EVIDENCE-BASED MEDICINE IN EQUINE CLINICAL PRACTICE

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by

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Abstract

The principles of Evidence-Based Medicine (EBM) have been well documented in the medical literature, with many examples of the successful application of these principles to the clinical environment. Despite this widespread acceptance of these principles throughout the medical profession, there has been resistance to adopt such an approach in the veterinary profession. To date, there are few examples in the literature of the application of the principles of evidence-based medicine to either clinical or scientific research. The aim of this study was to design a series of investigations of equine diseases, and implement them at three private equine hospitals. A variety of study designs were used, providing different classes of evidence when using the classification system proposed by Yusuf *et al.* (1998). The main focus of this investigation was to ascertain whether it was possible to apply the ethos of EBM to the veterinary profession, and provide good quality research and evidence form private practice.

It was found that 85.6% of horses (95% C.I. 81.3 to 89.3) treated for septic arthritis were successfully discharged from the hospital, with 65% of these horses (95% C.I. 57.9 to 71.6) able to return to their previous level of athletic function. When considering those horses treated for septic digital tenosynovitis, 87.8% survived to be discharged from the hospital. However, the prognosis for future soundness was poorer than that achieved following resolution of septic arthritis, with only 50% of horses treated for septic digital tenosynovitis able to return to their previous level of athletic function. Racing Thoroughbreds, both neonates and mature horses, were identified as an important subset of the population. It was found that the occurrence of septic arthritis in neonatal Thoroughbreds significantly reduced the likelihood of those foals going on to make at least one start on a racecourse, with those foals being 3.5 times less likely to start on a racecourse when compared to their siblings. In contrast, when considering mature Thoroughbred racehorses it was found that the occurrence of septic arthritis did not affect the likelihood that they would make at least one start on a racecourse when compared to their siblings, or be able to achieve an Official Rating awarded by the British Horseracing Board's handicappers equal to, or higher than, either the highest rating achieved prior to the onset of sepsis in cases in which horses had raced previously, or equal to the highest rating achieved by their siblings.

In a controlled, randomised trial it was found that 31.6% (95% C.I. 17.5 to 48.7) of horses wearing a belly band following an exploratory laparotomy developed incisional complications, compared with 76.6% (95% C.I. 62.0 to 87.7) of horses where no belly band was used. If a belly band was used following an exploratory laparotomy, the risk of developing post-operative incisional complications was reduced by 45% compared to those cases where no belly band was used.

Following a clinical audit of elective surgical procedures at three private equine hospitals, there was found to be a higher rate of post-operative complications, when compared to results reported in both the medical and small animal veterinary literature.

It was concluded that it was possible to apply the ethos of EBM to the veterinary profession, and provide good quality research and evidence from research performed in private practice. However, in order to be able to achieve sufficient case numbers to provide answers that are directly relevant to practice-based clinical situations, multi-centre studies are likely to be the best way forward.

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Acknowledgements

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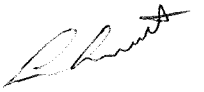
AUTHOR'S DECLARATION

The work presented in this thesis was performed solely by the author except where the assistance of others has been acknowledged. It has not been submitted in any form for another degree or professional qualification.



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Some of the work presented in this thesis has been the subject of the following publications:

Smith, L.J., Reid, S.W.J., Payne, R.J., Stoneham, S.J. and Marr, C.M. (2004) What is the likelihood of a Thoroughbred foal treated for septic arthritis racing, compared to its siblings? *Equine Vet. Journal.* **36** (5) 452-456

Smith, L.J., Mellor, D.J., Marr, C.M. and Mair, T.S. (2006) What is the likelihood that a horse treated for septic digital tenosynovitis will return to its previous level of athletic function? *Equine Vet. Journal* **38** (4) 337-341

Smith, L.J., Mellor, D.J., Marr, C.M., Reid, S.W.J. and Mair, T.S. (2007) Incisional complications following exploratory celiotomy: does an abdominal bandage reduce the risk? *Equine Vet. Journal* **39** (3) 227-283

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Smith, L.J., Marr, C.M, Payne, R.J., Stoneham, S.J., Reid, S.W.J. (2004) Are Thoroughbred foals treated for septic arthritis capable of racing. *43rd British Equine Veterinary Association Congress, Birmingham.*

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Smith, L.J. and Mair, T.S. (2005) Incisional complications following exploratory celiotomy: does a belly band reduce the risk? *44th British Equine Veterinary Association Congress, Harrogate.*

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LIST OF ACRONYMS

AF = Attributable fraction

AR = Attributable risk

ARR = Absolute risk reduction

BDDS = Biodegradable drug delivery system

CI = Confidence interval

CPD = Continuing professional development

DMSO = Dimethyl sulfoxide

EBM = Evidence-based medicine

EBVM = Evidence-based veterinary medicine

HAC = Hydroxyapatite cement

LRT = Likelihood ratio test

MIC = Minimum inhibitory concentration

NSAID = Non-steroidal anti-inflammatory drug

OR = Odds ratio

PMMA = Polymethyl methacrylate

RCT = Randomised controlled trial

RCVS = Royal College of Veterinary Surgeons

ROC = Receiver operating characteristic

SE = Standard error

TG-ROC = Two-graph receiver operating characteristic

Chapter 1

Introduction and review of the literature

1.1. Introduction

In one year alone approximately 1081 scientific papers are published in the mainstream veterinary literature, investigating new treatments, diseases and diagnostic tests, with 317 of these aimed specifically at the equine practitioner. This wealth of new information is not simply adding to and complementing existing knowledge, but also replacing knowledge that is out-of-date or obsolete (Cockroft and Holmes, 2003). As these information resources continue to grow, it becomes increasingly more time consuming for a busy practitioner to read and assimilate all these data (EBM Working Group, 1992; Sackett *et al.* 1996; Cockroft and Holmes, 2003). However, if a practitioner is to keep up–to-date with all the important progress in a field experiencing expansion in the techniques and technologies available, the ability to assimilate overwhelming volumes of information becomes vital (EBM Working Group, 1992; Sackett *et al.* 1996; Cockroft and Holmes, 2003). It is the veterinarian, as the reader of these studies, who must decide whether they offer any information that is either new or clinically relevant (Muir, 2003). However, to do this he or she must be able to understand the principles behind the study design and data analyses, in order to evaluate accurately the relevance of the information (Muir, 2003).

In order for a veterinarian to be able to provide his or her clients with the most efficacious diagnostic or treatment options available, he or she must be able to update their knowledge on a regular basis (Malynicz, 1998; Cockroft and Holmes, 2003). Evidence-based medicine (EBM) offers an efficient way of pursuing knowledge, as it focuses on identification of evidence that directly addresses problems encountered in patients (Malynicz, 1998; Cockroft and Holmes, 2003; Marr, 2003). However, many vets rely on textbooks or the traditional forms of Continuing Professional Development (CPD), such as meetings or conferences, to provide access to clinical knowledge (Cockroft and Holmes, 2003; Marr, 2003). At CPD meetings, veterinarians are frequently subjected to personal opinion and conjecture and, whilst this may convey some important information, it is not necessarily the best, or the most up to date (Holmes and Cockroft, 2004).

The ethos of evidence-base medicine (EBM) necessitates the use of current best evidence in making decisions about the care of individual patients (Sackett *et al.* 1996; Shaw, 2001). With the advent of information technology bringing huge resources of this evidence into both the home and the workplace (EBM Working Group, 1992; Cockroft and Holmes, 2003; Marr, 2003; Holmes and Cockroft, 2004), the opportunity to practice EBM has increased. A further motivation may be that this increase in access to information resources is not limited to the clinician, but has extended to the client as well (Cockroft and Holmes, 2003; Marr, 2003; Holmes and Cockroft, 2004). As a result, clients may be very well informed and prepared to challenge clinicians on their choice of patient management options.

Practitioners should use both their own individual clinical expertise and the best available external evidence, for neither by itself is sufficient to ensure the highest quality of patient care (Sackett *et al.* 1996). Without clinical expertise a clinician does not have sufficient background knowledge to assess the evidence, for even the best external evidence may be inapplicable to, or inappropriate for, an individual patient (EBM Working Group, 1992; Sackett *et al.* 1996), and only clinical experience can allow this judgement to be made. Without current best evidence, practice will rapidly become out-of-date, to the detriment of the patients (Sackett *et al.* 1996).

Much has been made in the veterinary literature of the lack of scientific evidence in target species for the use of alternative medicine (Fogle, 1998; Anderson, 2000a,b; Kruesi, 2000; Ramey and Rollin, 2001; Shaw, 2001), yet veterinarians are often guilty of utilising conventional therapies themselves that have no substantiating scientific evidence (Ross *et al.* 2001). The onus is increasingly on the veterinary profession to prove its right to exclusivity in the diagnosis and treatment of animals (Ramey and Rollin, 2001; Holmes and Cockroft, 2004), and the application of scientific evidence – evidence based veterinary medicine (EBVM) - in diagnosis and treatment is seen as the best way to proceed (Ramey and Rollin, 2001), to enable practitioners to continue to provide the best care for both the animals and their owners. In order for EBVM to develop further, a large body of high quality, patient-centred research is required (Keene, 2000; Holmes and Cockroft, 2004; Viner, 2005), and therefore a collaboration is necessary between first-opinion practitioners and academics, to allow sufficient case numbers to be generated and to allow answers to the most relevant questions to emerge (Marr, 2003; Mair and Cohen, 2003; Browning, 2004; Holmes and Cockroft, 2004; Viner, 2005).

1.2. Development of Evidence-Based Medicine

1.2.1. Historical background

Although it may be assumed by the general populace as a whole that all medical treatments are founded on good scientific evidence, and all actions performed by a doctor are the best available for the patient, this is not always the case. Dubinsky and Ferguson (1990) said that only between 10 and 20% of all treatments carried out by physicians were actually based on scientific evidence, thereby inferring that 80-90% of treatments were based on clinical experience, opinion of colleagues, and conjecture.

In 1992, a team at McMasters University in Ontario first proposed the idea of evidence based medicine (EBM Working Group, Guyatt *et al.* 1992). What was proposed was not supposed to be an entirely new concept to the medical profession, merely an amalgamation of a number of ideas (best research evidence, clinical expertise, patient values) in a logical order that would lead to the best outcome for the patient.

Evidence based medicine (EBM) was first formulated as a new approach to the practice of medicine, in recognition of some growing problems within the medical profession that needed to be addressed (Sackett *et al.* 2000):

- The daily need for valid information about diagnosis, prognosis, therapy and prevention
- The inadequacy of traditional sources for this information because they are either: out-of-date (textbooks), frequently inaccurate (expert opinion), ineffective (traditional forms of continuing professional education) or too overwhelming in volume (along with being wildly variable in validity) for practical clinical use (journals).
- The growing disparity between diagnostic skills and clinical judgement, which increase with experience, and up-to-date knowledge and clinical performance, which decline with experience.
- Under current arrangements in most clinical practices, the inability to afford more than a few seconds per patient for finding and assimilating this evidence, or to set aside more than half an hour per week for general study and reading.

Although these problems were researched exclusively based on the medical profession, they can equally be applied to the modern, busy general veterinary practitioner, for whom the pressure to see a large number of clients in a short space of time also exists. However, EBM as a separate entity in the veterinary profession - evidence based veterinary medicine (EBVM) - has been much slower to develop (Malynicz, 1998; Fogle, 1998; Roper, 1998; Roper, 2001; Cockroft and Holmes, 2003), and is only now being recognised as a valuable tool to be utilised in the class room as well as the consulting room (AVTRW, 2003).

1.2.2. Principles of evidence-based medicine

1.2.2.1. Defining evidence-based medicine

The definition of evidence-based medicine is popularly accepted as: the conscientious, judicious and explicit use of current best evidence in making decisions about the care of individual patients (Sackett *et al.* 1996), with the practice of evidence-based medicine meaning integrating individual clinical expertise with the best available external clinical evidence from systematic research (Sackett *et al.* 1996; Sackett *et al.* 2000; Marr, 2003; Muir, 2003). Individual clinical expertise is the proficiency and judgement acquired through clinical experience and practice (Sackett *et al.* 1996), whilst the best available external clinical evidence is clinically relevant research, but especially patient-centred clinical research (Sackett *et al.* 1996). External clinical evidence might invalidate previously accepted diagnostic tests or treatments and replace them with new ones (Sackett *et al.* 1996; Cockroft and Holmes, 2003). However, it might also serve to support the continued use of these diagnostic tests or therapies.

The increasing difficulties faced by busy clinicians in keeping abreast of the latest advances reported in primary journals are obvious from a comparison of the time required for reading these articles with the time available (Sackett *et al.* 1996; Browning, 2004; Holmes and Cockroft, 2004). It was reported that to stay abreast of recent developments a practitioner would have to read 17 articles per day, every day of the year (Davidoff *et al.* 1995), whereas practitioners only found one hour per week to assimilate all this information (Sackett *et al.* 1996). A mainstay of EBM is the encouragement of the

practitioner to target his/her reading time to address issues raised by specific patient problems (Sackett *et al.* 1996; Cockroft and Holmes, 2003). The benefits are two-fold:

1. Benefiting an individual patient,
2. Simultaneously increasing the clinician's knowledge base and keeping it appropriate to the patients' needs (Cockroft and Holmes, 2003).

The practice of EBM incorporates five steps (Sackett, *et al.* 2000):

- Converting the need for information into an answerable question
- Tracking down the best evidence with which to answer that question
- Critically appraising the evidence for validity, applicability and impact
- Integrating the clinical appraisal with clinical expertise and with a patient's unique biology, values and circumstances
- Evaluating both efficacy and efficiency in applying the above steps and looking for ways to improve them for the future

1.2.2.2. Asking an answerable question

Obviously, to be able to apply EBM to a clinical problem there is a need to be able to execute the first step – formulating an answerable question to a particular clinical situation (Sackett, *et al.* 2000; Marr, 2003; Cockroft and Holmes, 2004). There are two types of question commonly proposed in the quest for knowledge - those referring to background knowledge and those to foreground knowledge (Sackett *et al.* 2000; Marr, 2003). Background knowledge is the type of information an undergraduate student would commonly be seeking to attain (Cockroft and Holmes, 2003; Marr, 2003). Background knowledge refers to the fundamental principles behind all aspects of clinical science which are essential to the understanding of disease processes and management (Marr, 2003). Accumulation of background knowledge continues throughout a career (Marr, 2003). Background questions are formed of two components: a question root with a verb, and some aspect of the disorder itself (Sackett *et al.* 2000).

An answerable question is constructed to fill in the gaps in foreground knowledge, i.e. evidence that relates to a specific question, for which the driving force for acquisition is the patient and their problem (EBM Working Group, 1992; Sackett *et al.* 2000; Marr, 2003; Cockroft and Holmes, 2004). This foreground knowledge is most likely to come from

appraisal of recent, primary literature (Cockroft and Holmes, 2003). A question relating to this foreground knowledge can be subdivided into four steps that, if each are fulfilled, will result in an answerable question with which to continue (Sackett *et al.* 2000; Badenoch and Heneghan, 2002; Marr, 2003):

- Patient or problem
- Intervention
- Comparison intervention (where appropriate)
- Outcome

The breadth of the search will depend upon the specificity of the question: a more general question will require a broader search, whereas a very specific question, ideally targeted at an individual patient or clinical group of interest, will result in a much narrower search (Badenoch and Heneghan, 2002).

1.2.2.3. Tracking down the best evidence

There are different ways in which clinicians can search for the best available evidence (EBM Working Group, 1992; Oxman *et al.* 1993; Sackett *et al.* 2000). Looking in a textbook is an option followed by many practitioners, coupled with following up references cited by the author; however, a textbook is only as up to date as its most recent reference, therefore, by definition, it is already partially out of date by the time it is printed (Oxman *et al.* 1993; Sackett *et al.* 2000; Cockroft and Holmes, 2003). However, the information contained in these textbooks will only have been superceded if further research into that field has taken place, refuting the findings of the prior research. Asking a colleague or consultant is also a highly efficient way of discovering new information, although such individuals are also only as up-to-date as the latest clinical research that they have read or been involved with, and there is a reliance on them to have assessed the evidence accurately and drawn appropriate conclusions (Oxman *et al.* 1993). It must also be borne in mind that some of this information will be subjective and therefore, care must be taken to discern valid information from personal opinion (Cockroft and Holmes, 2003). Finally, there is searching through bibliographic databases (Oxman *et al.* 1993; Rosenberg and Donald, 1995; Badenoch and Heneghan, 2002; Cockroft and Holmes, 2003). However, although bibliographic databases are thought to provide the most up-to-date evidence, they will only find those manuscripts that have been published in scientific

journals. In these journals there is a reliance on the peer-review system to ensure that those manuscripts that are published report high quality evidence and utilise appropriate statistical analyses.

When the concept of EBM was first introduced, easy access to relevant information was limited. Database systems were poorly designed and searches were time consuming (Rafuse, 1994; Davidoff *et al.* 1995). Physicians, when faced with the time pressures of practice, faced difficulty in finding current clinical information and were more likely to be influenced by drug companies than by medical literature (Rafuse, 1994). However, as integrated computer networks grew, access to central databanks and current best evidence increased (Rafuse, 1994; Davidoff, 1995; Rosenberg and Donald, 1995; Sackett *et al.* 2001; Badenoch and Heneghan, 2002) including access to bibliographic databases, secondary journals and critically appraised topics (CATs). However, increased access to information did not provide physicians with the necessary tools to evaluate critically the rapidly growing body of electronic evidence (Kerridge *et al.* 1998).

1.2.2.4. Interpreting the available evidence

Having developed an appropriate question and performed the relevant literature searches, the EBM practitioner must then be able to assess the available evidence, to appreciate both any advantages offered, as well as limitations, by the study designs adopted (EBM Working Group, 1992; Oxman *et al.* 1993; Rosenberg & Donald, 1995; Kerridge *et al.* 1998; Mair, 2001; Muir, 2003). To interpret the results accurately the clinician must consider three questions (Oxman *et al.* 1993):

- Are the results of the study valid?
- What are the results?
- Will the results help in caring for patients?

It is necessary to decide whether the evidence is valid, and, if so, whether it is of clinical importance (Rosenberg and Donald, 1995; Muir, 2003). Claims of significant therapeutic or clinical findings must be backed up by appropriate statistical analyses; a feature often lacking in both the veterinary and medical literature (Lund et al, 1998; Greene et al, 2000; Christley & Reid, 2003; Muir, 2003), for a clinician to be able to assess whether the results can be applied to a particular clinical situation.

Unfortunately there are no easy 'yes/no' answers to these questions, because much of the evidence is considered to be suggestive as opposed to definitive (Oxman *et al.* 1993; Taylor, 1995). 'Grey zones' appear where evidence relating to different clinical options is either incomplete or contradictory, and the clinician must be able to understand the limitations imposed by different classes of evidence (EBM Working Group, 1992; Rosenberg and Donald, 1995; Kerridge *et al.* 1998; Yusuf, 1998; Mair, 2001; Sackett *et al.* 2001; Muir, 2003) and in doing so, recognise the level of certainty behind any decisions made (Taylor, 1995; CCDR, 1995)

In order to assist in this interpretation of evidence, a classification system of research studies was proposed, adapted from one originally generated by Sackett, reflecting the probability that the conclusions and recommendations of the study would be reliable (Yusuf *et al.* 1998):

- Class A: the most reliable form of evidence is obtained from the results of systematic reviews (e.g. meta-analyses) of multiple, randomised, blinded, placebo-controlled trials designed to address the clinical questions of interest. Individual, blinded, placebo-controlled, randomised clinical trials also provide Class A evidence, although this evidence is not as strong as that obtained from systematic reviews.
- Class B: non-randomised clinical trials using historical controls, providing significantly less reliable evidence.
- Class C: evidence obtained from uncontrolled case series, which can be difficult to assess
- Class D: evidence obtained from expert opinion and/or extrapolated evidence from basic research.

Although randomised trials have been cited as the 'gold standard' of evidence (Sackett *et al.* 1996; Keene, 2000; Mair, 2001; Cockroft and Holmes, 2003; Marr, 2003), they are not the most appropriate form of evidence to be used in every case. Whilst it is indisputable that randomised trials offer the best evidence when considering therapy (Sackett *et al.* 1996; Marr, 2003), where non-experimental approaches frequently give a false positive result, they are not always appropriate when considering either diagnostic tests or prognosis (Sackett *et al.* 1996; Marr, 2003).

Systematic reviews are an overview of several randomised trials for the same treatment in the same condition (EBM Working Group, 1992; Sackett *et al.* 2000). They will be able to provide more evidence than the results of a single study alone, as long as they are able to fulfil basic criteria: they must use (and specify) specific methods to search systematically and appraise critically the literature on a specific topic. If statistical analysis is then performed to combine the results of the individual studies, this review becomes a sub-set referred to as a meta-analysis (EBM Working Group, 1992; Sackett *et al.* 2000). It must also be specified whether the review utilises randomised, or non-randomised, clinical trials. If randomised clinical trials are reviewed, the systematic review will be able to reduce both bias and random error, resulting in the highest class of best available evidence (Sackett *et al.* 2000; Mair, 2001). In contrast, if non-randomised trials are reviewed, the problems of both bias and random error in individual trials can be compounded, resulting in a much poorer quality of evidence (Sackett *et al.* 2000).

A disproportionately large percentage of evidence derived from clinical trials utilising historical controls (Class B) has found in favour of the experimental therapy (Sacks *et al.* 1982; Schulz *et al.* 1995; Kunz and Oxman, 1998), with 84% of trials using historical controls finding the therapy in question effective, compared to only 11% of the randomised controlled trials, evaluating the same therapy, yielding a positive result (Sacks *et al.* 1982). It has been suggested that in general positive results from a trial utilising historical controls should be interpreted as a therapy worthy of further evaluation using a randomised, controlled trial (Keene, 2000). Where a negative result is reported by a study utilising historical controls, this is more likely to be a true finding (Keene, 2000).

In one study, it was found that clinical trials that lacked adequately concealed random allocation produced estimates of effect on average 40% larger than clinical trials with adequately concealed random allocation (Schulz *et al.* 1995). Authors of reviews comparing randomised and non-randomised trials (Sacks *et al.* 1982; Schulz *et al.* 1995; Kunz and Oxman, 1998) have hypothesised that this disparity in results may be due to a bias arising from the allocation of those patients with a poorer prognosis to the control group – a theory substantiated by the findings of one review (Kunz and Oxman, 1998). Similarly, evidence derived from multiple, uncontrolled case series (Class C) yielding a positive result can be disproved when the therapy is subjected to a randomised, controlled trial (Spilker, 1996), with the best known example being the administration of diethylstilboestrol to women in the 1940s and 1950s (Spilker, 1996; Keene, 2000).

1.2.2.5. Significance or equivalence?

With an increasing use of statistical methods to investigate whether a specific factor alters an outcome, it is common for researchers to report the results in terms of statistical significance. However, the use of the word 'significance' implies little more than statistical significance, and has no reflection on whether the finding is of clinical significance (Muir, 2003). To compound further the problem faced by the readership, a lack of statistical significance is often interpreted by authors as equivalence (Christley and Reid, 2003; Muir, 2003). However, if appropriate statistical testing is not performed to confirm this equivalence, this claim is erroneous (Christley and Reid, 2003; Muir, 2003) as all that has been proved is an absence of evidence of difference (Christley and Reid, 2003).

1.2.2.6. Sample size and power

Along with the use of appropriate statistical methods in the analysis of data, two important considerations in any study are the sample size and power, which provide an estimate of the relevance of the study (Muir, 2003; Holmes and Cockroft, 2004). Optimising sample size is the only way to provide a reliable statistical answer to the objective being investigated (Mann *et al.* 1991; Haimez 2002; Muir, 2003). If the sample size is smaller than the optimal number, the results are unlikely to be of either statistical or clinical significance (Muir, 2003; Holmes and Cockroft, 2004). It could also be considered wasteful of resources to have conducted a study whose results have little meaning. If the sample size is larger than is necessary, this too is wasteful of resources, and is potentially putting larger numbers of subjects in harm's way unnecessarily (Muir, 2003). The optimal sample size should be calculated at the outset of a study, either by using data available in the existing literature, or by conducting pilot experiments to provide the necessary information (Muir, 2003).

The power of a study is the probability of rejecting the null hypothesis when it is false (Curtis, *et al.* 1990; Holmes and Cockroft, 2004). Studies that have low power have a poor chance of detecting a difference when it exists (Muir, 2003; Holmes and Cockroft, 2004), therefore a study should be designed so that it has a high power (>0.8), particularly if it

relates to life-threatening decisions. The power is affected by the sample size, with power increasing as sample size increases, therefore power and sample size should be calculated together at the outset of the study (Muir, 2003).

1.2.2.7. Integration of evidence-based medicine in client care

Having searched the available literature and found the most relevant evidence to answer the question posed, it is necessary to integrate this critical appraisal with clinical expertise, in order to apply the results to clinical practice (Sackett, *et al.* 2000; Katz, 2001; Holmes and Cockroft, 2004). A form of such integration is decision analysis, where all the evidence available is applied, step-by-step, to the individual patient. At each step the evidence is weighed for applicability to the current situation, before a decision is made whether or not to act on the evidence (Cockroft and Holmes, 2003). In this way it is possible not only to apply evidence to a clinical situation, but to involve the patient in every step of the decision process, thereby making it a decision of informed consent (Cockroft and Holmes, 2003).

1.2.2.8. Evaluation

The fifth and final step when taking an evidence-based approach to medicine is self-evaluation (Sackett, *et al*, 2000). It is necessary to evaluate not only the ability to formulate and ask an appropriate question, but also the ability to interpret evidence correctly and then apply this new-found knowledge to a particular set of circumstances (Sackett *et al.* 2000). When evaluating the ability to ask a question, it is necessary to investigate both the questions formed, and the efficiency and effectiveness of the methods used in searching for, and finding, answers.

Even if evaluation confirms that the most appropriate questions are being asked, with answers being found efficiently, to have completed the process of EBM it is necessary to then take this information and integrate it with clinical expertise, thereby applying this information in a clinical setting.

Taking self-evaluation one step further is the performance of a clinical audit on EBM performances (Sackett *et al.* 2000). Audits such as these are important, as they not only give clinicians an accurate idea of how they are performing, but can also provide strategies

that can have a positive effect on clinical performance, for example individual feedback (Sackett *et al.* 2000).

1.2.2.9. The application of evidence-based medicine

Although EBM has been increasingly thought of as simply a comparison of treatment options (CCDR, 1995; Maynard, 1997; Ramey and Rollin, 2001), this is a narrow viewpoint. When used at its most basic level, EBM can be applied to a much broader range of clinical questions: clinical findings, aetiology, differential diagnosis, prognosis, therapy, prevention, and cost-effectiveness (Rosenberg and Donald, 1995; Badenoch and Heneghan, 2002). Of course, covering such a broad range of subjects, all of which are utilised on a daily basis in medicine, raises some difficulties in the application of EBM. For example, some of these concepts may be considered difficult to quantify, e.g. quality of life or pain (Kerridge *et al.* 1998), but this is a necessary step if statistical analysis is to be performed, and it should be possible in a properly designed and executed experiment (Maxwell, 1984; Stewart and Ware, 1992).

1.2.3. Limitations of evidence-based medicine

1.2.3.1. Using evidence-based medicine

Although appearing to be both a logical and beneficial way to approach patient care, EBM must be recognised to have its limitations (Rosenberg and Donald, 1995). Its basic concept relies on clinicians having easy, rapid access to the most up to date information (Rafuse, 1994; Rosenberg and Donald, 1995); without the best evidence being available they will not be able to make informed decisions. Coupled with this is the requirement for the clinician to interpret that evidence critically, deciding which evidence is relevant and which spurious (EBM Working Group, 1992; Oxman, 1993; Rafuse, 1994; Davidoff, 1995; Rosenberg and Donald, 1995; Kerridge *et al.* 1998).

Even with ready access to clinical research data, physicians have been resistant to the notion of EBM, which is considered by many to be a major paradigm shift in clinical practice. Concerns have been expressed that EBM would devalue clinical judgement, experience and the 'art of medicine' (EBM Working Group, 1992; Rafuse, 1994; Grahame-Smith, 1995; Rosenberg and Donald, 1995; Kerridge *et al.* 1998). When EBM

was first proposed this was a common misconception, as the proponents of EBM did not seek to replace current clinical practice but to augment it (EBM Working Group, 1992; Oxman, 1993; Rafuse, 1994; CCDR, 1995; Sackett, *et al.* 1996; Marr, 2003): it was still for the clinician to determine the severity of the patient's condition and then apply the evidence to the situation (EBM Working Group, 1992; Rafuse, 1994; Sackett *et al.* 1996). Undergraduate students were enthusiastic about the format of EBM-teaching, as were their teachers, and when these students graduated and carried their EBM ethos forward into practice this would in itself contribute to its success (Rafuse, 1994; Sackett *et al.* 1996).

1.2.3.2. The evidence base of cost-effectiveness

Doubts that had been raised over the validity of applying EBM in the workplace (Rafuse, 1994; Sackett *et al.* 1996; Kerridge *et al.* 1998) were refuted in a study by Paes *et al.* (1994), where it was established that a substantial cost saving was realised after the implementation of the principles of EBM. However, this in turn helped substantiate concerns that EBM would become the arena of policymakers and purchasers in an effort to curb spending (Rafuse, 1994; Grahame-Smith, 1995; Kerridge *et al.* 1998), even though this was a direct contradiction of the view held by many that EBM may raise the cost of health care. An increase in expenditure was predicted through the application of the most efficacious interventions to maximise the quality and quantity of life for individual patients (Sackett *et al.* 1996). As EBM developed, and indeed was focused on by governments and policy makers (CCDR, 1995; Maynard, 1997; Kerridge *et al.* 1998), this reckless attitude to an increase in spending for the benefit of the few rather than the many was challenged. In a publicly financed health care system such as the one that exists in the United Kingdom, social issues should be weighted as heavily as medical issues, leading to an 'evidence base of cost-effectiveness' (maximum gains in terms of population health from a finite budget) on which to base decisions (Maynard, 1997; Kerridge *et al.* 1998).

In proposing his defence of EBM Sackett (1996) unwittingly raised two controversial points:

1. even with the best evidence available, patient choice should still allow the patient the ultimate, although well informed, decision;
2. a limitation in the application of EBM. How can something be measured that appears to be un-quantifiable e.g. quality of life? In order to collect accurate data

to which statistical analysis can be applied, it is important to be able to measure a definable quantity.

1.2.4. Evidence based medicine – a new paradigm or a just new catchphrase?

Seizing on the concept that only 10-20% of clinical decisions were evidence-based (Dubinsky and Ferguson, 1990), Ellis (1995) designed and conducted a study in a university-affiliated district hospital investigating each clinical decision relating to diagnosis and treatment that was made in a one month period, and categorising this decision into one of three possibilities:

1. intervention with evidence from RCTs
2. intervention with convincing non-experimental evidence
3. intervention without substantial evidence

At the end of the study period the treatment decisions that had been made were reviewed, and it was found that 82% of clinical decisions made were considered to be evidence-based (category 1 and 2), with 53% of decisions substantiated by the results of randomised controlled clinical trials (category 1). The results of this study illustrated that the practice of EBM was not a new paradigm, as had been suggested (Rosenberg and Donald, 1995; Kerridge, *et al.* 1998), but was a way of supporting and substantiating many of the clinical decisions that were made.

Doubts over the validity of applying EBM in the workplace (Rafuse, 1994; Sackett *et al.* 1996) were also refuted (Paes *et al.* 1994; Ellis *et al.* 1995; Sackett *et al.* 1996) when the application of EBM to both hospital protocol and continuing medical education rounds was found to result in a significant reduction (from 50.5% to 6.9%) in the use of a specific, unnecessary, procedure in an intensive care nursery (Paes *et al.* 1994), without incurring patient morbidity. This decrease in the number of superficial cultures performed also realised a substantial cost saving.

The developments that allowed the concept of EBM to proceed into successful practical application were (Sackett *et al.* 2000):

- The development of strategies for efficiently tracking down and appraising the evidence

- The creation of systematic reviews and concise summaries on the effects of health care
- The creation of evidence-based journals of secondary publication
- The creation of information systems
- The identification and application of effective strategies for lifelong learning and for improving clinical performance.

1.2.5. Application of the principles of evidence-based medicine in veterinary research

Unfortunately, the narrow view of EBM was propagated in the veterinary profession, where some of the first calls for the increasing use of scientific evidence and statistical analysis were related to the increased use of alternative, or complementary, therapies in veterinary medicine (Fogle, 1998; Anderson, 2000a,b; Kruesi, 2000; Ramey & Rollin, 2001; Shaw, 2001). Evidence-based medicine was seen as a valuable tool to discredit the use of alternative therapies, as few studies containing scientific evidence and statistical analysis had been published (Anderson, 2000; Ramey and Rollin, 2001). However, the dissenting voices had failed to turn their attention to the remainder of the veterinary literature, where a similar argument could be made (Fogle, 1998; Ross *et al.* 2001).

A review of the literature in small animal medicine revealed that, in a 5 year period, 23 randomised controlled trials (class A evidence) were published (Lund *et al.* 1998). However, of these 23 papers, all were judged to have incomplete reporting in key areas, including group allocation, blinding, sample size and power and statistical reporting (Lund *et al.* 1998). Although the absence of reporting in key areas may merely have been a flaw in the written article, it casts doubt on the overall quality of the trials performed as it is incumbent on the authors of such studies to show readers this essential information to allow for the correct interpretation of the data (Lund *et al.* 1998). No such review has occurred in the equine medical literature, although it is unlikely to fare any better.

It is in the classification of evidence that the veterinary profession faces its biggest limitation in the utilisation of EBM. The most widely available form of evidence in veterinary medicine is Class D evidence, which is considered to be the least reliable

(Keene, 2000; Mair, 2001). Although this evidence is often of importance and correct, it should ideally be backed up by controlled clinical trials (Mair, 2001).

Whilst blinded, placebo-controlled, randomised clinical trials are widely accepted to provide the best available evidence (Keene, 2000), these trials are expensive to run, being demanding in terms of manpower and case requirements (Keene, 2000; Mair, 2001; Shaw, 2001). They are a rare occurrence in veterinary science as the veterinary pharmaceutical market comprises only a tiny fraction of the pharmaceutical industry as a whole and, in circumstances in which an industry is driven by profit margins, it will be unlikely to undertake such extensive research that is totally out of proportion to its potential returns (Keene, 2000; Mair, 2001). As a direct consequence systematic reviews are a rarity in the veterinary literature due to the paucity of randomised, controlled trials that have been performed on any single topic (Keene, 2000). However, in recent years some examples of systematic reviews have begun to emerge in the small animal veterinary literature (Olivry *et al.* 2003; Aragon and Budsburg, 2005).

In veterinary medicine (Keene, 2000), especially in equine medicine (Mair, 2001; Marr, 2003), randomised trials are few and far between, therefore the next class of best external evidence must be found (Sackett *et al.* 1996). To this end, a much greater importance is placed on the evidence that is actually available, i.e. class B (historical controls) and C (uncontrolled case series) evidence. These trials are cheaper to run and require lower case numbers (Keene, 2000). However, even if a study design is utilised that provides a lower class of evidence, the statistical methods used to analyse and interpret the data should be appropriate. One study investigating the use of statistical testing procedures in the veterinary literature reported that statistical analysis was not performed in 51% of articles published in one year (Hammer and Buffington, 1994), and an additional 26% of articles either supplied insufficient information to evaluate the statistical methods or had used inappropriate statistical methods (Hammer and Buffington, 1994). A more recent review concluded that 67% of the studies reviewed claiming clinical or therapeutic equivalency were based on a failure to detect significant differences (Christley and Reid, 2003). However, no further statistical investigation was conducted in these studies to support this conclusion of equivalency, which could lead to erroneous conclusions being drawn in relation to the question being researched (Christley and Reid, 2003).

It may be that all of these developments are yet to be realised in the veterinary field, but with advancements in information technology (Marr, 2003; Holmes and Cockroft, 2004), and increasing availability of access to information (Cockroft and Holmes, 2003; Marr, 2003), the concepts of EBM should now be able to be applied equally well in the veterinary consulting room as in the human.

In order for the practice of EBVM to progress further, a large body of high quality, patient-centred research, made available to veterinarians willing and able to access and critically appraise the quality and applicability of clinical trials, is required (Keene, 2000). A move towards this is beginning to occur, with increasing publication of patient-centred clinical research relating to small animal medicine. In the remainder of veterinary medicine, including equine medicine, such studies are unusual (Mair, 2001), although the Equine Veterinary Journal launched a Clinical Evidence Category in November 2003 to promote the principles of EBM in clinical research, with the intention that articles published in this category should help clinicians make specific and day-to-day decisions (Marr and Newton, 2006). In conjunction with this new section, the Clinical Evidence Notebook was launched in May 2005, to address issues relating to the collection, analysis and interpretation of data of clinical relevance (Marr and Rossdale, 2005). In a discipline that covers multiple species, the importance of data relating to that particular species, in contrast to data extrapolated from experimental studies using other species, cannot be underestimated.

To date in the equine veterinary literature there has been relatively few examples of evidence-based clinical research. Many of those that have been published have been in the clinical evidence category of the Equine Veterinary Journal (Edwards *et al.* 2003; Barakzai *et al.* 2004; Johnston *et al.* 2004; Smith *et al.* 2004; Proudman *et al.* 2005a,b; Smith *et al.* 2005; Valverde *et al.* 2005). Some studies containing good quality evidence are starting to emerge from research institutes and, although many of these studies (Spike-Pierce and Bramlage, 2003; Kane *et al.* 2003; Barakzai, *et al*, 2004; Smith *et al.* 2004, 2005) would be classified as providing class B evidence according to Yusuf *et al* (1998), this still represents an improvement not only in the quality of evidence provided, but also in the awareness for the need for such evidence. Recent studies have even included examples of studies (Denoix *et al.* 2003; Edwards *et al.* 2003; Johnston *et al*, 2004; Valverde *et al.* 2005) providing evidence that would be classified as class A according to Yusuf *et al* (1998), although not all have incorporated blinding in the study design (Valverde *et al.* 2005).

For further progress to be made it is necessary for veterinarians in first-opinion practice to work together with those in academia, in order to provide not only the case numbers required for such studies, but also to allow the most relevant questions to emerge (Marr, 2003; Mair & Cohen, 2003).

1.3. Epidemiology and Study Design

1.3.1. Epidemiology

Epidemiology is concerned primarily with the prevention and control of a disease within a population. An epidemiologist aims to identify specific events that could occur, and then evaluate their association with specific outcomes of interest, including health, welfare and, for veterinary epidemiologists, productivity.

1.3.2. What to study

In order to develop a research protocol, it is important to first think of the question to be addressed by the study, and then perform a literature search to establish if that question already has a definitive answer readily available. If such an answer is not apparent, then the original question, and the answer that might be expected, represent the hypothesis on which a study can then be based.

The capacity for evidence to support advances in veterinary medicine depends not just on the existence of such evidence, but also on its quality. Different methods of study design each carry with them their own intrinsic strengths and weaknesses, with implications for the quality of evidence produced and the appropriateness of the future application of this evidence. The design of the study therefore has a substantial impact on the quality of the evidence produced, including interpretability, reliability and applicability of the reported findings.

1.3.3. Classification of study design

There are two different classifications incorporating all study designs – those that are experimental and those that are investigational or observational in their data collection. In investigational studies, the investigators study the subjects 'as they find them': subjects are observed and relevant measurements are recorded, with no attempt made at intervention of any kind (Petrie and Watson, 1999; Noordhuizen *et al.* 2001). This type of study is susceptible to confounding. In an experimental study the investigator determines the method of selection of the animals studies, and the interventions they receive (Cockroft and Holmes, 2003; Dohoo *et al.* 2003).

1.3.4. Types of Investigational Study

There are 4 types of investigational study: longitudinal, cross-sectional, case-control and cohort studies.

1.3.4.1. Cross-sectional studies

A cross-sectional study measures the prevalence of health outcomes or determinants of health in a population at a specific point in time, or over a short time period (Petrie and Watson, 1999; Dohoo *et al.* 2003). It is a study design that can be used to explore aetiology (Katz, 2001). However, cross-sectional studies are able to provide only limited information, as they do not take into account the temporal relationship between the risk factors and the disease state (Petrie and Watson, 1999; Katz, 2001; Cockroft and Homes, 2003; Dohoo *et al.* 2003). They are most useful when the aims of the study are of a descriptive nature (Petrie and Watson, 1999; Katz, 2001). However, if cross-sectional studies are repeated at intervals they can be used to recognise trends in disease prevalence in a population over a period of time. Bias can arise due to selection of subjects into or out of the study population (Dohoo *et al.* 2003). It can also be difficult to differentiate between what is cause and what is effect when interpreting the data.

1.3.4.2. Longitudinal studies

A longitudinal study, which can be either prospective or retrospective in design, investigates changes over time (Petrie and Watson, 1999; Katz, 2001). There are two types of longitudinal study, defined primarily by the way the changes over time are investigated. When a longitudinal study is designed prospectively a cohort design can be used (Petrie and Watson, 1999) to compare those individuals that have been exposed to the factor of interest with those individuals that have not been exposed. With a retrospective study a case-control study design can be utilised (Petrie and Watson, 1999).

1.3.4.2.1. Cohort studies

At the outset of a cohort study the investigator must begin with a group of individuals apparently free from the disease of interest (Dohoo *et al.* 2003). This group of individuals is then subdivided into groups (cohorts) of animals, which must be defined according to the level of exposure of the animals in each group to the factor of interest (Petrie and Watson, 1999; Katz, 2001). These groups are then followed forward in time, to investigate which animals will go on to develop the disease under investigation, and compare the incidence of the disease between cohorts (Petrie and Watson, 1999; Katz, 2001; Cockroft and Holmes, 2003; Dohoo *et al.* 2003).

From the data collected incidence rates can be compared, and attributable and relative risk can be calculated (Petrie and Watson, 1999). The attributable risk (AR) is the proportion of the total risk of developing the outcome of interest that can be attributed to the factor of interest (Petrie and Watson, 1999), whilst the relative risk (RR) is the ratio of the risk of disease in the exposed group to the risk of disease in the unexposed group (Petrie and Watson, 1999). The RR provides a measure of the strength of association between the outcome of interest and exposure to the factor of interest (Petrie and Watson, 1999).

A difficulty arising if there is low disease incidence is that large and lengthy studies may be required to accrue sufficient case numbers in order to give adequate statistical power (Noordhuizen *et al.* 2001; Cockroft and Holmes, 2003). To counteract this problem, it is possible to carry out the study retrospectively, as long as the outcome of interest can be accurately measured in a retrospective manner, for example mortality rates, with a cohort of individuals identified based upon their attributes in the past (Katz, 2001). The disease

experience of the cohort is then followed, until some point in the more recent past or up to the present time.

1.3.4.2.2. Case-control studies

Case-control studies can frequently avoid the complications associated with prospective longitudinal studies where lengthy time periods may be required to accrue sufficient case numbers. Cases are identified and past exposures to suspected aetiological factors investigated, with results compared to suitable controls (Petrie and Watson, 1999; Cockroft and Holmes, 2003; Dohoo *et al.* 2003). In order for the findings of a clinical follow up study to be applicable to cases elsewhere (in this instance this would be other practice populations), it is necessary to precisely define how cases were selected for inclusion in the study (Dohoo *et al.* 2003). If characteristics of the subject are documented (age, sex, duration of clinical signs etc) it will also be possible to investigate the influence any of these variables may have on the outcome.

This study design allows for the estimation of odds ratios where differences exist between groups in terms of exposure to a risk factor, but not attributable risk (Petrie and Watson, 1999; Noordhuizen, *et al.* 2001). The odds ratio (OR) is the ratio of two odds. In this case it is the odds of exposure in the diseased group divided by the odds of exposure in the control group, thereby providing an estimate of the relative risk (Petrie and Watson, 1999). The odds ratio is a reasonable estimation of the relative risk, provided the incidence of the disease is low and the cases and controls represent a truly random sample of the population (Petrie and Watson, 1999).

Matching of cases to controls does not completely eliminate confounding (Katz, 2001) – to do this statistical adjustment would be required. Matching of cases to controls entails making the distribution of certain factors the same in the groups being compared, whereas confounding is where the effects of two or more factors of interest are inter-related and it is impossible to separate them into their individual effects. A suitable case definition must exist in order to identify cases eligible for inclusion in the study and, where possible, incident rather than prevalent cases should be used (Dohoo *et al.* 2003). Incidence relates to the number of new cases of a disease within a specific population in a defined time period, whereas prevalence relates to the number of cases of disease existing at a specific point in time (Dohoo *et al.* 2003). Prevalent cases are not considered suitable for inclusion

in a case-control study as there is often uncertainty as to when the disease actually began (Dohoo *et al.* 2003), and it is often difficult to separate factors that relate to the individual developing the disease initially from those factors that relate to the individual having the disease at a specific point in time (Dohoo *et al.* 2003).

In the selection of controls, their exposure to risk factors and confounders should be representative of that in the population considered to be 'at risk' of becoming cases (Katz, 2001; Dohoo *et al.* 2003). If there is low disease incidence, statistical confidence can be increased by increasing the number of controls for each case. However, there is a 'law of diminishing returns' in that it is usually not worth going beyond four or five controls per case, as the benefit of increasing the number of controls per case is frequently small, and must be balanced against the inherent difficulties of analysing large quantities of data, and the possibility of erroneously influencing the apparent significance of factors on the outcome of interest.

1.3.5. Experimental Studies

In experimental studies a form of intervention occurs as part of the study (Petrie and Watson, 1999; Dohoo *et al.* 2003). The effect this intervention exerts on the response of interest is then observed. There are 2 main forms of experimental study design: randomised controlled trials and cross-over studies. Randomisation is an essential element of both forms of experimental trials. To this end experimental studies are less susceptible to confounding, but ethical constraints are imposed on clinical research (Petrie and Watson, 1999), and experimental studies have a limited use in the investigation of aetiology. Their main use is in the evaluation of clinical interventions with randomised controlled trials.

1.3.5.1. Randomised Controlled Trials

Randomised controlled trials (RCTs) are commonly cited as the 'gold standard' of evidence (Katz, 2001; Dohoo *et al.* 2003). Although they may be the most appropriate form of evidence when considering therapy, they are not always an appropriate study design when considering either diagnostic tests or prognosis. The combination of size (RCTs generally require very large samples), length (many require years to complete) and

rigorous controls leads to enormous expense when designing and running RCTs (Katz, 2001).

An important consideration in any study is the sample size, in order to answer the frequently asked question of: 'how large a sample do I need to conduct a particular experiment?' (Noordhuizen *et al.* 2001; Muir, 2003). The sample size must be large enough to have a good chance of detecting any clinically relevant differences between groups (Noordhuizen *et al.* 2001; Dohoo *et al.* 2003; Muir, 2003; Holmes and Cockroft, 2004), without being so large as to be wasteful of individuals and resources (Petrie and Watson, 1999; Dohoo *et al.* 2003; Muir, 2003). If the sample size is inadequate, it may lead to clinically important differences being overlooked, and parameter estimates lacking precision (Petrie and Watson, 1999). A power calculation must be performed at the outset of the study, to determine the minimum numbers of individuals required in each group at a prescribed power (Dohoo *et al.* 2003). The power of a study relates to the chance of detecting a statistically significant true treatment difference of a pre-determined magnitude (Muir, 2003; Holmes and Cockroft, 2004). A pilot study is often conducted at the outset, in order to calculate the minimum number of individuals required in each group to permit the detection of real treatment effects in the full-scale trial (Petrie and Watson, 1999; Muir, 2003).

Although economics are likely to be the main reason for the paucity of RCTs in the veterinary literature, ethical considerations are also a limitation to the use of RCTs (Petrie and Watson, 1999; Katz, 2001). The welfare of the individuals participating in an RCT must lie with the investigators conducting the trial, and many important questions must be addressed before the trial can commence (Petrie and Watson, 1999; Dohoo *et al.* 2003). The ethics of withholding treatment from a group of diseased individuals to provide a negative control group for comparison to a novel treatment protocol are debatable (Petrie and Watson, 1999; Katz, 2001; Noordhuizen *et al.* 2001). If the disease is either debilitating or life-threatening it may be more appropriate to compare the novel treatment to the accepted current gold-standard treatment, if such a treatment exists (Petrie and Watson, 1999; Katz, 2001; Noordhuizen *et al.* 2001). If a standard treatment does not exist then the investigators must ensure the risk to participating individuals is minimal (Petrie and Watson, 1999). When conducting RCTs using animals as the subjects, all interventions must be approved and licensed by the Home Office, adding to the expense of conducting such a trial (Petrie and Watson, 1999).

At the outset of the study, the criteria for entry into the study group must be specified (Noordhuizen *et* al. 2001; Dohoo *et al.* 2003), and the subjects studied must be representative of the target population in which it is hoped to apply the results (Noordhuizen *et* al. 2001; Dohoo *et al.* 2003). Subjects are then randomly assigned to one of the different treatments being compared (Petrie and Watson, 1999; Noordhuizen *et* al. 2001; Dohoo *et al.* 2003), for example by the use of a table of random numbers, or a computer programme capable of generating sets of random numbers. Blinding, the withholding of the knowledge of the specific treatment administered from either the investigator and/or the individual, may be appropriate if other aspects of patient care will influence outcome (Petrie and Watson, 1999; Noordhuizen *et* al. 2001; Dohoo *et al.* 2003). Any criteria for withdrawing a patient from the prescribed treatment should be specified in advance (Petrie and Watson, 1999), although even after the treatment has been withdrawn follow up to the end point of the study should still continue. During the course of the study it is important to assess not just efficacy of treatment being investigated, but also any perceived side effects (Petrie and Watson, 1999).

1.3.5.2. Cross-over Studies

A cross-over study design is useful if the outcome is measured by the reporting of subjective symptoms, but it is only suitable in situations in which the effects of the treatment under investigation are short lived. Subjects receive each treatment sequentially, with an intervening 'wash out' period to eliminate any carry over effects (Petrie and Watson, 1999; Noordhuizen *et al.* 2001). It is important to establish the minimum duration of wash out period necessary between treatments to eliminate any carry over effect (Petrie and Watson, 1999). The order in which the treatments being compared are given is randomised, with the patients acting as their own controls (Petrie and Watson, 1999; Noordhuizen *et al.* 2001; Dohoo *et al.* 2003).

The aim is to compare the responses to treatment within, rather than between, the animals, thereby increasing the precision of the estimate of the difference between treatments (Petrie and Watson, 1999; Katz, 2001; Noordhuizen *et al.* 2001; Dohoo *et al.* 2003). However, this study design does not entirely eliminate individual variation (Petrie and Watson, 1999), as a period effect may exist (the treatments are given sequentially, not in parallel). Cross-over studies are considered to be ideal for comparing palliative treatments,

for example in chronic disease (Petrie and Watson, 1999; Noordhuizen *et al.* 2001). However, they are not suitable for comparing treatments that are considered to 'cure' the patient, as the disease must return in order to investigate the comparative treatment (Petrie and Watson, 1999; Noordhuizen *et al.* 2001).

1.4. Clinical Audit

1.4.1. What is clinical audit?

Although clinical audit may appear to be a relatively new concept, in particular in the veterinary profession, it is, in fact, a concept that has been recognised for many years (Rayment, 2002), although under a variety of different names, including quality assurance and clinical governance (Rayment, 2002). Clinical audit has been defined by the Department of Health as:

> The systematic and critical analysis of the quality of clinical care, including the procedures for diagnosis, treatment and care, the associated use of resources and the resulting outcome and quality of life for the patient.

Florence Nightingale was the first person actively to document the process of clinical audit in order to implement and maintain best practice, at which time she stated that: "for us who nurse, our nursing is a thing which unless we are making *progress* every year, every month, every week, take my word for it we are going *back.*"

It is this understanding that audit requires a team approach that has carried over with the implementation of audit in other professions, resulting in a more widely accepted definition of: "multi-disciplinary professional, patient focused audit, leading to cost-effective, high quality care delivery in clinical teams" (Batstone and Edwards, 1994), where the emphasis has been placed on a group working together to achieve optimal results (Rayment, 2002).

1.4.2. Why perform clinical audit?

The driving force behind the implementation of clinical audit has been aimed at the benefits to be offered to the patient, in terms of improved standards of patient care and a more effective service offered, both in terms of diagnosis, treatment and care (Mosedale, 1998; Rayment, 2002). Clinical audit not only allows a systematic approach to the investigation of specific topics (Mosedale, 1998), it also allows for the implementation of any necessary changes and an opportunity to evaluate the results of these changes (Mosedale, 1998; Rayment, 2002; Viner, 2005).

Clinical audit has been forced to the fore front in the veterinary profession, following the decision by the Royal College of Veterinary Surgeons (RCVS) to implement compulsory clinical audit for all practices that hold Tier 2 or 3 hospital status (RCVS 2005). The RCVS Practice Standards Scheme was established in January 2005, in order to "establish a quality assurance framework to promote and maintain the highest standards of veterinary care" (RCVS 2005). Three tiers were established to encompass all levels of veterinary practice:

1. Tier 1 – minimum requirement core standards relevant to all veterinary practices
2. Tier 2 – general standards
3. Tier 3 – veterinary hospital standards

The three tiers are cumulative, and represent the additional standards it is necessary for a practice to achieve in order to receive accreditation at the different levels (RCVS 2005). For those practices that are accredited as either Tier 2 or 3 practices, the requirements for clinical governance include: "a system for monitoring and discussing the clinical outcome of common procedures", whereas those achieving Tier 3 status are required to have: "regular morbidity and mortality meetings.....and demonstrate changes in procedure as resultant action", along with evidence of "an audit of standard hospital procedures" (RCVS 2005).

With the threat of mandatory audit forced upon them if they do not carry out their own internal auditing, practices are having to confront not only what auditing entails, but also how to implement clinical audit and the interpretation of the results. A major hurdle to the implementation of effective clinical audit is the time commitment required by those involved, and it can be hard in a busy practice to justify this extra expenditure in terms of

time and effort (Mosedale, 1998; Viner, 2005). It has been pointed out that "we should not accept uncritically what is urged upon us" (Ford and Walsh, 1994) – a mainstay of evidence-based medicine, where all ideas should be critically appraised for their relevance and applicability before being embraced. Similarly, in the application of clinical audit, a wise practitioner may consider whether practices that have implemented clinical audit have been seen to develop, with clear evidence of improvements in patient care, before committing both themselves and their practice resources.

1.4.3. Clinical audit or clinical research?

Confusion has arisen in the past between the practice of clinical audit and clinical research. The fundamental principles associated with the practice of clinical audit state that audit must (Department of Health):

- Be professionally led
- Be seen as an educational process
- Form part of routine clinical practice
- Be based on the setting of standards
- Generate results that can be used to improve outcome of quality of care
- Involve management in both the process and outcome of audit
- Be confidential at the individual patient/clinician level
- Be informed by the views of patients/clients

In contrast, it has been categorically stated that clinical audit is not (Clinical Resource and Audit Group):

- A system of ensuring that staff training are making satisfactory progress
- Performance appraisal of posts in organisational terms
- A disciplinary mechanism
- Research, which is concerned with establishing new knowledge
- Needs assessment

Clinical audit is viewed as the regular systematic review of the treatments and services health care professionals already provide – a means of monitoring the current system and looking for ways to improve (Mosedale, 1998; Rayment, 2002; Viner, 2005). In contrast

clinical research is aimed at the generation and development of new data and new ideas that in turn may lead to an improvement in treatments and services offered.

Clinical audit and evidence-based medicine, whilst being separate entities, cannot be considered to be mutually exclusive. When applied effectively, both approaches work synergistically, with involvement in clinical audit facilitating the review and appraisal of the latest available evidence. Clinical audit itself also provides valuable evidence both on the effectiveness of diagnostic techniques and treatment regimens, and also on the standards of care provided.

1.4.4. The practice of clinical audit

The four main stages of clinical audit form a continuous cycle (Mosedale, 1998; Rayment, 2002), made up of the following (Morrell *et al.* 1999):

1. defining best practice
2. implementing best practice
3. monitoring & comparing against best practice
4. taking action to improve

However, having completed the cycle once the process is not at that point complete, as you must then consider whether it is possible to raise the standard to move further towards best clinical practice.

1.4.5. Defining best practice

1.4.5.1. Identifying an area for clinical audit

One of the most critical areas for the implementation of clinical audit is the selection of a suitable area for investigation. The area identified must address important aspects of practice or concerns about quality of patient care (Mosedale, 1998; Rayment, 2002; Viner, 2005), in order to justify the commitment of practice resources. Once a suitable area for investigation has been selected, it is important to step back and take stock before initiating clinical audit. This will allow your current practice to be described in such a way to illustrate the existing problems and highlight possible areas for improvement.

1.4.5.2. Appraising the available evidence

The available evidence must then be critically appraised (Rayment, 2002; Viner, 2005), to make sure that it is of sufficient quality and current enough to be valid and reliable as a basis for practice. The more research that exists on a specific topic, the more informed a decision you will be able to make about effective practice (Rayment, 2002). However in order to utilise this wealth of information time and effort must be invested in order to locate and appraise the information appropriately.

1.4.5.3. Setting a standard

The next step in the process of audit involves setting a standard. This standard must set out what you recognise to be best practice, and give some indication of how that standard is to be achieved (Rayment, 2002; Viner, 2005). Standards are compiled from both objectives and criteria, with the criteria providing the more detailed information on how the objective is to be achieved (Viner, 2005). When faced with a long list of criteria it is important to refine this to the pertinent few, and this can be done by applying a simple mnemonic (DREAM) to each criterion to justify its inclusion (Morrell *et al.* 1999):

- Distinct – does it identify something new?
- Relevant – is it crucial to the achievement of the objective?
- Evidence-based – is the source of information clear?
- Achievable – is it realistic within current resources?
- Measurable – finally, and most importantly, can the criterion be measured?

1.4.6. Implementing best practice

1.4.6.1. Preparing to monitor

Having identified the area for audit and set a standard, you must now consider how best to measure the effect of the process (Rayment, 2002; Viner, 2005). A validated measurement tool may already be available, in the form of clinical guidelines, to form the basis of the criteria for audit, and if this is not the case the values of a particular measure should be compared to a number of key criteria before it is adopted (Morrell *et al.* 1999):

- Reliability and validity
- Responsiveness (sensitivity) to change
- Clinical utility
- Feasibility of data collection

1.4.6.2. Validity and Reliability

Validity and reliability are particularly important in the design of measurement tools (Petrie and Watson, 1999), as every audit criterion is measuring a particular variable, and it is vital to know how well the measurement tool is performing, i.e. how reliable is it, and how valid? Reliability refers to the ability for a test to be repeated over and over again, and achieving the same results each time, i.e. the repeatability of the test (Petrie and Watson, 1999). Validity describes the degree to which the criteria are actually measuring what they are supposed to be (Petrie and Watson, 1999). Without confidence in the level of reliability and validity of a particular measurement tool, you cannot have confidence in your data and any final conclusions drawn from it (Petrie and Watson, 1999).

1.4.6.3. Collection of baseline data

By performing a test run with the measurement tools of choice, prior to the main data collection phase, any limitations or problems can be highlighted and rectified, before they impact on the entire study (Rayment, 2002). Further refinement of the criteria is possible at this time, with collection of baseline data prior to the implementation of audit and the subsequent changes in the practice that will occur (Rayment, 2002). Collection of baseline data will provide a starting point against which any future progress can be measured, and if appropriate quantified.

1.4.7. Monitoring and comparing against best practice

1.4.7.1. Sources of data

Many sources of data exist that can be utilised in the institution of clinical audit (Rayment, 2002; Viner, 2005). These include questionnaires, interviews and direct observation, at

which time data are collected specifically for the purpose of clinical audit (Rayment, 2002; Viner, 2005). However, it must not be forgotten that a wealth of information already exists in data sources that are collected routinely. The most obvious of these pre-existing data sources would be patient records, although general practice information systems also contain a wealth of data. These data are often readily accessible, providing a saving both in terms of time and effort if the information they contain can be utilised.

1.4.7.2. Defining the sample

A sample population must be drawn that is considered to be representative of the target population (Mosedale, 1998), in order to allow extrapolation of results gained from the smaller sample to the larger population as a whole. The validity of an audit project will hinge on how the sample is selected, and whether this information can then be used to draw accurate, unbiased estimates of the characteristics of the larger population.

1.4.7.3. Comparison and analysis

Once clinical audit has been performed, the data must be collated, described and analysed appropriately in preparation for feedback (Viner, 2005), in the form of an audit summary. An audit aims at identifying patterns or deficiencies, not showing statistical significance in its findings (Mosedale, 1998; Rayment, 2002). The summary should be perceived as being constructive, highlighting both the high and low areas of achievement (Rayment, 2002; Viner, 2005).

1.4.8. Planning for Improvement

1.4.8.1. Feedback and Evaluation

The results are then disseminated to the relevant groups in order for results to be interpreted and an action plan for future development to be devised and eventually implemented in a systematic fashion (Rayment, 2002; Viner, 2005). Evaluation of the results is also important to ensure that all objectives of the audit were met, and if not, why not (Rayment, 2002; Viner, 2005).

1.4.8.2. Re-audit and Evaluation

A time-scale for the implementation of any changes must also be considered at this time, in order to set a realistic date for re-audit (Mosedale, 1998; Rayment, 2002). Comparison of the original and more recent sets of audit results then allow for evaluation and quantification of any improvements that have occurred (Mosedale, 1998; Rayment, 2002; Viner, 2005).

On completion of re-audit, the entire clinical audit cycle has undergone one revolution (Viner, 2005). At this point it can be decided whether there is further gain to be achieved by repeating the process immediately in order to further raise specific standards, or if the standards achieved now reflect best practice, in which case a timetable for regular re-audit in order to maintain these standards should be formulated.

1.5. Equine veterinary medicine and surgery

1.5.1. History

Although the practice of medical treatment of horses for a multitude of ailments had been around for centuries, the first printed texts on 'horse medicine' were published in the late fifteenth century (Hall, 1999). Farriers were responsible for much for the veterinary care provided, using secret remedies whose component parts were learnt during apprenticeships (Hall, 1999). However, it was the founding of the London Veterinary College in 1791, followed by the advent of the war with the French in 1793 that prompted the reorganisation and improvement in veterinary training with a scientific base, in order to provide care to the army's mounts and pack animals (Hall, 1999). Further conflicts around the world, and heavy losses of troop animals sustained by the British army continued the furtherment of the veterinary profession well into the early twentieth century, before horses were gradually phased out and replaced by mechanisation by the mid-twentieth century (Reilly, 1999). From this point a shift in emphasis was seen, from servant to one of the best kept domestic species of the modern day.

Even in the early twentieth century the practice of veterinary medicine was more of an art than a science, with the application of astringents, blisters and purgatives for a variety of ailments (Rossdale, 1999). It was not until the middle of the century with the advent of

such developments as antibiotics that the application of science became more commonplace, prior to the rapid acceleration in progress seen over the last few decades (Rossdale, 1999).

1.5.2. Modern practice

1.5.2.1. Organisation

With rapid developments in diagnostic imaging, surgery and therapeutics, along with the increasing capability of clinicians to apply these techniques, the inevitable path of specialisation of clinicians had begun to occur (Rossdale, 1999; Gripper, 2005). This has lead to the formation of group practices, in particular in areas of high density of the horse population, with the facilities and reputation to rival veterinary schools (Rossdale, 1999; Gripper, 2005).

With the rapid advances that have occurred in technology, and the increasing availability of these advanced technologies such as magnetic resonance imaging (MRI), nuclear scintigraphy and specialist surgical procedures, available to the veterinary profession, there is the inevitable cost that must be faced (Rossdale, 1999). Unlike in the medical profession, there is no version of the National Health Service to provide free veterinary care to domestic species (Gripper, 2005). Many horse owners are both willing and able to support the application of modern technologies by paying an appropriate fee, and this in turn will support the continued development of specialist practices (Rossdale, 1999), although some owners still hold the outdated view that the veterinary profession is an expensive commodity, rather than a highly skilled service industry (Gripper, 2005). For those owners that do not have the finances to cover oftentimes expensive medical interventions, they are faced with an unenviable decision.

For those owners who do not have the financial wherewithal to pay for advanced veterinary treatments out of their own pockets, insurance is a viable alternative (Buckton, 2003). However, despite the prospect of large veterinary bills for the treatment of any injury or disease, insurance for veterinary fees is still viewed by many as a luxury instead of a necessity (Keel, 2003). Different levels of horse insurance exist, ranging from all risks mortality (loss of the horse), through cover for veterinary fees, to loss of use where the horse is deemed incapable of performing the job for which it was insured. At one time

insurance for veterinary fees was viewed by many as a license to spend money (Buckton, 2003; Ordidge, 2003). However, increased regulation in the industry, brought about through increased competition amongst insurers, increased expectations by owners, spiralling costs of specialist veterinary treatment coupled with an increase in surgical interventions and the increased recognition of fraudulent claims by both owners and veterinarians, has led to the requirement for justification for expenditure on procedures, often before they are performed (Buckton, 2003). If this trend of increasing costs for veterinary treatment is to continue, it has been suggested that either owners will face large rises in premiums to the point that it is no longer economic to insure a horse, or veterinary fee cover may be withdrawn from the market altogether (Buckton, 2003).

With the increasing computerisation of practice records (Cockroft and Holmes, 2004), instead of the more traditional card filing systems there is now the ability to use practice data to provide practice specific information (Cockroft and Holmes, 2004). If the records are coded in a methodical and consistent manner, it is possible to use them to identify information such as the incidence of disease, post-operative complications and survival rates (Cockroft and Holmes, 2004). These detailed computerised records are also a vital tool in the implementation of clinical audit (Cockroft and Holmes, 2004).

1.5.2.2. The need for EBVM and clinical audit

In a time of increasing awareness of litigation, and tightening of European legislation (Rossdale, 1999), there is now an expectation for the veterinary profession to be able to defend many of its actions (Holmes and Cockroft, 2004). Clients will frequently no longer accept a veterinary surgeon's opinion at face value, but will wish to be involved in all aspects of the clinical decision making. With increasing access to electronic information sources clients are becoming well informed (Holmes and Cockroft, 2004) not only in alternative therapies, but also to the risks associated with those already widely accepted and employed. An owner, when faced with important decisions, will all too often ask a question that is rooted firmly in the principles of EBVM, beginning: 'what is the likelihood that....?' and they will expect the veterinary surgeon to be able to provide them with a well informed answer. With the recent loss of the exclusive right to dispense medicines to animals under their care (Gripper, 2005), and the increasing emergence of paraprofessionals, it must be accepted that the actions of the veterinary profession will

continue to come under increasing scrutiny, as people question the monopoly that they hold.

There are now a wide variety of easily accessible electronic information resources (Holmes and Cockroft, 2004) to allow a practitioner to apply the principles of EBVM to their work. It is becoming increasingly important that veterinary surgeons are able to account for any clinical decisions that they might make, especially in the event of an unfavourable outcome (Holmes and Cockroft, 2004). Similarly, access to these information resources will allow owners to make informed decisions in the care of their animal, along with avoiding unrealistic expectations of outcome (Holmes and Cockroft, 2004).

With the introduction of the Practice Standards Scheme in 2005, the Royal College of Veterinary Surgeons (RCVS) acknowledged that clients wished a means by which they could ensure that the services offered by a practice were safe and effective, conforming to a minimum standard of care (RCVS, 2005) . In order for the profession as a whole to be able to demonstrate, not only to clients but also to peers, that the expertise offered is reliable and can be held to account, clinical audit and the adoption of the principles of EBVM are a necessary step (Cockroft and Holmes, 2003).

In addition, with the introduction of the new Financial Services Authority (FSA) regulations, if a veterinary practice wished to play any part in giving advice or recommending a product to a client investigating the purchase of insurance cover, the practice must now be either directly authorised by the FSA, or an appointed representative of a firm that is (Keel, 2005). This involves not only specialist training, but also the performance of regular audits (Keel, 2005).

1.5.2.3. Limitations to the adoption of EBVM and clinical audit

Although both EBVM and clinical audit will play a vital role in the development of the veterinary profession in the future, they must be recognised to have their limitations. The process of performing an audit requires the mastering of new skills in investigation and appraisal, and once these skills have been acquired the actual auditing process is time-consuming. In a private veterinary practice, diversion of a clinician's time and energy from seeing cases to performing an audit is also costly (Viner, 2005). It is liable to be the actual expense, in terms of time and energy, of implementing an audit that will limit its use

in the veterinary practice. An additional complication in the inception of clinical audit is that in order to perform a true clinical audit, there must be pre-existing data with which to perform a comparison (Viner, 2005). If this data does not exist, a clinical audit cannot be performed until the benchmark data has been produced.

The practice of EBVM is also viewed to be time-consuming, by the time a question is formulated, the literature searched and appraised, and this knowledge then integrated into clinical work (Viner, 2005). Not only will an already busy clinician have to contend with the time-pressure of applying EBVM, they are also faced with the minefield of poor evidence that currently exists in the veterinary literature (Viner, 2005). It has been argued that it is inappropriate to practice EBVM at the current time, due to the insufficient depth and breadth in the veterinary scientific literature (Cockroft and Holmes, 2003). However, a lack of evidence is not a defence for not searching for the best available evidence (Cockroft and Holmes, 2003). An understanding of statistical techniques is also vital to interpret the appropriateness of their use in clinical studies, and the prospect of learning these techniques can be daunting.

The practice of EBVM is likely to be slow in its inception, in order to allow for time for the education of practitioners in matters such as statistical analysis, and the publication of studies that contain research of a higher quality of evidence than that which is currently available (Cockroft and Homes, 2003; Viner, 2005). As in the medical profession, it is liable to be new graduates and their teachers that embrace the principles of EBVM with enthusiasm (Rafuse, 1994; Sackett *et al.* 1996), whilst the established practitioners will no doubt greet it with something more akin to scepticism. The education of practitioners is being assisted by the formation of programmes designed to educate practitioners in methods of clinical research and data analysis, for example the clinical research outreach programme run by the Cambridge Infectious Disease Consortium, through the University of Cambridge (Viner, 2005). The purpose of this programme is to provide short residential courses with a well organised ongoing support structure, to enable practitioners to perform clinical research projects and then get the results published (Viner, 2005). By encouraging practitioners to answer questions through practice-based clinical research, it is hoped to promote not only the ethos of EBVM, but also the analytical skills necessary for both clinical research and clinical audit. For those wishing to advance their skills in clinical research still further, there is a Masters programme run by the Society of Practising Veterinary Surgeons (SPVS) to encourage work-based research (Viner, 2005), and the

RCVS is currently reviewing a proposal for a Certificate in Advanced Veterinary Practice, which would involve the study of research methodologies and the carrying out of work-based research (Viner, 2005).

1.6. Aims of this study

1.6.1. Study Design

The purpose of this study was to design a series of investigations of equine diseases, and implement them at three private equine hospitals in southern England. The diseases investigated were all different forms of sepsis associated with either elective or emergency surgical procedures, ranging from sepsis as a result of surgical intervention to sepsis requiring surgical intervention. A variety of study designs were used, each providing a different class of evidence when using the classification system generated by Yusuf *et al* 1998. The principles of EBM were followed, in an attempt to provide the evidence required to answer specific questions that could be posed by a veterinary practitioner, and to highlight both the strengths and short-comings of different types of study design, along with the quality of evidence different study designs could provide.

Four studies involving the retrospective analysis of case records were conducted, to investigate the short and long term prognosis for foals and mature horses treated for either septic arthritis or septic digital tenosyinovitis. Two of these studies, investigating the short and long term prognosis in Thoroughbred foals and mature horses treated for septic arthritis, were case-control studies, utilising siblings as the comparison population (Chapter 5). The remaining two retrospective studies were case series (Chapters 3 and 4). The final two studies conducted were prospective. One was a clinical audit of post-operative complications following elective surgery (Chapter 7), with the final study being a randomised, controlled clinical trial investigating whether the use of belly bands following exploratory laparotomy reduced the prevalence of incisional complications (Chapter 6). Due to the diverse nature of the specific conditions investigated, each separate study has a review of the literature relevant to that study at the beginning of the appropriate chapter.

1.6.2. Providing answers relevant to practice

The main focus of this investigation was to ascertain whether it was possible to apply the ethos of EBM to the veterinary profession, and provide good quality research and evidence from private practice.

A frequent comment when discussing the quality and relevance of publications in the equine veterinary literature is that, although studies are well designed and often provide significant findings, these findings are of little relevance to the general practitioner, or may be worded in such a way that the relevance of results can be difficult to interpret. It was thought that in order to provide answers relevant to the general practitioner, the original question should stem from a practice population.

In order to further this aim, studies were carried out on conditions encountered commonly in equine practice, where a large amount of information has already been published in the literature, frequently of a conflicting nature, and also of a poor quality of evidence as defined by Yusuf *et al* (1998). By addressing these issues, it was intended that data generated in these studies would then have a direct relevance to the general practitioner.

Chapter 2

General Materials and Methods

2.1. Introduction

The purpose of the study was to conduct a series of investigations into common equine problems, applying the principles of evidence-based medicine. Areas for investigation were identified by questioning equine clinicians on conditions that were commonly encountered in equine practice requiring surgical intervention, where existing evidence was considered to be either conflicting or poor. Searches were then performed for each condition of interest, in order to identify any studies already existing in the literature, and these studies were then classified on the 'class' of evidence that they provided in EBM terms, according to the classification system proposed by Yusuf *et al.* (1998).

At the outset of the study there were few examples of the application of the principles of EBM to clinical research in the equine veterinary literature (Denoix *et al.* 2003; Edwards *et al.* 2003; Kane *et al.* 2003; Spike-Pierce and Bramlage, 2003), although during the study period more papers were published (Barakzai *et al.* 2004; Johnston *et al.* 2004; Smith *et al.* 2004; Proudman *et al.* 2005a,b; Smith *et al.* 2005; Valverde *et al.* 2005). One intention of the study was to investigate whether it was plausible to conduct practice-based clinical research using the principles of EBM.

2.2. General Study Design

2.2.1. Recruitment of Veterinary Practices

Three private equine clinics in the South of England were approached to participate in either some, or all, of the clinical research studies. These three practices were selected due to pre-existing close links with the primary surgeons, their known willingness to participate in clinical research studies, and their interest in, and support for, EBM. It was decided not to include veterinary schools in the studies, as the participation of veterinary students in the evaluation and care of the cases in addition to that of trained veterinary nurses and veterinary surgeons could lead to over-interpretation of specific outcomes, and the introduction of bias into the studies. The practice populations treated by the three

private practices, along with the standard treatment regimens employed in these practices, were also felt to be more comparable with one another than with those of a veterinary school. Furthermore, since the intention of the overall study was to provide evidence for use by all practitioners, it was considered important to avoid the inevitably biased population of animals that are typically referred to veterinary school clinics. In all studies, necessary sample size was a critical design consideration, hence the need to have horses from up to three clinics available.

At the outset of the study formal presentations were made to the veterinary surgeons at each of the three participating clinics, in order to explain the reasons for the general study and the aims of the individual studies being conducted, along with the data collection requirements. At this point, surgeons were invited to provide feedback including: areas they would like to see investigated further that were within the scope of any of the studies, and where they perceived problems could arise, either in case management or data collection. Where possible, the results of this feedback were then incorporated into the study design.

2.3.1.1. Participating Veterinary Clinics

2.3.1.1.1. Rossdales Equine Hospital

Rossdale and Partners was first founded in 1959 as an ambulatory practice based in Newmarket, and in 1991 the practice was expanded to two sites. Since that time, the practice has continued to expand to the current total of 25 veterinary surgeons, and it is thought to be the largest private equine practice in the United Kingdom. The ambulatory part of the practice, Beaufort Cottage Stables, is still based at the original site off Newmarket High Street, performing first opinion work for a variety of Thoroughbred studs, racehorse trainers and private stables. The Rossdales Diagnostic Centre and Rossdales Equine Hospital are both based on the Exning Estate, in Exning, The hospital was opened in 1998, in order to 'provide a state of the art surgical facility to deal with the ever-increasing surgical caseload, both from the local practice and referred by veterinary surgeons'. It is accredited as a Tier 3 hospital under the RCVS Practice Standards Scheme, with a surgical caseload evenly divided between orthopaedic and soft tissue cases, although a large proportion of the caseload is from the Thoroughbred breeding and racing industry.

2.3.1.1.2. Bell Equine Veterinary Clinic

Bell Equine Veterinary Clinic was established in central Kent as a small, specialist equine clinic in 1991. Since that time, it has continued to expand, moving into purpose built premises and now employing 14 veterinary surgeons. Although there are two parts to the practice (the first opinion practice and the hospital practice, for both surgical and referral cases), both sides of the practice are fully integrated with each other, with the main clientele of the practice being pleasure horses. The practice is accredited as a Tier 3 hospital under the RCVS Practice Standards Scheme, and is committed not only to providing a high level of veterinary care, but also to clinical research and development, and the further education of both clients and veterinary surgeons.

2.3.1.1.3. Bushy Equine Veterinary Clinic

Bushy Equine Veterinary Clinic is part of the Vale Veterinary Group, and is based in Gloucestershire. It offers first opinion care for horses and ponies within Gloucestershire and Somerset, as well as receiving referrals from the South West of England and Wales. Although seven vets work at Bushy Equine Veterinary Clinic and it offers full hospitalisation and surgical facilities, it is not accredited under the RCVS Practice Standards Scheme. However, the Vale Veterinary Group has both Tier 2 general small animal practices and a Tier 3 small animal hospital accredited under the scheme.

2.3.2. Study design principles

A retrospective study design was chosen for four of the studies, in order to provide sufficient case numbers to achieve sufficient statistical power for clinically meaningful outcomes, without the necessity for a lengthy study period. The conditions investigated were not suitably common that an adequate number of cases would be generated in the available time period if a prospective study design was used. The data that were required for statistical analyses were all routinely recorded in the hospital records for each horse, and although it was accepted that some data may have been missing from some of the records, it was anticipated that sufficient data should be present to allow for meaningful statistical analyses to be performed.

A prospective study design was chosen for the remaining two studies in order to answer specific clinical questions that could not be answered by using pre-existing records. The prospective design allowed one study to be both controlled and randomised, providing a high quality of evidence in EBM terms, whereas if historical controls had been utilised through access to case records the resultant conclusions would have constituted a poorer quality of evidence. As the two conditions investigated using a prospective study design were encountered on a regular basis in the participating practices, it was possible to achieve a sufficiently large sample size to achieve sufficient statistical power for a clinically meaningful outcome, without having to implement a prohibitively lengthy study period.

2.3.3. Record Keeping

2.3.3.1. Methods of record keeping within the practices

The records at Rossdales Equine Hospital and Bushy Equine Veterinary Clinic are all paper records, with all daily occurrences noted in the horse's records and then the record is filed when the horse is discharged from the hospital. All hospital records are then archived by year, in alphabetical order by horse name.

At Rossdales Equine Hospital, if a horse already had a record existing from a previous visit, all new records were archived with the original record under the year of the first visit. For horses with multiple visits, especially for the treatment of different conditions, this rendered it impossible to search easily for case records when the name of the horse and the year of treatment were known. It was also necessary to know whether the horse had ever been treated previously, including whether this had occurred under either a different horse or owner name. It was possible to perform a computerised search for a condition, but only if the horse had been referred to the hospital from outside the main practice, as referral letters written after discharge were archived on a computer system under both name and condition treated. It was still necessary to then search for the case records in the paper archive for all relevant day-to-day case information.

At Bell Equine Veterinary Clinic, both a paper record and a computer record existed for every horse treated. The computer system used for recording clinical and billing details is 4D, from QVetIT, Quaesitor Solutions Limited, and a brief summary of clinical progress is

entered on a daily basis in each record, along with any relevant billing information so that a running total of the bill to date is kept. The paper records are filled out in detail on a daily basis, and then at the time of discharge the paper records are scanned into another computerised database (E-file) prior to archiving. Both these computerised databases allow for searching by horse or owner name, date of treatment or category of condition treated.

2.3.3.2. Design of data recording forms

The forms used for recording the relevant data in each of the studies were designed to be as simple as possible (Appendices 1, 3, 7 and 10). The design of the forms was important, as staff at all the participating practices had stressed that forms requiring long written answers would take too much time to complete, leading to poor compliance. The name and signalment for each horse were written in a series of blank spaces next to appropriate sub-headings. Where appropriate, there were a number of choices in answer to a simple question, with a tick-box beside each choice. It was only possible to select one answer in response to each question.

2.3.3.3. Data collection

A small group of people was identified at each practice to be responsible for all the identification of cases for inclusion in the prospective studies, and the daily data collection for these studies. Study-specific inclusion criteria were listed at the outset of each study, and a written and laminated copy of these criteria supplied to each of the participating practices for easy reference. The people responsible for data collection were the nurses at Rossdales Equine Hospital, and the hospital interns at Bell Equine Veterinary Clinic and Bushy Equine Veterinary Clinic. The surgeons participating in the study filled out a surgeon's report form for each case, but did not participate in any of the post-operative data collection to eliminate any bias that this might introduce. The completed data collection forms were then collected by the author on a regular basis, for collation and analysis.

In the retrospective studies, all cases eligible for inclusion in studies were identified by analysis of medical records. This case identification and the subsequent data retrieval from the medical records was performed solely by the author. The follow-up information was

then collected using telephone questionnaires administered to each horse's caretaker, performed solely by the author in all retrospective studies.

2.4. Hardware and Software

A Hi-Grade Notino 4400 laptop computer was purchased at the outset of the study, in July 2003, for collation and analysis of all data. Microsoft Office Professional 2000 incorporating Microsoft Excel, Microsoft Word and Microsoft PowerPoint, was installed on the computer, along with Minitab 13.31 for performing all statistical analysis, WINPEPI 4.0 for combined regression analysis and Win Episcope 2.0 for performing power studies.

All raw data were entered into study-specific spreadsheets in Microsoft Excel. Data were then transferred to worksheets in study-specific projects in Minitab 13.31, where data could be manipulated or coded into a form suitable for statistical analysis. Reports, and where appropriate graphs, could then be generated in Minitab 13.31 at the conclusion of all necessary statistical analyses.

2.5. Literature Search

A detailed search of the existing literature was performed for each of the conditions of interest at the outset of the study. Each search was conducted using the bibliographic databases available through the University of Glasgow Library website, accessed via OVID Online. Through this site, it is possible to access multiple electronic bibliographic databases, and perform the same search in each database. All searches were initially performed in MEDLINE, the electronic library of the United Stated National Library for Medicine, via OVID Online, before repeating the searches in CAB Abstracts, providing access to agriculture-based scientific literature abstracts, also accessed via OVID Online. Both MEDLINE and CAB Abstracts allow for search topics to be combined or refined to keywords, specific journals, authors or years using their advanced search settings, and they also recognise the need to search using both the American and British spelling of key words. All relevant references identified in this manner were then investigated, and all references cited by each paper were also accessed.

2.6. Statistical Methods Applied

At the outset of each study, the project team met and carefully considered the clinical problem in question and agreed on the aims and objectives for each study. Central to this was the definition of biologically meaningful effects which were used to inform sample size calculations. A power calculation was performed at the outset of each study, to determine the minimum sample size necessary to detect the existence of a statistically significant difference for a clinically meaningful outcome. The number of horses required (n) for each study, using a significance level of 5%, and study power of 80%, was calculated using the statistical freeware software Win Episcope 2.0, which used the standard formulae as appropriate for each study (Snedecor and Cochran, 1980):

$$n = [(Za + Zb)/(P_0 - P_1)]^2 * (P_1Q_1 + P_0Q_0)$$

where Za is the value of Student's t distribution at the specified confidence level, calculated to be 1.96, and Zb is the value of Student's t distribution at the specified power, calculated to be -0.842, with P_0 being the proportion of horses that successfully attain their expected level of athletic performance following treatment, Q_0 being $(1-P_0)$, P_1 is the proportion of horses in the control population that attain their expected level of athletic performance, and Q_1 is $(1-P_1)$. Each power calculation was parameterised with data derived from existing literature, where available.

Data were initially tabulated, summarised and subjected to exploratory data analysis with tests for normality and descriptive analyses, using either the chi-squared test for discreet data, or a Student's t-test for continuous data, as appropriate using the statistical software package Minitab 13.31. Following the initial analysis, categorical variables with more than two levels were coded as indicator variables using Minitab 13.31, prior to univariable and multivariable logistic regression analyses. For the majority of studies, a dichotomous outcome variable, i.e. survival or not; recovery or not; dictated that logistic regression analysis would be the most appropriate statistical modelling approach. Univariable analysis was used to screen all variables, and from this, all variables with a p-value ≤ 0.20 were included in a backward elimination process to fit a multivariable model. The inclusion criterion for backward elimination was set at $p \leq 0.05$. The goodness-of-fit of the models was assessed using Minitab 13.31, by the Hosmer-Lemeshow goodness-of-fit test,

to test the null hypothesis that the model was considered to be a good fit, with the null hypothesis rejected at a p-value ≤ 0.05.

Once the main effects model had been fitted, two-way interaction between variables was assessed using Minitab 13.31. Variable selection was determined by biological plausibility. Assessment between models was obtained using a likelihood ratio test (LRT) with significance set at $p \leq 0.05$.

Additional statistical analyses, specific to each study, were also performed, and are described in detail in the relevant chapters.

On completion of data analyses, findings were considered and discussed. In particular, their relevance in EBVM terms was considered with particular attention to the quality of evidence provided and their value to the veterinary practitioners.

Chapter 3

What is the likelihood that a horse treated for septic digital tenosynovitis will return to its previous level of athletic function?

3.1. Introduction

Synovial sepsis in adult horses is a serious clinical problem (Bertone *et al.* 1987a; Schneider *et al.* 1992a; Booth *et al.* 2001) that usually affects a single synovial structure (Cook & Bertone, 1998). The potential exists to cause permanent fibrosis, damage to tendons, adhesion formation and unsoundness when infection is not rapidly eliminated from the synovial space (Schneider *et al.* 1992a; Tremaine, 2000). Rupture of the tendons within the sheath, secondary to ongoing sepsis, has also been reported (Honnas *et al.* 1991; McIlwraith 2002; Kidd *et al.* 2004), presumably due to enzymatic degradation of the tendon fibres by bacteria and inflammatory cells present within the sheath. The digital flexor tendon sheath is the most commonly affected synovial sheath (Jackman *et al.* 1989; Honnas *et al.* 1991), although sepsis has also been reported frequently in the tarsal, carpal and extensor tendon sheaths (Nixon, 1990; Platt and Wright, 1997; Santschi *et al.* 1997; Cauvin *et al.* 1999).

3.2. The occurrence of septic digital tenosynovitis

3.2.1. Routes of infection

Septic tenosynovitis is caused by the inoculation of a synovial sheath with bacteria, with viable organisms overwhelming natural host defences and becoming established. There are three recognised routes by which bacteria may become established within a synovial cavity (McIlwraith, 1983).

1. Sepsis can follow a traumatic insult to the tissues overlying the synovial structure (Rose & Love, 1979; Madison *et al.* 1991, Schneider *et al.* 1992a; Tremaine, 2000)
2. It may be of iatrogenic origin, for example following an intra-synovial injection or surgery (Van Pelt, 1971; McIlwraith, 1983; Martens *et al.* 1986; Schneider *et al.* 1992a; Tremaine, 2000)

3. More rarely in adults, it can be the result of haematogenous spread from an infectious focus elsewhere in the body (Martens *et al.* 1986; Schneider *et al.* 1992a). In the vast majority of reported cases (Schneider *et al.* 1992a; Chan *et al.* 2000; Summerhays, 2000; Frees *et al.* 2002) the route of infection has been identified as traumatic in origin. Occasionally, the inciting cause of sepsis is not identified.

3.2.2. Clinical signs associated with sepsis

Acute severe lameness, synovial effusion, heat and pain on palpation of the joint, localised swelling, pyrexia, cellulitis and distal limb oedema are the most commonly reported clinical findings (Van Pelt, 1971; Rose & Love, 1979; McIlwraith, 1983; Bertone *et al.* 1987a; Honnas *et al.* 1991; Schneider *et al.* 1992a; Cook & Bertone, 1998; Tremaine, 2000; Chan *et al.* 2000), although synovial effusion and lameness may not be as marked if the synovial structure is open and draining (McIlwraith, 1983; Honnas *et al.* 1991).

3.2.3. Involvement of other structures

When synovial sepsis is a sequel to a traumatic laceration of the digital flexor tendon sheath it is also possible for the horse to sustain either a laceration to, or complete transection of, the superficial and/or deep digital flexor tendons (Fraser and Bladon, 2004). Even if the synovial sepsis is successfully resolved, these concurrent injuries will have serious implications on the likelihood of that horse becoming sound.

Rupture of either the superficial or deep digital flexor tendons has been reported in cases of untreated or ongoing sepsis (Honnas *et al.*1991; Kidd *et al* 2004) of the digital flexor tendon sheath, presumably due to the ongoing degradation of the tendon fibres by lysosomal enzymes

3.2.4. Principles of treatment

The basic principles for successful resolution of synovial sepsis are treatment with broad-spectrum systemic antimicrobials and lavage of the septic structure, although the most efficacious form of lavage remains a contentious issue. Although many additional treatment strategies have been proposed, including open drainage (Schneider *et al*, 1992b;

Chan and Munroe, 1997), intra-thecal antimicrobials (Schneider *et al.* 1992a,b), regional limb perfusion with antimicrobials (Whitehair *et al.* 1992) and transection of the proximal palmar/plantar annular ligament (Honnas *et al* 1991; Phillips, 1997), these can only be described as being complementary to the basic principles of systemic antimicrobials and lavage.

3.2.5. Treatment Failure

The main causes of treatment failure are the inability to eliminate the causative agent (Bertone *et al.* 1987a; Schneider *et al.* 1992a; Meijer *et al.* 2000) and to disrupt effectively the vicious cycle of fibrosis and subsequent adhesion formation through accumulation of inflammatory products (Orsini, 1984; Stover, 1990; Bertone, 1999; McIlwraith 2002). If digital tendon sheath sepsis has not been resolved after a single lavage, and there is no obvious reason for ongoing sepsis, it must be considered that a focus of infection remains within the sheath which will result in re-seeding of bacteria after surgical lavage. Cases have been reported in which a small foreign body has been present within the sheath, acting as a focus of infection (Magee, *et al*, 1997); similarly, if necrosis of tendon fibres has occurred (Booth *et al*, 2000), or osteomyelitis of a sesamoid bone (Chan and Munroe, 1997), as a consequence of the initial injury, these foci of infection will continuously reseed the tendon sheath until the underlying cause of infection is addressed and resolved. Even if there is no focus of infection identified, bacteria can sequester in the synovial membrane, leading to re-infection of the sheath after surgical lavage if all bacteria and inflammatory cells are not effectively removed.

3.2.6. Outcome and prognosis

There are few published studies investigating the long term outcome following septic tenosynovitis, specifically septic digital tenosynovitis. Previous studies have frequently reported only short term follow up, with the end point commonly being discharge form the hospital. Only three studies (Honnas *et al.* 1991; Chan *et al.* 2000; Frees *et al.* 2002) have followed the outcome of horses after they have been discharged from the hospital following treatment for septic digital tenosynovitis, and all have included relatively small numbers of cases (25, 12 and 20 horses respectively). Between 80% (20/25; Honnas *et al.* 1991) and 100% (14/14; Schneider *et al.* 1992) of mature horses treated for septic digital tenosynovitis were successfully discharged from the hospital, while the long term studies

found that between 50% of horses (10/20; Frees *et al.* 2002) and 91% (11/12; Chan *et al.* 2000) were able to return to their original level of athletic function, with no adverse affects related to the occurrence of septic digital tenosynovitis. Many of the recommended treatments for the management of septic digital tenosynovitis are extrapolated from data generated from controlled trials investigating the success of treatments for septic arthritis. Whilst it is widely accepted that systemic antimicrobial therapy and synovial drainage are necessary for the successful resolution of septic digital tenosynovitis, other factors that may influence either the short or long term prognosis prior to the commencement of treatment have not been examined. Potential factors that could influence the prognosis include the age of the horse at the time of admission to the hospital for treatment, whether a forelimb or hindlimb is affected, the exact location on the limb of the inciting cause of synovial sepsis and the duration of sepsis prior to referral for treatment.

For the purpose of this study, it was hypothesised that the occurrence of septic digital tenosynovitis would significantly reduce the likelihood of a horse returning to its previous level of athletic function when compared to a horse treated for septic arthritis in the same practice population.

3.3. Materials and Methods

3.3.1. Power calculation

The number of horses required (n) for this study, using a significance level of 5%, and study power of 80%, was calculated using the standard formula (Snedecor and Cochran, 1980):

$$n = [(Za + Zb)/(P_0 - P_1)]^2 * (P_1Q_1 + P_0Q_0)$$

where Za is the value of Student's t distribution at the specified confidence level and Zb is the value of Student's t distribution at the specified power, with P_0 being the proportion of horses that successfully return to their previous level of athletic performance following treatment for septic arthritis, Q_0 being $(1-P_0)$, P_1 is the proportion of horses that return to their previous level of exercise following treatment for septic digital tenosynovitis, and Q_1 is $(1-P_1)$. With P_0 estimated to be 50%, based on data gathered from the same practice population, over the same time period, as part of a separate study (see chapter 4) and P_1

estimated to be 71%, based on previously published data (Chan *et al.* 2000; Frees *et al.* 2002), the required number of horses for the study was, therefore, 83.

3.3.2. Data retrieval

3.3.2.1. Study group

The admission records for Bell Equine Veterinary Clinic between January 1994 and December 2003 were reviewed to identify horses that had been admitted with suspected digital sheath pathology, and medical histories were then retrieved. In cases in which septic digital tenosynovitis was suspected on the basis of clinical signs, diagnosis was confirmed on the result of synoviocentesis of the digital sheath, where an increased nucleated cell count (upper end of normal reference limit for laboratory: 3×10^9 cells/l) in conjunction with an increased total protein concentration (upper end of normal reference limit: 15g/l) and the presence of a neutrophilia (>90%) with degenerative polymorphonuclear cells on cytological analysis were considered to be diagnostic.

Information retrieved from the medical records included age, sex, breed, evidence of any other pathology outside the digital sheath, the suspected route of infection, anatomical location of any wound that may have contributed to the development of synovial sepsis, time from onset of clinical signs to presentation at the clinic for treatment, the white cell count of the synovial fluid at the time of admission to the hospital, results of bacterial culture of the synovial fluid, details of antimicrobial therapy and lavage procedures performed and whether the horse was discharged from the hospital following treatment.

3.3.2.2. Control Group

Over an identical study period, the same baseline data were collected for horses admitted to the clinic for evaluation of suspected septic arthritis. The diagnosis of septic arthritis was made based on similar criteria to those used in the diagnosis of septic digital tenosynovitis (4.4.1.). The basic information derived from the results of the analysis of these data were used to inform the power calculation performed at the outset of the current study (3.3.1.).

3.3.3. Outcome Measures

Outcomes that were statistically evaluated included discharge from the hospital and whether the horse eventually returned to its previous level, or a higher level, of performance. Outcome was determined by evaluation of medical records to determine whether the horses were successfully discharged from the hospital. Long term follow up was then obtained by means of a questionnaire administered to owners by telephone (Appendix 1). The purpose of the questionnaire was to establish the level of athletic performance the horse had achieved prior to the occurrence of septic digital tenosynovitis and whether, in the owner's opinion, the horse had been able to return to this level of performance after discharge from the hospital. If the owner did not consider the horse to have successfully returned to its previous level of performance it was established whether this was directly attributable to the occurrence of septic digital tenosynovitis, or whether there were other factors that had contributed to the eventual outcome.

3.3.4. Data Analysis

Variables that were statistically evaluated included age, sex, whether a forelimb or hindlimb was affected, location on the limb of any penetrating wound, inciting cause of sepsis and duration of onset of sepsis until commencement of treatment. Categorical variables with more than two levels were coded as indicator variables.

Binary logistic regression was used to analyse these data as both outcomes of interest were dichotomous. Two binary logistic regression models were constructed using these data. Analyses were implemented with the statistical software MINITAB (version 13.31).

Univariable logistic regression was used to screen all variables, and from this all variables with a p-value ≤ 0.20 were included in a backward elimination process to fit a multivariable model. The inclusion criterion for backward elimination was set at $p \leq 0.05$. The goodness-of-fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, to test the null hypothesis that the model was a good fit, with the null hypothesis accepted at a p-value ≤ 0.05.

Once the main effects model had been fitted, two-way interaction between variables was assessed. Variable selection was determined by biological plausibility. Assessment

between models was obtained using a likelihood ratio test (LRT) with significance set at $p \leq 0.05$.

Comparison of outcomes for those horses treated for septic arthritis and those treated for septic digital tenosynovitis were made using univariate analysis of odds ratios and 95% confidence intervals, along with a χ^2 test. Differences were considered significant at $p \leq 0.05$.

3.4. Results

3.4.1. Descriptive Statistics

3.4.1.1. Study group

Ninety horses met the criteria for inclusion in the study, thereby satisfying the power study performed at the outset. Forty-three horses were male and forty-seven were female. The age at the time of admission was recorded in 85 cases, with the age ranging from 1 month old to 30 years old, and the median age was 9 years old (inter-quartile range 5 – 14 years old) at the time of admission. Fifteen of the 90 horses (17%) had no breed recorded on their admission papers. Of the remaining 75 horses, the breed distribution included 23 Thoroughbreds (31%), 19 part-bred Thoroughbreds (25%), 11 Warmbloods (15%), and the remaining 22 horses (29%) were a variety of native pony breeds, or of mixed breeding, which was considered to be representative of the population of horses treated at the hospital during the study period. The athletic use at the time of admission was recorded in 76 cases (84.4%), with 90.8% of these (69/76) being general purpose riding horses at the time of admission.

All horses had sepsis in a single digital synovial sheath, with no other digital sheath affected. However, seven horses also had sepsis present in at least one other synovial structure (one in a tibio-tarsal joint, four in a metacarpo/metatarsophalangeal joint, one in the tarsal sheath and one with sepsis of the distal inter-phalangeal joint and navicular bursa). The cause of sepsis was recorded in all cases (Table 1). No horse developed sepsis subsequent to haematogenous spread, and no foals with septic digital tenosynovitis secondary to septicaemia were recorded in the 10 year study period.

Among the 90 horses, 38 forelimbs were affected and 52 hindlimbs. The site of the injury was recorded in all cases (Table 2). One horse developing sepsis as the result of regional anaesthesia had a low four-point nerve block performed on a front limb, and thus the site of inoculation was at the level of the fetlock joint; one horse developed sepsis in a hindlimb following surgical exploration of the digital sheath at the level of the pastern. The presence of a wound at the level of the pastern causing synovial sepsis was found to be statistically significantly over-represented (p=0.008, 95% CI 0.54 to 0.74), whilst numbers in the other two categories (wound at the level of the fetlock and solar penetration) were low.

Table 1: Cause of sepsis of the digital flexor tendon sheath in 90 horses

Cause of sepsis	Number	%
Trauma	88	97.8
Subsequent to diagnostic regional anaesthesia	1	1.1
Subsequent to surgical exploration of sheath	1	1.1

Table 2: Site of injury in 90 horses with sepsis of the digital flexor tendon sheath

	Forelimb		Hindlimb	
Site of Injury	Number	%	Number	%
Overall	38	42.2	52	57.8
Solar Penetration	1	1.1	1	1.1
Palmar/Plantar pastern	25	27.8	33	36.7
Palmar/Plantar fetlock	12	13.3	18	20.0

The time between onset of clinical signs and presentation at the hospital for treatment was recorded in 87 cases. Of these, 57.5% of horses (50/87; 95% C.I. 0.464 to 0.680; p=0.198) were admitted to the clinic for investigation of suspected septic digital tenosynovitis within 24 hours of the original inciting incident occurring (in the majority of cases the time period was, in fact, less than 12 hours after the incident). A further 33.3% (29/87; 95% C.I. 0.236 to 0.443; p=0.002) were admitted to the clinic between 1 and 7 days of the original wound occurring, and 9.2% (8/87; 95% C.I. 0.041 to 0.173; $p < 0.001$) after more than 7 days.

The range for time of wound to admission at the clinic for treatment ranged from less than 1 hour to 6 weeks. The number of horses that presented for treatment more than 7 days after the onset of sepsis was very low compared to those in the other two categories (within 24 hours and between 1 and 7 days).

3.4.1.2. Control group

One hundred and thirty-six horses met the criteria for inclusion in the study, thereby satisfying the power study performed at the outset. Seventy-six horses were male and sixty were female. The age at the time of admission was recorded in 134 cases, with the age ranging from 6 months old to 30 years old, and the median age was 8 years old (inter-quartile range 5 – 13 years old) at the time of admission. Twelve of the 136 horses (8.9%) had no breed recorded on their admission papers. Of the remaining 124 horses, the breed distribution included 28 Thoroughbreds (22.6%), 31 part-bred Thoroughbreds (25%), 16 Warmbloods (12.9%), and the remaining 49 horses (39.5%) were a variety of native pony breeds, or of mixed breeding, which was considered to be representative of the population of horses treated at the hospital during the study period. The athletic use at the time of admission was recorded in all cases, with 92.6% of these (126/136) being general purpose riding horses at the time of admission.

All horses had sepsis in at least one joint, with three horses (2.2%) also having sepsis present in one other synovial structure (all three horses had sepsis of the distal inter-phalangeal joint with concomitant sepsis of the navicular bursa). The cause of sepsis was recorded in all cases, with the most common cause being sepsis subsequent to external trauma (130/136; 95.6%). No horse developed sepsis subsequent to haematogenous spread in the 10 year study period.

The time between onset of clinical signs and presentation at the hospital for treatment was recorded in 135 cases. Of these, 59.3% of horses (80/135; 95% C.I. 50.5to 69.6; p=0.038) were admitted to the clinic for investigation of suspected septic arthritis within 24 hours of the original inciting incident occurring (in the majority of cases the time period was in fact less than 12 hours after the incident). A further 25.2% (34/135; 95% C.I. 11.7to 25.3; $p < 0.001$) were admitted to the clinic between 1 and 7 days of the original wound occurring, and 15.5% (21/135; 95% C.I. 9.9 to 22.8; $p < 0.001$) after more than 7 days. The range for

time of wound to admission at the clinic for treatment ranged from less than 1 hour to 60 days.

3.4.2. Treatment Options

Although all horses were treated with systemic broad spectrum antimicrobials and digital sheath lavage, there was no standardised treatment protocol. The initial digital sheath lavage was performed under general anaesthesia. Affected sheaths were usually lavaged on alternate days until a clinical improvement was seen, with lavage being performed between one and five times in total (median = 1 lavage). Of the 85 horses that recovered successfully from general anaesthesia, 62.4% (53/85) had only one lavage, along with a course of parenteral antimicrobials, with no other treatment necessary to eliminate the infection from the sheath. Other procedures included transection of the palmar/plantar annular ligament of the metacarpo/metatarso-phalangeal joint (10 horses), tenoscopy (14 horses), or standing lavage of the sheath after insertion of a fenestrated drainage tube during lavage under general anaesthesia (8 horses). Eight horses received a combination of treatments. Standard practice was to review the antimicrobial regimen if antimicrobial sensitivity indicated that the organisms cultured were resistant to the initial antimicrobial choice, or if there was a failure to respond to treatment. Horses were discharged from the hospital when the clinical signs of infection had resolved, although all cases were still receiving antimicrobials at the time of discharge. Digital sheath sepsis was deemed to have resolved if two synovial fluid samples obtained forty-eight hours apart, with the first sample obtained a minimum of forty-eight hours post-operatively, showed no further evidence of ongoing sepsis.

3.4.3. Factors affecting survival

Of the ninety horses admitted to the hospital for evaluation and treatment of septic digital tenosynovitis, 79 horses (87.8%) were successfully discharged from the hospital. Of the eleven horses euthanased, only six were euthanased due to a failure of the septic digital tenosynovitis to respond to treatment (Table 3).

Univariable logistic regression analysis showed that none of the variables evaluated were associated with an increased risk of a horse failing to survive to be discharged from the hospital following treatment for septic digital tenosynovitis (Appendix 2.1).

Table 3: Short term follow up of 90 horses treated for septic digital tenosynovitis

Discharged from hospital	**79/90**	**87.8%**	
Euthanased	**11/90**	**12.2%**	
Euthanased prior to treatment	2/11	For financial reasons	1
		Due to concurrent injuries	1
Euthanased under GA	3/11	Due to concurrent injuries	1
		Due to anaesthetic complications	2
Euthanased due to failure to respond to treatment	**6/11**		

A multivariable logistic regression model was constructed using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criterion for backward elimination was set at $p \leq 0.05$. None of the variables evaluated were associated with an increased risk of a horse failing to survive to be discharged from the hospital following treatment for septic digital tenosynovitis.

3.4.4. Long-term follow-up

Long term follow up was available for 91.1% of cases (72/79) (Table 4). Of these seventy-two horses , thirty-nine (54.2%) returned to their intended use as performance horses, although a further six horses (8.3%) were sound and would have been capable of returning to their intended use; however, they were retired to pasture with no attempt at a return to exercise as an elective decision of their owners. Six horses (8.3%) were euthanased after discharge from the hospital due to complications associated with the occurrence of septic digital tenosyovitis.

Of the seven horses that had another septic synovial structure in addition to septic digital tenosynovitis, five horses were successfully discharged (Table 5), with 57.1% (4/7) being able to return to their previous level of athletic function.

Univariable logistic regression analysis showed that the only variable that was associated with an increased risk of a horse being unable to return to its previous level of athletic function was the length of time between the onset of sepsis and treatment (Appendix 2.2).

Table 4: Long term follow up available in 72/79 cases (91.1%) discharged following treatment for septic digital tenosynovitis

	Number		%	95% CI
Returned to intended use	**39**		**54.2**	**42.6 to 65.7**
Returned to lower level of exercise	**3**		**4.2**	**0.0 to 8.9**
Retired to pasture with no attempt to return to exercise as elective decision by owner	**6**		**8.3**	**1.8 to 14.8**
Chronically lame	**18**		**25**	**15.0 to 35.0**
	14/18	Directly attributable to sepsis within digital sheath		
	4/18	Due to concurrent injuries		
Euthanased due to complications associated with occurrence of septic tenosynovitis	**6**		**8.3**	**1.8 to 14.8**

Table 5: 7/90 horses had sepsis of another synovial structure in addition to septic digital tenosynovitis

	Number		%	95% CI
Discharged from hospital	**5**		**71.4**	
Euthanased prior to discharge	**2**		**28.6**	**0.0 to 62.1**
	1	Under GA due to concurrent injuries		
	1	Due to failure to respond to treatment		
Long term follow up				
Retired to pasture with no attempt to return to exercise as elective decision by owner	**1**		**14.3**	**0.0 to 40.2**
Returned to intended use	**4**		**57.1**	**20.4 to 93.8**

A multivariable logistic regression model was constructed using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criterion for backward elimination was set at $p \leq 0.05$. The only variable found to be associated with an increased risk of a horse being unable to return to its previous

level of athletic function was the length of time between the onset of sepsis and treatment (Table 6).

Table 6: Multivariable logistic regression analysis of factors affecting likelihood of a horse returning to its' previous level of athletic function following treatment for septic digital tenosynovitis

	Coefficient	S.E.	OR	95% C.I.	p
Constant	0.47	0.29			0.099
Time between onset of sepsis and treatment, with <24hrs as referent value					
1-7 ds	-2.08	0.83	0.13	0.02 – 0.63	0.012

3.4.5. Comparison of outcomes for septic arthritis and septic digital tenosynovitis

Comparison of survival rates for those horses treated for septic arthritis and those horses treated for septic digital tenosynovitis showed that there was no statistically significant difference in the outcome for either of the two groups. However, when comparing the likelihood of a horse being able to return to its previous level of athletic function it was found that those horses treated for septic digital tenosynovitis were significantly less likely to achieve this level of athletic activity compared to those horses treated for septic arthritis (O.R.: 2.67; 95% C.I. 1.26 – 5.67; p=0.005).

3.5. Discussion of results

3.5.1. Class of evidence

Previous studies reported in the literature, investigating septic digital tenosynovitis, only included data from low numbers of cases (Honnas *et al.* 1991; Schneider *et al* 1992a; Chan *et al.* 2000; Frees *et al.* 2002), and have frequently focused on the efficacy of a specific treatment regimen (Chan *et al.* 2000; Frees *et al.* 2002). When considered in the context of evidence-based medicine, these studies have only provided class C evidence when using the classification system proposed by Yusuf *et al.* (1998). Whilst these studies contain a wealth of useful information, some of their conclusions must be viewed with caution due to inadequacies of the study design. By designing a study utilising a comparison population, it was hoped that the current study would provide findings in a higher class of evidence (class B) than those previously reported.

3.5.2. Comparison of survival rates

The purpose of this study was not to investigate the influence of a specific treatment regime on either the short or long term outcome for each case, but to ascertain whether the exact location of the inciting cause of sepsis, or the duration from onset of clinical signs to presentation at the hospital for treatment influenced either the short or long term outcome for the horse. One previous study reported that 100% of cases treated for septic digital tenosynovitis survived to be discharged from the hospital (Schneider *et al.* 1992a). Whilst the current study did not find such a high survival rate (87.8%; 95% CI 81.1 to 94.6), it is comparable to the survival rates of between 75% and 91% reported in other studies (Honnas *et al.* 1991; Chan *et al.* 2000; Frees *et al.* 2002).

3.5.3. Factors affecting short and long term prognosis

The numbers of male and female horses were evenly represented in the study population, as were the numbers of forelimbs and hindlimbs affected. Gender, the age of the horse at presentation and the limb affected were not found to have a significant influence on either the short or long term prognosis. A majority of the cases treated in the study period (64%) had sustained an injury at the level of the pastern, which had resulted in the development of septic digital tenosynovitis. Similarly, when investigating the duration from the onset of clinical signs to presentation at the hospital for treatment, the majority of cases (50.6%) were presented within 24 hours of onset of clinical signs. It may be expected that a longer duration from onset of clinical signs to initiation of treatment would reduce the likelihood of that horse either surviving to be discharged from the hospital or returning to its original level of athletic function, as prolonged exposure of the synovial structures to both bacteria and proteolytic enzymes will increase fibrin production and the likelihood of adhesion formation. Previous studies have not found a delay in treatment to influence significantly the eventual outcome for horses treated for septic digital tenosynovitis (Honnas *et al.* 1991; Chan *et al.* 2000), although they have suggested that prompt institution of aggressive treatment may improve the proportion of horses with a more favourable outcome. Our study agreed with those previously reported, finding that the time between onset of clinical

signs and the initiation of treatment did not affect the short term prognosis. However, our study found that a delay of between 1 and 7 days between the onset of sepsis and treatment would reduce the likelihood of a horse being able to return to its previous level of athletic function by almost eight times, when compared to a horse treated within 24 hours. Although a delay of greater than 7 days between the onset of sepsis and treatment was not found to influence the likelihood that a horse would return to its previous level of athletic function, the number of horses in this category was very low.

3.5.4. Study design and power

Although the current study failed to associate many of the variables investigated with the outcome, this does not necessarily mean that these variables do not influence either of the outcomes investigated. Despite the careful study design, and the power study performed at the outset, there may be a lack of power for some of the variables, in order to be able to show a statistically significant difference. For example, when investigating how the limb affected (forelimb or hindlimb) affects the long term prognosis, no significant association was found. However, at a significance level of 5%, this calculation only has a study power of 44%, therefore the power, and also the sample size, are inadequate to be able to detect a statistically significant difference.

3.5.5. Quantification of outcome

As the majority of the horses included in the study were used primarily for general riding purposes at the time of admission to the hospital, it is impossible to quantify their return to athletic activity in terms of either competitive winnings or number of events entered. Follow up information was therefore obtained by telephone questionnaire to the owners, as a successful outcome following treatment was viewed as whether the horse was able to fulfil the owner's long-term athletic expectations.

3.5.6. Study limitations

Despite the large number of horses in the study, the retrospective study design, coupled with the fact that many horses received more than one antimicrobial and lavage technique, limits any conclusions that could be drawn regarding the relative efficacy of specific treatment modalities. However, the aim of the study was not to compare the relative

success associated with one specific treatment, but to investigate the long-term prognosis of horses that had survived until discharge from the hospital, and to establish whether the occurrence of septic digital tenosynovitis would affect the likelihood of them returning to their previous level of athletic function. Studies adopting a prospective, controlled design are required in order to be able to draw any conclusions on the efficacy of specific treatment regimens.

In addition, the use of a telephone questionnaire to investigate the long term outcome for horses treated for digital sheath sepsis introduces bias. Inevitably, decay of memory will occur over time, and the ability for accurate recall of details must be questioned, in particular in those cases identified early in the study period, where owners were asked to recall events that had occurred upto ten years earlier. In addition, the ability for the owner to recall events accurately may not only be tempered by time, but also by the success of the outcome. Where a horse went on to return to its' previous level of athletic function, owners are less likely to recall negative events that may have occurred during recovery.

3.5.7. Comparison between septic arthritis and septic digital tenosynovitis

A comparison of results was made between the current study and a separate study conducted at the same practice investigating the long-term prognosis for horses treated for septic arthritis (Chapter 4). This comparison showed that whilst there was no difference in survival rates between those horses treated for septic arthritis and those treated for septic digital tenosynovitis, those horses treated for septic digital tenosynovitis were significantly less likely to return to their previous level of athletic function than those treated for septic arthritis. Although the findings on survival rates are comparable to a previous study (Schneider *et al.* 1992a), no study has compared the long-term prognosis for these two conditions. The difference in long-term prognosis may suggest that it is inappropriate to extrapolate data from the management of septic arthritis and apply it to septic digital tenosynovitis (Schneider *et al.* 1992a). Future research should recognise septic digital tenosynovitis as a separate condition, as neonatal septic arthritis has been, with research targeted accordingly.

3.5.7. Classification within the literature pool

This study has provided results from a higher class of evidence than that previously reported (Honnas, *et al.* 1991; Schneider, *et al*, 1992a; Chan *et al.* 2000; Frees *et al.* 2002), by providing class B evidence, using the classification system proposed by Yusuf, *et al* (1998). This research is from a practice population primarily consisting of general purpose riding horses and not high level competition horses, therefore the results are applicable to many different practice populations, where the majority of horses seen are not high level competition animals. The current study contradicts a previous study (Schneider *et al.* 1992a) by finding that there is a significant difference between the outcome for horses treated for septic arthritis and septic digital tenosynovitis, therefore data from one condition should not be extrapolated to the other. This study also gives general practitioners information on the likely short and long-term prognosis for a horse treated for septic digital tenosynovitis.

3.5.8. Conclusions

The prognosis for survival following early identification and treatment of septic digital tenosynovitis in this particular population of horses is fair. If the infection is successfully eliminated from the synovial space, then over 50% of those horses that were discharged returned to their previous level, or a higher level, of exercise. However, horses where a delay of greater than seven days occurred between the onset of sepsis and the initiation of treatment, had a significantly poorer prognosis for returning to their previous level of athletic function compared to those horses where treatment was initiated earlier.

Therefore, horses that require treatment for septic digital tenosynovitis can be given a fair prognosis for return to full athletic function. However, the prognosis for return to future soundness is not as good as that for horses treated for septic arthritis.

Chapter 4

What is the likelihood that a mature horse treated for septic arthritis will be able to return to its' previous level of athletic performance?

4.1. Introduction

Septic arthritis in adult horses is a serious clinical problem (Bertone *et al.* 1987a,b; Tulamo *et al.* 1989a; Schneider *et al.* 1992b; Cook & Bertone, 1998; Booth *et al.* 2001), with the first case series of monarticular septic arthritis in adult horses described in the veterinary literature by Van Pelt in 1971. The potential exists to cause permanent degenerative joint disease (Bertone *et al.* 1987b), irreversible cartilage damage, fibrosis and unsoundness when infection is not rapidly eliminated from the synovial space (Tulamo *et al.* 1989a; Schneider *et al.* 1992a,b; Tremaine, 2000). Historically, joint sepsis was most readily recognised as a sequel to septicaemia in foals (Rooney, 1962; Van Pelt & Riley 1969; Coffman, 1970) and was thought to be only an infrequent problem in older horses (Van Pelt, 1971) although it is now recognised as a more common occurrence (Morris *et al.* 1980; Madison *et al.* 1991; Schneider *et al.* 1992a). Initially the prognosis for horses treated for septic arthritis had been described as guarded to poor (Martens & Auer, 1980; McIlwraith, 1983; Bowman *et al.* 1991; Brusie *et al.* 1992; Lapointe *et al.* 1992). However, as more has become known about both the aetiology of the disease and the most efficacious treatment regimens the literature has carried reports of a more favourable prognosis (Schneider *et al.* 1992a; Bertone, 1999; Meijer *et al.* 2000). The main causes of treatment failure are the inability to eliminate the causative agent (Bertone *et al.* 1987a; Schneider *et al.* 1992a,b; Meijer *et al.* 2000) and to disrupt effectively the vicious cycle of articular cartilage destruction through inflammatory products (Orsini, 1984; Stover, 1990; Bertone, 1999).

4.2. The occurrence of septic arthritis

4.2.1. Aetiology and clinical signs of septic arthritis

Septic arthritis is caused by the inoculation of a synovial cavity with bacteria, with viable organisms readily becoming established. Normally, synovium is capable of eliminating a certain number of bacteria (Gustafson, McIlwraith & Jones, 1989a; Hardy, Bertone & Malemud, 1998; Tremaine, 2000), although these natural defences can be overcome if the bacterial load is overwhelming, the organism is highly pathogenic, and therefore able to adhere to the synovium and either bypass or compromise the natural defence mechanisms, or the synovium is compromised (Cook & Bertone, 1998; Tremaine, 2000). In adult horses septic arthritis commonly affects only a single joint (Cook & Bertone, 1998). There are three recognised routes by which bacteria may become established within a synovial cavity (McIlwraith, 1983):

1. Sepsis can be seen following a traumatic insult to the tissues overlying the joint, be it an apparently innocuous puncture wound or a larger laceration (Rose & Love, 1979; Madison *et al.* 1991, Schneider *et al.* 1992a; Tremaine, 2000);
2. following surgery involving a joint or joint injection, therefore of iatrogenic origin (Van Pelt, 1971; Leitch, 1979; Koch, 1979; McIlwraith, 1983; Martens *et al.* 1986; Schneider *et al.* 1992a; Tremaine, 2000);
3. more rarely in adults, it can be the result of haematogenous spread from an infectious focus elsewhere in the body (Martens *et al.* 1986; Schneider *et al.* 1992a).

Occasionally, the inciting cause of sepsis is never recognised. Acute severe lameness, synovial effusion, heat and pain on palpation of the joint, periarticular swelling, pyrexia, cellulitis and distal limb oedema are the most commonly reported clinical findings (Van Pelt, 1971; Rose & Love, 1979; McIlwraith, 1983; Bertone *et al.* 1987a.b; Gibson *et al.* 1989; Tulamo *et al.* 1989; Bowman *et al.* 1991; Peremans *et al.* 1991; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a; Cook & Bertone, 1998; Bertone, 1999; Meijer *et al.* 2000; Tremaine, 2000), although synovial effusion and lameness may not be as marked if the joint is open and draining (McIlwraith, 1983; Gibson *et al.* 1989; Honnas *et al.* 1992a).

4.2.2. Causative organisms of septic arthritis

4.2.2.1. Response of a synovial structure to bacteria

The response of a synovial structure to invasion by bacteria has been the subject of a large body of experimental research, and the sequence of events is well documented. Once bacteria have entered the joint, they localise in the synovial membrane and provoke a profound inflammatory reaction, with exudation of proteins and polymorphonuclear cells into the synovial cavity (Leitch, 1979; Bertone *et al.* 1987a; Cook & Bertone, 1998; Tremaine, 2000). Release of cellular enzymes, plasmin and prostaglandins leads to depletion of proteoglycans from the cartilage matrix within a matter of days (Leitch, 1979; McIlwraith, 1983; Bertone *et al.* 1987a; Peremans *et al.* 1991; Cook & Bertone, 1998; Tremaine, 2000), alteration in cartilage pliability, and subsequent collagen breakdown from increased vulnerability to mechanical forces (McIlwraith, 1983; Bertone *et al.* 1987a; Peremans *et al.* 1991; Tremaine, 2000). The nutritional capacity of the synovial fluid is diminished due to the inflammatory changes occurring, and interference with the synovial fluid-cartilage interface occurs due to exudates, pannus or granulation tissue, resulting in further articular cartilage destruction (Leitch, 1979; Martens & Auer, 1980; McIlwraith, 1983; Peremans *et al.* 1991; Tremaine, 2000). These changes within the synovial cavity are reflected in the gross appearance of synovial fluid. Following the onset of sepsis synovial fluid typically becomes grossly turbid, watery and discoloured (Van Pelt, 1971; Rose & Love, 1979; Gibson *et al.* 1989; Tulamo *et al.* 1989; Peremans *et al.* 1991; Lapointe *et al.* 1992; Bertone, 1999; Tremaine, 2000). Laboratory analysis yields an increased total protein concentration, increasing with time from onset of sepsis, due to synovial inflammation resulting in an increase in synovial permeability (Van Pelt, 1971; Gibson *et al.* 1989; Tulamo *et al.* 1989; Peremans *et al.* 1991; Schneider *et al.* 1992a; Bertone, 1999; Tremaine, 2000). A significant increase in the total white blood cell count within the synovial fluid, increasing with time from onset of sepsis, is also seen, with a profound neutrophilia consistent with the onset of clinical signs (Van Pelt, 1971; Rose & Love, 1979; Gibson *et al.* 1989; Tulamo *et al.* 1989; Peremans *et al.* 1991; Lapointe *et al.* 1992; Schneider *et al.* 1992a; Bertone, 1999; Tremaine, 2000). Degeneration of the neutrophils is an infrequent finding (Van Pelt, 1971; Koch, 1979; Tulamo *et al.* 1989; Bertone, 1999). Synovial fluid pH, normally close in value to blood pH (Tulamo *et al.* 1989) will rapidly become acidic following the onset of joint sepsis (Tulamo *et al.* 1989; Peremans *et al.* 1991).

4.2.2.2. Culture and identification of causative organisms

It has been widely reported in the literature that bacterial culture from cases of suspected septic arthritis is unrewarding (Van Pelt & Riley, 1969; Van Pelt, 1971; Koch, 1979; McIlwraith, 1983; Madison *et al.* 1991; Peremans *et al.* 1991), particularly in adult horses (Schneider *et al.* 1992a). Historically, culture was attempted on samples of synovial fluid, but a number of factors exist that may have prevented a positive culture. Synovial fluid is itself bactericidal in action, prior administration of antimicrobials will impede bacterial growth in culture (Koch, 1979; Martens *et al.* 1980; McIlwraith, 1983), and most importantly, when considering the action of bacteria within a joint, the site of multiplication is within the synovium rather than the synovial fluid (Martens & Auer, 1980). However, although it would appear logical that synovial membrane biopsy and culture would give an increased bacterial isolation rate (McIlwraith, 1983; Martens *et al.* 1986; Madison *et al.* 1991), this has frequently proved not to be the case. Studies in which culture of synovial membrane has been performed found either an identical isolation rate for synovial fluid and membrane (Bertone *et al.* 1987a), or a significantly lower isolation rate from synovial membrane compared to the results of isolation of organisms from synovial fluid (Madison *et al.* 1991; Ross *et al.* 1991). None of the studies investigated why culturing organisms from the synovial membrane was less successful than expected. One study (Bertone *et al.* 1987a) suggested that this may have been due to the enrichment broth used as a transport medium for synovial fluid, inhibiting the antimicrobial activity of the systemic antimicrobials used, and also the complement and lysozyme activity, thereby achieving a higher isolation rate of organisms. Alternatively, the site from which the biopsy was taken may be the cause of the poor culture results. Biopsy samples may contain only some of the joint capsule (Madison *et al.* 1991), or the sample may not have been taken at a site where bacteria are sequestered and multiplying.

When bacteria have been successfully cultured from joints in which sepsis is suspected, a mixed growth of bacteria is typically found in joints in which sepsis is due to a traumatic incident (Gibson *et al.* 1989; Madison *et al.* 1991; Schneider *et al.* 1992a). However, in joints where sepsis has occurred following joint injection or surgery, *Staphylococcus aureus* is the most common bacterial isolate (Koch, 1979; McIlwraith, 1983; Schneider *et al.* 1992a). Studies using an experimental model of septic arthritis have commonly used

Staphylococcus aureus as their bacterium of choice to induce sepsis (Bertone *et al.* 1987a,b; Tulamo, Bramlage & Gabel, 1989a; Gustafson *et al.* 1989a,b), despite the fact that this may restrict the wider application of their results to the general population. Joints act in a very individual way when responding to inoculation of bacteria, with factors such as type, number and virulence of the organism (McIlwraith, 1983; Cook & Bertone, 1998), as well as the local and general resistance of the host playing important roles (Leitch, 1979; McIlwraith, 1983; Gustafson *et al.* 1989a; Schneider *et al.* 1992a). The exact anatomical joint infected also has an effect on the likely outcome (Peremans *et al.* 1991; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a). Where surgical access to a joint is poor (Honnas *et al.* 1992a,b; Booth *et al.* 2001), or the anatomical structure of a joint is complex (Peremans *et al.* 1991), it may prohibit thorough lavage and removal of all bacteria and inflammatory products. To this end, it is important to study naturally occurring joint sepsis, as well as experimentally induced sepsis, in a large population of horses in order to evaluate treatment (McIlwraith, 1983; Schneider *et al.* 1992a).

The effect of different 'doses' of bacteria has been reported in only one study, in which small numbers of joints were inoculated (Gustafson *et al.* 1989a). Results showed that, at a specified dose of bacterial inoculum (between 10^2 and 7×10^2), only four out of five horses developed septic arthritis, supporting the theory of the individuality of the response by a joint to infection. Similarly, at a lower dose of bacterial inoculum ($<10^2$ organisms), all joints showed clinical signs consistent with joint sepsis (heat in joint, joint effusion, oedema and lameness), although these signs had resolved without therapy within forty-eight hours. It has also been documented that traumatic septic arthritis is typically due to a mixed growth of bacteria, although *Enterobacteriaceae* are the most common isolate within this group (Schneider *et al.* 1992a) when culture of an organism is possible. It is unknown whether equine joints inoculated with these bacteria respond differently to both sepsis and the different treatment modalities suggested, when compared to those joints with a pure growth of *Staphylococcus aureus*, as has been found in human septic arthritis (Lapointe *et al.* 1992). It is known that the quantity of bacteria inoculated into joints, along with the virulence of the organism, can have a profound effect on the response of the joint to sepsis (Leitch, 1979; McIlwraith, 1983; Cook & Bertone, 1998), as it has been shown that the reaction of synovial tissue in an infected joint appears to be proportional to the extent to which the causative organism can multiply (Ropes & Bauer, 1953).

4.2.3. Treatment options for septic arthritis

Successful resolution of septic arthritis involves treatment with broad-spectrum antimicrobials and joint drainage (Ross *et al.* 1991; Moore *et al.* 1992; Meijer *et al.* 2000), although controversy exists over the most efficacious form of drainage. There are many proposed treatment regimens for the successful resolution of septic arthritis, including: synovial fluid aspiration (Van Pelt & Riley, 1969), through-and-through lavage (Koch, 1979; Leitch, 1979; Morris, 1980; McIlwraith, 1983; Martens *et al.* 1986; Bertone *et al.* 1987a,b; Peremans *et al.* 1991; Schneider *et al.* 1992a,b), systemic antimicrobials (Van Pelt, 1969; Koch, 1979; Leitch, 1979; Morris, 1980; Martens *et al.* 1986; Bertone *et al.* 1987a,b; Peremans *et al.* 1991; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a,b), intra-articular antimicrobials, including continuous drug delivery systems (Stover & Pool, 1985; Lloyd *et al.* 1990; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a,b; Holcombe *et al.* 1997; Cook *et al.* 1999; Lescun *et al.* 2000; Adams & Lescun, 2000; Summerhays, 2000; Booth *et al.* 2001), arthroscopy (Koch, 1979; Morris, 1980; Ross *et al.* 1991; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a,b), arthrotomy (Leitch, 1979; Morris, 1980; Martens *et al.* 1986; Bertone *et al.* 1992; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a,b), synovectomy (Leitch, 1979; Martens *et al.* 1986; Bertone *et al.* 1992), intra-articular drains (Leitch, 1979; Martens *et al.* 1986; Ross *et al.* 1991), regional perfusion with antimicrobials (Whitehair *et al.* 1992; McClure *et al.* 1993; Murphey *et al.* 1999; Butt *et al.* 2001; Scheuch *et al.* 2001), and non-steroidal anti-inflammatory drugs (Koch, 1979; Leitch, 1979; Morris, 1980; McIlwraith, 1983; Martens *et al.* 1986; Bertone *et al.* 1987a,b; Honnas *et al*, 1992a; Schneider *et al.* 1992a,b; Meijer *et al.* 2000).

4.2.3.1. Medical Therapy

4.2.3.1.1. Historical treatment options

The first suggestions for treatment of septic arthritis in adult horses were based on sound scientific principles. Lameness is initially caused due to massive joint distension, therefore aspiration of the synovial fluid would not only relieve the local pressure build up within the joint, but also reduce the bacterial load within that joint (Van Pelt & Riley, 1969; Van Pelt, 1971). Culture of the aspirated fluid was attempted, although no bacteria were isolated (Van Pelt, 1971). Injection of an antimicrobial directly into the affected joint was performed after aspiration of the synovial fluid, with a broad-spectrum antimicrobial

advocated (Van Pelt, 1971). In some cases, this antimicrobial was in combination with a steroid, and in some cases this therapy was combined with systemic administration of antimicrobials (Van Pelt & Riley, 1969; Van Pelt, 1971). The majority of horses in these studies were reported to have a satisfactory outcome following treatment.

4.2.3.1.2. Systemic antimicrobials

Administration of broad-spectrum, systemic antimicrobials is recognised as an important treatment for septic arthritis (Leitch, 1979; Bertone *et* al. 1987a; Gibson *et al.* 1989; Peremans *et al.* 1991; Ross *et al.* 1991; Honnas *et al.* 1992a; Moore *et al.* 1992; Schneider *et al.* 1992a; Bertone, 1999; Tremaine, 2000). Treatment should ideally be started once an initial synovial fluid sample has been obtained, because even if the antimicrobial is ineffective against the bacterium within the joint, it may still interfere with successful culture of that organism (Peremans *et al.* 1991). However, antimicrobial therapy should be initiated immediately after synovial fluid aspiration, without waiting for culture results (McIlwraith, 1983; Gibson *et al.* 1989; Peremans *et al.* 1991; Meijer *et al.* 2000; Tremaine, 2000).

Antimicrobials have been shown to relieve systemic signs associated with joint sepsis, such as pain and pyrexia, (Bertone *et al.* 1987a; Bertone, 1999; Tremaine, 2000) and will diffuse into the synovial space (Bertone *et al.* 1992; Cook *et al.* 1999; Errecalde *et al.* 2001), although their trough concentrations may be below the minimum inhibitory concentration (MIC) for most isolates (Bertone *et al.* 1992; Cook *et al.* 1999), especially in the face of ongoing sepsis lowering the pH. The intravenous route of administration is recommended at the onset of treatment (Bertone, 1999) in order to achieve therapeutic blood and tissue concentrations rapidly, with penicillin in combination with an aminoglycoside (Ross *et al.* 1991; Moore *et al.* 1992; Schneider *et al.* 1992a), or a third-generation cephalosporin (Schneider *et al.* 1992a), being the most common antimicrobials used (Bertone, 1999).

Early experimental work investigated the efficacy of trimethoprim-sulphadiazine combinations in the treatment of *Staphylococcus aureus* induced septic arthritis (Bertone *et al.* 1987a; Bertone *et al.* 1988). These studies found that, at the manufacturers recommended oral daily dose rate, concentrations of trimethoprim or sulphadiazine were not effectively maintained above the MIC for *S. aureus* in the infected synovial fluid, nor

in the serum in the case of trimethoprim. However, doubling the recommended daily dose rate was effective in maintaining serum and synovial concentrations in excess of the MIC for the infective organism, resulting in a significant decrease in the isolation rate of *S. aureus* by the termination of the study (Bertone *et al.* 1987a; Bertone *et al.* 1988).

Although administration of systemic antimicrobials with no lavage of the joint (Bertone *et al.* 1987a) was found to be effective in reducing the bacterial load within the joint in an experimental study, further studies looking at naturally occurring sepsis found conflicting evidence (Gibson *et al.* 1989), with an unfavourable outcome resulting when antimicrobials alone were used to treat septic arthritis. An oral trimethoprim/sulfa combination was used as the treatment of choice in the treatment of both iatrogenic and traumatic septic arthritis (Meijer *et al.* 2000), in combination with through-and-through joint lavage, with 81% of cases resulting in the resolution of sepsis. Antimicrobials were only changed if indicated by bacterial culture and sensitivity, although in the majority of cases the infective organism isolated was found to be sensitive to the trimethoprim/sulfa combination. Although use of a trimethoprim/sulfa combination as a first choice antimicrobial in the treatment of septic arthritis has proved successful (Meijer *et al.* 2000), its narrow spectrum of action against many common pathogenic organisms may limit its use in the face of mixed bacterial infections (Moore *et al.* 1992).

A study investigating the antimicrobial susceptibility of bacterial isolates from 233 horses with musculoskeletal infections (Moore *et al.* 1992) found that *Enterobacteriaceae* were the most common isolate (28.8%), with only 38.5% of these isolates being sensitive to trimethoprim/sulfa, and coagulase-positive staphylococci only comprised 11.8% of isolates. Amikacin proved to be the most efficacious antimicrobial, providing broad-spectrum coverage, especially when in combination with a penicillin, although the cost of amikacin precludes its use as the routine drug of choice. This study (Moore *et al.* 1992) advocated the use of broad-spectrum antimicrobials in the management of orthopaedic infections pending culture results, citing a penicillin/aminoglycoside combination as being both an effective, and affordable choice, switching only to an oral antimicrobial such as trimethoprim/sulfa if indicated by culture and sensitivity. Other studies (Schneider *et al.* 1992a), whilst starting with broad-spectrum intravenous antimicrobials (normally a penicillin/aminoglycoside combination) have switched to oral trimethoprim/sulfa combinations following culture and sensitivity results. All recent studies advocate the use of systemic antimicrobials in the treatment of septic arthritis (McIlwraith, 1983; Gibson *et*

al. 1991; Peremans *et al.* 1991; Honnas *et al.* 1992a; Schneider *et al.* 1992a; Meijer *et al.* 2000), with the initial selection of drug based on the source of infection and the suspected organism (Moore *et al.* 1992), until culture and sensitivity results dictate otherwise.

4.2.3.1.3. Regional limb perfusion

Regional limb perfusion has been shown to be effective in delivering antimicrobials under pressure to a selected region of the limb through the venous system (Whitehair *et al.* 1992; Murphey *et al*, 1999; Butt *et al.* 2001; Scheuch *et al.* 2002). In an experimentally induced septic arthritis, the mean concentration of gentamicin present in the synovial fluid was significantly higher than following intravenous administration (Whitehair *et al.* 1992). Results showed that regional perfusion with gentamicin was successful in sufficiently decreasing the number of micro-organisms present so as to prevent culture of *S. aureus* (Whitehair *et al.* 1992). Studies have also investigated intra-osseous perfusion of antimicrobials (Butt *et al.* 2001; Scheuch *et al.* 2002). Whilst this route of administration also achieved high concentrations of antimicrobial within the target joint, the concentrations were not as high as those achieved using the intravenous route (Butt *et al.* 2001; Scheuch *et al.* 2002).

4.2.3.1.4. Intra-articular use of antimicrobials

In order to achieve intra-articular antimicrobial concentrations above the MIC for the suspected organism, intra-articular administration of antimicrobials is also possible. Although initially thought to be contra-indicated due to the chemical synovitis it would produce, (Koch 1979; Leitch, 1979; McIlwraith, 1983), more recent studies have shown that the beneficial effects of intra-articular administration of appropriate antimicrobials are greater than any possible detrimental effects (Stover & Pool, 1985; Lloyd *et al.* 1990; Schneider & Bramlage, 1991; Mills *et al.* 2000). Intra-articular administration of aminoglycosides and third generation cephalosporins has also been shown to provide higher concentrations of antimicrobial within the synovia, maintaining therapeutic concentrations for a longer period of time, compared with intravenous administration of antimicrobial (Lloyd *et al.* 1990; Mills *et al.* 2000). Stover & Pool (1985) demonstrated that it could not be the acidic nature of the antimicrobial inducing the characteristic synovitis seen, with a greater inflammatory response seen following the intra-articular

injection of saline (pH 4.5-7.0) when compared to intra-articular injection of gentamicin (pH 3.2). Intra-articular administration of antimicrobials has been included in the treatment strategy of many studies investigating septic arthritis in horses (McClure *et al.* 1993). Although it is possible to achieve these sustained high concentrations of antimicrobials within a joint by daily injection (Cook *et al.* 1999), the act of introducing a needle into a joint not only increases the risk of introducing infectious organisms (Cook *et al.* 1999), but it has also been shown to induce a synovitis (Cook *et al.* 1999). Alternative drug delivery methods have been investigated (Holcombe *et al.* 1997; Cook *et al.* 1999; Ethell *et al.* 2000; Lescun *et al.* 2000; Summerhays, 2000), including the use of flow-control tubing and balloon infusers (Adams & Lescun, 2000; Lescun *et al.* 2000), to provide a continuous infusion of antimicrobial into the joint. Balloon infusers were filled with gentamicin, with flow control tubing running from the infuser to an infusion catheter within the tibio-tarsal joint (Adams & Lescun, 2000; Lescun *et al.* 2000). Results indicated that use of an infusion system would be an effective way of maintaining a high concentration of gentamicin within a joint for a prolonged period of time (Adams & Lescun, 2000; Lescun *et al.* 2000). Although 29% of infusion catheters developed complications these were resolved by replacement of either the catheter or the balloon infuser, with an air lock of the flow control tubing being the most likely complication. Further work showed that a continuous infusion of gentamicin into tibio-tarsal joints for a period of five days did not cause significant synovial inflammation or articular cartilage damage, with any changes seen improving over a further nine day period (Lescun *et al.* 2002). Antimicrobial-impregnated polymethyl methacrylate (PMMA) and antimicrobial-impregnated hydroxyapatite cement (HAC) has been shown to be effective in providing sustained high concentrations of antimicrobials locally when used in human patients, whilst maintaining low serum concentrations, thereby limiting the potential for toxic side effects (Butson *et al.* 1996; Tobias *et al.* 1996; Holcombe *et al.* 1997; Cook *et al.* 1999; Booth *et al.* 2001; Farnsworth *et al.* 2001). Many different antimicrobials have been shown to be suitable for combination with both PMMA and HAC in the treatment of orthopaedic infections (Holcombe *et al.* 1997; Bertone, 1999; Ethell *et al.* 2000), with HAC exhibiting a better elution rate and duration of action than PMMA (Ethell *et al.* 2000), and where excessive cost may prohibit systemic administration of an antimicrobial for prolonged periods, use of an impregnated implant provides a feasible alternative (Holcombe *et al.* 1997; Ethell *et al.* 2000). The limitation to the use of PMMA beads in the treatment of septic arthritis may be that they are non-absorbable and removal of the beads is suggested (Summerhays, 2000; Farnsworth *et al.* 2001), although it can be

difficult to determine when these implants should be removed. If beads were left within the joint in a freely exercising horse, they could contribute to synovial inflammation and cartilage erosion (Summerhays, 2000; Farnsworth *et al.* 2001). Experimental studies have focused on the use of biodegradable drug delivery systems (BDDS) which, whilst providing the benefits of sustained high local concentrations of antimicrobials with low risk of toxic side effects, would not have the disadvantage of requiring removal at a later date (Cook *et al.* 1999). Collagen sponges were also proposed as a suitable biodegradable implant for use in septic arthritis (Summerhays, 2000), providing similar benefits to BDDS.

4.2.3.1.5. Non-steroidal anti-inflammatory drugs

The judicious use of non-steroidal anti-inflammatory drugs has been advocated in many studies on septic arthritis (Leitch, 1979; Rose & Love, 1979; Peremans *et al.* 1991; Ross *et al.* 1991; Schneider *et al.* 1992a; Meijer *et al.* 2000). Whilst they are unable, by themselves, to resolve the infection (Bertone *et al.* 1987a) they are important in both their analgesic and anti-inflammatory roles (Peremans *et al.* 1991; Ross *et al.* 1991; Honnas *et al.* 1992a; Schneider *et al.* 1992a), although over use may mask signs of ongoing sepsis within the joint (McIlwraith, 1983; Bertone, 1999).

4.2.3.2. Surgical therapy

4.2.3.2.1. Joint lavage

Distension-irrigation and through-and-through lavage were later considered as alternatives to simple aspiration of the synovial fluid, as dilution of both the bacteria and the accompanying white cells (which produce lysosomal enzymes) were thought to be an important consideration (Rose & Love, 1979; Bertone *et al.* 1987a,b; Leitch, 1979; Schneider *et al.* 1992a,b; Meijer *et al.* 2000). Bertone *et al.* (1987a,b; 1992) performed experimental studies inoculating *Staphylococcus aureus* into the joint in order to induce sepsis, to investigate the effect of different treatment modalities.

The first study compared the efficacy of administration of systemic antimicrobials with either joint lavage, intra-articular and systemic antimicrobials, or joint lavage, arthrotomy, intra-articular and systemic antimicrobials. There was also a control group (four joints) that received analgesia only following inoculation of bacteria. The conclusions drawn were that when no treatment was given, horses were euthanased on humane grounds (pain non-responsive to analgesia) within seven days. Using a high dose (double the manufacturer's recommended dose) of systemic antimicrobials significantly reduced the rate of isolation of *Staphylococcus aureus* from the joint at the termination of the study, although no clinical benefits from using arthrotomy, as opposed to through-and-through joint lavage alone, were apparent. This study was both randomised and controlled, thereby classifying it as providing class A evidence when using the classification system proposed by Yusuf *et al* (1998), although there was no blinding in the study design. However, the numbers in each of the study groups were very low, with only two horses (four joints) in each group. The suitability of the control group could also be questioned. The control horses were only treated with oral non-steroidal anti-inflammatory drugs, which, if used by itself, is not an appropriate treatment for septic arthritis.

The second study compared two different lavage solutions for their efficacy in resolving sepsis, with the horse acting as a self-control (the two tibio-tarsal joints in a horse were allocated, one to each treatment group). All horses in the study also received systemic antimicrobial therapy and analgesia. Synovial membrane and articular cartilage samples collected at necropsy were analysed histologically for evidence of synovitis and articular cartilage damage. Results indicated that there was no significant difference in the response of the joint between using a neutral-pH, isotonic-balanced electrolyte solution compared to a dilute, 0.1% povidone/iodine solution as lavage solutions. A high proportion of both synovial fluid and synovial membrane samples remained culture positive for *Staphylococcus aureus* at the termination of the study. This study was in fact a sub-group of the previous study (Bertone *et al.* 1987a). Similarly, as it is both randomised and controlled, it is classified as class A evidence. However, as in the previous study the numbers in each of the study groups were low, with only two horses per group.

The third study (Bertone *et al.* 1992) investigated the efficacy of arthrotomy versus arthroscopy and partial synovectomy for the treatment of experimentally induced infectious arthritis. All horses in the study received systemic antimicrobial therapy and analgesia. Synovial membrane and articular cartilage samples were collected at necropsy

for histologic and histochemical evaluation. Results indicated that arthrotomy eliminated the experimentally induced infection faster than arthroscopy and synovectomy, although both treatments had eliminated infection from all but a single joint by the termination of the study. Again, this study could be classified as class A evidence, as joints were randomly assigned to each treatment group. As each horse had one tibio-tarsal joint in each group, the horses acted as self-controls. However, although the numbers in each study group are slightly higher than previously reported studies (Bertone *et al.* 1987 a,b), the numbers are still low with only four horses in each study group.

All three of these studies did not find the results from the treatment under investigation (arthrotomy; povidone/iodine lavage solution; arthroscopy and synovectomy) significantly different from the standard treatment regime used as a comparison. However, a difference in outcome that is not found to be statistically significant does not necessarily indicate that different treatment regimes are equivalent. The case numbers in each of the study groups were very low, therefore the studies may have lacked sufficient power to achieve statistical significance. If these studies were repeated with a much larger sample size, the outcome may be different. An additional consideration is that these three studies utilised an experimental septic arthritis model, induced by the inoculation of *S. aureus* into the tibio-tarsal joint. Any extrapolation of results from this study to a practice population should be viewed with caution, as a number of important factors (causative organism, bacterial load, virulence of organism, joint affected, degree of tissue trauma and bacterial contamination) will differ between the study and practice populations.

The other studies were uncontrolled case series (class C evidence), utilising through-and-through joint lavage as part of a combination of therapies (Gibson *et al.* 1991; Ross *et al.* 1991; Peremans *et al.* 1991; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a,b; Meijer *et al.* 2000). All concluded that thorough lavage of the joint was vital for the successful resolution of synovial sepsis.

Whilst many studies have used polyionic solutions, or lactated ringers solution, when lavaging a septic joint, alternatives have been used (Bertone *et al.* 1987b; Gibson *et al.* 1991; Peremans *et al.* 1991; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a,b). The addition of povidone/iodine to the lavage solution (Bertone *et al.* 1987b; Gibson *et al.* 1991; Peremans *et al.* 1991; Ross *et al.* 1991; Schneider *et al.* 1992a) was found to have no beneficial effect in reducing the bacterial load when compared to neutral-pH, isotonic-

balanced electrolyte solutions (Bertone *et al.* 1987b; Gibson *et al.* 1991), although there was less fibrin found in the joint following treatment with povidone/iodine (Bertone *et al.* 1987b). Other additives used have included dimethyl-sulfoxide (DMSO), thought to be beneficial through its potent analgesic and anti-inflammatory actions (Honnas *et al.* 1992a,b; Bertone, 1999) and antimicrobials (Ross *et al.* 1991; Schneider *et al.* 1992a). No conclusions were drawn as to whether these solutions were more beneficial than using a polyionic solution alone, although it was suggested that incorporating DMSO into the lavage solution may have contributed to the successful outcome of those horses in which it was used (Honnas *et al.* 1992a).

4.2.3.2.2. Arthroscopy and arthrotomy

Although simple through-and-through lavage may be effective in many cases in the treatment of septic arthritis, the needles can rapidly become occluded if fibrin is present within the joint (Meijer *et al.* 2000). Arthroscopy is felt to be superior to lavage in this way, as it not only allows good visualisation of the articular surfaces and other synovial structures, but also allows removal of fibrin and debridement of any infected areas (Ross *et al.* 1991; Bertone *et al.* 1992; Honnas *et al.* 1992a; Schneider *et al.* 1992a,b; Bertone, 1999; Meijer *et al.* 2000; Tremaine, 2000). Synovectomy, to decrease the bacterial load and remove excess inflammatory cells sequestered in the synovium, can also be performed at this time (Ross *et al.* 1991; Bertone *et al.* 1992; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a,b; Bertone, 1999; Meijer *et al.* 2000; Tremaine, 2000).

Arthrotomy has been found to be superior to arthroscopic lavage, as it allows continuous drainage of fluid from the joint, decreasing the bacterial load faster (Bertone *et al.* 1992; Honnas *et al.* 1992a; Bertone, 1999) and preventing the discomfort associated with joint distension (Gibson *et al.* 1991; Bertone *et al.* 1992; Honnas *et al.* 1992a; Lapointe *et al.* 1992 Schneider *et al.* 1992b; Bertone, 1999). In some instances of open joint injury, distension of the joint for arthroscopic evaluation is not possible, leaving arthrotomy as a suitable alternative (Honnas *et al.* 1992a). Although it would appear to be a beneficial treatment, studies showed that there was a delayed healing time of the arthrotomy incisions (Bertone *et al.* 1987a; Bertone *et al.* 1992; Lapointe *et al.* 1992; Schneider *et al.* 1992b; Bertone, 1999), predisposing them to the formation of exuberant granulation tissue, and increasing the risk of ascending infection entering the joint (Bertone *et al.* 1987a; Bertone *et al.* 1992; Honnas *et al.* 1992a). Synovectomy can also be performed through an

arthrotomy incision (Leitch, 1979; Schneider *et al* 1992b) although this will not allow such wide access to the joint compared with arthroscopy (Meijer *et al.* 2000)

Although arthrotomy allows passive, open drainage of the joint to occur, closed-suction drainage has also been used for continuous removal of excess synovial fluid, bacteria and inflammatory products from the joint (Leitch, 1979; Ross *et al.* 1991; Honnas *et al.* 1992a; Lapointe *et al.* 1992). Continuous decompression of the joint increases the comfort of the horse, and precludes the need for repeated general anaesthesia to lavage the joint (Ross *et al.* 1991; Honnas *et al.* 1992a)

4.2.4. Outcome

The prognosis for a successful return to athletic function has been variously described from guarded or poor (Martens & Auer, 1980; McIlwraith, 1983; Gibson *et al.* 1989; Bowman *et al.* 1991; Brusie *et al.* 1992; Lapointe *et al.* 1992) to favourable, or even good (Ross *et al.* 1991; Schneider *et al.* 1992a,b; Bertone, 1999; Meijer *et al.* 2000; Summerhays, 2000; Booth *et al.* 2001). It has been shown that time between onset of sepsis and initiation of therapy (Gibson *et al.* 1989; Peremans *et al.* 1991; Honnas *et al.* 1992a), and the joint infected (Peremans *et al.* 1991; Booth *et al.* 2000) are both influential when considering the likely outcome. Whilst it is widely accepted that systemic antimicrobial therapy and joint drainage are necessary for the successful resolution of septic arthritis, many different treatment regimens exist, and no study has critically evaluated these treatments to see if one offers advantages over the others. The majority of studies are retrospective case series utilising multiple treatment regimens, rendering it difficult to draw definitive conclusions regarding the best method of treatment (Gibson *et al.* 1989; Schneider *et al.* 1992a).

4.3. Study aims

The purpose of this study was to evaluate critically data from two centres over the last ten years, in order to investigate factors associated with survival and return to previous level of athletic function following septic arthritis. An additional aim of this study was to evaluate appropriate prognostic cut-off values for diagnostic tests in relation to these outcomes.

4.4. Materials and methods

4.4.1. Data retrieval

The admission records for Bell Equine Veterinary Clinic and Rossdales Equine Hospital between 1992 and 2002 were reviewed to identify horses that had been admitted for investigation of suspected septic arthritis, and medical records were then retrieved. In order to be eligible for inclusion in the study horses had to be at least six months old at the time of admission to the hospital. In cases in which septic arthritis was suspected on the basis of clinical signs, diagnosis was confirmed on the result of synoviocentesis of the affected joint, where an increased nucleated cell count (upper end of normal reference limit for laboratory: 3×10^9 cells/l) in conjunction with an increased total protein concentration (upper end of normal reference limit: 15g/l) and the presence of a neutrophilia (>90%) with degenerative polymorphonuclear cells on cytological analysis were considered to be diagnostic.

Information retrieved from the medical records included age, sex, breed and athletic use of the horse at the time of admission; number and location of affected joints; the suspected route of infection; evidence of any radiographic abnormalities at the time of admission; time from onset of clinical signs to presentation at the clinic for treatment; the white cell count of the synovial fluid at the time of admission to the hospital; results of bacterial culture of the synovial fluid; details of antimicrobial therapy and lavage procedures performed and whether the horse was discharged from the hospital following treatment. The outcomes of interest were whether the horse survived to be discharged from the hospital, and whether the horse returned to its' previous, or higher, level of performance.

4.4.2. Data Analysis

Variables that were statistically evaluated included age and sex; specific joint infected and suspected route of infection; duration of sepsis prior to treatment; synovial white cell count at the time of admission and whether there was any evidence of radiographic abnormalities at time of admission. Categorical variables with more than two levels were coded as indicator variables.

Outcomes that were statistically evaluated for each variable included discharge from the hospital and whether the horse eventually returned to its previous level, or a higher level, of performance. Outcome was determined by evaluation of medical records to determine whether the horses were successfully discharged from the hospital. Long term follow up was then obtained by means of a questionnaire administered to owners by telephone (Appendix 3). The purpose of the questionnaire was to establish the level of athletic performance the horse had achieved prior to the occurrence of septic arthritis and whether, in the owner's opinion, the horse had been able to return to this level of performance after discharge from the hospital. If the owner did not consider the horse to have successfully returned to its previous level of performance, it was established whether this was directly attributable to the occurrence of septic arthritis, or whether there were other factors that had contributed to the eventual outcome.

Binary logistic regression was used to analyse these data, as both outcomes of interest were dichotomous. Two binary logistic regression models were developed using these data. Analyses were implemented with the statistical software MINITAB (version 13.31).

Univariable logistic regression was used to screen all variables, and from this all variables with a p-value ≤ 0.20 were included in a backward elimination process to fit a multivariable model. The inclusion criterion for backward elimination was set at $p \leq 0.05$. The goodness-of-fit of the models was assessed using the Hosmer-Lemeshow goodness-of-fit test, to test the null hypothesis that the model was considered to be a good fit, with the null hypothesis rejected at a p-value ≤ 0.05.

Once the main effects model had been fitted, two-way interaction between variables was assessed. Variable selection was determined by biological plausibility. Assessment between models was obtained using a likelihood ratio test (LRT) with significance set at $p \leq 0.05$.

A Receiver Operating Characteristic (ROC) curve allows for the evaluation of an appropriate cut-off value for a diagnostic test, in order for the test to be a worthwhile prognostic indicator. This is done by plotting the sensitivity of a test versus the false positive rate calculated at a number of different cut-points, in order to select the optimum cut-point for distinguishing between those animals with positive and negative outcomes. The closer the ROC curve is to the top left hand corner of the graph, the better the ability

of the test to discriminate between those animals with a positive and negative outcome. A Two-graph Receiver Operating Characteristic (TG-ROC) curve allows the simultaneous evaluation of how both the sensitivity and specificity of a test vary as the cut-point is changed. Non-parametric TG-ROC curves were generated to investigate the sensitivity and specificity of the nucleated white blood cell count of the synovial fluid at the time of admission as a predictor for each outcome of interest, using each observed value of the white blood cell count following synovial fluid analysis as a cut-point.

4.5. Results

4.5.1. Descriptive statistics

Three hundred and twenty horses met the criteria for inclusion in the study. One hundred and seventy eight horses were male and one hundred and forty-one were female, with the sex not recorded in one case. The age at the time of admission was recorded in 314 cases, with the age ranging from 6 months old to 30 years old, and the median age was 7 years old (inter-quartile range 4 – 11 years old) at the time of admission. The athletic use at the time of admission was recorded in all cases, with 103 horses (32.2%) considered to be performing at a high athletic level (racing, polo, international eventing, dressage and showjumping), 209 horses (65.3%) were general purpose riding horses, and eight (2.5%) were used exclusively for breeding.

Nine of the 320 horses (2.8%; 95% C.I. 1.3 to 5.3; $p<0.001$) had more than one synovial structure affected at the time of admission (Table 7). The joint involved was recorded in 317 cases, with the most commonly affected joint being the tibio-tarsal joint (Table 7). The inciting cause of sepsis was recorded in 298 cases (93.1%); the vast majority of horses developing septic arthritis subsequent to a traumatic event (Table 7), and only 1 horse developed septic arthritis subsequent to haematogenous spread of organisms from an infectious focus elsewhere in the body. Results of the cytological analyses of the synovial fluid collected at the time of admission were available in 170 cases (53.1%). Nucleated cell counts on admission (range: 3.9×10^9 cells/l to 285.0×10^9 cells/l; median: 52.0×10^9 cells/l; inter-quartile range: 21.15×10^9 cells/l to 102.25×10^9 cells/l) exceeded the reference limit (3.0×10^9 cells/l) in all cases.

The time between onset of clinical signs and presentation at the hospital for treatment was recorded in 310 cases (96.9%), with more than 60% of cases being presented at the hospital for treatment within 24 hours of the event perceived to have incited sepsis (Table 7). Radiographs of the affected joint were taken in 298 cases (93.1%) at the time of admission, with abnormalities evident in 58 cases (19.5%; 95% C.I. 15.1 to 24.4; $p < 0.001$). Synovial fluid was submitted for bacterial culture and sensitivity prior to the administration of any systemic antimicrobials in 121 cases (37.8%), with 75 samples (62%; 95% C.I. 52.7 to 70.7; p=0.011) yielding no growth and, of the remaining samples, the most common isolate was a pure growth of *Staphylococcus aureus* (20 cases; 16.5%; 95% C.I. 10.4 to 24.4; $p < 0.001$).

Table 7: Classification of joint affected, inciting cause of sepsis and time between onset of sepsis and initiation of treatment in horses treated for septic arthritis.

	Number	%
>1 synovial structure affected	9/320	2.8
Joint involved recorded	317/320	99.1
Tibio-tarsal joint	98/317	30.9
Metatarsophalangeal joint	63/317	19.9
Carpus	49/317	15.5
Metacarpophalangeal joint	31/317	9.8
Femoropatellar joint +/- femorotibial joint	22/317	6.9
Proximal inter-phalangeal joint	15/317	4.7
Elbow	14/317	4.4
Distal inter-phalangeal joint	13/317	4.1
Navicular bursa	9/317	2.8
Distal inter-phalangeal joint and navicular bursa	5/317	1.6
Inciting cause of sepsis recorded	298/320	93.1
Trauma	279/298	93.6
Joint injection or surgery	18/298	6
Haematogenous spread	1/298	0.3
Time between onset of sepsis and treatment	310/320	96.9
<24 hours	202/310	65.2
1-7 days	51/310	16.5
>7 days	57/310	18.4

4.5.2. Treatment options

Although all horses were treated with broad-spectrum systemic antimicrobials and joint lavage, there was no standardised treatment protocol. The initial joint lavage was performed under general anaesthesia in 282 cases (88.1%), with the remaining horses being treated with a standing, through-and-through needle lavage under heavy sedation for the intial lavage. Affected joints were usually lavaged on alternate days until a clinical improvement was seen, with lavage being performed between one and eleven times (median = 1.00 lavage; inter-quartile range: 1 – 2 lavages). Of the 320 horses, 201 (62.8%; 95% C.I. 57.3 to 68.1; $p < 0.001$) had only one lavage, along with a course of parenteral antimicrobials, with no other treatment necessary to eliminate the infection from the affected joint. Other procedures performed included arthroscopy (119, 37.2%; 95% C.I. 31.5 to 42.7; $p<0.001$); standing lavage after insertion of a fenestrated drainage tube during lavage under general anaesthesia (55, 17.2%; 95% C.I. 13.2 to 21.8; $p<0.001$); insertion of an indwelling, continuous antimicrobial infusion system; and insertion of antimicrobial impregnated, poly-methyl methacrylate beads, with some horses receiving a combination of treatments. Standard practice was to review the antimicrobial regimen if antimicrobial sensitivity indicated that the organisms cultured were resistant to the initial antimicrobial choice; or if there was a failure to respond to treatment. Horses were discharged from the hospital when the clinical signs of infection had resolved, although all horses were still receiving systemic antimicrobials at the time of discharge.

4.5.3. Factors affecting survival

Of the 320 horses admitted to the hospitals for evaluation and treatment of septic arthritis, 274 (85.6%) were successfully discharged from the hospitals. Of the 46 horses euthanased, six (8.7%) were euthanased whilst under general anaesthesia due to a hopeless prognosis for recovery; two (4.3%) were euthanased during hospitalisation due to financial constraints; two (4.3%) were euthanased during hospitalisation due to concurrent medical problems (development of weight-bearing laminitis in the contralateral limb in one case and subluxation of the affected joint in one case); with the remaining 36 cases (78.3%) being euthanased during treatment due to non-resolution of sepsis.

The synovial white cell count at the time of admission, age of the horse at the time of admission, specific joint affected, presence of radiographic changes in the affected joint at the time of admission, route of infection, duration from onset of sepsis to commencement of treatment, duration of hospitalisation and number of lavages performed during hospitalisation were all investigated for their influence on both the short and long-term outcome. Univariable binary logistic regression analysis showed that those variables that were associated with an increased risk of a horse failing to survive to discharge were time from onset of sepsis to admission to the hospital for treatment; the presence of radiographic abnormalities at the time of admission; age of the horse at the time of admission; and the specific joint involved (Table 8). Those variables found not to be associated with an increased risk of a horse failing to survive to be discharged from the hospital included: results of cytological analysis of synovial fluid at time of admission; duration of hospitalisation; and number of lavages performed (Appendix 4.1).

Table 8: Variables found to be associated with a decreased likelihood of survival to discharge following treatment for septic arthritis.

	Coefficient	S.E.	OR	95% CI	P
Presence of radiographic abnormalities	-1.20	0.35	0.30	0.15 – 0.60	0.001
Duration between onset of sepsis and treatment (referent <24hrs)					
>7ds	-1.61	0.37	0.20	0.10 – 0.41	<0.001
Age (referent <8yrs)					
8-15 yrs	-0.84	0.35	0.43	0.22 – 0.85	0.016
Specific joint affected (referent metatarso-phalangeal joint)					
Stifle	-2.47	0.86	0.08	0.02 – 0.46	0.004
Distal inter-phalangeal joint	-2.64	0.94	0.07	0.01 – 0.45	0.005
Distal inter-phalangeal joint and navicular bursa	-3.05	1.16	0.05	0.00 – 0.46	0.009
Navicular bursa	-3.23	0.98	0.04	0.01 – 0.27	0.001
Elbow	-2.53	0.93	0.08	0.01 – 0.49	0.006
Proximal inter-phalangeal joint	-3.04	0.89	0.05	0.01 – 0.27	0.001

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criterion for backward elimination was set at $p \leq 0.05$. Those variables found to be associated with an increased risk of a horse failing to survive to discharge at the multivariable level were the presence of radiographic abnormalities at the time of admission; involvement of the stifle,

distal inter-phalangeal joint, distal inter-phalangeal joint with concurrent involvement of the navicular bursa, navicular bursa, proximal inter-phalangeal joint or elbow, and sepsis in the affected joint for more than seven days prior to the initiation of treatment (Table 9).

Table 9: Variables found to be associated with a decreased likelihood of survival to be discharged from the hospital at the multivariable level, following treatment for septic arthritis.

	Coefficient	S.E.	OR	95% CI	P
Constant	4.28	0.80			<0.001
Presence of radiographic abnormalities	-2.49	0.60	0.08	0.03 – 0.27	<0.001
Duration between onset of sepsis and treatment (referent <24hrs)					
>7ds	-2.13	0.53	0.12	0.04 – 0.34	<0.001
Specific joint affected (referent metatarso-phalangeal joint)					
Stifle	-1.89	0.92	0.15	0.02 – 0.92	0.040
Distal inter-phalangeal joint	-2.58	1.02	0.08	0.01 – 0.56	0.012
Distal inter-phalangeal joint and navicular bursa	-2.89	1.29	0.06	0.00 – 0.69	0.025
Navicular bursa	-3.25	1.08	0.04	0.00 – 0.32	0.003
Elbow	-2.24	1.01	0.11	0.01 – 0.78	0.027
Proximal inter-phalangeal joint	-3.02	0.97	0.05	0.01 – 0.33	0.002
Interaction terms of significance					
Radiographic abnormalities * Duration 1-7ds	1.21	1.15	3.36	0.35 – 31.93	0.291
Radiographic abnormalities * Duration >7ds	2.95	0.89	19.01	3.32 – 108.85	0.001

The only two-way interaction term that was found to be significant in the final model was an interaction between the presence of radiographic abnormalities and the time delay between the onset of sepsis and the commencement of treatment (Table 9). The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit, with insufficient evidence to reject the null hypothesis at $p > 0.05$.

4.5.4. Factors affecting long-term outcome

Long-term follow up was available in 72% (197/274) cases that survived to be discharged from the hospital. Of these 197 cases, 128 (65%) were able to return to their intended use as performance horses. A further 17 cases (8.6%) would have been capable of returning to

their intended use, although they were retired to pasture with no attempt to return to exercise as an elective decision of their owners. Thirty-six horses (18.3%) were too lame to return to ridden work, but were comfortably retired to pasture, with the remaining 16 cases (8.1%) euthanased after discharge from the hospital due to complications directly associated with the occurrence of septic arthritis.

Univariable logistic regression analysis showed that the only variable that was found to be associated with an increased risk of a horse being unable to return to the level of athletic function attained prior to the onset of sepsis was the presence of radiographic abnormalities in the affected joint at the time of admission (Table 10). Other variables investigated were not found to be associated with the long-term outcome for horses treated for septic arthritis (Appendix 4.2).

Table 10: Those variables found to be associated with a decreased likelihood of a horse being able to return to its' previous level of athletic function following treatment for septic arthritis.

	Coefficient	S.E.	OR	95% CI	P
Presence of radiographic abnormalities	-1.20	0.43	0.30	0.13 – 0.70	0.005

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criterion for backward elimination was set at $p \leq 0.05$. Those variables found to be associated with an increased risk of a horse being unable to return to its previous level of athletic function at the multivariable level were the presence of radiographic abnormalities in the joint at the time of admission and the duration of hospitalisation (Table 11).

No two-way interaction terms were found to be significant. The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit, with insufficient evidence to reject the null hypothesis at $p > 0.05$.

Table 11: Variables found to be associated with a decreased likelihood of a horse being able to return to its previous level of athletic function, at the multivariable level, following treatment for septic arthritis.

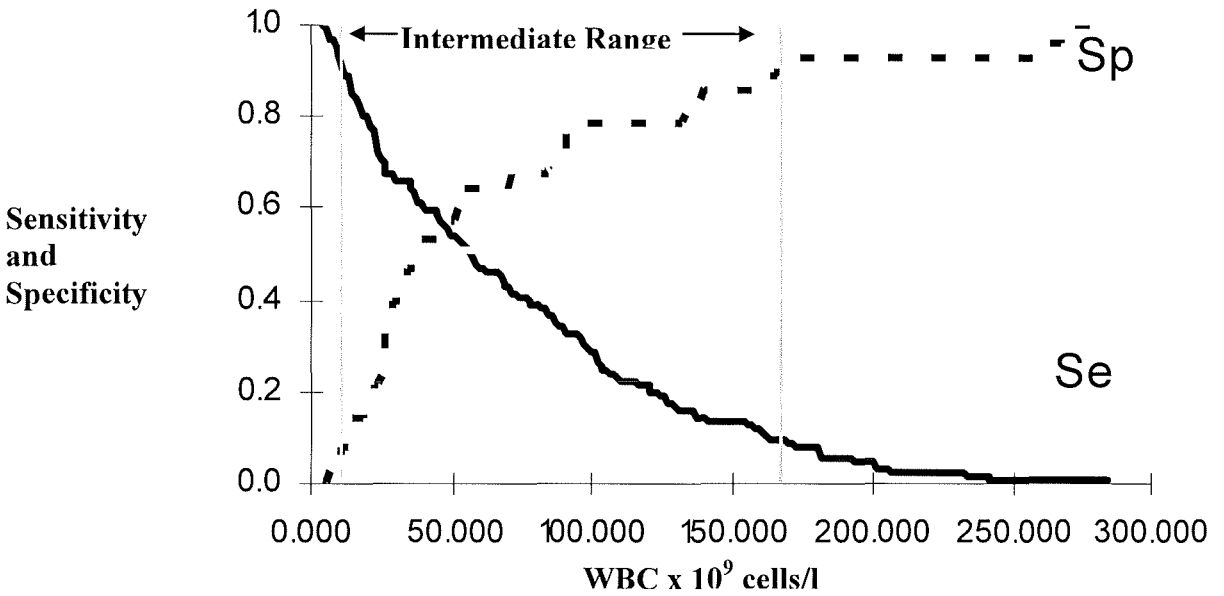
	Coefficient	S.E.	OR	95% CI	p
Constant	0.46	0.37			0.213
Radiographic abnormalities at the time of admission	-1.29	0.46	0.27	0.11 – 0.67	0.005
Duration of hospitalisation (referent <5 ds)					
5-9 ds	1.13	0.51	3.11	1.14 – 8.44	0.026

4.5.5. Two-graph receiver operating characteristic (TG-ROC) analysis

4.5.5.1. TG-ROC analysis for survival

A two graph-receiver operating characteristic (TG-ROC) curve was generated to investigate the sensitivity and specificity of the nucleated white blood cell count of the synovial fluid at admission as a predictor for whether or not the horse would survive to be discharged from the hospital (Figure 1). At a cut-point of 46.91 x 10^9 cells/l, the sensitivity and specificity are both 0.57. Any change in the cut-point to increase the sensitivity of the test, would result in a large decrease in the specificity, with the opposite also being true. The intermediate range (IR) – 10.00 to 167.00 x 10^9 cells/l – indicates the range of values where the sensitivity and specificity are both below 0.95. For example, changing the cut-point to 20.95 x 10^9 cells/l would increase the sensitivity to 0.8, however a concurrent drop in the specificity to 0.2 is also seen, therefore whilst being able to identify those horses likely to survive to be discharged with some accuracy, there will also be a large number of horses identified as likely to survive that would not be discharged successfully. The white blood cell count of the synovial fluid at the time of admission, therefore, is a poor predictor of whether the horse will survive to be discharged from the hospital.

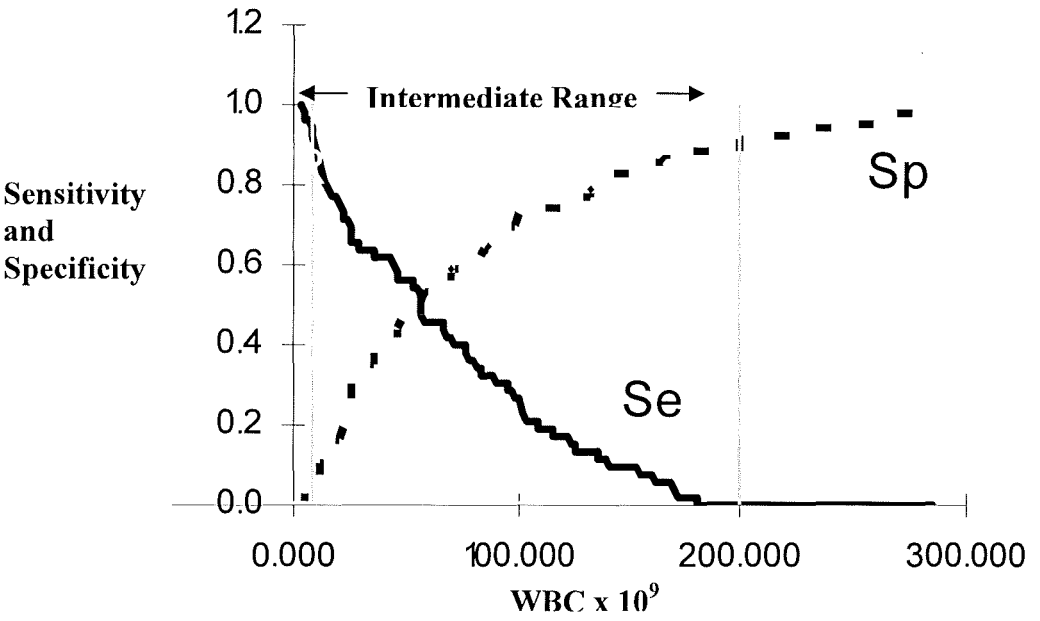
Figure 1: Two graph receiver operating characteristic curve (TG-ROC) showing Sensitivity (Se) and Specificity (Sp) the nucleated white blood cell count (WBC) of synovial fluid, as a predictor for survival to discharge.



4.5.5.2. TG-ROC analysis for long-term outcome

An additional TG-ROC curve was generated to investigate whether the white blood cell count of the synovial fluid at the time of admission may be a useful predictor of whether a horse may be able to return to its original level of athletic function following treatment for septic arthritis (Figure 2). At a cut-point of 55.94 x 10^9 cells/l, the sensitivity and specificity are both 0.51. Any change in the cut-point to increase the sensitivity of the test would result in a substantial decrease in the specificity, with the opposite also being true. The intermediate range (IR) – 9.20 – 200.00 x 10^9 cells/l – indicates the range of values where the sensitivity and specificity are both below 0.90.

Figure 2: Two graph receiver operating characteristic curve (TG-ROC) showing Sensitivity (Se) and Specificity (Sp) the nucleated white blood cell count (WBC) of synovial fluid, as a predictor for return to original level of athletic function.



4.6. Discussion

4.6.1. Class of evidence

Whilst many retrospective studies investigating the treatment of septic arthritis exist in the literature, there is little information on the long-term prognosis for return to athletic function in general riding horses, although some information exists for Thoroughbred racehorses (Schneider, *et al*, 1992) and Standardbred racehorses (LaPointe *et al.* 1992). No previous studies have performed a multivariable analysis to identify factors affecting either the short or long-term prognosis, allowing consideration of all the variables of interest simultaneously, and taking into consideration how these variables may affect one another.

Many of the earlier studies investigating septic arthritis (Schneider *et al.* 1992; LaPointe *et al.* 1992) were retrospective case series, therefore they would constitute class C evidence

using the classification system proposed by Yusuf *et al* (1998). However, some studies of a higher class of evidence do exist. Studies using an experimental model of septic arthritis could be classified as providing class A evidence (Bertone, *et al.* 1987a,b; Bertone *et al.* 1988; Bertone *et al.* 1992; Brusie *et al.* 1992; Whitehair *et al.* 1992; Cook *et al.* 1999), although they lack the placebo control and blinding necessary to fulfil all the criteria for this classification. However, these studies have commonly used *S. aureus* as their bacterium of choice to induce sepsis, thereby restricting the wider application of their results to the general population, where a mixed growth of organisms is typically found in septic joints.

4.6.2. Study limitations

Despite the large number of horses in the study, the retrospective study design and the fact that many horses received more than one antimicrobial and lavage technique, preclude any conclusions being drawn regarding the relative efficacy of specific treatment modalities. However, the aim of the study was not to compare the relative success associated with one specific treatment, but to look at the long-term prognosis of horses that had survived until discharge from the hospital. Studies adopting a controlled, prospective design would be required to investigate the efficacy of specific treatment regimens. Similarly, attempts to examine the effects of the specific joint involved, number of joints and existence of concurrent pathology on survival and long-term prognosis should be viewed with caution, as this study relies on the retrospective analysis of medical records.

In addition, the use of a telephone questionnaire introduces bias. Not only have you the bias associated with long-term memory recall (3.5.6), but there are also losses to follow up. These are inevitable, as people move house, change phone number or prove to be impossible to contact despite numerous attempts. It is unknown how significant an effect these losses to follow-up may have had on the overall interpretation of results.

4.6.3. Short-term prognosis

Survival rates reported here (85.6%) are similar to those reported in previous studies (LaPointe *et al.* 1992; Schneider *et al.* 1992a; Meijer *et al.* 2000). As the majority of horses included in this study were used primarily for general riding purposes at the time of admission to the hospital, it is impossible to quantify their return to athletic activity in

terms of either competitive winnings or number of events entered. Follow up information was therefore obtained by telephone questionnaire to the owners, as a successful outcome following treatment was viewed as whether the horse was able to fulfil the owner's long-term athletic expectations.

4.6.4. Factors affecting the outcome

The most commonly affected joint in our study was the tibio-tarsal joint – a finding that concurs with previous studies (Schneider *et al.* 1992a; Meijer *et al.* 2000) in which a higher incidence of involvement of the larger joints was reported. The statistically significant findings that were associated with the joint involved included: involvement of the stifle, proximal inter-phalangeal joint, elbow, distal inter-phalangeal joint or navicular bursa decreasing the likelihood of the horse surviving to be discharged from the hospital. These findings are similar to previously reported findings, where joints that were small, with limited surgical access, or of a complex nature, were associated with a poorer prognosis for survival (Peremans *et al.* 1991; Honnas *et al.* 1992a,b; Booth *et al.* 2001). Similarly, the current study concurred with a previous study (Peremans *et al.* 1991) in that a significant delay before the onset of treatment (7 days in this study) was associated with a poorer prognosis for survival to be discharged from the hospital. It may be expected that a longer duration from onset of clinical signs to initiation of treatment would reduce the likelihood of that horse either surviving to be discharged from the hospital or returning to its original level of athletic function, as prolonged exposure of the articular structure to both bacteria and proteolytic enzymes would be expected to deplete the proteoglycans from the cartilage matrix, leading to collagen breakdown. However this finding has only been sparsely reported (Peremans, *et al.* 1991), although many other studies have suggested that prompt institution of aggressive treatment may improve the proportion of horses with a more favourable outcome.

At the univariable level the age of the horse was also found to be associated with the risk of that horse surviving to be discharged from the hospital in the current study – a finding that has not been previously reported. However, age was not found to be a significant factor in the multivariable model. Horses less than eight years of age that were treated for septic arthritis were found to be significantly more likely to be discharged from the hospital than those aged between eight and fifteen years of age. If the age rose above fifteen years this was not found to influence the likelihood of survival to discharge,

although the low number of horses in this category (27/320; 8.4%) may have led to inadequate power to achieve statistical significance. The age of the horse may be expected to have a significant influence on both the short and long-term prognosis for horses treated for septic arthritis. Older horses would have been more likely to have degenerative changes within the joint, with associated inflammation of the synovium. Synovial inflammation can compromise the natural defence mechanisms within the synovial cavity, with synovial proliferation allowing the sequestration of bacteria within the membrane.

It may be expected that those horses requiring a greater number of surgical lavages to resolve the synovial sepsis would have a poorer prognosis both for survival and return to their original level of athletic function, because the articular structure would be exposed to bacteria and phagocytic enzymes for a prolonged period of time. However, this finding has not been reported in previous studies. The current study did not find that the number of surgical lavages performed had an adverse effect on either the likelihood of the horse surviving to be discharged from the hospital or returning to its previous level of athletic function. The vast majority of horses (62.8%) in this study only required one surgical lavage to eliminate the infection from the joint, with low numbers requiring more than one lavage. Therefore it may be that there were inadequate numbers to prove statistical significance as opposed to this being an unimportant factor.

The current study found that those horses that were hospitalised for between 5 and 9 days were more likely to return to their original level of athletic function than those discharged sooner. This finding is in direct contrast to what might be expected, as horses that required only one lavage were routinely discharged within 5 days, therefore you might expect these horses to have the best prognosis for return to athletic function. Those horses that remained in the hospital for more than 5 days did so either because they required more than one lavage to eliminate the sepsis, or the wound had not sealed and still communicated freely with the joint.

The presence of radiographic abnormalities within a joint (chip fractures, articular fractures, osteomyelitis) will initiate a profound inflammatory response, with degenerative joint disease subsequently developing, regardless of the concurrent presence of sepsis. It could, therefore, be expected that the presence of radiographic abnormalities detected within the affected joint at the time of admission would be associated with a poorer prognosis for future soundness. No previous study has investigated whether this could be a

significant factor in whether a horse is able to return to athletic activity following treatment for septic arthritis. In the current study this was found to be a significant factor both in terms of whether the horse survived to be discharged form the hospital, and whether those that were discharged were able to return to their original level of athletic function.

A significant interaction was found to exist between the presence of radiographic abnormalities and the time duration between the inciting cause of sepsis and the onset of treatment, when considering the likelihood of a horse surviving to be discharged from the hospital.

4.6.5. TG-ROC analysis

A wide variation was seen in the white blood cell count of the synovial fluid at the time of admission, and this study concurred with a previous study (Peremans *et al.* 1991) in finding that the white cell count alone was a poor predictor of both the short and long-term prognosis for any horse treated for septic arthritis. If the results of the synovial fluid analysis were used as the sole basis on which to recommend whether treatment for septic arthritis should be attempted, then the diagnostic test should have a good predictive ability, and therefore have a high sensitivity. An additional consideration in the treatment of septic arthritis is the high cost involved, not only for the initial treatment but also in the subsequent rehabilitation. Where economics can be an important issue, a test with a high specificity would also be needed in order to avoid needlessly wasting money on a case that has a poor prognosis. Although the white blood cell count of the synovial fluid at the time of admission does not appear to be a useful discriminatory test, when taken on its own, with regard to either of the outcomes of interest for this study, it is not superseded by any other single diagnostic test. To this end the result must be considered in conjunction with other contributing factors before a conclusion on either the short or long-term prognosis can be reached.

4.6.6. Classification in the literature pool

As an uncontrolled case series, the current study would also be classified as providing class C evidence. However, the large case numbers in this study, in conjunction with the more advanced methods of statistical analysis used, render it a valid addition to the current literature pool.

Earlier studies that reported the long-term prognosis for horses treated for septic arthritis focused on specific study groups: either Thoroughbred or Standardbred racehorses (LaPointe *et al.* 1992; Schneider *et al.* 1992); or horses that received a specific treatment regimen (Summerhays, 2000; Booth *et al.* 2001). The current study reported both the short and long-term prognosis for horses from a study population where the vast majority of horses were general purpose riding horses (209/320; 65.3%), and a variety of different treatment regimes were used. When considering the population of horses on which this study was performed, the results could be more widely extrapolated to other practice populations where the vast majority of horses are pleasure horses, when compared to previous studies that have a much more specific study population (LaPointe *et al.* 1992; Schneider *et al.* 1992a).

4.6.7. The benefits of multivariable analysis

The multivariable logistic regression analysis used in the current study showed that some factors identified as significant following univariable analysis were in fact not significant in the final model. Similarly, it also identified factors that were not considered significant after univariable analysis, that were in fact significant in the final model. In addition, the use of multivariable analysis highlighted the interaction that exists between some of the factors – a finding which would not have been identified if only univariable analysis was performed. The identification of interaction terms is important when considering the final model, as it shows how the effect on the final outcome exerted by one variable may also be dependent on another variable.

4.6.8. Conclusion

The prognosis for survival following early identification and treatment of septic arthritis in this particular population of horses was good, with 85.6% (95% C.I. 81.3 – 89.3) of horses surviving to be discharged form the hospital. If infection was eliminated from the synovial space then 65% (95% C.I. 57.9 – 71.6) of horses successfully discharged returned to their original level, or a higher level, of exercise. Therefore, horses that require treatment for septic arthritis can be given a fair prognosis for return to full athletic function. However, if there is a delay in treatment of more than seven days, evidence of radiographic abnormalities in the affected joint, or involvement of the stifle, distal inter-phalangeal

joint, proximal inter-phalangeal joint, elbow or the navicular bursa, then a more guarded prognosis should be given.

Chapter 5

What is the likelihood that Thoroughbreds treated for septic arthritis will race?

5.1 Introduction

Septic arthritis, in both mature horses and neonates, is recognised as a serious clinical problem (Bertone *et al.* 1987a,b; Tulamo *et al.* 1989; Schneider *et al.* 1992b; Cook and Bertone, 1998; Booth *et al.* 2001). The potential exists to cause permanent degenerative joint disease, irreversible cartilage damage, fibrosis and unsoundness if the infection is not rapidly eliminated from the synovial space (Van Pelt & Riley, 1969; Martens & Auer, 1980; McIlwraith, 1983; Martens *et al.* 1986; Stoneham, 1997; Waterhouse & Marr, 1997; Steel *et al.* 1999).

5.2. What is the likelihood that Thoroughbred foals treated for septic arthritis will race?

5.2.1. Introduction

Septic arthritis in foals, also referred to as joint-ill, was first described in the veterinary literature by Rooney in 1962, with reports estimating that between 1-5% of foals may be affected (Martens & Auer, 1980). In the neonate, the presentation is often complicated by underlying pathology (Martens & Auer, 1980; Schneider *et al.* 1992a): septic arthritis has been frequently described as a common sequel to neonatal septicaemia or failure of passive transfer of immunity, with haematogenous spread of organisms (Rooney, 1962; Van Pelt & Riley, 1969; Platt, 1973; 1977; Martens & Auer, 1980; McIlwraith, 1983; McClure, 1981; Carter & Martens, 1986; Martens *et al* 1986; Stoneham, 1997; Hance, 1998; Steel *et al.* 1999; Meijer *et al.* 2000; Tremaine, 2000; White, 2002), although it can develop from haematogenous spread with no other signs of systemic disease (Martens & Auer, 1980; Carter & Martens, 1986). It has been described as part of the septic arthritis/osteomyelitis syndrome (Martens & Auer, 1980; Firth *et al.* 1985; Martens *et al.* 1986; Steel *et al.* 1999; Meijer *et al.* 2000), also associated with neonatal septicaemia. Although less common, it can occur following trauma to the joint, or be of iatrogenic origin, subsequent to joint

injection or surgery (Van Pelt & Riley, 1969). The clinical signs associated with septic arthritis in foals depend on the presence of any underlying pathology. If the joint sepsis is of traumatic or iatrogenic origin, or from haematogenous spread without concurrent systemic signs of disease, then the most commonly reported clinical signs are (Martens & Auer, 1980; Firth, 1983; McIlwraith, 1983; Hance, 1988; Schneider *et al.* 1992a):

1. pyrexia,
2. joint effusion,
3. oedema over the joint,
4. heat and pain on palpation of the joint,
5. either lameness in the affected limb or a reluctance to move.

If there is an underlying septicaemia with resultant seeding out of bacteria into the joint then foals are more likely to present as dull, depressed and recumbent, with septic arthritis an incidental finding (Martens & Auer, 1980; McIlwraith, 1983; Carter & Martens, 1986; Martens *et al.* 1986; Stoneham, 1997). It is common for more than one joint to be involved (Van Pelt & Riley, 1969; Platt, 1973; Martens & Auer, 1980; McIlwraith, 1983; Carter & Martens, 1986; Schneider *et al.* 1992a; Steel *et al.* 1999; Meijer *et al.* 2000). The prognosis for recovery from septic arthritis in foals has widely been described as poor or unfavourable (Platt, 1977; Martens & Auer, 1980; Firth, 1983; Martens *et al.* 1986; Brewer & Koterba, 1990; Schneider *et al.* 1992a; Hance *et al.* 1993; Zamos *et al.* 1993; Raisis *et al.* 1996; Steel *et al.* 1999; Meijer *et al.* 2000), although this is often due to complications attributed to underlying disease (Firth, 1983; Brewer & Koterba, 1990; Schneider *et al.* 1992a; Steel *et al.* 1999; Meijer *et al.* 2000), as opposed to failure to resolve the joint sepsis (Steel *et al.* 1999; Meijer *et al.* 2000).

5.2.2. Aetiology of disease

5.2.2.1. Failure of passive transfer in foals

Total or partial failure of passive transfer of immunity has been recognised as a predisposing factor in the development of a variety of infectious conditions in neonates (Martens & Auer, 1980; McClure, 1981; Firth, 1983; Brewer & Mair, 1988; Robinson *et al.* 1993; Raidal, 1996; Hance, 1998; Steel *et al.* 1999). Colostral antibody temporarily protects foals until the immune system is able to respond adequately to challenge by environmental pathogens (Jeffcott, 1974; Platt, 1977; Koterba *et al.* 1984; Carter &

Martens, 1986; Brewer & Mair, 1988; Clabough *et al.* 1991; LeBlanc *et al.* 1992; Robinson *et al.* 1993; Stoneham, 1997; Meijer *et al.* 2000). Failure of passive transfer occurs when either the foal fails to ingest sufficient colostrum (Jeffcott, 1974; McGuire *et al.* 1975; Koterba *et al.* 1984; Jeffcott, 1985; Brewer & Mair, 1988; Clabough *et al.* 1991), the foal ingests colostrum but fails to absorb the antibodies (Jeffcott, 1974; McGuire *et al.* 1975; Jeffcott, 1985; Brewer & Mair, 1988; Clabough *et al.* 1991) or there are insufficient antibodies present in the colostrum, either through pre-partum loss of colostrum or poor quality of colostrum (Jeffcott, 1974; McGuire *et al.* 1975; Koterba *et al.* 1984; Brewer & Mair, 1988; LeBlanc *et al.* 1992). If recognised early, failure of passive transfer of immunity can be readily treated by administration of colostrum or transfusion of plasma (McGuire *et al.* 1975; Firth, 1983), although it is unknown what quantity of serum immunoglobulins should be considered sufficient, thereby not requiring supplementation (Brewer & Mair, 1988; Baldwin *et al.* 1989; Baldwin *et al.* 1991; Raidal, 1996).

The necessity for supplementation is itself a contentious issue (Brewer & Mair, 1988; Baldwin *et al.* 1989; Baldwin *et al.* 1991; Koterba, 1991; Hoffman *et al.* 1992; Raidal, 1996) as, although total or partial failure of passive transfer predisposes the foal to development of infection, it is not absolute that a foal with failure of passive transfer will subsequently develop an infection (Brewer & Mair, 1988; Baldwin *et al.* 1989; Baldwin *et al.* 1991; Hoffman *et al.* 1992). Studies have been done that show that many foals with apparently low concentrations of serum immunoglobulins remain healthy (Baldwin *et al.* 1989; Baldwin *et al.* 1991; Koterba, 1991), therefore it is thought that other factors must act in conjunction with a low serum immunoglobulin concentration to induce septicaemia (Martens & Auer, 1980; Firth, 1983; Baldwin *et al.* 1989; Baldwin *et al.* 1991; Koterba, 1991).

Many infections are caused by the opportunistic invasion of organisms that are ubiquitous in the environment of the newborn foal (Platt, 1973; Schneider *et al.* 1992a). The causative organisms usually gain entrance via the placenta, respiratory and digestive tracts or umbilicus (McIlwraith, 1983; Martens & Auer, 1980; Martens *et al.* 1986; Meijer *et al.* 2000; Kettner *et al.* 2003). Although infection of the umbilicus has been described as the most likely cause of haematogenous infection in the neonate (Firth, 1983; McIlwraith, 1983) its role in the development of septic arthritis is now thought to be overstated (Hance, 1998), as many foals will have a normal umbilicus on ultrasound evaluation, in the face of ongoing sepsis. Regardless of the initial route of entry of the infectious organism,

septicaemia will develop rapidly, spreading to involve multiple organs (Van Pelt & Riley, 1969; Platt, 1973; Firth, 1983). Apart from the clinical signs seen associated with septic shock, pathology will often be found in either one or more of the respiratory tract, gastro-intestinal tract, umbilicus, bones and joints (Van Pelt & Riley, 1969; Platt, 1973; Martens & Auer, 1980; Firth, 1983; Raisis *et al.* 1996). Once a concurrent infectious process develops the prognosis for survival becomes poor (Raisis *et al.* 1996; Steel *et al.* 1999; Meijer *et al.* 2000).

5.2.2.2. Aetiology of septic arthritis

The vascular system in the bones and joints of foals predisposes them to seed out bacteria (McIlwraith, 1983; Martens *et al.* 1986; Hance, 1998; Meijer *et al.* 2000; Kettner *et al.* 2003). The blood flow in the immature bone has a metaphyseal vascular loop immediately prior to the transphyseal vessel, which has low blood flow, allowing bacteria to settle out and potentially colonise. The transphyseal vessels disseminate bacteria to the physis, epiphysis and synovial membrane (Martens *et al.* 1986; Hance, 1998; Kettner *et al.* 2003). In addition there are extensive capillary tufts in the synovia that are thought to entrap micro organisms, allowing the subsequent colonisation of bacteria (McIlwraith, 1983).

Septic arthritis is caused by the inoculation of a synovial cavity with bacteria, with viable organisms readily becoming established. Normally, synovium is capable of eliminating a certain number of bacteria (Gustafson, McIlwraith & Jones, 1989; Hardy, Bertone & Malemud, 1998; Tremaine, 2000), although these natural defences can be overcome if:

1. the bacterial load is overwhelming,
2. the organism is highly pathogenic and therefore able to adhere to the synovium and either bypass or compromise the natural defence mechanisms,
3. the synovium is compromised (Cook & Bertone, 1998; Tremaine, 2000).

It has been suggested that the configuration of the capillary tufts in the synovial membrane favour entrapment of microorganisms (McIlwraith, 1983; Hance, 1998; Kettner *et al.* 2003), thereby predisposing septicaemic foals to develop concurrent septic arthritis.

5.2.2.3. Septic arthritis/osteomyelitis syndrome

One survey revealed that more than 75% of foals diagnosed with septic arthritis also had a clinically diagnosed, concomitant osteomyelitis (Martens & Auer, 1980), although later studies reported lower numbers of between 33-52% of foals treated for septic arthritis having concomitant osteomyelitis (Schneider *et al.* 1992a; Steel *et al.* 1999). Septic arthritis/osteomyelitis is seen in foals usually less than 60 days of age (Martens *et al.* 1986). There is frequently more than one joint involved (Martens *et al.* 1986; Steel *et al.* 1999) and it is commonly the larger joints that are involved, although this is not always the case (Martens & Auer, 1980; McIlwraith, 1983). There is generally a site of primary sepsis elsewhere in the body (Martens *et al*, 1986), although it is not always readily apparent (Martens & Auer, 1980).

The septic arthritis/osteomyelitis syndrome is classified according to the location of the lesions (Firth, 1983; Martens *et al.* 1986). A foal with S-type septic arthritis/osteomyelitis syndrome characteristically has synovitis without gross evidence of osteomyelitis. Foals with E-type have osteomyelitis of the epiphysis at the subchondral bone/cartilage junction. Foals with P-type have osteomyelitis directly adjacent to the physis, and a predisposition for the formation of these bone lesions has been reported in the lower limbs of foals (Firth, 1983). It is impossible to differentiate between S and E-type by clinical signs and synovial fluid evaluation (Firth, 1983). The diagnosis of E-type is confirmed by demonstration of the characteristic radiographic changes in the epiphysis or affected joints (Firth, 1983). The area of diseased bone is generally more extensive than is appreciable radiographically (Firth, 1983) and can be so extensive as to have caused loss of extensive areas of articular cartilage and epiphyseal bone (Firth, 1983).

The same joint can have a single type or any combination of types present at any one time (Firth, 1983), although most foals with infectious synovitis also have concurrent bone lesions (Firth, 1983; Martens *et al.* 1986). In the larger joints, bone lesions may be the result of local vascular spread from the synovial membrane to the adjacent epiphysis, whose vascular supply arises from common vessels (Firth, 1983). It was reported (Firth, 1983) that no foal was found with an E-type defect in the absence of purulent changes in the synovia of the adjacent joint. In P-type defects bone infection may occur before involvement of the adjacent joint (Firth, 1983). Once synovial effusion occurs this may be the result of either the presence of infection in an adjacent area or of extension of infection

from bone to synovial membrane (Firth, 1983). Lesions can be so extensive as to threaten to, or have already caused, pathological fracture of the affected bone (Firth, 1983). Whilst it is unclear why the predisposition sites in the lower limb for bone lesions occur, it has been suggested that it may be linked to trauma, as a history of recent trauma was reported in relation to bone infection in children (Firth, 1983). The lower limbs of foals are more likely to sustain either external traumatic insults or functional trauma when compared to the upper limb, which could then predispose them to the formation of bone lesions (Firth, 1983).

5.2.2.4. Synovial response to sepsis

The response of a synovial structure to invasion by bacteria has been the subject of a large body of experimental research, and the sequence of events is well documented (4.2.2.1.).

5.2.2.5. Bone response to sepsis

Osteomyelitis develops via the haematogenous route when a bacterial embolus present in the circulation settles out to the periphery of metaphyseal veins, causing the development of a venous thrombosis (Martens & Auer, 1980; Orsini, 1984; Martens *et al.* 1986; Hance *et al.* 1993; White, 2002). Feeding capillaries are gradually blocked by the retrograde progression of the clot and local marrow necrosis occurs, resulting in a perfect environment for the growth and colonisation of bacteria (Martens & Auer, 1980; Orsini, 1984; Martens *et al.* 1986; Hance *et al.* 1993). Thrombosis prevents immune defence mechanisms from reaching the colonised bacteria. Endosteal blood supply is lost due to the thrombosis of the nutrient artery, resulting in sequestrum formation. The dead bone becomes separated during necrosis and is surrounded by purulent material (Orsini, 1984; White, 2002). It is the osteolysis caused by the cycle of inflammation followed by ischaemia and necrosis that is visible radiographically, allowing accurate diagnosis of the condition (Martens & Auer, 1980; Hance *et al.* 1993).

5.2.2.6. Culture of causative organisms

It has been widely reported in the literature that bacterial culture from cases of suspected septic arthritis is unrewarding (4.2.2.2.).

It is recommended that in foals in which septicaemia is suspected, blood cultures be performed to identify the causative organism, in order to institute appropriate antimicrobial therapy (McIlwraith, 1983; Koterba *et al.* 1984; Martens *et al.* 1986; Bertone, 1999; Tremaine, 2000), with positive blood cultures achieved in approximately 80% of cases that were identified as septicaemic (Wilson & Madigan, 1989). It has been reported when septicaemic foals with concurrent septic arthritis had both their blood and synovial fluid from the affected joint cultured, that in between 50-85% of the cases in which a positive culture was obtained, identical organisms were isolated (Vatistas *et al.* 1993; Steel *et al.* 1999). When osteomyelitis is present, culture of any purulent exudates and necrotic material is also recommended (Martens & Auer, 1980; Martens *et al.* 1986), in order to increase further the likelihood of achieving a positive culture as microorganisms frequently colonise within the bone (Martens & Auer, 1980). Studies have found that, whilst a mixed growth of bacteria is commonly found when culturing synovial fluid from foals with septic arthritis (Schneider *et al.* 1992a; Bertone, 1999), the bacteria are predominantly Enterobacteriaceae, with *Escherichia coli* being the main isolate (Schneider *et al.* 1992a). This is probably related to the prevalence of these organisms in the environment, increasing the likelihood that faecal or soil contamination of compromised surfaces, for example an unsealed umbilicus, will result in infection (Platt, 1973; Schneider *et al.* 1992a).

5.2.2.7. Radiography in diagnosis

It is important when first examining a foal with suspected septic arthritis to identify any underlying disease processes and treat these accordingly, in order to eliminate them as a source of future pathogens capable of perpetuating the infection, in conjunction with treatment of the affected joint(s) (Martens & Auer, 1980; McIlwraith, 1983; Stoneham, 1997; Meijer *et al.* 2000). Without treatment of any other foci of infection, successful resolution of the septic arthritis will not be achieved. Any suspect joints should be radiographed for signs of osteomyelitis (Martens & Auer, 1980; Zamos *et al.* 1993; Raisis *et al.* 1996; Waterhouse & Marr, 1997; Stoneham, 1997; Hance, 1998), with between 33 and 52% of foals treated for septic arthritis found to have concurrent signs of osteomyelitis (Schneider *et al.* 1992a; Steel *et al.* 1999), although one survey reported more than 75% of foals treated for septic arthritis as having clinically diagnosed concurrent osteomyelitis (Martens & Auer, 1980).

If no radiographic evidence of osteomyelitis is seen, the joints should be re-radiographed every three to five days for the duration of treatment (Martens & Auer, 1980; Firth, 1983; Martens *et al.* 1986; Zamos *et al.* 1993; Stoneham, 1997; Hance, 1998; White, 2002), as there is frequently a latent period between the onset of clinical signs and the development of radiographically visible lesions (Zamos *et al.* 1993; Stoneham, 1997; White, 2002).

5.2.3. Treatment

5.2.3.1. Medical Therapy

5.2.3.1.1. Systemic antimicrobial therapy

Systemic antimicrobial therapy and lavage of the affected joint are the two most important aspects of treatment for septic arthritis (McIlwraith, 1983; Martens *et al.* 1986; Hance, 1998). Therapy should only be started once any blood and synovial fluid to be submitted for culture has been taken, maximising the likelihood of obtaining a positive culture result (Firth, 1983; Steel *et al.* 1999). Systemic antimicrobials should then be started immediately, without waiting for any culture results. The results of any culture and sensitivity can be used later to guide a change in antimicrobial therapy if a clinical response to treatment is not seen (Martens & Auer, 1980; Waterhouse & Marr, 1997; Steel *et al.* 1999).

The antimicrobials selected initially should be broad spectrum (Martens & Auer, 1980; McIlwraith, 1983; Koterba, 1991; Hance *et al.* 1993) although many infections in young foals are gram negative (Schneider *et al.* 1992a; Meijer *et al.* 2000), mixed bacterial infections cannot be ruled out without a positive culture result (Schneider *et al.* 1992a). The antimicrobials should also be bactericidal, as a sick neonate may have a compromised immune system (Firth, 1983; Stoneham, 1997), and they must be capable of achieving therapeutic concentrations for prolonged periods within both bone and synovia (Stoneham, 1997).

Care must be taken in considering both excretion and metabolism when selecting a suitable antimicrobial, as drugs administered at a standard dose can reach nephrotoxic concentrations if renal compromise exists (Bowman *et al.* 1991; Stoneham, 1997). Studies have shown that neonates, particularly when septic (Bowman *et al.* 1991; Wichtel *et al.* 1992; Green & Conlon, 1993), are prone to developing nephrotoxicity at standard antimicrobial dosages (Baggot & Short, 1984; Geor & Brashier, 1991; Wichtel *et al.* 1992; Bertone, 1999), therefore therapeutic monitoring may be appropriate in order to establish whether a non-toxic dose achieves therapeutic concentrations (Bowman *et al.* 1991).

The first choice of antimicrobials are a penicillin in combination with an aminoglycoside (Koterba, 1991; Schneider *et* al. 1992a; Stoneham, 1997; Waterhouse & Marr, 1997; Hance, 1998; Bertone, 1999; Steel *et al.* 1999; Meijer *et al.* 2000), although a third generation cephalosporin has also been used effectively (Schneider *et al.* 1992a; Zamos *et al.* 1993; Stoneham, 1997; Bertone, 1999). The use of amikacin in foals has been associated with less nephrotoxicity (Koterba, 1991), as well as less resistance amongst likely organisms when compared to gentamicin (Brewer & Koterba, 1985; Koterba, 1991).

Systemic antimicrobial therapy alone may be sufficient if osteomyelitis is diagnosed early in its clinical course (Martens & Auer, 1980; Martens *et al.* 1986; Zamos *et al.* 1993; Kettner *et al.* 2003), although ischaemia is an important aspect of osteomyelitis and microorganisms thrive in the avascular tissue. Once evidence of abscessation, sequestration or severe lysis is seen radiographically, surgical decompression will be required, with excision of the dead bone and associated infected tissue (Martens & Auer, 1980; Martens *et al.* 1986; Zamos *et al.* 1993; White, 2002).

Depending on the site of the lesion, surgical debridement may not be feasible (Hance *et al.* 1993; Kettner *et al.* 2003). Instances of osteomyelitis of the femoral condyle have been reported where no gross involvement of the articular cartilage was evident, despite changes in the synovial fluid suggestive of sepsis, therefore surgical curettage of the lesion would require removal of the overlying cartilage, creating additional damage to the joint (Hance *et al.* 1993). Similarly, in P-type osteomyelitis, if the bony lesion is at the centre of the growth plate, surgical curettage would result in extensive damage to both the growth plate

and adjacent bone (Kettner *et al.* 2003). Even after successful surgical debridement of a lesion and resolution of joint sepsis, foals require a prolonged course of antimicrobials for a number of months that extends far beyond the resolution of clinical signs (Martens & Auer, 1980; Firth, 1983; Martens *et al.* 1986; Hance *et al.* 1993). This is necessary because bacteria are capable of surviving for a long time in the bone and physeal cartilage, providing an ongoing source of infection (Martens & Auer, 1980; Orsini, 1984; Martens *et al.* 1986). If the antimicrobials are stopped prematurely, the infection will often recur (Martens & Auer, 1980; Firth, 1983; Martens *et al.* 1986).

5.2.3.1.2. Intra-articular antimicrobials and regional perfusion

Intra-articular antimicrobial therapy remains controversial in the treatment of septic arthritis (4.2.3.1.4.). The use of intra-articular antimicrobials in foals has been only infrequently reported (Schneider *et al.* 1992a; Zamos *et al.* 1993; Steel *et al.* 1999), and their requirement questioned (Waterhouse & Marr, 1997), as it is likely that multiple organ systems are involved in the disease process, and this would necessitate the systemic use of antimicrobial therapy (Waterhouse & Marr, 1997).

Regional perfusion of antimicrobials has been proposed as a viable method of treatment for septic arthritis and osteomyelitis in foals (Hance, 1998). Regional perfusion has been shown to be effective in delivering antimicrobials under pressure to a selected region of the limb through the venous system (Whitehair *et al.* 1992; Murphey *et al*, 1999; Butt *et al.* 2001; Scheuch *et al.* 2002). This allows antimicrobials to reach ischaemic areas by diffusion from the surrounding vascular tissue, resulting in higher local concentrations of antimicrobials within the bone lesions associated with osteomyelitis (Kettner *et al.* 2003). Regional perfusion has been studied using both the intravenous and intra-osseous route of administration of antimicrobials (Whitehair *et al.* 1992; Kettner *et al.* 2003). The intra-osseous route is thought to be advantageous as it does not require serial catheterisation of veins (Kettner *et al.* 2003), and when treating osteomyelitis it is unknown if antimicrobial concentrations are as high in bone following intravenous administration of antimicrobials when compared to the intra-osseous route (Kettner *et al.* 2003).

5.2.3.1.3. Non-steroidal anti-inflammatory drug therapy

Anti-inflammatory drug therapy is important in minimising damage to the articular surface (Martens & Auer, 1980; Schneider & Bramlage, 1991; Zamos *et al.* 1993; Stoneham, 1997). Chronically inflamed tissue and the associated by-products can perpetuate cartilage destruction even in the absence of sepsis, resulting in the occurrence of degenerative joint disease (Martens & Auer, 1980; Martens *et al*, 1986; Meijer *et al.* 2000). Whilst the judicious use of non-steroidal anti-inflammatory drugs (NSAIDs) is widely accepted as being beneficial in the treatment of septic arthritis in adult horses (Schneider & Bramlage, 1991; Bertone, 1999), they should only be used with care in the management of foals (Martens *et al.* 1986; Stoneham, 1997; Hance, 1998). They are known to contribute to gastric ulcer syndrome in foals (Martens *et al.* 1986; Stoneham, 1997; Waterhouse & Marr, 1997; Hance, 1998), therefore prophylactic anti-ulcer medication is recommended. They can induce a profound improvement in the degree of lameness seen in foals (Hance, 1998), even if the therapy employed is not being wholly effective, leading to a false sense of optimism, and they limit any febrile episodes, which are also an indicator of ongoing sepsis (Hance, 1998).

5.2.3.1.4. Anti-ulcer therapy

Anti-ulcer medication is recommended in the management of foals with septic arthritis (Zamos *et al.* 1993; Stoneham, 1997; Waterhouse & Marr, 1997). Many foals will receive NSAIDs as part of their therapy, which are known to be ulcerogenic, and when 'stressed' foals are more prone to develop gastric ulcers (Stoneham, 1997; Waterhouse & Marr, 1997)

5.2.3.1.5. Therapy for neonatal septicaemia

If the foal is septicaemic, this must be treated alongside treatment of septic arthritis and osteomyelitis. Systemic antimicrobial therapy should be instituted (McClure, 1981), with blood cultures confirming organism type and sensitivity. As failure of passive transfer in foals is recognised to predispose them to the development of septic conditions, immunoglobulin concentrations should be established, with hypogammaglobulinaemic foals receiving supplementary administration of antibodies through the intravenous transfusion of either plasma or serum (Martens & Auer, 1980; McClure, 1981; Meijer *et al.*

2000). It has been shown that clinically ill foals display a significantly lower rise in serum immunoglobulin concentrations following treatment with plasma than clinically healthy foals (LeBlanc, 1988), therefore a larger volume of plasma may be necessary to increase the serum immunoglobulin concentration an acceptable amount. It may be beneficial to administer plasma even in foals that were known to have acceptable concentrations of circulating immunoglobulins soon after birth, as it has been suggested that infection may lower the concentration of circulating immunoglobulins (LeBlanc, 1988) as serum proteins leak out into the infected tissues and body cavities (Brewer & Mair, 1988), and it is unknown how marked this drop in serum immunoglobulin concentration can be (Robinson *et al.* 1993).

5.2.3.2. Surgical Therapy

5.2.3.2.1. Joint lavage

Through-and-through lavage using a balanced polyionic solution, although reported to be ineffective in removing the fibrin-white blood cell coagulum within the joint (Martens *et al.* 1986; Schneider *et al.* 1992b), is a simple and quick technique frequently used in the treatment of septic arthritis in foals (Martens & Auer, 1980; Martens *et al.* 1986; Stoneham, 1997; Waterhouse & Marr, 1997; Meijer *et al.* 2000; Tremaine, 2000; Parviainen, 2002). It has the added advantage in the foal that it can be performed on a sedated animal in a suitably clean environment (Stoneham, 1997; Waterhouse & Marr, 1997; Meijer *et al.* 2000; Tremaine, 2000), negating the need for serial general anaesthesia in an animal that may also have systemic disease (Meijer *et al.* 2000), and rendering it a suitable treatment option where hospital facilities are not available (Tremaine, 2000).

There are few reports on the use of lavage solutions other than a balanced, polyionic solution, in the treatment of septic arthritis in foals. Studies have cited the use of either a 0.1% povidone-iodine solution, or the use of a dimethyl-sulfoxide (DMSO) solution (Honnas *et al.* 1992a,b; Schneider *et al.* 1992a; Zamos *et al.* 1993). The addition of 0.1% povidone-iodine has been shown to be no more beneficial than the use of a balanced, polyionic solution in the treatment of an experimentally induced septic arthritis in adult horses (Bertone, 1987b). The addition of DMSO to an articular lavage solution is thought to inhibit prostaglandin production and phagocytic cellular influx (Honnas *et al.* 1992a;

Zamos *et al.* 1993), although it is unknown if this is any more beneficial than a balanced, polyionic solution in the treatment of septic arthritis in foals.

5.2.3.2.2. Arthroscopy and arthrotomy

Arthroscopy and arthrotomy are surgical procedures that can be used in conjunction with lavage, in situations in which excessive fibrin within the joint interferes with thorough lavage using the through-and-through technique (4.2.3.2.2.). It has been suggested that arthroscopy should be a suitable first-choice treatment, as it would allow visualisation and subsequent curettage of any osteomyelitic lesions, along with removal of fibrin and inflammatory debris from the joint (Zamos *et al.* 1993; Meijer *et al.* 2000; Tremaine, 2000). It allows greater visualisation of the joint and the physis when compared to arthrotomy (Zamos *et al.* 1993; Tremaine, 2000), along with the ability to perform synovectomy at a site remote to the incision (Zamos *et al.* 1993; Tremaine, 2000).

5.2.3.3. Follow up

When treating osteomyelitis, repeat radiographs can be an effective means of monitoring the efficacy of treatment. If the lesion is continuing to progress into adjacent bony tissue despite antimicrobial therapy, then the drugs chosen are either not penetrating the lesion (Parviainen, 2002), or are not effective against the causative organism (Parviainen, 2002). However, if the lesion appears static after approximately 7 days of treatment, this would suggest that the antimicrobial regimen is effective (Hance, 1998; Kettner *et al.* 2003). Radiographs can also be used to determine the length of treatment required, based on the rate of regression of any bony lesions evident (Hance, 1998).

5.2.4. Outcome and prognosis

The outcome for foals with septic arthritis, with or without concurrent osteomyelitis, is generally described as poor (Martens & Auer, 1980; Schneider *et al.* 1992a; Steel *et al.* 1999; Meijer *et al.* 2000). Although young animals have a greater capacity for regeneration of articular cartilage than adults (Martens & Auer, 1980; McIlwraith, 1983) a guarded prognosis for future athletic capability is still indicated (Martens & Auer, 1980).

Foals are frequently euthanased before successful resolution of joint sepsis due to complications attributed to underlying disease processes (Schneider *et al.* 1992a; Steel *et al.* 1999; Meijer *et al.* 2000), failure of the joint sepsis to respond to treatment (Koterba *et al.* 1984; Hance *et al.* 1993; Steel *et al.* 1999; Meijer *et al.* 2000), or occurrence of musculoskeletal sepsis at other sites during the course of treatment (Koterba *et al.* 1984; Raisis *et al.* 1996; Steel *et al.* 1999). An inverse relationship has been described between the number of joints affected and the likelihood of recovery from the sepsis (Martens & Auer, 1980; Raisis *et al.* 1996; Steel *et al.* 1999). Presence of concurrent osteomyelitis, hypogammaglobulinaemia and the presence of multi-system disease are all thought negatively to influence the prognosis for a favourable outcome from septic arthritis (Firth, 1983; Bertone, 1999; Steel *et al.* 1999; Meijer *et al.* 2000). The treatment of septic arthritis and osteomyelitis in foals is complicated by the presence of underlying disease. There are few studies in existence that have incorporated large numbers of foals, with the studies that have done so being retrospective case series utilising a number of different treatment regimens (Schneider *et al.* 1992a; Steel *et al.* 1999), rendering it difficult to compare the efficacy of individual methods of treatment (Schneider *et al.* 1992a; Steel *et al.* 1999).

5.2.5. Study aims

The purpose of this study was to evaluate data from an equine hospital over the last 13 years, and to compare each study group to a suitable control population, so as to investigate the likely long term athletic prognosis for Thoroughbred neonates treated for septic arthritis. It was hypothesised that the occurrence of septic arthritis in a Thoroughbred neonate would significantly reduce the likelihood of that foal starting on a racecourse when compared to its siblings. The aim was to test this hypothesis using a retrospective study.

5.2.6. Material and Methods

5.2.6.1. Power calculation

The number of foals required (n) for this study, using a significance level of 5%, and study power of 80%, was calculated using the standard formula (Snedecor and Cochran, 1980):

$$n = [(Za + Zb)/(P_0 - P_1)]^2 * (P_1Q_1 + P_0Q_0)$$

where Za, calculated to be 1.96, is the value of Student's t distribution at the specified confidence level and Zb, calculated to be -0.842, is the value of Student's t distribution at the specified power, with P_0 being the proportion of Thoroughbred foals that successfully start on a racecourse following treatment for septic arhtirits, Q_0 being $(1-P_0)$, P_1 is the proportion of Thoroughbred siblings that start on a racecourse, and Q_1 is $(1-P_1)$. With P_0 estimated to be 40%, based on previously published data (Steel *et al.* 1999) and P_1 estimated to be 65%, based on statistics published by Weatherbys, the required number of foals for the study was, therefore, 67.

5.2.6.2. Data retrieval

5.2.6.2.1. Case identification

The admission records for Rossdales Equine Hospital between 1988 and 2001 were reviewed to identify Thoroughbred foals that had been admitted with suspected joint pathology, and medical histories were then retrieved. To be eligible for inclusion in the study, foals had to be Thoroughbreds, intended for use as racehorses, and had to be less than 4 months old at the time of admission. Any Thoroughbred foals which were not intended solely as racehorses were excluded from the study. Where septic arthritis was suspected on the basis of clinical signs, diagnosis was confirmed on the result of synoviocentesis of the affected joint, in which an increased nucleated cell count (upper end of normal reference limit for laboratory: 3×10^9 cells/l) in conjunction with an increased total protein concentration (upper end of normal reference limit: 15g/l) and the presence of a neutrophilia with degenerative polymorphonuclear cells on cytological analysis were considered to be diagnostic. Information retrieved from the medical records included sex, evidence of multi-system disease, the number of joints infected, anatomical location of the joint(s) involved, the white cell count of the synovial fluid at the time of admission to the hospital, and details of antimicrobial therapy and lavage procedures performed.

5.2.6.2.2. Comparison population identification

The foaling history of each foal's dam was then reviewed using Weatherbys stud book and racing records, in order to obtain the registration details of the affected foal, along with the details of two siblings. Two siblings were used as controls wherever possible in order to

increase the statistical power of the study. In instances in which mares had produced fewer than two live foals in the years prior to the affected foal being born, the closest siblings in age born after the affected foal were selected for comparison, provided that they had attained racing age within the study period, in order that each foal treated for septic arthritis might have two siblings as controls. In the case of mares that had failed to produce two other live foals of racing age in the study period, only one sibling was available for comparison.

5.2.6.3. Data Analysis

5.2.6.3.1. Study group analysis

Outcomes that were statistically evaluated within the study group included discharge from the hospital and whether the foal eventually raced. Outcome was determined by evaluation of medical records to determine whether the foals were successfully discharged from the hospital. Lifetime race records were then obtained for all the foals that had been successfully discharged following treatment for septic arthritis. Race records were obtained from when foals were $\geq$ 2 years old until 1st December 2003, and the time from birth until the first start and the number of starts were recorded.

Variables that were statistically evaluated included infection in more than one joint, the presence of multi-system disease and the specific joint involved. Analyses of categorical variables were conducted for each outcome. Comparisons among groups of discreet data were initially made using univariable analyses of odds ratios and 95% confidence intervals, along with a χ^2 test for independence, attributable risk and absolute risk increase.

5.2.6.3.2. Comparative analysis between study and control groups

The outcome that was statistically evaluated was whether the foal eventually raced. Outcome was determined by obtaining the lifetime race records for all control foals, and all the foals that had been successfully discharged following treatment for septic arthritis. Race records were obtained from when foals were $\geq$ 2 years old until 1st December 2003, and the time from birth until the first start, and the total number of starts was recorded.

To compare the likelihood of a foal starting on a racecourse from the study group with their siblings in the control group, data were analysed using conditional logistic regression analysis, using the statistical software package PAIRSetc version 0.86, Win PEPI version 4.0. This analysis allows exposed individuals (those in the study group) to have varying numbers of individually matched controls (those in the control group). This matching of cases and their siblings thereby clusters data by dam, to test the null hypothesis that septic arthritis as a foal did not affect the likelihood of that Thoroughbred foal starting on a racecourse, when compared to its siblings.

Kaplan-Meier survival curves were generated depicting the age at first race of male and female foals in both the study group and the control population, and the age at first race of the study group and the control population. Survival curves were compared using the Log-rank test. Differences were considered significant at $p < 0.05$.

The attributable risk (AR), indicating the increase in the probability of failing to start on a racecourse in the study group, beyond the baseline risk experienced by the control population, resulting from the development of septic arthritis was calculated using the standard formula (Dohoo *et al.* 2003):

$$AR = (a_1/n_1) - (a_0/n_0)$$

Where:

a_1: is number of foals with septic arthritis that failed to start on a racecourse

n_1: is total number of foals with septic arthritis

a_0: is number of control foals that failed to start on a racecourse

n_0: is total number of control foals

The attributable fraction (AF), indicating the proportion of foals in the study group failing to start on a racecourse due to the occurrence of septic arthritis, using the standard formula (Dohoo *et al.* 2003):

$$AF = [(a_1/n_1) - (a_0/n_0)]/(a_1/n_1)$$

Where:

a_1: is number of foals with septic arthritis that failed to start on a racecourse

n_1: is total number of foals with septic arthritis

a_0: is number of control foals that failed to start on a racecourse

n_0: is total number of control foals

5.2.7. Results

5.2.7.1. Descriptive statistics

Sixty-nine Thoroughbred foals met the criteria for inclusion in the study, thereby satisfying the power calculation performed at the outset of the study. Thirty-eight foals were male and thirty-one foals were female. Of the 69 foals, five had two affected joints at presentation and the remaining 64 foals had only one affected joint. The joint involved was recorded in 57 cases and included: femoropatellar joint with or without involvement of the femorotibial joint (17 foals), tibiotarsal joint (15), metacarpophalangeal or metatarsophalangeal joint (10), radiocarpal joint (6), humeroulnar joint (5), coxofemoral joint (2), scapulohumeral joint (1) and distal interphalangeal joint (1). In four of the five foals with > 1 joint involved, it was the same joint but in contra-lateral limbs. The specific joints affected were not recorded for the fifth foal. Results of the cytological analyses of the synovial fluid collected at the time of admission were available for 44 foals. Nucleated cell counts on admission (range: 5.0×10^9 cells/l to 194×10^9 cells/l; median: 38×10^9 cells/l; inter-quartile range: 20.25×10^9 cells/l to 95.50×10^9 cells/l) exceeded the reference limit (3.0×10^9 cells/l) in all cases. Duration of clinical signs prior to presentation at the hospital was recorded in 51 cases, with clinical signs first being noticed < 24 hours prior to admission at the hospital for treatment in 38 cases (74.5%).

5.2.7.2. Treatment options

Although all foals were treated with systemic, broad spectrum antimicrobials and joint lavage there was no standardised treatment protocol, with the specific antimicrobials and lavage technique used varying with the preference of the treating veterinarian. Affected joints were usually lavaged on alternate days until a clinical improvement was seen, with lavage being performed between one and six times in total (median=1 lavage). Standard practice was to review the antimicrobial regimen if antimicrobial sensitivity indicated that the organisms cultured were resistant to the initial antimicrobial choice, or if there was a failure to respond to treatment. Foals were discharged from the hospital when the clinical

signs of infection had resolved, although all foals were still receiving antimicrobials at the time of discharge.

5.2.7.3. Factors affecting survival

Of the 69 foals admitted to the hospital for treatment of septic arthritis, 84.1% (58/69) survived to be discharged from the hospital, with long-term follow-up available for all the foals discharged. Of the 11 foals that were euthanased prior to discharge from the hospital, one foal was euthanased due to a disease process other than septic arthritis. The remaining 10 foals were all euthanased due to a failure of the septic arthritis to respond to treatment.

Three of the five foals with more than one affected joint failed to survive to discharge from the hospital. The remaining two foals were successfully discharged but did not race. Further statistical analysis to demonstrate an association between the presence of infection in more than one joint and either a reduced likelihood of foals surviving to discharge or a reduced likelihood of starting on a racecourse was not performed, as there was insufficient power to prove a statistically significant difference.

Eight of 69 foals (11.6%) had evidence of a disease process outside the synovial cavity – one foal had concurrent osteomyelitis, one had a ruptured bladder, one foal had pneumonia and five foals had infected umbilical remnants requiring surgical resection. Of these eight foals, four failed to survive until discharge. Of the remaining four that were discharged, two failed to race. The presence of multi-system disease was associated with a decreased likelihood of the affected foal surviving to be successfully discharged from the hospital (O.R. 0.13; 95% C.I. 0.02 to 0.90; p=0.005). However, of those foals successfully discharged, the presence of multi-system disease did not affect the likelihood that they would start in at least one race compared to the foals treated for septic arthritis that were not affected with multi-system disease (O.R. 0.45; 95% C.I. 0.04 to 2.81; p=0.34).

5.2.7.4. Long-term follow-up

Twenty-eight foals (40.5%; 95% C.I. 28.9 to 53.1; p=0.148) with septic arthritis subsequently started in ≥1 race, and 17 (24.6%) raced ≥ 5 times. Thus, 28 of the 58 (48.3%) foals that were discharged from the hospital following treatment started in a race. Of the 130 foals in the control group, 86 (66.2%; 95% C.I. 57.3 to 74.2; $p < 0.001$)

subsequently started in ≥1 race, and 69 (53.1%) raced ≥ 5 times. Data analysed using combined regression analysis confirmed that the occurrence of septic arthritis as a neonate resulted in a Thoroughbred foal being 3.5 times less likely to start on a racecourse compared to its siblings prior to the commencement of treatment (O.R. 0.28; 95% C.I. 0.12 to 0.62, p=0.001). If the foal was successfully discharged from the hospital following resolution of joint sepsis, it would be 2.8 times less likely to start on a racecourse compared to its siblings (O.R. 0.36; 95% C.I. 0.15 to 0.83, p=0.008). Within those foals that started on a racecourse at least once, foals that had been treated for septic arthritis were no less likely to start ≥ 5 times as the sibling population (O.R. 0.38; 95% C.I. 0.14 to 1.08; p=0.037).

Calculation of the attributable risk showed that there was an increase by 0.256 in the risk of foals in the study group failing to start on a racecourse, beyond the baseline risk of failing to start on a racecourse experienced by those foals in the control group, due to the occurrence of septic arthritis. Calculation of the attributable fraction showed that in 43% of those foals in the study group that failed to start on a racecourse, this failure was due to the occurrence of septic arthritis. Therefore, if all the foals in the study group had not developed septic arthritis, an additional 43% could have been expected to start on a racecourse.

5.2.7.5. Comparison population

Two siblings for comparison were identified in 61 cases, with the remaining eight foals in the study group only having one sibling available for comparison. Therefore, there were 130 foals in the control group.

Of the 130 foals in the control group, 64 were female and 66 were male. A significantly larger proportion of the male foals started on a racecourse compared to the female foals (O.R. 2.82; 95% C.I. 1.24 to 6.49; p=0.007). In comparison, no statistically significant difference was found between the number of male and female foals treated for septic arthritis that started on a racecourse (O.R. 1.89; 95% CI. 0.64 to 5.74; p=0.20). Overall, male foals that were treated for septic arthritis were less likely to start on a racecourse when compared to the male foals in the control group (O.R. 0.26; 95% C.I. 0.10 to 0.68; p=0.002). The same was not found to be true of female foals treated for septic arthritis,

when compared to the female population in the control group (O.R. 0.39; 95% C.I. 0.14 to 1.05; p=0.04).

5.2.7.6. Survival anlaysis

Kaplan-Meier survival curves were generated comparing age at first race with the sex of the foal, and comparing age at first race between the study and sibling groups. Data from foals that failed to start in a race were censored. Log-rank comparison of the survival curves confirmed that foals discharged successfully following treatment for septic arthritis took significantly longer to appear on a racetrack for the first time compared to the sibling population (mean age of study group=1757 days; 95% C.I. 1604 to 1909; mean age of sibling group=1273 days; 95% C.I. 1197 to 1349; p=0.0006; Figure 3).

Within the healthy sibling population male foals appeared on a racetrack at an earlier age then female foals (mean age of male foals = 1172 days; 95% C.I. 1074 to 1270; mean age of female foals = 1208 days; 95% C.I. 1144 to 1273 p=0.002; Figure 4). However, within the study group sex was not statistically associated with the age of the foal at its first race (mean age of male foals = 1692 days; 95% C.I. 1487 to 1896; mean age of female foals = 1333 days; 95% C.I. 1242 to 1424; p=0.24; Figure 4). Although the difference in the mean age at first racecourse appearance was greater between male and female foals in the study group than in the control group, the sex of the foal in the study group was not found to be statistically significant due to the low number of foals in this group providing inadequate power to detect a statistically significant difference.

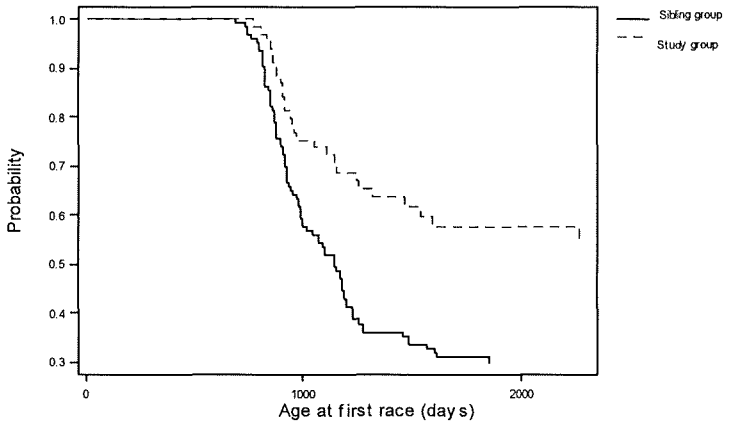


Figure 3: Kaplan-Meier plot of the probability of a Thoroughbred foal not starting on a racecourse, for the sibling and study groups.

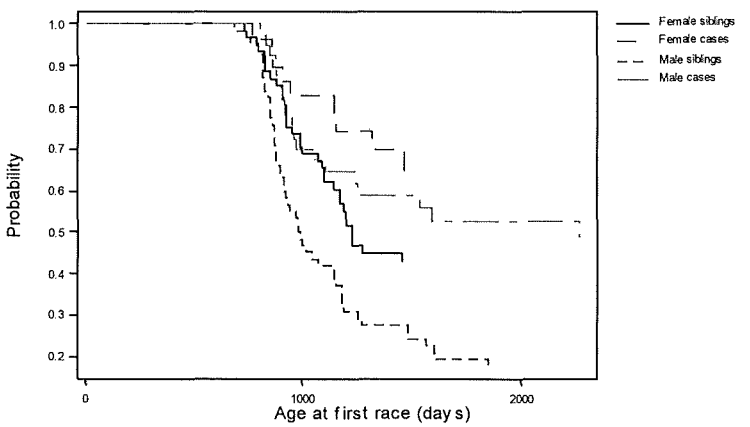


Figure 4: Kaplan-Meier plot of the probability of the sibling and study populations not starting on a racecourse, for male and female foals.

5.2.8. Discussion

5.2.8.1. Limitations of the study

Survival rates reported here for foals treated for septic arthritis are higher than those in other reports (Schneider *et al.* 1992a; Steel *et al.* 1999; Meijer *et al.* 2000). This may be the result of early recognition and treatment of joint sepsis. All the foals were resident at large studs, where the awareness of the importance of adequate colostrum consumption, along with thorough daily checks of foals, contributes to a better management regimen. The majority of cases were admitted to the hospital by members of the practice rather than being a referral population as described by previous reports, in which it might be expected that there is a bias towards more severely affected animals. In addition, the practice in question is a large, specialist equine hospital, well equipped both in terms of facilities and experienced personnel, where staff are familiar with neonatal septic arthritis and are therefore able to detect subtle clinical signs of early sepsis.

Despite the large number of publications in the literature on septic arthritis, limited data are available on the prognosis for neonatal septic arthritis (Schneider *et al.* 1992a; Steel *et al.* 1999; Meijer *et al.* 2000), particularly in an athletic breed such as the Thoroughbred, with only two studies extending follow-up beyond discharge from the hospital (Platt, 1977; Steel *et al.* 1999). Although both these studies contain valid data and conclusions, in EBM terms they would be classified as providing class C evidence, using the classification system proposed by Yusuf *et al* (1998), as they are case series, using no control groups. The purpose of the current study was to investigate the long term prognosis for Thoroughbred foals treated for septic arthritis, with the intention of conducting a study that would provide a higher class of evidence than those studies already published in the literature. By using a retrospective case series as a study design, with older siblings used as a comparison population, the current study would be classified as providing class B evidence.

5.2.8.2. Factors affecting long-term prognosis

Although many studies have examined the efficacy of different treatment regimens in the management of septic arthritis, no study has focused on such a specific study group, or compared the long-term outcome following treatment for septic arthritis to a suitable

control group. The purpose of this study was not to compare the specific treatment regimes used and their effect on the long-term prognosis, but to assess whether a Thoroughbred foal treated successfully for septic arthritis would race. All foals admitted to the hospital for treatment of septic arthritis were matched with two of their siblings of racing age as controls, for comparison of the number of starts achieved in their career (Mitten *et al.* 1995). Older siblings were selected where possible. Where two siblings of racing age were not available, one sibling was used as a control. Statistics published by Weatherbys suggest that approximately 65% of Thoroughbred foals born in one year will start at least once on a racecourse – a figure that has not changed over the past decade. Our figures showed that 66.2% of the siblings successfully started in at least one race – an almost identical result to the predicted average. In comparison, only 48.3% of all foals successfully discharged following treatment for septic arthritis started in at least one race in their career. This result is higher than two previous studies reporting the long term outcome of Thoroughbred foals treated for septic arthritis, in which only 30% (Platt, 1977) and 37% (Steel *et al.* 1999) of foals subsequently raced. The outcome may have been better than that previously reported, due to the nature of the study population. They were not a true referral population, as reported by Steel *et al.* (1999), but were resident at large studs where all foals were checked on a daily basis. In addition, daily veterinary visits were standard practice, allowing for prompt institution of treatment in cases where either septicaemia or septic arthritis was suspected.

Although young animals have a greater capacity for regeneration of articular cartilage than adults (Martens & Auer, 1980; McIlwraith, 1983) the severe degenerative changes that occur subsequent to infection are likely to have contributed to the higher number of foals that failed to race following successful resolution of sepsis, when compared to the sibling population. However, it is impossible to ascertain from lifetime racing records alone the reason that some of the foals that were discharged from the hospital failed to make at least one start on a racecourse.

Unlike previous studies (Martens & Auer, 1980; Steel *et al.* 1999), infection of multiple joints was not associated with either a reduced likelihood of foals surviving to discharge, or a reduced likelihood of racing. However, the total number of foals treated with multiple joint involvement was very low (5/69; 7%), compared with previous studies where a significantly higher proportion of multiple joint involvement was recorded – 50% (Schneider *et al.* 1992a) and 50.6% (Steel *et al.* 1999). The very small numbers of foals

that had multiple joint involvement in the current study rendered the statistical power too small to detect any significant difference. This finding highlights the fact that despite the careful study design and a power and sample size calculation being performed at the outset of the study, subsequent subdivision of the study group for investigation of different variables on the outcomes of interest will lower the power. However, the investigation of the affect these variables might have on the outcomes of interest was not the primary aim of this study.

The affected joint (femoropatellar, tibiotarsal joint, metacarpo/metatarsophalangeal) did not have a significant effect on either survival to discharge or the long term prognosis. Other joints were not affected in sufficient numbers to allow for accurate evaluation. The presence of multi-system disease was associated with an increased likelihood of the affected foal not surviving to be discharged from the hospital. However, of those foals discharged, the presence of multi-system disease did not affect the likelihood that they would start in at least one race.

Despite the large number of foals in the study, the retrospective study design, coupled with the fact that many foals received more than one antimicrobial and lavage technique precludes any conclusions being drawn regarding the relative efficacy of specific treatment modalities. However, the aim of the study was not to compare the relative success associated with one specific treatment, but to investigate the long-term prognosis of foals that had survived until discharge from the hospital, and whether the occurrence of septic arthritis as a neonate would affect the likelihood of them starting on a racecourse. It was not possible to draw any conclusions from this study as to whether the occurrence of septic arthritis as a neonate affected the racing performance of those foals in the study group. However, it would not be possible to investigate this adequately in a retrospective study, due to the multiple factors that influence a foal's ability to race successfully.

Studies adopting a prospective, controlled design are required in order to be able to draw any conclusions on the efficacy of specific treatment regimens. Similarly, attempts to examine the effects of the joint involved, number of joints and existence of concurrent pathology on survival and long-term prognosis should be viewed with caution as this study relies on retrospective analysis of medical records. When attempting to draw conclusions from the effects of multiple joint involvement or multi-system disease, the very low numbers of foals in each of these categories dramatically reduces the power of that

component of the study. In order to fully investigate the influence any of these variables might have on the outcomes of interest, it would be necessary to design a study that would take into consideration the relative prevalence of each of these variables, and an appropriate power and sample size calculation should be performed.

5.2.8.3. Conclusions

The prognosis for survival following early identification and treatment of septic arthritis in this particular population of Thoroughbred neonates is guarded to fair, although it is reduced significantly by the presence of multi-system disease. If the infection is eliminated from the synovial space then almost 50% of foals successfully started in at least one race. However, the prognosis for starting in a race, when compared to their siblings, is poor.

5.3. What factors affect the likelihood that mature Thoroughbred racehorses treated for septic arthritis will race?

5.3.1. Routes of infection

Septic arthritis in adult horses is a serious clinical problem (Bertone *et al.* 1987a,b; Tulamo *et al.* 1989; Schneider *et al.* 1992b; Cook and Bertone, 1998; Booth *et al.* 2001) which, unlike in the neonate, commonly affects only a single joint (Cook and Bertone, 1998). There are three recognised routes by which bacteria may become established within a synovial cavity (4.2.1.):

1. trauma
2. iatrogenic origin
3. haematogenous spread

Occasionally, the inciting cause of sepsis if never identified.

5.3.2. Prognosis following resolution of sepsis

The prognosis for a successful return to athletic function has been variously described from guarded or poor (Martens & Auer, 1980; McIlwraith, 1983; Gibson *et al.* 1989; Bowman *et al.* 1991; Brusie *et al.* 1992; Lapointe *et al.* 1992) to favourable or even good (Ross *et al.* 1991; Schneider *et al.* 1992a,b; Bertone, 1999; Meijer *et al.* 2000; Summerhays, 2000; Booth *et al.* 2001). It has been shown that time between onset of sepsis and initiation of therapy (Gibson *et al.* 1989; Peremans *et al.* 1991; Honnas *et al.* 1992a), and the joint infected (Peremans *et al.* 1991; Booth *et al.* 2000) are both influential when considering the likely outcome. The main causes of treatment failure are the inability to eliminate the causative agent (Bertone *et al.* 1987a; Schneider *et al.* 1992a,b; Meijer *et al.* 2000) and to disrupt effectively the vicious cycle of articular cartilage destruction mediated by inflammatory products (Orsini, 1984; Stover, 1990; Bertone, 1999).

Previous studies have frequently reported only short term follow up, with the end point commonly being discharge form the hospital. Only three studies (Ross *et al.* 1991; Lapointe *et al.* 1992; Schneider *et al.* 1992a) have followed the outcome of horses after they have been discharged from the hospital following treatment for septic arthritis. Studies have reported that between 41.7% (Honnas *et al.* 1992) and 85% (Schneider *et al.* 1992a) of mature horses treated for septic arthritis were successfully discharged from the hospital. Of those studies that reported longer term follow up, it was found that 25% (LaPointe *et al.* 1992) to 56.5% (Schneider *et al.* 1992a) of horses were able to return to their original level of athletic function, with no adverse affects related to the occurrence of septic arthritis. No study has followed up a large number of horses over an extended time period to assess the long term outcome following treatment for septic arthritis.

5.3.3. Study aims

The purpose of this study was to evaluate data from an equine hospital over the last 10 years, and to compare each study group to a suitable control population, so as to investigate the likely long term athletic prognosis for mature Thoroughbred racehorses treated for septic arthritis. In this study it was hypothesised that the occurrence of septic arthritis in mature Thoroughbred racehorses would significantly reduce the likelihood of these horses returning to their previous level of athletic function. The study aim was to test this hypothesis using a retrospective study.

5.3.4. Material and Methods

5.3.4.1. Data retrieval

The admission records for Rossdales Equine Hospital between 1993 and 2002 were reviewed to identify mature Thoroughbred horses that had been admitted with suspected joint pathology, and medical records were then retrieved. To be eligible for inclusion in the study horses had to be Thoroughbreds, either in training or intended for use as racehorses, and had to be $\geq$ 6 months old at the time of admission. Any Thoroughbred horses which were not intended solely as racehorses were excluded from the study. If age was not specified on the medical records, those horses were excluded from the study. In cases in which septic arthritis was suspected on the basis of clinical signs, diagnosis was confirmed on the result of synoviocentesis of the affected joint, where an increased nucleated cell count (upper end of normal reference limit for laboratory: 3×10^9 cells/l) in conjunction with an increased total protein concentration (upper end of normal reference limit: 15g/l) and the presence of a neutrophilia with degenerative polymorphonuclear cells on cytological analysis were considered to be diagnostic. Information retrieved from the medical records included age, sex, number of joints infected, anatomical location of joint(s) involved, the suspected route of infection, the white cell count of the synovial fluid at the time of admission to the hospital, radiographic findings, results of culture of the synovial fluid, details of antimicrobial therapy and lavage procedures performed and whether the horse was discharged from the hospital following treatment.

The foaling history of each horse's dam was then reviewed in order to obtain the details of two siblings, in order to match the case with two controls for analysis. In situations in which mares had produced fewer than two live foals in the years prior to the affected horse being born, the closest siblings in age born after the affected horse were selected for comparison, provided that they had attained racing age within the study period, in order that each horse treated for septic arthritis might have two siblings as controls. In the case of mares that had failed to produce two other live foals of racing age in the study period, only one sibling was available for comparison.

5.3.4.2. Data analysis

5.3.4.2.1. Study group analysis

Variables that were statistically evaluated included age, sex, location of affected joint, inciting cause of sepsis, evidence of radiographic changes at the time of admission, synovial white cell count at the time of admission, duration of onset of sepsis until commencement of treatment and the number of lavages performed. Categorical variables with more than two levels were coded as indicator variables.

Outcomes that were statistically evaluated included discharge from the hospital and whether the horse started on a race course following treatment for septic arthritis. Outcome was determined by evaluation of medical records to determine whether the horses were successfully discharged from the hospital. Lifetime race records were then obtained for all the horses that had been successfully discharged following treatment for septic arthritis. Race records were obtained from when horses were $\geq$ 2 years old until 1st December 2004. For horses in the study group, the highest Official Rating awarded to each horse by the British Horseracing Board's handicappers, both before and after treatment for septic arthritis, was retrieved.

Binary logistic regression was used to analyse these data, as both outcomes of interest were dichotomous. Analyses were implemented with the statistical software MINITAB (version 13.31).

Univariable logistic regression was used to screen all variables, and from this all variables with a p-value $\leq$0.20 were included in a backward elimination process to fit a multivariable model. The inclusion criterion for backward elimination was set at $p \leq 0.05$. The goodness-of-fit of the models was assessed using the Hosmer-Lemeshow goodness-of-fit test, to test the null hypothesis that the model was a good fit, with the null hypothesis accepted at a p-value ≥ 0.05.

Once the main effects model had been fitted, two-way interaction between variables was assessed. Variable selection was determined by biological plausibility. Assessment between models was obtained using a likelihood ratio test (LRT) with significance set at p ≤ 0.05.

5.3.4.2.2. Comparative analysis between study and control groups

The outcome that was statistically evaluated was whether the horse started on a race course following treatment for septic arthritis. Outcome was determined by obtaining lifetime race records for all the horses in the control group, and all the horses that had been successfully discharged following treatment for septic arthritis. Race records were obtained from when horses were $\geq$ 2 years old until 1st December 2004. For horses in the study group, the highest Official Rating awarded to each horse by the British Horseracing Board's handicappers, both before and after treatment for septic arthritis, was retrieved. The highest lifetime Official Rating awarded was retrieved for each horse in the comparison group. Data were then analysed using a general linear model, which allowed a univariate analysis of variance to be performed with an unbalanced design, as there was more than one control available for comparison with each case.

Data were also analysed using combined regression analysis, which allows for matching of cases and their siblings thereby clustering data by dam, to test the null hypothesis that the occurrence of septic arthritis did not affect the likelihood that an unraced Thoroughbred would start on a racecourse, when compared to its siblings. Comparison of Official Ratings between the study group and their matched controls was made using a general linear model. Differences were considered significant at $p < 0.05$.

A Wilcoxon signed rank test was used to compare the highest Official Rating achieved after resolution of septic arthritis with the highest Official Rating achieved prior to the onset of sepsis, for those horses that had raced at least once prior to the onset of sepsis. The null hypothesis, that there was no significant difference between the distribution or median of the paired samples, was rejected at p-values ≤ 0.05.

5.3.5. Results

5.3.5.1. Descriptive statistics

Sixty-five mature Thoroughbred horses met the criteria for inclusion in the study. Thirty-eight horses were male and twenty-seven horses were female. The age at the time of admission was recorded for all the horses, and ranged from 1 year old to 12 years old, with

the median age being 2 years old (inter-quartile range: 2 to 4 years old). None of the 65 horses had two or more affected joints at presentation.

5.3.5.2. Factors affecting survival

Of the 65 horses admitted to the hospital for treatment of septic arthritis, 87.7% (57/65; 95% C.I.: 77.2 to 94.5; $p < 0.001$) survived to be discharged from the hospital, with long-term follow-up available for all the horses discharged. Of the eight horses that were euthanased prior to discharge from the hospital, all horses were euthanased due to a failure of the septic arthritis to respond to treatment. Two of the eight horses that were euthanased had been successfully discharged from the hospital, then were re-admitted due to a recurrence of the synovial sepsis.

The age and gender of the horse at the time of admission, synovial white cell count at the time of admission, specific joint affected, presence of radiographic changes in the affected joint at the time of admission, route of infection, duration from onset of sepsis to commencement of treatment and number of lavages performed were all investigated for each outcome. The only variables found to be associated with an increased risk of a horse failing to survive to be discharged from the hospital were the involvement of the proximal inter-phalangeal joint and a delay of at least five days between the onset of sepsis and the commencement of treatment (Table 12). None of the other variables investigated were associated with an increased risk of a horse failing to survive to be discharged (Appendix 5.1).

Table 12: Univariable analysis of factors affecting survival of mature Thoroughbred racehorses following treatment for septic arthritis.

	Coefficient	S.E.	OR	95% CI	p
Joint affected (referent metatarso-phalangeal joint)					
Proximal inter-phalangeal joint	-3.05	1.43	0.05	0.00 – 0.79	0.033
Delay between onset of sepsis and treatment (referent <1d)					
>5 ds	-1.90	0.86	0.15	0.03 – 0.80	0.027

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criterion for backward elimination was set at $p \leq 0.05$. The only variable found to be associated with an

increased risk of a horse failing to survive to discharge at the multivariable level was a delay of more than 5 days between the onset of sepsis and treatment (Table 13). However, due to the low number of horses that failed to survive to be discharged from the hospital (8/65; 12.3%) the statistical power to detect a significant difference is very small.

Table 13: Multivariable analysis of factors associated with a decreased likelihood of mature Thoroughbred racehorses surviving following treatment for septic arthritis.

	Coefficient	S.E.	OR	95% CI	p
Constant	2.99	0.92			0.001
Delay between onset of sepsis and treatment (referent <1d)					
>5 ds	-2.68	1.23	0.07	0.01 – 0.77	0.030

5.3.5.3. Factors affecting long-term prognosis

Thirty-six horses (55.4%; 95% C.I. 42.5 to 67.7; p=0.457) with septic arthritis started in at least one race following discharge from the hospital. Thus, thirty-six of the fifty-seven horses (63.2%; 95% C.I. 49.3 to 79.6; p=0.063) that were successfully discharged from the hospital went on to start on a racecourse.

Univariable logistic regression analysis did not find that any of the variables investigated were associated with an increased risk of a horse that was successfully discharged following treatment for septic arthritis failing to start on a racecourse (Appendix 5.2).

5.3.5.4. Comparison population

Of the one hundred and twenty horses in the comparison group, 83 (69.2%; 95% C.I. 60.1 to 77.3; $p < 0.001$) subsequently started in ≥ 1 race, with the remaining thirty-seven horses failing to make a start on a racecourse. Sixty-four of those horses were female and fifty-six were male. The sex of the horse did not have a significant effect on whether the horse would start on a racecourse (OR 0.70; 95% CI 0.29 to 1.64; p= 0.37). A retrospective power calculation, with a 5% significance level, showed that with 36/65 (55.4%) horses in the study group starting in a race following resolution of septic arthritis, compared to 83/120 (69.2%) horses in the comparison group, the power of this component of the study to detect a significant difference between the two groups was only 37%. However, even if

the study design had provided significant power to detect a meaningful difference, it could be argued that there may be little clinical significance in the difference in proportions (55.4% and 69.2%) of horses starting on a racecourse.

5.3.5.5. Comparison between study and sibling populations

5.3.5.5.1. Raced prior to septic arthritis

Of the sixty-five horses in the study group, thirty-one horses (47.7%) had started in at least one race prior to the occurrence of septic arthritis. Of these horses, five (16.1%, 95% C.I. 5.0 to 34.0)) were euthanased prior to discharge from the hospital. Of the twenty-six horses successfully discharged from the hospital following resolution of the septic arthritis, eleven horses (42.3%, 95% C.I. 23.0 to 63.0) went on to make at least one subsequent start on a racecourse. Of these eleven horses, only one horse (9.1%; 95% C.I. 2.0 to 41.3) failed to achieve an equal or higher Official Rating awarded by the British Horseracing Board's handicappers, compared to the one allocated to it before the occurrence of septic arthritis. The highest Official Rating achieved by each horse following resolution of sepsis was compared to the highest rating achieved prior to the onset of sepsis using the Wilcoxon signed rank test. The highest rating achieved following resolution of sepsis was not found to be significantly different to that achieved prior to sepsis, with a p-value >0.05, therefore the null hypothesis could not be rejected. However, the limited number of horses available limited the power of the study to detect a significant difference.

5.3.5.5.2. Never raced prior to septic arthritis

The remaining thirty-four horses in the study group (52.3%) were all in training at the time of the occurrence of septic arthritis, but had not made their first start on a racecourse. Of these horses, three were euthanased prior to discharge from the hospital, and of those that were successfully discharged following resolution of the septic arthritis, twenty-five horses (80.6%, 95% C.I. 63.0 to 93.0) went on to make at least one subsequent start on a racecourse. Of the fifty-six siblings in the comparison group for these cases, thirty-seven horses (66%) made at least one appearance on a racecourse. Data analysed using combined regression analysis confirmed that the occurrence of septic arthritis in a mature Thoroughbred racehorse, prior to its first start in a race, did not affect the likelihood that it would make at least one appearance on a racecourse when compared to its siblings (OR

2.75; 95% C.I. 0.72 to 15.6; p=0.11). Of the twenty-five cases that started on a racecourse at least once after discharge from the hospital, four horses failed to achieve an Official Rating either equal or higher to that awarded by the British Horseracing Board's handicappers to its siblings.

When considering the likelihood of those horses that had already raced prior to the onset of septic arthritis returning to the racecourse, compared to the likelihood of those horses that had yet to make their first appearance on a racecourse prior to the onset of septic arthritis starting in a race, the horses that had yet to make their first appearance on a racecourse were significantly more likely to race after resolution of septic arthritis than those that had raced prior to the onset of septic arthritis (OR 0.20; 95% C.I. 0.07 to 0.58; p=0.002).

5.3.5.6. Official Ratings

Of the 36 cases that started in a race after successful treatment for septic arthritis, a general linear model was used to compare the highest Official Rating achieved by those cases in the study group successfully discharged from the hospital that went on to start on a racecourse, with the highest Official Rating achieved by their siblings in the comparison population (Table 14; Appendix 3). Whether a horse was a member of the study or control population was treated as a fixed effect in the model, whilst the code referring a member of the control population to its sibling in the study population was treated as a random effect. The model found that the F-statistic was significant, therefore there was a significant difference between variances in the study and control groups (Table 14). The coefficient indicated that those horses in the study group had, on average, an Official Rating 12.97 points higher than their siblings in the control group (Appendix 6).

Table 14: Comparison of highest Official Rating achieved between study and comparison populations of mature Thoroughbred racehorses, using a General Linear Model.

	Degrees of Freedom	Sequential Sums of Squares	Adjusted Sums of Squares	Adjusted Means Squares	F-test statistic	p-value
Case	1	12090	12567	12567	9.43	0.004
Sibling code	35	70520	70520	2015	1.51	0.093
Error	47	62630	62630	1333		
Total	83	145240				

Where: Case = member of study group; Sibling code = code referring member of control group to sibling in study group; Error = difference between observed value of observation and value predicted by model

5.3.6. Discussion

5.3.6.1. Class of evidence

Although there have been many studies published in the literature on septic arthritis, only a few have reported on the long-term prognosis for those horses successfully discharged from a hospital following resolution of sepsis (Ross *et al.* 1991; LaPointe *et al.* 1992; Schneider *et al.* 1992a). These three studies have all been case series, which would be classified in EBM terms as providing class C evidence using the classification system proposed by Yusuf *et al* (1998). The aim of this study was not merely to add another retrospective study to the literature pool, but to utilise a suitable comparison population, thereby reporting on a study providing a higher class of evidence (class B) than those previously reported.

5.3.6.2. Factors affecting the outcome

Survival rates reported here are similar to those from previous studies (LaPointe *et al.* 1992; Schneider *et al.* 1992a; Meijer *et al.* 2000). The majority of cases were admitted to the hospital by members of the practice rather than being a referral population as described

by previous reports, where it might have been expected that there would be a bias towards more severely affected animals.

The most commonly affected joint in our study was the metatarsophalangeal joint – a small joint with a relatively simple structure. Previous studies have reported a higher incidence of involvement of the larger joints (tibio-tarsal joint) (Schneider *et al.* 1992a; Meijer *et al.* 2000). The only statistically significant finding associated with the joint affected was that involvement of the proximal inter-phalangeal joint was associated with a decreased likelihood of surviving to be discharged from the hospital. This is similar to previously reported findings, where joints that were small, with limited surgical access, were associated with a poorer prognosis for survival (Peremans *et al.* 1991; Honnas *et al.* 1992; Booth *et al.* 2001). Similarly, our study concurred with a previous study (Peremans *et al.* 1991) in that a substantial time delay (at least 5 days in this study) was associated with a decreased likelihood of surviving to be discharged from the hospital. Although it could be expected that a delay between the onset of sepsis and treatment would lead to a poorer prognosis for survival, due to the prolonged exposure of the articular structure to both bacteria and proteolytic enzymes, this finding has only been sparsely reported (Peremans *et al.* 1991). However, the low numbers of horses presented for treatment more than 24 hours after the inciting caurse of sepsis reduces the power of that component of the study.

5.3.6.3. Limitations of the study

Despite the large number of horses included in the study, the retrospective study design, coupled with the fact that many horses received more than one antimicrobial and lavage technique, precludes any conclusions being drawn regarding the relative efficacy of specific treatment modalities. However, the aim of the study was not to compare the relative success associated with one specific treatment, but to investigate the long-term prognosis of horses that had survived until discharge from the hospital, and whether the occurrence of septic arthritis would affect the likelihood of them starting on a racecourse compared to their siblings.

Although many studies have examined the efficacy of different treatment regimens in the management of septic arthritis, no study has focused on such a specific study group, or compared the long-term outcome following treatment for septic arthritis to a suitable control group. All horses admitted to the hospital for treatment of septic arthritis were

matched with two of their siblings of racing age as controls, for comparison of whether they ever started on a racecourse (Mitten *et al.* 1995). Older siblings were selected where possible. Where two siblings of racing age were not available, one sibling was used as a control. Of those horses in the study group that were successfully discharged from the hospital, 63.2% started on a racecourse following treatment for septic arthritis – an almost identical result to the predicted average (5.2.6.1). However, it is impossible to know from medical records and racing records alone how many of these horses were capable of returning to racing but did not for other reasons. This could only be determined by long term follow up through contact with either the owner or trainer. It is possible that bias occurred in the long term follow up, with horses only being returned to training following a potentially expensive treatment for septic arthritis if owners or trainers were confident that they would be successful on a racecourse. Without direct communication with either the owners or trainers it is impossible to establish whether horses were not returned to training, and therefore racing, due to complications directly attributable to the occurrence of septic arthritis or if there was an ulterior motive. Due to the retrospective nature of the study, and the limited case numbers available, the power of this component of the study was low (40%). In order to improve the power of the study a larger study population should be compared with a suitable control group. However, sufficient case numbers may be difficult to recruit without a lengthy study period.

Evaluation of the official rating issued by the British Horseracing Board's handicappers showed that, of the horses that returned to racing, the occurrence of septic arthritis did not prevent horses returning to their best previous rating, or a higher rating. Similarly, over 90% of horses that returned to racing were able to attain a rating either equal to or higher than the highest rating achieved by their siblings. Therefore the occurrence of septic arthritis, whilst decreasing the likelihood that a mature Thoroughbred will return to racing compared to its siblings, does not appear to affect adversely the performance of those horses that do make at least one start on a racetrack after successful resolution of synovial sepsis.

5.3.6.4. Conclusions

The prognosis for survival following early identification and treatment of septic arthritis in this particular population of Thoroughbred racehorses is favourable. If the infection is eliminated from the synovial space, then almost 65% of horses successfully discharged

started in at least one race. In conclusion, the prognosis for starting in a race, following resolution of sepsis, is good.

5.4. Overall Conclusions

Overall, the prognosis for both surviving to be discharged form the hospital, and starting in at least one race, is porr for Thoroughbred neonates treated for septic arthritis. In direct contrast, the prognosis for a mature Thoroughbred racehorse treated for septic arthritis is much better, being described as favourable, or good, for either surviving to be discharged from the hospital or starting in at least one race.

Chapter 6

Incisional complications following exploratory celiotomy: does a belly band reduce the risk?

6.1. Introduction

As the rate of post-operative survival has increased over the last three decades, complications following exploratory laparotomy for abdominal pain in the horse have become more apparent (Freeman *et al*, 2000; French *et al*. 2002). These post-operative complications are coming under increasing scrutiny as their relative importance increases in terms of the overall cost of treatment and the length of time to recovery.

6.2. Complications following exploratory laparotomy

The main postoperative complications documented following colic surgery include (Ducharme *et al*. 1983; Hunt *et al*. 1986; Phillips and Walmsley, 1993; Freeman *et al*. 2000; French *et al*. 2002; Proudman *et al*. 2002; Mair and Smith, 2005a,b):

1. incisional infection, herniation and dehiscence
2. jugular vein thrombophlebitis
3. post-operative ileus
4. recurrent episodes of colic
5. post-operative shock
6. laminitis
7. colitis/diarrhoea
8. septic peritonitis

The nature of post-operative complications identified in these studies was similar, although there was variation in the prevalence of the complications between different studies. Some of this variability may be due to the changes in the peri- and post-operative management of horses undergoing colic surgery, along with the trend towards earlier referral and surgery, which has occurred over the last two decades.

6.2.1. Morbidity associated with complications

Although many post-operative complications are amenable to medical management, some of these complications are potentially life-threatening. The most common causes of euthanasia in the immediate post-operative period include: anastomotic leakage (MacDonald *et al.* 1989); septic peritonitis (Phillips and Walmsley, 1993); post-operative pain (Mair and Smith, 2005a) and shock (Ducharme *et al.* 1983). In some instances of post-operative pain, the decision for euthanasia was based on economic constraints (Mair and Smith, 2005a), instead of proceeding to a repeat laparotomy.

Even with complications associated with low mortality, the increased post-operative morbidity results in an increase in the length of hospitalisation of the patient (Mair and Smith, 2005a,b), both increasing the overall cost of the treatment (Mair and Smith, 2005a,b) and prolonging the eventual return to work. There has also been a direct link recognised between some of the more minor complications, for example incisional infections, and some of the more serious complications, for example incisional herniation (Gibson *et al.* 1989).

For these reasons, much research is now being directed at the identification of risk factors contributing to post-operative complications (Kobluk *et al.* 1989; Roussel *et al.* 2001; French *et al.* 2002; Morton and Blikslager, 2002; Proudman *et al.* 2002), and strategies that may help avoid these complications developing (Galuppo *et al.* 1999; Coomer *et al.* 2005).

6.3. Incisional complications following exploratory laparotomy

6.3.1. Classification of colic surgery

Using the classification system proposed by the Committee on Trauma of the National Research Council (1964), few colic surgeries are classified as clean surgical procedures, with many procedures being classified as clean-contaminated or even contaminated, depending on the lesion identified. With the classification of a procedure as either clean-contaminated or contaminated, the increased likelihood of possible exposure of the incision to a source of contamination is likely to contribute to this increased rate of incisional infections seen after an emergency celiotomy (Phillips & Walmsley, 1993; Honnas & Cohen, 1997).

6.3.2. Incidence of incisional complications

A higher incidence of incisional complications following clean-contaminated emergency surgical procedures has been reported in *Equidae* compared to other species, with rates of 5% (Vasseur *et al.* 1985; Vasseur *et al.* 1988) and 15% (Desrochers *et al.* 1996) reported for small animals and cattle respectively, compared to 24% in horses (Ingle-Fehr *et al.* 1997). Incisional complications, ranging from oedema and drainage to more serious complications including infection and acute dehiscence, occur relatively commonly following exploratory celiotomy (Kobluk *et al.* 1989). Some studies have associated this high incidence rate with intra-operative incisional trauma, primarily from the manipulation and evacuation of the large colon (Phillips and Walmsley, 1993).

6.3.3. Drainage from an incision

Any form of drainage from the celiotomy incision is now frequently considered to be synonymous with incisional infection, even when a bacterial culture of the fluid has not been performed. Previous studies (Kobluk *et al*, 1989; Honnas and Cohen, 1997) have shown that a large proportion of celiotomy incisions that are draining any fluid, be it serous, sero-sanguineous or purulent, will yield a positive bacterial culture.

Incisional drainage may not just be evidence of incisional infection, but can also be a precursor to the more serious incisional complications that could occur (herniation or dehiscence), as previous studies (French *et al.* 2002; Mair and Smith, 2005) have found that these complications have frequently been associated with prior incisional drainage.

6.3.4. Incisional infections

The prevalence of incisional infections after celiotomy incisions in horses is variable, with proportions from 4% (Mair, 2003; Mair and Smith, 2005b), to 9.9% (Kobluk *et al.* 1989), 24% (Ingle-Fehr *et al.* 1997), 25.4% (Honnas & Cohen, 1997) and 27% (Wilson, Baker & Boero, 1995) reported. Although there is wide variation in these figures, there was also a difference in classification of the definition of 'wound infection', ranging from any incisional drainage (Wilson, Baker & Boero, 1995; Ingle-Fehr *et al.* 1997), through purulent incisional drainage with associated heat and pain on palpation (Mair and Smith,

2005b) to positive bacterial culture (Honnas & Cohen, 1997), which may account for some of the variation. Similarly, whilst some studies were restricted to celiotomies for colic (Kobluk *et al.* 1989; Honnas & Cohen, 1997; Mair, 2003; Mair and Smith, 2005b) other studies included all forms of abdominal surgery (Wilson, Baker & Boero, 1995), which would alter the expected rate of incisional complications.

An increased occurrence of incisional complications was also reported following repeat celiotomies (Kobluk *et al.* 1989; Phillips and Walmsley, 1993; Mair, 2003; Mair and Smith, 2005b), from between 57% (Mair and Smith, 2005b) and 87.5% (Kobluk *et al.* 1989) reported.

6.3.5. Risk Factors for Incisional Complications

Many studies have identified risk factors that could contribute to the overall likelihood of incisional complications following exploratory laparotomy, including: manipulation of the gastro-intestinal tract traumatising the incisional edges (McIlwraith, 1978; Phillips & Walmsley, 1993; Honnas & Cohen, 1997); exposure of the incision to potential sources of contamination during either routine enterotomy or gastro-intestinal resection (Phillips & Walmsley, 1993; Honnas & Cohen, 1997); use of certain suture materials when closing the *linea alba*, specifically polyglactin 910 (Honnas and Cohen, 1997) and the development of post-operative endotoxaemia predisposing to infection. Although these have all been identified as potential risk factors, their contribution to the overall incidence of incisional complications has not been either investigated or quantified.

6.3.5.1. Suture Material

Polyglactin 910, a braided suture material, has been reported to be the suture material of choice when closing the abdomen, unless an excessive amount of contamination has occurred (Ducharme, *et al.* 1992). In cases of excessive contamination, it is thought that this multifilament braided material will provide crevices where bacteria can survive and remain protected from both the host immune response, and the effect of any systemic antimicrobials administered.

In one study, the use of polyglactin 910 in the closure of the *linea alba* was associated with a greater number of wound infections using both univariable and multivariable analyses,

when compared to polydioxanone and polyglycolic acid (Honnas and Cohen, 1997). It was proposed that the contamination resulting from an enterotomy may leave sufficient numbers of bacteria remaining in the abdomen to contaminate the suture material, thereby allowing establishment of post-operative wound infections (Honnas and Cohen, 1997).

6.3.5.2. Suture Pattern

The use of a near-far-far-near suture pattern when closing the *linea alba* was reported in one study to be associated with an increased incidence of incisional complications (Kobluk *et al.* 1989). The authors proposed that the dead space created when undermining tissue to place the sutures contributed to this increased occurrence of incisional infection (Kobluk, *et al.* 1989).

A later study that investigated the influence of suture pattern as a factor in the development of incisional infection did not find the use of a near-far-far-near suture pattern statistically associated with an increased incidence of incisonal complications (Honnas and Cohen, 1997. In this study, no undermining of tissues occurred prior to the placement of the sutures, thereby minimising the dead space created at the incision. It was proposed that this lack of dead space when using this suture pattern helped avoid the development of incisonal infection (Honnas and Cohen, 1997). A more recent study (Mair and Smith, 2005b) found that when the fascial tissues were dissected from the *linea alba* prior to closure, the horse was almost four times more likely to experience post-operative wound complications than those where no dissection occurred, although all horses in this study had their *linea alba* closed using a simple continuous suture pattern. This report concurs with the earlier studies (Kobluk *et al.* 1989; Honnas and Cohen, 1997) in which it was proposed that the increased incidence of complications may be associated with the undermining of tissues and creation of dead space, as opposed to the specific suture pattern used.

6.3.5.3. Repeat Celiotomy

Horses that undergo a second laparotomy early in the post-operative period (prior to discharge from the hospital) are recognised to have a significantly higher likelihood of developing post-operative incisional complications than those horses that underwent a single surgical procedure (Kobluk *et al.* 1989; Phillips and Walmsley, 1993; Freeman *et al.*

2002; Mair and Smith, 2005b). It has been proposed that the increased incidence of incisional infection following repeat laparotomy has been caused by the transfer of bacteria from the raw edges of the wound and diminished resistance in the friable and oedematous tissues (Freeman *et al.* 2002).

In one large retrospective study, the prevalence of incisional drainage following a repeat laparotomy was 57%, compared to only 29% following a single laparotomy (Mair and Smith, 2005b). Similarly, the likelihood of developing an incisional hernia increased following a repeat laparotomy, from 7.2% to 25% (Mair and Smith, 2005b).

6.3.6. Means of reducing complications

Previous studies have indicated a number of factors that may contribute to the high prevalence of post-operative complications following exploratory laparotomy. However, no study has evaluated the efficacy of specific strategies to reduce the incidence of incisional complications. It has been suggested that the use of a protective belly band (abdominal bandage) will reduce environmental contamination of the ventral abdominal incision, as well as providing increased support of the incision and a more optimal environment for wound healing, thereby leading to a reduction in the prevalence of post-operative incisional complications. However, to date no prospective study has been designed specifically to investigate this matter.

6.4. Study Aim

The aim of this controlled, randomised study was to test the hypothesis that the use of a belly band following colic surgery through a celiotomy incision would significantly reduce the prevalence of post-operative incisional complications.

6.5. Materials and Methods

6.5.1. Power Calculation

Based on previously published data (Mair and Smith, 2005b), in which the prevalence of incisional complications at Bell Equine Veterinary Clinic following exploratory laparotomy over a ten year period was found to be 26%, the number of horses required for

this study, using a significance level of 5% and a study power of 80%, was calculated using MINITAB®. This revealed that in order to show a significant reduction in the prevalence of complications, so that it was comparable to the complication rate of 5% identified in small animals following clean-contaminated surgery, it would be necessary to have 46 horses in each group, therefore 92 horses in total in the study.

6.5.2. Inclusion Criteria

Horses admitted to Bell Equine Veterinary Clinic between December 2003 and July 2005 were eligible for inclusion in the study if they fulfilled the following criteria:

1. They underwent an exploratory celiotomy for the investigation of abdominal pain
2. They recovered successfully from anaesthesia
3. They were not euthanased prior to discharge from the hospital

Horses that were undergoing a repeat celiotomy prior to discharge from the hospital were excluded from the study.

6.5.3. Randomisation

A table of random numbers was used to generate the randomisation data, for allocation of horses to one of two study groups. Horses either had an Elastoplast belly band applied immediately after recovery from general anaesthesia (study group), or the celiotomy incision was left uncovered, with no further form of intervention following recovery from anaesthesia (control group). All horses were subject to the same peri- and post-operative management.

6.5.4. The belly band

An Elastoplast belly band was used instead of one of the commercial elastic belly bands available, as it has been the author's experience at the clinic that they did not provide a good fit to the majority of the caseload, who encompassed a wide variety of sizes and shapes. The belly band consisted of two gamgee pads, one placed on the ventral midline incision and one on the dorsal spine to protect against pressure sores, before Elastoplast was wrapped around the abdomen, covering the entire length of the incision.

6.5.5. Data collection

The outcomes of interest for the study were: whether there was any evidence of post-operative swelling at the surgical site; any drainage from the surgical site, along with the nature of the drainage; partial or complete dehiscence of the surgical site; pyrexia; and hernia formation, defined for this study as both a palpable and visible defect in the ventral body wall (Appendix 8).

Variables evaluated for each outcome included: age, sex and weight of horse; heart rate and haematocrit at presentation; degree of abdominal pain at presentation and duration of colic signs; duration of general anaesthetic; duration of the surgical procedure; primary lesion identified; anatomical location of primary lesion; length of surgical incision; whether an enterotomy or resection was performed; degree of contamination of the abdomen during surgery; suture pattern used for closure of deep tissues, sub-cutaneous tissues and skin; suture material used in closure of each layer; whether the *linea alba* was lavaged with sterile saline prior to closure of the subcutaneous tissues and skin; whether crystalline sodium benzylpenicillin was applied to the *linea alba* prior to the closure of the subcutaneous tissues and skin; whether a belly band was applied following recovery from general anaesthesia (Appendix 8). Male horses were not routinely catheterised prior to an exploratory laparotomy being performed. In order to prevent urine contamination of the incision, the prepuce was packed with sterile swabs and a purse-string suture pattern used to close the prepuce. Horses had a urinary catheter placed to empty the bladder immediately prior to entering the recovery box.

Data were recorded at four key points during the study (Appendix 7). When horses entered into the study, a pre-operative assessment was carried out, recording the name, signalment and weight of the horse; rectal temperature, heart rate and respiratory rate; evidence of endotoxaemia; degree of abdominal discomfort displayed; duration of colic signs; along with the results of any haematological or biochemical analysis of blood if these were performed (Appendix 7). During the peri- and immediate post-operative period, a surgery report was completed, including such information as the primary lesion identified; anatomical location of the primary lesion whether an enterotomy or resection was performed; degree of contamination of the abdomen during surgery; duration of both general anaesthesia and surgery; length of incision made; the suture materials and suture

patterns used during closure of the individual tissue layers; whether the *linea alba* was lavaged with sterile saline or had crystalline sodium benzylpenicillin applied prior to closure of the subcutaneous tissues and skin (Appendix 7).

Once the horse had recovered successfully from general anaesthesia, it was assessed daily for any of the outcomes of interest in the study (Appendix 7), with a final assessment for any of the outcomes of interest being performed when the horse was discharged from the hospital. The post-operative assessment was not performed by the surgeon involved with the case, but by the team of staff responsible for the daily care of the horse, in order to remove any bias that may have occurred from a surgeon assessing their own work.

6.5.6. Post-operative management

Once the horse had recovered successfully from general anaesthesia, the iodophore impregnated self-adhesive drape (Ioban 2, 3M Health Care) used to protect the incision during the recovery period was removed. Horses that had been assigned to the study group had an Elastoplast belly band applied, and those horses assigned to the control group had no further form of intervention.

In the post-operative period, all horses received a 4 day course of intravenous systemic antimicrobials (sodium benzylpenicillin and gentamicin), supplemented in some cases with oral metronidazole. Intravenous flunixin meglumine was administered for 48 hours post-operatively at 1.1mg/kg, before the dose was reduced for a further 48 hours to 0.25mg/kg. All horses received intravenous fluid therapy for 24 hours post-operatively, supplemented where necessary with either calcium or potassium. Some horses received intravenous hypermune plasma in addition to the fluid therapy, and some horses received intravenous fluid therapy for longer than 24 hours. In some cases, the intravenous fluids were supplemented with the prokinetic drug lignocaine hydrochloride.

6.5.7. Assessment of incision

In the control group, the celiotomy incision was inspected daily, and evidence of any swelling, oedema, pain on palpation, discharge (including the nature of the discharge), dehiscence or herniation was noted. In the study group belly bands were changed 24 hours post-operatively, then every 48 hours until the horse was discharged from the hospital,

unless they required changing sooner due to loosening, slipping, external contamination or strike through. Once the horse had been discharged from the hospital, the belly band was changed after 7 days, and then removed 14 days after discharge. When the belly band was changed, the incision was inspected for any evidence of swelling, oedema, pain on palpation, discharge (including the nature of the discharge), dehiscence or herniation, and the gamgee pad was examined for any evidence of incisional drainage.

6.5.8. Follow-up information

Follow up telephone interviews with the horses' caretakers were conducted at 14 days, 30 days and 3 months post-discharge. At this time, it was ascertained whether there had been any oedema, drainage from the incision (including the nature of the drainage), dehiscence or herniation.

These time points were chosen to reflect both the findings from earlier studies, and the post-operative management of the patients. An earlier study found that the most likely time for the onset of incisional drainage was approximately 2 weeks post-discharge from the hospital (Galuppo *et al.* 1999); therefore assessment of the incision at 14 days post-discharge would allow the assessment of the number of incisions that developed complications in the immediate post-discharge period. Horses were routinely confined to a stable with in-hand walking for the first 30 days post-discharge, before beginning small paddock turnout. At 30 days the skin incision should have healed, although the *linea alba* will not have regained its full strength by this point. The final post-operative assessment was made at 3 months post-discharge, when the skin incision should have completely healed, and it is at this time that horses are beginning to return to light ridden work following their rehabilitation.

6.5.9. Data Analysis

Binary logistic regression was used to analyse these data, as all outcomes of interest were dichotomous. Categorical variables with more than two levels were coded as indicator variables. Analyses were implemented using the statistical software MINITAB (version 13.31).

Univariable logistic regression was used to screen all variables, and from this all variables with a p-value ≤ 0.20 were included in a backward elimination procedure to fit a multivariable model. The inclusion criterion for backward elimination was set at $p \leq 0.05$.

Once the main effects model had been fitted, two-way interaction between variables was assessed. Variable selection was determined by biological plausibility. Assessment between models was obtained using a likelihood ratio test (LRT) with significance set at $p \leq 0.05$. The goodness-of-fit of the models was assessed using the Hosmer-Lemeshow goodness-of-fit test, with the model considered to be a good fit with a p-value > 0.05.

The nature of the incisional discharge (serous, sero-sanguinous, purulent) was considered to be a nominal variable. Therefore, in order to investigate whether the use of a belly band post-operatively influenced the type of incisional drainage seen, nominal logistic regression analysis was used.

A decision analysis was performed to evaluate whether the additional expense of using a belly band outweighed the expense of a horse developing a post-operative incisional infection.

6.6. Results

6.6.1. Descriptive Statistics

Eighty-five horses met the inclusion criteria for the study: 38 in the study group (belly bands) and 47 in the control group (no belly bands). The age of the horses in the study group ranged from 8 months old to 30 years old, and in the control group the age ranged from 8 months old to 32 years old (Table 16). Overall there were 48 male horses in the study (35 in the control group and 13 in the study group) and 37 female horses (12 in the control group and 25 in the study group) (Table 15).

The signs of abdominal discomfort each horse was exhibiting at the time of presentation to the clinic for evaluation were qualified as mild, moderate or severe (Table 15). The duration of signs of abdominal discomfort ranged from 2 hours to 60 days in the study group (see table 16) and from 3 hours to 60 days in the control group (Table 16). On initial

examination, the heart rate ranged from 32 to 96 bpm (Table 16), and the haematocrit from 19.3 to 52.0% in the study group (Table 16). In the control group, the heart rate ranged from 36 to 100 bpm (Table 16), and the haematocrit ranged from 23.1 to 56.0% (Table 16).

An emergency midline laparotomy was performed in all cases for the investigation of abdominal discomfort. At surgery the primary lesion identified involved the large bowel in the majority of cases in both the study and control groups (Table 15). In one case no primary pathology could be identified (Table 15). In the study group the most commonly identified primary lesion was a large colon torsion (Table 15). In the control group no one primary lesion predominated, with the most frequently identified lesions being: large colon torsion; strangulating lesion of the small intestine; and non-strangulating lesion of the small intestine (Table 15). Only one horse overall presented with an inflammatory infiltrate of the bowel wall (Table 15). Three horses (all in the study group) had full thickness biopsy samples of the bowel wall taken during surgery (Table 15), and a further 20 horses had a resection of either the caecum or small bowel performed at surgery (Table 15). The length of resected intestine ranged from 0.2m to 5.5m (Table 16).

The duration of general anaesthesia ranged from 65-180 minutes (Table 16), and the duration of surgery ranged from 40-160 minutes (Table 16) in the study group, and in the control group the duration of general anaesthesia ranged from 60 – 205 minutes (Table 16), and the duration of surgery from 40 – 190 minutes (Table 16). The incision made on the ventral midline ranged from 20 to 35cm in length in the study group, and from 16 to 35cm in the control group. During surgery the degree of contamination of the abdomen and visceral surfaces was assessed by the surgeon and judged to be mild in the majority of cases in both the study and control groups (Table 15), with severe contamination only recorded in one case (Table 15).

The *linea alba* was closed in all cases using double-stranded, 5 metric polyglactin 910, in a simple continuous pattern. In 54 cases (63.5%; Table 15), a sub-cutaneous suture layer was placed, using 3.5 metric polyglactin 910 in a simple continuous pattern, and the skin was closed in all cases using 2 metric polyglactin 910 in a simple continuous pattern. The linea alba was lavaged using a sterile saline solution in 51 cases (60%; Table 15) prior to closure of the sub-cutaneous and skin layers, and in 5 cases (5.9%; Table 15) crystalline sodium benzylpenicillin was applied to the *linea alba* prior to closure of the sub-cutaneous and skin layers.

Table 15: Descriptive variables investigated for an association with an increased risk of the development of post-operative incisional complications following exploratory laparotomy, for both the study and control groups.

	Study Group (n=38)		Control Group (n=47)	
	No.	%	No.	%
Gender				
Male	13	34.2	35	74.5
Female	25	65.8	12	25.6
Level of abdominal discomfort				
Mild	12	31.6	18	38.3
Moderate	13	34.2	16	34.0
Severe	13	34.2	13	27.7
Evidence of endotoxaemia at admission	11	28.9	15	31.9
Location of primary lesion				
Large Intestine	23	60.5	22	46.8
Small Intestine	14	36.8	20	42.6
Caecum	1	2.6	4	8.5
No pathology identified	0	0	1	2.1
Primary lesion identified				
Large bowel displacement	7	18.4	6	12.8
Large colon torsion	15	39.5	7	14.9
Large colon impaction	1	2.6	4	8.5
Physical obstruction of colon	1	2.6	6	12.8
Inflammatory infiltrate of bowel wall	1	2.6	0	0
Entrapment of small intestine in epiploic foramen	3	7.9	6	12.8
Strangulating lesion of small intestine	5	13.2	7	14.9
Non-strangulating lesion of small intestine	5	13.2	7	14.9
Distension and loss of motility with no obvious obstruction	0	0	3	6.4
Full thickness biopsy performed				
Large bowel	2	5.3	0	0
Small intestine	1	2.6	0	0
Resection performed				
Caecum	0	0	2	4.3
Small intestine	6	15.8	12	25.5

Table continued overleaf

Table 15 (continued):

	Study Group (n=38)		Control Group (n=47)	
	No.	%	No.	%
Pelvic flexure enterotomy performed	34	89.5	37	78.7
Degree of contamination of visceral surfaces				
Mild	37	97.4	37	78.7
Moderate	1	2.6	9	19.1
Subcutaneous suture layer placed	25	65.8	29	61.7
Incision lavaged with sterile saline	27	71.1	24	51.1
Crystalline sodium benzylpenicillin applied to incision	4	10.5	1	2.1

Table 16: Descriptive variables of interest for all cases undergoing an exploratory laparotomy for the investigation of abdominal discomfort

	Study Group (n=38)		Control Group (n=47)	
	Median	Inter-quartile Range	Median	Inter-quartile Range
Age (years)	12	6 – 16	9	5 – 16
Duration of abdominal discomfort prior to presentation (hrs)	6	5 – 17	8	6 – 18
Heart rate at presentation (bpm)	51	41.5 – 60	48	40 – 61.5
Haematocrit at presentation (%)	33.7	28.8 – 38.0	32.5	29.3 – 38.55
Length of intestine resected (m)	0.4	0.1 – 0.8	2.0	1.0 – 4.0
Duration of general anaesthesia (mins)	100	80 – 117.50	110	95 – 140
Duration of surgery (mins)	80	60 – 95	85	70 – 115
Length of incision (cm)	30	25 – 30	30	25 – 30

6.6.2. Analysis of data

6.6.2.1. Overall analysis of data

When considering all of the data for the entire follow-up period as one dataset, with the dichotomous outcome of whether the horse developed some form of incisional drainage, acute partial or total incisional dehiscence, or incisional hernia formation, it was found that 12/38 horses in the study group (31.6%; 95% C.I. 17.5 to 48.7), compared to 36/47 horses in the control group (76.6%; 95% C.I. 62.0 to 87.7). It was considered to be a normal finding for horses in both the study and control groups to have a very small volume of sero-sanguinous discharge in the 12 hours immediately following recovery from general anaesthesia. Therefore, as long as there was no further incisional drainage and no other incisional complication developed, these horses were excluded from this analysis.

There was an absolute risk reduction (ARR) of the likelihood of developing a post-operative incisional complication of 45% when using a belly band, compared to not using a belly band in the post-operative period. Therefore, it would be necessary to treat 2.2 horses with a belly band in order to prevent one horse developing any of these unwanted, and potentially both serious and expensive, post-operative incisional complications.

6.6.2.2. Hospitalisation data

6.6.2.2.1. Descriptive Statistics

Complications recorded during hospitalisation included: pyrexia, incisional swelling, incisional drainage and one horse had partial dehiscence of the skin sutures (Table 17). Of the 15 horses that were pyrexic during hospitalisation, 6/15 (40%) also had incisional drainage.

No horse in the study group had an acute dehiscence of the skin incision during hospitalisation (Table 17). Of the five horses that were pyrexic during hospitalisation, two horses (40%) also had incisional drainage. One horse in the control group had acute dehiscence of the skin incision during hospitalisation (Table 17). Of the 10 horses in the

control group that were pyrexic during hospitalisation, seven horses (70%) also had incisional drainage.

At the time of discharge more than 80% of horses had experienced some form of incisional complication (Table 18), with the formation of pitting oedema around the incision being the most common complication (69/85; 81.2%). Incisional drainage had resolved prior to discharge on more than 50% of the cases, with only 21 horses (24.7%) experiencing some form of incisional drainage at the time of discharge from the hospital. Of those horses that were pyrexic during hospitalisation, 6/15 (40%) had drainage from their incision at the time of discharge.

Table 17: Complications recorded during hospitalisation for all horses undergoing an exploratory laparotomy for the investigation of abdominal discomfort

	All Cases (n=85)		Study Group (n=38)		Control Group (n=47)	
	No.	%	No.	%	No.	%
Pyrexia	15	17.6	5	13.2	10	21.3
Swelling	64	75.3	24	63.2	40	85.1
Oedema	69	81.2	25	65.8	44	93.6
Drainage	49	57.6	19	50.0	31	66.0
Serous	*7*	*14.3*	*4*	*21.1*	*1*	*3.2*
Sero-sanguinous	*26*	*53.1*	*9*	*47.4*	*17*	*54.8*
Purulent	*16*	*32.7*	*6*	*31.6*	*10*	*32.3*
Dehiscence	1	1.1	0	0.0	1	2.1
Pain	1	1.1	0	0.0	1	2.1

Incisional complications were recorded in 71.1% of horses in the study group (Table 18). Of the five horses that were pyrexic during hospitalisation, only one horse had incisional drainage at discharge. Of the 19 horses that had some form of incisional drainage during hospitalisation, only five horses (26.3%) still had drainage at discharge, with the majority of these horses (80%) having purulent drainage. Horses that had purulent incisional drainage during hospitalisation were more likely to still have incisional drainage at discharge than those with either serous or sero-sanguineous discharge (p=0.007).

Incisional complications were recorded in 91.5% of horses in the control group (Table 18), including acute dehiscence of the skin incision in one case. When considering the 10 horses that had been pyrexic during hospitalisation, five had incisional drainage at discharge. Of the 31 horses that had some form of incisional discharge during hospitalisation, 51.6% still had incisional drainage at discharge, with the most common type of drainage being purulent (56.3%). Horses that had purulent drainage during hospitalisation were significantly more likely to still have incisional drainage at discharge than those with either serous or sero-sanguinous drainage (p=0.009). The horse that had an acute dehiscence of the skin incision had had purulent drainage from the incision prior to dehiscence.

Table 18: Incisional complications recorded at discharge for all horses undergoing an exploratory laparotomy for the investigation of abdominal discomfort

	All Cases (n=85)		Study Group (n=38)		Control Group (n=47)	
	No.	%	No.	%	No.	%
Swelling	61	71.8	22	57.9	39	83.0
Oedema	63	74.1	24	63.2	39	83.0
Drainage	21	24.7	5	13.2	16	34.0
Sero-sanguinous	*8*	*38.1*	*1*	*20.0*	*7*	*43.8*
Purulent	*13*	*61.9*	*4*	*80.0*	*9*	*56.3*
Dehiscence	1	1.1	0	0.0	1	2.1
Pain	3	3.3	1	2.6	2	4.2

6.6.2.2.2. Factors affecting the likelihood of the development of incisional complications

6.6.2.2.2.1. During Hospitalisation

When considering all the cases in the study, univariable binary logistic regression analysis showed that the only variables associated with an increased risk of a horse developing incisional drainage during hospitalisation were the duration of either the general

anaesthetic or surgery, or the length of the incision. No other variables were found to be significant (Appendix 9.1).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. The only factor that was found to be associated with an increased risk of a horse developing incisional drainage during hospitalisation was the duration of surgery (Table 19).

Table 19: Variables found to be associated with an increased risk of a horse having incisional drainage during hospitalisation following multivariable logistic regression

	Coeffic	S.E.	Adjusted O.R.	95% C.I.	P
Constant	-0.13	0.30			0.66
Duration of surgery (referent <85mins)					
>85mins	1.16	0.47	2.51	1.03 – 6.12	0.043

Univariable nominal logistic regression was performed to investigate whether the use of a belly band would influence the nature of the incisional drainage (serous, sero-sanguinous or purulent). It was found that the use of a belly band during hospitalisation was not associated with the risk of a horse developing incisional drainage, or the nature of that drainage (Appendix 9.2).

Univariable binary logistic regression analysis showed that, when considering all the possible incisional complications together, the use of a belly band significantly reduced the likelihood of a horse having any one incisional complication at discharge from the hospital (Appendix 9.3).

6.6.2.2.2.2. Discharge from the hospital

When considering all the cases, univariable binary logistic regression analysis showed that the variables that were associated with an increased risk of a horse having incisional drainage at the time of discharge from the hospital included: duration of colic prior to

presentation, presence of endotoxaemia, involvement of the small intestine, duration of either general anaesthesia or surgery and length of incision. No other variables were found to be significant (Appendix 9.4).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. The factors that were found to be associated with an increased risk of a horse having incisional drainage at the time of discharge from the hospital were: duration of general anaesthesia; and whether a subcutaneous suture layer was used (Table 20).

Table 20: Variables found to be associated with an increased risk of a horse having incisional drainage at the time of discharge from the hospital, following multivariable logistic regression

	Coeffic	S.E.	Adjusted O.R.	95% C.I.	P
Constant	-1.30	0.49			0.008
Duration of general anaesthesia (referent <110mins)					
>110mins	2.61	0.70	13.67	3.45 – 54.21	<0.001
Subcutaneous suture layer	-1.67	0.71	0.19	0.05 – 0.76	0.019

No two-way interaction terms were found to be significant. The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit.

Univariable nominal logistic regression was performed to investigate whether the use of a belly band was associated with the nature of the incisional drainage (sero-sanguinous or purulent). It was found that the use of a belly band was not associated with the risk of a horse having incisional drainage, or the nature of that drainage, at the time of discharge from the hospital (Appendix 9.5).

6.6.2.3. Fourteen day follow-up data

6.6.2.3.1. Descriptive Statistics

At 14 days post-discharge from the hospital, five of the 85 cases (5.9%) had been euthanased, two from the study group and three from the control group, all due to a recurrence of colic. Follow-up information was available for all of the remaining 80 horses. Incisional complications were still present in 90% of horses. Incisional complications recorded included oedema, drainage and acute dehiscence of the skin incision (Table 21). The skin incision had completely healed in 48.8% of cases, although 30 of these horses (76.9%) still had significant oedema associated with the site of the incision. Of the nine horses that had acute dehiscence of the skin incision, five of these (55.6%) had not had any incisional drainage at discharge.

Incisional complications were recorded in 77.8% of cases in the study group (Table 21). The skin incision had healed completely in 69.4% of cases, although 17 of these (68%) still had oedema associated with the site of the incision. Two of the three horses that had acute dehiscence of the skin incision had a history of incisional drainage at the time of discharge from the hospital.

Table 21: Incisional complications recorded at 14 days after discharge in both the study and control groups.

	All cases (n=80)		Study Group (n=36)		Control Group (n=44)	
	No.	%	No.	%	No.	%
Swelling	3	3.8	2	5.6	1	2.3
Oedema	68	85	26	72.2	42	95.5
Drainage	41	51.3	11	30.6	30	68.1
Dehiscence	9	11.3	3	8.3	6	13.6
Heal	39	48.8	25	69.4	14	31.8

In the control group incisional complications were recorded in all cases (Table 21). The skin incision had completely healed in 31.8% of cases, although 13 of these (92.9%) still had significant oedema associated with the site of the incision. Of the six horses that had acute dehiscence of the skin incision, three had prior incisional drainage recorded at the time of discharge from the hospital.

6.6.2.3.2. Factors affecting the likelihood of the development of incisional complications at 14 days post-discharge from the hospital

Univariable binary logistic regression analysis showed that the variables that were associated with an increased risk of a horse having incisional drainage at 14 days post-discharge included: the duration of colic prior to presentation; length of incision; whether a belly band was used; if the incision had drained during hospitalisation or at discharge, and the nature of that drainage; and if there was oedema associated with the incision either during hospitalisation or at discharge. No other variables were found to be significant (Appendix 9.6).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. Those factors that were found to be associated with an increased risk that a horse would have incisional drainage at 14 days post-discharge included: duration of colic prior to presentation; heart rate at presentation; primary lesion identified; whether a belly band was used; and whether the horse was pyrexic during hospitalisation (Table 22).

No two-way interaction terms were found to be significant. The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit.

Univariable binary logistic regression analysis showed that the only variables that were associated with an increased risk of a skin incision having dehisced by 14 days post discharge were: whether the horse was pyrexic during hospitalisation; whether a subcutaneous suture layer was used; and whether the incision was draining at the time of discharge from the hospital. No other factors were found to be significant (Appendix 9.7).

Table 22: Variables found to be associated with the risk of a horse having incisional drainage at fourteen days post-discharge following multivariable logistic regression.

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	P
Constant	0.66	1.00			0.513
Duration of colic signs prior to presentation (referent <8hrs)					
8-24hrs	2.35	0.91	10.50	1.75 – 62.85	0.010
>24hrs	2.59	1.15	13.29	1.39 – 126.67	0.025
Heart rate at presentation (referent <40bpm)					
>60bpm	3.35	1.13	28.38	3.09 – 260.19	0.003
Primary lesion identified at surgery (referent displacement)					
Large bowel obstruction	-3.68	1.60	0.03	0.00 – 0.58	0.022
Small intestinal strangulation	-3.58	1.39	0.03	0.00 – 0.43	0.010
Use of a belly band	-2.59	0.82	0.08	0.02 – 0.37	0.002
Pyrexic during hospitalisation	2.76	1.21	15.85	1.49 – 168.41	0.022

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. Those factors that were found to be associated with the risk of a skin incision having dehisced by 14 days post-discharge were: whether the primary lesion involved the small intestine; if a pelvic flexure enterotomy was performed; use of a subcutaneous suture layer; and whether the incision was draining at the time of discharge form the hospital (Table 23).

Table 23: Variables found to be associated with the risk of a skin incision having dehisced by fourteen days post-discharge, following multivariable logistic regression.

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	P
Constant	2.39	1.68			0.157
Affected bowel (referent large bowel)					
Small Intestine	-4.18	1.76	0.02	0.00 – 0.48	0.018
Pelvic flexure enterotomy performed	-3.64	1.61	0.03	0.00 – 0.62	0.024
Subcutaneous suture layer	-3.00	1.26	0.05	0.00 – 0.58	0.017
Incisional drainage at discharge	2.34	1.03	10.37	1.37 – 78.31	0.023

No two-way interaction terms were found to be significant. The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit.

Univariable binary logistic regression analysis showed that the variables that were associated with the risk of a skin incision having not healed by 14 days post discharge were: the duration of colic prior to presentation; the length of the incision; whether a belly band was used; whether there had been any incisional drainage either during hospitalisation or at discharge, and the nature of that drainage; and whether there was any oedema associated with the incision either during hospitalisation or at discharge. No other factors were found to be significant (Appendix 9.8).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. The factors that were found to be associated with an increased risk that an incision would not have healed by 14 days post-discharge included: the duration of colic prior to presentation; the heart rate at presentation; the primary lesion identified; whether a belly band was used; and whether the horse had been pyrexic during hospitalisation (Table 24).

Table 24: Variables found to be associated with a decreased likelihood of the skin incision having healed by fourteen days post-discharge, following multivariable logistic regression.

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	P
Constant	-0.66	1.00			0.513
Duration of colic signs prior to presentation (referent <8hrs)					
8-24hrs	-2.35	0.91	0.10	0.02 – 0.57	0.010
>24hrs	-2.59	1.15	0.08	0.01 – 0.72	0.025
Heart rate at presentation (referent <40bpm)					
>60bpm	-3.35	1.13	0.04	0.00 – 0.32	0.003
Primary lesion identified at surgery (referent displacement)					
Large bowel obstruction	3.68	1.60	39.69	1.72 – 916.44	0.022
Small intestinal strangulation	3.58	1.39	35.70	2.33 – 546.16	0.010
Use of a belly band	2.59	0.82	13.28	2.69 – 65.65	0.002
Pyrexic during hospitalisation	-2.76	1.21	0.06	0.01 – 0.67	0.022

No two-way interaction terms were found to be significant in the final model. The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit.

6.6.2.4. Thirty day follow-up data

6.6.2.4.1. Descriptive statistics

A further seven horses (8.8%) had been euthanased by 30 days after discharge from the hospital, five from the study group and two from the control group. Follow-up information was available for all of the remaining 73 cases. Incisional complications recorded at this time included: oedema, drainage, acute dehiscence and formation of granulation tissue where an incision was healing by second intention (Table 25). The skin incision had completely healed in 53.4% of cases, although 32 of these cases (82.1%) still had oedema associated with the site of the incision. Of the 10 cases where the skin incision had dehisced, one horse had formed a large bed of healthy granulation tissue as the wound attempted to heal by second intention.

In the study group the skin incision had completely healed in 74.2% of cases (Table 25), although there was still oedema associated with the site of the incision in 19 cases (82.6%). Of the five horses where the skin incision had dehisced, one horse (20%) had formed a large bed of healthy granulation tissue where the wound was beginning to heal by second intention.

The skin incision had completely healed in 38.1% of cases in the control group (Table 25), although there was still oedema associated with the site of the incision in 13 cases (81.3%). Of the five horses that had acute dehiscence of the skin incision, none of these cases showed evidence of formation of a healthy granulation bed, indicative of the process of healing by second intention.

Table 25: Incisional complications recorded 30 days after discharge in both the study and control groups.

	All Cases (n=73)		Study Group (n=31)		Control Group (n=42)	
	No.	%	No.	%	No.	%
Granulating	1	1.4	1	3.2	0	0
Oedema	63	86.3	24	77.4	39	92.9
Drainage	34	46.6	8	25.8	26	61.9
Dehiscence	10	13.7	5	16.1	5	11.9
Heal	39	53.4	23	74.2	16	38.1

6.6.2.4.2. Factors affecting the likelihood of the development of incisional complications at 30 days post-discharge

Univariable binary logistic regression analysis showed that the variables that were associated with an increased risk of having incisional drainage at 30 days post discharge were: the level of pain on presentation; the duration of colic prior to presentation; the length of the incision; whether the horse was pyrexic during hospitalisation; whether a belly band was used; whether the incision was draining either during hospitalisation, at the time of discharge from the hospital or at 14 days post-discharge, and the nature of the drainage; and whether there was any oedema associated with the incision either during hospitalisation or at discharge. No other factors were found to be significant (Appendix 9.9).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criterion for backward elimination was set at $p \leq 0.05$. Those factors found to be associated with the risk of incisional drainage at 30 days post-discharge included: whether incisional oedema had been present during hospitalisation; whether the incision was draining at the time of discharge from the hospital; and whether the incision was draining at 14 days post-discharge (Table 26).

Table 26: Variables found to be associated with the risk of having incisional drainage at thirty days post-discharge, following multivariable logistic regression.

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
Constant	-4.14	1.45			0.004
Oedema during hospitalisation	2.78	1.39	16.19	1.07 – 244.44	0.044
Incisional drainage at discharge	2.04	0.85	7.67	1.46 – 40.42	0.016
Incisional drainage at fourteen days post-discharge	1.78	0.63	5.95	1.74 – 20.41	0.005

No two-way interaction terms were found to be significant. The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit.

Univariable binary logistic regression analysis showed that the variables that were associated with the risk of the skin incision having dehisced by 30 days post discharge were: the weight of the horse; the duration of colic prior to presentation; whether there was involvement of the small intestine; if a subcutaneous suture layer was used; if there was any purulent incisional drainage during hospitalisation; and whether the skin incision had dehisced by 14 days post-discharge. No other factors were found to be significant (Appendix 9.10).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. The only factors found to be associated with an increased risk of a skin incision having dehisced by 30 days post-discharge was: the weight of the horse; and whether a subcutaneous suture layer had been used (Table 27).

No two-way interaction terms were found to be significant. The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit.

Table 27: Variables found to be associated with an increased risk of the skin incision having dehisced by thirty days post-discharge, following multivariable logistic regression.

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
Constant	-1.98	0.77			0.010
Weight of horse at induction (referent <500kgs)					
>500 kgs	1.95	0.89	7.04	1.24 – 40.00	0.028
Subcutaneous suture layer	-2.04	0.80	0.13	0.03 – 0.62	0.011

Univariable binary logistic regression analysis showed that the variables that were associated with an increased risk of the skin incision having not healed by 30 days post discharge were: the level of pain on presentation; the duration of colic prior to presentation; the length of the incision; whether the horse was pyrexic during hospitalisation; whether a belly band was used; whether there was purulent incisional drainage during hospitalisation, or oedema associated with the incision during hospitalisation; if there was any incisional drainage at discharge and the nature of that drainage; if there was oedema associated with the incision at discharge; and whether there was any incisional drainage evident 14 days post-discharge. No other factors were found to be significant (Appendix 9.11).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. Those factors found to be associated with the risk of a skin incision having not healed by 30 days post-discharge included: degree of pain on presentation; duration of colic prior to presentation; use of a belly band; and whether there had been any incisional drainage at 14 days post-discharge (Table 28).

No two-way interaction terms were found to be significant. The fit of the model was evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the model was a good fit.

Table 28: Variables found to be associated with the decreased likelihood of the skin incision having healed by thirty days post-discharge, following multivariable logistic regression.

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
Constant	2.40	1.06			0.023
Pain on presentation (referent mild)					
Severe	-2.98	1.21	0.05	0.00 – 0.55	0.014
Duration (referent <8hrs)					
8-24hrs	-2.21	0.99	0.11	0.02 – 0.76	0.026
Belly Band	2.16	0.83	8.60	1.70 – 43.58	0.009
Drainage at 14d	-2.49	0.79	0.08	0.02 – 0.39	0.002

6.6.2.5. Three month follow-up data

6.6.2.5.1. Descriptive Statistics

One further horse (1.4%), from the control group, was euthanased between 30 days and 3 months post-discharge from the hospital, and one horse (1.4%), also from the control group, was lost to follow-up. Follow-up information was available for the remaining 71 cases. Incisional complications recorded included: hernia formation, drainage and dehiscence (Table 29). At this time the skin incision had completely healed in 95.8% of cases, with the skin having not healed in only three horses. Two of these horses had formed a healthy bed of granulation tissue as the wound healed by second intention. However, the third horse showed no evidence of granulation tissue formation at this stage, with the wound still draining purulent material. Of the 10 horses that had developed an incisional hernia, nine cases had incisional drainage at 30 days post-discharge, whist the remaining horse had had incisional drainage at 14 days post-discharge.

The skin incision had completely healed in 96.8% of cases in the study group (Table 29), leaving only one case where the incision had yet to heal. This horse still had purulent fluid draining from his wound, with no evidence of granulation tissue formation. Two horses (6.5%) had developed an incisional hernia, both of which had had fluid draining from their incision at 30 days post-discharge.

Table 29: Incisional complications recorded 3 months after discharge in both the study and control groups.

	All cases (n=71)		Study Group (n=31)		Control Group (n=40)	
	No.	%	No.	%	No.	%
Hernia	10	14.1	2	6.5	8	20.0
Drainage	1	1.4	1	3.2	0	0.0
Granulating	2	2.8	0	0.0	2	5.0
Dehiscence	3	4.2	1	3.2	2	5.0
Heal	68	95.8	30	96.8	38	95.0

At this time the skin incision was completely healed in 95% of cases in the control group (Table 29). The remaining two horses no longer had any incisional drainage and both had formed healthy beds of granulation tissue, as the wounds healed by second intention. Eight horses (20%) had developed an incisional hernia, with seven of these horses (87.5%) having a history of incisional drainage at 30 days post-discharge. The eighth horse did not have incisional drainage at 30 days, but incisional drainage had been present at 14 days post-discharge.

6.6.2.5.2. Factors affecting the likelihood of the development of incisional complications at 3 months post-discharge

Univariable binary logistic regression analysis showed that the variables that were associated with an increased risk of the skin incision having failed to heal by 3 months post discharge were: whether there was any dehiscence of the skin incision at either 14 or 30 days post-discharge. No other factors were found to be significant (Appendix 9.12).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. The only factor found to be associated with the risk of the skin incision having failed to heal by 3 months post-discharge was: whether the skin incision had dehisced by 14 days post-discharge (Table 30).

Table 30: Variables found to be associated with the decreased likelihood of the skin incision having healed by three months post-discharge, following multivariable logistic regression.

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	P
Constant	4.13	1.01			<0.001
Dehiscence at 14ds	-3.03	1.30	0.05	0.00 – 0.62	0.020

Univariable binary logistic regression analysis showed that the variables that were associated with an increased risk of the formation of an incisional hernia by 3 months post discharge were: whether there was any dehiscence of the skin incision at either 14 or 30 days post-discharge. No other factors were found to be significant (Appendix 9.13).

A multivariable logistic model was built using backward elimination, with all variables with $p \leq 0.20$ at the univariable level included in the analysis. The inclusion criteria for backward elimination was set at $p \leq 0.05$. The only factor found to be associated with an increased risk of the formation of an incisional hernia by 3 months post-discharge was: whether the incision was draining at 30 days post-discharge (Table 31).

Table 31: Variables found to influence likelihood of formation of incisional hernia by three months post-discharge, following multivariable logistic regression.

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	P
Constant	-3.56	1.01			<0.001
Drainage at 30ds	2.58	1.09	13.12	1.56 – 110.48	0.018

6.6.2.6. Decision analysis

A decision analysis was performed to investigate whether the cost of using a belly band was greater than the cost of the necessary treatment when a horse developed a post-operative incisional infection (Table 32). The assumptions made were that the treatment was for a 500kgs horse, requiring a 5 day course of oral antimicrobials (Norodine and Baytril) in order to resolve an incisional infection.

Table 32: Decision analysis comparing cost of using a belly band with that of the treatment of a post-operative incisional infection.

Problem	Decision	Outcome	Probability	Cost (£)	Probability x Cost (£)	Assumptions for 500kgs horse
	Belly Band	**Incisional infection**	0.32	-2(87.66)-(34.30)-(90.72)-2(30.00)-2(39.50)	-140.59	5ds Norodine (trimethoprim sulphonamide) = £34.30
		None	0.68	-2(87.66)-(30.00)-(39.50)	-166.48	5ds Baytril (enrofloxacin) = £90.72
				Total	**£307.07**	
Incisional infection						Examination fee = £30.00
	None	**Incisional infection**	0.77	-(34.30)-(90.72)-2(30.00)-2(39.50)	-203.30	Visit for veterinary attention= £39.50
		None	0.23	-(30.00)-(39.50)	-15.99	Elastoplast belly band = £87.66
				Total	**£219.29**	

When considering all of the data for the entire follow-up period as one dataset, it was found that 12 of the 38 horses in the study group developed a post-operative incisional complication. Therefore, the probability that a horse would develop a post-operative incisional complication was 0.32. In the control group 36 of 47 horses developed a post-operative incisional complication, resulting in a probability of developing a post-operative incisional complication of 0.77.

The decision analysis showed that the costs incurred when a horse that was wearing a belly band developed an incisional complication were less than those incurred in a horse without a belly band, when taking into consideration the probability of the likely outcomes.

6.7. Discussion

6.7.1. Sample size and Power

The power calculation performed at the outset of the study found that 92 horses were needed, 46 in each group, in order to have sufficient power to detect a statistically significant, clinically meaningful outcome, defined as a reduction in complications from 26% to less than 5%. Although this number was not achieved, the final number of horses enrolled in the study was close to that identified in the original power study. In addition, the magnitude of the difference found for the prevalence of incisional complications between the study and control groups was greater than anticipated in the study design, such that a statistically significant difference was identified between the study and control groups, even though slightly fewer horses were recruited to the study than originally considered necessary.

6.7.2. Using a belly band

The current study has found that using a belly band, although not 100% effective at preventing complications, did reduce both the incidence and the severity of incisional complications following colic surgery. Those horses that had a belly band applied following colic surgery had the risk of developing a post-operative incisional complication reduced by 45%, when compared to those horses that did not have a belly band applied. Expressed in another way, in the parlance of EBM, it would only be necessary to apply a

belly band to 2.2 horses in order to prevent one horse developing post-operative incisional complications.

By 14 days post-discharge, horses in the study group were significantly less likely to have any incisional complications than those in the control group. More specifically, it was found that using a belly band reduced the likelihood of incisional drainage at this time by more than twelve times. In addition, those horses that were wearing a belly band were more than twelve times more likely to have a healed skin incision by 14 days post-discharge than those in the control group. An incision that continues to drain for a prolonged period post-discharge is a complication that is both unsightly and unwanted for the owner, who has already invested a large amount of both time and money in electing to have an exploratory laparotomy performed. In addition, a draining incision may be a precursor to more serious complications such as hernia formation, which can be more than a visible blemish. Once the skin incision has healed, this will protect the deeper tissue layers from contamination and ascending infection.

In order to quantify the advantages of using a belly band further, a cost-benefit analysis should be performed, to answer the question: does the additional expense of a belly band cost less than the additional expense of an incisional infection, with all the associated costs (antimicrobials, veterinary attention), based on the associated probabilities that these events will occur. The decision analysis performed confirmed that the cost of a belly band was less than the cost of treating an incisional infection, even without taking into account the additional cost that could be incurred with more serious complications such as an incisional hernia repair.

In this study the horses had three different belly bands applied during hospitalisation alone, with at least one more applied after discharge. In retrospect, it may not have been necessary to change the belly band so frequently. However, as it was unknown how the use of a belly band would influence the likelihood of developing incisional complications, it was vital to check the incision on a regular basis for the welfare of the horse. In future, the use of a washable, reusable belly band would allow regular inspections of the incision with no increase in cost, provided it proves as effective as those used in this study. However, the commercially available reusable belly bands that have been used in the past at the participating clinic frequently slipped back, exposing the incision to sources of external contamination. They were also a poor fit for many of the horses, which could lead

to urine contamination of the wound and the formation of pressure sores. More companies are now producing washable, reusable belly bands, and with the increased choice on the market there are now more suitable options that are applicable to a wider range of shapes and sizes of horse.

6.7.3. Factors affecting the outcome

6.7.3.1. Factors affecting the likelihood of post-operative incisional complications

Earlier studies have investigated many factors that might influence the likelihood of a horse surviving after undergoing colic surgery, including: duration of colic prior to referral (Reeves *et al.* 1986; Phillips and Walmsley, 1993; Mair and Smith, 2005a); evidence of endotoxaemic shock on presentation (Mair and Smith, 2005a); severity of pain on presentation and heart rate (Morton and Blikslager, 2002; Proudman *et al.* 2002; Mair and Smith, 2005a); duration of surgery (Honnas and Cohen, 1997; Mair and Smith, 2005a); and the nature of the primary lesion identified (Ducharme *et al.* 1983; Pascoe *et al.* 1983; Mair and Smith, 2005a). Only a few of these studies have identified factors that may be associated with the occurrence of post-operative incisional complications (Turner *et al.* 1978; Kobluk, *et al.* 1989; Phillips and Walmsley, 1993; Honnas and Cohen, 1997; Ingle-Fehr *et al.* 1997; French *et al.* 2002; Coomer *et al.* 2005; Mair and Smith, 2005).

Factors that were investigated by these earlier studies to establish whether they influenced the likelihood of the occurrence of post-operative incisional complications included:

1. duration of colic signs (Honnas and Cohen, 1997; French *et al.* 2002), although no relationship between duration of signs and post-operative complications was identified
2. evidence of endotxaemia (Turner *et al*, 1978), where endotoxaemia was recognised to predispose horses to developing post-operative incisional complications
3. involvement of the large intestine and caecum (Phillips and Walmsley, 1993) was associated with an increased incidence of incisional complications
4. performing a pelvic flexure enterotomy, which has been variably reported to either increase (Honnas and Cohen, 1997), or not affect (Kobluk, *et al.* 1989; Phillips and Walmsley, 1993; Mair and Smith, 2005b), the likelihood of a horse developing incisional complications

5. post-operative pyrexia (Ingle-Fehr, *et al.* 1997), where a positive correlation was identified between pyrexia and the development of incisional drainage
6. use of a subcutaneous suture layer (Coomer, *et al.* 2005)

The current study concurred with earlier studies when it found that clinical signs of endotoxaemia at presentation, prolonged duration of general anaesthesia (> 110mins) and post-operative pyrexia were all associated with an increased incidence of post-operative incisional complications. An excessive duration of general anaesthesia has been shown to increase the likelihood of developing incisional complications even in healthy individuals (Romatowski 1989; MacDonald *et al.* 1994; Brown *et al.* 1997; Beal *et al.* 2000). General anaesthesia can induce hypoxia, hypotension and cold, all of which individually are known to cause an increase rate of incisional infections. However, a number of factors will influence the overall length of surgery, including the nature of the lesion identified and the surgical techniques required. In the current study longer durations of both general anaesthesia and surgery were associated with an increased likelihood of developing incisonal drainage. This is probably a reflection of the severity of the lesion identified at surgery, and the degree of manipulation of the gastro-intestinal tract to correct the problem. Pyrexia was associated with an increased likelihood of incisional drainage in the follow-up period, and a decreased likelihood of the incision having healed. Even if the source of the post-operative pyrexia is not an incisional infection, active infections at sites remote from the surgical site have been found to increase the incidence of incisional infections (Romatowski, 1989).

However, unlike the earlier studies, the current study did not find that performing a pelvic flexure enterotomy or use of a subcutaneous suture layer were associated with an increased incidence of incisional complications. In addition, the current study contradicted an earlier study as it found that when the primary lesion identified at surgery involved the small intestine there was an increased likelihood of the development of post-operative incisional complications, compared to lesions involving the large intestine.

The current study identified a relationship between the duration of colic signs prior to presentation and the occurrence of post-operative incisional complications – a relationship which earlier studies failed to identify. Unlike these earlier studies, the current study found that those horses that were presented at the hospital for evaluation within 8 hours of first exhibiting colic signs were significantly less likely to develop incisional drainage or

dehiscence of the skin incision than those horses presented between 8 and 24 hours after first displaying signs of colic, and the skin incision was more likely to have healed by 14 days in those horses presented rapidly.

The current study also found that: those horses whose heart rate was elevated above 60bpm were significantly more likely to experience incisonal drainage and delayed incisional healing in the post-operative period, compared to those horses with a heart rate below 40bpm on presentation; and that those horses that were showing signs of severe pain on presentation were more likely to have longer term incisional complications than those horses showing lesser signs of abdominal discomfort, and there was a decreased likelihood of the incision having healed by thirty days. The delayed healing process and apparently increased likelihood of incisional complications is probable a reflection of the degree of compromise to their cardiovascular status at the time of presentation. Heart rate is also a good reflection of the degree of cardiovascular compromise, therefore you would expect heart rate to influence the outcome in a manner similar to endotoxaemic shock.

6.7.3.2. Incisional complications

Oedema associated with the incision was the most common complication noted after surgery, lasting in nearly all cases (86.3%) for more than 30 days after discharge, even though many of the skin incisions (53.4%) had completely healed by this time.

Incisional drainage that occurred during hospitalisation appeared to be transient in many cases, with more than 50% of those cases resolving prior to discharge from the hospital. However, by 14 days post-discharge the number of horses that had incisional drainage had doubled, with nearly all cases having resolved by 3 months post-discharge. These findings would suggest that the biggest risk period for developing incisional drainage is in the first 2 weeks after surgery, a finding that concurs with that of an earlier study (Honnas and Cohen, 1997). Where horses had purulent incisional drainage, they were more likely to have complications longer into the follow-up period than those with either sero-sanguinous or no drainage (Appendices 7 and 10). Purulent incisional drainage in the early post-operative period was also associated with an increased likelihood of dehiscence of the skin incision (Appendix 11) and incisional hernia formation (Appendix 14).

6.7.4. Incisional drainage

By 14 days post-discharge, 51% of horses still had incisional drainage, with 46% of these incisions still draining at 30 days post-discharge. However, in the study group only 31% of horses had incisional drainage at 14 days post-discharge, compared to 68% in the control group, and by 30 days only 26% of horses in the study group had incisional drainage, compared to 62% in the control group.

Following univariable analysis, using a belly band was found to significantly reduce the likelihood that the incision would be draining at either 14 or 30 days post-discharge from the hospital. If the incision is not draining, there is no need for systemic antimicrobials, thereby reducing the cost to the client and protecting the horse from the possible unwanted side-effects of long-term antimicrobial use.

6.7.5. Incisional healing

Once the skin incision has healed, it provides an impermeable barrier to protect the deeper tissues against ascending infection and contamination. By 14 days post-discharge from the hospital the skin incision was completely healed in almost 50% of cases (Table 21). However, when considering those horses in the study group, almost 70% of the skin incisions had healed, compared to only 30% in the control group. Multivariable analysis found that, when considering all other factors, using a belly band increased the likelihood of a skin incision having healed by 14 days post-discharge by more than twelve times.

Following univariable analysis, using a belly band was found to increase the likelihood of a skin incision having healed by either 14 or 30 days post-discharge.

6.7.6. Hernia Formation

This study concurred with earlier studies (Mair and Smith, 2005b) where it was found that those horses that had incisional drainage were significantly more likely to develop an incisional hernia. However, this study only found incisional drainage at either 14 or 30 days post-discharge to be a significant factor in whether a hernia would develop. Horses that had incisional drainage either during hospitalisation or at discharge were not more

likely to develop a hernia than those with no drainage, unless the drainage was purulent in nature. The current study also found that a longer duration of anaesthesia increased the likelihood of hernia formation. Whilst there would not appear to be a direct link between general anaesthesia and hernia formation, it is worth noting that the length of anaesthesia was also a significant factor in the development of incisional drainage either during hospitalisation (Appendix 2) and at discharge (Table 20). Excessive duration of general anaesthesia has also been reported to delay the healing of incisions (Chapter 7) which could contribute to incisional hernia formation.

6.7.7. Study limitations

Although this was both a randomised and controlled trial, there were still substantial limitations to the study. Whilst the horses remained hospitalised, their care and assessment could be standardised. However, once the horses had been discharged there was a heavy reliance on owner compliance when following post-operative care instructions. To illustrate this point it may be worth noting that one of the horses in the study group was turned out early in the rehabilitation period, leading to soiling of the belly band and subsequent fly strike of the incision. This resulted in the development of purulent drainage and dehiscence of the skin incision. If the owner had followed the post-operative care instructions it is highly unlikely that this would have been the eventual outcome. Similarly, one horse was euthanased on the advice of a referring veterinarian as it had developed a purulent incisional discharge. Outcomes such as these highlight the need for further education of both clients and veterinarians in the management of horses following colic surgery, along with the possible complications that may occur. These cases highlight the fact that in spite of a careful study design, providing what would be classified as class A evidence using the system proposed by Yusuf *et al.* (1998), events beyond the control of the study can have an effect on the final outcome.

6.7.8. Class of evidence

Until now, there has only been one published study investigating the efficacy of a specific strategy to reduce the incidence of incisonal complications following colic surgery (Coomer *et al.* 2005), and this only featured preliminary results. Many earlier studies have been retrospective analyses of case records, attempting to identify factors that may contribute to either the survival rate or post-operative complication rate in horses following

colic surgery (Kobluk *et al.* 1989; Phillips and Walmsley, 1993; Honnas and Cohen, 1997; Mair and Smith. 2005). Whilst identifying important areas for future research, these studies do not provide such robust evidence as that which can be generated by prospective studies. Therefore, in EBM terms they are considered to be a relatively poor class of evidence (class C) (Yusuf *et al.* 1998).

The current study would be considered to provide class A evidence (Yusuf *et al.* 1998), although it was not possible to introduce blinding into the study design.

6.7.9. Conclusion

Although incisional complications continue to be a problem following an exploratory celiotomy for colic, the proportion of horses affected and the severity of the complications appear to be significantly reduced by the use of a belly band. There was an absolute risk reduction in the likelihood of developing post-operative incisional complications of 45% when using a belly band in the post-operative period, compared to those cases where no belly band was used.

Chapter 7

Investigation into the prevalence of post-operative complications following elective surgical procedures.

7.1. Introduction

Drainage from an ostensibly clean surgical incision is an unwanted sequel to any surgical procedure, both for the surgeon and the patient (Romatowski, 1989). It has long been recognised that surgical intervention in animals can have associated complications, ranging from anaesthetic complications to problems directly associated with the surgical procedure. Incisional infections are one of the most common complications associated with elective surgical procedures in animals (Orsini, 1992; Speirs, 1992), despite rigid adherence to aseptic techniques, and many clients will attribute this unsatisfactory outcome to carelessness on the part of the surgeon (Romatowski, 1989), regardless of whether the actual procedure was a success.

Infection has been defined as "the successful attachment and multiplication of micro-organisms on or within a host that result in a measurable host response" (Trostle & Hartmann, 1992). The majority of studies in human surgery that have investigated the occurrence of surgical infections have focused primarily on the development of incisional infections, using large scale epidemiological surveys to allow physicians to quantify risk factors for infection in a wide range of surgical procedures (Romatowski, 1989). An overall infection rate of 4.7% has been reported, with a rate of 1.5% reported for clean surgical procedures in one prospective study of 62,939 wounds (Cruse & Foord, 1980). Other studies have reported comparable rates of 1.6% and 1.9% for clean surgical procedures (Leissner, 1976; Olson *et al.* 1984). Due to the large number of animals required, and financial constraints, such large-scale studies have not been performed in small animal surgery (Romatowski, 1989; Brown *et al.* 1997), although the limited studies that are available report incisional infection rates that are comparable to those reported for human medicine - $\leq$ 2.5% - 4.8% for clean surgical procedures (Vasseur *et al.* 1985; Vasseur *et al.* 1988; Brown *et al.* 1997; Beal *et al.* 2000) and an overall rate of 5.1% - 5.5% (Vasseur *et al.* 1985; Vasseur *et al.* 1988; Brown *et al.* 1997). Although much research has been conducted on specific problems in small animals, little has been reported

in the equine literature, with the majority of reports focusing on complications associated with emergency celiotomies and different types of colic surgery (Kobluk *et al.* 1989; Honnas & Cohen, 1997; Ingle-Fehr *et al.* 1997), where it has been recognised that the development of an incisional infection will significantly increase the likelihood of the subsequent development of an incisional hernia (Gibson *et al.* 1989; Honnas & Cohen, 1997; Ingle-Fehr *et al.* 1997; Mair, 2003). The incidence of incisional infections has been sparsely reported in elective equine surgery, with rates of 1.43% - 8.1% reported for clean surgical procedures (Macdonald *et al.* 1994; Smith & Ross, 2002). Studies considering the incidence of infection for celiotomy incisions have reported rates of between 4% - 25.4% (Kobluk *et al.* 1989; Honnas & Cohen, 1997; Ingle-Fehr *et al.* 1997; Mair, 2003). However, no differentiation is made between clean, clean-contaminated or contaminated procedures, which would also be expected to influence the infection rates.

Although extrapolation from data from the human to the veterinary literature may not be precisely appropriate, surgical infection control techniques that have been developed in human hospitals are applicable across the species (Romatowski, 1989). A number of factors have been found in the human literature to influence the occurrence of incisional infections, including malnutrition, obesity, old age and active infection at sites distant from the surgical incision (Romatowski, 1989).

7.2. Surgical wound classification

In 1964, a committee appointed by the National Research Council defined four general categories of surgery, based on the expected degree of bacterial contamination, ranging from clean surgery to dirty surgery. A clean surgical procedure was defined as: "an elective procedure in which the wound is closed to heal by primary intention and without mechanical drainage, trauma, inflammation, or break in aseptic technique. The respiratory, alimentary, genitourinary, and oropharyngeal tracts are not entered." A clean-contaminated procedure is where: "the surgeon enters the respiratory, alimentary, or genitourinary tract under controlled conditions and without unusual contamination."

If all other factors are equal, the incidence of wound infection would be expected to increase as the degree of bacterial contamination increased (Romatwoski, 1989; Holmberg, 1985; Laitinen, 2001). It has been established that there is excessive variation within these broad categories, as surgical procedures within the same category can vary widely in their

associated post-operative infection rates (Vasseur *et al.* 1985; Vasseur *et al.* 1988; Romatowski, 1989; Macdonald *et al.* 1994; Brown *et al*, 1997). However, these categories provide vital information for a wound infection surveillance programme, and results of surveys can provide benchmark data for future comparison (Vasseur *et al.* 19895; Romatowski, 1989; Brown *et al*, 1997).

All surgical wounds, despite the best aseptic techniques, are invariably contaminated to some degree, but only a small percentage of these wounds become infected, as a healthy patient is able to resist the attempts of bacteria to grow in living tissue (Hackett *et al.* 1983; Romatowski, 1989).

7.3. Wound healing

7.3.1. Host response to a wound

The basic response to any wound is the inflammatory process – a cascade of events initiated by the injury (Silver, 1982; Lees *et al.* 1989). The predominant cells in the early stages of inflammation are polymorphonuclear leukocytes, whose primary role is the destruction of any infective organisms (Silver, 1982). In a clean wound these can effectively eliminate bacteria within four hours (Silver, 1982; Lees *et al.* 1989), when they will then be superseded by monocytes and macrophages, which have a wider range of functions than polymorphs, playing an essential role in wound healing (Silver, 1982). Necrotic tissue and foreign material is phagocytosed and removed from the wound (Lees *et al.* 1989; Johnston, 1990) by the macrophages, or multinucleate giant cells formed by coalescence of monocytes (Johnston, 1990), although if organisms or debris are lying within large masses of dead tissue they will be protected from the action of these cells (Lees *et al.* 1989; Johnston, 1990). In surgical incisions, surrounding tissue trauma must be minimised, in order to prevent non-viable tissue acting as a reservoir for bacterial proliferation (Johnston, 1990).

Once haemostasis has been achieved, the primary objective of wound healing is to re-establish the integrity of the epidermis (Silver, 1982) – not only is it important in forming a barrier to prevent the evaporation of water, but it also forms a barrier to the entry of organisms (Silver, 1982). In a simple incision with little dead space or dehydration of

tissues, the epithelial cells will migrate directly across the wound under the scab, joining up with cells migrating in from the other side (Silver, 1982). Depending on the size of the wound, this process can be complete within thirty-six hours (Silver, 1982). If there is an open wound, where dehydration of the surface tissue has occurred, the epithelial cells must cut through the underlying dermal connective tissue (Silver, 1982) – a process which is both energy consuming and slow (Silver, 1982). The cell migration rate, as it is an energy-dependant process, will also vary according to the supply of oxygen available (Silver, 1982; Johnston, 1990). In tissues, if the blood supply is inadequate due to trauma, cell migration rates will be significantly reduced (Silver, 1982; Johnston, 1990).

In a surgical wound, especially if it has been sutured, the same steps in wound healing occur (Johnston, 1990), although as there is minimal dead space, minimal tissue damage and good approximation of the wound edges healing is much more rapid (Johnston, 1990). Minimal debridement of the wound by inflammatory cells is required before epithelial cells are able to migrate across the intra-incisional clot beneath the scab (Johnston, 1990).

7.3.2. Inhibition of wound healing

A number of factors can affect the rate of wound healing. Hard exercise and other stresses will reduce the rate of wound healing, by increasing the concentrations of circulating glucocorticoids and by mechanical breakdown of newly formed collagen with resultant pulling open of the wound (Silver, 1982). Cold will also have a negative effect on the rate of wound healing, by causing a reduction in the metabolic rate and vasoconstriction, therefore reducing the blood supply to the wound (Silver, 1982; Johnston, 1990; Beal *et al.* 2000). Hypovolaemia will exert a similar influence (Silver, 1982; Lees *et al.* 1989; Johnston, 1990). In animals mechanical irritation through self-trauma is an important consideration, as it will prolong the inflammatory response (Silver, 1982), necessitating either good bandaging, or restraint of the animal. Nutrition is also important at both extremes of the scale, with delayed wound healing evident in both obese and malnourished animals (Silver, 1982; Lees *et al.* 1989; Johnston, 1990; Brown *et al.* 1997).

Local tissue injury will affect the rate of wound healing (Johnston, 1990). Although some trauma is inevitable, an excess of trauma to the tissues will increase the amount of debris that must be removed by phagocytosis and will decrease the activity of the phagocytic cells

(Johnston, 1990). The inflammatory phase of healing will be prolonged, with an increase in the possibility of the development of infection (Johnston, 1990). Excessive tissue trauma will also promote the formation of seromas and haematomas between the tissue layers, preventing proper apposition of the tissues and interfering with the blood supply to the wound edges (Johnston, 1990). Seromas and haematomas allow bacterial proliferation, whilst inhibiting the normal host response to bacteria. Prolonged exposure of tissues, associated with a long surgical time, will result in dessication of the tissue and delayed healing (Johnston, 1990) – this is thought to be a contributing factor in the increased incidence of incisional infections that are seen in long operative procedures (Johnston, 1990; Brown *et al.* 1997). The experience of the surgeon has been shown to have a significant effect on the incidence of wound infections, with the rate of infection decreasing as the surgeon's experience increases (Vasseur *et al.* 1988; Hofmann *et al.* 1999). It is thought that surgical experience results in a decrease both in local tissue trauma and duration of surgery (Vasseur *et al.* 1988; Hofmann *et al.* 1999).

Old age has been recognised in human surgery to have a negative effect on the rate of wound healing, thereby increasing the likelihood of the development of an incisional infection (Lees *et al.* 1989; Romatowski, 1989). It is an area that has been poorly investigated in veterinary surgery, although it is a risk factor cited in many veterinary surgical textbooks. In the only study in the veterinary literature where it was investigated as a risk factor, a statistically significant difference in wound infection rates with respect to age of the animal was not reported (Brown *et al.* 1997). No data have been reported in the equine literature on the influence of age on the incidence of incisional complications.

It has long been recognised that the presence of infectious organisms in a wound will have a deleterious effect on the rate of repair of that wound. These organisms should be killed off by the polymorphs and phagocytes, which are attracted to the wound in the early stages of inflammation and wound healing. If these organisms survive and multiply they inhibit healing by (Silver, 1982):

1. stimulating excessive inflammatory exudates leading to waterlogging tissues; consuming oxygen vital to tissue repair
2. attracting excessive numbers of phagocytic cells, which not only deplete the available oxygen levels but also release lytic enzymes causing further tissue destruction
3. produce toxins which kill cells directly

4. inhibiting epithelialisation by killing epithelial cells and washing them off the wound surface through excessive exudates.

General anaesthesia can induce hypoxia, hypotension and cold, all of which are known individually to cause an increased rate of incisional infections. Excessive depth of anaesthesia, or prolonged total anaesthetic time (Romatowski, 1989; Macdonald *et al.* 1994; Brown *et al.* 1997; Beal *et al.* 2000) will contribute to an increased rate of incisional infection.

7.3.3. Sources of bacterial contamination

Bacteria causing wound contamination can be either endogenous or exogenous in origin (Galuppo *et al.* 1999). Endogenous factors include resident and transient bacterial flora of the skin (Galuppo *et al.* 1999). Bacterial virulence and host resistance are also considered endogenous factors (Galuppo *et al.* 1999). Exogenous factors include operating room contamination, recovery room contamination and surgical site preparation (Galuppo *et al.* 1999).

Although endogenous bacteria are widely reported as being the predominant cause of incisional infections (Osuna *et al.* 1990), studies have shown that positive cultures from incisional and intra-operative swabs do not show a good correlation with the subsequent development of infection (Holmberg, 1985; Ingle-Fehr *et al.* 1997; Whittem *et al.* 1999).

7.3.4. Routes of infection

The basic tenets of aseptic surgery – disinfection of both the surgeon and the surgical site, sterilisation of instruments, sterile technique – have been established in human surgery since 1895. This had led, by the 1910s, to the reduction of surgical infection rates at some institutions to a level equivalent to those reported today in the medical literature (Romatowski, 1989). Largely due to economic considerations, aseptic technique was not adopted in the veterinary profession until the mid-1940s in small animal surgery (Romatowski, 1989), with large animal surgery lagging behind still further. With strict adherence to the principles of surgery, contamination of the wound can be minimised, therefore removing the reliance on antimicrobials.

The condition of the wound at the end of surgery and the degree of bacterial contamination that has occurred are the primary determinants for post-operative infection (Honnas & Cohen, 1997). Traumatic tissue handling, excessive use of electrocautery causing charring, inappropriate selection of suture materials and inadequate haemostasis leading to haematoma formation are among the factors that reduce resistance to infection. They all result in increased dead space between the tissue layers of the wound and excessive loss of potentially viable tissue (Kobluk *et al.* 1989; Honnas & Cohen, 1997), increasing the likelihood of the development of wound infection (Kobluk *et al.* 1989; Honnas & Cohen, 1997). Traumatised tissue will support bacterial growth, whilst having impaired host defences, along with a reduced oxygen content promoting the proliferation of anaerobic bacteria.

7.3.5. Natural host resistance to infection

Whether bacteria in a wound cause infection depends on the number and type of microorganisms present (Hackett *et al.* 1983; Holmberg, 1985; Kobluk *et al.* 1989; Lees *et al.* 1989; Trostle & Hartmann, 1992; Honnas & Cohen, 1997), as well as on the local and general resistance of the patient (Hackett *et al.* 1983; Kobluk *et al.* 1989; Lees *et al.* 1989; Trostle & Hartmann, 1992; Honnas & Cohen, 1997), and the degree of tissue destruction present (Kobluk *et al.* 1989; Honnas & Cohen, 1997). In order for infection to develop in a closed wound, not compromised by other systemic or local factors, a minimal number of bacteria must be present (Hackett *et al.* 1983; Lees *et al.* 1989), with 10^5 or more organisms/g of tissue being the critical tissue level of viable bacteria necessary to cause infection (Hackett *et al.* 1983; Lees *et al.* 1989).

Normal host defence mechanisms are a combination of humoral factors present in the wound fluid and phagocytic cells that migrate into the wound. The wound fluid is a serosanguinous exudate that contains antimicrobial substances which have been shown to inhibit the growth of bacteria. However, an excess of this wound fluid will also promote the incidence of post-operative infection, as it hinders migration of phagocytic cells. The phagocytic cells are the single most important host defence against incisional infection.

7.4. Celiotomy incisions in horses

The prevalence of incisional infections after celiotomy incisions in horses is variable, with rates of 4% (Mair, 2003), 9.9% (Kobluk *et al.* 1989), 24% (Ingle-Fehr *et al.* 1997), 25.4% (Honnas & Cohen, 1997) and 27% (Wilson, Baker & Boero, 1995) reported. Although there is wide variation in these figures, there was also a difference in classification of the definition of "wound infection", ranging from any incisional drainage (Wilson, Baker & Boero, 1995; Ingle-Fehr *et al.* 1997) to positive bacterial culture (Honnas & Cohen, 1997), which may account for some of the variation. Similarly, whilst some studies were restricted to celiotomies for colic (Kobluk *et al.* 1989; Honnas & Cohen, 1997; Mair, 2003) other studies included all forms of abdominal surgery (Wilson, Baker & Boero, 1995), which would alter the expected rate of incisional complications. An increased incidence of incisional complications was also reported following repeat celiotomies (Kobluk *et al.* 1989; Mair, 2003), although only one study gave a numerical value to the increased incidence, with a rate of 87.5% (Kobluk *et al.* 1989) reported.

Few colic surgeries are classified as clean surgical procedures, with many being classified as clean-contaminated or contaminated procedures. The possible exposure of the incision to a source of contamination, along with trauma to the incisional borders caused during exteriorisation and manipulation of the gastro-intestinal tract, are likely to contribute to this increased rate of incisional infection (Phillips & Walmsley, 1993; Honnas & Cohen, 1997). Depending on the type of lesion discovered during an exploratory celiotomy, colicking horses are often sick and endotoxaemic, which will also increase the likelihood of the development of an incisional infection.

7.5. Post-operative pyrexia

It has been reported in the human literature that development of a post-operative fever is a positive predictor of bacterial infection (Mellors *et al.* 1988), with a likelihood of 16% of incisional infection with the occurrence of post-operative fever (Mellors *et al.* 1988). The occurrence of post-operative pyrexia has only been reported in one study in the equine literature, where a positive correlation was found between post-operative pyrexia and the development of incisional drainage (Ingle-Fehr *et al.* 1997). It was reported that 62% of horses that underwent a ventral midline celiotomy became febrile during their hospitalisation (Ingle-Fehr *et al.* 1997). Of those horses that became pyrexic during

hospitalisation, 29% subsequently developed incisional drainage (Ingle-Fehr *et al.* 1997). Although multiple factors were put forward as the possible cause of this pyrexia, no investigation was performed to identify if these suggestions were accurate (Ingle-Fehr *et al.* 1997).

7.6. The prophylactic use of antimicrobials in clean surgical procedures – a contentious issue

7.6.1. The use of antimicrobials

The prophylactic use of antimicrobials in clean surgical procedures remains a controversial point in small animal veterinary surgery (Holmberg, 1985; Vasseur *et al.* 1985; Whittem *et al.* 1999). Whilst large, prospective studies in human surgery have established that antimicrobial prophylaxis is not routinely necessary in clean surgical procedures (Vasseur *et al.* 1985), and can in fact be detrimental (Vasseur *et al.* 1985; Lizan-Garcia *et al.* 1997), conflicting data has been reported in the veterinary literature (Holmberg, 1985; Vasseur *et al.* 1985; Whittem *et al.* 1999). Improper use of prophylactic antimicrobial therapy has been observed to contribute to the development of superinfections, resistant bacterial species and nosocomial infections (Holmberg, 1985; Van den Bogaard & Weidema, 1985; Vasseur *et al.* 1985). Although several reports in the veterinary literature concurred with the finding that routine use of antimicrobial prophylaxis in clean procedures was unnecessary (Holmberg, 1985; Vasseur *et al.* 1985; Brown *et al.* 1997), few controlled studies have been reported (Holmberg, 1985; Vasseur *et al.* 1985) and the theory remains controversial (Whittem *et al.* 1999). The limited number of studies that have compared the prevalence of incisional infections in clean procedures, both with and without antimicrobial prophylaxis, have found both for (Holmberg, 1985; Vasseur *et al.* 1985) and against (Vasseur *et al.* 1988; Whittem *et al.* 1999) this theory, with different studies reporting a widely variable prevalence of incisional infection (Holmberg, 1985; Vasseur *et al.* 1985; Whittem *et al.* 1985). In the equine literature no controlled studies have been performed to investigate the incidence of incisional infection in clean surgical procedures without the use of prophylactic antimicrobials. All surgical centres that have published data routinely use prophylactic antimicrobials for all surgical procedures, although the antimicrobial protocols employed vary between the institutions.

Numerous studies in human surgery have confirmed the significant reduction in wound infection associated with the prophylactic use of antimicrobials in clean-contaminated surgical procedures (Romatowski, 1989).

7.6.2. Potential side effects associated with prophylactic antimicrobial use

The prophylactic use of antimicrobials is not without its risks (Van den Bogaard & Weidema, 1985). Side effects include drug toxicity, allergic reactions and the evolution of bacterial resistance (Van den Bogaard & Weidema, 1985; Rosin *et al.* 1993). Superinfection by resistant strains, as well as non-susceptible bacteria, has also been reported (Van den Bogaard & Weidema, 1985). In both human and small animal surgery it has been recommended that, where prophylactic antimicrobials are used, careful selection and dosage of antimicrobials should be employed (Van den Bogaard & Weidema, 1985; Rosin *et al.* 1993), targeting the antimicrobial at the suspected bacterial contaminants and utilising as narrow a spectrum of antimicrobial as possible (Van den Bogaard & Weidema, 1985; Rosin *et al.* 1993). The antimicrobials should also be used for a short period of time only – twenty-four hours is a time period that has frequently been cited in the literature (Van den Bogaard & Weidema, 1985; Whittem *et al.* 1999).

Whilst reactions have been documented in the equine literature to specific antimicrobials (Baker & Leyland, 1973; Cook, 1973; White & Prior, 1982; Blue *et al.*1987; Dick & White, 1987; Sweeney *et al.* 1991; Mahrt, 1992; McConnico *et al.* 1992; Riond *et al.* 1992; van Duijkeren *et al.* 1994), little appears to have been reported as to the prevalence of adverse reactions to prophylactic antimicrobials used during clean surgical procedures. Adverse reactions that have been reported in commonly used antimicrobials include severe colitis following oxytetracycline administration (Baker & Leyland, 1973; Cook, 1973; White & Prior, 1982); local irritation after intra-muscular administration of ceftiofur sodium (Mahrt, 1992); severe cardio-vascular abnormalities, collapse and death after administration of doxycycline (Riond *et al.* 1992); cardiac irregularities and sudden death following intravenous administration of trimethoprim-sulphonamide (Dick & White, 1987; van Duijkeren *et al.* 1994); inappetance associated with oral metronidazole (Sweeney *et al.* 1991); and immune-mediated haemolytic anaemia associated with administration of penicillin (Blue *et al.* 1987; McConnico *et al.* 1992; Robbins *et al.* 1993).

7.7. Conclusion

The integrity of an incision remains a vital factor in the recovery of a horse from any surgical procedure. Little information is currently available in the equine literature regarding the incidence of incisional infections, and any risk factors that may increase the occurrence of what is a potentially life-threatening complication (Kobluk *et al.* 1989; Honnas & Cohen, 1997).

7.8. Study aims

Due to the lack of information on the subject of complications following elective equine surgery in the literature to use as a suitable comparison, a true clinical audit could not be performed. The purpose of this study, therefore, was to investigate the elective surgical case load at three private surgical facilities, in order to identify risk factors that may predispose horses to developing incisional complications. If any alterable perioperative risk factors could be identified, steps could then be taken to decrease the development of incisional drainage and infection. An additional aim of this study was to provide benchmark data for future comparison, and identify and complications associated with prophylactic antimicrobial use.

7.9. Materials and Methods

7.9.1. Inclusion criteria

Any horse admitted to the three participating private equine hospitals during the study period for an elective surgical procedure under general anaesthesia that fulfilled all of the inclusion criteria, were eligible for inclusion in the study. The study period of interest was from the 1st October 2003 until the 30th September 2004. The risk period under investigation was from the time that the surgical procedure was performed until the horse was discharged from the hospital.

The inclusion criteria for this study were:

1. the surgical procedure had to be considered elective and, for the purpose of this study, 'elective' was defined as a procedure that could be postponed up to twenty-four hours without having a detrimental effect on the outcome

2. the procedure had to be performed under general anaesthesia
3. there had to be at least one full thickness skin incision, although this incision did not have to have a primary closure
4. the skin at the surgical site must be intact and free from any gross pathology prior to the induction of anaesthesia
5. there must be no evidence of concurrent systemic infection or localised infection at the surgical site.

Prior to the commencement of the study, all surgical procedures were defined by an equine surgeon as either clean or clean-contaminated; and if any degree of post-operative swelling or incisional drainage was considered normal for a particular procedure this was identified, with the amount of expected swelling or drainage quantified.

7.9.2. Data collection

The outcomes of interest for the study were (Appendix 11):

1. whether there was any evidence of post-operative swelling at the surgical site, and whether this could be considered a normal finding for that procedure
2. any drainage from the surgical site, along with the nature of the drainage, and whether this was a normal or abnormal finding for this procedure
3. partial or complete dehiscence of the surgical site
4. pyrexia
5. diarrhoea
6. catheter site infection or jugular thrombus formation associated with an intravenous catheter.

Variables evaluated for each outcome included (Appendix 11):

1. age, sex and weight of horse
2. haematological abnormalities prior to induction
3. whether the surgical site was clipped prior to induction, and if so how long before induction
4. whether the surgical site was shaved at preparation
5. if there was evidence of a local skin reaction after preparation of surgical site
6. duration of general anaesthetic
7. duration of the surgical procedure

8. classification of surgical procedure performed
    - clean vs. clean-contaminated
9. type of surgical procedure performed
    - orthopaedic or soft tissue
10. specific procedure performed
11. anatomical location of surgical procedure
12. number of full thickness skin incisions made
13. length of surgical incision
14. suture pattern used for closure of deep tissues, subcutaneous tissues and skin
15. suture material used in closure of each layer
16. volume of dead space left at the end of surgery
17. whether a dressing was used post-operatively, and the type of dressing used post-operatively
18. whether systemic antimicrobials were administered prior to induction of anaesthesia, and if so, the systemic antimicrobials used.

Data were recorded at four key points during the study (Appendix 10).

1. When horses entered into the study a pre-operative assessment was carried out, recording:
    - the name, signalment and weight of the horse
    - rectal temperature, heart rate and respiratory rate
    - the results of any routine haematological or biochemical analyses of blood if they were performed.
2. During the peri- and immediate post-operative period, a surgery report was completed, including such information as:
    - the surgical procedure performed
    - the nature of the surgical procedure performed as defined by the National Research Council
    - identity of the surgeon
    - whether the surgical site was clipped or shaved, including whether this had occurred prior to induction for anaesthesia and if so, how long before induction
    - whether there was any evidence of local skin reaction following the preparation of the surgical site

- duration of both general anaesthesia and surgery
- length and site of incision made
- the suture materials and suture patterns used during closure of the individual tissue layers
- the volume of dead space left after surgery
- whether an indwelling drain had been placed, and if so what type of drain
- and the nature of any dressings used to protect the incision post-operatively

3. Once the horse had recovered successfully from general anaesthesia it was assessed daily for any of the outcomes of interest in the study.
4. A final assessment for any of the outcomes of interest was performed when the horse was discharged from the hospital.

The post-operative assessment was not performed by the surgeon involved with the case, but by the team of staff responsible for the daily care of the horse, in order to remove any bias that may occur from a surgeon assessing their own work.

7.9.3. Data Analysis

Binary logistic regression was used to analyse these data as all outcomes of interest were dichotomous. Categorical variables with more than two levels were coded as indicator variables, using the quartiles to define the parameters of each indicator variable. Analyses were implemented using the statistical software MINITAB (version 13.31).

Univariable logistic regression was used to screen all variables, and from this all variables with a p-value ≤ 0.20 were included in a backward elimination procedure to fit a multivariable model. The inclusion criterion for backward elimination was set at $p \leq 0.05$.

Once the main effects model had been fitted, two-way interaction between variables was assessed. Variable selection was determined by biological plausibility. Assessment between models was obtained using a likelihood ratio test (LRT) with significance set at $p \leq 0.05$.

The goodness-of-fit of the models was assessed using the Hosmer-Lemeshow goodness-of-fit test, to test the null hypothesis that the model was considered to be a good fit, with the null hypothesis rejected at a p-value ≤ 0.05.

7.10. Results

7.10.1. Descriptive statistics

7.10.1.1. All cases

Four hundred and thirty-three horses were found to be eligible for inclusion in the study. There were 139 female horses, 156 geldings and 138 entire male horses in the study, with an age range of between 3 days old and 19 years old at the time of admission to the hospital (median: 5 years old; inter-quartile range: 2 to 9 years old).

Table 33: Classification, according to National research Council, of all elective surgical procedures performed.

Classification	Procedure	Number	Percentage (%)
Total		433	100
Clean		376/433	86.8
	Orthopaedic	272/376	72.3
	Arthroscopy/Tenoscopy	110/272	40.4
	Neurectomy	57/272	21.0
	Fracture repair	47/272	17.3
	Desmotomy	25/272	9.2
	Other orthopaedic procedures	33/272	12.1
	Soft Tissue	104/376	27.7
	Castration	71/104	68.2
	Laparotomy	10/104	9.6
	Enucleation	5/104	4.8
	Myectomy	4/104	3.8
	Other soft tissue procedures	14/104	13.5
Clean-Contaminated		57/433	13.2
	Laryngoplasty	23/57	40.4
	Sinus surgery	12/57	21.1
	Dental surgery	7/57	12.3
	Penile surgery	7/57	12.3
	Other procedures	8/57	14.0

Three hundred and seventy six horses (86.8%) underwent a clean surgical procedure, and the remaining 57 horses (13.2%) underwent a clean-contaminated surgical procedure. Of the clean surgical procedures performed, 272 (72.3%) were orthopaedic procedures and 104 horses (27.7%) underwent a soft tissue procedure (Table 33).

Post-operative complications recorded during hospitalisation for the 433 surgical procedures performed included: pyrexia (10, 2.3%; 95% C.I. 1.1 to 4.2); diarrhoea (7, 1.6%; 95% C.I. 0.7 to 3.3); incisional swelling considered abnormal for the surgical procedure performed (93, 21.5%; 95% C.I. 17.7 to 25.7); incisional drainage considered abnormal for the surgical procedure performed (101, 23.3%; 95% C.I. 19.4 to 27.6); and partial or total dehiscence of the incision (7, 1.6%; 95% C.I. 0.7 to 3.3). Other complications recorded included: a pronounced pain response on palpation of the surgical site (15, 3.5%; 95% C.I. 2.0 to 5.6); and seroma or haematoma formation at the surgical site (10, 2.3%; 95% C.I. 1.1 to 4.2). (Table 34).

7.10.1.2. Clean surgical procedures

Three hundred and seventy six clean surgical procedures were performed (Table 33). There were 128 female horses, 118 geldings and 130 entire male horses. The age at admission ranged from 3 days old to 19 yrs (median: 4.0 yrs; inter-quartile range: 2 to 9 years old). Post-operative complications recorded during hospitalisation in all clean surgical procedures included: pyrexia, diarrhoea, incisional swelling, discharge from the surgical site and either partial or total dehiscence of the surgical site (Table 34). Other complications recorded included: a pronounced pain response on palpation of the surgical site, and seroma or haematoma formation at the surgical site (Table 34).

Seven horses undergoing clean surgical procedures were euthanased during the period of hospitalisation: five cases (1.3%) due to complications attributable to general anaesthesia in the horse (malignant hyperthermia (n=1), pleuropneumonia (n=1), myopathy (n=3)); one case (0.3%) due to implant failure; and one case (0.3%) due to the results of histopathologcial analysis. Of those cases that survived to be discharged from the hospital, complications recorded at discharge included: swelling, considered to be abnormal for that surgical procedure (39, 10.4%) drainage from the surgical site, considered to be abnormal for that surgical procedure (17, 4.5%); and partial or total dehiscence of the surgical site (5, 1.3%). Three horses (0.8%) were still observed to show a marked pain response on palpation of their surgical site at the time of discharge from the hospital (Table 35).

7.10.1.3. Clean-contaminated surgical procedures

Fifty seven horses underwent a surgical procedure that was classified as clean-contaminated (Table 33). There were 11 female horses, 38 geldings and eight entire male horses. The age at the time of admission ranged from 2 months old to 18 yrs (median: 7 yrs; inter-quartile range: 3.25 to 11 years old). Post-operative complications recorded for all clean-contaminated surgical procedures included: pyrexia, diarrhoea, incisional swelling, discharge from the surgical site, and partial or total dehiscence of the surgical site (Table 34). Other complications recorded included: a marked pain response on palpation of the surgical site, and seroma or haematoma formation at the surgical site (Table 34).

Two horses undergoing clean-contaminated surgical procedures were euthanased during hospitalisation, at the request of their owners for reasons unrelated to either general anaesthesia or the surgical procedure itself. Of those horses that survived to be discharged from the hospital, complications recorded at discharge included: swelling; drainage from the surgical site, considered to be abnormal for that surgical procedure (2, 3.5%); and partial or total dehiscence of the surgical site (2, 3.5%). (Table 35).

7.10.1.4. Orthopaedic procedures

Two hundred and seventy two orthopaedic procedures were performed during the study. There were 111 female horses, 111 geldings and 50 entire male horses. The age at the time of admission ranged from 3 days old to 19 years (median: 6 yrs; inter-quartile range: 3 to 10 years old).

Table 34: Post-operative complications recorded during hospitalization following an elective surgical procedure.

	Pyrexia		Diarrhoea		Swelling		Abnormal Swelling		Drainage		Abnormal Drainage		Dehiscence		Pain		Seroma/ Haematoma	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
All surgical procedures	10	2.3	7	1.6	166	38.3	93	21.5	120	27.7	101	23.3	7	1.6	15	3.5	10	2.3
Clean	8	2.1	6	1.6	145	38.6	82	21.8	99	26.3	78	20.7	5	1.3	13	3.5	9	2.4
Orthopaedic	4	1.5	4	1.5	87	32.0	81	29.8	76	27.9	72	26.5	3	1.1	9	3.3	4	1.5
Soft Tissue	4	3.8	2	1.9	58	55.8	1	1.0	23	22.1	6	5.8	2	1.9	4	3.8	5	4.8
Clean-contaminated	2	3.5	1	1.8	21	36.8	11	19.3	27	47.4	23	40.4	2	3.5	2	3.5	1	1.8

Table 35: Post-operative complications recorded at discharge from the hospital following an elective surgical procedure.

	Swelling		Abnormal Swelling		Drainage		Abnormal Drainage		Dehiscence		Pain		PTS	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
All surgical procedures	99	22.9	39	9.0	49	11.3	19	4.4	7	1.6	3	0.7	9	2.1
Clean	91	24.2	39	10.4	35	9.3	17	4.5	5	1.3	3	0.8	7	1.9
Orthopaedic	40	14.7	39	14.3	20	7.4	16	5.9	3	1.1	1	0.4	4	1.5
Soft Tissue	51	49.0	0	0	15	14.4	1	1.0	2	1.9	2	1.9	3	2.9
Clean-contaminated	8	14.0	0	0	14	24.6	2	3.5	2	3.5	0	0	2	3.5

7.10.1.5. Soft tissue procedures

One hundred and four soft-tissue procedures were performed during the study. There were 17 female horses, 7 geldings and 80 entire male horses. The age at the time of admission ranged from 3 weeks old to 14 years (median: 2yrs; inter-quartile range: 1.86 to 4 years old).

7.10.2. Analysis of all data

7.10.2.1. All cases

When considering data from all the surgical procedures performed, binary logistic regression at the univariable level showed that the only variable found to be associated with an increased risk of a horse developing pyrexia post-operatively was the use of the suture material PDS in the closure of the deep layer of the surgical incision (Appendix 12.1).

No variables were found to be associated with whether a horse undergoing an elective surgical procedure developed post-operative diarrhoea.

Univariable analyses using binary logistic regression were then performed for each of the incisional outcomes: abnormal swelling; abnormal drainage and either partial or complete incisional dehiscence (Appendix 12.6).

A multivariable logistic model was then built using backward elimination, for each outcome of interest. All variables with $p \leq 0.20$ at the univariable level were included in the analyses, with the inclusion criterion for backward elimination set at $p \leq 0.05$.

In the multivariable model, no variables were found to be associated with an increased risk of a horse developing post-operative diarrhoea. Those variables that were found to be associated with an increased risk of a horse developing post-operative pyrexia were: whether a laparotomy had been performed, and whether a horse developed post-operative incisional swelling that was considered abnormal for that procedure (Table 36).

Those variables found to be associated with an increased risk of the occurrence of either partial or total dehiscence of the surgical incision were: the length of the incision, and whether a deep suture layer was used (Table 37). No two-way interaction terms were found to be significant in the final model.

Table 36: Logistic regression analysis of factors associated with the development of post-operative pyrexia following an elective surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-4.26	1.33			0.001
Surgical procedure performed (referent arthroscopy and tenoscopy)					
Laparotomy	3.57	1.59	35.55	1.59 – 796.51	0.024
Development of abnormal incisional swelling	2.15	0.96	8.58	1.31 – 56.20	0.025

Table 37: Logistic regression analysis of factors associated with the development of either partial or total incisional dehiscence following an elective surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-5.02	0.71			<0.001
Length of surgical incision (referent <5cm)					
>10cm	2.56	0.93	12.99	2.10 – 80.39	0.006

Those variables found to be associated with an increased risk of a horse developing post-operative incisional swelling, considered to be abnormal for the surgical procedure performed, included: the age of the horse; the duration of general anaesthesia; the suture pattern used to close the skin; the suture material used in closure of the deep and subcutaneous layers; antimicrobial used; surgical procedure performed; and whether there was either partial or total incisional dehiscence (Table 38). Significant interaction was found to occur between the age of the horse, and the use of vicryl in the closure of the subcutaneous layer compared to the referent category of no closure of the subcutaneous layer.

Table 38: Logistic regression analysis of factors associated with the development of post-operative incisonal swelling considered to be an abnormal finding for the specific surgical procedure performed, following an elective surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	1.34	1.49			0.369
Age of horse at induction, in comparison to ≤ 2 yrs old					
3 – 5yrs old	1.00	0.57	2.73	0.90 – 8.26	0.076
6 – 9yrs old	1.59	0.67	4.90	1.31 – 18.38	0.018
Duration of general anaesthesia (referent < 60mins)					
≥110mins	1.17	0.57	3.21	1.05 – 9.80	0.041
Suture material used in closure of deep layer (referent none)					
Vicryl	-1.76	0.50	0.17	0.06 – 0.46	<0.001
Suture material used in closure of subcutaneous layer (referent none)					
Vicryl	1.87	0.85	6.46	1.23 – 34.02	0.028
Antimicrobials administered prior to induction (referent no antimicrobials given)					
Procaine penicillin or sodium penicillin	-2.81	1.38	0.06	0.00 – 0.90	0.042
Procaine penicillin and gentamicin	-2.97	1.44	0.05	0.00 – 0.87	0.040
Sodium penicillin and gentamicin	-3.64	1.47	0.03	0.00 – 0.55	0.018
Antimicrobials other than penicillin +/- gentamicin	-4.63	1.72	0.01	0.00 – 0.29	0.007
Surgical procedure performed (referent arthroscopy and tenoscopy)					
Other orthopaedic procedure	-3.06	1.08	0.05	0.01 – 0.39	0.005
Other soft tissue procedure	-2.85	1.25	0.06	0.01 – 0.67	0.022
3-5yrs * Vicryl in subcutaneous layer	-2.08	0.92	0.13	0.02 – 0.75	0.023

Those variables found to be associated with an increased risk of the development of post-operative incisional drainage considered to be an abnormal finding for the specific surgical procedure performed included: gender of the horse; duration of surgical procedure; clipping of surgical site prior to induction; classification of surgical procedure; and antimicrobials used (Table 39). No two-way interaction terms were found to be significant.

Table 39: Logistic regression analysis of factors associated with the development of post-operative incisonal drainage considered to be an abnormal finding for the specific surgical procedure performed, following an elective surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-1.00	0.93			0.287
Gender of horse (referent female)					
Entire male	-1.59	0.50	0.20	0.08 – 0.54	0.001
Duration of surgical procedure (referent <30 mins)					
30-50 mins	0.87	0.42	2.39	1.05 – 5.41	0.038
>65 mins	0.96	0.45	2.60	1.08 – 6.26	0.033
Surgical site clipped prior to induction (referent not clipped)					
>24hrs	1.38	0.34	3.99	2.03 – 7.85	<0.001
Classification of surgical procedure (referent clean)					
Clean-contaminated	1.37	0.41	3.95	1.77 – 8.78	0.001
Antimicrobials given prior to induction (referent no antimicrobials given)					
Antimicrobial other than penicillin +/- gentamicin	-3.32	1.41	0.04	0.00 – 0.58	0.019

The fit of the models were evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the models were a good fit.

7.10.3. Clean surgical procedures

Univariable analyses using binary logistic regression were performed for each outcome of interest (Appendices 12.2 and 12.7). Following a clean surgical procedure, no variables were found to be associated with an increased risk of a horse developing post-operative diarrhoea.

After the backward elimination of variables for data from all the clean surgical procedures, no variables were found to be associated with an increased risk of a horse developing post-operative diarrhoea. Those variables that were found to be associated with an increased risk of horses developing post-operative pyrexia included: the weight of the horse; the length of the surgical incision; and the suture material used to close the deep layer of the incision (Table 40). No two-way interaction terms were found to be significant.

Table 40: Logistic regression analysis of factors associated with the development of post-operative pyrexia following a clean surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-5.71	1.55			<0.001
Age of horse (referent < 2 yrs)					
> 9 yrs	3.42	1.41	30.69	1.93 – 488.49	0.015
Anatomical location of surgical incision (referent distal limb)					
Head and neck	2.91	1.35	18.28	1.29 – 258.24	0.032
Abnormal incisional swelling	3.28	1.39	26.46	1.74 – 402.98	0.018

Those variables found to be associated with an increased risk of a horse developing post-operative incisional swelling that was considered to be abnormal for the specific surgical procedure performed included: the duration of general anaesthesia; the type of dressing used; the suture material used in the closure of the deep and subcutaneous layers; and the surgical procedure performed (Table 41). No two-way interaction terms were found to be significant in the final model.

Those variables found to be associated with an increased risk of a horse developing post-operative incisional drainage that would be considered an abnormal finding for the specific surgical procedure included: whether the surgical site was clipped prior to induction; and the suture material used in the closure of the skin (Table 42). No two-way interaction terms were found to be significant in the final model.

Table 41: Logistic regression analysis of factors associated with the development of post-operative incisional swelling considered to be abnormal the surgical procedure following a clean surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-3.25	0.92			<0.001
Duration of general anaesthesia (referent <60mins)					
>110mins	1.71	0.60	5.50	1.70 – 17.86	0.005
Type of dressing used (referent none)					
Cast	3.40	1.41	29.95	1.88 – 476.33	0.016
Bandage	1.84	0.85	6.32	1.20 – 33.20	0.029
Suture material used in closure of deep layers (referent none)					
Vicryl	-1.73	0.54	0.18	0.06 – 0.52	0.001
Suture material used in closure of subcutaneous layers (referent none)					
Vicryl	1.42	0.60	4.14	1.28 – 13.37	0.018
Surgical procedure performed (referent arthroscopy or tenoscopy)					
Fracture	-3.37	1.19	0.03	0.00 – 0.35	0.005
Other orthopaedic procedure	-2.68	0.91	0.07	0.01 – 0.41	0.003

Table 42: Logistic regression analysis of factors associated with the development of post-operative incisional drainage considered to be abnormal for the specific surgical procedure, following a clean surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-1.16	0.33			<0.001
Surgical site clipped prior to induction of general anaesthesia (referent not clipped)					
Clipped >24hrs prior to induction	1.19	0.31	3.30	1.78 – 6.11	<0.001
Suture material used in closure of the skin (referent none)					
Vicryl	-2.13	0.67	0.12	0.03 – 0.44	0.001

The only variable found to be associated with an increased risk of a horse developing partial of total incisional dehiscence was the anatomical location of the surgical procedure (Table 43).

Table 43: Logistic regression analysis of factors associated with the development of partial or total incisional dehiscence, following a clean surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-4.67	0.71			<0.001
Length of incision (referent <5 cm)					
>10 cm	2.99	0.94	19.84	3.15 – 125.05	0.001

7.10.4. Clean-contaminated surgical procedures

Univariable logistic regression analysis showed that no single variable was associated with an increased risk of a horse developing post-operative pyrexia or diarrhoea following a clean-contaminated surgical procedure (Appendix 12.3). Univariable logistic regression analysis was then performed for each of the incisional outcomes (swelling, abnormal swelling, drainage from the incision, abnormal drainage and either partial or complete incisional dehiscence). (Appendix 12.8).

A multivariable logistic model built using a backward elimination procedure for each of the outcomes of interest. No variables were found to be associated with an increased risk of a horse developing post-operative pyrexia, diarrhoea, or partial or total incisional dehiscence.

Table 44: Logistic regression analysis of factors associated with the development of post-operative swelling considered to be abnormal for the surgical procedure, following a clean-contaminated surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-1.50	0.65			0.020
Abnormal post-operative incisional drainage	1.85	0.82	6.38	1.29 – 31.57	0.023
Suture material used in closure of the deep layer (referent none)					
Vicryl	-2.26	0.89	0.10	0.02 – 0.60	0.011

Those variables found to be associated with an increased risk of a horse developing post-operative incisional swelling considered to be abnormal for the specific surgical procedure performed included: the suture material used in closure of the deep layer; and whether there was any post-operative incisional drainage (Table 44). No two-way interaction terms were found to be significant in the final model.

Those variables found to be associated with an increased risk of a horse developing post-operative incisional drainage considered to be abnormal for the surgical procedure performed were: the age of the horse; and whether post-operative incisional swelling considered to be an abnormal finding for the surgical procedure occurred (Table 45). No two-way interaction terms were found to be significant in the final model.

Table 45: Logistic regression analysis of factors associated with the development of post-operative incisional drainage considered to be abnormal for the surgical procedure, following a clean-contaminated surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-1.88	0.77			0.015
Age of horse (referent <3 yrs) >11 yrs	3.31	1.34	27.26	1.96 – 378.46	0.014
Abnormal post-operative incisional swelling	1.93	0.82	6.88	1.37 – 34.45	0.019

The fit of the models were evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the models were a good fit.

7.10.5. Orthopaedic procedures

Univariable binary logistic regression was performed for each outcome of interest (Appendices 12.4 and 12.9).

Following backward elimination of variables for all orthopaedic procedures no variables were found to influence the likelihood of a horse developing post-operative pyrexia, diarrhoea or partial or total dehiscence of the surgical incision.

Those variables found to be associated with an increased risk of a horse developing post-operative incisional swelling considered to be an abnormal finding for the surgical procedure performed included: the gender and weight of the horse; the suture material used in the closure of the deep and subcutaneous layers; and the surgical procedure performed (Table 46). Significant interaction was found to occur between the gender of the horse, and the weight of the horse at induction.

Those variables found to be associated with an increased risk of a horse developing post-operative incisional drainage that is considered to be abnormal for the surgical procedure performed were the duration of general anaesthesia and whether the surgical site was clipped greater than twenty-four hours prior to induction of general anaesthesia (Table 47). No two-way interaction terms were found to be significant in the final model.

The fit of the models were evaluated using the Hosmer-Lemeshow goodness-of-fit test, and it was found that the models were a good fit.

Table 46: Logistic regression analysis of factors associated with the development of post-operative incisional swelling considered to be abnormal for the surgical procedure performed, following an orthopaedic surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	**-1.00**	**0.50**			**0.043**
Gender of horse (referent female)					
Gelding	**1.44**	**1.17**	**4.20**	**0.42 – 41.84**	**0.221**
Weight of horse (referent <400kgs)					
400 – 600 kgs	**1.27**	**0.54**	**3.56**	**1.23 – 10.30**	**0.019**
Suture material used in closure of the deep layer (referent none)					
Vicryl	**-1.55**	**0.55**	**0.21**	**0.07 – 0.62**	**0.005**
Suture material used in closure of subcutaneous layer (referent none)					
Vicryl	**1.67**	**0.63**	**5.31**	**1.53 – 18.39**	**0.009**
Surgical procedure performed (referent arthroscopy or tenoscopy)					
Fracture repair	**-1.77**	**0.69**	**0.17**	**0.04 – 0.67**	**0.011**
Other orthopaedic procedure	**-2.69**	**0.94**	**0.07**	**0.01 – 0.43**	**0.004**
Gelding * 400-600 kgs	**-2.77**	**1.24**	**0.06**	**0.01 – 0.71**	**0.026**

Table 47: Logistic regression analysis of factors associated with the development of post-operative incisional drainage considered to be abnormal for the surgical procedure, following an orthopaedic surgical procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-2.29	0.43			<0.001
Duration of general anaesthesia (referent <75 mins)					
> 115 mins	1.13	0.50	3.09	1.17 – 8.17	0.023
Surgical site clipped prior to induction of general anaesthesia (referent not clipped)					
Clipped >24 hrs prior to induction	1.40	0.34	4.06	2.10 – 7.85	<0.001

7.10.6. Soft Tissue procedures

Univariable binary logistic regression analysis was carried out for all outcomes of interest (Appendices 12.5 and 12.10). Following backward elimination of variables for each outcome of interest, no variables were found to be associated with an increased risk of: a horse developing post-operative diarrhoea; either post-operative incisional swelling or drainage considered to be an abnormal finding for the specific surgical procedure performed; or partial or total incisional dehiscence. The only variable found to be associated with an increased risk of a horse developing post-operative pyrexia was the type of dressing applied to the surgical site (Table 48).

Table 48: Logistic regression analysis of factors associated with the development of post-operative pyrexia following an elective soft tissue procedure.

Factor	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
(Constant)	-2.74	0.73			<0.001
Type of dressing used (referent none)					
Adhesive dressing or stent	2.34	1.17	10.33	1.05 – 102.08	0.046

7.11. Discussion

7.11.1. Class of evidence

No prospective study has previously been reported in the equine veterinary literature, investigating the prevalence of complications following clean and clean-contaminated elective surgery. Complication rates following clean, elective orthopaedic surgical procedures have been sparsely reported (Macdonald *et al.* 1994), as have those following specific clean and clean-contaminated elective procedures (Smith & Ross, 2002). A practitioner survey of castration complications has also been reported in the equine veterinary literature (Moll *et al.* 1995). These studies would be considered to provide class C (Macdonald *et al.* 1994; Smith & Ross, 2002) or even class D (Moll *et al.* 1995) evidence, using the classification system proposed by Yusuf *et al.* 1998. In contrast, many of those studies published in the small animal literature are of a higher classification: class A (Holmberg, 1985; Vasseur *et al.* 1985; Osuna *et al.* 1990) and class B (Brown *et al.* 1997; Heldmann *et al.* 1999; Beal *et al.* 2000).

More information is available on complications associated with emergency exploratory celiotomies in horses (Gibson *et al.* 1989; Kobluk *et al.* 1989; Honnas & Cohen, 1997; Ingle-Fehr *et al.* 1997; Mair, 2003; Mair and Smith, 2005a,b). These studies would predominantly be classified as class C evidence (Kobluk *et al.* 1989; Honnas & Cohen, 1997; Ingle-Fehr *et al.* 1997; Mair, 2003; Mair and Smith, 2005a,b), as they are retrospective case series.

7.11.2. Normal or abnormal?

Although the development of swelling at the surgical site, along with any form of drainage from the incision, could be considered an unwelcome sequel to any surgery, they are widely accepted as being an incidental finding following certain procedures. The purpose of leaving a castration site open is to allow free drainage of fluid in the post-operative period, preventing the accumulation of secretions that are associated with the inhibition of phagocytic cells and the increased incidence of incisional infections; therefore some sero-sanguinous discharge would be considered perfectly normal following a castration and would not be considered as a complication. However, if this drainage was noted following a fracture repair, this would be an abnormal finding, and may be indicative of an

underlying infection. A similar story is true with swelling around the surgical site – any surgical incision will result in some degree of trauma to, and contamination of, the skin edges thereby inducing an inflammatory response, however it is when this inflammatory response becomes marked that it will begin to interfere with wound healing and natural host-resistance to infection. One problem encountered in this study was a method of differentiating between those post-operative findings that could be considered normal for that specific surgical procedure and those that were considered to be true complications. In order to address this issue, a surgeon who was not involved in the study was asked to identify those procedures where post-operative swelling or surgical site drainage could be a normal feature, and then quantify that which would be considered normal and that which would be considered abnormal. If this had not occurred, the reported prevalence of incisional complications such as swelling and surgical site drainage would have been significantly higher than the value reported herein.

7.11.3. Types of Outcome

A distinction must be made between those complications directly associated with the surgical procedure, and those that could be attributed to general anaesthesia, hospitalisation and systemic antimicrobial therapy. Those complications attributed to hospitalisation, anaesthesia and the administration of systemic antimicrobials include post-operative pyrexia and diarrhoea. In contrast, those complications directly associated with the surgical procedure include: swelling of the surgical site; drainage from the incision; and partial or total dehiscence of the incision.

7.11.3.1. Hospitalisation Complications

7.11.3.1.1. Post-operative Pyrexia

Post-operative pyrexia has been reported in the human literature to be a positive predictor of bacterial infection (Mellors *et al.* 1988). The prevalence of post-operative pyrexia has only been reported in one study in the equine literature, where a positive correlation was found between post-operative pyrexia and the development of incisional drainage (Ingle-Fehr *et al.* 1997), although this study was investigating complications following midline celiotomies for the investigation of abdominal pain.

In our study the prevalence of post-operative pyrexia was low and the only positive correlations that were identified between the development of pyrexia and surgical site complications were: the age of the horse, with horses over nine years of age undergoing a clean surgical procedure more likely to develop post-operative pyrexia than those in the referent category of less than 2 years old (Table 40); the location of the surgical incision when a horse underwent a clean surgical procedure (Table 40); the surgical procedure performed, with horses undergoing a laparotomy more likely to become pyrexic than those undergoing arthroscopy or tenoscopy (Table 36); and the occurrence of incisional swelling that was considered to be an abnormal finding for the specific surgical procedure performed would increase the likelihood of a horse developing post-operative pyrexia (Tables 36 and 40). However, one hospital contributed the vast majority of cases to this study, and it was standard practice at this hospital not to take the rectal temperature of horses unless they had undergone a surgical procedure involving placement of an implant (fracture repair, laryngoplasty) or the horse was displaying clinical signs of systemic disease (inappetance, lethargy). Taking this into account, the true prevalence of post-operative pyrexia in the population of interest may have been much higher than that recorded in this study if it remained at the sub-clinical level, without the horse displaying signs of systemic disease. Therefore it is not possible to investigate accurately whether post-operative pyrexia could be a positive predictor for surgical site complications. The prevalence of post-operative pyrexia was found to be 10/433 (2.3%), however a more accurate figure would be obtained if you were to only consider those cases where the rectal temperature was taken twice daily, which would result in a prevalence of 10/162 (6.2%).

7.11.3.1.2. Post-operative diarrhoea

In both human and small animal surgery it has been recommended that, where prophylactic antimicrobials are used, careful selection and dosage of antimicrobials should be employed (Van den Bogaard & Weidema, 1985; Rosin *et al.* 1993; Seim, 1997), utilising as narrow a spectrum of antimicrobial as possible (Van den Bogaard & Weidema, 1985; Rosin *et al.* 1993; Seim, 1997). The antimicrobials should also be used for a short period of time only – twenty-four hours is a time period that has frequently been cited in the literature (Van den Bogaard & Weidema, 1985; Whittem *et al.* 1999). These recommendations were made in order to reduce the possibility of drug toxicity, allergic reaction and the evolution of resistant strains of bacteria.

All three hospitals that participated in this study routinely used broad-spectrum prophylactic antimicrobials in the post-operative period, for longer than the recommended twenty-four hours. Whilst reactions have been documented in the equine literature to specific antimicrobials (Baker & Leyland, 1973; Cook, 1973; White & Prior, 1982; Blue *et al.*1987; Dick & White, 1987; Sweeney *et al.* 1991; Mahrt, 1992; McConnico *et al.* 1992; Riond *et al.* 1992; van Duijkeren *et al.* 1994), very few horses developed complications in this study that could be attributed to the use of prophylactic antimicrobials, with only 7 horses (1.6%) developing diarrhoea in the post-operative period. No single factor was found to influence the likelihood that a horse would develop post-operative diarrhoea.

7.11.3.2. Incisional Complications

Those factors that were found to influence the prevalence of post-operative incisional complications in the human literature included: old age (Lees *et al.* 1989; Romatowski, 1989), long surgical time (desiccation of wound edges) (Johnston, 1990), general anaesthesia time (excessive depth or prolonged total time) (Johnston, 1990; Brown *et al.* 1997; Seim, 1997), hypoxia (Romatowski, 1989; Macdonald *et al.* 1994; Brown *et al.* 1997; Beal *et al.* 2000), hypotension (Romatowski, 1989; Macdonald *et al.* 1994; Brown *et al.* 1997; Beal *et al.* 2000), cold (Silver, 1982; Johnston, 1990; Beal *et al.* 2000), experience of the surgeon (traumatisation of tissues, duration of surgery) (Vasseur *et al.* 1988; Hofmann *et al.* 1999), malnutrition, obesity, and active infection at sites remote from the surgical incision. Those factors found to contribute to the prevalence of post-operative incisional complications in the small animal veterinary literature include: cold (Silver, 1982), hypovolaemia (Silver, 1982; Romatowski, 1989; Macdonald *et al.* 1994; Brown *et al.* 1997; Beal *et al.* 2000), malnutrition or obesity (Silver, 1982; Lees *et al.* 1989; Johnston, 1990; Brown *et al.* 1997), mechanical irritation through self-trauma (Silver, 1982), and general anaesthesia and surgery times (Romatowski, 1989; Macdonald *et al.* 1994; Brown *et al.* 1997; Beal *et al.* 2000). The only study that investigated the effect of old age on the prevalence of post-operative incisional complications did not report a statistically significant difference in complication rates with respect to the age of the animal (Brown *et al.* 1997).

In the equine veterinary literature, those factors that have been reported to affect the prevalence of post-operative complications in elective surgical procedures include: classification of surgical procedure (MacDonald *et al.* 1994), duration of surgery (MacDonald *et al.* 1994), the use of pre-operative antimicrobials (MacDonald *et al.* 1994), and the gender of the patient (MacDonald *et al.* 1994). Variables not found to be associated with the incidence of post-operative infection included the age of the patient (MacDonald *et al.* 1994), and the training level of the primary surgeon (MacDonald *et al.* 1994).

The current study found that when considering all the data, those factors that exerted an influence on the prevalence of post-operative complications included:

1. the age and gender of the horse
2. the duration of general anaesthesia and the duration of the surgical procedure
3. the use of antimicrobials prior to induction
4. whether the surgical site was clipped prior to induction
5. the specific surgical procedure performed
6. the classification of the surgical procedure performed, as classified by the National Research Council
7. the length of the surgical incision made
8. the suture materials used in the closure of the incision
9. the suture patterns used in the closure of the incision

The weight of the horse, type of dressing used to cover the surgical incision, and the anatomical location of the surgical incision were significant when considering specific types of surgical procedure (those classified as clean or orthopaedic procedures).

7.11.4. Variables of interest

7.11.4.1. Weight

Both obesity and malnutrition have been reported to delay wound healing (Silver, 1982; Johnston, 1990; Brown *et al.* 1997) and to contribute to an increase occurrence of incisional infections (Silver, 1982; Johnston, 1990; Brown *et al.* 1997). In this study every horse was weighed prior to induction of anaesthesia. However, the weight alone is not an accurate guide to the overall body condition of the animal, due to the wide range of

sizes and types of horse that this study encompasses. The weight recorded is merely an index of the total body mass of each horse.

This study found that the weight of the horse was only an important factor when considering orthopaedic procedures, when horses weighing more than 600kgs were more likely to develop post-operative incisional swelling that was considered to be an abnormal finding for the specific surgical procedure performed (Table 46). Significant interaction was found to occur between the gender of the horse and the weight of the horse.

7.11.4.2. Gender

A previous study found that female horses were almost three times as likely to develop incisional infections post-operatively as male horses (MacDonald *et al.* 1994). It was postulated that this may be the result of a hormonal influence on neutrophil function. However, due to the retrospective nature of the study it was impossible to ascertain whether or not this was merely conjecture.

The current study concurred with the previously reported findings, as male horses were found to be significantly less likely to develop post-operative complications following an elective surgical procedure than female horses, in particular if they underwent an orthopaedic procedure (Tables 39 and 46). When considering horses undergoing orthopaedic procedures, significant interaction was found to occur between the weight of the horse and the gender of the horse (Table 46).

7.11.4.3. Age

Old age has been recognised in human surgery to have a negative effect on the rate of wound healing post-operatively, thereby increasing the likelihood of developing incisional complications (Lees *et al.* 1989; Romatowski, 1989). Although sparsely reported in the veterinary literature, those studies that have investigated the effect of age on the likelihood of developing post-operative incisional complications have not found it to be a significant factor (MacDonald, *et al.* 1994; Brown *et al.* 1997).

In the current study the increasing age of the animal was found to be a significant factor for the development of post-operative incisional complications following either clean-

contaminated or orthopaedic procedures (Tables 38, 40 and 45). Older horses were more than twenty-seven times more likely to develop post-operative incisional drainage following a clean-contaminated procedure than their younger counterparts. This may be a feature unique to this particular population, as the majority of horses that underwent a clean-contaminated surgical procedure were older than the reference age group.

The caseload of one hospital was primarily young, fit Thoroughbred racehorses in training, and this hospital provided most of the data for the study. The referent group when investigating whether age was a significant factor in the development of post-operative complications was the first quartile, which was ≤ 2 years of age. Young, fit horses such as these could be expected to heal faster than their older counterparts, who may have sub-clinical health problems that could compromise their healing potential.

7.11.4.4. Pre-operative antimicrobials

In direct contrast to an earlier study (MacDonald *et al.* 1994), an increased likelihood of developing post-operative incisional complications was not seen following the administration of antimicrobials prior to induction. When considering the data for all surgical procedures, it was found that the administration of antimicrobials prior to induction would significantly reduce the likelihood of the horse developing post-operative incisional swelling or drainage, considered to be an abnormal finding for the specific surgical procedure performed (Tables 38 and 39).

7.11.4.5. Clean vs. Clean-contaminated

As long ago as 1964, when a committee appointed by the National Research Council defined four general categories of surgery, based upon the expected degree of bacterial contamination, it has been recognised that the nature of the surgical procedure will influence the likelihood that post-operative complications will develop (Romatowski, 1989; Holmberg, 1985; MacDonald *et al.* 1994; Brown *et al.* 1997; Laitinen, 2001). Although it has been established that there is excessive variation within the broad categories defined by the National Research Council, it is still accepted that the expected rate of complications for a clean surgical procedure will be lower than that for a clean-contaminated surgical procedure (MacDonald *et al.* 1994; Brown *et al.* 1997), as the exposure of the surgical incision to possible sources of contamination, and the resultant

bacterial load, increases. The results of this study supported this theory, with those horses undergoing a clean-contaminated surgical procedure almost four times more likely to develop post-operative incisional complications than those horses that underwent a clean surgical procedure (Table 39).

7.11.4.6. Pre-operative preparation

Preparation of the skin pre-operatively can influence the prevalence of post-operative complications. Close clipping and shaving of the surgical site is thought to cause microtrauma to the skin barrier, producing small cuts in which bacteria could colonise, thus predisposing patients to post-operative wound infection (Brown *et al.* 1997; Smith and Ross, 2002). In small animal surgery clipping the surgical site within four hours of induction of anaesthesia was found to increase the likelihood of post-operative incisional complications three-fold, compared to clipping the site after induction of anaesthesia (Brown *et al.* 1997).

In the current study, clipping the surgical site was found to affect the likelihood of developing post-operative incisional complications for all surgical procedures (Tables 39 and 42), and in particular those horses that underwent an orthopaedic surgical procedure (Table 47). This finding may be due to the fact that many horses undergoing orthopaedic surgery had the affected area clipped for the performance of diagnostic regional or synovial anaesthesia, or an ultrasonographic examination, prior to the decision of performing a surgical intervention was made. In many cases this would occur at least twenty-four hours prior to the surgery being performed. When exposed to a typical stable environment, this would allow bacteria to populate any abrasions created in the otherwise impermeable skin barrier, prior to a surgical incision being made. Shaving the surgical site at the time of skin preparation could be expected to cause further superficial trauma to the skin surface. However, shaving was only found to be significant following univariable analysis, but not after the final model was constructed. Not every horse undergoing an orthopaedic procedure had the surgical site shaved, with this routinely performed only for neurectomies and tenoscopies.

Horses undergoing either soft tissue or clean-contaminated surgical procedures were only infrequently clipped prior to induction for anaesthesia. No horse undergoing either a soft-

tissue or clean-contaminated surgical procedure had the surgical site shaved at the time of skin preparation.

7.11.4.7. Duration of Anaesthesia

The duration of anaesthesia is thought to increase the likelihood of developing incisional complications through a number of mechanisms. General anaesthesia can induce hypoxia, hypotension and hypothermia, each of which individually is known to cause an increased rate of incisional infections, by causing a reduction in the metabolic rate and vasoconstriction (Silver, 1982; Johnston, 1990). Excessive depth of anaesthesia or prolonged total anaesthetic time (Romatowski, 1989; Macdonald *et al.* 1994; Brown *et al.* 1997; Beal *et al.* 2000) will also contribute to an increased rate of incisional infection.

When considering data from all surgical procedures performed, and procedures classified as clean or orthopaedic, the current study found that when the duration of general anaesthesia exceeded 110 minutes, this was associated with a significant increase in the likelihood of the development of post-operative incisional swelling or drainage, considered to be abnormal for the surgical procedure performed (Tables 38, 41 and 47). This finding concurs with previous studies (Romatowski, 1989; Macdonald *et al.* 1994; Brown *et al.* 1997; Beal *et al.* 2000) where it was found that a prolonged total anaesthetic time contributed to an increased rate of incisional infection.

When the duration of surgery exceeded the reference value of 30 minutes, this was found to significantly increase the likelihood of developing incisional swelling or drainage (Table 39). A longer surgical procedure will automatically result in a longer duration of general anaesthesia. However, longer surgical procedures also result in increased handling of the tissues, and potentially increased trauma to the tissues through excessive handling and desiccation. This may also have contributed to the increase in post-operative incisional complications associated with longer surgical procedures (Johnston, 1990; Brown *et al.* 1997).

7.11.4.8. Suture Materials and Patterns

The ideal suture material, with a high tensile strength and eliciting minimal tissue reaction without inducing an environment favourable to bacterial growth (Blackford and

Blackford, 1999) does not exist. Many suture materials exist, each with their own associated advantages and disadvantages. Whilst much is known about the chemical composition and tensile strength of individual suture materials, there is a paucity of information in the equine literature about their performance *in vivo* (Turner and McIlwraith, 1989), leading to extrapolation of data from the human and small animal literature.

It has been reported that the use of polyglactin 910 (Vicryl) has been associated with an increased risk of incisional complications (Honnas and Cohen, 1997), although the study that reported this was a retrospective case series, only providing class C evidence, and later studies have not concurred with this finding.

In the current study, the use of polyglactin 910 (Vicryl) in the closure of the deep or skin layers was found to significantly decrease the likelihood of the development of unwanted sequelae to an elective surgical procedure (Tables 38, 41, 42, 44 and 46), a finding in direct contrast to that reported previously (Honnas and Cohen, 1997). However, the use of Vicryl in the closure of the subcutaneous tissue layer was associated with an increased likelihood of the development of post-operative incisional swelling, compared to those incisions where no subcutaneous suture layer was placed (Tables 38, 41 and 46). This finding may support the theory currently being investigated that the use of a subcutaneous suture layer will lead to an increase in post-operative incisional complications, due to increased tissue handling and an increase in the quantity of foreign material within a surgical incision (Coomer *et al.* 2005).

The most commonly used suture patterns are simple continuous and simple interrupted, with the continuous pattern recommended for tissues that are elastic, and that are not subject to a lot of tension (Turner and McIlwraith, 1989). In the current study, no associations were found between the suture pattern used and any of the outcomes of interest.

7.11.4.9. Dead Space

Studies in both the human and the veterinary literature have recognised that large volumes of dead space left after surgery increase the risk of incisional complications (Lees *et al.* 1989). Dead space potentiates incisional infection due to the accumulation of tissue fluid

in the dead space (Lees *et al.* 1989), which will prevent the migration of phagocytic cells. These cells are the primary host defence against the development of incisional infection.

In the current study the volume of dead space left after surgery was not found to be a significant factor in the development of post-operative complications in any of the final models constructed.

7.11.5. Sources of bacterial contamination

Previous studies investigating the prevalence of incisional complications in equine surgery have recognised the contribution of the recovery room environment to the bacterial load (Smith and Ross, 2002). Unlike in both human and small animal surgery, it is impossible to accurately control a horse during the recovery period. Ineffectual attempts to stand prematurely can result in excessive trauma to the surgical site, leading to an exaggerated inflammatory response, local tissue trauma and partial or total dehiscence of the incision (Silver, 1982). Trauma is not the only factor in the recovery room environment that will contribute to the overall bacterial load. A strong positive correlation has been identified between the recovery room environment and the prevalence of incisional infections, with recovery room hygiene and maintenance considered to be important contributing factors (Galuppo *et al.* 1999; Smith and Ross, 2002). Poorly disinfected drains, or cracks in the padded lining to the recovery room, have proven to be ideal breeding grounds for bacteria, which in turn will readily colonise fresh surgical incisions. The incision can be protected to some degree by the application of a padded dressing, although this is not always either appropriate or feasible, depending on the nature of the surgical procedure and the site of the incision.

Using a dressing not only protects the incision from sources of trauma and bacterial contamination, but will also provide an improved environment for wound healing (Silver, 1982). A dressing will prevent evaporation and help keep the surface of the wound moist, allowing the epithelium to move straight along the damaged surface of the connective tissue, or even migrate straight through the wound exudates (Silver, 1982). However, a balance must be struck as an excess of this wound exudate will slow down the migration of the phagocytic cells, promoting the incidence of post-operative infection (Rosin *et al.* 1993).

In the current study the use of a protective dressing post-operatively was found to significantly increase the likelihood of a horse developing an abnormal amount of post-operative incisional swelling following a clean surgical procedure (Table 41). This is an unexpected finding, which may be due to the fact that those incisions most susceptible to either external trauma or where excessive tissue handling has occurred were preferentially covered by surgeons, for example casting of limbs following fracture repair, in comparison to those incisions where relatively few complications were anticipated, and therefore the incision was left uncovered.

7.11.6. Study Limitations

The risk period was under investigation was defined as running from the time of the surgical procedure being performed, until the horse was discharged from the hospital. It has been reported that most incisional complications occur approximately 14 days post-operatively in horses that have undergone and exploratory laparotomy (Galuppo *et al.* 1999), therefore it is possible that complications were potentially missed due to the short risk period under investigation. However, it was important to the study that all horses were evaluated at the end of the risk period by an impartial observer, and this would not have been possible in all cases if the risk period extended beyond the point of discharge from the hospital.

7.11.7. Conclusion

The results of our study showed that the prevalence of post-operative complications following an elective surgical procedure was higher than that previously reported, both when comparing results to the human literature and the veterinary literature, with almost 25% of horses undergoing a surgical procedure experiencing a complication. When looking exclusively at the prevalence of incisional complications, the prevalence reported was 23.3%. This figure is higher than that previously reported when compared to both the human and the veterinary literature. All post-operative complications appeared to be transient, with the majority resolving prior to the horse's discharge from the hospital, although no data is available on whether horses experienced any complications subsequent to discharge from the hospital.

Chapter 8

Conclusions and General Discussion

The purpose of this research was to perform a series of studies that would investigate a number of surgical conditions in the horse, both elective and emergency procedures, focusing on different aspects of sepsis. The sepsis ranged from intra-synovial sepsis that would require a form of surgical intervention in order to have a successful outcome, to sepsis as a direct result of a form of surgical intervention.

All the areas investigated were of a direct relevance to the general equine practitioner, and were also amenable to an EBM approach. There is a paucity of information available in the equine veterinary literature covering the investigation of the prevalence of complications following elective surgery (Macdonald *et al.* 1994; Smith & Ross, 2002), and in particular what factors may contribute to the development of post-operative complications. Similarly, when looking at complications arising from emergency surgery, whilst previous studies have hypothesised about factors that may either increase or decrease the risk of developing these complications (Turner *et al.* 1978; Kobluk, *et al.* 1989; Phillips and Walmsley, 1993; Honnas and Cohen, 1997; Ingle-Fehr *et al.* 1997; French *et al.* 2002; Coomer *et al.* 2005; Mair and Smith, 2005), no study has previously been published that investigates the influence of any risk factors on the prevalence of complications, or the success of any preventive measures to reduce the prevalence.

In contrast, when investigating the literature available on synovial sepsis in the horse, there is a wealth of information (Van Pelt & Riley, 1969; Koch, 1979; Leitch, 1979; Morris, 1980; McIlwraith, 1983; Stover & Pool, 1985; Martens *et al.* 1986; Bertone *et al.* 1987a,b; Lloyd *et al.* 1990; Peremans *et al.* 1991; Ross *et al.* 1991; Honnas *et al.* 1992a,b; Schneider *et al.* 1992a,b; Whitehair *et al.* 1992; McClure *et al.* 1993; Holcombe *et al.* 1997; Cook *et al.* 1999; Murphey *et al.* 1999; Lescun *et al.* 2000; Adams & Lescun, 2000; Meijer *et al.* 2000; Summerhays, 2000; Booth *et al.* 2001; Butt *et al.* 2001; Scheuch *et al.* 2001). However, much of this information is conflicting and of a 'poor quality' of evidence in EBM terms. The majority of studies are retrospective, with low case numbers (Van Pelt & Riley, 1969; Ross *et al.* 1991; Honnas *et al.* 1992a,b; Schneider *et al.* 1992b; Lescun *et al.* 2000; Adams & Lescun, 2000; Summerhays, 2000; Booth *et al.* 2001; Meijer *et al.* 2000), which limits the conclusions that can be drawn from the results, with many conclusions

being based on personal experience and anecdote rather than strongly supported by factual evidence. Those studies that exist that are of a prospective nature, for example the clinical trials performed by Bertone *et al.* (1987a,b), contain only small case numbers and focus on a very specific study population in which synovial sepsis was caused by inoculation of the synovial structure with *S. aureus*, thereby limiting the application of the findings to a wider population.

The studies reported here have made estimates of the likelihood of horses with either septic arthritis or septic digital tenosynovitis surviving, and going on to return to their previous, or anticipated, level of exercise. It was found that the presence of multi-system disease in neonatal Thoroughbreds treated for septic arthritis significantly reduced the likelihood that the foal would survive to be discharged from the hospital, compared to those foals with no disease process outside the synovial cavity. It was not possible to investigate whether involvement of more than one joint had an adverse effect on survival, as there was insufficient power to support a statistically significant effect. It was also found that the occurrence of septic arthritis in neonatal Thoroughbreds significantly reduced the likelihood of those foals going on to make at least one start on a racecourse, with those foals being 3.5 times less likely to start on a racecourse when compared to their siblings. When considering mature Thoroughbred racehorses treated for septic arthritis, only one factor was found to influence survival in the final model: a delay of more than five days between the onset of sepsis and commencement of treatment, with those horses being thirteen times less likely to survive than horses where treatment was started earlier. The occurrence of septic arthritis in a mature Thoroughbred racehorse did not reduce the likelihood of that horse starting on a racecourse when compared to its siblings, or of achieving an Official Rating issued by the British Horseracing Board's handicappers equal to either the highest rating achieved prior to the onset of sepsis in cases in which horses had raced previously, or equal to the highest rating achieved by their siblings.

When considering the overall population of mature horses treated for septic arthritis, it was found that the presence of radiographic abnormalities at the time of admission; a delay of more than seven days between the onset of sepsis and the commencement of treatment; and involvement of the stifle, elbow, proximal inter-phalangeal joint, distal inter-phalangeal joint or navicular bursa significantly decreased the likelihood that the horse would survive to be discharged from the hospital. The single factor that was found to influence the likelihood of horses being able to return to their previous level of athletic function

following the successful resolution of septic arthritis was whether there were any radiographic abnormalities evident in the affected joint at the time of admission for treatment. The only factor found to influence the likelihood of horses treated for septic digital tenosynovitis either surviving to be discharged from the hospital, or returning to their previous level of performance, was a delay in more than seven days between the onset of sepsis and the commencement of treatment.

These four studies were all retrospective studies, and therefore susceptible to many of the disadvantages commonly associated with these designs. Missing data in the case records are always a potential problem in this type of study, although did not affect the statistical analyses performed in the studies. Due to the wide variation in the treatment regimens employed, it was impossible to draw any conclusions regarding the relative efficacy of specific treatment modalities, although this was never the primary aim of these studies. In order to be able to draw conclusions about the relative efficacy of different treatment regimens it would be necessary to perform a controlled, prospective study, with sufficient case numbers to achieve statistical significance for medically meaningful outcomes. In addition, all long-term follow-up information was obtained by telephone questionnaire to the horses' caretakers. It was not possible to contact the caretaker of every horse in these studies, leading to the exclusion of some data from the final analyses. In those cases in which it was possible to contact the horse's caretaker, all information obtained was reliant on the ability of the caretaker to recall relevant events accurately and without bias, and it was up to the caretaker to decide subjectively whether they thought the horse had been able to return to its previous level of performance. In some cases there was a time lag of ten years between the horse being treated and follow-up information being obtained. However, at the outset of these studies, it was decided that a successful outcome would be the ability of the horse to satisfy the owner's long-term athletic expectations following treatment. As many horses were used primarily for general purposes at the time of admission to the hospital, it was impossible to quantify their return to athletic activity in terms of either competitive winnings or number of events entered.

The final two studies investigated the prevalence of complications following elective surgical procedures, and whether the use of a belly band would reduce the occurrence of incisional complications following an exploratory celiotomy for the investigation of abdominal pain. It was found that those horses that had an exploratory laparotomy

performed as an elective surgical procedure were 35 times more likely to develop post-operative pyrexia than horses undergoing the referent surgical procedure (arthroscopy or tenoscopy), and those risk factors found to influence the likelihood of a horse experiencing either partial or total incisional dehiscence in the risk period of interest were: having an incision that exceeded 5cm in length, compared to the referent value of less than 5cm; and whether the incision had a simple continuous suture pattern used in the closure of the deep tissue layers, compared to the referent value of no closure in the deep tissue layer. Those variables found to influence the likelihood of a horse developing post-operative incisional swelling, considered to be abnormal for the surgical procedure performed, included: the gender of the horse; the age of the horse; the duration of general anaesthesia; the suture pattern used to close the skin; the suture material used in closure of the deep and subcutaneous layers; the antimicrobials used; the surgical procedure performed; and whether either partial or total incisional dehiscence occurred during the risk period. Those variables found to influence the likelihood of the development of post-operative incisional drainage, considered to be an abnormal finding for the specific surgical procedure performed, included: the gender of the horse; duration of the surgical procedure; clipping of the surgical site prior to induction; classification of surgical procedure; and the antimicrobials used.

The use of an elastoplast belly band following an exploratory laparotomy for the investigation of abdominal pain was found to significantly reduce the likelihood of a horse developing post-operative incisional complications, with the risk of post-operative incisional complications reduced by 45% when compared to those horses in which no further form of intervention was used following recovery from general anaesthesia. In addition, it was found that in those horses that wore belly bands, the skin incision was more than twelve times more likely to have healed by 14 days post-discharge than those horses that did not wear belly bands. An incision that continues to drain for a prolonged period post-discharge is a complication that is both unsightly and unwanted for the owner, who has already invested a large amount of both time and money in electing to have an exploratory laparotomy performed. A draining incision is also a precursor to more serious complications such as incisional hernia formation, which can be more than just a visible blemish. Once the skin incision has healed, it will protect the deeper tissue layers from contamination and ascending infection.

All of the individual studies reported here were conducted in busy private practices. The questions formulated were directly relevant to practitioners, and were questions that had been faced by members of these practices countless times. Reviews of the available literature confirmed that no answers to these questions were immediately forthcoming and, therefore, they were suitable areas for further research. All data were collected as part of the normal case recording carried out on a daily basis for hospitalised patients, with minimal extra time required for the noting of results in case records. The study populations were the general populations encountered by each of the three private practices. As the studies were carried out in three general practice populations of horses, the results obtained should be broadly applicable to the horse population of the United Kingdom as a whole. An important subset of the practice population was identified at one practice, where there was a higher level of athletic expectation for Thoroughbred racehorses compared to the other practice populations. As a result, further analysis of this subset was also performed.

The subsequent collation and analysis of the data was time consuming, and required the acquisition of skills in statistical analysis. However, once these skills have been acquired, it would be possible to perform these analyses whilst working in a private practice, although time away from clinical duties would be beneficial. This demonstrates that it is possible to conduct good quality, practice-based clinical research, although a suitable support structure allowing the acquisition of further statistical skills and a reduction in clinical duties would be advantageous. It is with this aim in mind that the Cambridge Infectious Disease Consortium created their clinical research outreach programme, with the added incentive of a financial reimbursement for all participating practices to cover the expense encountered when employing a locum veterinarian. Indeed, if more practices were to adopt a similar approach, it may encourage many young veterinarians to venture into becoming involved in clinical research, without having to leave a clinical position for one in academia, especially if suitable sustainable partnerships between practices and interested academic departments could be maintained.

It could be argued that it does not have to be a veterinarian that performs the literature reviews, collection and collation of data, or the subsequent analysis of these data. In this way it would not be necessary for clinicians to take time away from their clinical duties in order for practice-based research to be performed. However, it is the veterinarian who is able to identify questions that are directly relevant to their practice population, where no

answer currently exists. There is also much to be gained by a clinician in performing a literature review of the relevant area, both in terms of increasing their existing knowledge base, but also in appreciating fully how to review studies, recognising both their advantages and their short-comings. This appreciation of study design and statistical analysis can then be transferred to future articles read in veterinary journals, allowing the clinician to appraise them and decide whether they are of a good quality of evidence, in EBM terms, and whether the results are directly relevant to the clinician's individual practice population. Similarly, by learning how to perform some simple statistical analyses, a greater understanding, not only of the results of the clinician's own research, but also of the results reported in the published literature, can be achieved.

The results provided by the studies performed here all answered a clinically relevant question, and the results are directly applicable to the intended end user: the general equine practitioner. In addition, they have provided a higher 'class' of evidence in EBM terms than was previously available. Although only one study could be classified as providing class A evidence, when using the classification system proposed by Yusuf *et al.* (1998), the other studies were all classified as class B evidence, thereby still providing a valuable addition to the current literature pool. The next step would be to conduct randomised trials investigating the efficacy of the different treatment regimens employed in these studies. However, in order to achieve sufficient case numbers, it would be necessary to either have a lengthy study period, or conduct a multi-centre study. Conducting a multi-centre study would require a considerable level of commitment from the participating practices, relying on the goodwill of the participants to agree on and adhere to a particular treatment regimen, then collect the relevant data accurately. As has already been demonstrated in the medical profession (Cruse & Foord, 1980), multi-centre studies are likely to be the best way forward for veterinary clinical research, in order to achieve sufficient case numbers to provide answers that are directly relevant to practice-based clinical situations.

One apparent shortcoming of the current study was the lack of opportunity to discuss the findings of the individual studies with practitioners, and gain feedback from them on how relevant they perceived the results to be to their practice situation. The fifth, and final, step in the application of the principles of EBM is the critical evaluation of the outcome of all the preceding steps. Although the current study performed self-evaluation, a more rigorous test of the applicability of the results to the intended target audience would have been the dissemination of the results to such an audience. A review of the results by practitioners

would then have provided a more accurate assessment of whether the underlying aim of the study had been achieved: the application of the principles of EBM to equine practice, in order to generate, and then answer, clinically relevant questions.

Although many in academia have been keen to embrace the principles of Evidence-Based Medicine, general practitioners are still left questioning the necessity of such an approach. The question of whether the application of EBM to a common problem will actually change the outcome is a valid one, and one that must be addressed. Evidence-based medicine will be perceived to be of little relevance to the equine practitioner if the studies performed and the results obtained cannot be applied to general practice (Mair, 2001; Mair and Cohen, 2003; Marr, 2003). In fact, this approach would be a direct contraindication of the original ethos of EBM. It must be remembered that EBM should be answering questions relevant to an individual's situation and therefore the questions that are addressed must pertain to general practice for a practitioner to be able to utilise the results (Mair, 2001; Mair and Cohen, 2003; Marr, 2003).

There has recently been encouragement for general practitioners to contribute to future research, either by providing the questions that are relevant to practice, thereby giving researchers guidance as to where to focus future research, or by participating in practice-based research. In reality, many of the veterinarians who hold an active interest in research work are already in academic institutions, in order to gain access to a wide range of facilities and funding opportunities that enable high quality research to be conducted. Those practitioners that are keen to participate in clinical research are often at a loss as to how to start when planning a practice-based research project, and any aspirations to publish in a prestigious, peer-reviewed journal are often shelved at the prospect of having to undertake the rigours of the writing and peer-review process. The peer-review process is to ensure that only high quality, relevant research is published, yet this may leave many practitioners feeling that any contribution they may have to make would be inadequate in such a forum.

Currently, the results of research utilising the principles of EBM are published in veterinary journals, having been subjected to the peer-review process. However, it could be asked whether journals really are the most appropriate vehicle for disseminating new, and potentially ground-breaking, research. Many such journals have a long backlog of accepted manuscripts, leading to a substantial delay between the research being conducted

and the results being disseminated to a target audience. Theoretically, this delay could lead to the results being out-of-date by the time they are published, even though they are being published as some of the most up-to-date and applicable results in their field. This delay in publication and dissemination of results is the anathema of the ethos of EBM. The medical profession has addressed this problem by the creation and utilisation of on-line journals for research following the principles of EBM, allowing the results to be both rapidly and widely disseminated to the target audience. However, with no on-line EBM journals available to the veterinary profession, at the current time it would be appear that printed journals are the most efficient way for results to be communicated to the profession as a whole.

In order for the results of a manuscript to reach its target audience, it must be published in an appropriate journal. If a practitioner were to attempt to read all the journals available – both the general and specialised – there would be insufficient time both to review and digest all the relevant results on top of a normal workload. In addition, there would be a substantial cost incurred in subscribing to the plethora of publications that are available. As a rule, general practitioners are more likely to read one of the many broad-spectrum journals available to the profession, as opposed to a specialist, or scientific, journal if they wish to keep abreast of all the new developments. To this end, research must then be published in a journal appropriate to the intended target audience. However, authors may be attracted to the more specialised journals for the publication of their research, in particular in light of research assessment exercises and impact factor pressures, thereby taking that information away from the readership for which it was intended.

If it is to be accepted that journals are, at this time, the most appropriate method for the communication of relevant research to the profession, then how manuscripts are accepted for publication must itself be reviewed. Many journals utilise the peer-review system, where manuscripts are passed on to members of the profession with a specific interest in that field, for review. The onus is then on the reviewer to decide whether the manuscript is suitable for publication, and whether any amendments should be made. Journals rely on the goodwill of reviewers to add to their normal workload by taking on such responsibilities. An obvious flaw in the review process is that there is no formal training in either how to review a manuscript appropriately or the understanding of statistical techniques, with many learning through personal experience. The potential also exists for the introduction of deliberate bias into the review process, or a reviewer's judgement being

influenced by personal interests. Without any standardisation of the review process, this results in a wide variation in the personal opinion of reviewers when considering the same manuscript. In addition, there is inevitably a delay until reviewers can find an appropriate break in their workload to examine the manuscript thoroughly and prepare a report. This delay will add to the delay faced by a manuscript awaiting publication, thereby increasing the time-lag between the submission of research and the dissemination of that research to the wider population.

The Equine Veterinary Journal launched a section dedicated to Clinical Evidence Articles in November 2003, in order to disseminate results of clinically relevant studies rapidly, addressing common and important diseases and promote the principles of EBM within the veterinary profession (Rossdale *et al.* 2003). Since the launch of the Clinical Evidence section in the Equine Veterinary Journal, only eight articles have been published that fulfil the inclusion criteria for this section (Edwards *et al.* 2003; Barakzai *et al.* 2004; Johnston *et al.* 2004; Smith *et al.* 2004; Proudman *et al.* 2005a,b; Smith *et al.* 2005; Valverde *et al.* 2005), whilst the General Articles section of the journal continues to be inundated with manuscripts. This poor response to an avenue offering fast-track publication for manuscripts fulfilling the inclusion criteria must be queried. It could be that the rigorous inclusion criteria, along with the stringent requirements on the overall length of the manuscript, are prohibitive. The main criterion is that the article must address a clinically relevant question, which is clearly defined at the outset. Furthermore, a sample size calculation must be performed at the outset of the study to ensure that there will be sufficient power to detect a statistically significant difference for a medically meaningful outcome. The case definition criteria and outcomes of interest must be unambiguous, rigorously applied and explicitly reported at all stages of the study. Controls, randomisation and blinding should be utilised as appropriate, and reported accordingly, and appropriate analytical methods applied to the data. Authors may believe that it is not possible to fulfil all these inclusion criteria in sufficient detail, and still produce a manuscript that conforms to the length of general articles. Another possible explanation is the lack of clinical research that is submitted. The majority of articles submitted from academic institutions are reporting results of bench or basic science research. This is unlikely to be wholly because they believe that these areas are more worthy, or interesting, to research than questions that are more pressing to general practitioners. Academic institutions must attract funding from the research councils or charities to support their research interests, and inevitably, the sources of this funding to some extent dictate the

nature of the research undertaken. Funding for basic science research is, generally, more widely available and the findings of such research are, generally, more amenable to publication in high impact factor journals, which greatly influence the rating of the scientists and their institute. Hence, clinically orientated research faces many difficulties in gaining points with basic science.

It could be argued that it takes time to:

1. identify an area suitable for, and in need of, further research,
2. design an appropriate study,
3. implement this study, collecting all the relevant data,
4. process these data,
5. interpret and present these data in a comprehensible fashion.

Despite these difficulties, the initiative of the Equine Veterinary Journal is to be applauded and it is to be hoped that the volume of well-founded research will start to grow steadily over the coming years. In the meantime, many of the early studies have re-investigated areas that have already been covered extensively in the literature. These studies have not contradicted their earlier counterparts, but have reinforced the findings of prior research, as well as contributing new results to the literature pool. This finding should encourage further implementation of the principles of EBM in veterinary research, instead of shying away from it with the fear that a 'new science' may disprove widely accepted, long-standing beliefs. The Equine Veterinary Journal has itself been proactive in encouraging the use of the principles of EBM in future research, and promoting the understanding of the principles of EBM, both through the Clinical Evidence section, and the Clinical Evidence Notebook, launched in May 2005. The Notebook was intended to complement research articles and address a wide range of issues relating to the collection, analysis and interpretation of data of clinical relevance (Marr and Rossdale, 2005).

The current study should be viewed as 'the tip of the iceberg', demonstrating that it is entirely possible to conduct modest, practice-based clinical studies within private practices, and generating worthwhile results from these studies that are applicable to a wider audience. The knowledge gained from this, and hopefully other future studies, will provide answers to questions that are directly relevant to equine practitioners. In addition to providing a good quality of evidence to support the most up-to-date and relevant knowledge, they provide substance to support clinical decision making. In this way, the

veterinary profession can be seen to be demonstrating a commitment to best practice and effective self-regulation.

Appendix 1

Survey of horse owners to obtain long-term follow-up of horses treated for septic digital tenosynovitis – Questionnaire

What is the likelihood that a horse treated for septic digital tenosynovitis will return to its previous level of athletic function?

Horse: **Owner:**

What best describes the intended use of the horse at the time of purchase?

Breeding	☐	Eventing	☐	Polo	☐
General Purpose	☐	Show jumping	☐	Hunting	☐
Showing	☐	Flat racing	☐	Team chasing	☐
Dressage	☐	Jump racing	☐		

What best describes the use of the horse at the time of the injury?

Breeding	☐	Eventing	☐	Polo	☐
General Purpose	☐	Show jumping	☐	Hunting	☐
Showing	☐	Flat racing	☐	Team chasing	☐
Dressage	☐	Jump racing	☐		

Has the horse returned to the same type of work after the injury?

Yes ☐
No ☐

If no, is the reason directly attributable to the injury (ie lameness associated with the tendon or tendon sheath) or is it due to any other unrelated injuries/illnesses?

Related ☐
Unrelated ☐

Has the horse returned to the same level of work after the injury?

Yes ☐
No ☐

If no, is the reason directly attributable to the injury (ie lameness associated with the tendon or tendon sheath) or is it due to any other unrelated injuries/illnesses?

Related ☐
Unrelated ☐

Has the horse attained its originally intended use after the injury?

Yes ☐
No ☐

If no, is the reason directly attributable to the injury (ie lameness associated with the tendon or tendon sheath) or is it due to any other unrelated injuries/illnesses?

Related ☐
Unrelated ☐

Have there been any long term/recurrent lameness problems associated with the initial injury?

Yes ☐
No ☐

Appendix 2

Univariable analysis of factors influencing short and long term prognosis following treatment for septic digital tenosynovitis.

Appendix 2.1: Univariable analysis of factors influencing likelihood of survival following treatment for septic digital tenosynovitis

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
Age of horse at presentation (referent <5 yrs)					
5 – 10 yrs	-2.04	1.11	0.14	0.01 – 1.15	0.067
10 – 14 yrs	19	10163	∞	0.00 - ∞	0.998
> 14 yrs	-0.89	1.27	0.41	0.03 – 4.89	4.80
Gender of horse (referent female)					
Male	0.106	0.646	1.11	0.31 – 3.95	0.869
Limb affected (referent forelimb)					
Hindlimb	-0.28	0.67	0.76	0.20 – 2.79	0.675
Location of wound (referent fetlock)					
Pastern	-0.36	0.72	0.69	0.17 – 2.84	0.611
Foot	20	28097	∞	0.00 - ∞	0.999
Delay between onset of sepsis and commencement of treatment (referent <24 hrs)					
1-7ds	20	11295	∞	0.00 - ∞	0.999
>7 ds	-0.76	0.89	0.47	0.08 – 2.67	0.391

Appendix 2.2: Univariable analysis of factors affecting likelihood of return to previous level of performance following treatment for septic digital tenosynovitis

	Coefficient	S.E.	Adjusted O.R.	95% C.I.	p
Age of horse at presentation (referent <5 yrs)					
5 – 10 yrs	1.10	0.68	3.00	0.80 – 11.31	0.105
10 – 14 yrs	0.81	0.70	2.25	0.57 – 8.82	2.45
> 14 yrs	0.29	0.67	1.33	0.36 – 4.93	0.666
Gender of horse (referent female)					
Male	0.41	0.47	1.50	0.59 – 3.80	3.89
Limb affected (referent forelimb)					
Hindlimb	-0.55	0.48	0.57	0.22 – 1.47	0.249
Location of wound (referent fetlock)					
Pastern	0.07	0.49	1.07	0.41 – 2.83	0.889
Foot	-21	17307	∞	0.00 - ∞	0.999
Delay between onset of sepsis and commencement of treatment (referent <24 hrs)					
1-7ds	-2.08	0.83	0.13	0.02 – 0.63	0.012
>7 ds	1.14	1.13	3.12	0.34 – 28.73	0.314

Appendix 3

Survey of horse owners to obtain long-term follow-up of horses treated for septic arthritis - Questionnaire

What is the likelihood that a mature horse treated for septic arthritis will be able to return to its' previous level of athletic performance?

Horse: **Owner:** **Clinic:**

What best describes the intended use of the horse at the time of purchase?

Breeding	☐	Eventing	☐	Polo	☐
General Purpose	☐	Show jumping	☐	Hunting	☐
Showing	☐	Flat racing	☐	Team chasing	☐
Dressage	☐	Jump racing	☐		

What best describes the use of the horse at the time of the injury?

Breeding	☐	Eventing	☐	Polo	☐
General Purpose	☐	Show jumping	☐	Hunting	☐
Showing	☐	Flat racing	☐	Team chasing	☐
Dressage	☐	Jump racing	☐		

Has the horse returned to the same type of work after the injury?

Yes ☐
No ☐

If no, is the reason directly attributable to the injury (ie lameness associated with that joint) or is it due to any other unrelated injuries/illnesses?

Related ☐
Unrelated ☐

Has the horse returned to the same level of work after the injury?

Yes ☐
No ☐

If no, is the reason directly attributable to the injury (ie lameness associated with that joint) or is it due to any other unrelated injuries/illnesses?

Related ☐
Unrelated ☐

Has the horse attained its originally intended use after the injury?

Yes ☐
No ☐

If no, is the reason directly attributable to the injury (ie lameness associated with that joint) or is it due to any other unrelated injuries/illnesses?

Related ☐
Unrelated ☐

Have there been any long term/recurrent lameness problems associated with the initial injury?

Yes ☐
No ☐

Appendix 4

Univariable analysis of factors influencing short and long term prognosis following treatment for septic arthritis.

Appendix 4.1: Univariable logistic regression analysis of factors affecting survival following treatment for septic arthritis

	Coefficient	S.E.	OR	95% CI	p
Rads	-1.20	0.35	0.30	0.15 – 0.60	0.001
Duration (referent <24hrs)					
1 – 7ds	-0.21	0.50	0.81	0.31 – 2.14	0.670
>7ds	-1.61	0.37	0.20	0.10 – 0.41	<0.001
Age (referent <8yrs)					
8-15 yrs	-0.84	0.35	0.43	0.22 – 0.85	0.016
>15 yrs	-0.94	0.50	0.39	0.15 – 1.03	0.058
Specific joint affected (referent metatarso-phalangeal joint)					
Carpus	-1.28	0.86	0.28	0.05 – 1.51	0.138
Stifle	-2.47	0.86	0.08	0.02 – 0.46	0.004
Hock	-1.39	0.79	0.25	0.05 – 1.16	0.076
Metacarpo-phalangeal joint	-0.81	1.03	0.44	0.06 – 3.32	0.429
Distal inter-phalangeal joint	-2.64	0.94	0.07	0.01 – 0.45	0.005
Distal inter-phalangeal joint and navicular bursa	-3.05	1.16	0.05	0.00 – 0.46	0.009
Navicular bursa	-3.23	0.98	0.04	0.01 – 0.27	0.001
Elbow	-2.53	0.93	0.08	0.01 – 0.49	0.006
Proximal inter-phalangeal joint	-3.04	0.89	0.05	0.01 – 0.27	0.001
Route of infection (referent trauma)					
Iatrogenic	-0.99	0.56	0.37	0.13 – 1.11	0.076
Haematogenous	20.00	~	∞	0.00 – ∞	1.000
Synovial white cell count (referent <21 x 10^9 cells/l)					
21 – 71	-0.51	0.54	0.60	0.21 – 1.74	0.349
71 – 102	0.25	0.76	1.28	0.29 – 5.62	0.746
>102	0.00	0.62	1.00	0.29 – 3.39	1.000
Duration hospitalisation (referent <5ds)					
5-9 ds	22.00	~	∞	0.00 – ∞	0.996
9-12 ds	22.00	~	∞	0.00 – ∞	0.996
>12 ds	22.00	~	∞	0.00 – ∞	0.996
Number lavages performed (referent 1)					
2-4	0.35	0.36	1.42	0.69 – 2.90	0.338
>4	-1.23	0.76	0.29	0.07 – 1.29	0.104

Appendix 4.2: Univariable logistic regression analysis of factors affecting likelihood of return to original athletic function following treatment for septic arthritis

	Coefficient	S.E.	OR	95% CI	p
Rads	-1.20	0.43	0.30	0.13 – 0.70	0.005
Duration (referent <24hrs)					
1 – 7ds	-0.07	0.45	0.93	0.39 – 2.23	0.867
>7ds	-0.82	0.42	0.44	0.19 – 1.01	0.052
Age (referent <8yrs)					
8-15 yrs	-0.12	0.35	0.89	0.45 – 1.74	0.728
>15 yrs	-0.61	0.52	0.54	0.19 – 1.51	0.242
Specific joint affected (referent metatarso-phalangeal joint)					
Carpus	0.12	0.47	1.13	0.45 – 2.84	0.803
Stifle	0.41	0.74	1.50	0.35 – 6.38	0.583
Hock	0.33	0.41	1.39	0.62 – 3.11	0.424
Metacarpo-phalangeal joint	-0.12	0.57	0.88	0.29 – 2.68	0.827
Distal inter-phalangeal joint	0.12	0.91	1.13	0.19 – 6.76	0.898
Distal inter-phalangeal joint and navicular bursa	-1.27	1.26	0.28	0.02 – 3.32	0.314
Navicular bursa	0.81	1.16	2.25	0.23 – 21.70	0.483
Elbow	0.12	1.26	1.13	0.10 – 13.29	0.926
Proximal inter-phalangeal joint	-2.19	1.13	0.11	0.01 – 1.04	0.054
Route of infection (referent trauma)					
Iatrogenic	-0.76	0.60	0.47	0.14 – 1.52	0.208
Haematogenous	-22.00	∞	0.00	0.00 – ∞	0.999
Synovial white cell count (referent <21 x 10^9 cells/l)					
21 – 71	-0.50	0.57	0.61	0.20 – 1.87	0.386
71 – 102	-0.38	0.67	0.69	0.19 – 2.54	0.572
>102	-0.63	0.60	0.53	0.16 – 1.72	0.294
Duration hospitalisation (referent <5ds)					
5-9 ds	0.95	0.50	2.58	0.97 – 6.87	0.057
9-12 ds	-0.15	0.46	0.86	0.35 – 2.14	0.747
>12 ds	-0.15	0.46	0.86	0.35 – 2.14	0.747
Number lavages performed (referent 1)					
2-4	-0.17	0.32	0.84	0.45 – 1.57	0.595
>4	-2.14	1.14	0.12	0.01 – 1.09	0.059

Appendix 5

Univariable analysis of factors influencing short and long term prognosis in mature Thoroughbred racehorses following treatment for septic arthritis.

Appendix 5.1: Univariable analysis of factors affecting survival in mature Thoroughbred racehorses following treatment for septic arthritis

	Coefficient	S.E.	OR	95% CI	p
Gender (referent male)	0.85	0.86	2.34	0.44 – 12.62	0.321
Radiographic abnormalities at admission	20	20140	∞	0.00 – ∞	0.999
Duration (referent <24hrs)					
1 – 5ds	-0.80	1.24	0.45	0.04 – 5.06	0.518
>5ds	-1.90	0.86	0.15	0.03 – 0.80	0.027
Age (referent ≤2yrs)					
3-4 yrs	0.32	0.89	1.38	0.24 – 7.94	0.719
>4 yrs	0.73	1.15	2.07	0.22 – 19.63	0.527
Specific joint affected (referent metatarso-phalangeal joint)					
Carpus	19	8104	∞	0.00 – ∞	0.998
Stifle	-2.35	1.60	0.10	0.00 – 2.18	0.141
Hock	-0.97	1.34	0.38	0.03 – 5.27	0.472
Metacarpo-phalangeal joint	-0.56	1.31	0.57	0.04 – 7.44	0.669
Distal inter-phalangeal joint	19	17507	∞	0.00 – ∞	0.999
Distal inter-phalangeal joint and navicular bursa	19	30324	∞	0.00 – ∞	0.999
Navicular bursa	-0.97	1.34	0.38	0.03 – 5.27	0.472
Proximal inter-phalangeal joint	-3.05	1.43	0.05	0.00 – 0.79	0.033
Route of infection (referent trauma)					
Iatrogenic	-0.02	1.15	0.98	0.10 – 9.39	0.984
Haematogenous	20	39965	∞	0.00 – ∞	1.000
Synovial white cell count (referent <50)					
50 – 120	21	11854	∞	0.00 – ∞	0.999
>120	0.41	1.30	1.50	0.12 – 19.24	0.755
Number lavages performed (referent 1)					
>1	0.00	0.87	1.00	0.18 – 5.53	1.000

Appendix 5.2: Univariable analysis of factors affecting likelihood of racing in mature Thoroughbred racehorses, following treatment for septic arthritis

	Coefficient	S.E.	OR	95% CI	p
Gender (referent male)	-0.84	0.58	0.43	0.14 – 1.34	0.146
Radiographic abnormalities at admission	-1.79	1.20	0.17	0.02 – 1.74	0.134
Duration (referent <24hrs)					
1 – 5ds	-0.77	0.89	0.46	0.08 – 2.63	0.384
>5ds	-0.49	0.84	0.62	0.12 – 3.19	0.563
Age (referent ≤2yrs)					
2-4 yrs	-21	8655	0.00	0.00 – ∞	0.998
>4 yrs	-21	8655	0.00	0.00 – ∞	0.998
Specific joint affected (referent metatarso-phalangeal joint)					
Carpus	-0.33	0.72	0.72	0.18 – 2.92	0.643
Stifle	21	25687	∞	0.00 – ∞	0.999
Hock	0.48	1.25	1.62	0.14 – 18.58	0.700
Metacarpo-phalangeal joint	-0.21	1.03	0.81	0.11 – 6.04	0.835
Distal inter-phalangeal joint	0.07	1.31	1.08	0.08 – 14.08	0.955
Navicular bursa	0.48	1.25	1.62	0.14 – 18.58	0.700
Proximal inter-phalangeal joint	-22	26303	0.00	0.00 – ∞	0.999
Route of infection (referent trauma)					
Iatrogenic	-0.44	0.84	0.64	0.12 – 3.30	0.596
Haematogenous	-22	26726	0.00	0.00 – ∞	0.999
Synovial white cell count (referent <50)					
50-120	0.45	0.80	1.57	0.33 – 7.48	0.570
>120	-0.11	0.89	0.89	0.16 – 5.11	0.899
Number lavages performed (referent 1)					
>1	-1.00	0.65	0.37	0.10 – 1.33	0.126

Appendix 6

General Linear Model comparing highest Official Rating achieved by mature Thoroughbred racehorses treated for septic arthritis, and the comparison population.

Term	Coefficient	S.E.	p
Constant	54.08	4.23	<0.001
Case/Sib			
Case	-12.97	4.23	0.004
Sib code			
1	37.24	20.95	0.082
2	-54.08	25.44	0.039
3	11.91	20.95	0.572
4	21.94	35.99	0.545
5	-34.08	25.44	0.187
6	27.94	35.99	0.441
7	-3.42	20.95	0.871
8	10.58	20.95	0.616
9	-5.76	20.95	0.785
10	44.24	20.95	0.040
11	13.92	25.44	0.587
12	15.24	20.95	0.470
13	8.92	25.44	0.727
14	-5.58	25.44	0.827
15	9.42	25.44	0.713
16	31.42	25.44	0.223
17	-22.09	20.95	0.297
18	26.91	20.95	0.205
19	-16.58	25.44	0.518
20	-5.06	35.99	0.889
21	-67.06	35.99	0.069
22	22.91	20.95	0.280
23	42.91	20.95	0.046
24	28.91	20.59	0.174
25	-14.08	25.44	0.582
26	-49.76	20.95	0.022
27	-30.08	25.44	0.243
28	-4.58	25.44	0.858
29	15.92	25.44	0.535
30	-49.76	20.95	0.022
31	26.92	25.44	0.295
32	-0.76	20.95	0.971
33	-49.76	20.95	0.022
34	-4.58	25.44	0.858
35	29.92	25.44	0.245

Appendix 7

Incisional complications following exploratory celiotomy: does a belly band reduce the risk? – Data collection forms

Sheet 1

Case details

Horse name: Owner name: Date of surgery:

Age: Sex: M F MN Breed:

Use: Weight (kgs):

Duration of signs of abdominal discomfort prior to induction:

Severity of discomfort prior to induction: **mild / moderate / severe**

Evidence of endotoxaemia present prior to induction: **Y / N**

Pre-op. rectal temperature (°C), heart rate (bpm) and respiratory rate (bpm):

T: **P:** **R:**

Rectal findings:

Pre-op. haematology:
WBC:

Neutrophils:

Hct:

TP:

Pre-op. antibiotics:

Drugs	Total Dose	IM / IV / PO

Pre-op. analgesia:

Drugs	Total Dose	IM / IV / PO

Any evidence of pre-existing site of infection?

	Y/N
Skin wound remote to surgical site	
Nasal discharge	
Diarrhoea	

Sheet 2

Surgery Report Form

Date: **Surgeon:** **Nurse:**

Horse name: **Owner name:**

Duration of anaesthesia (mins): **Duration of surgery (mins):**

Surgical scrub solution used: pevidine / hibiscrub **Duration of surgical scrub (mins):**

Evidence of local skin reaction following surgical clip & scrub: **Y / N**

Surgical report (to include: nature of lesion found including anatomical location, any gut resected including site of resection, reason for resection, length of resection and type of anastomosis performed, viability and motility of gut prior to closure of abdomen):

Degree of peritoneal contamination: mild / moderate / severe

Length of incision (cm): **Linea lavaged after closure: Y / N** **Crystapen applied to linea: Y / N**

Deep layer closure (select as appropriate):

continuous ☐ interrupted: simple ☐ cruciate ☐ mattress ☐ near-far ☐ far-near ☐ other : ☐

Suture material (select as appropriate):

Vicryl ☐ Polysorb ☐ Biosyn ☐ PDS ☐ other: ☐ **SIZE:**

Subcutaneous closure (select as appropriate):

continuous ☐ interrupted: simple ☐ cruciate ☐ mattress ☐ other : ☐

Suture material (select as appropriate):

Vicryl ☐ other: ☐ **SIZE:**

Skin closure (select as appropriate):

continuous ☐ interrupted: simple ☐ cruciate ☐ mattress ☐ other : ☐

Suture material (select as appropriate):

Vicryl ☐ Nylon ☐ Prolene ☐ Staples ☐ **SIZE:**

Drain inserted: Y / N

Sheet 3

Horse name: **Owner name:**

Belly band applied: Y / N

Type of belly band used: Elasticated / Elastoplast

Daily wound assessment (answer yes/no as appropriate):

Post-op. day	Heat	Swelling	Pitting oedema	Pain on palpation	Serous discharge	Serosanguinous discharge	Purulent discharge	Partial wound dehiscence	Total wound dehiscence	Seroma / haematoma	Strike through on dressing	Dressing slipped prior to change	AM T(°C) P(bpm) R(bpm)	PM T(°C) P(bpm) R(bpm)	Initials
1															
2															
3															
4															
5															
6															
7															

Did horse receive any antibiotics other than Crystapen and Gentamicin: Y / N

If yes, please state which antibiotics and reason for change:

Sheet 4

Discharge Sheet

Horse name: **Owner name:**

Date of discharge:

Was horse pyrexic at any time during hospitalistion? Y / N

Was pyrexia attributed to (please check box as appropriate):

Respiratory tract infection	☐	Thrombophlebitis of jugular vein	☐
Gastro-intestinal tract infection	☐	Catheter site infection	☐
Wound infection	☐	Pyrexia of unknown origin	☐

Wound assessment at discharge – any evidence of (please check box as appropriate):

Heat	☐	Discharge from incision	☐
Pain on palpation	☐	Partial dehiscence of incision	☐
Swelling	☐	Total dehiscence of incision	☐
Pitting oedema	☐		

Please attach copies of results of all bloodwork, and any other laboratory investigations performed during hospitalization, to this sheet.

Appendix 8

Incisional complications following exploratory celiotomy: does a belly band reduce the risk? Definitions of outcomes

Definitions of outcomes

Post operative period

- defined as starting immediately following recovery of the horse from general anaesthesia, ie. post-op. day 1 is the same day as the surgical procedure.

Pyrexia

- identified by twice daily assessment of rectal temperature.
- rectal temperature > 39 ^{o}C at any one time.

Jugular thrombosis

- identified by observation and palpation of the ventral neck of the horse on a daily basis.
- swelling of, or palpable thrombus formation within, jugular vein in which an intra-venous catheter has been placed during hospitalization, ideally confirmed as narrowing or complete obstruction of jugular vein by the use of ultrasound.

Catheter site infection

- identified by observation and palpation of the catheter insertion site on a daily basis.
- localized swelling, heat or abscess formation, without associated thrombosis of underlying vessel, in the skin directly around the site of insertion of an intra-venous catheter, ideally confirmed by the use of ultrasound.

Diarrhoea

- identified by twice daily inspection of faeces.
- loose faeces for $\geq$ 24 hours.

Respiratory tract infection

- rectal temperature elevated >39 ^{o}C, associated with any two of the following criteria identifying the respiratory tract as the source of the pyrexia: nasal discharge (serous/purulent); increased respiratory rate; increased lung sounds on thoracic auscultation.

Gastro-intestinal tract infection

- rectal temperature elevated >39 °C, associated with diarrhoea of >24 hours duration.

Pyrexia of unknown origin

- rectal temperature elevated >39 °C, associated with non-specific signs of illness (eg. lethargy, inappetance), where no infectious cause is identified.

Definition of surgical terms

Anaesthesia time

- defined as the time from induction to the time that the gaseous anaesthetic agent was turned off.

Surgery time

- defined as the time from the first surgical incision until all surgical intervention (suturing, application of dressing, etc) had ceased.

Peritoneal contamination

- defined as any material from the lumen of the gastro-intestinal tract entering the peritoneal cavity.
- Mild – small particles of ingesta seen on the serosal surface of the gut, easily removed by lavage (eg after an enterotomy incision)
- Moderate – some ingesta seen on the serosal surface of the gut, where the amount renders it unlikely that all contamination will be removed following lavage.
- Severe – frank contamination of abdomen with significant quantities of ingesta, or evidence of peritonitis already present at time of closure of incision.

Identification and definition of complications during hospitalisation

Pain

- Mild – occasional pawing, may lie quietly in sternal / lateral recumbancy with no repeated attempts to roll. Responds readily, for prolonged periods, to administration of analgesia.

- Moderate – intermittent episodes of pawing and lieing down to roll, however when roused into a standing position will stand quietly. Responds well to analgesia, however only for a short time (hours).
- Severe – persistent pawing and rolling. Hard to maintain in a standing position, with administration of analgesia resulting in a poor response (< 1hr).

Endotoxaemia

- defined as exhibiting any two of the three following signs when being assessed prior to surgery: congested mucous membranes with prolonged capillary refill time, significantly elevated heart rate (>50 bpm), significantly elevated haematocrit (>50 l/l).

Drainage from incision

- identified by visual inspection of the surgical incision at every bandage/dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- any fluid seen to be leaking from the surgical site.

Serous drainage

- identified by visual inspection of the surgical incision at every bandage/dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- clear, straw coloured fluid leaking from incision.

Serosanguinous drainage

- identified by visual inspection of the surgical incision at every bandage/dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- clear, blood tinged fluid leaking from incision.

Purulent drainage

- identified by visual inspection of the surgical incision at every bandage/dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- cloudy, cellular fluid leaking from incision.

Heat

- identified by palpation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- incision palpably warmer compared to either temperature of surrounding skin, or to a comparable region, ie with a skin incision on neck, compare to other side of neck.

Pain on palpation of wound

- identified by gentle palpation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis
- horse flinches or makes an attempt to move away when incision is palpated

Swelling of incision

- identified by observation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- margins of incision raised above level of surrounding skin more than would be anticipated with the suture pattern used.

Oedema of incision

- identified by observation and palpation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- margins of incision raised above level of surrounding skin more than would be anticipated with the suture pattern used, and when digital pressure is applied to this area a visible indent remains for >5secs.

Partial wound dehiscence

- identified by observation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- disruption of less than 75% of the surgical wound.

Total wound dehiscence

- identified by observation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.

- disruption of at least 75% of the surgical wound.

Seroma/haematoma

- identified by observation and palpation of surgical incision on a daily basis.
- localized, fluid filled pocket in area of surgical wound.

Appendix 9

Univariable analysis of factors affecting the likelihood of the development of post-operative incisional complications following exploratory celiotomy

Appendix 9.1: Univariable analysis of factors affecting likelihood of the development of incisional drainage during hospitalisation following exploratory laparotomy for the investigation of abdominal discomfort

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	0.53	0.62	1.69	0.50 – 5.68	0.395
10 – 16 yrs	-0.17	0.61	0.85	0.26 – 2.78	0.783
>16 yrs	0.37	0.63	1.45	0.42 – 4.96	0.553
Gender (referent male)					
Female	-0.73	0.47	0.48	0.19 – 1.21	0.120
Weight (referent <500kgs)					
>500 kgs	0.77	0.46	2.17	0.88 – 5.35	0.094
Pain on presentation (referent mild)					
Moderate	1.02	0.55	2.76	0.94 – 8.07	0.064
Severe	0.90	0.55	2.47	0.84 – 7.30	0.102
Duration (referent <8hrs)					
8-24hrs	-0.17	0.53	0.85	0.30 – 2.39	0.754
>24hrs	-0.79	0.59	0.46	0.14 – 1.45	0.183
Endotoxic	0.93	0.51	2.53	0.92 – 6.94	0.071
Heart rate (referent <40 bpm)					
40-60 bpm	0.47	0.52	1.60	0.58 – 4.43	0.367
>60 bpm	1.20	0.66	3.31	0.90 – 12.13	0.071
Haematocrit (referent <33.2%)					
>33.2%	0.37	0.46	1.45	0.59 – 3.54	0.418
Affected bowel (referent large bowel)					
Small intestine	0.39	0.46	1.47	0.59 – 3.66	0.403
Caecum	21	11168	∞	0.00 – ∞	0.998
Primary lesion (referent displacement)					
Torsion	-0.37	0.72	0.69	0.17 – 2.81	0.602
Impaction	-0.88	1.08	0.42	0.05 – 3.43	0.416
Obstruction	-0.18	0.95	0.83	0.14 – 5.40	0.848
IBD	-22	25141	0.00	0.00 – ∞	0.999
EFE	0.78	0.98	2.19	0.32 – 15.04	0.426
Strangulating SI	0.22	0.84	1.25	0.24 – 6.44	0.790
Non strangulating SI	-0.47	0.81	0.63	0.13 – 3.07	0.562
LI distension	21	14418	∞	0.00 – ∞	0.999
Resection	0.40	0.51	1.49	0.55 – 4.03	0.433
Enterotomy	0.06	0.59	1.06	0.33 – 3.38	0.921
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	1.23	0.51	3.41	1.25 – 9.30	0.016

Appendix 9.1 continued overleaf

Appendix 9.1 contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	1.16	0.47	3.20	1.26 – 8.11	0.014
Length of incision (referent <28cm)					
>28 cms	0.92	0.45	2.51	1.03 – 6.12	0.043
Contamination of abdomen (referent mild)					
Moderate	2.06	1.08	7.85	0.95 – 65.14	0.056
Severe	21	24886	∞	0.00 – ∞	0.999
Lavage LA	-0.03	0.45	0.97	0.40 – 2.34	0.940
Crystapen on LA	-0.79	0.94	0.45	0.07 – 2.87	0.401
Subcutaneous suture layer	-0.11	0.46	0.90	0.36 – 2.23	0.817
Belly band	-0.72	0.45	0.49	0.20 – 1.18	0.112
Pyrexia	0.43	0.60	1.54	0.48 – 4.98	0.472

Appendix 9.2: Nominal logistic regression to investigate whether the use of a belly band influenced either whether a horse would develop incisional drainage or the nature of the drainage, during hospitalisation following an exploratory laparotomy for the investigation of abdominal discomfort

	Coefficient	S.E.	O.R.	95% C.I.	p
Sero-sanguinous (referent purulent)	-0.13	0.66	0.88	0.24 – 3.22	0.850
Serous (referent purulent)	0.80	0.92	2.22	0.36 – 13.54	0.386
None (referent purulent)	0.57	0.62	1.76	0.53 – 5.92	0.358

Appendix 9.3: Variable that influences likelihood of development of incisional complications at discharge from the hospital, subsequent to an exploratory laparotomy, following univariable binary logistic regression

	Coefficient	S.E.	O.R.	95% C.I.	p
Use of a belly band	1.67	0.70	0.19	0.05 – 0.75	0.018

Appendix 9.4: Univariable analysis of factors affecting likelihood of incisional drainage at discharge from the hospital, subsequent to an exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	-0.50	0.72	0.61	0.15 – 2.48	0.487
10 – 16 yrs	0.27	0.65	1.31	0.37 – 4.67	0.679
>16 yrs	-0.79	0.77	0.46	0.10 – 2.07	0.309
Gender (referent male)					
Female	-0.32	0.55	0.73	0.25 – 2.14	0.563
Weight (referent <500kgs)					
>500 kgs	0.36	0.51	1.44	0.53 – 3.90	0.475
Pain on presentation (referent mild)					
Moderate	0.09	0.65	1.09	0.31 – 3.89	0.893
Severe	0.81	0.62	2.25	0.67 – 7.56	0.189
Duration (referent <8hrs)					
8-24hrs	1.38	0.58	3.96	1.27 – 12.30	0.017
>24hrs	0.17	0.75	1.19	0.27 – 5.20	0.820
Endotoxic	1.05	0.53	2.85	1.01 – 8.02	0.047
Heart rate (referent <40 bpm)					
40-60 bpm	-0.85	0.67	0.43	0.11 – 1.60	0.207
>60 bpm	1.10	0.67	3.00	0.81 – 11.08	0.099
Haematocrit (referent <33.2%)					
>33.2%	0.78	0.54	2.18	0.75 – 6.31	0.152
Affected bowel (referent large bowel)					
Small intestine	1.11	0.55	3.02	1.03 – 8.85	0.044
Caecum	1.26	1.00	3.52	0.49 – 25.10	0.209
Primary lesion (referent displacement)					
Torsion	-0.24	0.86	0.78	0.14 – 4.24	0.778
Impaction	-20	12953	0.00	0.00 – ∞	0.999
Obstruction	-0.59	0.127	0.56	0.05 – 6.63	0.642
IBD	-20	28963	0.00	0.00 – ∞	0.999
EFE	1.43	0.94	4.17	0.66 – 26.29	0.129
Strangulating SI	0.87	0.88	2.38	0.42 – 13.39	0.325
Non strangulating SI	-0.30	1.02	0.74	0.10 – 5.49	0.769
LI distension	0.51	1.39	1.67	0.11 – 25.43	0.713
Resection	0.94	0.54	2.57	0.90 – 7.34	0.078
Enterotomy	-0.20	0.65	0.82	0.23 – 2.95	0.758
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	2.04	0.57	7.67	2.52 – 23.30	<0.001

Appendix 9.4 continued overleaf

Appendix 9.4, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	1.74	0.58	5.67	1.83 – 17.60	0.003
Length of incision (referent <28cm)					
>28 cms	1.58	0.61	4.84	1.06 – 16.03	0.010
Contamination of abdomen (referent mild)					
Moderate	1.34	0.70	3.80	0.97 – 14.86	0.055
Severe	23	35550	∞	0.00 – ∞	0.999
Lavage LA	-0.10	0.51	0.90	0.33 – 2.45	0.838
Crystapen on LA	-21	13013	0.00	0.00 – ∞	0.999
Subcutaneous suture layer	-0.72	0.52	0.49	0.18 – 1.34	0.162
Belly band	-1.23	0.57	0.29	0.10 – 0.90	0.132
Pyrexia	0.86	0.60	2.36	0.72 – 7.68	0.155
Drainage during hospitalisation	21	4918	∞	0.00 – ∞	0.997
Oedema during hospitalisation	0.92	0.81	2.52	0.52 – 12.24	0.252
Nature of drainage (referent none)					
Serous	0	12048	1.00	0.00 – ∞	1.000
Sero-sanguinous	21	4918	∞	0.00 – ∞	0.997
Purulent	23	4918	∞	0.00 – ∞	0.996

Appendix 9.5: Nominal logistic regression to investigate whether the use of a belly band influenced either whether a horse had incisional drainage, or the nature of the drainage, at discharge from the hospital following an exploratory laparotomy

	Coefficient	S.E.	O.R.	95% C.I.	P
Sero-sanguinous (referent purulent)					
	-1.14	1.23	0.32	0.03 – 3.56	0.355
None (referent purulent)					
	0.88	0.65	2.40	0.67 – 8.62	0.180

Appendix 9.6: Univariable analysis of factors affecting likelihood of incisional drainage at fourteen days post-discharge subsequent to an exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	0.36	0.64	1.43	0.41 – 5.01	0.577
10 – 16 yrs	-0.18	0.62	0.83	0.25 – 2.80	0.768
>16 yrs	-0.72	0.64	0.49	0.14 – 1.70	0.260
Gender (referent male)					
Female	0.04	0.47	1.04	0.41 – 2.62	0.939
Weight (referent <500kgs)					
>500 kgs	0.11	0.45	1.12	0.46 – 2.72	0.807
Pain on presentation (referent mild)					
Moderate	0.54	0.55	1.71	0.59 – 5.02	0.326
Severe	0.05	0.54	1.05	0.36 – 3.05	0.921
Duration (referent <8hrs)					
8-24hrs	1.25	0.58	3.50	1.13 – 10.80	0.029
>24hrs	0.81	0.61	2.25	0.68 – 7.42	0.183
Endotoxic	0.80	0.51	2.24	0.82 – 6.10	0.116
Heart rate (referent <40 bpm)					
40-60 bpm	-0.04	0.52	0.96	0.34 – 2.67	0.933
>60 bpm	1.04	0.67	2.84	0.76 – 10.58	0.121
Haematocrit (referent <33.2%)					
>33.2%	0.37	0.46	1.45	0.59 – 3.61	0.420
Affected bowel (referent large bowel)					
Small intestine	-0.13	0.47	0.88	0.35 – 2.22	0.790
Caecum	1.39	1.16	4.00	0.41 – 38.84	0.232
Primary lesion (referent displacement)					
Torsion	-1.30	0.75	0.27	0.06 – 1.19	0.084
Impaction	-0.81	1.17	0.44	0.05 – 4.37	0.487
Obstruction	-0.81	1.01	0.44	0.06 – 3.24	0.424
IBD	-22	24381	0.00	0.00 – ∞	0.999
EFE	-0.59	0.90	0.56	0.10 – 3.25	0.514
Strangulating SI	-0.81	0.83	0.44	0.09 – 2.28	0.330
Non strangulating SI	-1.22	0.88	0.30	0.05 – 1.67	0.168
LI distension	20	14077	∞	0.00 – ∞	0.999
Resection	-0.19	0.49	0.82	0.31 – 2.17	0.697
Enterotomy	-0.65	0.61	0.52	0.16 – 1.73	0.288
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	0.88	0.48	2.42	0.94 – 6.24	0.068

Appendix 9.6 continued overleaf

Appendix 9.6, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	0.57	0.46	1.78	0.73 – 4.34	0.208
Length of incision (referent <28cm)					
>28 cms	1.03	0.47	2.79	1.12 – 6.94	0.028
Contamination of abdomen (referent mild)					
Moderate	0.43	0.69	1.54	0.40 – 5.96	0.528
Severe	21	24390	∞	0.00 – ∞	0.999
Lavage LA	-0.33	0.46	0.72	0.29 – 1.76	0.466
Crystapen on LA	-0.49	0.94	0.62	0.10 – 3.90	0.606
Subcutaneous suture layer	-0.25	0.47	0.78	0.31 – 1.95	0.597
Belly band	-1.58	0.49	0.21	0.08 – 0.53	0.001
Pyrexia	1.35	0.70	3.87	0.98 – 15.34	0.054
Drainage during hospitalisation	1.26	0.48	3.53	1.38 – 9.01	0.008
Nature of drainage (referent none)					
Serous	1.39	0.94	4.00	0.63 – 25.32	0.141
Sero-sanguinous	0.61	0.54	1.85	0.63 – 5.37	0.260
Purulent	2.64	0.84	14.00	2.69 – 72.82	0.002
Oedema during hospitalisation	2.16	0.80	8.67	1.79 – 41.88	0.007
Drainage at discharge	2.77	0.79	15.98	3.39 – 75.25	<0.001
Nature of drainage (referent none)					
Sero-sanguinous	2.47	1.10	11.77	1.36 – 102.16	0.025
Purulent	3.00	1.08	20.18	2.45 – 165.98	0.005
Oedema at discharge	2.18	0.68	8.81	2.31 – 33.57	0.001

Appendix 9.7: Univariable analysis of factors affecting likelihood of having dehiscence of skin incision at fourteen days post-discharge, subsequent to exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	0.63	0.97	1.88	0.28 – 12.61	0.518
10 – 16 yrs	0.57	0.97	1.76	0.26 – 11.83	0.558
>16 yrs	-0.59	1.27	0.56	0.05 – 6.66	0.643
Gender (referent male)					
Female	-0.02	0.75	0.98	0.23 – 4.26	0.978
Weight (referent <500kgs)					
>500 kgs	1.57	0.84	4.83	0.93 – 24.95	0.060
Pain on presentation (referent mild)					
Moderate	0.98	0.91	2.67	0.45 – 15.96	0.283
Severe	0.65	0.96	1.91	0.29 – 12.44	0.499
Duration (referent <8hrs)					
8-24hrs	1.25	0.82	3.50	0.70 – 17.40	0.126
>24hrs	0.77	0.97	2.15	0.32 – 14.32	0.427
Endotoxic	0.24	0.75	1.28	0.29 – 5.60	0.748
Heart rate (referent <40 bpm)					
40-60 bpm	-0.53	0.76	0.59	0.13 – 2.62	0.486
>60 bpm	-1.16	1.17	0.31	0.03 – 3.08	0.319
Haematocrit (referent <33.2%)					
>33.2%	0.75	0.75	2.12	0.49 – 9.22	0.314
Affected bowel (referent large bowel)					
Small intestine	-1.10	0.84	0.33	0.06 – 1.73	0.191
Caecum	-21	18353	0.00	0.00 – ∞	0.999
Primary lesion (referent displacement)					
Torsion	-1.05	0.99	0.35	0.05 – 2.46	0.292
Impaction	1.20	1.20	3.33	0.32 – 34.83	0.315
Obstruction	-21	16754	0.00	0.00 – ∞	0.999
IBD	-21	41038	0.00	0.00 – ∞	1.000
EFE	-0.88	1.25	0.42	0.04 – 4.81	0.483
Strangulating SI	-21	11847	0.00	0.00 – ∞	0.999
Non strangulating SI	-0.99	1.24	0.37	0.03 – 4.23	0.424
LI distension	-21	23693	0.00	0.00 – ∞	0.999
Resection	-1.28	1.09	0.28	0.03 – 2.36	0.241
Enterotomy	-1.00	0.78	0.37	0.08 – 1.69	0.198
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	-0.17	0.75	0.85	0.19 – 3.67	0.824

Appendix 9.7 conitnued overleaf

Appendix 9.7, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	-0.64	0.75	0.53	0.12 – 2.29	0.394
Length of incision (referent <28cm)					
>28 cms	2.00	1.09	7.35	0.87 – 61.88	0.066
Contamination of abdomen (referent mild)					
Moderate	-0.17	1.12	0.85	0.09 – 7.60	0.882
Severe	-20	41277	0.00	0.00 – ∞	1.000
Lavage LA	-0.21	0.71	0.81	0.20 – 3.30	0.773
Crystapen on LA	0.74	1.18	2.09	0.21 – 21.11	0.531
Subcutaneous suture layer	-2.05	0.84	0.13	0.02 – 0.67	0.015
Belly band	-0.55	0.75	0.58	0.13 – 2.48	0.459
Pyrexia	1.71	0.76	5.51	1.24 – 24.43	0.025
Drainage during hospitalisation	1.00	0.84	2.71	0.53 – 13.98	0.233
Nature of drainage (referent none)					
Serous	-20	16851	0.00	0.00 – ∞	0.999
Sero-sanguinous	0.75	0.95	2.11	0.33 – 13.72	0.433
Purulent	1.64	0.93	5.17	0.93 – 32.00	0.078
Oedema during hospitalisation	0.58	1.10	1.79	0.21 – 15.61	0.597
Drainage at discharge	1.46	0.73	4.30	1.03 – 17.92	0.045
Nature of drainage (referent none)					
Sero-sanguinous	1.52	0.97	4.58	0.69 – 30.49	0.115
Purulent	1.42	0.84	4.13	0.80 – 21.30	0.091
Oedema at discharge	1.00	1.10	2.72	0.32 – 23.24	0.361

Appendix 9.8: Univariable analysis of factors affecting likelihood of skin incision having healed by fourteen days post-discharge, subsequent to an exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	-0.36	0.64	0.70	0.20 – 2.45	0.577
10 – 16 yrs	0.18	0.62	1.20	0.36 – 4.04	0.768
>16 yrs	0.72	0.64	2.06	0.59 – 7.21	0.260
Gender (referent male)					
Female	-0.04	0.47	0.96	0.38 – 2.44	0.939
Weight (referent <500kgs)					
>500 kgs	-0.11	0.45	0.89	0.37 – 2.18	0.807
Pain on presentation (referent mild)					
Moderate	-0.54	0.55	0.58	0.20 – 1.71	0.326
Severe	-0.05	0.54	0.95	0.33 – 2.74	0.921
Duration (referent <8hrs)					
8-24hrs	-1.25	0.58	0.29	0.09 – 0.88	0.029
>24hrs	-0.81	0.61	0.44	0.13 – 1.47	0.183
Endotoxic	-0.80	0.51	0.45	0.16 – 1.22	0.116
Heart rate (referent <40 bpm)					
40-60 bpm	0.04	0.52	1.05	0.37 – 2.92	0.933
>60 bpm	-1.04	0.67	0.35	0.09 – 1.32	0.121
Haematocrit (referent <33.2%)					
>33.2%	-0.37	0.46	0.69	0.28 – 1.71	0.420
Affected bowel (referent large bowel)					
Small intestine	0.13	0.47	1.13	0.45 – 2.85	0.790
Caecum	-1.39	1.16	0.25	0.03 – 2.43	0.232
Primary lesion (referent displacement)					
Torsion	1.30	0.75	3.66	0.84 – 15.91	0.084
Impaction	0.81	1.17	2.25	0.23 – 22.14	0.487
Obstruction	0.81	1.01	2.25	0.31 – 16.41	0.424
IBD	22	24381	∞	0.00 – ∞	0.999
EFE	0.59	0.90	1.80	0.31 – 10.52	0.514
Strangulating SI	0.81	0.83	2.25	0.44 – 11.52	0.330
Non strangulating SI	1.22	0.88	3.37	0.60 – 19.01	0.168
LI distension	-20	14077	0.00	0.00 – ∞	0.999
Resection	0.19	0.49	1.21	0.46 – 3.20	0.697
Enterotomy	0.65	0.61	1.91	0.58 – 6.32	0.288
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	-0.88	0.48	0.41	0.16 – 1.07	0.068

Appendix 9.8 continued overleaf

Appendix 9.8, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	-0.57	0.46	0.56	0.23 – 1.38	0.208
Length of incision (referent <28cm)					
>28 cms	-1.03	0.47	0.36	0.14 – 0.89	0.028
Contamination of abdomen (referent mild)					
Moderate	-0.43	0.69	0.65	0.17 – 2.50	0.528
Severe	-21	24390	0.00	0.00 – ∞	0.999
Lavage LA	0.33	0.46	1.40	0.57 – 3.43	0.466
Crystapen on LA	0.49	0.94	1.62	0.26 – 10.29	0.606
Subcutaneous suture layer	0.25	0.47	1.28	0.51 – 3.20	0.597
Belly band	1.58	0.49	4.87	1.88 – 12.61	0.001
Pyrexia	-1.35	0.70	0.26	0.07 – 1.02	0.054
Drainage during hospitalisation	-1.26	0.48	0.28	0.11 – 0.72	0.008
Nature of drainage (referent none)					
Serous	-1.39	0.94	0.25	0.04 – 1.58	0.141
Sero-sanguinous	-0.61	0.54	0.54	0.19 – 1.58	0.260
Purulent	-2.64	0.84	0.07	0.01 – 0.37	0.002
Oedema during hospitalisation	-2.16	0.80	0.12	0.02 – 0.56	0.007
Drainage at discharge	-2.77	0.79	0.06	0.01 – 0.29	<0.001
Nature of drainage (referent none)					
Sero-sanguinous	-2.47	1.10	0.08	0.01 – 0.74	0.025
Purulent	-3.00	1.08	0.05	0.01 – 0.41	0.005
Oedema at discharge	-2.18	0.68	0.11	0.03 – 0.43	0.001

Appendix 9.9: Univariable analysis of factors affecting likelihood of incisional drainage at thirty days post-discharge, subsequent to an exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	0.56	0.67	1.75	0.47 – 6.45	0.403
10 – 16 yrs	0.68	0.68	1.96	0.52 – 7.41	0.319
>16 yrs	0.00	0.68	1.00	0.26 – 3.82	1.000
Gender (referent male)					
Female	-0.16	0.50	0.85	0.32 – 2.26	0.750
Weight (referent <500kgs)					
>500 kgs	0.50	0.48	1.65	0.64 – 4.23	0.297
Pain on presentation (referent mild)					
Moderate	0.36	0.58	1.43	0.46 – 4.47	0.540
Severe	1.46	0.61	4.29	1.29 – 14.26	0.018
Duration (referent <8hrs)					
8-24hrs	1.48	0.61	4.37	1.32 – 14.50	0.016
>24hrs	-0.36	0.68	0.69	0.18 – 2.64	0.592
Endotoxic	0.88	0.53	2.40	0.85 – 6.79	0.099
Heart rate (referent <40 bpm)					
40-60 bpm	-0.29	0.55	0.75	0.26 – 2.19	0.598
>60 bpm	0.13	0.67	1.14	0.31 – 4.25	0.842
Haematocrit (referent <33.2%)					
>33.2%	0.27	0.49	1.31	0.50 – 3.42	0.585
Affected bowel (referent large bowel)					
Small intestine	0.32	0.49	1.37	0.53 – 3.60	0.517
Caecum	0.32	1.05	1.37	0.17 – 10.82	0.762
Primary lesion (referent displacement)					
Torsion	0.76	0.83	2.13	0.42 – 10.78	0.359
Impaction	2.08	1.34	8.00	0.58 – 110.27	0.120
Obstruction	-0.63	1.29	0.53	0.04 – 6.66	0.625
IBD	-20	24509	0.00	0.00 – ∞	0.999
EFE	1.27	1.02	3.56	0.48 – 26.28	0.214
Strangulating SI	1.32	0.90	3.73	0.65 – 21.58	0.141
Non strangulating SI	0.58	0.94	1.78	0.28 – 11.12	0.538
LI distension	22	14159	∞	0.00 – ∞	0.999
Resection	0.19	0.53	1.21	0.43 – 3.38	0.719
Enterotomy	-0.57	0.64	0.57	0.16 – 1.99	0.375
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	0.66	0.50	1.94	0.73 – 5.14	0.183

Appendix 9.9 continued overleaf

Appendix 9.9, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	0.32	0.48	1.37	0.54 – 3.49	0.503
Length of incision (referent <28cm)					
>28 cms	1.03	0.49	2.80	1.06 – 7.39	0.037
Contamination of abdomen (referent mild)					
Moderate	1.17	0.74	3.23	0.76 – 13.68	0.111
Severe	22	24476	∞	0.00 – ∞	0.999
Lavage LA	0.12	0.48	1.12	0.44 – 2.88	0.808
Crystapen on LA	-1.01	1.18	0.36	0.04 – 3.67	0.391
Subcutaneous suture layer	-0.95	0.50	0.39	0.14 – 1.04	0.060
Belly band	-1.54	0.52	0.21	0.08 – 0.59	0.003
Pyrexia	1.90	0.82	6.66	1.33 – 33.45	0.021
Drainage during hospitalisation	0.93	0.49	2.53	0.96 – 6.66	0.061
Nature of drainage (referent none)					
Serous	0	0.95	1.00	0.16 – 6.42	1.000
Sero-sanguinous	0.79	0.58	2.20	0.70 – 6.91	0.177
Purulent	1.48	0.66	4.40	1.20 – 16.17	0.026
Oedema during hospitalisation	2.56	1.08	12.96	1.57 – 106.73	0.017
Drainage at discharge	2.37	0.69	10.67	2.75 – 41.42	0.001
Nature of drainage (referent none)					
Sero-sanguinous	22	9992	∞	0.00 – ∞	0.998
Purulent	1.90	0.72	6.67	1.63 – 27.27	0.008
Oedema at discharge	1.64	0.69	5.17	1.33 – 20.12	0.018
Drainage at 14d	2.47	0.57	11.88	3.86 – 36.56	<0.001
Oedema at 14d	0.60	0.90	1.83	0.31 – 10.67	0.502
Dehiscence at 14d	22	8653	∞	0.00 – ∞	0.998

Appendix 9.10: Univariable analysis of factors affecting likelihood of skin incision having dehisced by thirty days post-discharge, subsequent to an exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	1.80	1.15	6.07	0.63 – 58.22	0.118
10 – 16 yrs	1.22	1.21	3.40	0.32 – 36.27	0.311
>16 yrs	0.00	1.46	1.00	0.06 – 17.33	1.000
Gender (referent male)					
Female	0.29	0.70	1.33	0.34 – 5.24	0.681
Weight (referent <500kgs)					
>500 kgs	1.68	0.83	5.38	1.05 – 27.50	0.043
Pain on presentation (referent mild)					
Moderate	1.19	0.89	3.29	0.57 – 18.83	0.181
Severe	0.68	0.96	1.97	0.30 – 13.01	0.480
Duration (referent <8hrs)					
8-24hrs	1.77	0.78	5.85	1.28 – 26.79	0.023
>24hrs	0.05	1.20	1.06	0.10 – 11.12	0.964
Endotoxic	0.07	0.74	1.07	0.25 – 4.61	0.926
Heart rate (referent <40 bpm)					
40-60 bpm	-1.14	0.79	0.32	0.07 – 1.50	0.148
>60 bpm	-0.65	0.91	0.52	0.09 – 3.14	0.478
Haematocrit (referent <33.2%)					
>33.2%	0.34	0.70	1.40	0.36 – 5.49	0.629
Affected bowel (referent large bowel)					
Small intestine	-2.20	1.09	0.11	0.01 – 0.93	0.043
Caecum	-21	18749	0.00	0.00 – ∞	0.999
Primary lesion (referent displacement)					
Torsion	0.55	0.94	1.73	0.27 – 10.97	0.560
Impaction	1.50	1.27	4.50	0.37 – 54.16	0.236
Obstruction	-21	15308	0.00	0.00 – ∞	0.999
IBD	-21	37498	0.00	0.00 – ∞	1.000
EFE	-0.29	1.33	0.75	0.05 – 10.23	0.829
Strangulating SI	-21	10825	0.00	0.00 – ∞	0.998
Non strangulating SI	-21	11858	0.00	0.00 – ∞	0.999
LI distension	-21	21649	0.00	0.00 – ∞	0.999
Resection	-1.36	1.09	0.26	0.03 – 2.18	0.213
Enterotomy	0.64	1.11	1.90	0.22 – 16.61	0.560
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	-0.32	0.74	0.73	0.17 – 3.09	0.666

Appendix 9.10 continued overleaf

Appendix 9.10, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	-0.78	0.74	0.46	0.11 – 1.93	0.287
Length of incision (referent <28cm)					
>28 cms	0.62	0.74	1.87	0.44 – 7.89	0.396
Contamination of abdomen (referent mild)					
Moderate	-0.42	1.11	0.65	0.07 – 5.81	0.703
Severe	-20	37731	0.00	0.00 – ∞	1.000
Lavage LA	0.49	0.74	1.64	0.39 – 6.94	0.502
Crystapen on LA	0.80	1.21	2.22	0.21 – 23.75	0.509
Subcutaneous suture layer	-1.69	0.74	0.19	0.04 – 0.79	0.023
Belly band	0.35	0.68	1.42	0.37 – 5.42	0.605
Pyrexia	1.08	0.79	2.95	0.63 – 13.78	0.170
Drainage during hospitalisation	1.16	0.83	3.20	0.63 – 16.29	0.161
Nature of drainage (referent none)					
Serous	1.03	1.32	2.80	0.21 – 37.03	0.434
Sero-sanguinous	0.39	1.04	1.47	0.19 – 11.39	0.710
Purulent	1.85	0.91	6.36	1.07 – 37.81	0.042
Oedema during hospitalisation	0.64	1.11	1.90	0.22 – 16.61	0.560
Drainage at discharge	1.25	0.70	3.50	0.89 – 13.84	0.074
Nature of drainage (referent none)					
Sero-sanguinous	0.67	1.19	1.96	0.19 – 20.26	0.572
Purulent	1.47	0.76	4.36	0.98 – 19.42	0.054
Oedema at discharge	1.03	1.10	2.81	0.33 – 24.04	0.345
Drainage at 14d	21	6471	∞	0.00 – ∞	0.997
Oedema at 14d	-1.30	0.94	0.27	0.04 – 1.73	0.167
Dehiscence at 14d	4.97	1.22	144.67	13.20 – 1585.70	<0.001

Appendix 9.11: Univariable analysis of factors affecting likelihood of skin incision having healed by thirty days post-discharge, subsequent to an exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	-0.56	0.67	0.57	0.15 – 2.12	0.403
10 – 16 yrs	-0.68	0.68	0.51	0.13 – 1.92	0.319
>16 yrs	0.00	0.68	1.00	0.26 – 3.82	1.000
Gender (referent male)					
Female	0.16	0.50	1.17	0.44 – 3.09	0.750
Weight (referent <500kgs)					
>500 kgs	-0.50	0.48	0.61	0.24 – 1.55	0.297
Pain on presentation (referent mild)					
Moderate	-0.36	0.58	0.70	0.22 – 2.19	0.540
Severe	-1.46	0.61	0.23	0.07 – 0.78	0.018
Duration (referent <8hrs)					
8-24hrs	-1.48	0.61	0.23	0.07 – 0.76	0.016
>24hrs	0.36	0.68	1.44	0.38 – 5.47	0.592
Endotoxic	-0.88	0.53	0.42	0.15 – 1.18	0.099
Heart rate (referent <40 bpm)					
40-60 bpm	0.29	0.55	1.33	0.46 – 3.89	0.598
>60 bpm	-0.13	0.67	0.88	0.24 – 3.26	0.842
Haematocrit (referent <33.2%)					
>33.2%	-0.27	0.49	0.76	0.29 – 2.00	0.585
Affected bowel (referent large bowel)					
Small intestine	-0.32	0.49	0.73	0.28 – 1.90	0.517
Caecum	-0.32	1.05	0.73	0.09 – 5.72	0.762
Primary lesion (referent displacement)					
Torsion	-0.76	0.83	0.47	0.09 – 2.37	0.359
Impaction	-2.08	1.34	0.13	0.01 – 1.72	0.120
Obstruction	0.63	1.29	1.87	0.15 – 23.40	0.625
IBD	20	24509	∞	0.00 – ∞	0.999
EFE	-1.27	1.02	0.28	0.04 – 2.08	0.214
Strangulating SI	-1.32	0.90	0.27	0.05 – 1.55	0.141
Non strangulating SI	-0.58	0.94	0.56	0.09 – 3.52	0.538
LI distension	-22	14159	0.00	0.00 – ∞	0.999
Resection	-0.19	0.53	0.83	0.30 – 2.32	0.719
Enterotomy	0.57	0.64	1.76	0.50 – 6.18	0.375
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	-0.66	0.50	0.52	0.19 – 1.37	0.183

Appendix 9.11 continued overleaf

Appendix 9.11, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	-0.32	0.48	0.73	0.29 – 1.85	0.503
Length of incision (referent <28cm)					
>28 cms	-1.03	0.49	0.36	0.14 – 0.94	0.037
Contamination of abdomen (referent mild)					
Moderate	-1.17	0.74	0.31	0.07 – 1.31	0.111
Severe	-22	24476	0.00	0.00 – ∞	0.999
Lavage LA	-0.12	0.48	0.89	0.35 – 2.28	0.808
Crystapen on LA	1.01	1.18	2.75	0.27 – 27.76	0.391
Subcutaneous suture layer	0.95	0.50	2.58	0.96 – 6.90	0.060
Belly band	1.54	0.52	4.67	1.69 - 12.92	0.003
Pyrexia	-1.90	0.82	0.15	0.03 – 0.75	0.021
Drainage during hospitalisation	-0.93	0.49	0.40	0.15 – 1.04	0.061
Nature of drainage (referent none)					
Serous	0	0.95	1.00	0.16 – 6.42	1.000
Sero-sanguinous	-0.79	0.58	0.45	0.14 – 1.43	0.177
Purulent	-1.48	0.66	0.23	0.06 – 0.84	0.026
Oedema during hospitalisation	-2.56	1.08	0.08	0.01 – 0.64	0.017
Drainage at discharge	-2.37	0.69	0.09	0.02 – 0.36	0.001
Nature of drainage (referent none)					
Sero-sanguinous	-22	9992	0.00	0.00 – ∞	0.998
Purulent	-1.90	0.72	0.15	0.04 – 0.61	0.008
Oedema at discharge	-1.64	0.69	0.19	0.05 – 0.75	0.018
Drainage at 14d	-2.47	0.57	0.08	0.03 – 0.26	<0.001
Oedema at 14d	-0.60	0.90	0.55	0.09 – 3.19	0.502
Dehiscence at 14d	-22	8653	0.00	0.00 – ∞	0.998

Appendix 9.12: Univariable analysis of factors affecting likelihood of skin incision having healed by three months post-discharge, subsequent to an exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Age (referent <5 yrs)					
5 – 10 yrs	-20	15964	0.00	0.00 – ∞	0.999
10 – 16 yrs	-21	15964	0.00	0.00 – ∞	0.999
>16 yrs	0	22261	0.00	0.00 – ∞	1.000
Gender (referent male)					
Female	21	13164	∞	0.00 – ∞	0.999
Weight (referent <500kgs)					
>500 kgs	-21	10819	0.00	0.00 – ∞	0.998
Pain on presentation (referent mild)					
Moderate	-0.87	1.26	0.42	0.04 – 4.96	0.491
Severe	20	14033	∞	0.00 – ∞	0.999
Duration (referent <8hrs)					
8-24hrs	-21	10407	0.00	0.00 – ∞	0.998
>24hrs	-21	10407	0.00	0.00 – ∞	0.998
Endotoxic	20	14364	∞	0.00 – ∞	0.999
Heart rate (referent <40 bpm)					
40-60 bpm	0.58	1.44	1.79	0.11 – 30.27	0.687
>60 bpm	-0.31	1.46	0.74	0.04 – 12.82	0.834
Haematocrit (referent <33.2%)					
>33.2%	0.92	1.25	2.50	0.22 – 29.01	0.464
Affected bowel (referent large bowel)					
Small intestine	-0.28	1.44	0.76	0.05 – 12.63	0.846
Caecum	-2.51	1.54	0.08	0.00 – 1.65	0.102
Primary lesion (referent displacement)					
Torsion	-20	15414	0.00	0.00 – ∞	0.999
Impaction	0	29848	1.00	0.00 – ∞	1.000
Obstruction	0	25945	1.00	0.00 – ∞	1.000
IBD	0	53394	1.00	0.00 – ∞	1.000
EFE	-21	15414	0.00	0.00 – ∞	0.999
Strangulating SI	0	21339	1.00	0.00 – ∞	1.000
Non strangulating SI	0	22336	1.00	0.00 – ∞	1.000
LI distension	-22	15414	0.00	0.00 – ∞	0.999
Resection	-0.25	1.25	0.78	0.07 – 9.06	0.839
Enterotomy	1.07	1.27	2.90	0.24 – 35.07	0.402
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	0.11	1.25	1.12	0.10 – 12.96	0.930

Appendix 9.12 continued overleaf

Appendix 9.12, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	p
Duration of surgery (referent <85 minutes)					
>85 minutes	0.54	1.25	1.72	0.15 – 19.92	0.663
Length of incision (referent <28cm)					
>28 cms	-21	11822	0.00	0.00 – ∞	0.999
Contamination of abdomen (referent mild)					
Moderate	20	20815	∞	0.00 – ∞	0.999
Severe	-43	1000000	0.00	0.00 – ∞	1.000
Lavage LA	-0.21	1.25	0.81	0.07 – 9.36	0.864
Crystapen on LA	20	32911	∞	0.00 – ∞	1.000
Subcutaneous suture layer	1.30	1.25	3.67	0.32 – 42.55	0.299
Belly band	0.46	1.25	1.58	0.14 – 18.26	0.715
Pyrexia	-1.07	1.27	0.34	0.03 – 4.17	0.402
Drainage during hospitalisation	-21	12223	0.00	0.00 – ∞	0.999
Nature of drainage (referent none)					
Serous	0	29521	1.00	0.00 – ∞	1.000
Sero-sanguinous	-20	12223	0.00	0.00 – ∞	0.999
Purulent	-21	12223	0.00	0.00 – ∞	0.999
Oedema during hospitalisation	-20	19001	0.00	0.00 – ∞	0.999
Drainage at discharge	-22	9128	0.00	0.00 – ∞	0.999
Nature of drainage (referent none)					
Sero-sanguinous	-21	7089	0.00	0.00 – ∞	0.998
Purulent	-21	7089	0.00	0.00 – ∞	0.998
Oedema at discharge	-20	16456	0.00	0.00 – ∞	0.999
Drainage at 14d	-21	11458	0.00	0.00 – ∞	0.999
Oedema at 14d	1.84	1.31	6.30	0.48 – 82.10	0.160
Dehiscence at 14d	-3.03	1.30	0.05	0.00 – 0.62	0.020
Oedema at 30d	1.19	1.28	3.28	0.27 – 39.97	0.352
Drainage at 30d	-21	10678	0.00	0.00 – ∞	0.998
Dehiscence at 30d	-2.71	1.28	0.07	0.01 – 0.82	0.035

Appendix 9.13: Univariable analysis of factors affecting likelihood of incisional hernia formation by three months post-discharge, subsequent to an exploratory laparotomy

Factor	Coefficient	S.E.	O.R.	95% C.I.	P
Age (referent <5 yrs)					
5 – 10 yrs	0.62	0.95	1.86	0.29 – 11.90	0.514
10 – 16 yrs	-0.96	1.28	0.38	0.03 – 4.69	0.452
>16 yrs	0.26	0.99	1.30	0.19 – 9.02	0.791
Gender (referent male)					
Female	-0.94	0.83	0.39	0.08 – 2.01	0.261
Weight (referent <500kgs)					
>500 kgs	0.90	0.75	2.46	0.56 – 10.81	0.233
Pain on presentation (referent mild)					
Moderate	1.67	1.16	5.33	0.55 – 51.88	0.149
Severe	1.95	1.14	7.06	0.76 – 65.99	0.087
Duration (referent <8hrs)					
8-24hrs	0.03	0.77	1.03	0.23 – 4.66	0.968
>24hrs	-0.60	1.14	0.55	0.06 – 5.13	0.600
Endotoxic	1.08	0.70	2.93	0.74 – 11.56	0.124
Heart rate (referent <40 bpm)					
40-60 bpm	0.35	0.89	1.42	0.25 – 8.11	0.696
>60 bpm	0.75	0.99	2.12	0.31 – 14.73	0.445
Haematocrit (referent <33.2%)					
>33.2%	0.30	0.78	1.34	0.29 – 6.18	0.704
Affected bowel (referent large bowel)					
Small intestine	0.29	0.69	1.33	0.35 – 5.13	0.676
Caecum	-20	21240	0.00	0.00 – ∞	0.999
Primary lesion (referent displacement)					
Torsion	0.69	1.23	2.00	0.18 – 2..06	0.571
Impaction	1.20	1.56	3.33	0.16 – 70.91	0.440
Obstruction	-20	18395	0.00	0.00 – ∞	0.999
IBD	-20	36789	0.00	0.00 – ∞	1.000
EFE	1.61	1.36	5.00	0.35 – 71.90	0.237
Strangulating SI	0.69	1.30	2.00	0.16 – 25.76	0.595
Non strangulating SI	0.11	1.49	1.11	0.06 – 20.49	0.944
LI distension	-20	21240	0.00	0.00 – ∞	0.999
Resection	0.06	0.75	1.06	0.24 – 4.58	0.939
Enterotomy	0.61	1.11	1.84	0.21 – 16.17	0.584
Duration of general anaesthesia (referent <110minutes)					
>110 minutes	1.73	0.75	5.63	1.30 – 24.37	0.021

Appendix 9.13 continued overleaf

Appendix 9.13, contd.

Factor	Coefficient	S.E.	O.R.	95% C.I.	P
Duration of surgery (referent <85 minutes)					
>85 minutes	1.20	0.74	3.31	0.78 – 14.09	0.106
Length of incision (referent <28cm)					
>28 cms	0.68	0.74	1.97	0.46 – 8.36	0.359
Contamination of abdomen (referent mild)					
Moderate	0.60	0.89	1.82	0.32 – 10.37	0.499
Severe	-20	36789	0.00	0.00 – ∞	1.000
Lavage LA	-0.19	0.70	0.83	0.21 – 3.27	0.789
Crystapen on LA	-20	18395	0.00	0.00 – ∞	0.999
Subcutaneous suture layer	-0.19	0.70	0.83	0.21 – 3.27	0.789
Belly band	-1.35	0.83	0.26	0.05 – 1.32	0.104
Pyrexia	0.47	0.88	1.59	0.29 – 8.90	0.595
Drainage during hospitalisation	1.22	0.83	3.38	0.66 – 17.26	0.144
Nature of drainage (referent none)					
Serous	0.96	1.32	2.60	0.20 – 34.46	0.469
Sero-sanguinous	0.37	1.05	1.44	0.19 – 11.22	0.725
Purulent	1.87	0.92	6.50	1.08 – 39.12	0.041
Oedema during hospitalisation	20	10620	∞	0.00 – ∞	0.998
Drainage at discharge	1.26	0.71	3.54	0.89 – 14.12	0.074
Nature of drainage (referent none)					
Sero-sanguinous	0.61	1.19	1.84	0.18 – 19.05	0.609
Purulent	1.53	0.77	4.60	1.01 – 20.91	0.048
Oedema at discharge	21	9499	∞	0.00 – ∞	0.998
Drainage at 14d	2.30	1.09	9.96	1.19 – 83.69	0.034
Oedema at 14d	20	15019	∞	0.00 – ∞	0.999
Dehiscence at 14d	0.79	0.90	2.21	0.38 – 12.89	0.379
Drainage at 30d	2.58	1.09	13.12	1.56 – 110.48	0.018
Dehiscence at 30d	1.77	0.78	5.89	1.29 – 26.95	0.022

Appendix 10

Investigation into the prevalence of post-operative complications following elective surgical procedures – Data Collection forms

Sheet 1

Clinic ID:

Case details

Horse name: Owner name: Date of surgery:

Age: Sex: M F MN Breed:

Use:

Approx. height (hh): Weight (kgs):

Pre-op. rectal temperature (°C), heart rate (bpm) and respiratory rate (bpm):

T: **P:** **R:**

Pre-op. haematology normal: **Y / N**

Pre-op. antibiotics:

Drugs	Total Dose	IM / IV / PO

Pre-op. analgesia:

Drugs	Total Dose	IM / IV / PO

Any evidence of pre-existing site of infection?

	Y/N
Skin wound remote to surgical site	
Nasal discharge	
Diarrhoea	

Sheet 2

Clinic ID:

Surgery Report Form

Date: **Surgeon:**

Horse name: **Owner name:**

Site of surgery: induction or recovery room / clean surgical suite / dirty surgical suite

Duration of anaesthesia (mins): **Duration of surgery (mins):**

Evidence of local skin reaction following surgical clip & scrub: **Y / N**

Surgical scrub solution used: **pevidine / hibiscrub / other**

Surgical spirit used after scrub: **Y / N**

Surgical procedure: **Length of incision (cm):**

Site of incision (please check box):

F.limb prox.	☐	Hindquarters	☐	Neck	☐	Inguinal region	☐
F.limb dist.	☐	Flank	☐	Chest	☐	Sheath /penis	☐
H.limb prox.	☐	Ventral abdomen	☐	Head	☐	Hoof	☐
H.limb dist.	☐	Thorax	☐	Dorsal spine	☐	Perineum/ vulva	☐

Deep layer closure (select as appropriate):

continuous ☐ interrupted

simple	☐
cruciate	☐
mattress	☐
near-far	☐
far-near	☐
other :	☐

Suture material (select as appropriate):

vicryl	☐
polysorb	☐
biosyn	☐
PDS	☐
other:	☐

Subcutaneous closure (select as appropriate):

continuous ☐ interrupted

simple	☐
cruciate	☐
mattress	☐
other :	☐

Suture material (select as appropriate):

vicryl	☐
polysorb	☐
other:	☐

Skin closure (select as appropriate):

continuous ☐ interrupted

simple	☐
cruciate	☐
mattress	☐
other :	☐

Suture material (select as appropriate):

vicryl	☐
nylon	☐
prolene	☐
staples	☐

Drain inserted: Y / N **Type of drain:** penrose / multi-lumen

Volume of dead space left: small / moderate / large

Wound dressing: bandage / cast / stent / adhesive dressing / no dressing

Sheet 3

Clinic ID:

Appendix 10

Horse name: **Owner name:**

Daily wound assessment (answer yes/no as appropriate):

Post-op. day	Heat	Swelling	Pain on palpation	Serous discharge	Serosanguinous discharge	Purulent discharge	Partial wound dehiscence	Total wound dehiscence	Seroma / haematoma	Strike through on dressing	Dressing slipped / chewed prior to change	Bandage applied	Stent applied	Cast applied	Adhesive dressing	No dressing	Initials
1																	
2																	
3																	
4																	
5																	
6																	
7																	

Post-op day	1	2	3	4	5	6	7
IV catheter used for admin of IV drugs (Y/N)							
Type of catheter Used							
Catheter replaced (Y/N)							
Extension set used (Y/N)							
Extension set replaced (Y/N)							
Bung used (Y/N)							
Bung Replaced (Y/N)							

Sheet 4

Clinic ID:

Horse name: **Owner name:**

Daily horse assessment and treatment:

	AM						PM					
Post-op. day	T(°C) P(bpm) R(bpm)	Antibiotics	Dose/ route of admin.	Analgesia	Dose/ route of admin.	Diarrhoea (Y/N)	T(°C) P(bpm) R(bpm)	Antibiotics	Dose/ route of admin.	Analgesia	Dose/ route of admin.	Diarrhoea (Y/N)
1												
2												
3												
4												
5												
6												
7												

Sheet 5

Clinic ID:

Discharge Sheet

Horse name: **Owner name:**

Date of discharge:

Was horse pyrexic at any time during hospitalistion? Y / N

Was pyrexia attributed to (please check box as appropriate)**:**

Respiratory tract infection		Thrombophlebitis of jugular vein	
Gastro-intestinal tract infection		Catheter site infection	
Wound infection		Pyrexia of unknown origin	

Wound assessment at discharge – any evidence of (please check box as appropriate)**:**

Heat		Discharge from incision	
Pain on palpation		Partial dehiscence of incision	
Swelling		Total dehiscence of incision	

Appendix 11

Investigation into the prevalence of post-operative complications following elective surgical procedures – Definitions of outcomes

Definitions of outcomes

Wound infection defined as the presence of at least two of the following three criteria:

- wound drainage
- pain on palpation
- localized heat on palpation

Post operative period

- defined as starting immediately following recovery of the horse from general anaesthesia, ie. post-op. day 1 is the same day as the surgical procedure.

Pyrexia

- identified by twice daily assessment of rectal temperature.
- rectal temperature > 39 °C at any one time.

Jugular thrombosis

- identified by observation and palpation of the ventral neck of the horse on a daily basis.
- swelling of, or palpable thrombus formation within, jugular vein in which an intra-venous catheter has been placed during hospitalization, ideally confirmed as narrowing or complete obstruction of jugular vein by the use of ultrasound.

Catheter site infection

- identified by observation and palpation of the catheter insertion site on a daily basis.
- localized swelling, heat or abscess formation, without associated thrombosis of underlying vessel, in the skin directly around the site of insertion of an intra-venous catheter, ideally confirmed by the use of ultrasound.

Diarrhoea

- identified by twice daily inspection of faeces.
- loose faeces for ≥ 24 hours.

Respiratory tract infection

- rectal temperature elevated >39 °C, associated with any two of the following criteria identifying the respiratory tract as the source of the pyrexia: nasal discharge (serous/purulent); increased respiratory rate; increased lung sounds on thoracic auscultation.

Gastro-intestinal tract infection

- rectal temperature elevated >39 °C, associated with diarrhea of >24 hours duration.

Pyrexia of unknown origin

- rectal temperature elevated >39 °C, associated with non-specific signs of illness (eg. lethargy, inappetance), where no infectious cause is identified.

Definition of surgical terms

Hoof

- all tissue distal to coronary band on both fore and hindlimbs

Proximal forelimb
- from the level of the distal radius to the proximal border of the scapula.

Distal forelimb
- forelimb distal to, and including, the carpus, although excluding the hoof.

Proximal hindlimb
- from the level of the distal tibia to the level of the greater trochanter of the femur.

Distal hindlimb
- hindlimb distal to, and including, the tarsus, although excluding the hoof.

Hindquarters
- area extending from tuber coxae to tail-head, incorporating gluteal muscle mass, semitendinosus and semimembranosus muscles.

Flank
- area extending from caudal aspect of last rib to the level of the tuber coxae, including the abdominal oblique muscles.

Ventral abdomen
- area from xiphoid process to sheath/mammary glands that is on ventral aspect of body

Thorax
- area delineated by ribcage, excluding pectoral region and dorsal spine.

Chest
- area between the forelimbs, incorporating the pectoral musculature, extending dorsally to the base of the jugular furrow.

Neck
- area extending from poll to withers and from the cranial border of the wings of the atlas to the cranial border of the scapula.

Anaesthesia time
- defined as the time from induction to the time that the gaseous anaesthetic agent was turned off. In the case of total intravenous anesthesia, the end point was the time that all external stimuli had ceased (surgery, application of dressing, etc).

Surgery time
- defined as the time from the first surgical incision until all surgical intervention (suturing, application of dressing, etc) had ceased.

Identification and definition of complications during hospitalisation

Drainage from incision
- identified by visual inspection of the surgical incision at every bandage/dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- any fluid seen to be leaking from the surgical site.

Serous drainage

- identified by visual inspection of the surgical incision at every bandage/dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- clear, straw coloured fluid leaking from incision.

Serosanguinous drainage

- identified by visual inspection of the surgical incision at every bandage/dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- clear, blood tinged fluid leaking from incision.

Purulent drainage

- identified by visual inspection of the surgical incision at every bandage/dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- cloudy, cellular fluid leaking from incision.

Heat

- identified by palpation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- incision palpably warmer compared to either temperature of surrounding skin, or to a comparable region, ie with a skin incision on neck, compare to other side of neck.

Pain on palpation of wound

- identified by palpation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis
- horse flinches or makes an attempt to move away when incision is palpated

Swelling of incision

- identified by observation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- margins of incision raised above level of surrounding skin more than would be anticipated with the suture pattern used.

Strike through on bandage

- identified by observation of the dressing/bandage prior to every dressing change.
- fluid has leaked through to the outermost layer of the dressing/bandage covering the surgical wound.

Bandage/dressing slipped or chewed

- identified by observation of the dressing/bandage prior to every dressing change.
- integrity of the outer layers of the bandage has been disrupted, or the bandage/dressing has slipped in such a way as to expose part, or all, of the surgical site.

Partial wound dehiscence

- identified by observation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- disruption of less than 75% of the surgical wound.

Total wound dehiscence

- identified by observation of the surgical incision at every dressing change. If no dressing is used then the wound will be assessed on a daily basis.
- disruption of at least 75% of the surgical wound.

Seroma/haematoma

- identified by observation and palpation of surgical incision on a daily basis.
- localized, fluid filled pocket in area of surgical wound.

Volume of dead space left at surgery

- assessed by surgeon at time of surgical procedure.
- perfect tissue apposition cannot be achieved, leaving an unoccupied space within tissue layers in the surgical field.
- subjectively quantified as:

small	space left only between tissue/fascial layers
moderate	small space left within surgical field, eg laryngoplasty
large	tissues surrounding surgical field cannot be adequately apposed, eg myectomy incision

Appendix 12

Univariable analysis of factors affecting the likelihood of the development of post-operative complications following elective surgical procedures

Appendix 12.1: Comparison of hospitalisation related outcomes by variable for all elective surgical procedures

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Age (referent < 2 yrs)						
2 – 6 yrs	0.918	1.11	0.15 – 8.22	0.481	2.38	0.21 – 26.63
6 – 9 yrs	0.573	1.79	0.24 – 13.38	0.817	1.39	0.09 – 22.50
> 9 yrs	0.272	3.26	0.51 – 20.87	0.245	3.87	0.40 – 37.75
Gender (referent female)						
M	0.850	0.86	0.18 – 4.05	0.648	1.52	0.25 – 9.25
MN	0.770	0.79	0.17 – 3.72	0.918	0.90	0.13 – 6.49
Weight (referent <400kgs)						
400-600 kgs	0.897	1.12	0.20 – 6.33			
>600 kgs	0.124	5.10	0.64 – 40.57			
Duration of GA (referent < 60 mins)						
60 – 90 mins	0.887	0.87	0.12 – 6.40	0.819	1.24	0.20 – 7.52
90 – 110 mins	0.787	1.41	0.12 – 16.58	0.999	0.00	0.00 - ∞
> 110 mins	0.349	2.31	0.40 – 13.29	0.854	1.20	0.17 – 8.72
Duration of Sx (referent < 30 mins)						
30 – 50 mins	0.473	2.32	0.23 – 23.14	0.318	3.07	0.34 – 27.89
50 – 65 mins	0.642	1.95	0.12 – 32.80	0.999	0.00	0.00 - ∞
> 65 mins	0.184	4.56	0.49 – 42.65	0.466	2.46	0.22 – 27.52
Length of incision (referent <5cm)						
5-10cm	0.596	1.49	0.34 – 6.55			
>10cm	0.249	2.77	0.49 – 15.68			
>1 incision	0.844	1.05	0.64 – 1.72			
Volume of dead space left (referent small)						
Moderate	0.926	1.06	0.29 – 3.94	0.892	1.13	0.20 – 6.23
Large	0.999	0.00	0.00 - ∞	0.352	2.89	0.31 – 26.85
Surgical site clipped prior to induction (referent not clipped)						
<24hrs	0.999	0.00	0.00 - ∞			
>24hrs	0.849	0.23	0.14 – 10.65			
Dressing used Y/N	0.727	0.79	0.21 – 2.92			
Type of dressing used (referent no dressing used)						
Cast	0.752	1.33	0.23 – 7.68			
Bandage	0.784	0.78	0.14 – 4.46			
Adhesive dressing/ stent	0.251	2.88	0.47 – 17.47			

Appendix 12.1 continued overleaf

Appendix 12.1, contd.

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Classification of surgical procedure (referent clean)						
Clean-contaminated	0.899	0.90	0.18 – 4.45			
Type of clean surgical procedure (referent orthopaedic)						
Soft tissue	0.213	2.50	0.59 – 10.57			
Suture material used in closure of deep layer (referent none)						
Vicryl/ polysorb	0.668	0.73	0.17 – 3.15			
PDS/biosyn	**0.033**	**8.10**	**1.18 – 55.40**			
Suture material used in closure of subcutaneous layer (referent none)						
Vicryl/polysorb	0.998	0.00	0.00 - ∞			
PDS/biosyn	0.998	0.00	0.00 - ∞			
Suture material used in closure of skin (referent none)						
Staples	0.812	0.76	0.08 – 7.41			
Nylon/prolene	0.999	0.00	0.00 - ∞			
Vicryl/polysorb	0.724	1.55	0.14 – 17.44			
PDS/biosyn	0.221	5.91	0.34 – 101.60			
Type of antimicrobials used prior to induction (referent none used)						
Procaine penicillin or sodium penicillin	0.99	0.00	0.00 - ∞	1.00	1.00	0.00 - ∞
Procaine penicillin and gentamicin	0.99	0.00	0.00 - ∞	1.00	1.00	0.00 - ∞
Sodium penicillin and gentamicin	0.99	0.00	0.00 - ∞	1.00	1.00	0.00 - ∞
Other combination	0.99	0.00	0.00 - ∞	1.00	1.00	0.00 - ∞
Surgical procedure performed (referent arthroscopy or tenoscopy)						
Neurectomy	~	~	~	0.645	1.93	0.12 – 31.42
Fracture repair	0.824	0.76	0.06 – 8.88	0.549	2.35	0.14 – 38.35
Desmotomy	0.415	3.40	0.18 – 64.69	0.294	4.50	0.27 – 74.52
Other orthopaedic procedure	0.998	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Castration	0.998	0.00	0.00 - ∞	0.355	3.13	0.28 – 35.18
Laparotomy	0.112	8.50	0.61 – 118.64	1.000	0.00	0.00 - ∞
Enucleation	0.341	4.25	0.22 – 83.52	1.000	0.00	0.00 - ∞
Other soft tissue procedure	0.226	4.86	0.38 – 62.63	0.999	0.00	0.00 - ∞

Appendix 12.1 continued overleaf

Appendix 12.1, contd.

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Surgical procedure performed (referent arthroscopy or tenoscopy)						
Laryngoplasty	0.859	0.77	0.05 – 13.27	0.999	0.00	0.00 - ∞
Sinus & Dental	0.999	0.00	0.00 - ∞	0.212	6.00	0.36 – 100.30
Penile	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Other clean-contaminated procedure	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Anatomical location of surgical procedure (referent distal limb)						
Proximal limb	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Body	0.105	8.63	0.64 – 116.54	0.999	0.00	0.00 - ∞
Head & neck	0.397	1.86	0.44 – 7.89	0.849	0.81	0.09 – 7.34
Ventral abdomen, inguinal & penis	0.607	0.56	0.06 – 5.19	0.827	1.21	0.22 – 6.73
Abnormal drainage for the surgical procedure	0.790	0.81	0.16 – 3.97	0.571	0.54	0.06 – 4.54
Partial or total incisional dehiscence	~	~	~	1.000	0.00	0.00 - ∞
Abnormal swelling for the surgical procedure	0.063	3.56	0.93 – 13.55	0.652	1.46	0.28 – 7.67

Appendix 12.2: Clean surgical procedures – hospitalisation outcome by variable

	Pyrexia			Diarrhoea		
	P	**OR**	**95% CI**	**P**	**OR**	**95% CI**
Age (referent < 2 yrs)						
2 – 6 yrs	0.788	1.47	0.09 – 24.35	0.424	2.68	0.24 – 30.05
6 – 9 yrs	0.246	4.27	0.37 – 49.68	0.999	0.00	0.00 - ∞
> 9 yrs	**0.046**	**10.85**	**1.04 – 113.17**	0.190	4.60	0.47 – 45.01
Gender (referent female)						
M	0.718	0.71	0.11 – 4.48	0.666	1.49	0.24 – 9.06
MN	0.615	1.53	0.29 – 8.11	0.625	0.55	0.05 – 6.12
Weight (referent <400kgs)						
400-600 kgs	0.964	1.04	0.17 – 6.48			
>600 kgs	**0.010**	**24.00**	**2.14 – 269.12**			
Duration of GA (referent < 60 mins)						
60 – 90 mins	0.874	0.85	0.11 – 6.36	0.870	0.85	0.12 – 6.13
90 – 110 mins	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
> 110 mins	0.599	1.65	0.26 – 10.51	0.796	1.30	0.18 – 9.43
Duration of Sx (referent < 30 mins)						
30 – 50 mins	0.487	2.27	0.22 – 22.87	0.461	2.35	0.24 – 22.97
50 – 65 mins	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
> 65 mins	0.311	3.32	0.33 – 33.80	0.399	2.83	0.25 – 31.84
Length of incision (referent <5cm)						
5-10cm	0.104	3.71	0.76 – 18.01	0.245	2.78	0.50 – 15.56
>10cm	0.493	2.22	0.23 – 21.90	0.999	0.00	0.00 - ∞
>1 incision	0.606	0.69	0.16 – 2.88	0.654	1.48	0.27 – 8.18
Volume of dead space left (referent small)						
Moderate	0.422	1.84	0.41 – 8.18	0.670	1.45	0.26 – 8.06
Large	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Surgical site clipped prior to induction (referent not clipped)						
<24hrs	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
>24hrs	0.715	1.51	0.17 – 13.66	0.621	0.58	0.07 – 5.04
Type of dressing used (referent no dressing used)						
Cast	0.732	1.42	0.19 – 10.76	0.632	1.81	0.16 – 20.78
Bandage	0.866	0.84	0.11 – 6.26	0.781	0.77	0.13 – 4.71
Adhesive dressing/ stent	0.251	3.36	0.42 – 26.72	0.999	0.00	0.00 - ∞

Appendix 12.2 continued overleaf

Appendix 12.2, contd.

	Pyrexia			Diarrhoea		
	P	**OR**	**95% CI**	**P**	**OR**	**95% CI**
Type of clean surgical procedure (referent orthopaedic)						
Soft tissue	0.213	2.50	0.59 – 10.57	0.761	1.30	0.24 – 7.23
Suture material used in closure of deep layer (referent none)						
Vicryl/ polysorb	0.727	0.73	0.13 – 4.17			
PDS/biosyn	**0.020**	**11.50**	**1.48 – 89.66**			
Suture material used in closure of subcutaneous layer (referent none)						
Vicryl/polysorb	0.998	0.00	0.00 - ∞			
PDS/biosyn	0.998	0.00	0.00 - ∞			
Suture material used in closure of skin (referent none)						
Staples	0.999	0.00	0.00 - ∞			
Nylon/prolene	1.000	1.00	0.00 - ∞			
Vicryl/polysorb	0.999	0.00	0.00 - ∞			
PDS/biosyn	0.999	0.00	0.00 - ∞			
Type of antimicrobials used prior to induction (referent none used)						
Procaine penicillin or sodium penicillin	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Sodium penicillin and gentamicin	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Other combination	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Surgical procedure performed (referent arthroscopy or tenoscopy)						
Neurectomy	~	~	~	0.645	1.93	0.12 – 31.42
Fracture repair	0.824	0.76	0.06 – 8.88	0.549	2.35	0.14 – 38.35
Desmotomy	0.415	3.40	0.18 – 64.69	0.294	4.50	0.27 – 74.52
Other orthopaedic procedure	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Castration	0.999	0.00	0.00 - ∞	0.355	3.13	0.28 – 35.18
Laparotomy	0.341	4.25	0.22 – 83.52	1.000	0.00	0.00 - ∞
Enucleation	0.341	4.25	0.22 – 83.52	1.000	0.00	0.00 - ∞
Other soft tissue procedure	0.226	4.86	0.38 – 62.63	0.999	0.00	0.00 - ∞

Appendix 12.2 continued overleaf

Appendix 12.2, contd.

	Pyrexia			Diarrhoea		
	P	**OR**	**95% CI**	**P**	**OR**	**95% CI**
Anatomical location of surgical procedure (referent distal limb)						
Proximal limb	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Body	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Head & neck	0.077	4.31	0.86 – 21.74	0.999	0.00	0.00 - ∞
Ventral abdomen, inguinal & penis	0.773	0.72	0.08 – 6.75	0.748	1.33	0.24 – 7.38
Abnormal drainage for the surgical procedure	0.602	0.57	0.07 – 4.82	0.999	0.00	0.00 - ∞
Partial or total incisional dehiscence	~	~	~	1.000	0.00	0.00 - ∞
Abnormal swelling for the surgical procedure	**0.027**	**5.26**	**1.21 – 22.89**	0.502	1.80	0.32 – 10.01

Appendix 12.3: Clean-contaminated procedures – hospitalisation outcome by variable

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Age (referent < 3 yrs)						
3 – 7 yrs	0.831	0.73	0.04 – 13.45	0.999	0.00	0.00 - ∞
7 – 11 yrs	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
> 11 yrs	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Gender (referent female)						
M	0.653	2.00	0.10 – 41.01	1.000	1.00	0.00 - ∞
MN	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Weight (referent <400kgs)						
400-600 kgs	1.000	0.00	0.00 - ∞			
>600 kgs	1.000	1.00	0.00 - ∞			
Duration of GA (referent < 67 mins)						
67 – 97 mins	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞
97 – 117 mins	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
> 117 mins	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Duration of Sx (referent < 40 mins)						
40 – 65 mins	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
65 – 80 mins	1.000	1.00	0.00 - ∞	1.000	1.00	0.00 - ∞
>80 mins	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Length of incision (referent <5cm)						
5-10cm	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
>10cm	0.653	2.00	0.10 – 41.01	1.000	1.00	0.00 - ∞
>1 incision	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Volume of dead space left (referent small)						
Moderate	0.097	0.07	0.00 – 1.62	1.000	0.00	0.00 - ∞
Large	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Surgical site clipped prior to induction (referent not clipped)						
<24hrs	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
>24hrs	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Type of dressing used (referent no dressing used)						
Cast	~	~	~	1.000	0.00	0.00 - ∞
Bandage	~	~	~	~	~	~
Adhesive dressing/ stent	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Suture material used in closure of deep layer (referent none)						
Vicryl/ polysorb	0.727	0.60	0.03 – 10.51			
PDS/biosyn	1.000	0.00	0.00 - ∞			
Suture material used in closure of subcutaneous layer (referent none)						
Vicryl/polysorb	0.999	0.00	0.00 - ∞			
PDS/biosyn	1.000	1.00	0.00 - ∞			

Appendix 12.3 continued overleaf

Appendix 12.3, contd.

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Suture material used in closure of skin (referent none)						
Staples	1.000	1.00	0.00 - ∞			
Nylon/prolene	1.000	0.00	0.00 - ∞			
Vicryl/polysorb	0.999	0.00	0.00 - ∞			
PDS/biosyn	~	~	~			
Type of antimicrobials used prior to induction (referent none used)						
Procaine penicillin or sodium penicillin	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	0.196	0.14	0.01 – 2.80	1.000	1.00	0.00 - ∞
Sodium penicillin and gentamicin	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Other combination	~	~	~	1.000	1.00	0.00 - ∞
Surgical procedure performed (referent arthroscopy or tenoscopy)						
Laryngoplasty	1.000	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Sinus & Dental	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Penile	1.000	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Other clean-contaminated procedure	1.000	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Anatomical location of surgical procedure (referent distal limb)						
Proximal limb	1.000	1.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Body	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Head & neck	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Ventral abdomen, inguinal & penis	~	~	~	~	~	~
Abnormal drainage for the surgical procedure	0.701	1.75	0.10 – 30.59	0.999	0.00	0.00 - ∞
Partial or total incisional dehiscence	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Abnormal swelling for the surgical procedure	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞

Appendix 12.4: Clean orthopaedic procedures – hospitalisation outcome by variable

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Age (referent < 3 yrs)						
3 – 6 yrs	0.999	0.00	0.00 - ∞	0.998	0.00	0.00 - ∞
6 – 10 yrs	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
> 10 yrs	0.524	2.25	0.19 – 27.31	0.998	0.00	0.00 - ∞
Gender (referent female)						
M	0.323	3.45	0.30 – 40.32	0.931	1.11	0.10 – 12.56
MN	0.771	1.52	0.09 – 25.44	0.579	0.50	0.05 – 5.65
Weight (referent <400kgs)						
400-600 kgs	0.999	0.00	0.00 - ∞			
>600 kgs	0.998	0.00	0.00 - ∞			
Duration of GA (referent < 75 mins)						
75 – 100 mins	0.999	0.00	0.00 - ∞	0.953	0.92	0.06 – 14.99
100 – 115 mins	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞
> 115 mins	0.999	0.00	0.00 - ∞	0.509	2.26	0.20 – 25.57
Duration of Sx (referent < 35 mins)						
35 – 55 mins	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
55 – 65 mins	1.000	1.00	0.00 - ∞	1.000	1.00	0.00 - ∞
> 65 mins	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Length of incision (referent <5cm)						
5-10cm	0.098	8.56	0.67 – 108.50			
>10cm	0.999	0.00	0.00 - ∞			
>1 incision	0.999	0.00	0.00 - ∞			
Volume of dead space left (referent small)						
Moderate	0.088	9.11	0.72 – 115.48			
Large	~	~	~			
Surgical site clipped prior to induction (referent not clipped)						
<24hrs	1.000	0.00	0.00 - ∞			
>24hrs	0.999	0.00	0.00 - ∞			
Type of dressing used (referent no dressing used)						
Cast	0.999	0.00	0.00 - ∞			
Bandage	0.999	0.00	0.00 - ∞			
Adhesive dressing/ stent	1.000	1.00	0.00 - ∞			
Suture material used in closure of deep layer (referent none)						
Vicryl/ polysorb	0.999	0.00	0.00 - ∞			
PDS/biosyn	1.000	0.00	0.00 - ∞			

Appendix 12.4 continued overleaf

Appendix 12.4, contd.

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Suture material used in closure of subcutaneous layer (referent none)						
Vicryl/polysorb	0.998	0.00	0.00 - ∞			
PDS/biosyn	0.998	0.00	0.00 - ∞			
Suture material used in closure of skin (referent none)						
Staples	1.000	0.00	0.00 - ∞			
Nylon/prolene	1.000	1.00	0.00 - ∞			
Vicryl/polysorb	1.000	1.00	0.00 - ∞			
PDS/biosyn	1.000	1.00	0.00 - ∞			
Type of antimicrobials used prior to induction (referent none used)						
Procaine penicillin or sodium penicillin	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	1.000	1.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Sodium penicillin and gentamicin	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Other combination	1.000	1.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Surgical procedure performed (referent arthroscopy or tenoscopy)						
Neurectomy	~	~	~	0.645	1.93	0.12 – 31.42
Fracture repair	0.824	0.76	0.06 – 8.88	0.549	2.35	0.14 – 38.35
Desmotomy	0.415	3.40	0.18 – 64.69	0.294	4.50	0.27 – 74.52
Other orthopaedic procedure	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Anatomical location of surgical procedure (referent distal limb)						
Proximal limb	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Body	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Head & neck	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Abnormal drainage for the surgical procedure	0.856	1.24	0.12 – 12.65	0.999	0.00	0.00 - ∞
Partial or total incisional dehiscence	~	~	~	1.000	0.00	0.00 - ∞
Abnormal swelling for the surgical procedure	**0.048**	**10.42**	**1.02 – 106.04**	0.393	2.37	0.33 – 17.10

Appendix 12.5: Clean soft-tissue procedures – hospitalisation outcome by variable

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Age (referent < 2 yrs)						
2 – 3 yrs	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞
3 – 4 yrs	1.000	1.00	0.00 - ∞	1.000	1.00	0.00 - ∞
> 4 yrs	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Gender (referent female)						
M	0.998	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
MN	0.683	1.60	0.17 – 15.27	1.000	1.00	0.00 - ∞
Weight (referent <400kgs)						
400-600 kgs	0.792	0.71	0.06 – 8.67			
>600 kgs	1.000	0.00	0.00 - ∞			
Duration of GA (referent < 50 mins)						
50 – 60 mins	0.910	0.85	0.05 – 15.16	0.673	0.55	.0.3 – 9.12
60 – 70 mins	0.173	11.00	0.35 – 345.08	0.999	0.00	0.00 - ∞
> 70 mins	0.892	1.22	0.07 – 22.40	0.999	0.00	0.00 - ∞
Duration of Sx (referent < 28 mins mins)						
28 – 39 mins	0.999	0.00	0.00 - ∞	0.793	0.69	0.04 – 11.51
39 – 45 mins	0.327	3.67	0.27 – 49.29	0.999	0.00	0.00 - ∞
> 45 mins	0.892	1.22	0.07 – 22.40	0.999	0.00	0.00 - ∞
Length of incision (referent <5cm)						
5-10cm	0.714	1.60	0.13 – 19.84			
>10cm	0.644	2.00	0.11 – 37.83			
>1 incision	0.999	0.00	0.00 - ∞			
Volume of dead space left (referent small)						
Moderate	0.227	0.27	0.03 – 2.27			
Large	1.000	0.00	0.00 - ∞			
Surgical site clipped prior to induction (referent not clipped)						
<24hrs	~	~	~			
>24hrs	1.000	0.00	0.00 - ∞			
Type of dressing used (referent no dressing used)						
Adhesive dressing/ stent	**0.046**	**10.33**	**1.05 – 102.08**			
Suture material used in closure of deep layer (referent none)						
Vicryl/ polysorb	0.678	0.58	0.05 – 7.43			
PDS/biosyn	0.590	2.33	0.11 – 50.99			
Suture material used in closure of subcutaneous layer (referent none)						
Vicryl/polysorb	0.999	0.00	0.00 - ∞			
PDS/biosyn	0.999	0.00	0.00 - ∞			

Appendix 12.5 continued overleaf

Appendix 12.5, contd.

	Pyrexia			Diarrhoea		
	P	OR	95% CI	P	OR	95% CI
Suture material used in closure of skin (referent none)						
Staples	0.999	0.00	0.00 - ∞			
Nylon/prolene	1.000	1.00	0.00 - ∞			
Vicryl/polysorb	0.999	0.00	0.00 - ∞			
PDS/biosyn	0.999	0.00	0.00 - ∞			
Type of antimicrobials used prior to induction (referent none used)						
Procaine penicillin or sodium penicillin	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Sodium penicillin and gentamicin	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Other combination	1.000	1.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Surgical procedure performed (referent arthroscopy or tenoscopy)						
Castration	0.998	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Laparotomy	0.923	0.88	0.06 – 12.98	1.000	1.00	0.00 - ∞
Enucleation	0.923	0.88	0.06 – 12.98	1.000	1.00	0.00 - ∞
Other soft tissue procedure	~	~	~	~	~	~
Anatomical location of surgical procedure (referent distal limb)						
Proximal limb	~	~	~	~	~	~
Body	~	~	~	1.000	0.00	0.00 - ∞
Head & neck	0.104	7.20	0.67 – 77.83	0.999	0.00	0.00 - ∞
Ventral abdomen, inguinal & penis	~	~	~	~	~	~
Abnormal drainage for the surgical procedure	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Partial or total incisional dehiscence	~	~	~	1.000	0.00	0.00 - ∞
Abnormal swelling for the surgical procedure	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞

Appendix 12.6: Comparison of incisional complications by variable, for all elective surgical procedures.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Age (referent < 2 yrs)									
2 – 6 yrs	0.151	1.70	0.82 – 3.52	0.140	1.89	0.81 – 4.41	0.869	1.18	0.16 – 8.53
6 – 9 yrs	**0.007**	**2.65**	**1.30 – 5.41**	**<0.001**	**6.92**	**3.19 – 14.99**	0.762	0.69	0.06 – 7.71
> 9 yrs	**0.001**	**3.32**	**1.67 – 6.60**	**<0.001**	**7.42**	**3.47 – 15.87**	0.816	1.27	0.18 – 9.14
Gender (referent female)									
M	**<0.001**	**0.24**	**0.13 – 0.47**	**<0.001**	**0.15**	**0.07 – 0.36**	0.648	1.52	0.25 – 9.25
MN	0.087	0.64	0.38 – 1.07	**0.032**	**1.73**	**1.05 – 2.85**	0.918	0.90	0.13 – 6.49
Weight (referent <400 kgs)									
400-600 kgs	0.084	1.80	0.92 – 3.51	**0.034**	**2.06**	**1.06 – 3.99**	0.539	0.58	0.11 – 3.24
>600 kgs	**0.040**	**2.54**	**1.05 – 6.16**	**0.040**	**2.54**	**1.05 – 6.16**	0.978	0.97	0.09 – 10.95
Duration of GA (referent < 60 mins)									
60 – 90 mins	**0.002**	**3.49**	**1.59 – 7.66**	**0.008**	**2.65**	**1.30 – 5.41**	0.999	0.00	0.00 - ∞
90 – 110 mins	**<0.001**	**4.67**	**2.01 – 10.82**	**<0.001**	**4.09**	**1.90 – 8.78**	1.000	1.00	0.00 - ∞
> 110 mins	**<0.001**	**4.88**	**2.17 – 10.97**	**<0.001**	**3.73**	**1.78 – 7.83**	0.000	0.00	0.00 - ∞
Duration of Surgery (referent < 30 mins)									
30 – 50 mins	0.362	1.36	0.70 – 2.61	**0.013**	**2.30**	**1.19 – 4.42**	0.735	1.52	0.14 – 16.94
50 – 65 mins	0.262	1.57	0.71 – 3.43	0.228	1.65	0.73 – 3.73	0.999	0.00	0.00 - ∞
> 65 mins	**0.004**	**2.67**	**1.36 – 5.25**	**0.001**	**3.25**	**1.62 – 6.49**	0.466	2.46	0.22 – 27.52
Length of incision (referent < 5cm)									
5-10cm	**0.002**	**0.29**	**0.14 – 0.63**	0.185	0.66	0.36 – 1.22	0.203	3.61	0.50 – 25.99
>10 cm	0.179	0.54	0.22 – 1.33	0.529	1.27	0.60 – 2.69	**0.006**	**12.99**	**2.10 – 80.39**
>1 incision	**<0.001**	**2.83**	**1.73 – 4.62**	0.207	1.34	0.85 – 2.10	0.091	0.16	0.02 – 1.34

Appendix 12.6 continued overleaf

Appendix 12.6, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Volume of dead space left (referent small)									
Moderate	**<0.001**	**0.10**	**0.04 – 0.26**	**0.002**	**0.39**	**0.21 – 0.71**	0.415	2.27	0.32 – 16.29
Large	0.930	0.96	0.39 – 2.39	**0.008**	**3.09**	**1.35 – 7.07**	**0.002**	**19.02**	**3.02 – 119.90**
Surgical site clipped prior to induction (referent not clipped)									
<24hrs	0.376	1.62	0.56 – 4.69	0.654	1.30	0.41 – 4.09	0.999	0.00	0.00 - ∞
>24hrs	**0.022**	**1.92**	**1.10 – 3.35**	**<0.001**	**3.84**	**2.26 – 6.53**	0.714	0.67	0.08 – 5.79
Surgical site shaved	0.902	1.04	0.53 – 2.08	**<0.001**	**3.74**	**2.07 – 6.75**	0.888	1.17	0.14 – 9.88
Type of dressing used (referent none used)									
Cast	**0.001**	**4.92**	**1.86 – 12.97**	0.073	0.16	0.02 – 1.19	0.999	0.00	0.00 - ∞
Bandage	**<0.001**	**4.81**	**2.52 – 9.17**	**0.009**	**1.96**	**1.18 – 3.25**	0.288	0.40	0.07 – 2.19
Adhesive /stent	**0.018**	**2.86**	**1.19 – 6.85**	0.980	0.01	0.46 – 2.24	0.777	0.73	0.08 – 6.64
Classification of surgical procedure performed (referent clean)									
Clean-contaminated	0.654	0.85	0.42 – 1.72	**0.002**	**2.57**	**1.43 – 4.61**	0.245	2.68	0.51 – 14.17
Suture pattern used in closure of deep layer (referent no deep closure)									
Simple interrupted	**0.008**	**0.14**	**0.03 – 0.60**	0.116	0.37	0.11 – 1.28	0.999	0.00	0.00 - ∞
Simple continuous	**<0.001**	**0.18**	**0.10 – 0.32**	0.696	1.10	0.69 – 1.73	0.137	0.20	0.02 – 1.67
Mattress/Near-far Far-near	0.999	0.00	0.00 - ∞	0.690	0.64	0.07 – 5.63	X	x	X
Suture pattern used in closure of subcutaneous layer (referent no closure)									
Simple interrupted	0.107	0.50	0.21 – 1.16	0.599	0.79	0.33 – 1.89	0.346	3.84	0.23 – 62.82
Simple continuous	**<0.001**	**0.29**	**0.18 – 0.48**	0.609	0.88	0.55 – 1.43	0.332	2.91	0.34 – 25.16
Mattress/Near-far Far-near	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞

Appendix 12.6 continued overleaf

Appendix 12.6, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Suture pattern used in closure of skin (referent none)									
Simple interrupted	0.335	1.38	0.72 – 2.67	**0.004**	**0.44**	**0.25 – 0.77**	0.732	1.45	0.17 – 12.24
Simple continuous	**0.026**	**0.09**	**0.01 – 0.75**	**0.003**	**0.20**	**0.07 – 0.57**	0.999	0.00	0.00 - ∞
Cruciate	0.999	0.00	0.00 - ∞	0.404	0.38	0.04 – 3.64	X	X	X
Mattress/Near-far Far-near	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	X	X	X
Suture material used in closure of deep layer (referent none)									
Vicryl/ polysorb	**<0.001**	**0.17**	**0.09 – 0.30**	0.990	1.00	0.64 – 1.56	0.742	0.78	0.17 – 3.51
PDS/biosyn	0.174	0.23	0.03 – 1.90	0.396	0.40	0.05 – 3.29	1.000	0.00	0.00 - ∞
Suture material used in closure of subcutaneous layer (referent none)									
Vicryl/polysorb	**<0.001**	**0.33**	**0.20 – 0.53**	0.539	0.86	0.54 – 1.38	0.296	3.11	0.37 – 26.08
PDS/biosyn	0.221	0.27	0.03 – 2.22	0.991	0.99	0.19 – 5.13	1.000	0.00	0.00 - ∞
Suture material used in closure of skin (referent none)									
Staples	0.123	1.68	0.87 – 3.27	**0.010**	**0.47**	**0.27 – 0.83**	0.998	1.00	0.00 - ∞
Nylon/prolene	0.731	0.68	0.08 – 6.15	0.578	0.62	0.11 – 3.41	0.998	1.00	0.00 - ∞
Vicryl/polysorb	**0.003**	**0.10**	**0.02 – 0.45**	**<0.001**	**0.14**	**0.05 – 0.34**	0.998	1.00	0.00 - ∞
PDS/biosyn	0.362	0.37	0.04 – 3.13	0.882	1.10	0.32 – 3.83	1.000	0.00	0.00 - ∞
Type of antimicrobials administered prior to induction of anaesthesia (referent none)									
Procaine penicillin/Sodium penicillin	0.914	1.09	0.22 – 5.38	0.513	0.62	0.15 – 2.56	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	0.700	0.71	0.13 – 3.96	0.782	0.81	0.18 – 3.61	1.000	0.00	0.00 - ∞
Sodium penicillin and gentamicin	0.908	1.11	0.20 – 6.05	0.556	0.63	0.14 – 2.92	1.000	1.00	0.00 - ∞
Other combination	0.122	0.13	0.01 – 1.71	**0.039**	**0.08**	**0.01 – 0.87**	1.000	1.00	0.00 - ∞

Appendix 12.6 continued overleaf

Appendix 12.6, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Surgical procedure performed (referent arthroscopy or tenoscopy)									
Neurectomy	**0.007**	**0.35**	**0.17 – 0.76**	**0.001**	**3.19**	**1.60 – 6.35**	0.645	1.93	0.12 – 31.42
Fracture repair	**0.045**	**0.45**	**0.21 – 0.98**	0.309	0.62	0.25 – 1.56	0.999	0.00	0.00 - ∞
Desmotomy	0.291	1.60	0.67 – 3.83	0.148	1.99	0.78 – 5.07	0.999	0.00	0.00 - ∞
Other orthopaedic procedure	**0.002**	**0.10**	**0.02 – 0.43**	0.434	0.66	0.23 – 1.89	0.382	3.48	0.21 – 57.32
Castration	0.995	0.00	0.00 - ∞	0.995	0.00	0.00 - ∞	0.998	0.00	0.00 - ∞
Laparotomy	0.998	0.00	0.00 - ∞	0.769	0.79	0.16 – 3.89	0.999	0.00	0.00 - ∞
Enucleation	0.999	0.00	0.00 - ∞	0.362	2.36	0.37 – 14.95	1.000	0.00	0.00 - ∞
Other soft tissue procedure	**0.020**	**0.09**	**0.01 – 0.68**	0.609	0.71	0.19 – 2.65	**0.038**	**13.50**	**1.16 – 157.58**
Laryngoplasty	**0.045**	**0.31**	**0.10 – 0.98**	0.673	1.25	0.44 – 3.52	0.999	0.00	0.00 - ∞
Sinus & Dental	0.051	0.28	0.08 – 1.01	0.068	2.58	0.93 – 7.12	0.212	6.00	0.36 – 100.30
Penile	0.999	0.00	0.00 - ∞	0.052	4.72	0.99 – 22.56	**0.050**	18.00	1.00 – 324 – 27
Other clean-contaminated procedure	0.390	1.97	0.42 – 9.23	0.052	4.72	0.99 – 22.56	1.000	0.00	0.00 - ∞
Anatomical location of surgical incision (referent distal limb)									
Proximal limb	0.828	1.08	0.54 – 2.18	0.978	0.99	0.48 – 2.05	0.999	0.00	0.00 - ∞
Body	0.093	0.17	0.02 – 1.34	0.273	0.43	0.09 – 1.96	**0.006**	**17.92**	**2.32 – 138.40**
Head & neck	**0.012**	**0.39**	**0.19 – 0.82**	0.783	1.09	0.60 – 1.99	0.236	3.31	0.46 – 23.95
Ventral abdomen, inguinal & penis	**<0.001**	**0.03**	**0.00 – 0.18**	**<0.001**	**0.18**	**0.08 – 0.44**	0.878	1.21	0.11 – 13.49

Appendix 12.6 continued overleaf

Appendix 12.6, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Abnormal incisional drainage	**0.005**	**2.05**	**1.24 – 3.38**	X	X	x	0.237	2.49	0.55 – 11.34
Partial or total incisional dehiscence	0.185	2.78	0.61 – 12.66	0.237	2.49	0.55 – 11.34	X	x	X
Abnormal incisional swelling	X	x	X	**0.005**	**2.05**	**1.24 – 3.38**	0.185	2.78	0.61 – 12.66

Appendix 12.7: Clean surgical procedures – incisional outcome by variable

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Age (referent < 2 yrs)									
2 – 6 yrs	0.105	1.87	0.88 – 4.01	0.261	1.70	0.67 – 4.30	0.778	1.33	0.18 – 9.62
6 – 9 yrs	**0.009**	**2.72**	**1.28 – 5.74**	**<0.001**	**6.71**	**2.95 – 15.25**	0.999	0.00	0.00 - ∞
> 9 yrs	**0.001**	**3.61**	**1.74 – 7.48**	**<0.001**	**6.23**	**2.74 – 14.17**	0.808	0.74	0.07 – 8.31
Gender (referent female)									
M	**<0.001**	**0.22**	**0.11 – 0.43**	**<0.001**	**0.16**	**0.06 – 0.39**	0.666	1.49	0.24 – 9.06
MN	0.054	0.57	0.32 – 1.01	**0.030**	**1.85**	**1.06 – 3.24**	0.999	0.00	0.00 - ∞
Weight (referent <400 kgs)									
400-600 kgs	0.078	1.87	0.93 – 3.77	**0.046**	**2.09**	**1.01 – 4.31**	0.426	0.48	0.08 – 2.92
>600 kgs	**0.005**	**3.93**	**1.51 – 10.22**	0.093	2.43	0.86 – 6.87	0.999	0.00	0.00 - ∞
Duration of GA (referent < 60 mins)									
60 – 90 mins	**0.001**	**4.52**	**1.89 – 10.52**	**0.020**	**2.54**	**1.16 – 5.57**	0.999	0.00	0.00 - ∞
90 – 110 mins	**<0.001**	**5.78**	**2.28 – 14.62**	**0.001**	**3.91**	**1.70 – 9.04**	1.000	1.00	0.00 - ∞
> 110 mins	**<0.001**	**5.57**	**2.25 – 13.82**	**0.007**	**3.12**	**1.36 – 7.13**	0.999	0.00	0.00 - ∞
Duration of Surgery (referent < 30 mins)									
30 – 50 mins	0.255	1.49	0.75 – 2.98	0.108	1.77	0.88 – 3.56	0.856	0.77	0.05 – 12.50
50 – 65 mins	0.119	1.91	0.85 – 4.31	0.140	1.88	0.81 – 4.34	0.999	0.00	0.00 - ∞
> 65 mins	**0.010**	**2.65**	**1.27 – 5.52**	**0.045**	2.20	1.02 – 4.73	0.814	1.40	0.09 0 22.71
Length of incision (referent < 5cm)									
5-10cm	**0.003**	**0.16**	**0.05 – 0.53**	**0.009**	**0.25**	**0.09 – 0.70**	0.999	0.00	0.00 - ∞
>10 cm	**0.035**	**0.11**	**0.02 – 0.86**	**0.046**	**0.13**	**0.02 – 0.96**	**0.001**	**19.84**	**3.15 – 125.05**
>1 incision	**<0.001**	**3.59**	**2.01 – 6.43**	**0.007**	**2.12**	**1.23 – 3.66**	0.127	0.18	0.02 – 1.63

Appendix 12.7 continued overleaf

Appendix 12.7, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Volume of dead space left (referent small)									
Moderate	**<0.001**	**0.05**	**0.01 – 0.22**	**<0.001**	**0.23**	**0.10 – 0.51**	0.781	0.73	0.08 – 6.63
Large	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	X	x	X
Surgical site clipped prior to induction (referent not clipped)									
<24hrs	0.353	1.93	0.48 – 7.78	0.503	1.72	0.35 – 8.51	1.000	0.00	0.00 - ∞
>24hrs	**0.030**	**1.90**	**1.06 – 3.39**	**<0.001**	**4.99**	**2.78 – 8.95**	0.983	0.98	0.10 – 9.51
Surgical site shaved	0.955	1.02	0.51 – 2.04	**<0.001**	**4.79**	**2.60 – 8.82**	0.723	1.49	0.16 – 13.60
Type of dressing used (referent none used)									
Cast	**<0.001**	**23.21**	**4.64 – 116.00**	0.516	0.49	0.06 – 4.18	0.999	0.00	0.00 - ∞
Bandage	**<0.001**	**21.57**	**5.15 – 90.43**	**<0.001**	**5.99**	**2.62 – 13.70**	0.508	0.51	0.07 – 3.70
Adhesive /stent	**0.001**	**13.15**	**2.79 – 61.95**	0.057	2.78	0.97 – 7.96	0.974	0.96	0.09 – 10.85
Type of surgical procedure performed (referent orthopaedic)									
Soft tissue	**<0.001**	**0.02**	**0.00 – 0.17**	**<0.001**	**0.17**	**0.07 – 0.40**	0.545	1.75	0.29 – 10.60
Suture pattern used in closure of deep layer (referent no deep closure)									
Simple interrupted	0.060	0.24	0.05 – 1.06	0.150	0.22	0.03 – 1.72	0.999	0.00	0.00 - ∞
Simple continuous	**<0.001**	**0.18**	**0.10 – 0.34**	0.645	1.13	0.68 – 1.87	0.282	0.30	0.03 – 2.70
Mattress/Near-far Far-near	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	X	x	X
Suture pattern used in closure of subcutaneous layer (referent no closure)									
Simple interrupted	0.493	0.72	0.28 – 1.84	0.176	0.42	0.12 – 1.48	0.999	0.00	0.00 - ∞
Simple continuous	**<0.001**	**0.31**	**0.18 – 0.53**	0.435	0.81	0.48 – 1.37	0.431	2.42	0.27 – 21.91
Mattress/Near-far Far-near	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞

Appendix 12.7 continued overleaf

Appendix 12.7, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Suture pattern used in closure of skin (referent none)									
Simple interrupted	0.094	1.92	0.89 – 4.11	**0.001**	**0.34**	**0.18 – 0.62**	0.921	0.89	0.10 – 8.14
Simple continuous	0.058	0.13	0.02 – 1.08	**0.001**	**0.11**	**0.03 – 0.41**	0.999	0.00	0.00 - ∞
Cruciate	0.999	0.00	0.00 - ∞	0.373	0.36	0.04 – 3.42	1.000	0.00	0.00 - ∞
Mattress/Near-far Far-near	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	X	X	X
Suture material used in closure of deep layer (referent none)									
Vicryl/ polysorb	**<0.001**	**0.18**	**0.10 – 0.33**	0.963	1.01	0.61 – 1.67	0.726	0.72	0.12 – 4.39
PDS/biosyn	0.226	0.27	0.03 – 2.25	0.569	0.54	0.06 – 4.51	1.000	0.00	0.00 - ∞
Suture material used in closure of subcutaneous layer (referent none)									
Vicryl/polysorb	**<0.001**	**0.36**	**0.22 – 0.60**	0.309	0.77	0.46 – 1.28	0.481	2.21	0.24 – 19.91
PDS/biosyn	0.398	0.39	0.04 – 3.45	0.688	0.64	0.07 – 5.68	1.000	0.00	0.00 - ∞
Suture material used in closure of skin (referent none)									
Staples	**0.020**	**2.49**	**1.16 – 5.36**	**0.002**	**0.38**	**0.20 – 0.71**	0.997	1.00	0.10 – 9.72
Nylon/prolene	0.999	0.00	0.00 - ∞	0.373	0.36	0.04 – 3.42	X	x	X
Vicryl/polysorb	**0.011**	**0.07**	**0.01 – 0.53**	**<0.001**	**0.06**	**0.02 – 0.20**	0.941	0.90	0.06 – 14.65
PDS/biosyn	0.501	0.47	0.05 – 4.15	0.970	1.02	0.29 – 3.63	X	X	X
Type of antimicrobials administered prior to induction of anaesthesia (referent none)									
Procaine penicillin/Sodium penicillin	0.469	2.18	0.26 – 18.09	0.834	0.84	0.17 – 4.28	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	0.703	1.56	0.16 – 15.12	0.817	0.81	0.13 – 4.91	1.000	0.00	0.00 - ∞
Sodium penicillin and gentamicin	0.498	2.14	0.24 – 19.33	0.922	0.92	0.16 – 5.21	1.000	1.00	0.00 - ∞
Other combination	0.478	0.35	0.02 – 6.38	0.998	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞

Appendix 12.7 continued overleaf

Appendix 12.7, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Surgical procedure performed (referent arthroscopy or tenoscopy)									
Neurectomy	**0.007**	**0.35**	**0.17 – 0.76**	**0.001**	**3.19**	**1.60 – 6.35**	0.645	1.93	0.12 – 31.42
Fracture repair	**0.045**	**0.45**	**0.21 – 0.98**	0.309	0.62	0.25 – 1.56	0.999	0.00	0.00 - ∞
Desmotomy	0.291	1.60	0.67 – 3.83	0.148	1.99	0.78 – 5.07	0.999	0.00	0.00 - ∞
Other orthopaedic procedure	**0.002**	**0.10**	**0.02 – 0.43**	0.434	0.66	0.23 – 1.89	0.382	3.48	0.21 – 57.32
Castration	0.995	0.00	0.00 - ∞	0.996	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Laparotomy	0.998	0.00	0.00 - ∞	0.387	0.39	0.05 – 3.26	0.999	0.00	0.00 - ∞
Enucleation	0.999	0.00	0.00 - ∞	0.362	2.36	0.37 – 14.95	1.000	0.00	0.00 - ∞
Other soft tissue procedure	**0.020**	**0.09**	**0.01 – 0.68**	0.609	0.71	0.19 – 2.65	**0.038**	**13.50**	**1.16 – 157.58**
Anatomical location of surgical incision (referent distal limb)									
Proximal limb	0.767	1.11	0.55 – 2.25	0.786	0.90	0.43 – 1.91	0.999	0.00	0.00 - ∞
Body	0.998	0.00	0.00 - ∞	0.998	0.00	0.00 - ∞	**0.004**	**21.40**	**2.73 – 167.91**
Head & neck	**0.030**	**0.11**	**0.01 – 0.80**	0.319	0.56	0.18 – 1.74	0.191	5.10	0.44 – 58.57
Ventral abdomen, inguinal & penis	0.995	0.00	0.00 - ∞	**<0.001**	**0.06**	**0.02 – 0.27**	0.998	0.00	0.00 - ∞
Abnormal incisional drainage	**0.035**	**1.82**	**1.04 – 3.19**	X	x	X	0.962	0.95	0.10 – 8.60
Partial or total incisional dehiscence	0.340	2.41	0.40 – 14.66	0.962	0.95	0.10 – 8.60	X	x	X
Abnormal incisional swelling	X	x	X	**0.035**	**1.82**	**1.04 – 3.19**	0.340	2.41	0.40 – 14.66

Appendix 12.8: Clean orthopaedic surgical procedures – incisional outcome by variable

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Age (referent < 3 yrs)									
3 – 6 yrs	0.546	1.26	0.59 – 2.69	**0.025**	**2.69**	**1.13 – 6.41**	0.999	0.00	0.00 - ∞
6 – 10 yrs	0.576	1.22	0.60 – 2.49	**0.002**	**3.50**	**1.56 – 7.84**	1.000	1.00	0.00 - ∞
> 10 yrs	0.149	1.71	0.83 – 3.56	**0.001**	**4.00**	**1.73 – 9.24**	0.999	0.00	0.00 - ∞
Gender (referent female)									
M	0.145	0.58	0.28 – 1.21	0.079	0.42	0.16 – 1.10	0.218	4.58	0.41 – 51.77
MN	**0.026**	**0.51**	**0.29 – 0.92**	0.065	1.73	0.97 – 3.11	0.998	0.00	0.00 - ∞
Weight (referent <400 kgs)									
400-600 kgs	0.237	1.59	0.74 – 3.51	0.063	2.27	0.96 – 5.38	0.999	0.00	0.00 - ∞
>600 kgs	0.080	2.47	0.90 – 6.78	0.209	2.08	0.66 – 6.50	1.000	1.00	0.00 - ∞
Duration of GA (referent < 75 mins)									
75 – 100 mins	0.947	1.02	0.49 – 2.12	0.066	2.10	0.95 – 4.63	0.999	0.00	0.00 - ∞
100 – 115 mins	0.335	1.45	0.68 – 3.09	0.212	1.73	0.73 – 4.07	0.999	0.00	0.00 - ∞
> 115 mins	0.701	1.16	0.55 – 2.46	0.052	2.25	0.99 – 5.09	0.940	1.11	0.07 – 18.17
Duration of Surgery (referent < 35 mins)									
35 – 55 mins	0.363	0.73	0.36 – 1.45	0.662	1.17	0.57 – 2.41	0.999	0.00	0.00 - ∞
55 – 65 mins	0.809	0.90	0.37 – 2.19	0.939	0.96	0.37 – 2.53	0.999	0.00	0.00 - ∞
> 65 mins	0.538	1.26	0.61 – 2.59	0.424	1.37	0.63 – 2.98	0.966	1.06	0.07 – 17.37
Length of incision (referent < 5cm)									
5-10cm	0.700	0.73	0.14 – 3.68	0.842	0.85	0.17 – 4.30	1.000	0.00	0.00 - ∞
>10 cm	0.104	0.18	0.02 – 1.42	0.998	0.00	0.00 - ∞	0.065	10.25	0.87 – 121.11
>1 incision	0.080	1.75	0.94 – 3.29	0.650	1.15	0.62 – 2.14	0.166	0.18	0.02 – 2.03

Appendix 12.8 continued overleaf

Appendix 12.8, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Volume of dead space left (referent small)									
Moderate	0.064	0.15	0.02 – 1.12	0.464	0.62	0.17 – 2.24	0.089	8.40	0.72 – 97.96
Surgical site clipped prior to induction (referent not clipped)									
<24hrs	0.939	0.95	0.23 – 3.84	0.834	1.19	0.24 – 5.95	1.000	0.00	0.00 - ∞
>24hrs	0.798	0.92	0.50 – 1.69	**<0.001**	**3.67**	**1.96 – 6.88**	0.999	0.00	0.00 - ∞
Surgical site shaved	0.166	0.61	0.30 – 1.23	**<0.001**	**3.43**	**1.84 – 6.41**	0.569	2.02	0.18 – 22.69
Type of dressing used (referent none used)									
Cast	0.856	1.18	0.19 – 7.32	0.071	0.09	0.01 – 1.23	1.000	1.00	0.00 - ∞
Bandage	0.896	1.12	0.21 – 5.93	0.874	1.15	0.22 – 6.07	1.000	0.00	0.00 - ∞
Adhesive /stent	0.761	0.76	0.13 – 4.52	0.545	0.57	0.09 – 3.49	1.000	0.00	0.00 - ∞
Suture pattern used in closure of deep layer (referent no deep closure)									
Simple interrupted	0.424	0.41	0.04 – 3.70	0.893	0.86	0.09 – 7.91	1.000	0.00	0.00 - ∞
Simple continuous	**<0.001**	**0.31**	**0.16 – 0.59**	**0.019**	**1.96**	**1.12 – 3.44**	0.999	0.00	0.00 - ∞
Mattress/Near-far Far-near	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	X	x	X
Suture pattern used in closure of subcutaneous layer (referent no closure)									
Simple interrupted	0.651	1.30	0.42 – 3.98	0.382	0.50	0.11 – 2.36	1.000	0.00	0.00 - ∞
Simple continuous	**0.012**	**0.49**	**0.28 – 0.86**	0.409	1.26	0.73 – 2.20	0.636	1.79	0.16 – 19.99
Mattress/Near-far Far-near	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Suture pattern used in closure of skin (referent none)									
Simple interrupted	0.089	1.97	0.90 – 4.32	**0.001**	**0.31**	**0.16 – 0.60**	0.999	0.00	0.00 - ∞
Simple continuous	1.000	1.00	0.10 – 10.07	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Cruciate	0.999	0.00	0.00 - ∞	0.246	0.26	0.03 – 2.52	1.000	1.00	0.00 - ∞

Appendix 12.8 continued overleaf

Appendix 12.8, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Suture material used in closure of deep layer (referent none)									
Vicryl/ polysorb	**<0.001**	**0.28**	**0.15 – 0.53**	**0.032**	**1.83**	**1.05 – 3.18**	0.939	0.91	0.08 – 10.16
PDS/biosyn	0.734	1.62	0.10 – 26.36	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Suture material used in closure of subcutaneous layer (referent none)									
Vicryl/polysorb	**0.029**	**0.56**	**0.33 – 0.94**	0.535	1.19	0.69 – 2.05	0.691	1.63	0.15 – 18.20
PDS/biosyn	0.702	1.73	0.11 – 28.31	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Suture material used in closure of skin (referent none)									
Staples	**0.080**	**2.01**	**0.92 – 4.42**	**<0.001**	**0.30**	**0.15 – 0.58**	0.999	0.00	0.00 - ∞
Nylon/prolene	0.999	0.00	0.00 - ∞	0.975	1.05	0.06 – 17.77	1.000	1.00	0.00 - ∞
Vicryl/polysorb	1.000	1.00	0.10 – 10.07	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
PDS/biosyn	0.538	0.50	0.06 – 4.53	0.398	0.51	0.12 – 2.35	1.000	1.00	0.00 - ∞
Type of antimicrobials administered prior to induction of anaesthesia (referent none)									
Procaine penicillin/Sodium penicillin	0.626	0.50	0.03 – 8.13	0.543	0.42	0.03 – 6.85	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	0.439	0.31	0.02 – 5.96	0.540	0.40	0.02 – 7.48	1.000	0.00	0.00 - ∞
Sodium penicillin and gentamicin	0.477	0.35	0.02 – 6.17	0.375	0.27	0.02 – 4.80	1.000	1.00	0.00 - ∞
Other combination	0.122	0.07	0.00 – 2.06	0.998	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Surgical procedure performed (referent arthroscopy or tenoscopy)									
Neurectomy	**0.007**	**0.35**	**0.17 – 0.76**	**0.001**	**3.19**	**1.60 – 6.35**	0.645	1.93	0.12 – 31.42
Fracture repair	**0.045**	**0.45**	**0.21 – 0.98**	0.309	0.62	0.25 – 1.56	0.999	0.00	0.00 - ∞
Desmotomy	0.291	1.60	0.67 – 3.83	0.148	1.99	0.78 – 5.07	0.999	0.00	0.00 - ∞
Other orthopaedic procedure	**0.002**	**0.10**	**0.02 – 0.43**	0.434	0.66	0.23 – 1.89	0.382	3.48	0.21 – 57.32

Appendix 12.8 continued overleaf

Appendix 12.8, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Anatomical location of surgical incision (referent distal limb)									
Proximal limb	0.767	1.11	0.55 – 2.25	0.786	0.90	0.43 – 1.91	0.999	0.00	0.00 - ∞
Body	0.998	0.00	0.00 - ∞	0.998	0.00	0.00 - ∞	0.051	11.89	0.98 – 143.60
Head & neck	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Abnormal incisional drainage	0.471	1.24	0.69 – 2.21	X	X	x	0.794	1.38	0.12 – 15.46
Partial or total incisional dehiscence	0.205	4.76	0.43 – 53.23	0.794	1.38	0.12 – 15.46	X	x	X
Abnormal incisional swelling	X	x	X	0.471	1.24	0.69 – 2.21	0.205	4.76	0.43 – 53.25

Appendix 12.9: Clean soft-tissue surgical procedures – incisional outcome by variable

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Age (referent < 2 yrs)									
2 – 3 yrs	1.000	1.00	0.00 - ∞	0.998	0.00	0.00 - ∞	0.998	0.00	0.00 - ∞
3 – 4 yrs	1.000	1.00	0.00 - ∞	0.455	3.00	0.17 – 53.71	0.999	0.00	0.00 - ∞
> 4 yrs	0.999	0.00	0.00 - ∞	0.124	6.00	0.61 – 58.71	0.999	0.00	0.00 - ∞
Gender (referent female)									
M	0.999	0.00	0.00 - ∞	0.997	0.00	0.00 - ∞	0.268	0.20	0.01 – 3.41
MN	1.000	0.00	0.00 - ∞	0.208	3.50	0.50 – 24.56	1.000	0.00	0.00 - ∞
Weight (referent <400 kgs)									
400-600 kgs	0.999	0.00	0.00 - ∞	0.444	0.52	0.10 – 2.74	0.999	0.00	0.00 - ∞
>600 kgs	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Duration of GA (referent < 50 mins)									
50 – 60 mins	1.000	1.00	0.00 - ∞	0.458	2.34	0.25 – 22.18	1.000	1.00	0.00 - ∞
60 – 70 mins	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
> 70 mins	1.000	1.00	0.00 - ∞	0.900	1.20	0.07 – 20.43	0.999	0.00	0.00 - ∞
Duration of Surgery (referent < 29 mins)									
29 – 39 mins	1.000	1.00	0.00 - ∞	0.998	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
39 – 45 mins	0.999	0.00	0.00 - ∞	0.162	5.05	0.52 – 49.03	0.999	0.00	0.00 - ∞
> 45 mins	1.000	1.00	0.00 - ∞	0.812	1.41	0.08 – 24.18	1.000	1.00	0.00 - ∞
Length of incision (referent < 5cm)									
5-10cm	0.999	0.00	0.00 - ∞	0.982	0.98	0.13 – 7.25	1.000	1.00	0.00 - ∞
>10 cm	1.000	1.00	0.00 - ∞	0.598	1.95	0.16 – 23.58	0.998	0.00	0.00 - ∞
>1 incision	0.999	0.00	0.00 - ∞	0.879	1.19	0.13 – 11.33	0.999	0.00	0.00 - ∞

Appendix 12.9 continued overleaf

Appendix 12.9, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Volume of dead space left (referent small)									
Moderate	0.999	0.00	0.00 - ∞	0.417	0.48	0.08 – 2.83	0.998	0.00	0.00 - ∞
Large	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞	X	x	X
Type of dressing used (referent none used)									
Bandage	1.000	1.00	0.00 - ∞	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Adhesive /stent	0.998	0.00	0.00 - ∞	0.495	2.20	0.23 – 21.21	1.000	0.00	0.00 - ∞
Suture pattern used in closure of deep layer (referent no deep closure)									
Simple interrupted	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Simple continuous	1.000	1.00	0.00 - ∞	0.843	1.25	0.14 – 11.42	0.316	0.24	0.01 – 3.97
Suture pattern used in closure of subcutaneous layer (referent no closure)									
Simple interrupted	0.999	0.00	0.00 - ∞	0.892	0.82	0.04 – 15.00	1.000	1.00	0.00 - ∞
Simple continuous	1.000	1.00	0.00 - ∞	0.509	0.46	0.05 – 4.59	0.999	0.00	0.00 - ∞
Suture pattern used in closure of skin (referent none)									
Simple interrupted	1.000	0.00	0.00 - ∞	0.462	0.39	0.03 – 4.75	0.364	0.27	0.02 – 4.58
Simple continuous	1.000	1.00	0.00 - ∞	0.937	0.91	0.08 – 9.74	0.999	0.00	0.00 - ∞
Mattress/Near-far Far-near	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞	X	x	X
Suture material used in closure of deep layer (referent none)									
Vicryl/ polysorb	0.999	0.00	0.00 - ∞	0.293	0.89	0.09 – 8.52	0.286	0.22	0.01 – 3.61
PDS/biosyn	1.000	1.00	0.00 - ∞	0.415	3.40	0.18 – 64.68	1.000	0.00	0.00 - ∞
Suture material used in closure of subcutaneous layer (referent none)									
Vicryl/polysorb	1.000	0.00	0.00 - ∞	0.457	0.42	0.04 – 4.16	0.999	0.00	0.00 - ∞
PDS/biosyn	1.000	1.00	0.00 - ∞	0.482	3.00	0.14 – 64.27	1.000	1.00	0.00 - ∞

Appendix 12.9 continued overleaf

Appendix 12.9, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Suture material used in closure of skin (referent none)									
Staples	0.999	0.00	0.00 - ∞	0.998	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞
Nylon/prolene	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞	X	x	X
Vicryl/polysorb	1.000	1.00	0.00 - ∞	0.460	0.41	0.04 – 4.34	0.284	0.21	0.01 – 3.59
PDS/biosyn	1.000	1.00	0.00 - ∞	0.063	20.00	0.85 – 471.60	X	x	X
Type of antimicrobials administered prior to induction of anaesthesia (referent none)									
Procaine penicillin/Sodium penicillin	1.000	1.00	0.00 - ∞	0.126	0.14	0.01 – 1.76	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	1.000	0.00	0.00 - ∞	0.602	0.45	0.02 – 8.83	1.000	1.00	0.00 - ∞
Sodium penicillin and gentamicin	1.000	1.00	0.00 - ∞	0.398	3.33	0.20 – 54.53	1.000	1.00	0.00 - ∞
Other combination	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Surgical procedure performed (referent arthroscopy or tenoscopy)									
Castration	0.999	0.00	0.00 - ∞	0.997	0.00	0.00 - ∞	0.998	0.00	0.00 - ∞
Laparotomy	0.999	0.00	0.00 - ∞	0.633	0.56	0.05 – 6.18	0.999	0.00	0.00 - ∞
Enucleation	1.000	0.00	0.00 - ∞	0.278	3.33	0.38 – 29.39	0.999	0.00	0.00 - ∞
Other soft tissue procedure	X	x	x	X	x	x	X	x	X
Anatomical location of surgical incision (referent distal limb)									
Proximal limb	X	x	X	X	x	X	X	x	X
Body	1.000	1.00	0.00 - ∞	1.000	0.00	0.00 - ∞	**<0.001**	**0.00**	**0.00** - ∞
Head & neck	0.999	0.00	0.00 - ∞	**0.011**	**10.00**	**1.69 – 59.31**	0.999	0.00	0.00 - ∞
Ventral abdomen, inguinal & penis	X	x	X	X	x	x	X	X	x

Appendix 12.9 continued overleaf

Appendix 12.9, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Abnormal incisional drainage	1.000	0.00	0.00 - ∞	X	x	X	1.000	0.00	0.00 - ∞
Partial or total incisional dehiscence	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞	X	x	x
Abnormal incisional swelling	X	x	X	1.000	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞

Appendix 12.10: Clean contaminated surgical procedures – incisional outcome by variable

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Age (referent < 3 yrs)									
3 – 7 yrs	0.517	0.52	0.07 – 3.70	0.546	1.67	0.32 – 8.74	1.000	1.00	0.00 - ∞
7 – 11 yrs	0.809	1.22	0.24 – 6.23	0.100	3.67	0.78 – 17.25	0.999	0.00	0.00 - ∞
> 11 yrs	0.808	0.73	0.06 – 8.92	**0.022**	**18.33**	**1.51 – 222.88**	1.000	1.00	0.00 - ∞
Gender (referent female)									
M	0.812	1.43	0.08 – 26.90	0.083	0.12	0.01 – 1.32	1.000	1.00	0.00 - ∞
MN	0.310	3.10	0.35 – 27.66	0.467	0.61	0.16 – 2.34	0.999	0.00	0.00 - ∞
Weight (referent <400 kgs)									
400-600 kgs	0.931	0.90	0.08 – 9.75	0.730	0.70	0.09 – 5.46	1.000	0.00	0.00 - ∞
>600 kgs	0.373	0.25	0.01 – 5.26	0.683	0.63	0.07 – 5.97	1.000	0.00	0.00 - ∞
Duration of GA (referent < 67 mins)									
67 – 97 mins	0.150	0.17	0.02 – 1.88	0.629	1.43	0.34 – 6.08	0.999	0.00	0.00 - ∞
97 – 117 mins	0.718	1.47	0.18 – 11.72	0.515	1.88	0.28 – 12.46	1.000	1.00	0.00 - ∞
> 117 mins	0.407	2.04	0.38 – 10.94	0.133	3.33	0.69 – 16.02	0.999	0.00	0.00 - ∞
Duration of Surgery (referent < 40 mins)									
40 – 65 mins	0.288	0.28	0.03 – 2.96	0.335	2.04	0.48 – 8.71	0.999	0.00	0.00 - ∞
65 – 80 mins	0.056	6.67	0.95 – 46.56	0.105	4.67	0.72 – 30.11	0.999	0.00	0.00 - ∞
> 80 mins	0.657	1.50	0.25 – 8.98	**0.032**	**5.60**	**1.16 – 27.08**	0.812	1.42	0.08 – 24.95
Length of incision (referent < 5cm)									
5-10cm	0.537	2.04	0.21 – 19.49	0.263	2.62	0.49 – 14.11	0.999	0.00	0.00 - ∞
>10 cm	0.105	6.87	0.67 – 70.82	**0.006**	**16.67**	**2.27 – 122.21**	1.000	1.00	0.00 - ∞
>1 incision	0.999	0.00	0.00 - ∞	0.778	0.150	0.09 – 25.26	1.000	0.00	0.00 - ∞

Appendix 12.10 continued overleaf

Appendix 12.10, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Volume of dead space left (referent small)									
Moderate	0.744	0.67	0.06 – 7.57	0.919	0.91	0.15 – 5.66	0.999	0.00	0.00 - ∞
Large	0.319	3.23	0.32 – 32.48	0.109	4.64	0.71 – 30.42	0.999	0.00	0.00 - ∞
Surgical site clipped prior to induction (referent not clipped)									
<24hrs	0.755	1.32	0.23 – 7.59	0.323	0.43	0.08 – 2.30	0.999	0.00	0.00 - ∞
>24hrs	0.514	2.31	0.19 – 28.72	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Type of dressing used (referent none used)									
Cast	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Adhesive /stent	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Suture pattern used in closure of deep layer (referent no deep closure)									
Simple interrupted	0.998	0.00	0.00 - ∞	0.130	0.26	0.05 – 1.48	0.999	0.00	0.00 - ∞
Simple continuous	**0.049**	**0.19**	**0.03 – 0.99**	0.956	0.97	0.29 – 3.18	0.998	0.00	0.00 - ∞
Mattress/Near-far Far-near	0.999	0.00	0.00 - ∞	0.910	1.18	0.07 – 21.18	X	x	X
Suture pattern used in closure of subcutaneous layer (referent no closure)									
Simple interrupted	0.058	0.11	0.01 – 1.08	0.870	1.14	0.23- 5.67	0.999	0.00	0.00 - ∞
Simple continuous	**0.020**	**0.17**	**0.04 – 0.76**	0.893	1.09	0.29 – 4.10	0.999	0.00	0.00 - ∞
Suture pattern used in closure of skin (referent none)									
Simple interrupted	0.100	0.28	0.06 – 1.27	0.525	1.62	0.37 – 7.10	0.999	0.00	0.00 - ∞
Simple continuous	0.999	0.00	0.00 - ∞	0.273	4.67	0.30 – 73.39	1.000	1.00	0.00 - ∞
Suture material used in closure of deep layer (referent none)									
Vicryl/ polysorb	**0.009**	**0.11**	**0.02 – 0.58**	0.531	0.71	0.24 – 2.08	0.836	0.74	0.04 – 12.50
PDS/biosyn	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞

Appendix 12.10 continued overleaf

Appendix 12.10, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Suture material used in closure of subcutaneous layer (referent none)									
Vicryl/polysorb	**0.012**	**0.16**	**0.04 – 0.66**	0.897	1.09	0.30 – 3.90	0.999	0.00	0.00 - ∞
PDS/biosyn	0.999	0.00	0.00 - ∞	0.758	1.60	0.08 – 31.77	1.000	1.00	0.00 - ∞
Suture material used in closure of skin (referent none)									
Staples	0.055	0.21	0.04 – 1.03	0.659	1.40	0.31 – 6.25	0.999	0.00	0.00 - ∞
Nylon/prolene	0.794	1.50	0.07 – 31.58	0.590	2.33	0.11 – 50.99	1.000	1.00	0.00 - ∞
Vicryl/polysorb	0.447	0.37	0.03 – 4.71	0.089	9.33	0.71 – 122.58	1.000	1.00	0.00 - ∞
Type of antimicrobials administered prior to induction of anaesthesia (referent none)									
Procaine penicillin/Sodium penicillin	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Procaine penicillin and gentamicin	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Sodium penicillin and gentamicin	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Other combination	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Surgical procedure performed (referent arthroscopy or tenoscopy)									
Laryngoplasty	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Sinus & Dental	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Penile	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Other clean-contaminated procedure	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞

Appendix 12.10 continued overleaf

Appendix 12.10, contd.

	Abnormal swelling			Abnormal drainage			Dehiscence		
	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI
Anatomical location of surgical incision (referent distal limb)									
Proximal limb	1.000	1.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Body	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	1.00	0.00 - ∞
Head & neck	0.999	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Ventral abdomen, inguinal & penis	1.000	0.00	0.00 - ∞	0.999	0.00	0.00 - ∞	1.000	0.00	0.00 - ∞
Abnormal incisional drainage	**0.022**	**5.51**	**1.28 – 23.80**	X	x	X	0.999	0.00	0.00 - ∞
Partial or total incisional dehiscence	0.302	4.50	0.26 – 78.21	0.999	0.00	0.00 - ∞	X	x	x
Abnormal incisional swelling	X	x	X	**0.022**	**5.51**	**1.28 – 23.81**	0.302	4.50	0.26 – 78.21

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