Surveillance of HIV Infection in Scotland

(A decade of HIV surveillance at SCIEH: 1984 - 1994)

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Abstract

The objectives of this thesis are to describe, analyse and evaluate the principal HIV surveillance schemes co-ordinated at the Scottish Centre for Infection and Environmental Health (SCIEH) between 1984 and 1994.

Chapter one begins with a brief review of surveillance, including examples of surveillance schemes and their benefits, followed by a detailed statement of the aims of this thesis. The chapter continues with a review of the first reports of AIDS, the discovery of HIV, the transmission of HIV, the immune response to HIV, and the development of a test for HIV antibodies. A brief introduction to the principal HIV surveillance schemes is given, with a description of the role of each scheme in the context of the overall HIV surveillance programme for Scotland. This is followed by an outline of the framework used, in chapter eight, to evaluate each surveillance scheme. Finally, the chapter concludes with a methods section.

Chapters two to six all follow a similar pattern, each concentrating on one particular HIV surveillance scheme. These are the AIDS Register (chapter two), HIV Register (chapter three), Denominator Study (chapter four), UAT surveillance (chapter five) and the CD4 Study (chapter six). Each chapter contains a detailed description of the surveillance scheme and an analysis of the data collected.

Chapter seven examines computer linkage of these HIV surveillance schemes, both with one another and with data from other surveillance schemes. It describes linkages that have already taken place, analyses results from them, and highlights areas for future work.

Chapter eight begins with an evaluation of key attributes of each of the HIV surveillance schemes described in chapters two to six. It continues with a demonstration of the importance of the linked HIV/AIDS Register, together with the CD4 and GUM Studies, in identifying where new infection may be occurring, and in estimating the prevalence of HIV infection. It also addresses a variety of issues regarding the performance, value and future role of the principal HIV surveillance schemes in Scotland.

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Summary

Introduction

In June 1981, a report was published about five previously-healthy homosexual men who had pneumocystis carinii pneumonia (PCP) and unexplained profound immune deficiency [1]. Throughout the next few months, it became apparent that there were many people presenting with a variety of infections and tumours associated with unexplained immune deficiency [2,3] and the term 'acquired immune deficiency syndrome' (AIDS) was introduced to encompass them [4].

In 1982, a retrovirus {later named the human immunodeficiency virus (HIV)} was discovered to be the causal agent of AIDS [5], although it was not until 1985 that a test for detecting antibodies to HIV, in serum samples, became readily available.

The AIDS Register

Since 1984, clinicians in Scotland have voluntarily reported AIDS cases to the Scottish Centre for Infection and Environmental Health (SCIEH), where a register of such cases is maintained. Analysis of this AIDS Register shows that by 30th June 1994, 518 cases of AIDS had been reported, of whom 366 (71 per cent) were known to have died [6]. Since 1989, the number of newly-reported AIDS diagnoses (ranging from 70 - 100 per year) has exceeded the number of deaths from AIDS, leading to an annual increase in the number of people living with AIDS [7]. Predictions show that this trend is expected to continue, so that by the year 1999 there will be approximately 270 people with AIDS living in Scotland [8].

Median survival, from AIDS diagnosis to death, is 17 months, with 37 per cent of AIDS cases surviving for two years from diagnosis, and 22 per cent surviving for three years. Analysis of survival following AIDS diagnosis shows that age and clinical presentation at diagnosis are important prognostic factors, with younger people surviving longer than older people.

The HIV Register

Since HIV testing began in Scotland in 1985, staff at NHS laboratories have reported all persons testing HIV antibody positive (HIV positive) to SCIEH where a register of these reports is maintained. Analysis of this HIV Register shows that by 30th June 1994, 2,129 HIV positive persons had been reported [6].

The number of HIV positive tests rose from 250 in 1984 to 325 in 1986 before falling to 248 in 1987. Of the 966 HIV-positive test results, from blood specimens taken before 1987, 66 per cent were attributable to injecting drug use, 20 per cent to homosexual/bisexual risk, 7 per cent to haemophiliacs receiving infected blood products, and 3 per cent to heterosexual risk. Since 1988, the number of HIV positive tests among IDUs has fallen, while the number attributable to heterosexual transmission has risen. Of the 915 HIV-positive test results reported since 1988, 38 per cent are attributed to homosexual/bisexual risk, 28 per cent attributed to injecting drug use, and 27 per cent attributed to heterosexual risk.

The Denominator Study

In 1988, the HIV reporting scheme was extended to include reports on everyone having an HIV antibody test, regardless of the test result. This extended scheme, the Denominator Study, allows HIV positive results to be interpreted in conjunction with the denominator of all HIV tests. This study shows that the number of persons having an HIV test has risen from approximately 9,000 in 1989 to 13,000 in 1992.

Most HIV test requests are made through the general practitioner setting (33 per cent), although most HIV positive results are found in the hospital setting. High rates of testing are found (for males and females) in the 20-24 year age group, and in Lothian Health Board. High rates of testing HIV positive are found among men aged 30-44 years, and in Tayside and Lothian Health Boards.

Logistic regression analysis of the 46,673 HIV test results reported between 1989 and 1992, shows that risk category, health board, reason for testing, source of test request, age, and presence of clinical symptoms, are all associated with the probability of testing HIV positive. In particular, men in the homosexual/bisexual category were found to be seven times more likely to test HIV positive than those with no known risk factors for HIV.

Unlinked Anonymous Testing

Both the HIV Register and the Denominator Study are based on test results of people who voluntarily seek HIV testing, and therefore cannot be used to provide estimates of prevalence of HIV in other population groups. In 1989, the UK Government announced that unlinked anonymous testing (UAT) for HIV antibodies in residual blood specimens could begin [9].

In UAT, the residual blood from another test (such as syphilis serology) is irreversibly unlinked from any patient-identifiable information before being tested for HIV. Hence, the HIV test result cannot be linked to a particular patient, but can be linked to information such as gender and age group.

In Scotland, the current network of UAT schemes was introduced between 1990 and 1992, covering different populations. These include people thought to be at high risk of acquiring HIV infection, such as genito-urinary medicine (GUM) clinic attenders, and those thought to be at lower risk, such as antenatal clinic attenders. These surveillance schemes provide estimates of the prevalence of HIV in their population groups, and trends in prevalence with time. Estimated prevalence of HIV among those participating in the GUM Study is 9 per 1000 in Edinburgh, and 5 per 1000 in Glasgow, compared with a prevalence among those participating in the Antenatal Study of less than 2 per 1000 in both Dundee and Edinburgh.

WHO Staging System : the CD4 Study

Several staging systems for HIV exist, each dividing the spectrum of HIV infection into distinct categories [10-12]. In 1991, an HIV surveillance scheme was introduced in Scotland, based on a WHO staging system [13]. All HIV positive adults who receive immunological monitoring, at one of five Scottish laboratories, participate in the surveillance scheme. The patient's clinical and immunological status are recorded every time he or she is monitored, and these results sent by the laboratory to SCIEH. From these records, a profile of the HIV infected population in Scotland (under monitoring) can be produced. Results show that 942 persons were monitored in 1993, 18 per cent of whom had late stage infection, and 40 per cent had CD4 counts of less than 200.

Computer Linkage of HIV Surveillance Schemes

Although each of the HIV surveillance schemes already mentioned is important in its own right, the value of these schemes (with the exception of UAT) will be increased by being linked to other schemes. This linkage is simplified by the centralisation and standardisation of data at SCIEH.

Linkages have been made between the AIDS and HIV registers, enabling progression from HIV to AIDS to be studied. Linkage between the HIV Register and the CD4 Study enables CD4 counts, pertaining to the time of HIV diagnosis, to be ascertained. Successful linkages have also been performed between the HIV Register and all deaths in Scotland (1980 - 1991), and between the HIV Register and hospital discharge data [14,15].

Evaluation of HIV Surveillance at SCIEH (1984 - 1994)

In the last chapter, each of the individual surveillance schemes is evaluated for attributes of simplicity, flexibility, acceptability, sensitivity, representativeness and timeliness. The focus then changes from individual surveillance schemes to broader issues concerning HIV surveillance in Scotland. Key information required by public health officials, clinicians and other professionals, involves identifying the occurrence of new infection, and assessing the resources required for those who are already infected [8,16-18]. By providing this information, the importance of the AIDS/HIV Register, together with the CD4 and GUM Studies, is demonstrated.

To conclude, the focus returns to the individual HIV surveillance schemes, where a variety of issues surrounding their performance, value and future role are addressed. These issues include discussion of the relevance of AIDS surveillance, the future of the Denominator and CD4 Studies, and the coverage of the UAT surveillance programme.

Chapter 1

Introduction

1.1 Background

1.1.1 Introduction to surveillance

The concept of surveillance is known to date from at least the fourth century BC, when Hippocrates followed the practice of observing, recording, and analysing data related to health, before deciding on a particular course of treatment. However, it was not until the pioneering work of Gottfried Wilhelm von Leibnitz, John Gaunt and William Petty in the 17th century, and William Farr, John Snow and Edwin Chadwick in the 19th century, that surveillance as we know it today began to develop [19].

Surveillance in the 19th century, and the first half of the 20th century, was primarily concerned with infectious diseases such as cholera, smallpox, and the plague, usually resulting in the isolation of infected individuals and the protection of those who had been in contact with them. In this second half of the 20th century, particularly in the developed world, surveillance has widened to include non-infectious diseases, chronic diseases, congenital defects, drug reactions, accidents, and a wide variety of environmental and occupational hazards.

1.1.2 Examples of surveillance schemes

(1) Mortality surveillance

The routine collection, analysis, and dissemination of information on deaths, particularly cause of death, has played an important role in public health surveillance since it was established in the 19th century. In particular, it has enabled data to be collected on the annual number of deaths due to specified causes, thus allowing yearly comparisons to be made, changes to be noticed and possible reasons investigated. For example, an increase in the number of deaths from asthma in the 1960s was found to coincide with an increase in the use of pressurised aerosols. The subsequent limitations imposed on the use of these aerosols was followed by a drop in the number of asthma-related deaths [20].

(2) Congenital malformations and birth defects

The surveillance of congenital malformation and birth defects has been demonstrated to be of particular importance in identifying possible causes of congenital malformation. This was highlighted in the 1940s when a link was discovered between infants exhibiting specific eye defects and the infection of their mothers with rubella during pregnancy [21]. It was again highlighted in 1962, when a link was identified between mothers taking the sedative drug thalidomide during pregnancy and the subsequent birth of infants with gross limb defects [22].

(3) Cardiovascular disease surveillance

Cardiovascular disease is a leading cause of death and disability throughout the world. Accordingly, the WHO cardiovascular unit in Geneva initiated a surveillance scheme for coronary heart disease and cerebrovascular disease. This scheme, known as the MONICA project, is run in 27 countries covering more than 12 million people [23]. One of the primary aims of MONICA is to test hypotheses relating coronary-risk to factors such as cholesterol, diastolic blood pressure and tobacco consumption.

(4) Cancer Surveillance

Cancer surveillance schemes were introduced in the UK between 1958 and 1962. They collect data on morbidity and mortality, which enable trends in incidence to be noticed and investigated. Data from such schemes have helped to justify the introduction of screening programmes for early diagnosis of cancer (such as cervical cancer and breast cancer). The data have also been used to calculate survival rates following cancer diagnosis, and have played an important role in evaluating the success both of these screening programmes and new methods of treatment.

Data from cancer surveillance schemes have been used very successfully to suggest possible aetiological hypotheses. For example, the number of cases of bladder cancer among workers in the rubber industry suggested a possible link to an antioxidant used in the rubber industry [24].

(5) Communicable diseases

Most microbiology laboratories in the United Kingdom voluntarily report any occurrence of specific infections (such as salmonella, chlamydia and hepatitis) to national surveillance centres in Glasgow and London. In addition to these laboratory reports, health professionals report notifiable diseases (such as chicken pox, rubella and tuberculosis) to these same centres. This information is collated and published weekly, together with data from the previous week and the previous year, for comparison purposes. This enables changes in incidence of infection to be identified and action to be taken. For example, in late 1993 and early 1994, an increase in the number of measles infections among school-age children was noticed, prompting a vacciniation programme to be implemented. Subsequent surveillance data showed that the incidence of measles dropped and a possible epidemic had been averted. Medical advances, such as the eradication of smallpox, together with the emergence of new infections, such as HIV, lead to changing requirements for the surveillance of communicable diseases.

1.2 The aims of this thesis

The discovery of AIDS and its causative agent HIV, in the early 1980's, were the catalysts for the introduction of a series of HIV surveillance schemes. However, in the haste to establish these surveillance schemes, the task of comprehensive detailed documentation was left largely undone. This lack of documentation occurred because priority was rightly given initially to data collection. Thus, there were early publications on the number of AIDS cases reported and the number of people testing HIV positive, while publications on the surveillance methodology lagged behind. This pattern was repeated with the introduction of the UAT schemes and the CD4 monitoring schemes, with the need to establish these schemes, and produce results, taking priority over documentation.

One of the aims of this thesis is to fill this gap by producing a reference document containing a historical record of the development of HIV surveillance at SCIEH, from 1985-1995, including detailed descriptions of the individual schemes together with their aims, the type of data collected, and how the schemes are managed. It is envisaged that this document will be of practical help to people currently working on these HIV surveillance schemes, those who will work on them in the future, and those who require to reference particular milestones in the development of HIV surveillance in Scotland.

A further aim of the thesis is to increase understanding of the spread of HIV in Scotland, by analysing data produced by the surveillance schemes.

For the HIV and AIDS Registers, this involves looking at trends in reported HIV infection and AIDS, with time, by factors such as age, gender, geographical region and risk category. Further analysis involves instigating a follow-up of all reported AIDS cases before carrying out a multivariate survival analysis from AIDS diagnosis to death.

For the Denominator Study, analysis includes looking at trends in HIV testing, with time, by factors such as age and gender, as well as calculation of testing rates in specific age bands. Further work includes estimating the effect of risk category, geographical region, reason for test, source of request, gender, age, presence of clinical symptoms, and year of test, on the probability of testing HIV positive.

For both the UAT and the CD4 schemes, analysis involves looking at trends in HIV testing, with time, by factors such as age, gender,

geographical region and risk category. In addition, the CD4 study includes analysis of the relationships between region, risk factor for HIV, and severity of HIV infection.

In addition to analysing each surveillance scheme separately, it is aimed to demonstrate the advantages to be gained by linking the data in the HIV and AIDS Registers with data from the CD4 Study. With this link established, various analyses are carried out, including estimation of the proportion of reported HIV positive persons who progressed to AIDS, and the CD4 values of people newly reported HIV positive.

The final aim of this thesis is to evaluate the HIV surveillance schemes currently co-ordinated at SCIEH. This includes looking at the utilisation of the data gathered, in particular what do these schemes tell us about the spread of HIV in the general population, the spread of HIV in high-risk categories, and about the magnitude of resources required for the care of HIV positive patients. This evaluation also involves looking at the biases inherent in each scheme and assessing each scheme for attributes such as simplicity, flexibility, acceptability, sensitivity, representativeness and timeliness. Finally, each scheme is examined for its contribution to the overall surveillance of HIV in Scotland.

1.3 First reports of AIDS

In June 1981, the Morbidity and Mortality Weekly Report (MMWR) published by the Centers for Disease Control (CDC) in Atlanta, Georgia, carried a report of five previously-healthy homosexual men in Los Angeles, California, who had pneumocystis carinii pneumonia (PCP) and unexplained profound immune deficiency [1]. Within the next month, twenty-six cases of a rare malignant tumour called Kaposi's sarcoma (KS), and an additional ten cases of PCP, were reported among homosexual men [2]. Soon it became apparent that there was a rapidly increasing epidemic of infections and tumours associated with unexplained immune deficiency [3].

When the immune system is impaired, persons affected become susceptible to a wide range of infections and tumours. The infections are often called 'opportunistic infections' because they take the opportunity provided by the deficiency in the person's immune system to cause diseases that would not normally occur. In 1982, the term 'acquired immune deficiency syndrome' (AIDS) was introduced, to encompass the range of infections and tumours that were being seen in people with unexplained immune deficiency. In September 1982, staff at CDC published the first AIDS-case definition [4]. In each of the years 1985, 1987 and 1993, the definition of AIDS was expanded to encompass a greater variety of opportunistic infections and clinical presentations [25-27].

1.3.1 AIDS cases world-wide

Between June 1981 and December 1994, 1,025,073 cases of AIDS were reported to the World Health Organization (WHO) in Geneva, Switzerland [28]. It is well known that this is an underestimate of the true figure because of under-diagnosis, under- reporting and late reporting. WHO estimated the true figure (at 31st December, 1994) to be over 4.5 million [28].

1.4 The discovery of HIV

The number of reported AIDS cases increased throughout 1982, and the same opportunistic infections associated with unexplained profound immune deficiency in homosexual men were reported in injecting drug users (IDUs) and haemophiliacs [4]. A virus was deemed the most likely cause of AIDS, because of the resemblance to the epidemiology of Hepatitis B. Hepatitis B was known to have a viral cause, and to be spread by sexual intercourse and through blood contact.

In 1983, a retrovirus was thought to be associated with the development of AIDS. This retrovirus was isolated by a team led by Dr L. Montagnier at the Institut Pasteur in Paris, France, and named 'lymphadenopathy associated virus' (LAV) [5]. By 1986, when the retrovirus was renamed the 'human immunodeficiency virus' (HIV), most epidemiologists agreed that HIV was the causal agent of AIDS. Although a few epidemiologists have remained unconvinced that HIV causes AIDS, this view has become increasingly untenable through time as evidence has increased that HIV does indeed cause AIDS [29,30].

1.4.1 Viruses and retroviruses

A virus is an infectious agent that invades cells of other organisms in order to replicate. A single virus particle (called a virion) consists of a core of deoxyribonucleic acid (DNA) surrounded by a protein shell and an outer layer of protein called the viral envelope. It attaches itself to a suitable cell of another organism, often called the host cell, then invades it. Viruses can only attach themselves to cells that have suitable receptors on their surfaces. The viral DNA uses the raw materials of the host cell to make large numbers of new copies of itself. These new virions then leave the host cell and invade other cells, thus continuing the replication process. The host cell may be destroyed in this process.

A retrovirus (like a virus) consists of a core of nucleic acid surrounded by a protein shell and a viral envelope but, in a retrovirus, the nucleic acid is ribonucleic acid (RNA). On entering a host cell, the RNA is converted to DNA before replicating and being released. Throughout this thesis, HIV is referred-to simply as a virus rather than more specifically as a retrovirus.

1.4.2 Immune response

When people with healthy immune systems are attacked by foreign organisms such as viruses, bacteria or fungi, the immune system reacts in a specific way. This immune response involves a range of different blood cells, including two specific types of white blood cells called B-lymphocytes and T-lymphocytes.

The first step in the immune response is to recognise the invading organism. A particular type of T-lymphocyte, called the T-helper lymphocyte, plays a crucial role in this recognition process, then "helps" other lymphocytes to mount an appropriate immune response. An important function of the T-helper lymphocyte is to stimulate B-lymphocytes and T-killer lymphocytes to multiply. B-lymphocytes then produce antibodies which may attach themselves to the antigen (foreign protein) on the surface of the invading organism. This, in turn, starts a process which enables the T-killer lymphocytes, and other white cells such as phagocytes, to destroy the resulting clusters of cells. Some of the B-cells and T-killer cells remain in the body as memory cells, so that if the organism should invade again, the immune response will be more rapid.

1.4.3 Immune response to HIV infection

HIV attaches itself to CD4 molecules which are found on the surface of T-helper cells, monocytes and macrophages. Thus, each of these types of cells may become infected with HIV. When HIV attaches itself to the T-helper cells, they are unable to function correctly, and a crucial part of the immune system is weakened. The person's immune response is then inadequately equipped to withstand subsequent attacks by other invading organisms, making the person susceptible to a whole range of opportunistic infections and tumours.

1.4.4 Transmission of HIV

There are three known routes of transmission of HIV :-

(1) Sexual intercourse

(2) Blood to blood transmission

(3) Mother to child transmission

Injecting drug users may become infected by blood to blood transmission, through injecting with needles previously used by an HIV-infected person.

1.4.5 Progression of HIV infection

Between three to twelve weeks after infection with HIV, almost 50 per cent of people will experience a flu-like illness, possibly accompanied by fever, lethargy, lymphadenopathy or a rash, called a seroconversion illness [31]. However, these symptoms occur so frequently in the general population that HIV is unlikely to be suspected as the cause of such symptoms. Infection is usually, but not necessarily, followed by a period when the patient is well. This time period when clinical symptoms are absent (commonly called the asymptomatic period) is very variable. After the asymptomatic period, opportunistic infections, which may be of long or short duration, will usually develop .

The median time from infection to the development of AIDS is estimated to be between 10 - 11 years [32,33]. Although progression to AIDS is the norm for HIV infected individuals, a number of persons who have been infected with HIV for many years, without developing AIDS, are beginning to be identified. There is much debate as to whether these people have developed immunity to HIV, or are simply very slow progressors [34-36].

HIV progression can be measured immunologically as well as clinically. The best known, and most widely used, of these immunological measurements is the absolute number of T-helper cells (also known as T4 cells or CD4 cells) per cubic millimetre of blood. This count (often called the CD4 count) is known to decline in HIV-infected people by approximately 40-80 counts per year, on average [13], although individual counts may fluctuate widely.

1.4.6 HIV antibody test

In 1985, a test for detecting antibodies to HIV, in samples of serum, became routinely available. Detectable antibodies to HIV will usually develop between three to twelve weeks after infection; this process is called seroconversion [31]. The period from HIV infection to the development of detectable antibodies is often referred to as the 'window period'.

An individual is said to be 'HIV positive', or have a 'positive test result', if the HIV test detects antibodies to HIV. If the HIV test does not detect HIV antibodies, the person is said to be 'HIV negative'. If a person is HIV positive then, with the exception of babies, they are regarded as being infected with HIV. A person who is HIV negative may still be infected with HIV if they are in the 'window period'. Babies born to HIV positive mothers, carry maternal antibodies which may be detected by HIV testing. Approximately 84 per cent of these infants later lose these maternal antibodies, and are found not to be infected with HIV [37].

1.4.7 HIV infection world-wide

WHO estimated (at 31st December 1994) that approximately 18 million adults and 1.5 million children have been infected with HIV since the epidemic began [28]. The worldwide distribution of these estimated cases is given in Figure 1.01.

1.5 Surveillance of HIV infection in Scotland

As the AIDS epidemic unfolded, staff at the Scottish Centre for Infection and Environmental Health (SCIEH) responded to the challenge of providing appropriate surveillance schemes. These schemes evolved naturally, as a test for antibodies to HIV became available, and as other immunological parameters became measurable. Another important step in the surveillance of HIV arose when the UK Government gave permission for the introduction of unlinked anonymous testing (UAT). These developments have led to a network of surveillance schemes which are mentioned briefly in this chapter and, in detail, in later chapters.

The Communicable Diseases (Scotland) Unit (CD(S)U) was established in 1969, to undertake surveillance of communicable diseases in Scotland. In 1993, it was amalgamated with the Environmental Health (Scotland) Unit (EH(S)U) to become the Communicable Diseases and Environmental Health (Scotland) Unit (CDEH(S)U). In 1994, it was renamed the Scottish Centre for Infection and Environmental Health (SCIEH). Throughout this thesis, irrespective of the time period, the surveillance centre is referred to as the Scottish Centre for Infection and Environmental Health (SCIEH).

Throughout this thesis, I have consistently analysed all the data available to me, from each individual surveillance scheme, at the time of the analysis. This has created different cut-off dates in different analyses, depending upon the date at which the analysis was performed. These different cut-off dates are the penalty paid for making the most effective use of all the available data.

Figure 1.02 shows the introduction of the HIV surveillance schemes, co-ordinated at SCIEH, against the background of cumulative HIV-positive test results reported to SCIEH.

1.5.1 The AIDS Register

Since 1982, all clinicians working in Scotland have been encouraged to report any AIDS cases in their care, in strict medical confidence, to the director of the AIDS/HIV surveillance programme at SCIEH. To date (31st December 1994) 604 cases of AIDS have been reported to the centre [38].

All AIDS cases are reported to SCIEH on a specially designed AIDS

report form. This form is used to record the opportunistic infections, or clinical presentations, at the time of AIDS diagnosis. The report form is also used to record possible routes of transmission for acquiring HIV, date of birth, gender, initials and health board of residence. Modification of the form has been necessary every time the AIDS definition has been widened. The latest version of the form, introduced in 1994, is described in detail in chapter two.

1.5.2 The HIV Register

In 1985, a register was initiated at SCIEH to record all persons who tested HIV positive as a result of 'voluntary-named' HIV testing in Scotland. The term 'voluntary-named' means that the person has agreed to be tested and is known, by name or clinic identifier, to the doctor requesting the test and to the HIV testing laboratory. The person's surname is encoded at the laboratory, and the code forwarded to SCIEH. Hence, the person's surname is not known to staff at SCIEH. It is important, however, that individuals who are tested at more than one laboratory are able to be detected. These individuals may be recognised by their encoded surname, date of birth, gender, and initials.

To date (31st December 1994) reports of 2,209 HIV positive persons are on this register [38]. This register is commonly called the 'HIV Register' and is examined more fully in chapter three.

1.5.3 The Denominator Study

It was soon realised that the HIV Register was difficult to interpret, because very little was known about the characteristics of the population who were coming forward for voluntary-named HIV tests. Accordingly at SCIEH, in 1989, a scheme was initiated to collect laboratory reports of all persons undergoing voluntary-named HIV tests in Scottish laboratories, regardless of the test result [39]. This was officially known as the 'Scottish National Collaborative HIV Seroprevalence Study', but soon became colloquially known as the 'Denominator Study'. This name was appropriate, since the study enabled the numerator of HIV positive tests to be interpreted in conjunction with the denominator of all HIV tests. This study is examined in detail in chapter four.

1.5.4 Reporting of mortality from HIV infection

Clinicians, who report AIDS cases to SCIEH, have always been encouraged to notify SCIEH of the death of any of their patients. In 1994, clinicians caring for AIDS patients were contacted to ascertain if any of their patients had died and their deaths not reported to SCIEH. The outcome of this exercise showed that the reporting system for AIDS deaths was working well (see section 2.6.1).

It is less easy to monitor mortality in the population of HIV-infected persons who have not developed AIDS. Accordingly, in 1989, an arrangement was made with the Registrar General for Scotland (RGS) to collect, and forward to SCIEH, information on HIV-related deaths.

This reporting system is examined more fully in chapter three.

1.5.5 Unlinked anonymous testing for HIV

In November 1989, the UK Government announced that Unlinked Anonymous Testing (UAT) of serum for HIV would begin, in certain areas of the UK, on a pilot basis [40]. The principles of UAT are :-

(1) To use only residual specimens from blood (or urine) originally collected for some other test.

(2) To ensure anonymity, by irreversibly unlinking the residual specimen from any information which would enable it to be linked to the individual from whom it came, but not from basic epidemiological data.

For example, the residual specimen would be unlinked from the name, address or exact date of birth, but remain linked to information on the gender, health board of residence and age group of the patient.

The main advantage of UAT is that it dispenses with the need to seek permission from, and provide counselling for, everyone to be tested, thereby minimising participation bias and counselling resources.

By displaying multilingual leaflets and posters at clinics taking part in UAT schemes, people are informed that their blood, or urine, may be tested anonymously for HIV, unless they choose not to participate. In practice, the compliance rate is over 98% in most of the studies (see chapter five).

The main disadvantage of UAT is that any specimen found to be HIV positive cannot be traced back to the person from whom it was taken, therefore that individual cannot be notified and helped. Between 1990 and 1992, a number of UAT studies were instigated, funded by the Medical Research Council (MRC). Details of these studies are provided in chapter five.

1.5.6 The CD4 Study

In July 1990, the World Health Organization (WHO) published a staging system for people who were infected with HIV [13]. This WHO staging system classifies people according to their CD4 count and their clinical symptoms. In November 1991, a surveillance scheme was introduced, applying the WHO staging system to all HIV-infected persons undergoing lymphocyte monitoring at three HIV immunology laboratories in Scotland. This surveillance scheme is called the 'CD4 Study'. Information from the CD4 Study has enabled epidemiologists to discover more about the health of the HIV-infected population in Scotland. In particular, it provides new and useful information on the large numbers of HIV-infected persons who have not progressed to AIDS. This study is described and analysed in chapter six.

1.6 Public health importance of HIV infection

The public health importance of an infection may be assessed by three main criteria :-

(1) Number of cases
(2) Severity of cases
(3) Preventability

With an estimated 4.5 million persons having developed AIDS since 1981, and almost 20 million persons having become infected with HIV world-wide, the number of cases of AIDS and HIV is obviously large enough to cause great concern.

There can be no doubt of the severity of HIV infection. With the exception of babies (see section 3.3), once a person is infected with HIV, he or she remains infected and infectious for life. It is estimated that nine years after infection, 40 per cent of people will have developed AIDS, with only 10 per cent remaining asymptomatic [31].

The third criterion, preventability, is of great importance in combating the spread of HIV. In the absence of a vaccine or a cure, emphasis must be placed on halting the spread of the virus. Transmission of HIV may be greatly reduced by behavioural changes. The acceptability of practising 'safe sex', by using condoms for penetrative sex, would reduce the spread of HIV and other sexually transmitted diseases. The use of 'clean needles', by injecting drug users, would likewise reduce the spread of HIV within this group. Making such behavioural changes and sustaining them is, at present, generally held to be the key to containing the epidemic [41].

It is clear that on all three criteria, HIV infection is an extremely important public health issue, and is likely to remain so for the foreseeable future.

1.7 Government response to HIV infection

Throughout the development of the HIV surveillance schemes, there has been close collaboration between SCIEH and the Scottish Office. The encouragement and financial support provided by the Scottish Office has been invaluable in the development and maintenance of these schemes. In addition, monies made available by the Scottish Office have been used to fund public-education campaigns, special AIDS units and needle-exchange schemes.

1.7.1 All-Party Parliamentary Group on AIDS

In October 1986, an All-Party Parliamentary Group on AIDS (APPGA) was set up to raise awareness of AIDS, to keep AIDS on the political agenda, and to "*encourage policies based on reliable sources of information*" [42]. In 1994, this group consisted of 174 members, 114 from the House of Commons and 60 from the House of Lords. It has provided a forum for various voluntary and statutory bodies to exchange both information and views on wide-ranging aspects of HIV infection.

In March 1993, the 'AIDS Awareness Trust' was launched with the objective of improving public education in issues related to AIDS and HIV infection. The trust provides financial support for the APPGA.

1.7.2 Ministerial task force

In July 1991, a ministerial task force was set up, led by Mr M. Forsyth (then Minister of State with responsibility for health at the Scottish Office). The task force included experts from the health services, the voluntary sector, social services and other relevant fields. It initially undertook to examine "*measures to reduce the spread of HIV and AIDS and to ensure services were provided and co-ordinated to best advantage*" [43]. The task force published a report, in March 1992 [41], which included recommendations for health education and for co-operation between groups working within HIV-related fields. The Health Education Board for Scotland (HEBS) were asked to take a major role in all HIV-related educational initiatives.

Issues highlighted under health education included :-

(1) Maintaining public awareness of HIV and AIDS.
(2) Reviewing health education in schools.
(3) Training on HIV/AIDS issues for teachers, police and others involved in community education.
(4) Establishing a liaison group to exchange views on HIV health-education issues.

To facilitate co-operation the task force recommended :-

(1) A strategic planning group to be established in each health board, to co-ordinate HIV-related issues within that health board.
(2) A national group to be established to co-ordinate HIV-related issues at a national level.
(3) Drug-related issues to be developed, including work in prisons.
(4) Voluntary HIV testing to be made more accessible.

1.7.3 Public health strategies

The importance attached by the Government to the problems associated with HIV infection, was demonstrated in a policy statement issued by the Scottish Office, in 1992, entitled 'Scotland's Health: A Challenge to us All' [44], by the specification of HIV/AIDS as a priority area.

A similar document, published by the Department of Health in 1992, entitled 'The Health of the Nation: A Strategy for Health in England' [45], included HIV/AIDS and sexual health as one of five key areas.

1.8 Evaluation of surveillance schemes

Evaluation of surveillance schemes is necessary to ensure that valuable resources are used as efficiently as possible. The inevitable changes in health-related problems are reflected in changing data requirements. While some surveillance schemes, originally of great value, may become redundant, others, originally of lesser value, may assume greater importance (such as the monitoring of the use of pentamidine, in the USA, which led to the identification of AIDS [46]).

Evaluation of surveillance schemes is extremely complex. The evaluation methods used in this thesis (see chapter 8) concentrate on the utilisation of individual schemes and on a critical review of their attributes. Evaluation of the finiancial benefits and costs of running the various HIV surveillance schemes described in this thesis was deemed outwith the scope of this thesis and has not been carried out.

1.8.1 Utilisation of surveillance

The value of surveillance is inextricably linked to the use made of the data collected. Surveillance data are used for many purposes, such as :-

(1) To determine the incidence and prevalence of a health problem, and to detect changes in incidence as early as possible so that appropriate action may be taken.

(2) To detect epidemics, outbreaks, or clusters of a health problem.

(3) To estimate the morbidity and mortality associated with a health problem.

(4) To identify those with a health problem (and their contacts) in order that they may be offered appropriate health care.

(5) To improve understanding of the health problem; for example :-

  (a) To determine the population at risk and identify vulnerable groups of people.

  (b) To identify possible risk factors.

  (c) To stimulate ideas for research, e.g. to provide hypotheses of the aetiology of a disease.

(6) To help evaluate an intervention, e.g. vaccination or screening.

(7) To help plan future health requirements.

1.8.2 Attributes of a surveillance scheme

A practical approach to evaluation of surveillance schemes involves assessing particular attributes common to most surveillance schemes, such as simplicity, flexibility, acceptability, sensitivity, representativeness and timeliness [47]. However, the relative importance of these attributes will vary between surveillance schemes; for example, timeliness is of critical importance in surveillance of infections such as influenza, where prompt control measures are necessary, but less important in cancer surveillance. Additionally, in certain surveillance schemes it may only be practicable to improve some attributes, e.g. sensitivity, at the expense of others, e.g. simplicity.

(1) Simplicity

Surveillance schemes should be as simple as possible in both structure and ease of operation, while still meeting their objectives. In particular, they should be as streamlined as is practicable and collect only necessary data.

(2) Flexibility

Surveillance schemes should be as flexible as possible in order to be able to adapt to changing needs. Changes occur naturally as knowledge about the health event improves (e.g. changing AIDS definitions in 1985, 1987, and 1992 [25-27]). Changes may also be caused by other factors such as varying data requirements. In general, simpler surveillance schemes will be more flexible.

(3) Acceptability

Surveillance schemes should be acceptable both to the people who are operating the surveillance scheme, such as clinicians, laboratory staff and clerical staff, and to those who are under surveillance. Measures of acceptability include participation rates, completeness of data on forms, reporting rates, and timeliness of reporting.

(4) Sensitivity

The sensitivity of a surveillance scheme is its ability to identify all occurrences of the health event under surveillance. Sensitivity is affected by the likelihood that a person with the health event seeks medical care, that the health event is correctly diagnosed, and that it is subsequently reported to the surveillance scheme. Sensitivity may be affected by heightened awareness of a health event, as well as introduction of new diagnostic tests or new treatments. Surveillance schemes not of high sensitivity may still be useful in monitoring trends, provided that the sensitivity remains relatively constant. Sensitivity may be measured by the completeness of case reporting.

(5) Representativeness

A highly representative surveillance scheme will describe accurately the occurrence of a health event over time, and its distribution throughout the population. The representativeness of a surveillance scheme is affected by sampling biases which may exclude certain sub-groups of the population or favour inclusion of other sub-groups. Change in reporting practice is another factor affecting representativeness.

(6) Timeliness

Surveillance schemes should be able process information as quickly as possible. There should be no undue delays between the component parts of the surveillance system. Timeliness can best be assessed by the ability of the system to take appropriate action based on the urgency of the health event. Four time points are of particular importance when considering timeliness, namely :-

(a) Time of onset of event.
(b) Time of diagnosis.
(c) Time of report to surveillance centre.
(d) Time of implementation of appropriate action.

1.9 Methods

From the start of my research it was clear to me that while the first recognised cases of AIDS, and the ensuing discovery of HIV, were extremely well documented, there was a lack of documentation on the surveillance schemes subsequently set up to monitor the spread of AIDS and HIV. However, few would argue that documentation is necessary, therefore the writing and compilation of such documentation should be undertaken as soon as resources permit, particularly since the opportunity to collaborate with the people who set up the surveillance schemes will decrease with time. Access to sources of information, such as informal correspondence and grant applications, is also easiest while key personnel are still in post. Thus, for the creation of documentation, there is a window of opportunity outside which the task must become much harder.

The sources of information available to me included :-

(1) Documentation

Early reports of AIDS and HIV were well documented in publications such as Morbidity and Mortality Weekly Report, and Science [1-3,5]. These early reports were soon followed by various historical accounts of the early days of the epidemic, e.g. [46].

In the 1980's, few sources of documentation relating to surveillance of HIV in Scotland were available, except for routine reports of early cases of AIDS and HIV, and informal correspondence and grant applications to funding bodies such as the Medical Research Council and the Scottish Office.

(2) Personal Contact

On my becoming a member of the AIDS/HIV team at SCIEH in 1991, I had daily contact with the people who were responsible for setting up the AIDS/HIV-related surveillance schemes in Scotland, and was able to discuss with them the beginning of each of these schemes. In addition to this, informal team meetings gave me the opportunity to assess how the schemes were operating, while formal meetings with colleagues working

in AIDS/HIV throughout Scotland gave me the further opportunity to assess how the schemes were perceived, and used, by other professionals. Scientific meetings, such as international AIDS conferences and MRC workshops, allowed me to discuss, formally and informally, the results of HIV surveillance in Scotland, and compare these results with those obtained from similar schemes elsewhere.

Chapter 2

The AIDS Register

2.1 Introduction to AIDS surveillance in the United Kingdom

In September 1982, fifteen months after the first reports appeared in the Morbidity and Mortality Weekly Report (MMWR) relating to unexplained profound immune deficiency in young men [1-3], a national surveillance scheme was introduced for the purpose of monitoring the spread of AIDS in the United Kingdom. This was a joint initiative by SCIEH and the Communicable Disease Surveillance Centre (CDSC), which is part of the Public Health Laboratory Service (PHLS). Clinicians are encouraged to report, to this surveillance scheme, any patients who develop an AIDS-defining illness. The objectives of this surveillance scheme are :-

(1) To detect cases of AIDS in the United Kingdom, and to monitor trends in incidence.

(2) To assist research into the epidemiology of AIDS.

2.1.1 First AIDS-case definition

It was soon apparent that people suffering from unexplained immune deficiency were developing a wide range of infections and tumours. To provide guidelines for surveillance purposes, a definition of AIDS was compiled by the Centers for Disease Control, Atlanta (CDC), in 1982 [4]. This defines a case of AIDS as a person who has both :-

(1) A reliably diagnosed disease that is, at least, moderately indicative of immune deficiency.

(2) No known underlying cause of immune deficiency.

The definition was made more specific by stating the diseases or conditions which were thought to be indicative of immune deficiency :-

(1) Kaposi's sarcoma (KS)

(2) Pneumocystis carinii pneumonia (PCP)

(3) Some specific forms of meningitis

(4) Some specific forms of encephalitis

(5) Oesophagitis due to candidiasis, cytomegalovirus or herpes simplex virus

(6) Progressive multifocal leukoencephalopathy (PML)

(7) Chronic entercolitis (more than four weeks) due to cryptosporidiosis

(8) Unusually extensive mucocutaneous herpes simplex (of more than five week's duration)

It was recognised that there would probably be manifestations of AIDS which the definition did not cover, but a MMWR report [4] stated that the "*absence of a reliable, inexpensive, widely available test for AIDS, however, may make the working case definition the best currently available for incidence monitoring.*"

By 1985, a reliable test for detecting antibodies to HIV was readily available, and other clinical presentations were known to be associated with immune deficiency. The first AIDS-case definition [4] was amended, in 1985, to encompass this new knowledge. The new AIDS-case definition included a list of other signs of immune deficiency, provided that they occurred in a person who had developed antibodies to HIV [25,48,49]. These other signs included :-

(1) Disseminated histoplasmosis
(2) Isosporiasis
(3) Bronchial or pulmonary candidiasis
(4) Non-Hodgkin's lymphoma

2.1.2 First reported AIDS cases in Scotland

By 31st December 1984, the first three cases of AIDS had been reported to SCIEH. Two had presented with opportunistic infections, and one with PCP; all were males over 30 years of age. One was homosexual, one was a haemophiliac, and one had received a blood transfusion abroad. Three years later, at 31st December 1987, a total of 39 cases of AIDS had been reported to SCIEH.

Table 2.01 shows the epidemiological characteristics of these 39 AIDS cases. It shows that 77 per cent of the AIDS cases were diagnosed in 1986 or 1987, 67 per cent were homosexual or bisexual men, 82 per cent were over 30 years of age, and 51 per cent presented with PCP. Only 4 IDUs (all female) were among these 39 AIDS cases.

2.1.3 Public Health Acts

The Public Health Act of 1899 enforced notification, to the proper authorities, of specified infectious diseases in the UK. AIDS, however, has not been added to the list of notifiable diseases, in the UK [50]. In January 1989, Mr D. Mellor (then Minister of State for Health), in response to a parliamentary question on why AIDS had not been made a

notifiable disease, said :-

> "*The department did not consider that there were any strong public health grounds for making AIDS a notifiable disease. To do so would be unlikely to improve the present reporting system or to assist health professionals in their work. Notification might also deter people from seeking help and so drive the infection underground.*" [51].

2.1.4 AIDS (Control) Act, 1987

On 15th May 1987, Parliament passed the 'AIDS (Control) Act, 1987'. The requirements of this act are :-

(1) Every health board in Scotland must submit a report to the Secretary of State.
(2) These reports will contain information specified in the act, and such "*other relevant information as the Secretary of State may direct*".
(3) These reports will be published.
(4) The Secretary of State may decide the form that the report will take and the period it will cover. This period must be one year or under.

The first reports were to be made to the Secretary of State and published by 31st December 1988. The information initially requested by the Secretary of State comprised :-

(1) The number of persons, known to each health board, to have AIDS diagnosed in the previous twelve months.
(2) The cumulative number of AIDS cases in each health board.
(3) The number of AIDS cases, known to the health board, to have died in the previous twelve months.
(4) The cumulative number of deaths among AIDS cases in each health board.
(5) Health boards are asked to give details of the facilities and services for HIV testing, HIV prevention, counselling and care, available within their respective areas.
(6) Health boards are asked to give the number of persons employed (full and part-time) in providing these services, in the

previous twelve months.

(7) Health boards are asked to provide an estimate of the facilities and services they expect to provide in the next twelve months.

(8) Health boards are asked to report what action has been taken, within the health board, in education, training for HIV counselling, and treatment of HIV-infected people.

On an annual basis, SCIEH provides all health boards with data from the AIDS and HIV Registers to assist them in the compilation of their reports to the Secretary of State for Scotland, in compliance with the Act. An example of such data is given in Figure 2.01.

A map showing the location of the health boards in Scotland, is provided in the back pocket of this thesis.

2.1.5 AIDS-case report form

To standardise AIDS-case data-collection throughout the United Kingdom, in 1987 a new reporting form was designed jointly by SCIEH and CDSC. The information requested falls into five main sections :-

(1) Name of the clinician reporting the AIDS case, and the hospital or clinic from which the case is reported. The health board of residence of the patient is also requested.

(2) The date of birth, gender and 'soundex code' of the surname of the patient.

To preserve patients' confidentiality, clinicians are encouraged to use 'soundex codes' as an alternative to using the patient's surname. The soundex code is derived by following a set of rules to convert the surname to a letter followed by three digits. The letter is simply the first letter of the surname. Each soundex code represents a group of surnames, with no soundex code being unique to a particular surname, thus preserving confidentiality. The soundex code can be derived by using a set of written instructions, by a pre-programmed calculator, or by using a computer program [52,53]. When the soundex code is used in conjunction with the person's date of birth, it is possible to detect probable duplicate reports which can then be investigated.

(3) All possible risk factors for acquiring HIV are requested. In some cases there will be more than one way in which the person may have become infected; for instance, injecting drug users who are sexually active might have acquired the virus sexually or through drug injecting.

To allocate people to risk categories, a hierarchical system is used. This hierarchy is given in Table 2.02. The risk is determined first by the risk activities of the patient, then by the risk activities of his or her partner(s). From Table 2.02, it can be seen that a person who is an injecting drug user, and a sexually active heterosexual, will be classified as an injecting drug user.

While this approach allows for consistency of classification, it will tend to over-estimate the number of persons who are in the categories at the top of the hierarchy, at the expense of those lower down. Thus, the number of infections attributed to IDU will appear higher (and the number attributed to heterosexual risk will appear lower) than they actually are. This, in turn, is likely to lead to underestimation of the extent of heterosexual spread of HIV, possibly causing unwarranted complacency in the heterosexual population.

(4) Dates of last HIV-negative test result, and first HIV-positive test result (if available).

(5) All AIDS-defining conditions present at time of AIDS diagnosis.

A hierarchical system, similar to the one already described for risk classification, is used to categorise clinical presentation at AIDS diagnosis. This hierarchy is given in Table 2.03. From this table it can be seen that a person presenting with both KS and HIV encephalopathy will be classified as presenting with KS. Once again, this hierarchical approach overestimates categories at the top of the hierarchy at the expense of those lower down.

2.1.6 United Kingdom collaboration on reporting of AIDS cases

All new AIDS cases, reported to either SCIEH or CDSC, are compared with those already reported within the United Kingdom, using date of birth, gender, and soundex code of surname to eliminate any duplicate

reports. The hierarchies shown in Tables 2.02 and 2.03 are used by both SCIEH and CDSC to obtain uniformity of classification, throughout the UK, of both risk and AIDS presentation. Staff at SCIEH and CDSC co-operate regularly to discuss surveillance issues and prepare reports [54-57].

2.1.7 AIDS-case definitions (1987 and 1993)

In September 1987, the original definition of an AIDS case [4] was expanded to include the many more opportunistic infections which were then known to be associated with AIDS [26]. In January 1993, the Centers for Disease Control (CDC) again adopted a new definition of an AIDS case [27,58]. This definition included three more AIDS-indicator diseases :-

(1) Recurrent pneumonia within a 12 month period
(2) Pulmonary tuberculosis
(3) Invasive cervical cancer

However, the main difference in the new CDC AIDS-case definition was the inclusion of all HIV-infected adults with a CD4 count of under 200, regardless of the presence of an AIDS-indicator disease. This new AIDS-case definition is substantially wider than the previous AIDS-case definition, with its introduction resulting in a large rise in the number of AIDS cases reported in the USA [59]. CDC stated that the use of the new definition would allow more people to be classified as AIDS cases which, in turn, would allow them access to additional medical and social benefits.

A European working group rejected the CDC revision. The reasons they gave for this were :-

(1) Lack of availability of CD4 monitoring throughout Europe. In countries where CD4 monitoring is available, there is a lack of adequate quality assurance.
(2) The undesirable psychological effect, of being categorised as an AIDS case, on HIV-infected people who may feel quite well.
(3) In Europe, unlike the USA, access to appropriate health care is not dependent on the person's illness being classified as AIDS, so there is no apparent medical benefit to the patient in widening the AIDS-case definition to include low CD4 counts.

However, the European working group did agree to add the three new AIDS-indicator diseases to the 1987 definition [60,61]. One important consequence of the changes in the 1993 definition of AIDS, is that AIDS statistics from the USA and Europe are no longer directly comparable.

2.1.8 AIDS-case report form (1993)

This new AIDS-case definition was adopted in the United Kingdom in January 1993 [61]. A new AIDS report form, including the three new AIDS-indicator diseases, was designed in the summer of 1993. With the reprinting of the form, the opportunity was taken to make some improvements to the design of the form. In particular, the sections on risk category and AIDS presentation were simplified, and a section was introduced to record the patient's initials. Three new sections were added to the form :-

(1) Clinical symptoms of HIV prior to the development of AIDS
(2) Details of prophylactic treatment and anti-retroviral drug therapy taken by the patient before AIDS diagnosis
(3) Cause of death (where applicable)

A copy of the new AIDS-case report form is included in the back pocket of this thesis.

2.2 Reporting delay for AIDS cases

The time elapsing between the clinician diagnosing a case of AIDS, and reporting that case, is called the 'reporting delay'. In Scotland, the median reporting delay is between three and six months. The reporting delay varies greatly among doctors, with some doctors preferring to wait until they have a batch of cases to report. There is little doubt that the time required to complete the AIDS-case registration form is one of the reasons for both under-reporting and delayed-reporting.

There is always the possibility that an AIDS case will be reported several years after diagnosis but, in Scotland, only eight cases of AIDS (1.5 per cent) have ever been reported more than three years after diagnosis.

2.2.1 Rosenberg's correction for reporting delay

A computationally attractive method of adjusting AIDS figures for reporting delay was developed by P. Rosenberg [62], requiring only the date of diagnosis and the date of report, for each AIDS case. This method makes two assumptions :-

(1) The reporting delay is independent of the date of the AIDS diagnosis.

(2) The reporting delay is always less than three years.

The first assumption is untrue, in that reporting delay was longer in the early years of AIDS (1983-1986) than it has been subsequently. This was mostly owing to the rarity of AIDS cases in Scotland at that time, lower awareness of the many presentations of AIDS, and a less developed reporting system. However, for cases reported from 1989 onwards, this assumption has appeared to be reasonable.

The second assumption has already been shown to be reasonable, since fewer than 2 per cent of all cases ever reported, in Scotland, have had a reporting delay of more than three years.

Applying Rosenberg's correction to the AIDS cases diagnosed in Scotland since January 1989, and reported to SCIEH by 31st December 1993 (see Table 2.04), it can be shown that 9 per cent of AIDS cases are reported within one month of diagnosis, 57 per cent within three months, and 82 per cent within one year. Throughout section 2.2, Rosenberg's method is used, whenever appropriate, to correct for reporting delay. The distribution of reporting delay is shown in Figure 2.02.

2.3 Reporting of mortality from AIDS in Scotland

Deaths are reported to SCIEH in two ways :-

(1) Directly by the clinician managing the AIDS case.

(2) The Registrar General for Scotland (RGS) notifies SCIEH of all deaths in Scotland if the cause of death is likely to be related to HIV infection.

Throughout the past ten years, in Scotland, the death toll from AIDS has risen steadily from 25 deaths having occurred by 31st December 1987, to 346 deaths by 30th April 1994 [63]. Figure 2.03 shows the number of deaths, in cases of AIDS reported to SCIEH, by year of death. Figure 2.04 shows the number of persons who are known to be dead, thought to be alive, or are of unknown vital status (at 30th April 1994), by the year of their AIDS diagnosis. There are twelve persons whose vital status is not known (at 30th April 1994). Eleven of these persons have come from abroad and have subsequently returned home, and one has not been seen by his doctor since the AIDS diagnosis was made in August 1991. Only two patients whose AIDS- defining illnesses were diagnosed before 1989 (one in 1984 and one in 1987), are known to be still alive (at 30th April 1994). All the other patients, who are assumed still to be alive, have had their AIDS-defining illnesses diagnosed from 1989 onwards.

2.4 Completeness of AIDS-case reporting

Since some AIDS cases are not diagnosed, not reported, or are reported late, the cumulative number of reported AIDS cases will always be fewer than the actual number of cases. In Scotland, the rate of under-reporting of AIDS cases is estimated to be approximately ten per cent [16]. This compares with an estimate of 20 per cent under-reporting in England and Wales [56,64], and 15 per cent in the USA [65].

2.5 Analysis of AIDS cases in Scotland

2.5.1 Year of AIDS diagnosis

By 30th April 1994, 512 AIDS cases had been reported to SCIEH [63]. Figure 2.05 shows these cases, by year of diagnosis. It shows a rise in the number of new AIDS cases diagnosed each year from 1988 to 1991, then a fall in 1992. Figure 2.06 shows the expected number of AIDS cases, by year of diagnosis, once adjustment for reporting delay has been made. The estimate for 1992 appears unusually low, and is thought to be a result of prophylaxis and anti-retroviral therapy delaying the onset of AIDS [7,66]

2.5.2 Living AIDS cases

Every year, from 1986 onwards, the number of new AIDS diagnoses has exceeded the number of deaths from AIDS. This has been reflected in an annual increase in the number of persons with AIDS who are still alive [7]. Figure 2.07 shows that in Greater Glasgow, Lothian, and Tayside Health Boards, the number of persons with AIDS who have been alive at the end of each calendar year, from 1990 to 1994, is rising through time.

2.5.3 Presentation at AIDS diagnosis

Table 2.05 shows that 50 per cent of AIDS cases have presented with PCP. Other opportunistic infections (OOI) account for 29 per cent of all AIDS diagnoses. KS accounted for 10 per cent of the early (pre 1988) AIDS diagnoses (see Table 2.01), but this has fallen to 6 per cent of the 512 cases reported by 30th April 1994.

2.5.4 Risk category of AIDS cases

Table 2.05 shows the allocated risk categories, by gender, for the 512 reported AIDS cases. It shows that 53 per cent of the male cases are classified as homosexual/bisexual, 31 per cent as IDUs, and 8 per cent as heterosexual. This contrasts with the risk classification for females where 60 per cent are classified as IDUs, and 24 per cent as heterosexual.

Figure 2.08 shows the number of cases of AIDS diagnosed each year, attributed to either homosexual/bisexual or IDU transmission.

These figures are adjusted for reporting delay, and do not include those who are both homosexual/bisexual and IDU. This figure shows that, from 1984 to 1988, the predominant route of infection of reported AIDS cases was homosexual/bisexual. Since 1986, there has been an increase in the number of reported AIDS cases attributed to injecting drug use. Figure 2.08 shows that the number of cases expected to be reported as diagnosed in 1993, after correcting for reporting delay, is greater for those classified as IDUs than for those classified as homosexual/bisexual.

2.5.4.1 Heterosexual risk category

In recent years, interest has focused on increasing reports of AIDS cases attributed to heterosexual transmission.

Heterosexual transmission is categorised into three hierarchical groups :-

(1) 'High risk' partner. Men or women who have had sexual intercourse with a person in a recognised high risk category such as IDU, bisexual, or a recipient of HIV-infected blood or blood products.

(2) 'Exposure abroad'. Men or women, not in group (1), who have had sexual intercourse abroad.

(3) 'Exposure United Kingdom'. Men or women who have had sexual intercourse in the UK and are not in groups (1) or (2).

Heterosexual transmissions are classified according to the risk activities of the partner, not the HIV status of the partner. This leads to the anomaly that a person may have a partner who is known to be HIV infected, but the partner will not be categorised as a 'high risk' partner unless he or she is in a recognised high risk category.

As with other hierarchies, this approach will overestimate the categories at the top of the hierarchy (e.g. 'high-risk partner'), at the expense of categories lower down (e.g. 'exposure (UK)').

Table 2.05 shows that fifty-six of the AIDS cases reported to SCIEH were classified as heterosexual. Fifteen (27 per cent) were categorised as 'high risk' partner, twenty-seven (48 per cent) as

'exposure abroad', and ten (18 per cent) 'exposure UK'. There are four cases where the transmission risk is only known to be heterosexual; these cases are under investigation to classify them more specifically to one of the heterosexual subgroups [63]. Figure 2.09 shows the expected number of AIDS cases attributed to each of the heterosexual risk categories, by year of diagnosis (adjusted for reporting delay). It shows a large increase in the expected number of AIDS diagnoses in 1993, attributed to 'high risk' partners, and also underlines the importance of 'exposure abroad'.

2.5.5 Health board of residence at AIDS diagnosis

Figure 2.10 shows the number of AIDS cases, by health board of residence at the time of AIDS diagnosis. It shows that 44 per cent of all AIDS cases were resident, at the time of their AIDS diagnosis, in Lothian Health Board, compared with 24 per cent resident in Greater Glasgow Health Board, and 13 per cent in Tayside Health Board.

2.6 Survival analysis

It is clearly important for the patient, the clinician, and those allocating resources for patient care, to know the expected survival rates following AIDS diagnosis. Although it is valuable to estimate survival rates based on data collected from those persons who have already reached AIDS diagnosis, some caution is required. The use of antiretroviral treatments, better patient management, and prophylaxis for opportunistic infections [67-71], have all played an important part in improving survival following infection with HIV. While it is reasonable to assume that improvements in survival will continue, pre-AIDS survival may increase at the expense of post-AIDS survival, by the onset of AIDS being delayed to a later stage of immune deficiency at which survival rates remain poor [7,72].

2.6.1 Following-up of adult AIDS cases

Of the 498 adult AIDS cases reported to SCIEH by 30th April 1994, 334 were known to have died [63]. Enquiries were made of the remaining 164 AIDS patients to ascertain when they last had their CD4 count measured, or were last seen by medical staff.

If SCIEH had not been notified of the death of a patient, and that patient had undergone CD4 monitoring in the period January to April 1994, then the patient was assumed to be still alive at 30th April 1994. There were 133 patients in this category.

Enquiries were made of the remaining 31 patients who had not undergone CD4 monitoring in the period January to April 1994, by contacting the clinicians who first reported them to SCIEH. Five of the 31 cases had recently died, and their deaths had not yet been reported to SCIEH. Eleven patients had left the country, and had their survival times ' censored' at the date they left. When a survival time is 'censored' it means that the patient is known to have survived for at least that time with AIDS. Only one patient had not been seen by his doctor since August 1991, hence his survival time was censored at that date. The other 14 patients had all been seen by their doctors in the previous six months, and were assumed to be still alive at 30 April 1994. All cases thought to be alive at 30 April 1994 had their survival times censored at that date.

All death certificates, received at SCIEH, were examined to

identify cases where the cause of death did not seem to be directly related to HIV. Five persons, who were on the AIDS Register, appeared to have died from causes other than AIDS. Three persons had died of drug overdoses, one of cirrhosis of the liver, and one of 'inhalation of gastric contents'. These five AIDS cases had their survival times censored at their date of death.

Survival times, from date of AIDS diagnosis to date of death, were calculated for all who had died from AIDS, and from date of diagnosis to date of censoring, for the remainder. Analysis was restricted to the 394 AIDS cases diagnosed by 31st December 1992, since it is thought that cases with shorter survival tend to be reported more quickly, thus underestimating survival in recent years [55].

2.6.2 Results of univariate survival analysis

Each of the variables used in the survival analysis was categorised into mutually exclusive groups. 'Age (in years) at AIDS diagnosis' was divided into five groups; 15-24, 25-29, 30-34, 35-44, and 45+. 'Year of AIDS diagnosis' was divided into three groups; pre 1988, 1988-1989, and 1990-1992. 'Geographical region' was divided into four groups according to the health board from which the patient was first reported as having AIDS; Greater Glasgow, Lothian, Tayside, and 'other'. 'Risk category for HIV transmission' was divided into five groups; homosexual/bisexual, IDU, heterosexual, haemophiliac or blood products, and 'other or unknown'. 'AIDS presentation at diagnosis' was divided into six groups :-

(1) PCP
(2) KS
(3) HIV encephalopathy
(4) Wasting attributed to HIV
(5) Other opportunistic infection (OOI)
(6) Other-cerebral lymphoma, non-Hodgkin's lymphoma and PML

Firstly, all variables were examined individually to produce a set of univariate analyses. For the univariate analyses, Kaplan Meier survival curves [73,74] were calculated, and the difference between curves assessed using a log rank test [75]. The analyses were carried out using SPSSPC+ [76], and the results summarised in Table 2.06. Following AIDS diagnosis, median survival for the 394 cases was 17 months. One

year after AIDS diagnosis, 60 per cent were still alive; by two years, 37 per cent were alive, and by three years only 22 per cent were still alive. Figure 2.11 shows a smoothed survival curve (based on the stepwise Kaplan Meier survival curve) from AIDS diagnosis to death. There were significant differences in survival between age groups at AIDS diagnosis, between presentations at AIDS diagnosis, and between health boards of AIDS diagnosis. These results are shown graphically, for selected categories, in Figures 2.12, 2.13 and 2.14.

2.6.3 Results of multivariate survival analysis

While univariate analyses are informative, it is important to make allowances for the effect of associations between the variables by using a multivariate analysis.

All the variables used in the univariate analysis were entered into a Cox's proportional hazard's model, to predict factors independently associated with survival [74,77]. The analysis was carried out using BMDP procedure P2L [78].

The results of the analysis are given in Table 2.07. This table shows the relative risk (RR) associated with each of the categories, compared to a baseline category, while making allowances for the effects of all the other variables. This analysis shows that people aged 45 years or over have poor survival compared to those aged 15-24 years. The 95 per cent confidence interval (95% CI) for the relative risk of survival for those aged 45 years or over, compared with those aged 15-24 years, is (1.4, 3.9).

Poorer survival was found to be associated with those who presented with HIV encephalopathy, HIV wasting syndrome, or 'other'; 'other' being cerebral lymphoma, non-Hodgkin's lymphoma or PML. The 95% CI for the RR of survival for those presenting with HIV encephalopathy, compared to those not-presenting with HIV encephalopathy, is (1.4, 19.9). Similar results were found for 'HIV wasting' (95% CI 1.6, 28.0) and for 'other' (95% CI 2.3, 34.9).

The independent effects of age and clinical presentation on survival, following AIDS diagnosis, have been well documented. These effects were noted, early in the HIV epidemic, in key papers on the survival experiences of 5,833 AIDS patients in New York [79], and of 4,323 AIDS patients in San Francisco [80]. More recent papers on the

survival experiences of 3,984 AIDS cases in the United Kingdom [55], 2,135 AIDS patients in Brazil [81], and 3,204 AIDS cases in Australia [82], show that these variables are still significantly related to survival.

Gender, risk category, and year of AIDS diagnosis were found not to be statistically significant predictors of survival. Survival, following AIDS diagnosis, was found to be poorer in Tayside Health Board than in Lothian Health Board. Possible explanations for this are :-

(1) Different diagnostic practices in different regions leading to earlier, or later, diagnosis of AIDS.

(2)Regional differences in treatment policies, such as the early use of zidovudine, which might delay the progression to AIDS [83].

Other studies have found that survival differs among regions [55,84], although the reasons for this are not clear. Additional data are necessary to examine this regional difference more closely, in particular CD4 counts at time of AIDS diagnosis, and knowledge of treatment practices in the different hospitals in the different regions.

2.7 AIDS predictions

2.7.1 AIDS predictions working groups

In June 1994, Dr R. Kendell (Chief Medical Officer for Scotland) convened a working group to be chaired by Professor D. Reid (director of SCIEH). The remit given to the working group was to estimate, for each of the years 1995 to 1999, the number of HIV-infected individuals, in Scotland, who :-

> "*(a) will develop AIDS or severe HIV immunodeficiency*
> *(b) will require substantial health care because of their HIV infection.*" [8].

This was the fourth working group convened to predict future numbers of cases of AIDS and severe HIV-related disease in Scotland.

The first working group, chaired by Mr W. Tayler, was convened in 1987, and provided predictions of AIDS cases in Scotland from 1987 to 1991 [18]. The second group, chaired by Dr B. McClelland, was convened in 1990, and provided predictions of AIDS cases and severe HIV-related disease from 1990 to 1993 [17]. The third group, chaired by Professor D. Reid, was convened in 1992, and provided predictions of AIDS and severe HIV-related disease to 1995 [16].

2.7.2 Problems associated with AIDS predictions

Several factors make predictions of future numbers of AIDS cases and cases of severe HIV-related disease difficult :-

(1) The very long and very variable incubation period from HIV to AIDS (median 10-11 years) [32,33].

(2) Those coming forward for an HIV test are an unknown proportion of all those infected with HIV.

(3) One of the primary routes of infection is sexual, and little is known about mixing patterns within, and between, different sexual groups. There are problems in obtaining accurate data on sexual behaviour, and there are further difficulties in assessing the influence of education and publicity on patterns of sexual behaviour. The lack of data on sexual behaviour has been redressed, to some extent, by the publication of the results

of studies of sexual behaviour [85-87].

(4) Advances in the use of antiretroviral treatments, better management of patients, and prophylaxis for opportunistic infections, all affect survival following HIV infection [67-71].

Should new treatments be introduced in the next few years, they may have a significant effect on survival which, in turn, will affect predictions of AIDS and severe HIV infection [8].

However, regardless of the problems, predictions of future AIDS cases and cases of severe HIV-related disease are essential, particularly for :-

(1) Planning purposes, to ensure adequate resources are made available for patient care.

(2) Targeting of education and support where it is most needed, and where it will be most effective.

2.7.3 AIDS predictions - results and assessment

The second Reid working-group predictions were completed in December 1995 [8], using the methodology from the previous report [16,88]. The predictions were based on AIDS cases, and deaths, reported to SCIEH by March 1995 [89], together with estimates of progression rates from HIV to AIDS [68,90-94], and estimates of the cumulative number of persons infected with HIV.

Predictions show that a gradual increase in new cases of AIDS is expected, from 140 cases in 1995 to 155 cases in 1999 [8]. The number of new AIDS cases, attributable to homosexual/bisexual risk and IDU risk, is expected to stay relatively constant, at approximately 40 cases per year and 60 cases per year respectively. The number of new AIDS cases, attributable to heterosexual risk, is expected to increase from 20 cases in 1995 to 55 cases in 1999.

The predictions also show that the number of persons with AIDS, and still alive, is expected to rise from 240 in 1995 to 270 in 1999, with the largest increase occurring in the heterosexual group [8].

The predictions of the second Reid working group are given in Figure 2.15, together with the predictions of the previous three working groups. Figure 2.15 shows that the predictions, produced by each working group, have successively decreased and have become more

accurate. It would, however, be unjust and over-simplistic to say that the previous working groups overestimated the scale of the AIDS epidemic. The earlier predictions drew the attention of the authorities to the potential severity of the problem. The reactions of these authorities, in the form of various public health initiatives, have almost certainly played an important role in preventing these earlier predictions from being fulfilled.

2.8 Distribution of AIDS data

Tables of cumulative and newly-reported AIDS cases are published every calendar quarter in a SCIEH publication 'ANSWER' (a copy of which is provided in the back pocket of this thesis). These tables show cumulative AIDS figures by health board of registration, gender, probable transmission route, and vital status. ANSWER is distributed, free of charge, to those who help to provide the data in all the HIV surveillance schemes co-ordinated at SCIEH. ANSWER is produced monthly, the other two issues in each calendar quarter containing original articles concerning HIV in Scotland.

Tables of cumulative and newly-reported AIDS cases are sent to CDSC every calendar quarter, to be included in the United Kingdom quarterly tables [57].

Tables of AIDS data are supplied to the Information and Statistics Division of the National Health Service in Scotland, for inclusion in an annual publication on the health of Scottish people [95].

In addition to these regular publications, AIDS figures are routinely presented at meetings such as :-

1) AIDS co-ordinator's meetings
2) HIV epidemiology and laboratory sub-committee (HEALS)
3) West of Scotland AIDS advisory and information committee
4) SCIEH review meetings

Beginning in January 1996, staff at SCIEH will produce an annual report consisting of an extremely comprehensive set of tables of data, together with figures and explanatory text, from all the AIDS/HIV surveillance schemes co-ordinated at SCIEH [96].

2.9 The future of AIDS surveillance

The main objective of the current AIDS surveillance scheme is to provide an estimate of the number of persons, in Scotland, who have AIDS, together with their epidemiological characteristics.

In the early 1980s, when this surveillance scheme began, it was the only means of collecting data about the number of persons affected by this newly-discovered and unexplained syndrome. However, the discovery of HIV as the causative agent of AIDS, the development of HIV surveillance, and the growth of immunological monitoring, have all played a part in displacing the importance of AIDS surveillance. This has led many people to consider whether or not AIDS surveillance is still important, or necessary. This issue is discussed further in chapter eight.

Chapter 3

The HIV Register

3.1 Introduction to HIV and HIV testing

Almost from the initial recognition, in 1981, of the symptoms of unexplained immune deficiency, which became known as AIDS [1-3], a viral cause seemed likely. The occurrence of AIDS among homosexual and bisexual men, injecting drug users who shared injecting equipment, and recipients of blood products (including haemophiliacs), suggested the presence of a virus which might spread through sexual contact or through blood products. These routes of transmission were already familiar to epidemiologists, through previously acquired knowledge of hepatitis B virus (HBV) which was known to be transmitted by sexual contact or through blood.

In 1982, a team of researchers in France, led by Dr L. Montagnier, removed some cells from a patient suffering from lymphadenopathy, then succeeded in isolating a virus from them. This virus appeared to be a new retrovirus, and was named 'lymphadenopathy associated virus' (LAV) [5].

One of the main difficulties faced by the scientists studying retroviruses in 1982, was propagating the retrovirus. In November 1983, a team of researchers in America, led by Dr R. Gallo, reported the scientific breakthrough which allowed the retrovirus to be propagated in large quantities [97]. The American team named the retrovirus on which they were working, the 'human T-cell leukaemia virus - type three' (HTLV-III). It later emerged that LAV and HTLV-III were the same retrovirus. In May 1986, at the International Committee on Taxonomy of Viruses, the retrovirus was renamed the 'human immunodeficiency virus' (HIV).

3.1.1 HIV antibody testing

By 1985, commercial test kits were available in National Health Service (NHS) laboratories in Scotland, for testing blood for antibodies to HIV. The test, known as an 'ELISA' test, is widely used in Scotland for screening blood for antibodies to HIV [98]. If antibodies to HIV are found, then a confirmatory test is carried out using a different technique. In Scotland, the confirmatory test most often used is known as 'Western blot' [98]. The combination of the initial test and the confirmatory test is required to be both very sensitive (ability to identify positives correctly) and very specific (ability to identify negatives correctly) [31].

3.1.2 Implications of the window period for HIV

In HIV testing, a major problem arises as a result of the naturally occurring time-lag between a person becoming infected with HIV and developing detectable antibodies to HIV. This period is called the 'window period'. An HIV-infected individual who has an HIV test while in this window period, will not be identified as HIV infected. As HIV tests have improved, the length of the window period has shortened, with the current estimate being approximately six weeks [99].

The presence of the window period has important implications for the Blood Transfusion Service (BTS). Since December 1985, all blood donated to the NHS has been screened for antibodies to HIV; anyone found to be HIV positive has been recalled by the BTS for counselling. Recognising that routine screening of blood could not detect people in the window period, additional steps were taken to safeguard the blood supply.

The most important of these steps was to introduce a set of guidelines to be implemented at each of the five BTS centres in Scotland. These guidelines have resulted in questionnaires being given to all new donors, drawing their attention to the transmission routes of HIV. The questionnaires request those who belong to certain specified high risk categories not to donate blood. However, some centres allow these donors to donate blood, but the blood will not to be used. This saves a homosexual or bisexual man, attending a donor unit with his peers, the potential embarrassment of being turned away without donating blood.

However, even if the optimistic assumption is made that these policies have been 100 per cent effective, following their introduction between 1985 and 1986, there is still a small but definite risk of HIV infected blood entering the blood bank. This risk comes from those who are not in (or do not admit to being in) the recognised high risk categories for HIV, but are HIV infected and are in the 'window period'. The probability of this happening is known to be influenced by three key parameters :-

(1) The incidence rate of new infection among those at low-risk of HIV infection.

(2) The length of the window period.

(3) The frequency with which donors return to donate blood [100,101].

In Scotland, this risk is thought to be very small, and has been estimated to be less than 1 in 100,000 [102]. However in 1986 a donor, who was in the window period, donated HIV infected blood which was subsequently given to two recipients [103]. As a consequence, at least one of the two recipients was infected with HIV; the second person died of his underlying illness shortly after his transfusion.

In 1993, Dr B. McClelland, Director of the South East of Scotland Blood Transfusion Service, approached Professor D. Reid, Director of SCIEH, with a request to set up a working group to determine the risk, to recipients, of acquiring HIV and other infections from blood provided through the BTS in Scotland. Recognising the scale and complexity of the problem, the working group approved the appointment of Dr J. McMenamin, Research Fellow, to work on this project [104-106].

3.2 The HIV Register in Scotland

From the start of HIV testing in Scotland, in 1985, the NHS laboratories have been informing SCIEH of all persons who test HIV positive. The confidentiality of data relating to persons testing HIV positive has always been of great importance. To preserve this confidentiality, the report from the HIV testing laboratory does not contain names, but simply the initials and the soundex code of the surname (see section 2.1.5). Should a person test HIV positive on more than one occasion, then only the earliest HIV test result is retained on the register. However, additional information gained on a subsequent test, such as more accurate risk information or a change of name, is used to update the HIV Register.

3.2.1 HIV test request form

As part of a nationwide programme to improve and standardise the collection of epidemiological data on all patients requesting an HIV test, a request form was designed. This form has been used throughout Scotland since 1989; a copy of the form is enclosed in the back pocket of this thesis.

From the form it can be seen that the information requested falls into several distinct sections :-

(1) Referral source: the name, address and signature of the doctor authorising the request.

(2) Patient details: basic epidemiological information on the person being tested. Initials, soundex code of surname, gender, date of birth, nationality, residential information and clinic number are all requested.

(3) Specimen date.

(4) Principal reason for testing.

(5) Risk factor information: this is a complex set of questions designed to collect as much information as possible about the person's risk of acquiring HIV.

(6) Clinical information: clinical symptoms commonly associated with HIV. These symptoms vary widely and include fever, weight loss and persistent fatigue.

(7) Previous HIV test: information is requested on whether or not the person has had a previous HIV test. If a test has been taken, then the time, place and laboratory reference number of

the previous test are requested.

(8) Additional information: any further information which the clinician feels may be relevant.

3.2.2 Computer support for HIV surveillance

A database was created by computing staff at SCIEH, using a software package called DATAEASE [107]. This database was designed to enable staff to enter data quickly and accurately. It makes extensive use of 'choice-fields', selected by one or two keystrokes, thus avoiding the need to type phrases such as 'Greater Glasgow Health Board', hence minimising errors and inconsistencies.

3.3 Revision of the HIV Register

During 1990, the late Dr G. Bath, formerly AIDS Co-ordinator for Lothian Health Board, instigated a revision of the Lothian Health Board HIV Register, using information from local laboratory reports and hospital records. This exercise proved that it was possible to improve substantially both the quality and quantity of the information held on this HIV Register. An important contributory factor was that clinicians were becoming more confident that, by revealing dates of birth and soundex codes of surnames of their HIV positive patients, they were not compromising confidentiality.

During 1991 and 1992, a revision of the entire HIV Register was undertaken by Dr B. Davis, then Registrar in Public Health Medicine at SCIEH, involving staff at SCIEH and staff at laboratories and hospital records offices throughout Scotland. The results of the Lothian register revision were made available to SCIEH by Dr Bath, thus saving duplication of effort. The revision of the register is described in detail in a separate publication [108]. By the end of the revision process, the HIV Register had improved substantially. In particular, soundex codes of surnames, which previously were mostly unavailable, were known for 95 per cent of the cases, date of birth was known for 98 per cent, gender for 99 per cent, and transmission category for 92 per cent. A total of 447 records were removed from the database, either because they were duplicate records, or because they lacked both date of birth and soundex code. Summary tables, from the revised register, were first published in ANSWER in July 1992 [109].

An important outcome of the revision was the resulting improvement in the procedures for reporting HIV positive test results in infants. Babies, born to HIV positive mothers, carry maternal antibodies that are detected by HIV testing. Approximately 84 per cent of these babies are not infected with HIV and, at a later stage, will test HIV negative because they will lose these maternal antibodies [37]. It was recognised that these infants should not remain on the HIV Register if they subsequently test HIV negative. The British Paediatric Association Surveillance Unit (BPASU) of the Institute of Child Health (ICH) maintains a register of all HIV infected children in the UK. Only those 22 infants who were confirmed by the ICH to be HIV infected were kept on the HIV Register, the other 95 infants were removed from the register. Reports of HIV positive tests, on infants, are now only included in the register after the ICH has confirmed that these infants are infected with HIV.

3.4 Problems associated with the HIV Register

There are two major problems associated with interpretation of the cases on the HIV Register :-

(1) These cases represent HIV infection among those persons who choose to come forward for HIV testing.

Not everyone who is HIV infected will suspect that they are infected or will wish to be tested, therefore the register will underestimate the number of persons who are HIV infected. The register therefore cannot be used as a direct estimate of HIV prevalence.

(2) It is not known whether a person testing HIV positive has been recently infected with HIV, or has been infected for several years.

The fact that a person testing HIV positive has been infected for an unknown time, means that newly-reported HIV positive test results cannot be interpreted as new infections.

The first problem has been partially resolved by the provision of a range of unlinked anonymous testing (UAT) studies, which are not subject to the participation bias of voluntary testing (see chapter five).

The second problem has been helped by the introduction of the CD4 Study (see chapter six). This enables the matching of people on the HIV Register to their CD4 count, if this has been measured at the time of their first positive HIV test. Hence, for many of the persons now testing HIV positive, their level of immune deficiency may be ascertained from their CD4 count at the time of their HIV test.

3.5 Analysis of the HIV Register

An analysis of the HIV Register was carried out using all the data available on the 2,129 HIV positive persons reported to SCIEH by 30th June 1994 [6].

3.5.1 Age group and gender of persons tested

Figure 3.01 shows the gender and age group, at time of test, of the 2,129 HIV positive persons, 75 per cent of whom are male. The modal age group of persons testing HIV positive is 20-24 years (28 per cent), followed by the 25-29 year age group (22 per cent). All age groups, from 0-4 years to over 65 years, are represented.

3.5.2 Setting of HIV test request

The setting in which people requested HIV tests has only been routinely documented since the introduction of the standard request form in 1989. Table 3.01 shows that 37 per cent of test requests have been made through the hospital setting, 20 per cent through the genito-urinary medicine (GUM) setting, 16 per cent through the general practitioner (GP) setting, and 11 per cent through the counselling clinic setting.

3.5.3 Reason for HIV test request

There are many reasons for people to seek, or to be recommended by a doctor to have, an HIV test :-

(1) Concern that their behaviour has exposed them to the risk of acquiring HIV.
(2) Concern that accidental injury, such as a needlestick injury, has exposed them to HIV.
(3) Physical symptoms may have developed that are associated with HIV.
(4) Learning (or suspecting) that a partner is HIV positive.
(5) Travelling to parts of the world which require proof of a negative HIV test before allowing entry [110].
(6) Requiring an HIV test for insurance purposes.
(7) Screening for HIV before renal dialysis or organ/semen donation.

The reason why a person requested an HIV test, has also only been routinely documented since the introduction of the standard request form in 1989. Table 3.01 shows that, for persons tested between January 1989 and June 1994, the modal reason for requesting an HIV test was 'patient concerned' (42 per cent) followed by 'doctor concerned' (35 per cent).

3.5.4 Health board of residence by health board of test request

Table 3.02 shows the health board of residence of the person being tested, by the health board from which the HIV test was requested (health board of request). Health board of residence is known for 68 per cent of those tested; health board of request is known for all cases. Table 3.02 shows that 48 per cent of all HIV positive tests have been requested from Lothian Health Board, 22 per cent from Greater Glasgow Health Board, and 16 per cent from Tayside Health Board. The other health boards together account for only 14 per cent of all HIV positive tests. Table 3.02 shows clearly that most people have an HIV test in their health board of residence.

3.5.5 Year of HIV specimen

The HIV Register contains three different dates pertaining to the HIV positive test. These are: the date the blood specimen was taken (specimen date), the date the blood specimen was tested (test date), and the date the result was reported to SCIEH (report date). In most cases, these three dates are within a few days of one another. However, in some instances, blood specimens, previously held in storage, were later tested for antibodies to HIV; under such circumstances the specimen date may precede the test date by several years.

Figure 3.02 shows the number of persons testing HIV positive, by the year of specimen. From 1981 to 1983, 84 specimens tested HIV positive. Between 1984 and 1987, the number of HIV positive specimens rose from 250 in 1984 to 325 in 1986, before falling to 248 in 1987. Since 1987, the number of HIV positive specimens has fluctuated between 125 and 175 per year.

3.5.6 Health board by year of specimen

Figure 3.03 shows the number of positive HIV tests resulting from those tests requested within Lothian, Greater Glasgow, and Tayside Health Boards, by year of specimen. This shows clearly that, within Lothian Health Board, a large number of persons tested HIV positive in the period before 1986, compared with either Greater Glasgow Health Board or Tayside Health Board. Since 1988, the number of positive HIV tests has been relatively stable, at approximately 50 per year from those requested in Lothian Health Board, and approximately 25 to 35 per year from those requested in each of Greater Glasgow and Tayside Health Boards.

3.5.7 Risk category for HIV infection

Where a person has more than one 'risk activity' for HIV infection, it is usually not known which of the possible routes of infection was the actual route. This is the case with sexually-active IDUs, who might have been infected either through sharing needles or through sexual contact. In the HIV Register, the hierarchical approach taken to classification is consistent with that taken in the AIDS Register, by first identifying the risk activities of the patient, and then those of the partner(s) (see section 2.1.5 and Table 2.02).

Ninety-seven per cent of the persons who tested HIV positive have been assigned a risk category. Table 3.03 shows that 49 per cent have been classified as IDU, 29 per cent as homosexual/bisexual, and 14 per cent as heterosexual.

3.5.7.1 Risk category by year of specimen

Table 3.04 shows each risk category by year of specimen, while Figure 3.04 shows only the homosexual/bisexual, IDU, and heterosexual risk categories by year of specimen. Figure 3.04 shows a high number of HIV positive tests among IDUs between 1984 and 1987, with a lower, relatively stable, number thereafter (between 30 and 50 tests per year). It also shows that the number of homosexuals/bisexuals testing HIV positive has been relatively stable and, since 1989, has been slightly greater than the number of IDUs testing HIV positive. The number of HIV positive tests

attributed to heterosexual risk increased sharply in 1986, then increased more steadily until 1992, before dropping slightly in 1993.

3.5.7.2 Risk category by year of specimen (Greater Glasgow HB)

Figure 3.05 shows the major risk categories, by year of specimen, for tests requested within Greater Glasgow Health Board. It shows that, since 1984, the number of HIV positive tests among homosexuals/bisexuals has been greater than those among IDUs or heterosexuals, with the exception of 1986 and 1987 when there were slightly more HIV positive tests among IDUs. Since 1989, the number of HIV positive tests among homosexuals/bisexuals has been more than twice that of any other risk category.

3.5.7.3 Risk category by year of specimen (Lothian HB)

Figure 3.06 shows the major risk categories, by year of specimen, for tests requested within Lothian Health Board. It shows that there were 195 HIV positive tests among IDUs in 1984, 107 in 1985 and 70 in 1986. Throughout the same period, there were 70 HIV positive tests among homosexuals/bisexuals. Since 1987, the number of HIV positive tests among those in all three major risk categories has been similar at 10 to 25 per year.

3.5.7.4 Risk category by year of specimen (Tayside HB)

Figure 3.07 shows the major risk categories, by year of specimen, for tests requested within Tayside Health Board. It shows a similar pattern to Lothian, but on a smaller scale, with most HIV positive tests, before 1987, being among IDUs. However, unlike Lothian, there have been very few HIV positive tests among homosexuals/bisexuals, at only 2 to 3 per year.

3.5.7.5 Injecting drug user (IDU) risk category

Figure 3.04 emphasises the scale of the spread of HIV infection among injecting drug users. Figures 3.05 and 3.06 show that most of these tests were requested within Lothian Health Board, with relatively few requested within Greater Glasgow Health Board.

Many papers have been published on the epidemic of HIV among injecting drug users in Edinburgh [111-114].

Since Glasgow and Edinburgh are both large cities, only 70 kilometres apart, with regular, rapid transport links between them, there has been much debate about the rapid spread of HIV among the estimated 3,000 IDUs in Edinburgh in the early 1980's [115], compared with the relative lack of spread of HIV among the estimated 10,000 IDUs in Glasgow at that time [116-118]. There is no doubt that the citizens of Glasgow benefited through the knowledge and experience accumulated from the epidemic in Edinburgh. This enabled timely implementation of preventative measures, in Glasgow, such as needle exchange programmes [119].

3.5.7.6 Heterosexual risk category

In recent years, there has been an increase in the number of HIV positive test results from people whose risk activity is classified as heterosexual (see Table 3.04). The numbers in this heterosexual category have risen since 1985, and are now similar to the number of IDUs and homosexuals/bisexuals testing HIV positive, at around 25-50 new tests per year. This has stimulated a great deal of interest [120-126].

Table 3.03 shows that 31 per cent, of the 294 persons who are classified as heterosexual, have a partner who is in a recognised high risk category. This 31 per cent includes persons who have had sex with IDUs, or with those infected through blood factor treatment or blood transfusion, or women who have had sex with bisexual men. Thirty per cent of those classified as heterosexual are classified as 'other partner (abroad)'; they have no other identified risks, but are thought to have been infected with HIV through sexual intercourse abroad. Twelve per cent are classified as 'other partner (United Kingdom)', and 27 per cent are classified as 'not known'. Figure 3.08 shows the heterosexual classifications by year of specimen; since 1985, there has been a rise in the number of persons in the 'high risk partner' category. Of those whose infection is attributed to 'other partner (abroad)', numbers have varied between 8 and 16 cases per year, but with no obvious pattern. 'Other partner (United Kingdom)' has always been the smallest of the heterosexual categories, with

between 1 and 8 cases per year.

In 1993, Ms F. Raeside (a research nurse at SCIEH) began the task of investigating those whose risk category was coded as 'heterosexual - not known' or 'unknown', to ascertain if these persons might be re-classified. Initially, this investigation made use of medical records and contacts with doctors. Only if the patient's risk could not be classified through any of these information sources, was permission sought from the clinician to interview the patient.

By 30th June 1994, 148 persons who had been classified as 'heterosexual - not known' or 'unknown' were re-classified. Twenty-one per cent were found to be homosexual or bisexual, 30 per cent were injecting drug users, and 18 per cent were found to be heterosexual with high risk partners [6,127].

3.5.7.7 Mother to child transmission of HIV

Table 3.04 shows that the number of HIV positive specimens, attributed to mother-to-child transmission, ranged from zero to five cases per year. This does not necessarily mean that this category will continue to contribute few cases to the overall epidemic. The increase in HIV infection, attributed to heterosexual spread, has led to an increase in the reported number of HIV positive specimens among women, most of whom are of childbearing age. Hence, this may lead to an increase in the number of pregnancies among HIV positive women. In turn, this may result in an increase in the number of babies born to HIV positive women, although the decision faced by such women, as to whether or not to continue their pregnancies, is likely to be influenced by current knowledge of the combined effects of treatment, pregnancy and HIV progression [128].

3.5.7.8 Transmission of HIV to haemophiliacs

Haemophilia is an inherited bleeding disorder caused by a deficiency of a blood component known as 'factor VIII'. Haemophiliacs are treated by regular injections of factor VIII obtained from several thousand individual blood donations. In the years preceding HIV testing, batches of factor VIII were contaminated by HIV infected blood, thereby infecting the haemophiliacs who received them. Since

April 1985, factor VIII has been subjected to heat treatment to inactivate HIV without reducing the effectiveness of the factor VIII.

When the plight of the HIV infected haemophiliacs was recognised, the Haemophilia Society placed pressure on the Government to provide financial compensation for the 1,215 haemophiliacs, in the UK, who were known to have been infected with HIV. In 1987, the Government announced that ten million pounds would be made available to the MacFarlane Trust, to be administered for the benefit of those HIV infected haemophiliacs and their families. The Government made an additional donation of 24 million pounds to the MacFarlane Trust in November 1989. The Haemophilia Society's campaign for compensation was finally dropped in December 1990, when the Government gave a further 42 million pounds to the Trust. Throughout the campaign for compensation, the Government admitted that it had a moral responsibility to those haemophiliacs who had become infected, but denied that it had been negligent [129].

Table 3.04 shows the number of HIV positive tests, by year of specimen, for haemophiliacs in Scotland. It shows that, by 1985, of the 74 haemophiliacs, 66 (89 per cent) were known to be HIV positive. Since 1990, only one haemophiliac has newly-tested HIV positive.

3.6 Reporting of mortality from HIV infection

Like deaths from AIDS, pre-AIDS deaths are reported to SCIEH in two ways :-

(1) Directly by the doctor responsible for the patient's care.

(2) The Registrar General for Scotland notifies SCIEH of all deaths, in Scotland, where the cause of death is likely to be related to HIV infection.

The information on cause of death, which is recorded on a form of particulars (FOP) for each death, is often inadequate to ascertain if HIV has been a principal cause of death. Doctors will often describe the cause of death in vague terms, in order to spare the deceased person's family the possible embarrassment of having AIDS or HIV specified as a cause of death [130]. In a cohort of AIDS patients, in New York, of which 2,834 deaths were reported, 13 per cent of the death certificates did not mention either HIV or AIDS as a cause of death [131].

In Scotland, conditions such as chronic viral illness, recurrent chest infections, generalised debility, pneumonia and bilateral bronchial pneumonia, are regularly written on FOPs as causes of death in HIV positive people, with no mention being made of HIV or AIDS. To obtain a more accurate cause of death, the Registrar General for Scotland arranged that FOPs would contain a specific box which doctors should tick if they were willing to provide, in confidence, more information on the cause of death, were this to be requested by the Registrar General. This arrangement has enabled more accurate information to be collected, and AIDS or HIV to be specified as a cause of death in cases where it had not previously been recorded.

By 30th June 1994, 536 deaths of persons on the HIV Register had been reported to SCIEH [6]. Figure 3.09 shows the number of deaths of persons on the HIV Register by year of death. It can be seen that the number of deaths rose steadily each year, from 13 in 1986 to 61 in 1990, then almost doubled to 120 in 1991. In 1992 and 1993, the numbers of deaths were approximately 100 per year.

3.7 Survival analysis

The ideal survival analysis would look at the time elapsing between HIV infection and death (or censoring). Unfortunately, with the exception of some haemophiliacs and blood transfusion recipients, the time of infection is usually unknown. Another difficulty lies in determining to what extent HIV infection contributes to many of the deaths, especially of injecting drug users [132,133]. Date of HIV test is a poor substitute for date of HIV infection. Some people will seek an HIV test because they have been at risk of HIV infection, others because they have developed symptoms that may be associated with HIV. At the time of testing, some will have recently become HIV infected, others will have been infected for many months or years. From the information available through the HIV Register, recent infections cannot be distinguished from earlier ones. Using the date of the first HIV positive test will always underestimate survival time from HIV infection to death.

Despite these caveats, some survival analysis is appropriate. The population studied, in June 1993, included adults aged 15 years or more whose HIV positive specimens pre-dated 31st December 1992. There were 1,668 HIV positive adults in the study.

In this analysis, survival time was defined as the time from the date of the earliest HIV positive blood sample (known to SCIEH) to the date of death (or censoring). Those whose deaths were not recorded, had their survival times censored at 30th June 1993.

3.7.1 Results of univariate analysis

Each of the variables used in the survival analysis was categorised. 'Age (in years) at first HIV positive specimen' was divided into four groups, 15-24, 25-34, 35-44, and 45+; 'risk' was divided into four categories, homosexual/bisexual, IDU, heterosexual, and 'other'; 'health board of test request' was divided into four groups, Greater Glasgow, Lothian, Tayside, and 'Other'. Kaplan Meier survival curves [73] were calculated using SPSSPC+ [76], and the difference between the curves assessed using a log rank test [75].

The results of the univariate analysis are summarised in Table 3.05, which shows that five years after first testing HIV positive, 82 per cent of the population are still alive, by ten years this has fallen to 62 per

cent. Since few HIV positive tests have resulted from blood specimens taken before 1983, survival rates beyond ten years are not estimated. A smoothed survival curve for the whole group, based on the Kaplan Meier survival curve, is given in Figure 3.10.

There are differences in survival between the categories of all four variables. In particular, IDUs appear to have better survival than homosexuals/bisexuals (shown in Figure 3.11), younger age groups survive longer than older age groups (shown in Figure 3.12), females survive longer than males, and those requesting HIV testing in Lothian Health Board survive longer than those from other health boards.

3.7.2 Results of multivariate analysis

The main problem with univariate analysis is that it cannot make allowances for the effect of associations between the variables. To investigate the independent effect of each variable, on survival, it is necessary to use multivariate analysis. All the variables used in the univariate analysis were entered into a Cox's proportional hazards model, to predict factors independently associated with survival [74,77]. The analysis was carried out using BMDP procedure P2L [78].

The results of this analysis are summarised in Table 3.06, and show that those who are aged over 35 years have poor survival compared to those in the baseline group of 15-24 years. The 95 per cent confidence interval (95% CI) for the relative risk (RR) of survival for those aged 35-44 years, compared with those aged 15-24 years is (1.5, 2.7); for those aged 45 years or over, compared with the same baseline group, it is (1.5, 3.0).

Being homosexual/bisexual was significantly associated with poorer survival than that of the baseline heterosexual category, with the 95% CI for RR being (1.1, 2.3). However, survival of IDUs was not significantly different from that of the heterosexual category. Comparing survival between the IDU and homosexual/bisexual categories, shows that survival in the IDU category is twice as long.

Those who were first tested for HIV in areas outside Greater Glasgow or Lothian Health Boards, show poorer survival. For those in Tayside the 95% CI for RR is (1.2, 2.0) compared with the baseline of Lothian; for those in the 'other' category it is (1.1, 2.0). Although survival of females appears to be longer than that of males, the difference was not statistically significant once the effect of the other variables was taken into account.

The independent effect of age on survival from HIV infection is well documented in other papers; in particular, in a study of IDUs in Edinburgh [92], a study of people infected by blood transfusions in Sweden [134], and a study of HIV-infected homosexuals and heterosexuals in Italy [135]. The effect of risk activity on survival from HIV infection is shown in studies from Edinburgh [68] and Italy [135].

3.8 Distribution of HIV data

Tables of HIV data are published quarterly in 'ANSWER', showing newly-reported and cumulative HIV infections, by risk category, gender, age, and health board; a copy of ANSWER is provided in the back pocket of this thesis.

Like AIDS data, summary data from the HIV Register are routinely presented at meetings attended by professional people working in HIV-related fields (see section 2.8).

In addition to this, SCIEH provides an information service, on HIV surveillance data held at SCIEH, to people from a wide range of disciplines, such as public health officials, students and the media.

Staff at SCIEH have often been asked to provide information in response to parliamentary questions, in particular regarding the number of persons thought to have been infected with HIV as a result of blood, or blood products, provided by the National Health Service (NHS). These persons included haemophiliacs living in Scotland who had become infected with HIV after receiving infected 'Factor VIII' [129].

3.9 The future of the HIV Register

The HIV Register is an extremely important component of HIV surveillance in Scotland, playing a crucial role in both routine publications, such as ANSWER [136], and in special studies such as AIDS predictions [8,16-18]. Its value has been increased even more by linkage to other surveillance schemes such as the CD4 Study and the Denominator Study.

It is clear that the HIV Register will continue to have a fundamental role in HIV surveillance for the foreseeable future.

Chapter 4

The Denominator Study

4.1 Introduction to the Denominator Study

While the HIV Register plays an undeniably important role in the surveillance of HIV infection in Scotland, it is often difficult to interpret because little is known about the population being tested. For example, an increase in the number of reported HIV positive persons might represent a genuine increase in prevalence of HIV, or reflect an increase in the number of persons coming forward for HIV testing [137].

4.1.1 Origin of the Denominator Study

In 1988, the 'Scottish National Collaborative HIV Sero-testing Study' was co-ordinated at SCIEH, with the financial support of the Home and Health Department of the Scottish Office [39]. The aim of the study is to collect epidemiological data on all persons coming forward for an HIV test. All National Health Service HIV testing laboratories participate, except those devoted exclusively to the processing of blood donations. The study is colloquially referred to as the 'Denominator Study' because, within this study, HIV positive results (the numerator) are interpreted in conjunction with all HIV test results (the denominator).

A similar study, but less extensive, involving eighteen HIV testing laboratories in England and Wales, was introduced at CDSC in 1986 [138].

4.1.2 Request form for the Denominator Study

A request form, designed specifically for this study, is used whenever an HIV test is requested. A description of this form was given in section 3.2.1, and a copy is provided in the back pocket of this thesis.

The use of a common request form helps to standardise data collection, but some difficulties remain :-

(1) The absence of requested information is difficult to interpret; e.g. the absence of clinical information may mean that either no clinical symptoms were present, or that symptoms were present but not recorded.

(2) Decisions may be made subjectively by the clinician; e.g. a person requesting a test, for insurance purposes, may be presumed by the clinician to be heterosexual with no risk factors for HIV.

4.1.3 Support for the Denominator Study

The HIV testing laboratories which are expected to test more than 1,500 specimens each year, are called the 'principal laboratories', while the others are called the 'small laboratories'. Clerical officers have been appointed, by SCIEH, to work in each principal laboratory, to collate the HIV test results, and to enquire about incomplete, absent or implausible information. The names and locations of these laboratories are found in Figure 4.01 and Table 4.01.

Concurrent with the development of the request form, computers were purchased and installed in all principal laboratories, to help the clerical officers manage their data. To enable data to be entered quickly and accurately, a database was designed at SCIEH, using a software package called DATAEASE [107], and installed on each of these computers. This database makes extensive use of 'choice-fields', which allow text (such as 'Greater Glasgow') to be entered by only one or two keystrokes, thereby minimising errors and inconsistencies in data-entry.

HIV positive test results, from all laboratories, are reported to SCIEH, promptly, by telephone. Once a month, all test results from the principal laboratories are transferred electronically to SCIEH. The small laboratories post their HIV test request forms and test results to SCIEH on a regular basis.

4.2 Analysis of data from the Denominator Study (1989-1992)

4.2.1 Number of HIV tests and repeat tests

For the purposes of this analysis, 'repeat tests' are defined as subsequent tests for the same person within a calendar year. The main reason for repeat testing is to ensure that a person still tests HIV negative after the window period (see section 3.1.2).

Following computer-entry of all the HIV test data for a calendar year, the data are examined to identify persons having repeat tests. Figure 4.02 shows that repeat tests account for approximately 8 per cent of all tests.

In July 1993, a data analysis was undertaken, covering the period 1989 to 1992. Haemophiliacs and children, people who had been recorded as 'known HIV positives', and people whose age or gender was not recorded, were excluded from the analysis. In any one calendar year, repeat tests were excluded unless seroconversion occurred between tests, when the positive test result was included instead of the earlier negative test result. The study population consisted of 46,673 test results.

4.2.2 Year of HIV test

Table 4.02 shows that the number of persons tested, per year, rose by 35 per cent from 9,651 in 1989 to 13,049 in 1992. It also shows that the rate of persons testing HIV positive has decreased from 13.0 per 1000 tested in 1989 to 9.8 per 1000 in 1992.

However, caution should be shown in interpreting these results, in particular a fall in the rate of persons testing HIV positive does not necessarily imply that prevalence of HIV is falling [137].

4.2.3 Testing rates in population groups of known size

Although it is valuable to analyse variations, through time, in the characteristics of those persons (belonging to a particular category or group) who requested HIV tests, the analysis may be enhanced by taking into account the total number of persons in that group. While this is not possible for variables where the numbers in each category are not known, such as risk category, it is certainly possible for variables such as age

group, gender and health board of residence.

4.2.3.1 Age group and gender of persons tested

Table 4.03 shows the number of persons tested, the number tested per 1000 population, the number testing HIV positive, and the number testing HIV positive per 1000 tested. Population data for Scotland are based on estimates provided in Scottish Health Statistics (1994) [139].

Table 4.03 shows that, for both males and females, the 20-24 year age group showed the highest rate of persons seeking an HIV test; for males, 7.7 per 1000 population sought testing, compared with 5.2 per 1000 for females. However, it is important to realise that high rates of testing do not necessarily mean high rates of testing HIV positive. The highest rates of testing HIV positive, for both males and females, were found in the 25-29 year age group at 18.8 per 1000 tested, for males, compared with 11.6 per 1000 for females.

High rates of testing HIV positive, within a group, indicate that more persons in that group should be encouraged to seek testing. The above results suggest that more testing should be encouraged among men in the 25-29 year age group.

4.2.3.2 Health board of residence of persons tested

Table 4.03 shows the number of tests by health board of residence. The highest rate of testing was found in Lothian with 5.5 tests per 1000 population per year, followed by Greater Glasgow with 3.7 tests per 1000. The highest rate of testing HIV positive was in Tayside where 19.1 of every 1000 tests were positive, followed by Lothian with 17.5 per 1000. Lower rates were found in Greater Glasgow with 8.4 positive tests per 1000 tests, and Grampian with 4.7 per 1000.

These results suggest that more testing should be encouraged in persons from both Tayside and Lothian Health Boards.

4.2.4 Reason for HIV test request

The reason for the test request is recorded for 99 per cent of persons tested; figure 4.03 shows the three main reasons given. 'Screening' includes HIV testing for purposes of travel, insurance, renal dialysis, and

organ/semen donors or recipients. In the 'patient concerned' group, there was a 104 per cent rise in the number of persons tested per year, from 4,411 in 1989 to 8,985 in 1992. The modal reason for testing was 'patient concerned' (57 per cent of persons tested), followed by 'screening' (23 per cent).

4.2.5 Setting of HIV test request

Figure 4.04 shows that the modal setting from which people requested HIV tests was the general practitioner (GP) setting. Tests requested through GUM clinics increased by 117 per cent, from 1,636 in 1989 to 3,554 in 1992. Tests requested through counselling clinics increased by 132 per cent, from 694 in 1989 to 1,616 in 1992.

4.2.6 Risk category for HIV infection

The approach used to categorise people by risk behaviour only differs from that described in Table 2.02 in that the heterosexual risk category has been simplified by referring to those who are 'heterosexual (high risk partner)' as 'heterosexual (high risk)' and the remainder as 'heterosexual (low risk)'. Seventy-eight per cent of the people being tested were assigned a risk category. Of those persons assigned a risk category, 58 per cent were attributed to heterosexual (low risk), 11 per cent to heterosexual (high risk), 15 per cent to IDU, 10 per cent to homosexual/bisexual, and 6 per cent to 'other' risk.

Figure 4.05 shows that the number of persons tested, in the heterosexual (low risk) category, rose by 77 per cent from 3,567 in 1989 to 6,324 in 1992. Figure 4.06 shows that, between 1989 and 1992, the rate of testing HIV positive was relatively stable in this category, at approximately 3.4 per 1000 tested. Although fewer persons tested were in the IDU and homosexual/bisexual risk categories, the rate of testing HIV positive, in these categories, was much higher at 28.9 per 1000 tested and 42.9 per 1000 respectively. In the homosexual/bisexual category, the high rate of men testing HIV positive suggests that it is extremely important to encourage more homosexual or bisexual men to come forward for testing.

4.3 Characteristics associated with testing HIV positive

4.3.1 Introduction to logistic regression

In July 1993, a logistic regression analysis was carried out using the study population described in section 4.2.1. The aims of this analysis were :-

(1) To investigate which characteristics, of those seeking HIV testing, are associated with testing HIV positive.

(2) To provide an estimate of the probability of testing HIV positive, for an individual person.

The logistic model specifies the probability of an event occurring, depending on the values of a set of explanatory variables [140]. In this analysis, the event of interest is the HIV test result. The logistic model is used to investigate the effect of the explanatory variables on the probability of testing HIV positive, and also to estimate the probability of a person testing HIV positive for any given set of explanatory variables. The analysis was carried out using the statistical procedure PROC LOGISTIC from SAS [141].

The following explanatory variables were chosen for inclusion in the logistic regression model. Risk category, gender, presence of HIV related clinical symptoms, year of HIV test, age group at time of HIV test, health board of test request, reason for HIV test, and setting of HIV test request.

4.3.2 Example of logistic regression using gender

Logistic regression, at its simplest, looks at each explanatory variable separately. The following example illustrates logistic regression using gender :-

$$P(\text{HIV positive}) = \exp(a)/\{1+\exp(a)\}$$

where $a = b_0 + b_1 x$

with $x = 0$ if the person is male,

or $x = 1$ if the person is female.

Using the data on gender from the study population, the logistic regression provides maximum likelihood estimates for b_0 and b_1, giving:

$b_0 = -4.293$ and $b_1 = -0.6307$

Thus:

P (HIV positive) = 0.013 for a male

P (HIV positive) = 0.007 for a female.

4.3.3 The odds ratio in logistic regression

The parameters in a logistic regression model may be expressed in terms of the odds ratio.

The odds of being HIV positive are :-

P (HIV positive) / P (HIV negative).

Using the example of section 4.3.2 :-

The odds of being HIV positive for a male are:

$[\exp(a) / \{1 + \exp(a)\}] / [1 / \{1 + \exp(a)\}]$

$= \exp(a)$ where $a = b_0$

Similarly, the odds of being HIV positive for a female are:

$[\exp(a) / \{1 + \exp(a)\}] / [1 / \{1 + \exp(a)\}]$

$= \exp(a)$ where $a = b_0 + b_1$

Thus the odds ratio (OR) for females, compared to males, is:

$\exp(b_0 + b_1) / \exp(b_0)$

$= \exp(b_1)$

$= \exp(-0.6307)$

$= 0.53$

The value $\exp(b_1)$ is called the 'odds ratio (unadjusted)'. It is unadjusted in the sense that gender is the only explanatory variable in the regression, and is therefore unadjusted for the effect of any other explanatory variable.

4.3.4 Reference categories for logistic regression

Each of the explanatory variables chosen for the logistic regression was treated as a categorical variable. In logistic regression, a statement can only be made about the effect of a particular category by comparing it with another category. For each variable, therefore, it was necessary to designate a particular category (the reference category) to be the one with which the other categories were compared. This was chosen to be the category which had the largest number of tests, with the exception of age group and year of test. For age group, the youngest age group was chosen to be the reference group; for year of test, the earliest year was chosen.

The results of these logistic regressions, for each explanatory variable separately, are given in Table 4.04.

4.3.5 Multivariate logistic regression

So far, the analysis has explored the association between each of the explanatory variables and the probability of testing HIV positive. It was limited to looking at each variable separately. It is important to investigate the effect of each variable on the probability of testing HIV positive, while allowing for the effects of all the other explanatory variables. This is particularly important if there are associations between the explanatory variables which might confound the results. Using the general logistic regression equation [140], gives the odds ratio adjusted for the effect of the other explanatory variables. These odds ratios, and their 95 per cent confidence intervals (95% CI), are given in the last two columns of Table 4.04.

4.3.6 Results of multivariate logistic regression

There were statistically significant odds of testing HIV positive, for each of the risk categories, compared to the reference category 'heterosexual (low risk)', once all the other explanatory variables were taken into account. The 95 per cent confidence interval (95% CI) for the adjusted odds ratio {OR(adj)} for 'homosexual/bisexual' was (5.56, 10.05), for 'IDU' (2.92, 5.32), and for 'heterosexual (high risk)' (2.22, 4.41).

The odds of testing HIV positive in Tayside Health Board were similar to the odds of testing HIV positive in Lothian Health Board, but

were lower in the rest of Scotland.

The reasons for test 'doctor concerned' and 'confirmatory test' were both independently associated with higher odds of testing HIV positive, compared with those whose reasons for testing were 'patient concerned'. Those who were tested for screening purposes, such as insurance or travel, were independently associated with lower odds of testing HIV positive, compared with the reference category 'patient concerned'.

The setting of the test request was also independently associated with higher odds of testing HIV positive, for those from hospital settings, GUM clinics, or counselling clinics, compared to those requesting an HIV test from their GPs. The higher odds associated with the counselling clinic are probably explained by the fact that, in Scotland, there are only three counselling clinics, all of which are attached to hospitals specialising in the treatment of HIV.

The presence of clinical symptoms was also independently associated with higher odds of testing HIV positive.

Females appeared to be associated with lower odds of testing HIV positive, until adjustment was made for the other explanatory variables when it was shown that males and females were equally likely to test HIV positive.

Similarly, later years of testing appeared to be associated with lower odds of testing HIV positive, until adjustment was made for the other explanatory variables, when it was shown that year of testing had no significant effect on testing HIV positive.

4.3.6.1 Multivariate logistic regression : interactions

The previous multivariate analysis was taken forward by including interaction terms in the general logistic regression equation; for example, gender by health board, gender by source of test request, risk category by gender, and risk category by source of test request. The interactions involving risk category were found to be statistically significant, hence a separate multivariate analysis was carried out for the three main risk categories; injecting drug users, homosexual/bisexual males, and heterosexuals.

For homosexuals and bisexuals, the odds of testing HIV positive were similar in Lothian Health Board and Greater Glasgow Health Board, but were significantly lower elsewhere ($P < 0.05$;

OR(adj) = 0.5). Significantly higher odds of testing HIV positive were found at counselling clinics (OR(adj) = 3.6) and hospitals (OR(adj) = 2.0) compared with persons tested by GPs. The odds of testing HIV positive were significantly higher for persons who exhibited clinical symptoms compared with those who did not (OR(adj) = 4.0). The odds of testing HIV positive rose significantly from age 20-24 (baseline for OR) to age 35-39 (OR(adj) = 3.0), then fell by age 40-44 (OR(adj) = 1.04). The odds of testing HIV positive remained relatively constant over the time period.

For injecting drug users, the odds of testing HIV positive were similar in Lothian Health Board and in Tayside Health Board, but were significantly lower elsewhere ($P < 0.05$, OR(adj) = 0.2). Significantly higher odds of testing HIV positive were found at counselling clinics (OR(adj) = 3.1) and GUM clinics (OR(adj) = 2.8) compared with persons tested by GPs. The odds of testing HIV positive were significantly higher for persons who exhibited clinical symptoms compared with those who did not (OR(adj) = 2.7). Females were significantly less likely to test HIV positive than males (OR(adj) = 0.49). The odds of testing HIV positive rose significantly from age 20-24 (baseline for OR) to age 30-34 (OR(adj) = 2.5), then fell by age 40-44 (OR(adj) = 1.39). The odds of testing HIV positive remained relatively constant over the time period.

For the heterosexual risk category, the odds of testing HIV positive were similar in Lothian Health Board and in Tayside Health Board, but were significantly lower elsewhere (OR(adj) = 0.5). Significantly higher odds of testing HIV positive were found in the hospital setting (OR(adj) = 2.9) and the GUM clinics (OR(adj) = 1.8) compared with persons tested by GPs. The odds of testing HIV positive were significantly higher for persons who exhibited clinical symptoms compared with those who did not (OR(adj) = 2.6). The odds of testing HIV positive were relatively constant over all age groups and for both males and females. The odds of testing HIV positive remained relatively constant over the time period.

From these analyses by risk category, several points are worth highlighting :-

(1) Although the highest odds of testing HIV positive are found in the counselling clinic setting, for homosexual/bisexuals and injecting drug users, the highest odds for heterosexuals are found in the hospital setting. This suggests that those who are infected heterosexually may not be aware of being at risk of HIV infection until symptoms arise which require hospital treatment. If this is true, then it is particularly important that hospital clinicians remain alert to the possibility of their patients being at risk of HIV infection, and persuade patients to have an HIV test.

(2) While the overall adjusted odds of testing HIV positive are equal for males and females, there are differences between the risk categories. In the injecting drug user category, males are twice as likely to test HIV positive as females, while in the heterosexual category, females are more likely to test HIV positive (OR(adj) = 1.31). The reasons for this are unclear and should be investigated further, possibly by running separate logistic regressions for male and female injecting drug users and heterosexuals.

(3) The heterosexual category differs from the other two categories with age having little effect on the odds of testing HIV positive. There is no typical age group for those infected heterosexually, unlike the other two risk categories with the typically older HIV-infected homosexual and typically younger HIV-infected injecting drug user. This again underlines the importance of hospital clinicians being alert to the possibility of their patients being at risk of HIV infection, regardless of typical stereotypes.

4.3.7 Probability of testing HIV positive

The estimated probability of any patient testing HIV positive may be calculated from the values of the coefficients of the relevant explanatory variables used in the multivariate logistic regression, as shown in the

following three examples :-

Example 1

During a visit to a GUM clinic in Glasgow in 1990, a thirty-year-old male homosexual requested an HIV test because his doctor was concerned that his clinical symptoms might be HIV related. Using the coefficients of the explanatory variables in Table 4.05 gives :-

P (HIV positive) = exp (a) / {1+ exp (a)}

where

a = -7.263 + 2.012 - 0.908 + 1.135 + 0.613 + 1.653 + 1.342 - 0.036

= -1.452

Thus P (HIV positive) = 0.234/ 1.234

= 0.19

Example 2

As example 1, except that the patient had no clinical symptoms.

a = -7.263 + 2.012 - 0.908 + 1.135 + 0.613 + 1.653 - 0.036

= -2.795

Thus P (HIV positive) = 0.061/ 1.061

= 0.06

Example 3

As example 2, except that the reason for testing was 'patient concerned'.

a = -7.263 + 2.012 - 0.908 + 0.613 + 1.653 - 0.036

= -3.930

Thus P (HIV positive) = 0.02/ 1.02

= 0.02

4.4 The future of the Denominator Study

The Denominator Study collects data on all HIV tests in Scotland, currently approximately 15,000 tests each year. To manage this data, the study utilises substantial resources, since clerical officers and computers are required in the principal laboratories. The time taken for each year's data to be published, together with the poor quality of information on many of the request forms, raises questions about the future direction of this surveillance scheme. These issues are discussed further in chapter eight.

Chapter 5

Unlinked Anonymous Testing

5.1 Unlinked Anonymous Testing (UAT)

Prior to 1989, surveillance of HIV in Scotland relied on the results of HIV tests performed only with the informed consent of the patient.

Between 1987 and 1989, several reports were published which showed that estimating the prevalence of HIV from data provided solely by voluntary testing, such as the HIV Register and the Denominator Study, was inadequate and undesirable [142-144].

Another report, produced by the Social Services Committee for the UK Government [145], stated that there was an urgent need for more reliable data on the prevalence of HIV in the United Kingdom. Several epidemiologists argued that a system of anonymous screening was the :-

> "*...most practical, most accurate and most ethical means of gauging the prevalence of HIV in the population as a whole and its emergence in groups currently considered low risk...*" [145].

One of the main obstacles to UAT concerned the ethical implications of testing a person's blood for HIV without that person's knowledge or consent. However, in 1989, the Standards Committee of the General Medical Council reported that no fundamental ethical principle is breached by the principles of UAT [146]. This report paved the way for the introduction of unlinked anonymous testing (UAT) for HIV infection within specific population groups, such as antenatal and GUM clinic attenders.

5.1.1 Principles of UAT

Unlinked anonymous testing involves the testing of residue from any specimen that has been taken from a person for some other purpose. The residue is irreversibly unlinked from any person-identifiable information (e.g. name, address or date of birth) before being tested, so that it is impossible to link the result with a particular person, thus fulfilling the key requirement of UAT that the anonymity of the individual is preserved. The purpose for which the specimen was initially taken must not be compromised in any way by UAT.

Information must be available describing the purpose of the UAT scheme, and stating that anyone may be tested for HIV, anonymously and

without prior consent, unless that person chooses not to participate. To this effect, those implementing UAT schemes are required to ensure that posters are on display, and leaflets available, to people at all centres where UAT is being carried out. Such literature is available in several languages; one of the leaflets is provided in the back pocket of this thesis.

Participation in a UAT scheme does not affect a person's right to request an HIV test, should one be wished.

5.1.2 The main advantages and disadvantages of UAT

The main advantage of UAT is that it is virtually free of participation bias since permission to test is not actively sought, therefore very few people object to participating. Another advantage is that surveillance is relatively inexpensive, since the patient cannot receive the test result, and therefore counselling is redundant. Hence, large numbers of people are able to be tested relatively cheaply, making this a particularly appropriate method of surveillance for a large population.

The main disadvantage of UAT is that the patient is unable to benefit directly, since the patient cannot be informed of the test result. However, knowledge of prevalence of an infection within a group of people is beneficial to the group as a whole. If the prevalence of the infection is low, the members of the group will be reassured by this; if the prevalence is high, then the group may be targeted and encouraged to come forward for further testing.

Another disadvantage of UAT is that only limited information, from the original specimen, is permitted to remain linked to the residue. For example, it is acceptable to retain the patient's gender, age group, geographical region and calendar quarter of test, but not the date of birth, name, address or date of test.

Vigilance is always necessary, when presenting results of UAT, to ensure that deductive disclosure cannot occur. For example, a man in the 80-84 year age group, from Grampian Health Board, testing HIV positive, would almost certainly compromise that individual's identity!

5.1.3 Government approval for UAT in UK

After much consultation and debate on the legal and ethical issues of UAT, Kenneth Clarke (then Secretary of State for Health) announced, in November 1988, that :-

> *"The Government sees no legal obstacle to such (anonymous) testing. From the layman's point of view, we also see no ethical objection to the testing for scientific purposes of blood samples taken properly in the first place for another purpose from a patient no longer identifiable."* [42].

A year later, in November 1989, Virginia Bottomley (then Minister for Health) announced that UAT would begin in the United Kingdom in January 1990; she said :-

> *"The surveys will be a valuable tool in assessing prevalence of HIV in this country, particularly amongst the heterosexual population for whom we lack information. These surveys will help us make more accurate predictions of the numbers of people throughout the population who will become infected. This will help us to plan and target both our prevention activities and services for those who are infected."* [9].

5.1.4 Network of UAT studies for HIV, in Scotland

Since 1990, five UAT surveillance schemes, for HIV in Scotland, have been introduced. They form a network of complementary studies, each providing data on HIV prevalence. The five studies are :-

(1) GUM Study: A study of men and women attending GUM clinics in Glasgow and Edinburgh.

(2) Hospital Study: A study of men attending two Glasgow hospitals, as in-patients or out-patients, or attending one of a small number of general practitioner clinics in Glasgow.

(3) Guthrie Study: A study of mothers of new-born babies. This study covers the whole of Scotland.

(4) Family Planning Study: A study of women attending a family planning centre in Glasgow.

(5) Antenatal Study: A study of women attending antenatal clinics in Edinburgh and Dundee.

A similar network of studies, co-ordinated at CDSC, was introduced in England and Wales [40,147-149].

5.2 GUM Study

The GUM study started, in October 1990, in three GUM clinics based at Edinburgh Royal Infirmary, Glasgow Royal Infirmary and Glasgow Southern General Hospital. This study was initially funded by the Medical Research Council (MRC) before being funded by SCIEH.

The purpose of the study is to estimate the prevalence of HIV, and to detect changes in prevalence, through time, among men and women attending GUM clinics.

Since people attending GUM clinics often present with sexually transmitted diseases (STDs), these people are thought to be more likely to have more sexual partners, and therefore to be at higher risk of acquiring HIV infection than the general population. If there is an increase in the heterosexual spread of HIV, then it is likely to be apparent first in this setting.

Persons attending one of these GUM clinics, and who have a blood sample taken, are included in the study if it is either, their first attendance in a calendar quarter or, their first attendance with a new STD.

In late 1992, the study was expanded to include GUM clinics in Aberdeen, Falkirk, Stirling, Dundee and Perth.

Results from the study have been presented at international AIDS conferences in Amsterdam and Berlin [150,151].

5.2.1 GUM Study : data collected

(1) GUM clinic attended
(2) Gender and age group
(3) Time period of specimen taken (in calendar quarters)
(4) The HIV status of the patient, if known
(5) Any objection, by the patient, to being tested for HIV
(6) Patient's risk factors for HIV
(7) Partner's risk factors for HIV (and HIV status if known)
(8) Diagnostic codes of current STDs
(9) Information about nationality of patient and partner(s)

An example of the survey form is included in the back pocket of this thesis.

5.2.2 GUM Study : results

An analysis of all tests conducted throughout the period 1st October 1990, to 30th June 1994, shows that the number of persons tested per calendar quarter, in both Glasgow and Edinburgh, has stayed relatively constant (see Figure 5.01 and Table 5.01). However, owing to the study design, it is not possible to tell how many different people have been tested overall.

There were 58 objections to participating in the study, 20 from Edinburgh and 38 from Glasgow. Twenty-six objections took place in the first six months of the study (0.5 per cent), but this fell to only two objections in the first six months of 1994 (0.05 per cent).

Table 5.01 shows that 16,103 tests were carried out in Edinburgh, compared with 18,289 in Glasgow. There were 146 HIV positive test results in Edinburgh, and 96 in Glasgow, over this time period. The rate of persons testing HIV positive (per 1000 tested) in Edinburgh was greater than that in Glasgow, in almost all calendar quarters, averaging 9.1 per 1000 and 5.2 per 1000 respectively.

Table 5.02 shows the number of tests classified by risk category, gender, and location of GUM clinic. Although the number of tests among IDUs at GUM clinics in Glasgow was higher than in Edinburgh, the rate of HIV positive tests, per 1000 tests, was substantially lower in Glasgow at 8 per 1000, compared with 142 per 1000 in Edinburgh. Tests among IDUs in Edinburgh accounted for 0.8 per cent of the total tests in Edinburgh, but 13 per cent of the HIV positive tests there. By contrast, tests among IDUs in Glasgow accounted for 1.3 per cent of the total tests there, and 2 per cent of the HIV positive tests.

The number of tests among homosexuals/bisexuals in Edinburgh and Glasgow were of similar magnitude, as were the rates of testing HIV positive, at 54 per 1000 in Edinburgh and 48 per 1000 in Glasgow.

Tests among homosexuals/bisexuals in Edinburgh accounted for 9 per cent of the Edinburgh HIV tests, but accounted for 55 per cent of the HIV positive results there. Similarly, in Glasgow they accounted for only 7 per cent of the HIV tests, but 63 per cent of the HIV positive results.

The number of HIV tests, on those classified as heterosexual risk, was higher in males than in females, in both Edinburgh and Glasgow. However, in Edinburgh, the rates of HIV positive tests, per 1000 tests, were very similar for males and females, at 3.0 per 1000 and 3.5 per 1000 respectively. In Glasgow, the rates were higher for males, at 2.6 per

1000, compared with 1.0 per 1000 for females.

There is, however, the unavoidable problem associated with classifying people, especially males, into risk categories, namely that they may withhold the truth about their sexual activities, thus being classified as heterosexual when they are either homosexual or bisexual. This potential bias means that the true rate among heterosexual males is likely to be lower than this study shows. The skill and attitude of the doctor interviewing the patient at the GUM clinic may affect the willingness of the patient to reveal risk factors for HIV transmission.

All persons are asked, at consultation, if they know their HIV status; those who say they are HIV positive are classified as 'known positives'. In the analysis, table 5.02 shows whether or not the person testing HIV positive was a known HIV positive. In Edinburgh, the number of known HIV positives, in the IDU and homosexual/bisexual categories, exceeded the number of unknown HIV positives. This was not the case in the heterosexual category, where unknown HIV infections outnumbered known HIV infections by two to one, in males, and three to one, in females. Overall, in Edinburgh, there were 75 known HIV positives and 70 unknown HIV positives.

In Glasgow, in the homosexual/bisexual category the unknown infections outnumbered known infections by three to one, in heterosexual males by approximately six to one, and in heterosexual females by two to one. There was very little infection, known or unknown, among the Glasgow IDUs. Overall, in Glasgow, there were 22 known HIV positives and 73 unknown HIV positives.

One of the aims of the GUM Study is to study trends in HIV prevalence over a period of time. The results of the analysis showed a relatively stable situation with no substantial changes in HIV prevalence in any of the risk categories, in either Glasgow or Edinburgh.

5.3 Hospital Study

In October, 1991, a one-year pilot study was initiated at SCIEH to estimate the prevalence of HIV infection among people, aged 16-49 years, attending two Glasgow hospitals, or attending a few GP clinics that were using the biochemistry laboratories of these hospitals. All patients attending these centres, who have a blood sample taken for urea and electrolyte testing, are eligible for the study. Repeat samples, provided by any one person within a twelve week period, are excluded from the study.

The pilot phase of this study was financed by the MRC, thereafter, financial responsibility passed to SCIEH.

From 1st May 1993, the study was restricted to males, since it was recognised that the GUM, Guthrie, antenatal and family planning studies were already providing sufficient HIV-prevalence data for females.

Results from the study have been presented at international AIDS conferences in Amsterdam and Berlin, and at an MRC workshop in Manchester in 1995 [152-154].

5.3.1 Hospital Study : data collected

(1) Hospital biochemistry department (Glasgow Royal Infirmary or Stobhill General Hospital)
(2) Gender and age group
(3) Time period of specimen taken (in calendar quarters)
(4) The HIV status of the patient, if known
(5) Any objection, by the patient, to being tested for HIV
(6) Medical section patient is attending i.e.
    General practitioner (GP)
    General medical
    Other

5.3.2 Hospital Study : results

The results of this study, for males only, covering the time period 1st October 1991, to 30th June 1994, are summarised in Table 5.03.

In this time period, 17,130 specimens were tested at Glasgow Royal Infirmary, compared with 9,942 specimens at Stobhill General Hospital, Glasgow. Among those tests from Glasgow Royal Infirmary, 201 HIV

positive tests were found, compared with only 10 from Stobhill General Hospital. This gave an average rate, per calendar quarter, for Glasgow Royal Infirmary, of 11.7 HIV positive tests per 1000 tested, compared with a rate of 1.04 per 1000 for Stobhill General Hospital.

Table 5.04 shows the results for each hospital, classified by the medical section being attended by the patient at the time the blood specimen was taken. Extremely high rates of testing HIV positive were found in the General Medical section at Glasgow Royal Infirmary, averaging 49.7 per 1000 tests. The rates for Stobhill General Hospital were all lower than those found at Glasgow Royal Infirmary. The highest rate at Stobhill was found in the General Medical section with 2.1 HIV positive tests per 1000 tests; the other medical sections had rates of under 1 per 1000 tests.

Table 5.04 also shows the distribution of the HIV positive test results among the different medical sections, at Glasgow Royal Infirmary, by knowledge of HIV status. In the General Medical section, where most of the HIV positive results were concentrated, the known HIV positives outnumbered the unknown HIV positives by a factor of ten. Of the remaining 21 HIV positive results, only 8 were known HIV positives. Only ten HIV positive results were found among those tested at Stobhill General Hospital, four of which were from known HIV positives.

Throughout this analysis there has been a marked difference between the results from the two hospitals. The number of HIV positive specimens (most of which were from known HIV positive persons) taken at Glasgow Royal Infirmary, has been greater (by a factor of 20) than the number of HIV positive specimens taken at Stobhill General Hospital. However, this is almost certainly brought about by the West of Scotland haemophilia unit being based at Glasgow Royal Infirmary. Haemophilia patients are frequently referred to other medical sections within the hospital for treatment and, if they are HIV infected, will usually be classified as 'known positives'.

The results from Stobhill General Hospital are likely to be representative of the prevalence of HIV infection among males (excluding haemophiliacs) attending hospital, and show no change in HIV prevalence over the study period. The results from Glasgow Royal Infirmary are, however, likely to reflect trends in the health-care needs of the HIV infected haemophiliac cohort in the West of Scotland.

5.4 Guthrie Study

In Scotland, blood samples taken from babies, between 8-14 days old, are routinely tested for an inherited disorder which, unless treated, usually leads to severe brain damage. This test, the Guthrie test, measures the amount of phenylketonuria in a spot of blood taken from the heel of the baby. All the blood samples, from babies throughout Scotland, are sent to one laboratory, at Stobhill General Hospital in Glasgow, for testing.

In January 1990, a UAT programme was started, to study changes in prevalence of HIV infection among the mothers of new-born babies in Scotland. This was based on HIV testing of residual blood from the Guthrie test [155,156]. Babies born to HIV infected mothers will have antibodies to HIV in their blood, but this does not necessarily mean that the baby is infected with HIV (see section 3.3). Thus, testing residual blood from the Guthrie test only provides the HIV status of the mother, not that of the baby.

Although each test specimen comes from a different baby, some mothers are counted more than once in any one calendar year, either by having a multiple birth or by having another baby within a calendar year.

This UAT study differs from all the other UAT studies in that babies are unable to object to their blood being tested for HIV, although a mother may object on her baby's behalf.

5.4.1 Guthrie Study : data collected

(1) First part of postcode of mother's residence
(2) Mother's age
(3) Baby's gender and calendar quarter of birth

5.4.2 Guthrie Study : results

The results of the Guthrie Study are presented for the four years 1990 to 1993. Table 5.05 shows that the number of tests per calendar quarter, and the rate of HIV positive tests, have shown little variation throughout the study period. Overall, 77 of the 262,508 specimens were HIV positive, giving a rate of 0.3 per 1000 tests.

Table 5.06 shows the number of mothers resident in Glasgow, Edinburgh and Dundee, by HIV test result and year of test. For each

location, averaging the rates of HIV positive tests, over the four years, shows Edinburgh had a rate of 1.7 per 1000 tests, Dundee had 1.3, and Glasgow had 0.12. The rate for the rest of Scotland was similar to that of Glasgow at the low rate of 0.13 per 1000 tests.

5.5 Antenatal Study

In December 1988, an HIV surveillance scheme was introduced to estimate HIV prevalence among women attending antenatal clinics in Edinburgh and Dundee. In this scheme, women who agreed to participate in HIV testing were given a choice of either a named, or anonymous, HIV test [157]. Results from this scheme have been presented at international AIDS conferences in Amsterdam and Berlin [150,151].

In July 1993, this 'mixed' surveillance scheme was replaced by a solely UAT surveillance scheme, again of women attending antenatal clinics in Edinburgh and Dundee, the objective being to determine changes, through time, in HIV prevalence among these women.

The following study results refer to the more recent UAT surveillance scheme.

5.5.1 Antenatal Study : data collected

(1) Clinic attended
(2) Woman's age group
(3) Time period of specimen taken (in calendar quarters)
(4) Woman's risk factors for HIV
(5) Partner's risk factors for HIV
(6) Any objection, by the woman, to being tested for HIV
(6) Setting from which the blood was taken
(7) Woman's choice for ongoing pregnancy or planned termination

5.5.2 Antenatal Study : results

Table 5.07 shows the number of persons in the Antenatal Study, in both Dundee and Edinburgh, from 1st July 1993 to 30th June 1994; in Dundee there were 3,749 HIV tests, and in Edinburgh, 15,258 tests.

Averaged over all the calendar quarters in this same period, the rate of testing HIV positive was remarkably similar in the two test-centres, at 1.3 per 1000 tests in Dundee, and 1.2 per 1000 tests in Edinburgh. Table 5.07 shows that, although few women were IDUs, or partners of IDUs, these categories contained most of the women who tested HIV positive. In Dundee, there were 5 HIV positive specimens; 4

were from IDUs, and 1 from a partner of an IDU. In Edinburgh, 19 HIV positive specimens were found, including 6 from IDUs and 5 from partners of IDUs.

Among women who were assumed to be at low risk of HIV, i.e. neither they nor their partners were IDUs, there were very few cases of HIV. In this low-risk category, no HIV positives were found in Dundee, and only 8 in Edinburgh (0.52 per 1000 tests).

5.6 Family Planning Study

In January 1992, a UAT study was started at a family planning clinic in Glasgow, with the aim of monitoring changes in HIV prevalence among women attending the clinic. The study was initially funded by the MRC before becoming funded by SCIEH. All women attending the clinic for pregnancy testing, for the first time in a calendar year, and who submit a urine specimen, are included in the study.

This study has a complementary role to the Guthrie and Antenatal Studies. The Family Planning Study includes women who think they may be pregnant, while the Antenatal Study is restricted to women who are pregnant, and the Guthrie Study to those who have given birth to a baby.

5.6.1 Family Planning Study : data collected

(1) Age group of the woman
(2) Time period of specimen taken (in calendar quarters)
(3) Any objection, by the woman, to being tested for HIV
(4) First part of the postcode of woman's residence
(5) Result of pregnancy test

5.6.2 Family Planning Study : results

Table 5.08 shows that 9,929 specimens were tested for HIV between January 1992 and June 1994. Only two of these specimens were HIV positive; one in the calendar quarter April to June 1992, the other in the quarter April to June 1993. Averaging the number of HIV positive tests per 1000 tests, over all calendar quarters in this period, gives the very low rate of 0.2 per 1000 tests.

5.7 UAT : summary of results

Figure 5.02 shows summary results from all the UAT schemes co-ordinated at SCIEH, based on data collected from January 1992 to June 1994. It shows that high prevalences of HIV are found in the GUM and Hospital Studies, with over 5 HIV positives per 1000 tests, compared with the other UAT studies showing under 2 per 1000 tests. The reasons for this may include :-

(1) People attending GUM clinics and hospitals are likely to be at higher risk of having HIV infection than people with no need to attend (see section 5.2).

(2) The Guthrie, Antenatal and Family Planning Studies do not include males, thereby excluding the homosexual risk category.

5.8 UAT : comparison of results with Denominator Study

The Denominator Study gives an HIV prevalence rate of 11 HIV positives per 1000 tested, which, as expected, is substantially higher than any results from the UAT studies. However, the prevalence rate from the Denominator Study, for those persons classified as low risk heterosexuals, is 4 per 1000 tested, which is lower than the prevalence rates found in the GUM and Hospital Studies, but higher than the rates found in the Antenatal, Guthrie and Family Planning Studies.

5.9 UAT : comparison with England and Wales

In January 1995, staff at CDSC produced a comprehensive report on the results of UAT surveillance schemes, in England and Wales, from the years 1990 to 1993 [149]. This report contains results from similar GUM, Guthrie and hospital surveillance schemes.

Results from 1992 and 1993, co-ordinated at CDSC for the GUM Study, are separated into three groups: Central London, London and the South East (excluding Central London), and England and Wales (excluding London and the South East). Very high HIV prevalence rates are found in Central London (49 HIV positives per 1000 tests), compared with the other two regions (4 per 1000 and 3 per 1000 respectively). From Table 5.01, it can be seen that the HIV prevalence rates, from the GUM Study in Scotland, are comparable to those found in England and Wales (excluding Central London).

Results from the Guthrie Study (from years 1990 to 1993), in England and Wales, show an HIV prevalence rate of 2 per 1000 tests in London and the South-East, compared with under 0.4 per 1000 tests in the rest of England and Wales. From Table 5.06, it can be seen that the rates from the Guthrie Study, in Edinburgh and Dundee, are similar to those in London and the South East, while the rates in Glasgow are similar to those in the rest of England and Wales.

Results of a hospital study from two London hospitals (from years 1991 to 1993), show that HIV prevalence rates among all patients receiving hospital care (excluding obstetrics) was 11 per 1000 tests, compared with 11.7 per 1000 tests found in a comparable study in one Glasgow hospital, and 1 per 1000 tests in another Glasgow hospital (see Table 5.03).

5.10 The future of UAT surveillance

The growth of UAT surveillance, in the early 1990s, has led to a network of UAT surveillance schemes. Many of these schemes have been modified at the end of their pilot phase; some have been curtailed, others expanded. While acknowledging that each UAT scheme has its own merits, it is nevertheless worthwhile to evaluate the relative importance of each scheme, and to question if they are all necessary. These issues are addressed further in chapter eight.

Chapter 6

The CD4 Study

6.1 Staging system for HIV infection

The progression of HIV infection is characterised by immunological changes and increasingly severe clinical manifestations which reflect the gradual deterioration of the immune system [31]. Staging systems for HIV infection have evolved as knowledge of the progression of HIV infection has improved. Of the earlier staging systems [11,12], one of the best known is the Walter Reed staging system, adopted by the United States Army in 1985 [10].

A staging system provides a framework for dividing the whole spectrum of HIV infection into mutually exclusive stages. In particular :-

(1) It helps to identify intermediate stages of disease progression between the asymptomatic stage and AIDS.

(2) It provides guidelines which may be used for such events as commencing (or ceasing) therapy, or drug trials.

(3) It facilitates communication between various groups of professionals in HIV-related fields by providing a framework in which all HIV positive people are able to be classified consistently.

6.1.1 WHO staging system for HIV infection

In July 1990, the World Health Organization (WHO) produced an interim proposal for a staging system for HIV infection and disease [13]. This system is applicable to HIV positive people aged thirteen or over. The progression of HIV infection in children and adults is different both clinically and immunologically, so it is inappropriate for them to share the same staging system.

The WHO staging system has two axes, one clinical and one immunological (see Table 6.01). The immunological axis is based on the absolute number of T4 cells per cubic millimetre of blood. This value is commonly referred to as the CD4 count. The absolute number of CD4 cells is calculated, from three separate laboratory measurements, using the formula :-

CD4 count = (WCC) x (%lymphocytes) x (%CD4 lymphocytes)

where:

WCC = white cell count

%lymphocytes = percentage of WCC that are lymphocytes

%CD4 = percentage of lymphocytes that are CD4 lymphocytes

For example, if a person has a WCC of $5.4x10^9$/L, of which 22 per cent are lymphocytes, and 35 per cent of these lymphocytes are CD4 lymphocytes, then :-

$$\begin{aligned} \text{CD4 count} &= 5.4 \times 10^9/\text{L} \times 0.22 \times 0.35 \\ &= 0.416 \times 10^9/\text{L} \\ &= 416 \times 10^6/\text{L} \end{aligned}$$

This is commonly referred to as a CD4 count of 416.

The CD4 count of a healthy person is around 1000 cells per cubic millimetre of blood. Following HIV infection, the CD4 count tends to fall, with time, by approximately 40 - 80 cells per cubic millimetre of blood per year on average [13], although individual counts may fluctuate widely.

In the WHO staging system the immunological axis is divided into three categories, A,B and C :-

(1) Stage A: CD4 count greater than 500

(2) Stage B: CD4 count between 200 and 500

(3) Stage C: CD4 count less than 200

The clinical axis has four mutually exclusive categories, stages 1 to 4, corresponding to a list of physical or clinical conditions associated with HIV.

Stage 1 means that, at the time of the CD4 request, the patient is asymptomatic, or has an acute retroviral infection, or has persistent generalised lymphadenopathy (PGL).

Stage 2 (early HIV infection) includes conditions such as herpes zoster and recurrent infections of the upper respiratory tract.

Stage 3 (intermediate HIV infection) embraces such clinical conditions as oral candidiasis, oral hairy leukoplakia and pulmonary tuberculosis.

Stage 4 (late HIV infection) includes patients with an AIDS

defining illness, in addition to those patients whose illness has confined them to bed for a considerable part of the month preceding the date of the CD4 request.

Patients may have symptoms that put them in stage 2 at one clinic visit, but be asymptomatic (stage 1) at the next. The WHO staging system classifies people according to highest stage ever reached, so these patients would remain in clinical stage 2 despite being asymptomatic at the time of their later visit.

When the CD4 count is combined with clinical information, there are twelve categories that cover the entire spectrum of HIV infection. Those in the 1A category (clinical stage 1 and immunological stage A) being relatively healthy, compared with those in the 4C category (clinical stage 4 and immunological stage C), whose HIV infection is more advanced. This system has been used and validated by a WHO international collaborating group [158].

6.1.2 WHO staging system in Scotland

In November 1990, a proposal was put forward to introduce a collaborative surveillance scheme, for HIV infected adults receiving health care in Scotland, based on the WHO staging system. Such a scheme began in Scotland in November 1991, after consultation with HIV immunologists and clinicians. Its purpose is to discover the number of HIV positive adults currently receiving immunological monitoring in Scotland, together with information on their current clinical and immunological health. This surveillance scheme is colloquially referred to as the 'CD4 Study'.

6.1.3 Surveillance form for the CD4 Study

A three-part request form, for those persons undergoing immunological monitoring in Scotland, was designed at SCIEH in order to standardise data collection for this surveillance scheme. A copy of this form is provided in the back pocket of this thesis. The clinician, who is requesting the lymphocyte count, completes the top copy of the form at the time of consultation, recording the clinical symptoms present according to his or her medical judgment. The top copy of the form is kept by the clinician, with the other two copies being forwarded to the

HIV immunology laboratory, together with the blood sample for lymphocyte analysis. The second copy of the form is retained by the laboratory. The third copy, which contains information from both the clinician and the laboratory, except for the patient's name, is forwarded to SCIEH.

As with the other surveillance schemes administered by SCIEH, the confidentiality of each person is maintained by collecting only limited information on identity, such as date of birth, initials and soundex code of surname.

6.1.4 Computer support for the CD4 Study

A request form is completed every time a CD4 count is requested and, since HIV positive people are monitored regularly, several forms will probably be completed for each person in the study.

Concurrent with the designing of the request form, a computer relational database was designed in DATAEASE [107] to track all records for each person in the study, and to collate, for each person, such summary information as highest clinical stage ever reached, most recent CD4 count, and date of most recent CD4 count.

6.1.5 Addition of risk category and death information

Since the person's name will usually be written on the top copy of the request form, it was decided that HIV risk factor information should not be collected; instead, risk information is sought from the HIV Register. This enables risk category to be entered onto the CD4 database while preserving the patient's confidentiality.

Information about deaths of HIV infected persons, received at SCIEH from either the Registrar General for Scotland (RGS) or clinicians, is also recorded on the CD4 database.

6.1.6 Interpretation of immunological axis

There are several ways of using the CD4 data to represent the immunological state of those under monitoring. It may be argued that the best choice will depend on the context in which the data are likely to be used :-

(1) If the data are to be used for allocation of resources, such as provision of out-patient facilities, hospital beds and staffing, it may be appropriate to look at the worst scenario by taking the lowest CD4 count within the time period of interest.
(2) If the data are being used to assess a patient's suitability to enter a drug trial, then the most recent CD4 count is likely to be the most appropriate.
(3) If the data are being used to describe the immunological condition of the population in any given time period, it may be appropriate to use the average CD4 count (averaged over all counts in the time period).

For the purpose of describing the staging of the population in any one year, it was decided to use the average CD4 count in that calendar year, together with the most severe stage ever reached. The tables and figures referred to, throughout this chapter, use this system of representation.

6.2 Results of the CD4 Study in Scotland

In June 1994, an analysis was carried out to compare the staging, in 1992, of those HIV positive adults who had their CD4 count measured in 1992, with the staging, in 1993, of those who had their CD4 count measured in 1993.

6.2.1 WHO staging of HIV positive adults (1992)

The staging, for the 928 HIV positive adults who had their CD4 count measured in 1992, is given in Table 6.02.

At the time of their last CD4 count measurement in 1992, 40 per cent of these 928 adults were in clinical stage 1, 16 per cent were in stage 2 (early HIV infection), 25 per cent in stage 3 (intermediate HIV infection), and 15 per cent in stage 4 (late HIV infection). The remaining 4 per cent had no clinical information recorded on any of their forms, and thus were unable to be clinically staged.

Taking the average of all CD4 counts, measured during 1992, for each of the 928 persons, 15 per cent had an average CD4 count of over 500, 44 per cent had an average count of between 200 and 500, and 39 per cent had an average count of under 200. The remaining 2 per cent had no CD4 count recorded on any of their forms.

From Table 6.02, it can be seen that the modal cell is 1B with 209 persons (22 per cent). The distribution of people in the staging system reflects the association between high clinical staging and low CD4 counts. No person in stage 4 had an average CD4 count of over 500. Of those persons with an average CD4 count of greater than 500, 71 per cent were in clinical stage 1, while, of those people with average CD4 count of less than 200, 70 per cent were in clinical stages three or four (intermediate or late HIV infection).

6.2.2 WHO staging of HIV positive adults (1993)

The staging, for the 942 HIV positive adults, who had their CD4 count measured in 1993, is given in Table 6.03 and represented in Figure 6.01.

At the time of their last CD4 count measurement in 1993, 39 per cent of these 942 adults were in clinical stage 1, 15 per cent were in stage 2 (early HIV infection), 20 per cent in stage 3 (intermediate HIV

infection), and 17 per cent in stage 4 (late HIV infection). The remaining 9 per cent had no clinical information recorded on any of their forms, and thus were unable to be clinically staged.

Taking the average of all CD4 counts, measured during 1993, for each of the 942 persons, 17 per cent had an average CD4 count of over 500, 42 per cent had an average count of between 200 and 500, and 40 per cent had an average count of under 200. The remaining 1 per cent had no CD4 count recorded on any of their forms.

It is apparent that the results in Tables 6.02 and 6.03 are almost identical, showing a stable population-profile for those who were monitored during 1992 and 1993. However, it can be seen from Figure 3.09 that approximately 100 HIV positive persons died in 1992, hence, this stability in population-profile masks substantial changes at individual level.

6.2.3 Regional variations in WHO staging (1993)

Figures 6.02, 6.03 and 6.04 show the distribution of WHO staging applied to all patients monitored, during 1993, at immunology laboratories in Edinburgh, Glasgow and Dundee. These laboratories all show a different distribution of staging: in Edinburgh, the modal stage was 1B with 27 per cent of the 481 persons monitored there; in Glasgow, the modal stage was the most severe stage, 4C, with 24 per cent of the 215 persons monitored; in Dundee, 3C was the modal stage with 20 per cent of 144 persons. From these figures, it appears that those persons currently under monitoring in Glasgow and Dundee are more likely to be at an advanced state of HIV disease than those in Edinburgh.

6.2.4 Risk category variations in WHO staging (1993)

Figures 6.05, 6.06 and 6.07 show the distribution of WHO staging as applied to the three main risk categories. The most striking difference is in the homosexual/bisexual category where 26 per cent of the 181 persons are in stage 4C, compared with 12 per cent of the IDU, and 12 per cent of the heterosexual, categories. From these figures it appears that, of those persons undergoing CD4 monitoring, those classified as homosexual/bisexual (males) are more likely to be at an advanced stage of HIV infection than those classified as either IDU or heterosexual.

6.3 Log-linear modelling of risk, region and severity of HIV infection

The associations among geographical region, risk category and severity of HIV infection are complex. A statistical technique known as log-linear modelling may be used to investigate such associations among categorical variables, by examining the number of entries in distinct categories of a multi-dimensional table [140]. In October 1993, this analysis was carried out using data collected from those persons under immunological monitoring during 1992.

For this analysis only, each of the twelve cells of the WHO staging system was classified as either 'severe' HIV infection or 'moderate' HIV infection. Using the WHO staging in Table 6.01, cells 1A, 2A, 3A, 1B, 2B and 3B became 'moderate' HIV infection, and cells 1C, 2C, 3C, 4A, 4B and 4C became 'severe' HIV infection. The 'severe' HIV classification conformed to the AIDS definition adopted in the United States of America in January 1993 [27,58].

The three immunology laboratories in Edinburgh, Glasgow and Dundee were used as a surrogate for the three geographical regions. Analysis was restricted to the three main risk categories, homosexual/bisexual, IDU, and heterosexual, giving a study population of 720 (see Table 6.04). A formal analysis was carried out using the statistical procedure HILOGLINEAR from the Advanced Statistics module of SPSSPC+ [159].

Table 6.05 shows the 95% confidence interval (95% CI) for the estimates of the main effects and two-way interactions produced by the log-linear model. The values of the parameters for the main effects confirm what is already well known about the HIV population under monitoring in Scotland; namely, that there are more HIV positive people in Edinburgh than either Glasgow or Dundee, that there are more HIV positive people whose risk activity is thought to be IDU than homosexual/bisexual or heterosexual, and more 'moderate' HIV infection than 'severe' HIV infection.

Of much greater interest than the main effects, are the interactions between region, risk, and severity of HIV infection. The interaction parameters indicate the change between the effects of the variables taken individually and taken collectively. They represent the additional effect associated with a particular combination of values.

Table 6.05 shows that statistically significant associations occur between region and risk category; in particular, it shows that Glasgow has more HIV positive homosexuals/bisexuals than expected, and that Dundee has fewer than expected. There are strong statistical associations between risk category and severity of HIV infection; in particular, homosexuals are more likely to have 'severe' HIV infection, while IDUs are more likely to have 'moderate' HIV infection. Despite the statistically significant association between region and risk category, and between risk category and severity of HIV infection, Table 6.05 shows that the association between region and severity of HIV infection is not statistically significant.

Some issues are raised by the results of these interactions :-

(1) The higher than expected number of HIV-infected male homosexuals in Glasgow indicates that this is the most important transmission route in this area, while the relatively low level of infection among the IDU and heterosexual risk categories suggests that these routes have been less important. This scenario is completely reversed in Dundee, with injecting drug use and heterosexual sex being the key routes of transmission, and homosexual spread being of little importance. These results emphasise the need to plan HIV-related services, such as prevention campaigns, to suit the different needs of the different areas.

(2) The higher than expected number of people with severe HIV infection among those infected homosexually, and the lower than expected number people with severe HIV infection among the other risk categories, have important consequences for future patient care. Although, at present, the majority of those infected by injecting drug use, or heterosexually, are still relatively well, these people will become less healthy as their infection progresses. Thus, in the future, these risk categories will need increasing levels of care. This will have important consequences for the future costs of care which will be significantly increased, particularly in Edinburgh and Dundee with their higher proportion of people infected either by injecting drug use or heterosexually.

6.4 HIV positive adults alive and under monitoring

Table 6.06 shows, for those HIV positive adults not known (at 31/12/94) to have died, the time period and value of their most recent CD4 count. These results include all CD4 counts reported to SCIEH by 15th February, 1995. The last time period, January to June 1995, is necessarily incomplete.

In Table 6.06, it is shown that 912 persons (81 per cent) had their CD4 count measured between 1st January 1994 and 15th February 1995, of whom 216 persons had their CD4 count measured in the first six weeks of 1995. There were 80 persons (7 per cent) who last had their CD4 count measured in 1992. These people may have died, and the death not reported to SCIEH, or have moved away from Scotland.

Table 6.07 shows the same information as Table 6.06, but categorised by the health board from which the most recent CD4 count was requested. This 'health board of request' is known for 1,098 persons (97 per cent). In Lothian Health Board, 486 persons (83 per cent) have had their CD4 count measured since 1st January 1994, compared with 195 (81 per cent) in Greater Glasgow Health Board, 143 (74 per cent) in Tayside Health Board, and 25 (83 per cent) in Grampian Health Board.

Table 6.08 shows the same information as Table 6.06 but categorised by risk. Risk categories have been assigned (see section 6.1.5) to 1,027 persons (91 per cent). Since 1st January 1994, 251 (88 per cent) of the HIV positive persons in the homosexual/bisexual category have undergone CD4 monitoring, compared with 430 (81 per cent) of those in the IDU category, and 140 (77 per cent) of those classified as heterosexual risk.

6.5 The future of the CD4 Study

Although the CD4 Study is relatively new, it has already become an extremely important component of HIV surveillance in Scotland. Information from the scheme is regularly requested by staff at the Scottish Office who are interested in the allocation of resources for HIV-related issues in Scotland [8].

However, as the study comes to the end of its pilot phase, there are concerns relating to its performance that need to be addressed. In particular, the quality of the clinical data is poor and data-entry is unnecessarily laborious. These issues are discussed further in chapter eight.

Chapter 7

Computer Linkage of HIV Surveillance Schemes

7.1 Linkage of HIV surveillance schemes

There is enormous potential to increase the information available from the surveillance of HIV in Scotland, by linking the records in the individual HIV surveillance schemes. This potential arises because, over a period of time, an HIV infected person is likely to appear in more than one surveillance scheme, as the following hypothetical example illustrates:-

> A woman IDU tests HIV negative in March 1989, tests HIV positive in January 1990, has her first CD4 count measured in February 1990, and has an AIDS-defining illness diagnosed in March 1994. This woman would appear first in the Denominator Study, then the HIV Register, the CD4 Study and finally the AIDS Register.

If each HIV surveillance scheme has sufficient common identifiers, such as date of birth, initials, and soundex code of surname, to enable its records to be linked to those in the other surveillance schemes, then it is possible to build up a profile, over a period of time, of HIV positive individuals. The uniformity of the use of identifiers, such as initials, date of birth, and soundex code of surname, together with the centralisation of all the surveillance data on computer at SCIEH, makes this task much easier than it would be otherwise.

However, unless the data-sets to be linked are of a similarly high quality, and the linkage is carried out with considerable care, it may present misleading information. In particular, if there are transcription errors in key identifiers such as date of birth, or if people are known by different surnames in different data-sets, then links will be missed. This may lead to an overestimation of the number of different persons contained in the new combined data-set.

Although the AIDS Register and the CD4 Study have always had good identifiers, it was not until the revision of the HIV Register was completed in 1992 [108], that the identifiers in that surveillance scheme became of a sufficiently high quality to link it with the other surveillance schemes. Since 1993, much time and effort has been expended by staff at SCIEH to identify people who are in more than one scheme.

7.2 Merger of the HIV and AIDS Registers

The first link to be made occurred in 1994, between the HIV Register and the AIDS Register. These two files were initially linked, then merged into one file, the HIV/AIDS Register, thereby providing many benefits. The following are some examples :-

(1) Data entry is simplified. Most people test HIV positive before developing an AIDS-defining illness. Such a person will have an HIV positive record, on the HIV/AIDS Register, already containing information such as initials, soundex code of surname, date of birth and probable transmission category. Hence, the record only needs to be updated with additional information pertinent to the AIDS diagnosis, e.g. date of onset of first AIDS-defining illness. If the person subsequently dies, then the date of death needs only to be entered in one combined file, instead of two separate files.

If a person has not previously tested HIV positive, then this will now be more noticeable than before the merger, prompting enquiries to be made, through the reporting clinician, about any previous HIV test which the person may have had.

(2) Data held on the HIV Register may be found to be out of date, e.g. the person may now be known to be homosexual, or may have changed name or address. With a merged file, it is easier to update the person's record with this new information.

(3) The merging of the two files allows other questions to be answered more easily, for example :-

(a) How many persons infected with HIV have progressed to AIDS?

(b) How many persons infected with HIV have died before developing an AIDS-defining illness?

7.2.1 Results from merger of HIV and AIDS Registers

Table 7.01 shows HIV positive persons and the year of their first HIV positive specimen, categorised by whether or not they have been reported to SCIEH as AIDS cases. Of the 2,209 HIV positive reports received at SCIEH by 31st December 1994 [38], it can be seen that 604 (27 per cent)

have been reported as AIDS cases.

However, contrary to expectations, Table 7.01 shows little difference between the percentage of reported AIDS cases among those persons known to be HIV positive in the early 1980s, and those not known to be HIV positive until the early 1990s. For instance, 25 per cent of people who were known to be HIV positive, in 1984, have progressed to AIDS, compared with 23 per cent of those who were first known to be HIV positive ten years later, in 1994. The figure of 25 per cent is at variance with published figures which show that, ten years after infection, 50 per cent of HIV infected people will have progressed to AIDS [31].

This apparently slow progression from HIV to AIDS might be artificial. Possible explanations are :-

(1) Some people on the HIV/AIDS Register may no longer be resident in Scotland.

(2) Some people may have had HIV tests under false names or dates of birth. For such people, it is unlikely that any subsequent AIDS reports will be capable of being matched to their original HIV positive tests. These people may appear twice on the HIV/AIDS Register, with their earlier HIV-positive test results possibly never being updated.

Table 7.02 shows information relating to deaths reported to SCIEH by 31st December 1994. Of those who were known to be HIV positive between 1983 and 1988, approximately 10 per cent have died without either having developed an AIDS defining illness, or without having being reported to SCIEH as an AIDS case.

7.3 Computer linkage of HIV/AIDS Register and CD4 Study

From the beginning of the CD4 Study, the HIV Register has been used to provide risk-category information for all patients in the CD4 Study. Since the name of the patient is on the surveillance form used to request a CD4 count, in order to preserve confidentiality it was deemed inappropriate to record risk factors for HIV on the same request form. Instead, ascertainment of the HIV risk category, for a person new to the CD4 Study, involves searching the HIV Register for the person's record, then copying the relevant information to the corresponding record in the CD4 Study database. This time-consuming procedure creates a temporary link between the person's records in both the HIV Register and the CD4 Study database, but the link is broken after the risk information has been copied.

It was clear that it would be desirable to make this link permanent. Computer linkage of the HIV/AIDS Register and CD4 Study database was started in July 1994, using the common identifiers of initials, soundex of surname and date of birth, to make the link. The format of the CD4 Study database, which collects all CD4 counts for all HIV positive persons, makes a single register, for all HIV/AIDS data and all CD4 data, too cumbersome to be easily manipulated.

In order to simplify the linkage process, each person in the HIV/AIDS Register is allocated a unique serial number (HIV record number), similarly, each person in the CD4 Study is allocated a unique serial number (CD4 record number). When a patient in the CD4 Study is identified in the HIV/AIDS Register, then the CD4 record number is copied to the HIV/AIDS Register, and the HIV record number copied to the CD4 summary record. Thus, these record numbers establish a permanent link between the two files, which remain separate, unlike the new linked HIV/AIDS Register, which is now held as one computer data file.

The main impetus for linking the two surveillance schemes is to provide answers to questions such as :-

(1) What proportion of HIV positives in each health board, and thought to be still alive, are currently under CD4 monitoring?

(2) Do persons who have only recently been tested as HIV positive have high or low CD4 counts?

7.3.1 HIV positives under CD4 monitoring

Table 7.03 shows that of the 1,591 HIV positive persons thought to be alive, 960 (60 per cent) are known to be in the CD4 Study. In all but three health boards, the number of people included in the CD4 Study is greater than the number not included in the study; the three exceptions being Dumfries and Galloway, Highland, and Grampian. The low participation rates in these three health boards may be a consequence of the practical difficulties of transporting blood specimens, from remote locations to the immunology laboratories, quickly enough for the CD4 count measurements to be viable.

From Table 7.03 it can be seen that there are 631 persons who have tested HIV positive, are thought to be alive, but are not in the CD4 Study. Further investigation is required to ascertain if these people are resident in Scotland and receiving care.

7.3.2 CD4 counts at first positive HIV test

The interpretation of CD4 counts, at HIV diagnosis, is not straightforward. The extent to which individual doctors succeed in persuading HIV positive people to encourage their partners to have HIV tests (commonly called 'contact tracing'), will affect the values of CD4 counts at HIV diagnosis. If partners test HIV positive, then their CD4 count at HIV diagnosis will almost certainly be higher than if they had waited until they had other reasons to seek HIV testing. Similarly, higher CD4 counts will occur if doctors encourage women, attending antenatal clinics, to have HIV tests. Attitudes to contact-tracing and antenatal testing may differ between doctors, hospitals and health boards, making the interpretation of CD4 counts, at HIV diagnosis, very difficult.

7.3.3 Results from linkage of HIV/AIDS Register and CD4 Study

In January 1995, using the HIV/AIDS Register linked to the CD4 Study database, an analysis was carried out to examine the CD4 counts, at time of HIV diagnosis, of persons first testing HIV positive in 1994. For 95 persons (69 per cent of the 138 persons first testing HIV positive in 1994), an HIV test and a CD4 count measurement had been conducted within

one month of each other.

Table 7.04 shows the CD4 counts for these 95 persons, classified by health board of CD4 request, risk category and gender. In particular, it is seen that 48 of the 95 persons (50 per cent) had a CD4 count of less than 200, suggesting that they were at a late stage of HIV infection, and had probably been infected with HIV several years before being identified as HIV positive. In contrast, 18 persons (19 per cent) had a CD4 count of over 500, suggesting that they were in the early stages of HIV infection.

Table 7.04 also shows that the largest group of newly identified HIV cases consisted of 28 homosexual/bisexual men from Lothian. Of these 28 men, 7 had CD4 counts of less than 200 at HIV diagnosis, compared with 7 who had CD4 counts of over 500. The second-largest group consisted of 19 homosexual/bisexual men from Greater Glasgow, of whom 9 had CD4 counts of under 200 at HIV diagnosis, and 2 had counts of over 500.

In Lothian, 15 new HIV cases were attributed to heterosexual transmission, compared with 6 in Greater Glasgow and 9 in Tayside. In each health board, there appeared to be a mixture of early-stage and late-stage HIV infection among those classified as heterosexual risk, with similar levels of immune deficiency in both males and females.

The smallest risk category was IDU, with 7 cases in Lothian, 5 in greater Glasgow and 8 in Tayside. Most persons in this category had low CD4 counts, suggesting that infection took place some years before. There were 3 male IDUs with counts of over 500, 2 in Tayside and 1 in Greater Glasgow, suggesting that there were a few early-stage infections in these groups.

A copy of a poster, presented at an MRC workshop in Manchester in 1995, showing CD4 counts at HIV diagnosis [160], is provided in the back pocket of this thesis.

7.4 Other computer linkage involving HIV surveillance data

Increasing computerisation of surveillance records at SCIEH, and at other centres, has increased the opportunity to create links between data held at different locations. This provides greater potential for additional information to be extracted from data already gathered.

When linkage of data held at SCIEH with data held in other centres is proposed, it is necessary to be extremely careful to consider all possible consequences of that linkage. In particular, there is a need to ensure that the confidentiality of the HIV surveillance data is preserved. Doctors who report AIDS cases, HIV positive test results and CD4 counts to SCIEH, do so in confidence, using soundex codes for surnames to protect their patients' identities. It is clearly wrong to use this data in such a way that patients' names or addresses might be identified.

Data, held within SCIEH, containing individual dates of birth and soundex codes, should not be made available to anyone outside SCIEH, except under very strict guidelines and with appropriate ethical approval.

In the past few years, SCIEH has approached (and has been approached by) other centres, with proposals to link the HIV Register with other data sources. In each case, a protocol has been agreed, and appropriate ethical committee approval sought, before the linkage has begun.

Two such linkages have already taken place :-

(1) Linkage of the HIV Register with data on all deaths in Scotland, between 1980 and 1991, held by the Registrar General for Scotland.

This has improved the record of deaths among those persons listed in the HIV Register, in particular by providing information on the cause of death [14].

(2) Linkage of the HIV Register with Scottish morbidity record (SMR) data collated on SMR-1 forms from 1981 to 1993.

SMR-1 forms are completed every time a patient is discharged from a ward in a Scottish hospital (excluding psychiatric wards and obstetric wards). They are also completed every time a person changes consultant or is transferred to another hospital [15]. This has enabled information to be generated on the use of hospital resources by those who are

known to be HIV positive. This includes information such as number of hospital admissions, length of stay and type of hospital. This information is clearly of great importance to those responsible for the planning of resources for patient care.

7.5 Computer linkage - the future

It is evident that computers will continue to play an increasingly important role in the collection of data. This, in turn, creates a climate that is ideal for computer linkage.

Results from computer linkage often point the way forward to new areas of research :-

(1) The results in Table 7.02 suggest that there should be more active following-up of the people who tested HIV positive in the early 1980's, and who have apparently not yet reached AIDS diagnosis, or died. A first approach might be to make enquiries as to whether, or not, any of these people are known to be registered as AIDS cases in England or Wales.

(2) The results in Table 7.03 suggest that it might be worthwhile to contact the health boards that show low participation rates in the CD4 Study, in order to investigate the extent of the immunological monitoring received by patients in these health boards.

(3) The results in Table 7.04 have implications for health education policies aimed at reducing the spread of HIV. The results indicate that preventative campaigns should be maintained, or strengthened, to encourage behavioural changes among homosexual/bisexual men.

Following the success of the linkage between the HIV Register and SMR-1 data, plans are being made to link the HIV Register with other SMR data-sets, including SMR-2 (maternity discharge records), SMR-4 (mental health in-patient admission/discharge records), and SMR-6 (cancer registration) [15].

Chapter 8

Evaluation of HIV Surveillance at SCIEH (1984 - 1994)

8.1 Evaluation of HIV surveillance

In the first six chapters of this thesis, the principal HIV surveillance schemes co-ordinated at SCIEH, between 1984 and 1994, have been examined in depth. In this final chapter, each of the principal surveillance schemes is evaluated for attributes such as simplicity, flexibility, acceptability, sensitivity, representativeness and timeliness. The schemes are also evaluated for their ability to help to answer key questions on the spread of HIV. Finally, this chapter returns to issues previously raised, in the first six chapters, about the individual surveillance schemes.

Throughout this chapter, I have expressed my own views on the value of certain aspects of HIV surveillance in Scotland. These views have been formed over the past five years, not in isolation, but after many discussions with clinicians, epidemiologists and statisticians working in the field of HIV surveillance.

8.2 Evaluation of attributes of HIV surveillance

In May 1988, CDC published guidelines for evaluating surveillance systems [47]. In this report (see section 1.8.2) the following attributes are listed as being important to a surveillance system :-

(1) Simplicity
(2) Flexibility
(3) Acceptability
(4) Sensitivity
(5) Representativeness
(6) Timeliness

8.2.1 Evaluation of attributes of the AIDS Register

The objective of the current AIDS surveillance scheme is to provide an estimate of the number of persons, in Scotland, who have AIDS, together with their epidemiological characteristics.

Clinicians throughout Scotland, who recognise that a patient has an AIDS-defining illness, are encouraged to complete an AIDS-registration form and forward it to SCIEH. This scheme relies on a patient with AIDS seeking medical help, the clinician recognising that the illness is an AIDS-defining illness, and the clinician reporting it to SCIEH.

Since almost all people who develop an AIDS-defining illness seek medical help, the level of under-reporting of AIDS cases is thought to be low, having been estimated at approximately ten per cent [8]. Hence, the sensitivity of the system is very high.

From clinical data collected by the CD4 Study, it is recognised that the AIDS-registration scheme appears to work well in the hospitals that treat a large number of AIDS patients, since these hospitals are more likely to be familiar with AIDS-defining illnesses and the AIDS-reporting scheme. However, this may not be the case in hospitals where AIDS patients are rarely seen, and consequently the reporting system is less well known. Hence, there may be a bias in favour of the larger AIDS centres in Edinburgh, Glasgow, and Dundee. However, despite this bias, the AIDS-reporting scheme rates highly for being representative of all AIDS cases in Scotland.

The AIDS-registration scheme undoubtably suffers from the complexity of the current AIDS definition, which consists of a long list of AIDS-defining illnesses [4,26,27]. In addition, the AIDS-registration form is time consuming to complete, leading often to a considerable delay between a clinician diagnosing a case of AIDS and reporting that case to SCIEH. Therefore, the AIDS-registration scheme rates poorly for simplicity, acceptability and timeliness.

The AIDS-registration scheme has proved that it is extremely flexible by coping with three changes in the AIDS-case definition between 1985 and 1993 [25-27].

8.2.2 Evaluation of attributes of the HIV Register

The purpose of the HIV-registration scheme is to provide estimates of the number of persons, in Scotland, who are infected with HIV, together with their epidemiological characteristics.

HIV surveillance relies on the HIV-infected person agreeing to have an HIV test, and also relies on that test result being reported to SCIEH. However, many HIV-infected people will not suspect that they are infected, especially if they are asymptomatic, therefore they will not seek an HIV test, hence this scheme is likely to under-represent people who are HIV infected and asymptomatic. Estimates from the GUM Study show that for every two persons known to be HIV infected there is another HIV-infected person whose infection is not known [8]. Therefore, this scheme rates poorly for both sensitivity and representativeness.

This surveillance scheme runs very smoothly, since there are few laboratories in Scotland where HIV testing is carried out, and it is relatively easy for laboratory staff promptly to report their HIV-antibody-positive test results to SCIEH. This scheme rates highly for simplicity, acceptability, flexibility and timeliness.

8.2.3 Evaluation of attributes of the Denominator Study

The purpose of the Denominator Study is to provide information about all those seeking HIV testing in Scotland, regardless of their test result.

This scheme shares many of the attributes of the HIV-registration scheme. Like the HIV Register, it relies on people seeking an HIV test and therefore shares the same problems of representativeness and sensitivity.

With almost 15,000 HIV tests carried out in Scotland every year, this surveillance scheme is much less simple to operate than the HIV Register, requiring substantial resources, particularly in staffing and computing. It is also much less timeous, with a long time delay (up to 18 months) between HIV tests being carried out and the results being published.

8.2.4 Evaluation of attributes of UAT

UAT surveillance was introduced in 1990 to provide unbiased estimates of HIV prevalence, in selected population groups, over a period of time. There are five such UAT schemes in Scotland, all of them operating in a similar way.

Since participation rates are extremely high, these surveillance schemes are all highly representative of the population groups targeted, with initial doubts about the acceptability of the schemes [145] having been shown to be unfounded. However, several of the schemes are extremely limited in their geographical spread; such as the Hospital Study which is limited to two Glasgow hospitals, the Family Planning Study which is limited to one Glasgow clinic, and the Antenatal Study which is limited to Glasgow and Edinburgh.

These schemes are all relatively simple to operate, and timeous, with results being available at SCIEH within a few months of the person attending the participating clinic. However, the schemes rate poorly for flexibility, since the collection of more information, such as risk factors or postcode of residence, may be seen as a threat to the confidentiality of the participants.

8.2.5 Evaluation of attributes of the CD4 Study

The objective of the CD4 surveillance scheme is to monitor the clinical and immunological health of those HIV-infected people, in Scotland, who are receiving CD4 monitoring.

Since there are only five immunology laboratories participating in the scheme, and their staff report all HIV-positive immunological requests promptly to SCIEH every month, this scheme rates highly for simplicity, sensitivity and timeliness. However, since many of the immunological measurements must be performed within a few hours of the patient giving the blood sample, these laboratories can only process blood samples from their own locality. Therefore, although this surveillance scheme is representative of those requiring treatment in the main cities, it does not represent those who live in the more remote parts of Scotland.

The quality of the data collected has been variable, with extremely good immunological information and extremely poor clinical data being returned. Analysis showed that approximately one third of all forms returned contained no clinical information. Hence, the scheme appears to be acceptable to the immunologists, but not acceptable to the clinicians.

This study is extremely flexible; as immunological advances continue and new markers of HIV progression are discovered, this scheme will have the flexibility to include any new immunological measurements that are appropriate.

8.3 Utilisation of HIV surveillance data

Surveillance has been defined as :-

> "*The ongoing systematic collection, analysis and interpretation of health data essential to the planning, implementation and evaluation of public health practice, closely linked with the timely dissemination of these data to those who need to know.*" [161].

Identification of the information required by those in a position to use it, is fundamental to good surveillance. In the surveillance of HIV, key areas where information is most useful include :-

(1) Monitoring the heterosexual spread of HIV among the general population.

(2) Identification of the epidemiological characteristics of those infected recently.

(3) Estimation of the current and future prevalence of HIV infection.

8.3.1 Monitoring the heterosexual spread of HIV in the general population

From the beginning of the HIV epidemic, it has been apparent that most of the reported cases of HIV, in Scotland, have been confined to specific risk categories, particularly IDUs and homosexual/bisexuals. Analysis of the HIV Register, to 30th June 1994, shows that of the 2,129 HIV positive reports, 50 per cent are attributed to injecting drug use, and a further 29 per cent to homosexual/bisexual risk [6].

The heterosexual spread of HIV, from the IDU and homosexual/bisexual risk categories to the rest of the general population, has stimulated a great deal of interest [120-126]. Accordingly, a series of UAT schemes were established, between 1990 and 1993, to examine this spread (see chapter 5).

In 1990, the GUM Study was introduced to monitor the spread of HIV among men and women presenting with a suspected sexually

transmitted disease at GUM clinics. It was recognised that if infection were to spread heterosexually into the general population, then this would first be apparent among this group. This study collects data on risk factors, therefore analysis can separate those whose risk factor is solely heterosexual from those who are either IDU or homosexual/bisexual. It includes both males and females, covering GUM clinics in Glasgow, Edinburgh, Dundee, Aberdeen, Falkirk, Stirling and Perth.

In addition to the GUM Study, other UAT studies were introduced to measure the spread of HIV in the general population. These included the Antenatal Study, the Guthrie Study, the Hospital Study and the Family Planning Study. Of these studies, the Hospital Study is the only one in which the spread of HIV among males is measured. However, the study design does not permit HIV-risk factors to be collected, hence its data is of limited value in assessing the heterosexual spread of HIV.

Similarly, the designs of both the Guthrie Study and the Family Planning Study do not permit risk factors to be collected. Despite this drawback, the Guthrie Study is extremely useful because it covers every baby who has a Guthrie test in Scotland, providing valuable data on the spread of HIV among childbearing women. Less useful are the Hospital Study, which is restricted to two Glasgow hospitals, and the Family Planning Study which is restricted to one Glasgow clinic.

The Antenatal Study is the only one of this group of studies to collect risk factors, thereby enabling measurement of the spread of HIV among women whose only risk factor for HIV is heterosexual. Unfortunately this study is restricted to antenatal clinics in Edinburgh and Dundee.

8.3.2 Identification of new infection

The identification of new infection is an important part of HIV surveillance. If infection is suspected to be occurring in identifiable groups of people, education can be targeted at those groups.

To determine where new HIV infection is occurring, is an extremely difficult task. The long and variable incubation period, between infection with HIV and the development of clinical symptoms, means that people who are infected with HIV may not know that they are infected. Even those who do know that they are infected, may not know

when, or how, they became infected.

The HIV Register provides information on newly reported infection, but it cannot be used to discriminate between new and old infection. Comparison with the Denominator Study has provided information on previous negative tests for about 4 per cent of persons on the HIV Register, thus narrowing the time of infection for these persons to a specific interval.

The data on the HIV Register may be further enhanced by linkage with the CD4 Register. For some people on the HIV Register, the CD4 Study provides CD4 counts at the time of their HIV diagnosis. Although a high CD4 count does not prove that a person has been recently infected, it is generally an indication of recent infection.

In this way, these three studies, the HIV Register, the Denominator Study and the CD4 Study, together help to identify recent infection.

8.3.3 Estimation of prevalence of HIV

Estimates of the prevalence of HIV are needed in order to assess the demand on resources. Some resources, such as provision of patient care, need to be planned some years in advance, which necessitates furnishing information not only on current numbers of HIV-infected people, but also on the numbers expected in the years ahead. However, it is extremely difficult to determine the prevalence of HIV.

The CD4 Study collects data on the immunological and clinical staging of only those HIV-infected people who are receiving lymphocyte monitoring at the participating immunology laboratories in Edinburgh, Glasgow, Dundee and Aberdeen. Hence the CD4 Study plays a key role in assessing the number of people currently requiring resources in these areas, but needs to be supplemented by information from the HIV Register about those thought to be living in other parts of Scotland.

Estimation of the prevalence of HIV, in Scotland, involves combining the number of persons known to be infected with HIV (i.e. on the HIV Register) with an estimate of the unknown number of persons infected with HIV (i.e. not on the HIV Register). This can be estimated using the results of the GUM Study.

The GUM Study provides estimates of the proportion of HIV positive people who are known to be HIV positive, classified by risk

category and region. Using data from this study it can be shown that approximately 66 per cent of all HIV positive people have had a positive HIV test and are known at SCIEH to be HIV positive, although this proportion varies between risk categories and regions [8]. Therefore, in general, for every two persons currently on the HIV Register, and assumed to be alive, there is another person with HIV infection who has not yet been reported.

Assessing future numbers of HIV-infected people, who will require substantial health care owing to their HIV infection, is a complex exercise which has been conducted by various working groups [8,16-18]. Methodology, to estimate future numbers of AIDS cases, has been developed using reports of AIDS cases, HIV infections, and deaths, in addition to estimates of HIV prevalence, and rates of progression from HIV infection to AIDS (see section 2.7). Estimates of future numbers of severe HIV infections have been based on previous, and current, CD4 counts.

Thus, for the estimation of the current and future prevalence of HIV infection, the key surveillance schemes are the AIDS Register, the HIV Register, the CD4 Study and the GUM Study.

8.4 Issues surrounding HIV surveillance in Scotland

If surveillance schemes are to remain effective, it is important to re-examine them regularly, and to look for possible improvements. This helps to optimise the use of resources made available for surveillance. Numerous questions have been asked concerning the performance and value of some of the HIV surveillance schemes. In particular, concern has been expressed as follows :-

(1) Is AIDS surveillance still relevant and useful?

(2) Should the Denominator Study be streamlined?

(3) Should the CD4 Study be modified?

(4) Are all the UAT schemes necessary?

8.4.1 Issues arising from AIDS surveillance

Many clinicians are sceptical about the value of the term AIDS. The clinician, who may have been caring for the patient from an early stage of HIV infection through to the later stages, often holds AIDS to be a rather artificial milestone of little consequence. Indeed, the awareness that such a milestone has been reached may create psychological problems for the patient [162].

The growth of immunological monitoring in Scotland (particularly CD4 monitoring) has played a large part in undermining the relevance of the term AIDS, since CD4 monitoring provides a means of measuring the deterioration of the immune system throughout all stages of HIV infection.

Is AIDS registration still relevant and useful? It is unquestionably true that, in the early 1980's, AIDS registrations were the only way of measuring the number of people affected by this newly discovered, and unexplained, immune deficiency syndrome. However, fifteen years later, this is no longer true, with the term 'AIDS' having become virtually redundant for many professionals working in HIV-related fields in Scotland. However, there are many reasons why AIDS surveillance will continue for the foreseeable future :-

(1) The AIDS Control Act (1987) makes it a statutory requirement to report the number of (and details concerning) AIDS cases in Scotland [163].
(2) Although immunological monitoring is widespread in Scotland, this is not the case in many other countries. Therefore, for the purposes of producing figures for comparison with other countries, reporting of AIDS cases will continue to be important.
(3) While the term 'AIDS' may be an anachronism to many professionals in Scotland, it is firmly established in the mind of the public. The concern of the public, and the media, regarding the number of people with AIDS, is unlikely to diminish in the near future.

In summary, the AIDS-registration scheme has many inherent problems, and is now playing a less important role in the surveillance of HIV infection in Scotland than it previously did. However, it has become an established means of reporting, has international importance, and will almost certainly remain an integral part of HIV surveillance in Scotland for the foreseeable future.

8.4.2 Issues arising from the Denominator Study

The long time delay between HIV tests being carried out and the results being published needs addressed. This is mostly attributable to the cumbersome task of checking for persons who have been tested on more than one occasion within any one calendar year. This task cannot be completed until all the tests for that calendar year have been reported. As a consequence, results from the Denominator Study, for any one year, are not usually available until the middle of the following year. The time-consuming nature of duplicate-checking raises doubts about the efficiency of this task.

If full responsibility for the identification of duplicate tests was transferred to the clerical officers employed by SCIEH at the principal laboratories, this would enable duplicates to be identified more accurately within each laboratory, at the expense of being unable to identify inter-laboratory duplicates. This would only leave SCIEH to identify duplicate tests within each of the smaller laboratories. In my opinion, the

Denominator Study should be streamlined by delegating the task of identifying duplicate tests to clerical officers at these laboratories.

Another issue arising from the Denominator Study involves the quality of the information collected. Many clinicians do not fill-in all the sections of the HIV test-request form, hence much of the data collected is incomplete. The clinicians need to be questioned about their reasons for these omissions: it may be necessary to modify or simplify the request form.

8.4.3 Issues arising from the CD4 Study

The CD4 Study is currently at the end of its pilot stage. Several issues have arisen concerning the operation of the study and the quality of the data collected.

The quality of the clinical data is poor. A new and simpler request form has been drafted, and will be used after consultation with the clinicians and immunologists.

Problems were also identified with data-entry at the immunology laboratories, leading to the installation of computers and standard DATAEASE software at the HIV immunology laboratories in Edinburgh, Glasgow and Dundee.

Concern has also been expressed about the use of CD4 counts as a measure of immune deficiency. The CD4 count is simply a measure of the quantity of cells, disregarding quality. The fact that difficulties may arise from the use of CD4 counts to measure progression, was demonstrated in the Concorde Study in which the aim was to determine whether or not symptom-free HIV positive people would benefit from starting treatment with zidovudine before they developed clinical disease. The Concorde Study showed statistically significant differences in CD4 counts between the groups, but there were no corresponding differences in either disease-progression or survival [164]. However, as immunological advances continue, and as new markers of HIV progression are discovered, such aspects can easily be incorporated into this flexible surveillance scheme.

8.4.4 Issues arising from UAT

At the end of the pilot stage, each study was assessed, leading to changes being made in the populations being studied in both the Hospital Study and the GUM Study. After its pilot phase, the Hospital Study was restricted to men, because sufficient information on HIV prevalence among women was available from other UAT studies. After the pilot phase of the GUM Study, it was expanded (from Glasgow and Edinburgh) to encompass GUM clinics in Aberdeen, Dundee, Falkirk, Perth and Stirling.

Each of the UAT studies makes its own unique contribution to the understanding of HIV prevalence in Scotland, its value being reflected in the value of the data collected :-

(1) The GUM Study measures HIV prevalence among men and women attending GUM clinics throughout a wide area of Scotland. It collects information on HIV risk as well as data on the person's current STDs. Hence, the data it provides are extremely valuable. Table 8.01 shows that the prevalence of HIV among people presenting with a new risk of a sexually transmitted disease, has remained relatively constant over the study period, at approximately 0.5 per cent in Glasgow and 1 per cent in Edinburgh.

(2) The Hospital Study measures HIV prevalence among men attending two Glasgow hospitals. Table 8.01 shows a relatively high prevalence of HIV among this group at approximately 0.8 per cent. Unfortunately, clinicians deemed it intrusive to seek risk category information about these men, so the data collected are hard to interpret, and contribute little to the overall understanding of HIV prevalence in Scotland.

(3) The Guthrie Study measures HIV prevalence among all women, in Scotland, whose baby is given a Guthrie test. Its main advantage is that it tests the mothers of over 99 per cent of all babies born in Scotland every year [155]. Thus, this study provides very valuable data on HIV prevalence. Table 8.01 shows that HIV prevalence among these women has remained relatively stable, at less than 0.03 per cent, in all areas of Scotland except Edinburgh and Dundee,

where prevalence has fluctuated between 0.1 per cent and 0.3 per cent.

(4) The Family Planning Study measured HIV prevalence among women attending a family-planning practice in Glasgow. Since this study was restricted to one centre, and did not collect risk factors, the data gathered contributed little to the overall understanding of HIV prevalence in Scotland. Accordingly, this study was terminated in 1995.

(5) The Antenatal Study, started in July 1994, collects data on HIV prevalence among women attending antenatal clinics in Edinburgh and Dundee. It collects risk category information, as well as information on the type of clinic attended, and the mother's intention to continue with her pregnancy. Hence, this study will be extremely valuable in measuring the prevalence of HIV among women considered to be at low risk of acquiring HIV.

While some of the UAT surveillance schemes are undoubtedly of more value than others, they all shed light on a different aspect of HIV infection in Scotland, with none having a monopoly on the truth. Indeed, the informal links between many of the studies makes the value of the surveillance programme, as a whole, far greater than the sum of its component parts.

Epilogue

The challenges posed by HIV to the scientific world have been immense. However, substantial progress has been made, and much has been discovered about the virus, its structure, and its effect on the immune system. Likewise, considerable progress has been made in the treatment of the illnesses that are associated with the virus.

It is also true that HIV has posed a great challenge to society, where the response has been handicapped by prejudice and fear, fuelled by misunderstanding and ignorance [46]. While much has been achieved, there is no room for complacency. With an estimated 6,000 people becoming infected with HIV every day, equivalent to one every 14 seconds [165], much remains to be done.

As the recent brochure [166] promoting the XI International Conference on AIDS in July 1996, in Vancouver, states :-

> "*The answers to our many questions about preventing, managing, and curing HIV/AIDS lie in our ability to unite, in our willingness to accept difference, and in the unwavering commitment of people and nations to one another.*"

It is largely as a result of the willingness of many professionals, in HIV-related disciplines, to work together for the benefit of all, that the surveillance schemes described in this thesis have been developed. It is only with their continuing support that these surveillance schemes will progress, leading to a better understanding of the spread of HIV infection in Scotland.

Tables

AIDS Cases Reported to SCIEH by 31/12/87

	AIDS CASES	
	Number	**Percentage**
TOTAL CASES	39	100.0%
GENDER		
Male	34	87.2%
Female	5	12.8%
RISK CATEGORY		
Homo/Bisex	26	66.7%
IDU	4	10.3%
Heterosex	1	2.6%
Haem/Blood	7	17.9%
Mother-to-Child	1	2.6%
YEAR OF AIDS DIAGNOSIS		
1983	1	2.6%
1984	4	10.3%
1985	4	10.3%
1986	9	23.1%
1987	21	53.8%
AGE GROUP AT AIDS DIAGNOSIS		
Male 0 - 9 (Years)	0	0.0%
10 - 19	2	5.1%
20 - 29	1	2.6%
30 - 39	17	43.6%
40 - 49	9	23.1%
50+	5	12.8%
Male Total	34	87.2%
Female 0 - 9 (Years)	1	2.6%
10 - 19	0	0.0%
20 - 29	3	7.7%
30 - 39	1	2.6%
40 - 49	0	0.0%
50+	0	0.0%
Female Total	5	12.8%
PRESENTATION AT AIDS DIAGNOSIS		
OOI	15	38.5%
PCP	19	48.7%
KS	4	10.3%
KS+PCP	1	2.6%

Table 2.01

Hierarchical Rules for Allocation of Risk Category

Level 1	Homosexual/bisexual Injecting drug user Homosexual/bisexual and injecting drug user Haemophiliac Mother to child Blood transfusion
Level 2	Heterosexual (high risk partner) ie partner belongs to level 1
Level 3	Heterosexual (abroad)
Level 4	Heterosexual (United Kingdom)

Notes :

1 Level 1 takes precedence over level 2, etc.

2 The risk level is determined first by the risk activities of the patient, then the partner. The HIV status of the partner is not considered.

Table 2.02

Hierarchical Rules for Allocation of Presentation at AIDS Diagnosis

Level 1	Kaposi's Sarcoma (KS) Pneumocistis Carinii Pneumonia (PCP) KS + PCP
Level 2	Other Opportunistic Infection (OOI)
Level 3	Cerebral lymphoma
Level 4	Non-Hodgkin's lymphoma
Level 5	Encephalopathy
Level 6	Lymphoid Interstitial Pneumonia (LIP)
Level 7	Progressive Multifocal Leukoencephalopathy (PML)
Level 8	Wasting

Note : Level 1 takes precedence over level 2, etc.

Table 2.03

AIDS Cases Diagnosed by 31/12/93

Calendar Quarter of Diagnosis by Reporting Delay

CALENDAR QUARTER	REPORTING DELAY (MONTHS)													TOTAL
	<1	1-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24	25-27	28-30	31-33	>33	
Jan-Mar '89	2	12	1	0	0	0	0	0	1	0	1	0	0	17
Apr-Jun '89	3	10	2	0	0	1	0	0	1	1	1	0	0	19
Jul-Sep '89	3	13	3	0	0	1	0	1	0	0	0	0	1	22
Oct-Dec '89	1	9	1	2	0	0	0	1	0	0	0	0	2	16
Jan-Mar '90	0	8	4	0	0	0	0	0	1	0	0	0	1	14
Apr-Jun '90	3	10	1	2	1	1	0	0	0	0	1	1	0	20
Jul-Sep '90	1	10	1	2	2	1	1	0	0	1	0	0	0	19
Oct-Dec '90	1	12	3	2	0	0	0	0	1	1	0	0	0	20
Jan-Mar '91	1	17	8	1	1	1	0	0	1	1	0	0	0	31
Apr-Jun '91	1	7	5	2	0	0	4	3	0	1	0	0	-	23
Jul-Sep '91	0	14	4	1	1	0	1	0	0	0	0	-	-	21
Oct-Dec '91	3	8	2	0	3	3	0	1	0	0	-	-	-	20
Jan-Mar '92	1	9	2	4	1	1	1	2	0	-	-	-	-	21
Apr-Jun '92	1	5	5	0	2	0	0	0	-	-	-	-	-	13
Jul-Sep '92	0	9	3	3	0	2	1	-	-	-	-	-	-	18
Oct-Dec '92	4	9	1	0	4	1	-	-	-	-	-	-	-	19
Jan-Mar '93	6	17	4	0	2	-	-	-	-	-	-	-	-	29
Apr-Jun '93	0	8	5	1	-	-	-	-	-	-	-	-	-	14
Jul-Sep '93	5	17	5	-	-	-	-	-	-	-	-	-	-	27
Oct-Dec '93	3	5	-	-	-	-	-	-	-	-	-	-	-	8
TOTAL	39	209	60	20	17	12	8	8	5	5	3	1	4	391

- Structural zero, insufficient time elapsed

Shaded areas are necessarily incomplete

Table 2.04

AIDS Cases Reported to SCIEH by 30/4/94

			AIDS CASES	
			Number	Percentage
TOTAL CASES			512	100.0%
RISK CATEGORY (by Gender)				
Male	Homo/Bisex		224	43.8%
	IDU		133	26.0%
	Heterosex		35	6.8%
	Haem/Blood		27	5.3%
	Mother-to-Child		3	0.6%
	Unknown		3	0.6%
		Male Total	425	83.0%
Female	Homo/Bisex		0	0.0%
	IDU		52	10.2%
	Heterosex		21	4.1%
	Haem/Blood		5	1.0%
	Mother-to-Child		8	1.6%
	Unknown		1	0.2%
		Female Total	87	17.0%
YEAR OF AIDS DIAGNOSIS				
	Pre 1990		162	31.6%
	1990		73	14.3%
	1991		99	0.0%
	1992		73	14.3%
	1993		91	17.8%
	1994		14	0.0%
AGE GROUP AT AIDS DIAGNOSIS				
Male	0 - 9	(Years)	4	0.8%
	10 - 19		7	1.4%
	20 - 29		124	24.2%
	30 - 39		164	32.0%
	40 - 49		91	17.8%
	50+		35	6.8%
		Male Total	425	83.0%
Female	0 - 9	(Years)	8	1.6%
	10 - 19		1	0.2%
	20 - 29		34	6.6%
	30 - 39		36	7.0%
	40 - 49		6	1.2%
	50+		2	0.4%
		Female Total	87	17.0%
PRESENTATION AT AIDS DIAGNOSIS				
	OOI		149	29.1%
	PCP		256	50.0%
	KS		29	5.7%
	KS+PCP		4	0.8%
	WASTING		17	3.3%
	OTHER		57	11.1%

Table 2.05

Results of Univariate Survival Analysis from AIDS Diagnosis to Death

	N	DEATHS *	MEDIAN SURVIVAL (Months)	SURVIVAL AT X YEARS (%) X=1	X=2	X=3	P VALUE
ALL CASES	394	304	17.04	59.64	36.68	21.59	
GENDER							P=0.08
Male	341	267	16.18	57.86	35.3	21.02	
Female	53	37	21.96	71.15	45.67	25.04	
RISK CATEGORY							P=0.06
Homo/Bisex	189	157	17.46	61.8	35.84	18.74	
IDU	136	95	18.83	60.74	41.86	27.54	
Heterosex	41	25	16.63	60	34.05	-	
Haem/Blood	26	25	9.75	38.46	-	-	
Unknown	2	2	-	-	-	-	
PERIOD OF AIDS DIAGNOSIS							P=0.02
Pre 1988	51	48	11.33	47.06	27.03	16.64	
1988 - 1989	104	89	22.45	73.4	46.52	21.92	
1990 - 1992	239	167	15.53	56.45	34.54	23.74	
AGE GROUP AT AIDS DIAGNOSIS							P<0.001
15 - 24 (Years)	36	30	20.96	69.44	43.4	23.37	
25 - 29	98	59	25.58	72.77	51.65	39.13	
30 - 34	97	79	13.96	53.37	32.71	17.84	
35 - 44	103	79	18.18	61.58	39.09	18.24	
45+	60	57	9.92	39.5	12.02	-	
PRESENTATION AT AIDS DIAGNOSIS							P<0.001
OOI	106	76	14.99	53.62	39.1	21.9	
Other	16	15	8	25	-	-	
HIV Enceph.	20	18	8.57	30	-	-	
KS	30	24	16.14	62.71	25.82	-	
PCP	211	162	20.34	68.97	41.69	24.04	
HIV Wasting	11	9	9	33.33	-	-	
HEALTH BOARD OF FIRST REPORT							P=0.01
Greater Glasgow	121	93	16.04	57.63	34.95	19.97	
Lothian	183	139	20.43	65.84	43.3	25.14	
Tayside	49	39	10.5	42.86	19.69	-	
Other	41	33	15.73	58.02	32.24	20.51	

* DEATHS refer to uncensored deaths only.

Table 2.06

Results of Multivariate Survival Analysis from AIDS Diagnosis to Death

	COEFFICIENT	RELATIVE RISK (R.R.)	STANDARD ERROR of R.R.	95% C.I. for R.R.
GENDER				
Male	0.000	1.000	-	-
Female	-0.214	0.807	0.198	(0.548 , 1.190)
RISK CATEGORY				
Heterosex	0.000	1.000	-	-
Homo/Bisex	-0.138	0.871	0.220	(0.566 , 1.342)
IDU	-0.108	0.898	0.224	(0.579 , 1.392)
Haem/Blood	0.333	1.395	0.291	(0.789 , 2.466)
Unknown	0.472	1.603	0.748	(0.370 , 6.937)
PERIOD OF AIDS DIAGNOSIS				
Pre 1988	0.000	1.000	-	-
1988 - 1989	-0.168	0.846	0.192	(0.581 , 1.231)
1990 - 1992	-0.145	0.865	0.186	(0.600 , 1.247)
AGE GROUP AT AIDS DIAGNOSIS				
15 - 24 (Years)	0.000	1.000	-	-
25 - 29	-0.149	0.862	0.243	(0.535 , 1.388)
30 - 34	0.370	1.448	0.237	(0.910 , 2.305)
35 - 44	0.233	1.262	0.242	(0.785 , 2.029)
45+	0.852	2.344	0.260	(1.410 , 3.898)
PRESENTATION AT AIDS DIAGNOSIS				
PCP absent	0.000	1.000	-	-
PCP present	1.163	3.201	0.628	(0.935 , 10.962)
KS absent	0.000	1.000	-	-
KS present	1.113	3.044	0.598	(0.944 , 9.820)
OOI absent	0.000	1.000	-	-
OOI present	1.248	3.483	0.645	(0.984 , 12.326)
HIV Enceph. absent	0.000	1.000	-	-
HIV Enceph. present	1.665	5.283	0.677	(1.402 , 19.914)
HIV Wasting absent	0.000	1.000	-	-
HIV Wasting present	1.905	6.719	0.729	(1.610 , 28.038)
OTHER absent	0.000	1.000	-	-
OTHER present	2.190	8.937	0.696	(2.286 , 34.945)
HEALTH BOARD OF FIRST REPORT				
Lothian	0.000	1.000	-	-
Greater Glasgow	0.118	1.125	0.147	(0.843 , 1.502)
Tayside	0.578	1.782	0.200	(1.204 , 2.637)
Other	0.109	1.115	0.205	(0.746 , 1.668)

Significant at 5% level.

Table 2.07

HIV+ Tests Reported to SCIEH from 1/1/89 to 30/6/94

	HIV+ TESTS	
	Number	**Percentage**
SOURCE OF HIV TEST REQUEST		
Hospital	261	37.1%
Gum Clinic	142	20.2%
Counselling Clinic	74	10.5%
GP	112	15.9%
Other	115	16.3%
TOTAL	**704**	**100.0%**
REASON FOR HIV TEST REQUEST		
Doctor Concerned	244	34.7%
Patient Concerned	297	42.2%
Other	67	9.5%
Unknown	96	13.6%
TOTAL	**704**	**100.0%**

Table 3.01

HIV+ Tests Reported to SCIEH by 30/6/94

by Health Board of Residence and Health Board of Test Request

HB OF RESIDENCE	HEALTH BOARD OF TEST REQUEST													TOTAL
	A&C	A&A	BORD	D&G	FIFE	FV	GRAMP	GG	HIGH	LAN	LOTH	TAYS	OTHER	
ARGYLL & CLYDE	13	0	0	0	0	1	0	32	0	1	0	0	0	47
AYRSHIRE & ARRAN	0	13	0	0	0	0	0	16	0	0	1	0	0	30
BORDERS	0	0	7	0	0	0	0	0	0	0	4	0	0	11
DUMFRIES & GALLOWAY	0	0	0	7	0	0	0	7	0	0	2	0	0	16
FIFE	0	0	0	0	22	1	0	0	0	0	6	5	0	34
FORTH VALLEY	0	0	0	0	0	16	0	10	0	0	2	0	0	28
GRAMPIAN	0	0	0	0	0	0	73	0	0	0	1	1	0	75
GREATER GLASGOW	1	0	0	0	0	8	0	305	0	12	5	2	0	333
HIGHLAND	0	0	0	0	0	0	1	0	20	0	1	0	0	22
LANARKSHIRE	0	0	0	0	0	0	0	20	0	26	0	0	0	46
LOTHIAN	0	0	2	0	0	10	0	4	0	1	498	2	0	517
TAYSIDE	0	0	0	0	0	4	0	1	0	0	3	270	0	278
UNKNOWN/OTHER	2	2	1	4	15	21	4	65	7	7	500	63	1	692
TOTAL	**16**	**15**	**10**	**11**	**37**	**61**	**78**	**460**	**27**	**47**	**1,023**	**343**	**1**	**2,129**

Table 3.02

HIV+ Tests Reported to SCIEH by 30/6/94
by Risk Category

RISK CATEGORY		HIV+ TESTS	
		Number	Percentage
HOMO / BISEX		609	28.6%
IDU		1,037	48.7%
HETEROSEX			
	High Risk Partner	92	
	Other Partner (Abroad)	88	
	Other Partner (United Kingdom)	35	
	Not Known	79	
		294	13.8%
HAEM/BLOOD		101	4.7%
MOTHER-TO-CHILD		23	1.1%
UNKNOWN / OTHER		65	3.1%
TOTAL		**2,129**	**100.0%**

Table 3.03

HIV+ Tests Reported to SCIEH by 30/6/94
by Year of Specimen and Risk Category

YEAR OF SPECIMEN	RISK CATEGORY						TOTAL
	Homo/Bisex	IDU	Heterosex	Haemophiliac	Mother-to-Child	Unknown/Other	
Pre 1984	25	63	1	21	0	6	**116**
1984	15	202	4	23	0	6	**250**
1985	71	167	2	22	4	9	**275**
1986	78	208	20	2	2	15	**325**
1987	68	136	24	2	4	14	**248**
1988	45	54	32	2	0	6	**139**
1989	44	38	24	1	2	5	**114**
1990	55	29	39	0	3	6	**132**
1991	60	50	40	0	5	8	**163**
1992	53	27	52	1	1	3	**137**
1993	62	51	38	0	2	5	**158**
1994	33	12	18	0	0	9	**72**
TOTAL	**609**	**1,037**	**294**	**74**	**23**	**92**	**2,129**

Table 3.04

Results of Univariate Survival Analysis from First HIV+ Specimen to Death

	N	DEATHS	SURVIVAL AT X YEARS (%)					P VALUE
			X=1	X=2	X=5	X=8	X=10	
ALL TESTS	1,668	430	96	93	82	70	62	
GENDER								P < 0.0001
Male	1,232	356	95	91	80	66	58	
Female	436	74	98	97	87	79	71	
RISK CATEGORY								P < 0.0001
Homo/Bisex	447	162	93	85	66	51	-	
Heterosex	226	37	92	92	83	-	-	
IDU	884	204	98	97	89	76	67	
Unknown/Other	111	27	95	90	-	-	-	
AGE GROUP AT FIRST HIV+ SPECIMEN								P < 0.0001
15 - 24 (Years)	648	144	99	98	90	77	68	
25 - 34	672	159	96	94	84	70	64	
35 - 44	222	78	94	88	68	51	-	
45+	126	49	86	72	65	-	-	
HEALTH BOARD OF FIRST HIV+ SPECIMEN								P < 0.0001
Greater Glasgow	334	97	92	87	75	64	-	
Lothian	850	205	98	96	87	74	65	
Tayside	260	64	96	92	81	68	-	
'Other'	224	64	94	89	83	-	-	

Table 3.05

Results of Multivariate Survival Analysis from First HIV+ Specimen to Death

	COEFFICIENT	RELATIVE RISK (R.R)	STANDARD ERROR of R.R	95% C.I. for R.R.
GENDER				
Male	0.000	1.00	-	-
Female	-0.266	0.77	0.140	(0.6 , 1.0)
RISK CATEGORY				
Heterosex	0.000	1.00	-	-
IDU	-0.257	0.77	0.192	(0.5 , 1.1)
Homo/Bisex	0.452	1.57	0.197	(1.1 , 2.3)
Unknown/Other	-0.452	0.64	0.265	(0.4 , 1.1)
AGE GROUP AT FIRST HIV+ SPECIMEN				
15 - 24 (Years)	0.000	1.00	-	-
25 - 34	0.160	1.17	0.120	(0.9 , 1.5)
35 - 44	0.702	2.02	0.151	(1.5 , 2.7)
45+	0.743	2.10	0.175	(1.5 , 3.0)
HEALTH BOARD OF FIRST HIV+ SPECIMEN				
Lothian	0.000	1.00	-	-
Greater Glasgow	0.189	1.21	0.133	(0.9 , 1.6)
Tayside	0.429	1.54	0.147	(1.2 , 2.0)
Other	0.373	1.45	0.151	(1.1 , 2.0)

Significant at 5% level.

Table 3.06

Average Number of HIV Tests per Year
by HIV Testing Laboratories

LABORATORY	LOCATION	HIV TESTS
Principal Laboratories		**Average No. per Year**
Aberdeen University	Aberdeen	1,738
Ninewells Hospital	Dundee	1,668
City Hospital	Edinburgh	2,661
East of Scotland HIV Ref. Lab.	Edinburgh	2,227
Ruchill Hospital	Glasgow	3,880
Western Infirmary	Glasgow	713
Small Laboratories		
Dumfries & Galloway Royal Infirmary	Dumfries	183
Victoria Infirmary	Kirkaldy	261
Inverclyde Royal Infirmary	Greenock	132
Crosshouse Hospital	Kilmarnock	376
Law Hospital	Carluke	90
Monklands District General Hospital	Airdrie	266
Stirling Royal Infirmary	Stirling	561
Royal Alexandra Hospital	Paisley	131
Raigmore Hospital	Inverness	421

Table 4.01

Persons Tested and Rate of Testing HIV+
by Gender, Age Group, and Year of HIV Test

	YEAR OF HIV TEST			
	1989	**1990**	**1991**	**1992**
NUMBER OF PERSONS TESTED				
Gender				
Male	6,228	6,678	8,076	8,100
Female	3,423	4,041	5,178	4,949
Total	**9,651**	**10,719**	**13,254**	**13,049**
Age Group				
15-19 (Years)	748	750	1,094	1,116
20 - 29	4,013	4,502	6,113	6,076
30 - 39	2,409	2,862	3,429	3,332
40 +	2,481	2,605	2,618	2,525
Total	**9,651**	**10,719**	**13,254**	**13,049**
PERSONS TESTING HIV+ (PER 1000 TESTED)				
Overall	**13.0**	**11.5**	**10.8**	**9.8**
Gender				
Male	16.1	14.2	13.7	10.8
Female	7.3	7.2	6.4	8.1
Age Group				
15 - 19 (Years)	4.0	4.0	1.8	1.8
20 - 29	18.4	13.8	11.6	9.9
30 - 39	12.9	15.4	12.0	13.5
40 +	6.9	5.4	11.5	7.9

Table 4.02

Persons Testing HIV+ and Test Rates
by Gender, Age Group, and Health Board

	TOTAL TESTS	POPULATION (Thousands)	TEST * RATE	NUMBER HIV+	HIV+ ** RATE
MALE					
Age Group					
15-19 (Years)	1,887	172.8	2.7	2	1.1
20-24	6,351	207.1	7.7	60	9.4
25-29	6,286	208.5	7.5	118	18.8
30-34	4,586	194.0	5.9	82	17.9
35-39	3,225	171.6	4.7	57	17.7
40-44	2,118	178.9	3.0	33	15.6
45+	4,629	837.7	1.4	39	8.4
FEMALE					
Age Group					
15-19 (Years)	1,821	166.0	2.7	8	4.4
20-24	4,188	203.3	5.2	44	10.5
25-29	3,879	207.5	4.7	45	11.6
30-34	2,586	193.9	3.3	12	4.6
35-39	1,635	171.2	2.4	10	6.1
40-44	888	179.4	1.2	1	1.1
45+	2,594	1048.2	0.6	8	3.1
HEALTH BOARD OF RESIDENCE					
Greater Glasgow	11,114	751.3	3.7	93	8.4
Lothian	13,669	619.5	5.5	239	17.5
Grampian	4,887	416.4	2.9	23	4.7
Tayside	4,409	320.9	3.4	84	19.1
Other	12,157	2032.5	1.5	75	6.2

* Test rate per 1000 population (per year).

** Number of persons testing HIV positive per 1000 tested.

Table 4.03

Results of Logistic Regression Analysis.

	TOTAL TESTS	NUMBER HIV+	HIV+ * RATE	ODDS RATIO (O.R.) (Unadjusted)	ODDS RATIO (O.R.) (Adjusted)	95% C.I. for O.R. (Adjusted)
ALL CASES	46,673	519	11.1	-	-	-
RISK CATEGORY						
Heterosex : Low Risk	21,015	80	3.8	1.00	1.00	-
Heterosex : High Risk	4,070	61	15.0	3.98	3.13	(2.22 , 4.41)
Injecting Drug User	5,570	161	28.9	7.78	3.94	(2.92 , 5.32)
Homo/Bisex	3,681	158	42.9	12.16	7.48	(5.56 , 10.05
Other	1,966	7	3.6	0.93	0.59	(0.27 , 1.29)
Unknown	10,371	52	5.0	1.28	1.40	(0.70 , 1.53)
HEALTH BOARD OF TEST REQUEST						
Lothian	14,269	241	16.9	1.00	1.00	-
Greater Glasgow	14,009	111	7.9	0.47	0.40	(0.32 , 0.51)
Tayside	4,677	90	19.2	1.14	1.21	(0.92 , 1.57)
Grampian	5,081	23	4.5	0.27	0.28	(0.18 , 0.44)
Other	8,436	54	6.4	0.37	0.41	(0.30 , 0.56)
Unknown	201	0	0.0	-	-	-
REASON FOR TEST						
Patient Concerned	26,643	246	9.2	1.00	1.00	-
Doctor Concerned	4,717	227	48.1	5.43	3.11	(2.42 , 4.00)
Screening	10,633	3	0.3	0.03	0.06	(0.02 , 0.19)
Confirmatory Test	185	17	91.9	10.86	4.99	(2.81 , 8.89)
Other	3,995	20	5.0	0.51	0.69	(0.52 , 1.46)
Unknown	500	6	12.0	2.04	3.46	(3.17 , 3.77)
SOURCE OF REQUEST						
GP	15,606	99	6.3	1.00	1.00	-
Hospital	10,221	204	20.0	3.19	1.86	(1.41 , 2.44)
GUM Clinic	10,376	117	11.3	1.79	1.85	(1.36 , 2.50)
Counselling Clinic	4,246	59	13.9	2.21	2.54	(1.79 , 3.67)
Other	6,013	40	6.7	1.02	1.65	(1.11 , 2.45)
Unknown	211	0	0.0	-	-	-
GENDER						
Male	29,082	391	13.4	1.00	1.00	-
Female	17,591	128	7.3	0.53	0.99	(0.78 , 1.24)
AGE GROUP						
15-19 (Years)	3,708	10	2.7	1.00	1.00	-
20-29	20,704	267	12.9	4.82	4.23	(2.24 , 8.00)
30-39	12,032	161	13.4	5.02	5.22	(2.74 , 9.97)
40-49	4,911	47	9.6	3.58	4.02	(2.01 , 8.06)
50+	5,318	34	6.4	2.40	3.61	(1.74 , 7.48)
CLINICAL SYMPTOMS						
Absent	28,532	197	6.9	1.00	1.00	-
Present	3,585	183	51.0	7.74	3.83	(3.02 , 4.86)
Unknown	14,556	139	9.5	1.39	1.58	(1.21 , 2.05)
YEAR OF TEST						
1989	9,651	125	13.0	1.00	1.00	-
1990	10,719	123	11.5	0.89	0.96	(0.74 , 1.25)
1991	13,254	144	10.9	0.83	1.01	(0.79 , 1.30)
1992	13,049	127	9.7	0.75	0.89	(0.69 , 1.16)

Significant at 5% level.

* Number of persons testing HIV positive per 1000 tested.

Table 4.04

Estimated Probability of Testing HIV+

	PARAMETER ESTIMATE	EXAMPLE 1	EXAMPLE 2	EXAMPLE 3
CONSTANT	-7.263	-7.263	-7.263	-7.263
RISK CATEGORY				
Heterosex : Low Risk	0.000	-	-	-
Heterosex : High Risk	1.141	-	-	-
Injecting Drug User	1.372	-	-	-
Homo/Bisex	2.012	2.012	2.012	2.012
Other	-0.531	-	-	-
Unknown	0.338	-	-	-
HEALTH BOARD OF TEST REQUEST				
Lothian	0.000	-	-	-
Greater Glasgow	-0.908	-0.908	-0.908	-0.908
Tayside	0.187	-	-	-
Grampian	-1.261	-	-	-
Other	-0.892	-	-	-
REASON FOR TEST				
Patient Concerned	0.000	-	-	0.000
Doctor Concerned	1.135	1.135	1.135	-
Screening	-2.828	-	-	-
Confirmatory Test	1.608	-	-	-
Other	-0.142	-	-	-
Unknown	1.241	-	-	-
SOURCE OF REQUEST				
GP	0.000	-	-	-
Hospital	0.618	-	-	-
GUM Clinic	0.613	0.613	0.613	0.613
Counselling Clinic	0.941	-	-	-
Other	0.500	-	-	-
GENDER				
Male	0.000	0.000	0.000	0.000
Female	-0.013	-	-	-
AGE GROUP				
15-19 (Years)	0.000	-	-	-
20-29	1.443	-	-	-
30-39	1.653	1.653	1.653	1.653
40-49	1.392	-	-	-
50+	1.283	-	-	-
CLINICAL SYMPTOMS				
Absent	0.000	-	0.000	0.000
Present	1.342	1.342	-	-
Unknown	0.456	-	-	-
YEAR OF TEST				
1989	0.000	-	-	-
1990	-0.036	-0.036	-0.036	-0.036
1991	0.012	-	-	-
1992	-0.115	-	-	-
a		-1.452	-2.795	-3.930
PROBABILITY (HIV+) *		**0.19**	**0.06**	**0.02**

* Probability (HIV+) = exp(a)/[1+exp(a)]

Table 4.05

Persons Testing HIV+ and Test Rate
by Date of Test and Test Centre

	TOTAL TESTS	NUMBER HIV+	HIV+ * RATE
EDINBURGH			
CALENDAR QUARTER :			
Oct - Dec 1990	957	10	10.4
Jan - Mar 1991	1,199	9	7.5
Apr - Jun 1991	1,149	18	15.7
Jul - Sep 1991	1,153	11	9.5
Oct - Dec 1991	1,207	10	8.3
Jan - Mar 1992	1,172	15	12.8
Apr - Jun 1992	1,073	12	11.2
Jul - Sep 1992	1,038	8	7.7
Oct - Dec 1992	1,022	11	10.8
Jan - Mar 1993	1,082	5	4.6
Apr - Jun 1993	976	5	5.1
Jul - Sep 1993	953	10	10.5
Oct - Dec 1993	990	9	9.1
Jan - Mar 1994	1,107	6	5.4
Apr - Jun 1994	1,025	7	6.8
EDINBURGH TOTAL	**16,103**	**146**	**9.1**
GLASGOW			
CALENDAR QUARTER :			
Oct - Dec 1990	1,072	6	5.6
Jan - Mar 1991	1,500	13	8.7
Apr - Jun 1991	1,395	7	5.0
Jul - Sep 1991	1,417	5	3.5
Oct - Dec 1991	1,197	5	4.2
Jan - Mar 1992	1,311	6	4.6
Apr - Jun 1992	1,213	6	4.9
Jul - Sep 1992	1,292	4	3.1
Oct - Dec 1992	1,174	10	8.5
Jan - Mar 1993	1,257	8	6.4
Apr - Jun 1993	1,054	4	3.8
Jul - Sep 1993	1,343	6	4.5
Oct - Dec 1993	1,010	6	5.9
Jan - Mar 1994	1,045	3	2.9
Apr - Jun 1994	1,009	7	6.9
GLASGOW TOTAL	**18,289**	**96**	**5.2**

* Number of persons testing HIV positive per 1000 tested.

Table 5.01

Persons Testing HIV+ and Test Rate

by Risk Category, Gender, Location and Knowledge of HIV Status

	MALE					FEMALE				
	TOTAL TESTS	NUMBER HIV+	HIV+ * RATE	KNOWN HIV+	UNKNOWN HIV+	TOTAL TESTS	NUMBER HIV+	HIV+ * RATE	KNOWN HIV+	UNKNOWN HIV+
(1) **EDINBURGH**										
IDU	85	11	129.4	10	1	42	7	166.7	4	3
HOMO/BISEX	1,473	80	54.3	47	33	0	0	0.0	0	0
HETEROSEX	7,870	24	3.0	8	16	6,512	23	3.5	6	17
TOTAL	**9,428**	**115**	**12.2**	**65**	**50**	**6,554**	**30**	**4.6**	**10**	**20**
(2) **GLASGOW**										
IDU	175	1	5.7	0	1	63	1	15.9	1	0
HOMO/BISEX	1,261	60	47.6	15	45	0	0	0.0	0	0
HETEROSEX	10,492	27	2.6	4	23	5,903	6	1.0	2	4
TOTAL	**11,928**	**88**	**7.4**	**19**	**69**	**5,966**	**7**	**1.2**	**3**	**4**

* Number of HIV positive tests per 1000 tests.

(1) 121 people not classified (Either GENDER or RISK CATEGORY is not known)

(2) 395 people not classified (Either GENDER or RISK CATEGORY is not known)

Table 5.02

Persons Testing HIV+ and Test Rate
by Date of Test and Hospital

	TOTAL TESTS	NUMBER HIV+	HIV+ * RATE
GLASGOW ROYAL INFIRMARY			
CALENDAR QUARTER :			
Oct - Dec 1991	1,050	17	16.2
Jan - Mar 1992	1,767	25	14.1
Apr - Jun 1992	1,478	22	14.9
Jul - Sep 1992	1,448	19	13.1
Oct - Dec 1992	1,611	21	13.0
Jan - Mar 1993	1,723	17	9.9
Apr - Jun 1993	1,625	20	12.3
Jul - Sep 1993	1,357	15	11.1
Oct - Dec 1993	1,625	11	6.8
Jan - Mar 1994	1,745	19	10.9
Apr - Jun 1994	1,701	15	8.8
GRI TOTAL	**17,130**	**201**	**11.7**
STOBHILL GENERAL HOSPITAL			
CALENDAR QUARTER :			
Oct - Dec 1991	772	1	1.3
Jan - Mar 1992	1,185	3	2.5
Apr - Jun 1992	1,171	2	1.7
Jul - Sep 1992	1,093	0	0.0
Oct - Dec 1992	907	1	1.1
Jan - Mar 1993	844	0	0.0
Apr - Jun 1993	741	1	1.3
Jul - Sep 1993	693	0	0.0
Oct - Dec 1993	805	1	1.2
Jan - Mar 1994	899	1	1.1
Apr - Jun 1994	832	0	0.0
SGH TOTAL	**9,942**	**10**	**1.0**

* Number of persons testing HIV positive per 1000 tested.

Table 5.03

Persons Testing HIV+ and Test Rate
by Hospital, Medical Section and Knowledge of HIV Status

	TOTAL TESTS	NUMBER HIV+	HIV+ * RATE	KNOWN HIV+	UNKNOWN HIV+
GLASGOW ROYAL INFIRMARY					
GP	2,776	4	1.4	1	3
GENERAL MEDICAL	3,623	180	49.7	164	16
OTHER	10,731	17	1.6	7	10
GRI TOTAL	**17,130**	**201**	**11.7**	**172**	**29**
STOBHILL GENERAL HOSPITAL					
GP	3,045	2	0.7	0	2
GENERAL MEDICAL	2,423	5	2.1	2	3
OTHER	4,474	3	0.7	2	1
SGH TOTAL	**9,942**	**10**	**1.0**	**4**	**6**

* Number of HIV positive tests per 1000 tests.

Table 5.04

Persons Testing HIV+ and Test Rate
by Date of Test

CALENDAR QUARTER	TOTAL TESTS	NUMBER HIV+	HIV+ * RATE
Jan - Mar 1990	15,673	6	0.38
Apr - Jun 1990	16,486	2	0.12
Jul - Sep 1990	17,242	6	0.35
Oct - Dec 1990	16,372	5	0.31
Jan - Mar 1991	16,419	4	0.24
Apr - Jun 1991	16,858	5	0.30
Jul - Sep 1991	17,531	6	0.34
Oct - Dec 1991	16,251	4	0.25
Jan - Mar 1992	16,310	9	0.55
Apr - Jun 1992	16,499	6	0.36
Jul - Sep 1992	17,062	3	0.18
Oct - Dec 1992	15,816	3	0.19
Jan - Mar 1993	15,709	5	0.32
Apr - Jun 1993	15,876	3	0.19
Jul - Sep 1993	16,975	7	0.41
Oct - Dec 1993	15,429	3	0.19
TOTAL	**262,508**	**77**	**0.29**

* Number of HIV positive tests per 1000 tests.

Table 5.05

HIV+ Tests and Test Rate
by Year of Test and Location

	YEAR OF TEST				TOTAL
	1990	1991	1992	1993	
GLASGOW					
Total Tests	16,308	16,781	16,237	15,887	**65,213**
Total HIV+ Tests	0	5	1	2	**8**
HIV+ Rate *	0.00	0.30	0.06	0.13	**0.12**
EDINBURGH					
Total Tests	5,276	5,471	5,237	5,093	**21,077**
Total HIV+ Tests	13	9	6	8	**36**
HIV+ Rate *	2.46	1.65	1.15	1.57	**1.71**
DUNDEE					
Total Tests	2,130	2,210	2,118	2,117	**8,575**
Total HIV+ Tests	3	0	6	2	**11**
HIV+ Rate *	1.41	0.00	2.83	0.94	**1.28**
OTHER					
Total Tests	42,059	42,597	42,095	40,892	**167,643**
Total HIV+ Tests	3	5	8	6	**22**
HIV+ Rate *	0.07	0.12	0.19	0.15	**0.13**

* Number of HIV positive tests per 1000 tests.

Table 5.06

Number of Tests, Persons Testing HIV+ and Test Rate
by Date of Test, Test Centre and Risk Category

TEST CENTRE	CALENDAR QUARTER	TOTAL TESTS	NUMBER HIV+	HIV+ * RATE	I D U		PARTNER OF IDU		NEITHER IDU NOR PARTNER OF IDU	
					TESTS	NUMBER HIV+	TESTS	NUMBER HIV+	TESTS	NUMBER HIV+
DUNDEE										
	Jul - Sep 1993	966	2	2.1	6	1	4	1	956	0
	Oct - Dec 1993	928	0	0.0	2	0	4	0	922	0
	Jan - Mar 1994	990	1	1.0	2	1	8	0	980	0
	Apr - Jun 1994	865	2	2.3	4	2	6	0	855	0
DUNDEE TOTAL		**3,749**	**5**	**1.3**	**14**	**4**	**22**	**1**	**3,713**	**0**
EDINBURGH										
	Jul - Sep 1993	4,351	5	1.1	7	1	2	0	4,342	4
	Oct - Dec 1993	3,824	4	1.0	2	0	11	3	3,811	1
	Jan - Mar 1994	3,667	5	1.4	12	3	5	0	3,650	2
	Apr - Jun 1994	3,416	5	1.5	16	2	20	2	3,380	1
EDINBURGH TOTAL		**15,258**	**19**	**1.2**	**37**	**6**	**38**	**5**	**15,183**	**8**

* Number of persons testing HIV positive per 1000 tested.

Table 5.07

Number of Tests and Persons Testing HIV+

by Date of Test

CALENDAR QUARTER	TOTAL TESTS	NUMBER HIV+
Jan - Mar 1992	846	0
Apr - Jun 1992	989	1
Jul - Sep 1992	1,051	0
Oct - Dec 1992	942	0
Jan - Mar 1993	1,111	0
Apr - Jun 1993	861	1
Jul - Sep 1993	1,051	0
Oct - Dec 1993	989	0
Jan - Mar 1994	1,014	0
Apr - Jun 1994	1,075	0
TOTAL	**9,929**	**2**

Table 5.08

WHO Staging System for HIV Infection and Disease

IMMUNOLOGICAL AXIS		CLINICAL AXIS			
		Asymptomatic / PGL	Early HIV Infection	Intermediate HIV Infection	Late HIV Infection
CD4 COUNT		1	2	3	4
0 - 199	C	1C	2C	3C	4C
200 - 500	B	1B	2B	3B	4B
> 500	A	1A	2A	3A	4A

Table 6.01

WHO Staging of HIV+ Adults Monitored in 1992

MEAN CD4 COUNT IN 1992	CLINICAL STAGE					TOTAL
	ASYMPTOMATIC / PGL	EARLY HIV INFECTION	INTERMEDIATE HIV INFECTION	LATE HIV INFECTION	NOT KNOWN	
0 - 199	59	46	124	126	10	**365**
200 - 500	209	77	87	13	20	**406**
> 500	93	20	18	0	9	**140**
NOT KNOWN	10	2	3	2	0	**17**
TOTAL	**371**	**145**	**232**	**141**	**39**	**928**

Table 6.02

WHO Staging of HIV+ Adults Monitored in 1993

MEAN CD4 COUNT IN 1993	CLINICAL STAGE					TOTAL
	ASYMPTOMATIC / PGL	EARLY HIV INFECTION	INTERMEDIATE HIV INFECTION	LATE HIV INFECTION	NOT KNOWN	
0 - 199	53	50	104	136	33	**376**
200 - 500	203	66	69	21	38	**397**
> 500	113	25	16	0	9	**163**
NOT KNOWN	1	1	2	2	0	**6**
TOTAL	**370**	**142**	**191**	**159**	**80**	**942**

Table 6.03

Number of HIV+ Adults Monitored in 1992
by Laboratory, Severity of HIV Infection and Risk Category

LABORATORY	SEVERITY OF HIV INFECTION	RISK CATEGORY			TOTAL
		Homo/Bisex	IDU	Heterosex	
GLASGOW	Moderate	38	44	17	**99**
	Severe	41	16	6	**63**
EDINBURGH	Moderate	38	153	44	**235**
	Severe	50	125	27	**202**
DUNDEE	Moderate	1	61	18	**80**
	Severe	3	27	11	**41**
TOTAL		**171**	**426**	**123**	**720**

Table 6.04

Results of Log-Linear Modelling Analysis

	95 % CONFIDENCE INTERVAL
MAIN EFFECTS	
Edinburgh	0.73 , 1.04
Glasgow	-0.26 , 0.09
Dundee	-1.04 , -0.55
Homosexual/Bisexual	-0.68 , -0.20
IDU	0.62 , 0.93
Heterosexual	-0.52 , -0.15
Moderate HIV Infection	0.15 , 0.29
Severe HIV Infection	-0.29 , -0.01
INTERACTIONS	
Edinburgh X Homo/Bisex	-0.12 , 0.39
Edinburgh X IDU	-0.11 , 0.24
Edinburgh X Heterosex	-0.41 , 0.01
Glasgow X Homo/bisex	0.74 , 1.28
Glasgow X IDU	-0.81 , -0.38
Glasgow X Heterosex	-0.67 , -0.15
Dundee X Homo/bisex	-1.58 , -0.70
Dundee X IDU	0.26 , 0.80
Dundee X Heterosex	0.31 , 0.91
Edinburgh X Moderate HIV	-0.24 , 0.07
Edinburgh X Severe HIV	-0.07 , 0.24
Glasgow X Moderate HIV	-0.01 , 0.34
Glasgow X Severe HIV	-0.34 , 0.01
Dundee X Moderate HIV	-0.16 , 0.32
Dundee X Severe HIV	-0.32 , 0.16
Homo/Bisex X Moderate HIV	-0.59 , -0.11
Homo/Bisex X Severe HIV	0.11 , 0.59
IDU X Moderate HIV	0.02 , 0.34
IDU X Severe HIV	-0.34 , -0.02
Heterosex X Moderate HIV	-0.01 , 0.35
Heterosex X Severe HIV	-0.35 , 0.01

Significant at 5% level.

Table 6.05

HIV+ Adults, Alive and Under Monitoring (at 31/12/94)
by Date, and Value of most recent CD4 Count

TIME PERIOD	CD4 COUNT			TOTAL
	0 - 199	200 - 500	> 500	
Jan - Jun 1992	10	22	15	**47**
Jul - Dec 1992	11	12	10	**33**
Jan - Jun 1993	16	24	12	**52**
Jul - Dec 1993	36	28	22	**86**
Jan - Jun 1994	78	83	47	**208**
Jul - Dec 1994	189	188	111	**488**
Jan - Jun 1995 *	110	83	23	**216**
TOTAL	**450**	**440**	**240**	**1,130**

* Incomplete Data.

Table 6.06

HIV+ Adults, Alive and Under Monitoring (at 31/12/94)

by Health Board, Date, and Value of most recent CD4 Count

HEALTH BOARD OF REQUEST	TIME PERIOD	CD4 COUNT			TOTAL
		0 - 199	200 - 500	> 500	
LOTHIAN	Jan - Jun 1992	7	15	7	29
	Jul - Dec 1992	6	6	2	14
	Jan - Jun 1993	5	16	3	24
	Jul - Dec 1993	14	15	6	35
	Jan - Jun 1994	31	31	20	82
	Jul - Dec 1994	94	113	64	271
	Jan - Jun 1995 *	70	49	14	133
LOTHIAN TOTAL		**227**	**245**	**116**	**588**
GREATER GLASGOW	Jan - Jun 1992	0	5	4	9
	Jul - Dec 1992	4	2	4	10
	Jan - Jun 1993	5	2	3	10
	Jul - Dec 1993	10	4	3	17
	Jan - Jun 1994	19	15	8	42
	Jul - Dec 1994	38	33	16	87
	Jan - Jun 1995 *	33	24	9	66
GREATER GLASGOW TOTAL		**109**	**85**	**47**	**241**
TAYSIDE	Jan - Jun 1992	1	1	3	5
	Jul - Dec 1992	1	3	3	7
	Jan - Jun 1993	6	3	5	14
	Jul - Dec 1993	6	8	9	23
	Jan - Jun 1994	11	24	15	50
	Jul - Dec 1994	42	24	22	88
	Jan - Jun 1995 *	2	3	0	5
TAYSIDE TOTAL		**69**	**66**	**57**	**192**
GRAMPIAN	Jan - Jun 1992	0	0	0	0
	Jul - Dec 1992	0	0	0	0
	Jan - Jun 1993	0	0	1	1
	Jul - Dec 1993	2	1	1	4
	Jan - Jun 1994	8	7	0	15
	Jul - Dec 1994	5	4	1	10
	Jan - Jun 1995 *	0	0	0	0
GRAMPIAN TOTAL		**15**	**12**	**3**	**30**
'OTHER'	Jan - Jun 1992	2	1	1	4
	Jul - Dec 1992	0	1	1	2
	Jan - Jun 1993	0	3	0	3
	Jul - Dec 1993	4	0	3	7
	Jan - Jun 1994	6	2	1	9
	Jul - Dec 1994	4	9	5	18
	Jan - Jun 1995 *	3	1	0	4
'OTHER' TOTAL		**19**	**17**	**11**	**47**

* Incomplete Data.

Table 6.07

HIV+ Adults, Alive and Under Monitoring (at 31/12/94)

by Risk Category, Date, and Value of most recent CD4 Count

RISK CATEGORY	TIME PERIOD	CD4 COUNT			TOTAL
		0 - 199	200 - 500	> 500	
HOMO/BISEX	Jan - Jun 1992	3	3	0	6
	Jul - Dec 1992	1	4	2	7
	Jan - Jun 1993	1	7	0	8
	Jul - Dec 1993	9	2	3	14
	Jan - Jun 1994	24	25	9	58
	Jul - Dec 1994	51	46	24	121
	Jan - Jun 1995 *	42	24	6	72
HOMO/BISEX TOTAL		**131**	**111**	**44**	**286**
IDU	Jan - Jun 1992	1	8	7	16
	Jul - Dec 1992	5	4	3	12
	Jan - Jun 1993	10	8	11	29
	Jul - Dec 1993	16	15	14	45
	Jan - Jun 1994	31	37	26	94
	Jul - Dec 1994	84	91	59	234
	Jan - Jun 1995 *	48	44	10	102
IDU TOTAL		**195**	**207**	**130**	**532**
HETEROSEX	Jan - Jun 1992	2	5	2	9
	Jul - Dec 1992	2	2	1	5
	Jan - Jun 1993	2	7	1	10
	Jul - Dec 1993	5	9	5	19
	Jan - Jun 1994	14	13	8	35
	Jul - Dec 1994	35	29	17	81
	Jan - Jun 1995 *	9	10	5	24
HETEROSEX TOTAL		**69**	**75**	**39**	**183**
HAEM/BLOOD	Jan - Jun 1992	2	0	1	3
	Jul - Dec 1992	0	0	1	1
	Jan - Jun 1993	2	0	0	2
	Jul - Dec 1993	0	0	0	0
	Jan - Jun 1994	3	1	0	4
	Jul - Dec 1994	6	3	1	10
	Jan - Jun 1995 *	4	2	0	6
HAEM/BLOOD TOTAL		**17**	**6**	**3**	**26**
UNKNOWN/OTHER	Jan - Jun 1992	2	6	5	13
	Jul - Dec 1992	3	2	3	8
	Jan - Jun 1993	1	2	0	3
	Jul - Dec 1993	6	2	0	8
	Jan - Jun 1994	6	7	4	17
	Jul - Dec 1994	13	19	10	42
	Jan - Jun 1995 *	7	3	2	12
UNKNOWN/OTHER TOTAL		**38**	**41**	**24**	**103**

* Incomplete Data.

Table 6.08

AIDS Cases Reported to SCIEH, by 31/12/94, and HIV+ Persons

by Year of First HIV+ Specimen

YEAR OF FIRST HIV+ SPECIMEN	NUMBER OF HIV+ PERSONS	REPORTED AS AIDS CASE		NOT REPORTED AS AIDS CASE	
		Number	%	Number	%
1981	3	0	0%	3	100%
1982	14	7	50%	7	50%
1983	69	23	33%	46	67%
1984	253	63	25%	190	75%
1985	279	75	27%	204	73%
1986	326	84	26%	242	74%
1987	251	72	29%	179	71%
1988	141	40	28%	101	72%
1989	117	42	36%	75	64%
1990	132	41	31%	91	69%
1991	173	58	34%	115	66%
1992	146	34	23%	112	77%
1993	167	33	20%	134	80%
1994	138	32	23%	106	77%
TOTAL	**2,209**	**604**	**27%**	**1,605**	**73%**

Table 7.01

AIDS Cases Reported to SCIEH, and HIV+ Persons
by Vital Status at 31/12/94, and Year of First HIV+ Specimen

YEAR OF FIRST HIV+ SPECIMEN	NUMBER OF HIV+ PERSONS	REPORTED AS AIDS CASE				NOT REPORTED AS AIDS CASE			
		Dead	%	Alive	%	Dead	%	Alive	%
1981	3	0	0%	0	0%	2	67%	1	33%
1982	14	7	50%	0	0%	0	0%	7	50%
1983	69	17	25%	6	9%	7	10%	39	57%
1984	253	52	21%	11	4%	33	13%	157	62%
1985	279	59	21%	16	6%	32	11%	172	62%
1986	326	64	20%	20	6%	33	10%	209	64%
1987	251	57	23%	15	6%	19	8%	160	64%
1988	141	27	19%	13	9%	17	12%	84	60%
1989	117	34	29%	8	7%	7	6%	68	58%
1990	132	34	26%	7	5%	12	9%	79	60%
1991	173	36	21%	22	13%	12	7%	103	60%
1992	146	19	13%	15	10%	6	4%	106	73%
1993	167	17	10%	16	10%	8	5%	126	75%
1994	138	6	4%	26	19%	1	1%	105	76%
TOTAL	**2,209**	**429**		**175**		**189**		**1,416**	

Table 7.02

HIV+ Persons

by Health Board, Vital Status at 31/12/94, and Participation in CD4 Study

HEALTH BOARD OF SOURCE OF SPECIMEN	NUMBER OF HIV+ PERSONS	REPORTED DEAD	ASSUMED ALIVE				
				IN CD4 STUDY		NOT IN CD4 STUDY	
		Number	Number	Number	%	Number	%
Argyll & Clyde	17	12	5	3	60%	2	40%
Ayrshire & Arran	16	5	11	6	55%	5	45%
Borders	10	4	6	5	83%	1	17%
Dumfries & Galloway	11	3	8	1	13%	7	88%
Fife	42	13	29	18	62%	11	38%
Forth Valley	64	18	46	27	59%	19	41%
Grampian	86	22	64	27	42%	37	58%
Greater Glasgow	475	142	333	197	59%	136	41%
Highland	27	2	25	2	8%	23	92%
Lanarkshire	49	12	37	22	59%	15	41%
Lothian	1,060	287	773	478	62%	295	38%
Shetland	1	0	1	1	100%	0	0%
Tayside	351	98	253	173	68%	80	32%
TOTAL	**2,209**	**618**	**1,591**	**960**	**60%**	**631**	**40%**

Table 7.03

Persons with CD4 Count Measured at HIV Diagnosis
by Health Board, CD4 Count, Risk Category and Gender

HEALTH BOARD OF REQUEST	CD4 COUNT	HOMO/ BISEX	IDU		HETEROSEX		UNKNOWN/ OTHER	TOTAL
			Male	Female	Male	Female		
LOTHIAN	0 - 199	7	2	0	3	2	1	15
	200 - 500	8	1	2	2	3	0	16
	> 500	7	0	0	0	0	2	9
	Not Known	6	1	1	3	2	4	17
LOTHIAN TOTAL		**28**	**4**	**3**	**8**	**7**	**7**	**57**
GREATER GLASGOW	0 - 199	9	1	1	1	0	3	15
	200 - 500	4	0	0	0	0	0	4
	> 500	2	1	0	0	2	0	5
	Not Known	4	2	0	1	2	0	9
GREATER GLASGOW TOTAL		**19**	**4**	**1**	**2**	**4**	**3**	**33**
TAYSIDE	0 - 199	0	3	0	3	0	0	6
	200 - 500	1	0	1	1	2	0	5
	> 500	0	2	0	0	2	0	4
	Not Known	1	1	1	1	0	1	5
TAYSIDE TOTAL		**2**	**6**	**2**	**5**	**4**	**1**	**20**
'OTHER'	0 - 199	3	2	0	2	4	1	12
	200 - 500	3	0	0	0	1	0	4
	> 500	0	0	0	0	0	0	0
	Not Known	9	1	0	1	1	0	12
'OTHER' TOTAL		**15**	**3**	**0**	**3**	**6**	**1**	**28**

Table 7.04

HIV Prevalence
by Year, Location and UAT Study

	YEAR			
	1990	1991	1992	1993
EDINBURGH				
GUM Study	n/a	1.02%	1.07%	0.73%
Guthrie Study	0.25%	0.17%	0.12%	0.16%
GLASGOW				
GUM Study	n/a	0.55%	0.52%	0.51%
Guthrie Study	0.00%	0.03%	0.01%	0.01%
Hospital Study	n/a	n/a	0.87%	0.69%
Family Planning Study	n/a	n/a	0.03%	0.03%
DUNDEE				
GUM Study	n/a	n/a	n/a	n/a
Guthrie Study	0.14%	0.00%	0.28%	0.09%
REST OF SCOTLAND				
GUM Study	n/a	n/a	n/a	n/a
Guthrie Study	0.01%	0.01%	0.01%	0.02%

Table 8.01

Figures

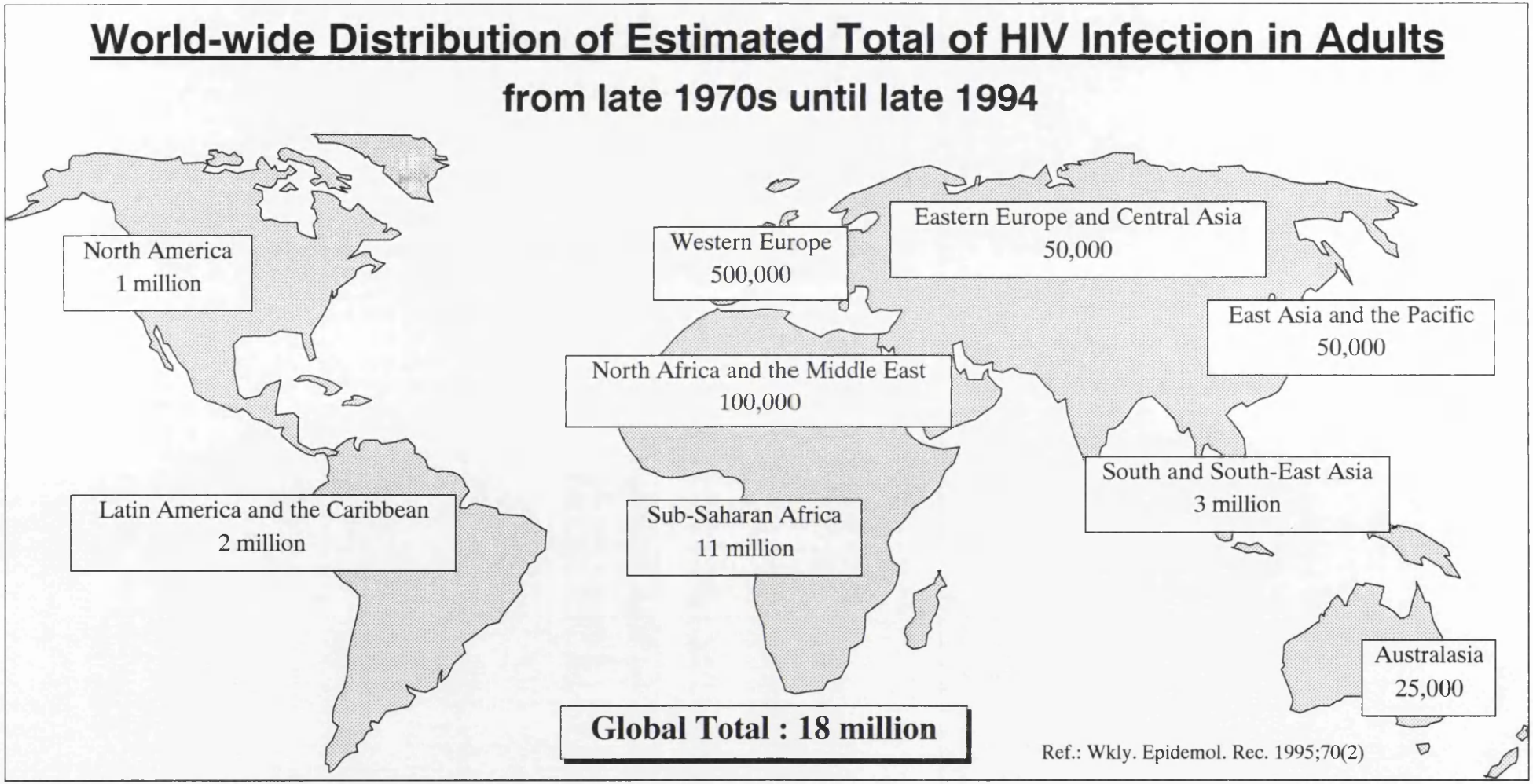
World-wide Distribution of Estimated Total of HIV Infection in Adults
from late 1970s until late 1994
North America
1 million
Western Europe
500,000
Eastern Europe and Central Asia
50,000
East Asia and the Pacific
50,000
North Africa and the Middle East
100,000
South and South-East Asia
3 million
Latin America and the Caribbean
2 million
Sub-Saharan Africa
11 million
Australasia
25,000
Global Total : 18 million
Ref.: Wkly. Epidemol. Rec. 1995;70(2)

Figure 1.01

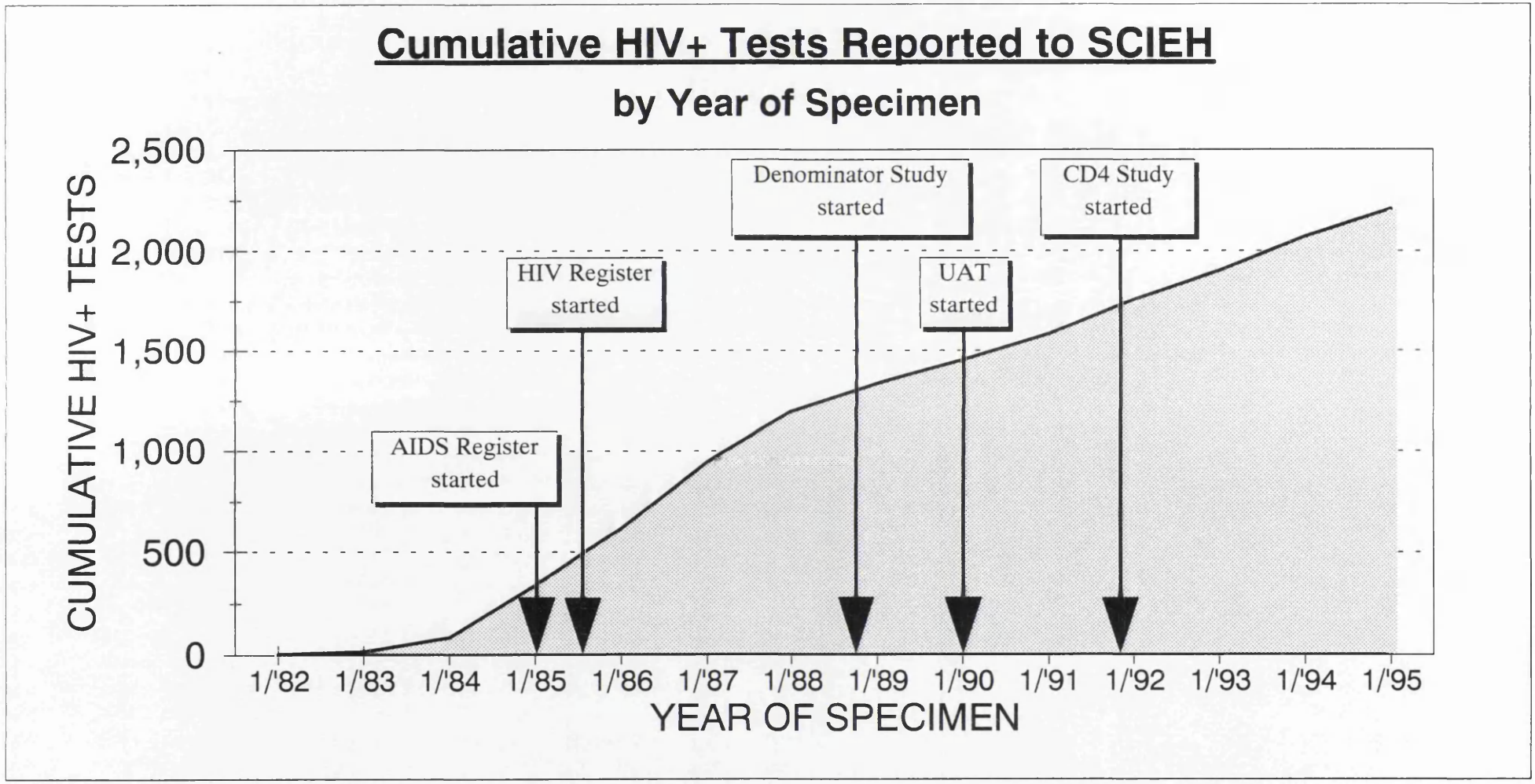
Cumulative HIV+ Tests Reported to SCIEH
by Year of Specimen
CUMULATIVE HIV+ TESTS
2,500
2,000
1,500
1,000
500
0
AIDS Register started
HIV Register started
Denominator Study started
UAT started
CD4 Study started
1/'82
1/'83
1/'84
1/'85
1/'86
1/'87
1/'88
1/'89
1/'90
1/'91
1/'92
1/'93
1/'94
1/'95
YEAR OF SPECIMEN

Figure 1.02

Sample Report Form : AIDS (Control) Act

Greater Glasgow Health Board (To 31/3/94)

A(C)A1

AIDS (CONTROL) ACT 1987 : STATISTICS ON REPORTED AIDS CASES AND DEATHS

Health Board : ***Greater Glasgow***

Year ending 31 March 1994

Signed : _____

Name : _____

Tel. No. : _____

Period	People With AIDS	First Reported From This Health Board	Known to be Resident of this Health Board
1 April 1993 to 31 March 1994	*- reported to, and accepted by SCIEH in period*	**42**	**34**
	- numbers of above known by 31 March 1994 to have died	**10**	**8**
Cumulative to 31 March 1994	*- cumulative number reported to, and accepted by SCIEH by end of period*	**151**	**118**
	- numbers of above known by 31 March to have died	**98**	**75**

Notes :

1. This form should be completed as part of the reports made by Health Boards under the AIDS (Control) Act 1987.

2. The form should be completed from information supplied by SCIEH

Figure 2.01

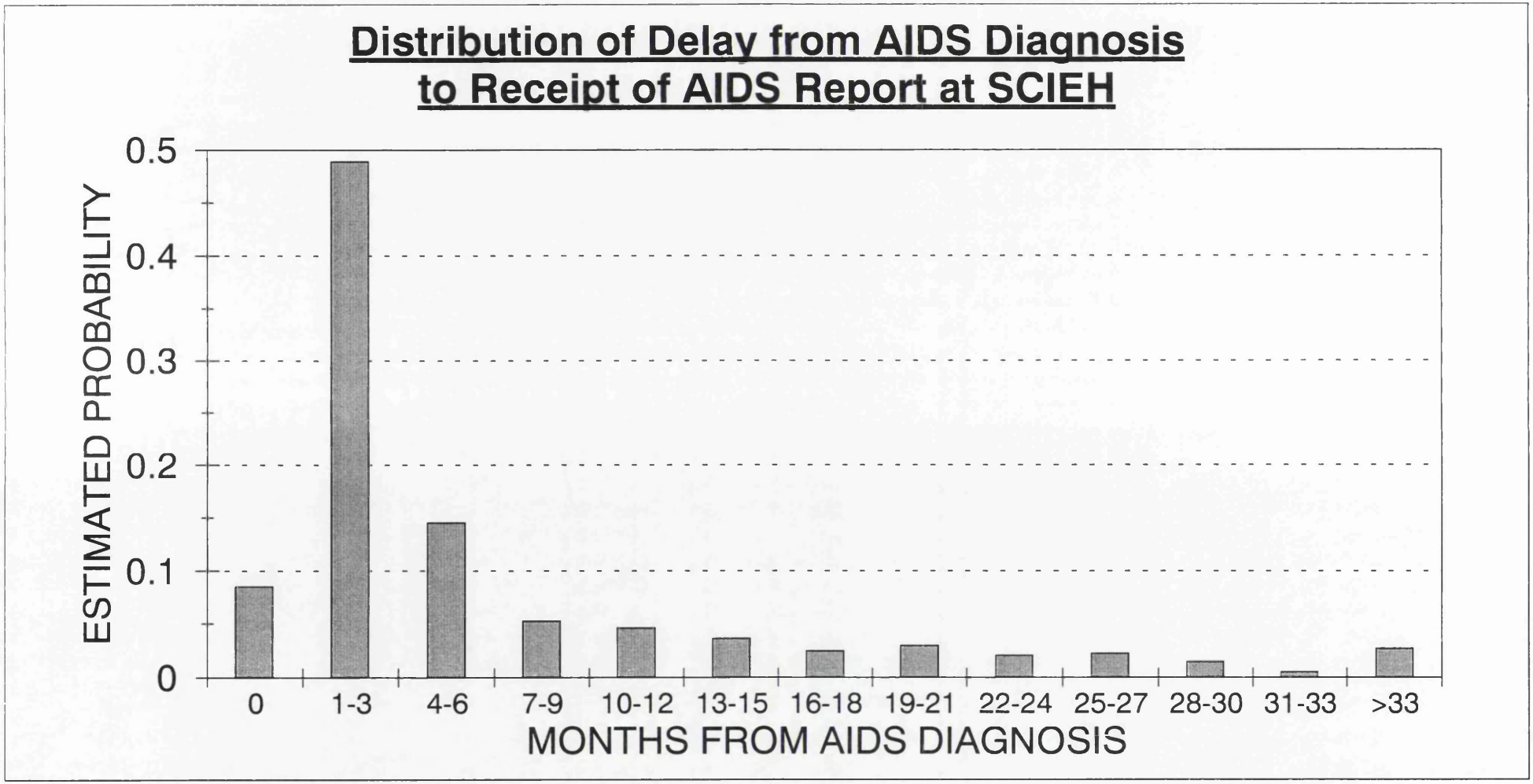
Distribution of Delay from AIDS Diagnosis
to Receipt of AIDS Report at SCIEH
ESTIMATED PROBABILITY
0.5
0.4
0.3
0.2
0.1
0
0
1-3
4-6
7-9
10-12
13-15
16-18
19-21
22-24
25-27
28-30
31-33
>33
MONTHS FROM AIDS DIAGNOSIS

Figure 2.02

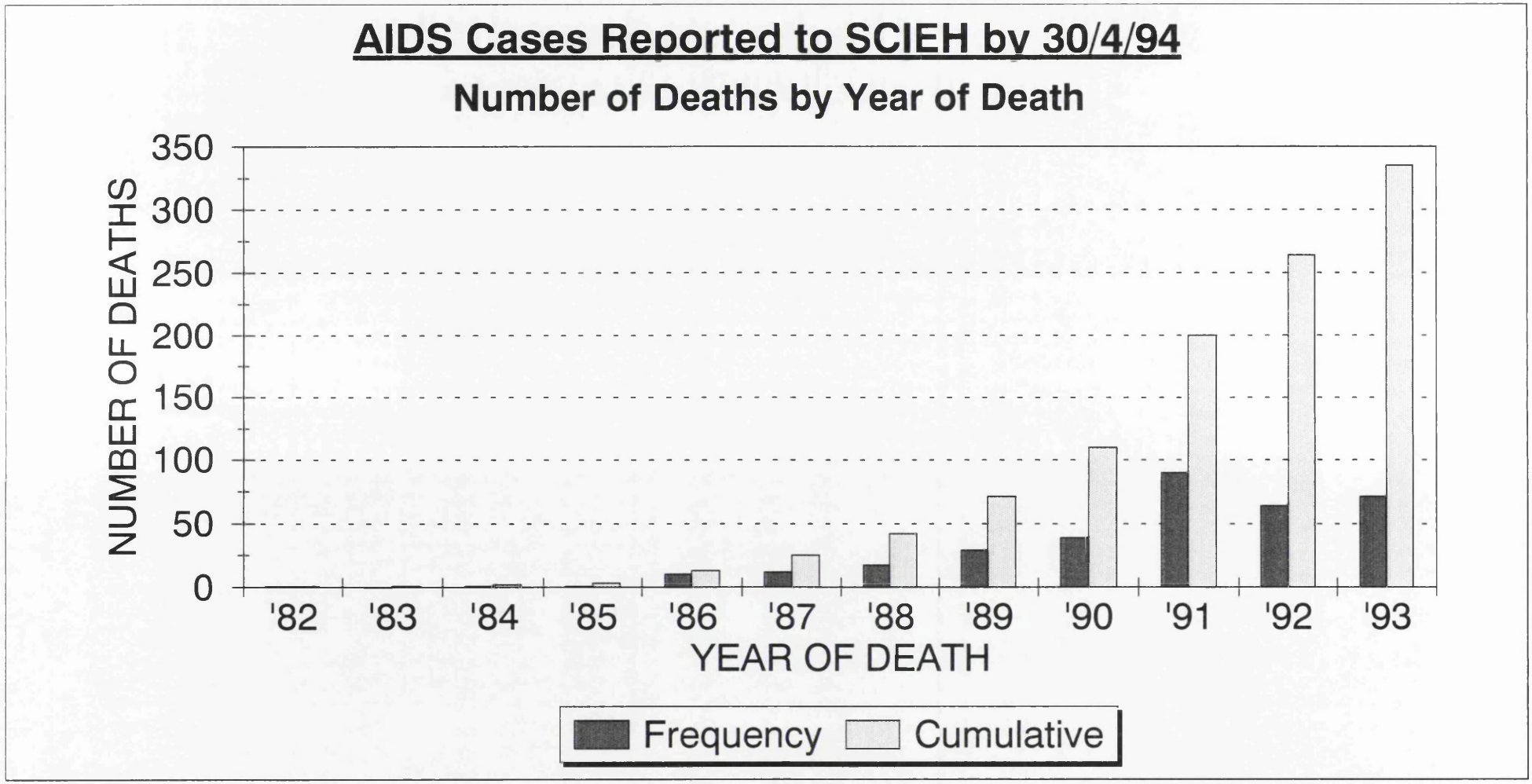
AIDS Cases Reported to SCIEH by 30/4/94
Number of Deaths by Year of Death
NUMBER OF DEATHS
350
300
250
200
150
100
50
0
'82
'83
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF DEATH
Frequency
Cumulative

Figure 2.03

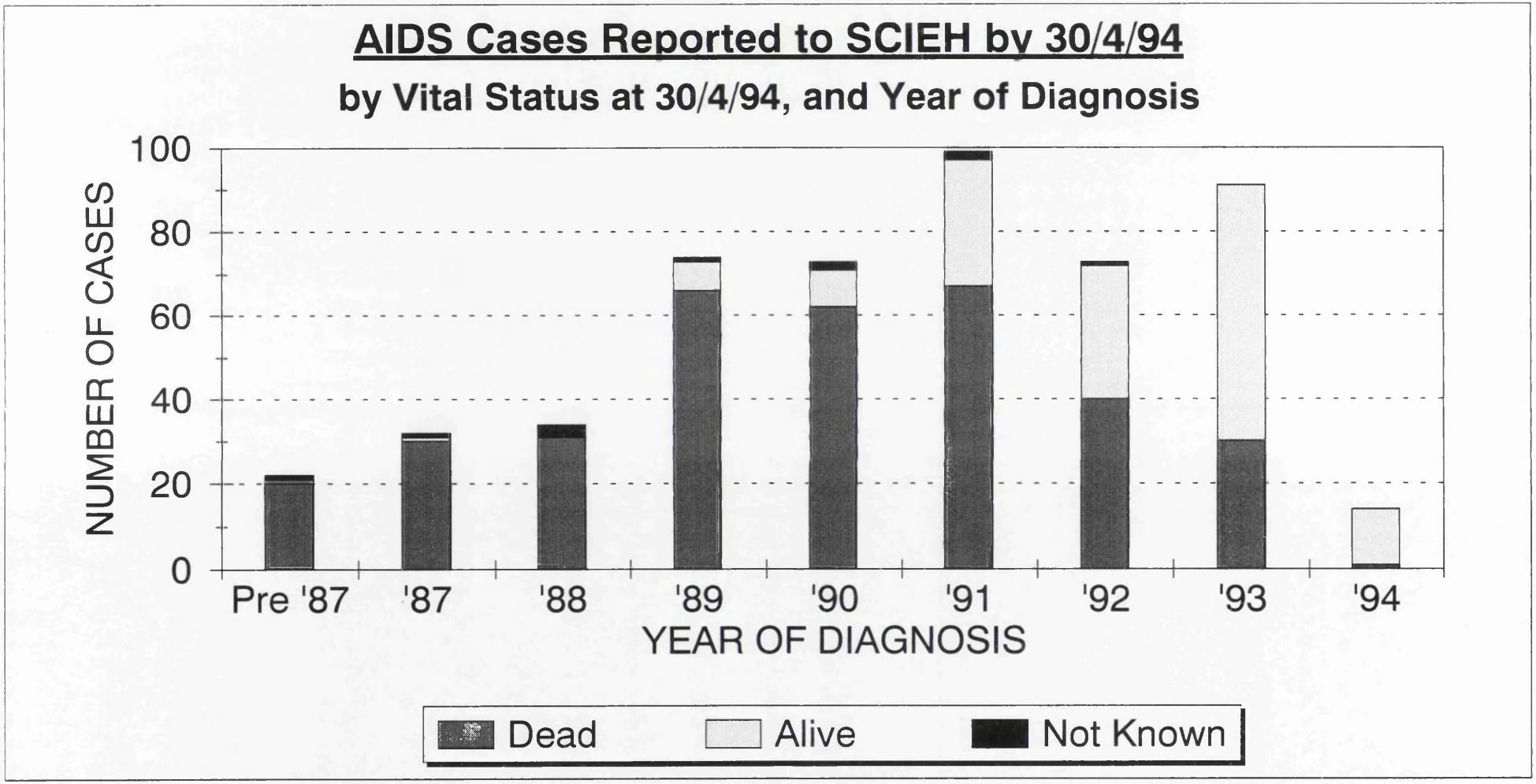
AIDS Cases Reported to SCIEH by 30/4/94
by Vital Status at 30/4/94, and Year of Diagnosis
NUMBER OF CASES
100
80
60
40
20
0
Pre '87
'87
'88
'89
'90
'91
'92
'93
'94
YEAR OF DIAGNOSIS
Dead
Alive
Not Known

Figure 2.04

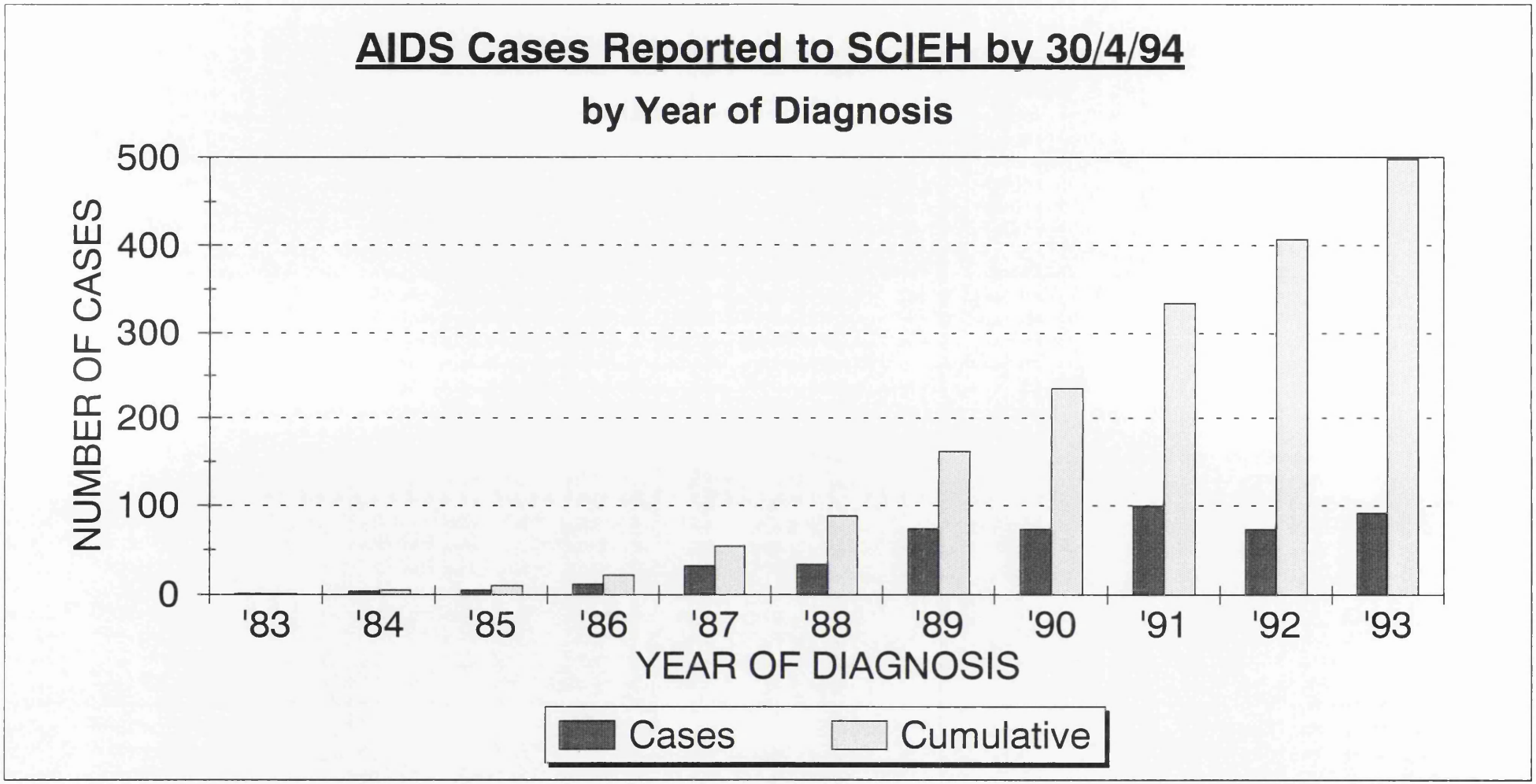
AIDS Cases Reported to SCIEH by 30/4/94
by Year of Diagnosis
NUMBER OF CASES
500
400
300
200
100
0
'83
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF DIAGNOSIS
Cases
Cumulative

Figure 2.05

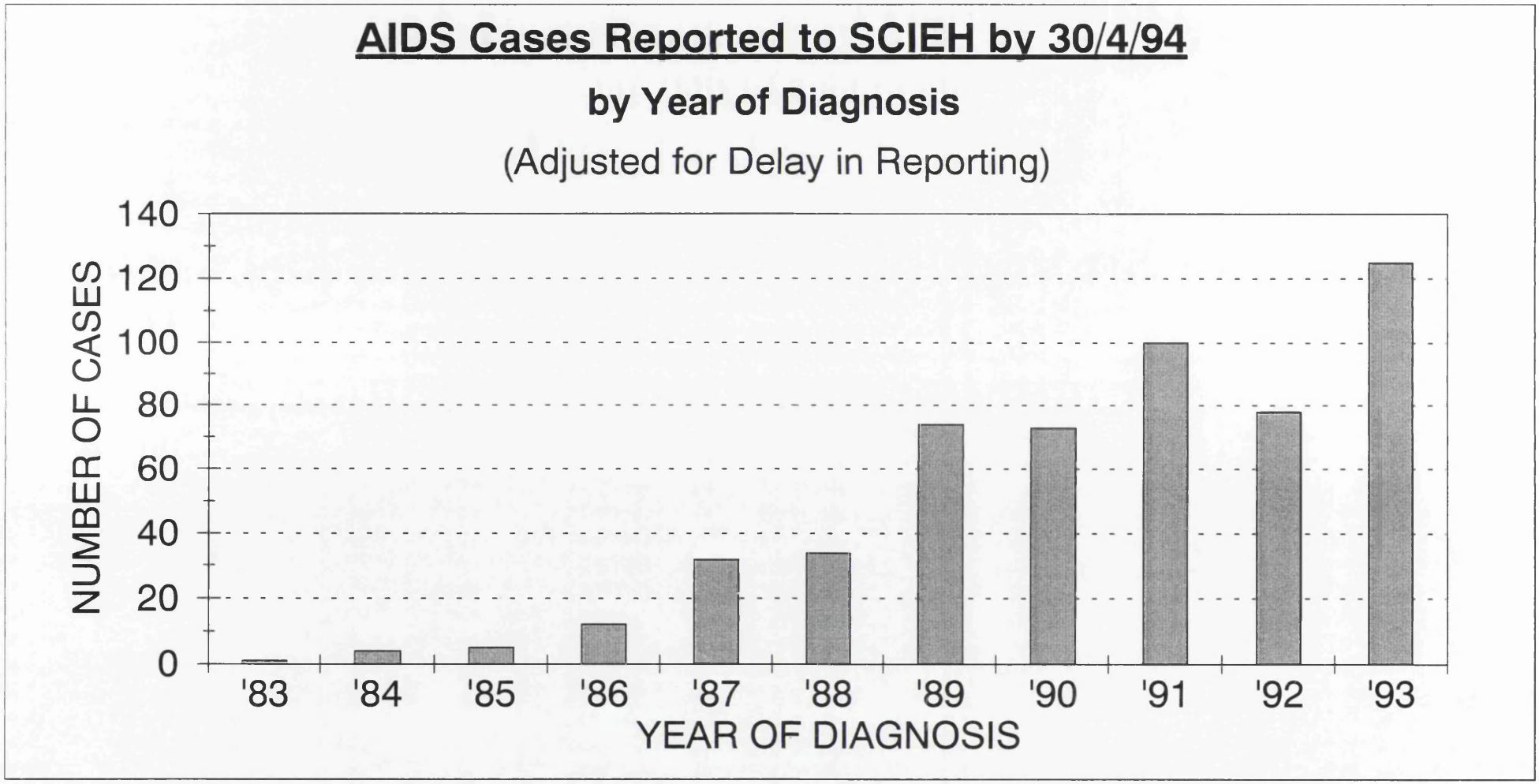
AIDS Cases Reported to SCIEH by 30/4/94
by Year of Diagnosis
(Adjusted for Delay in Reporting)
NUMBER OF CASES
140
120
100
80
60
40
20
0
'83
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF DIAGNOSIS

Figure 2.06

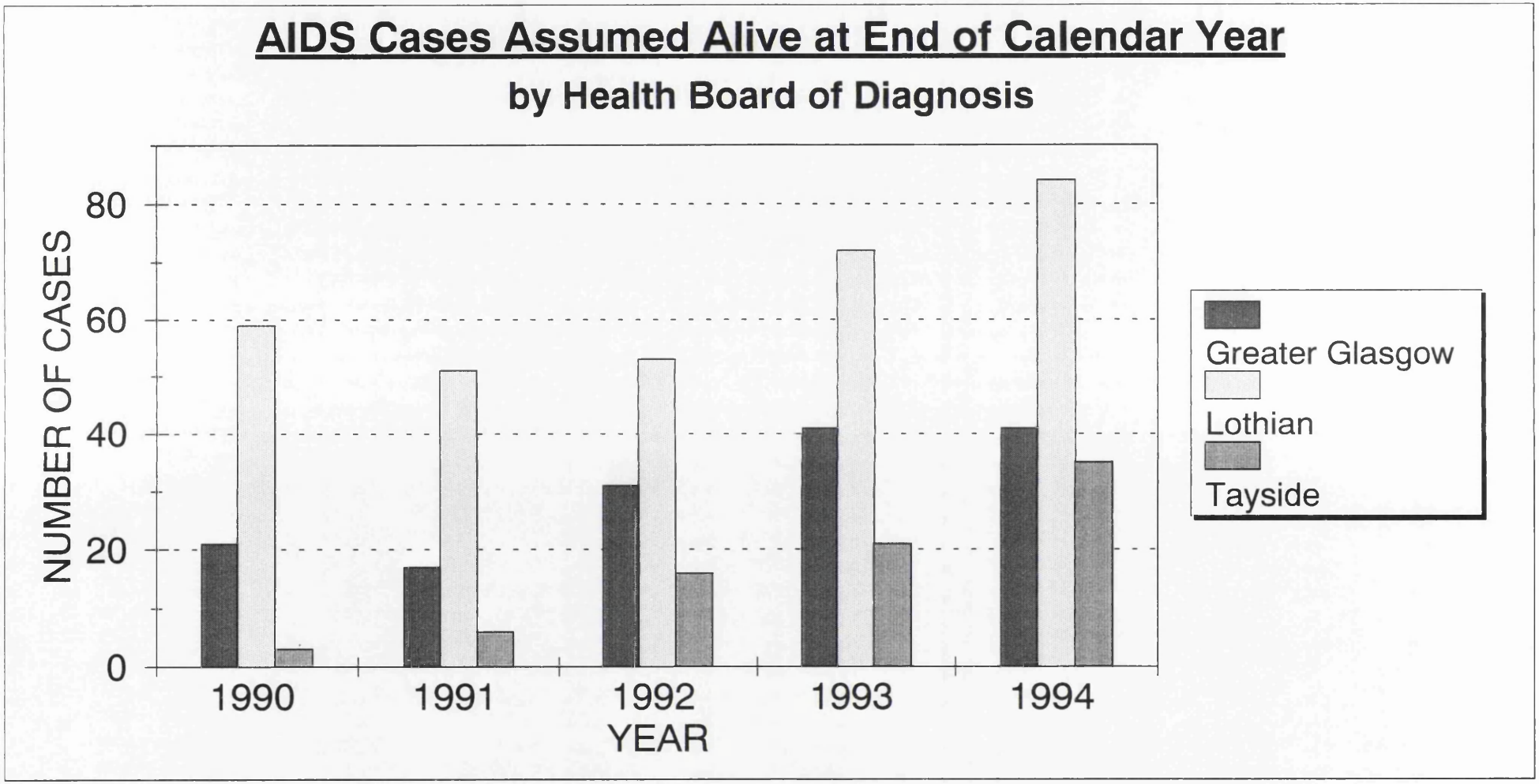
AIDS Cases Assumed Alive at End of Calendar Year
by Health Board of Diagnosis
NUMBER OF CASES
0
20
40
60
80
1990
1991
1992
1993
1994
YEAR
Greater Glasgow
Lothian
Tayside

Figure 2.07

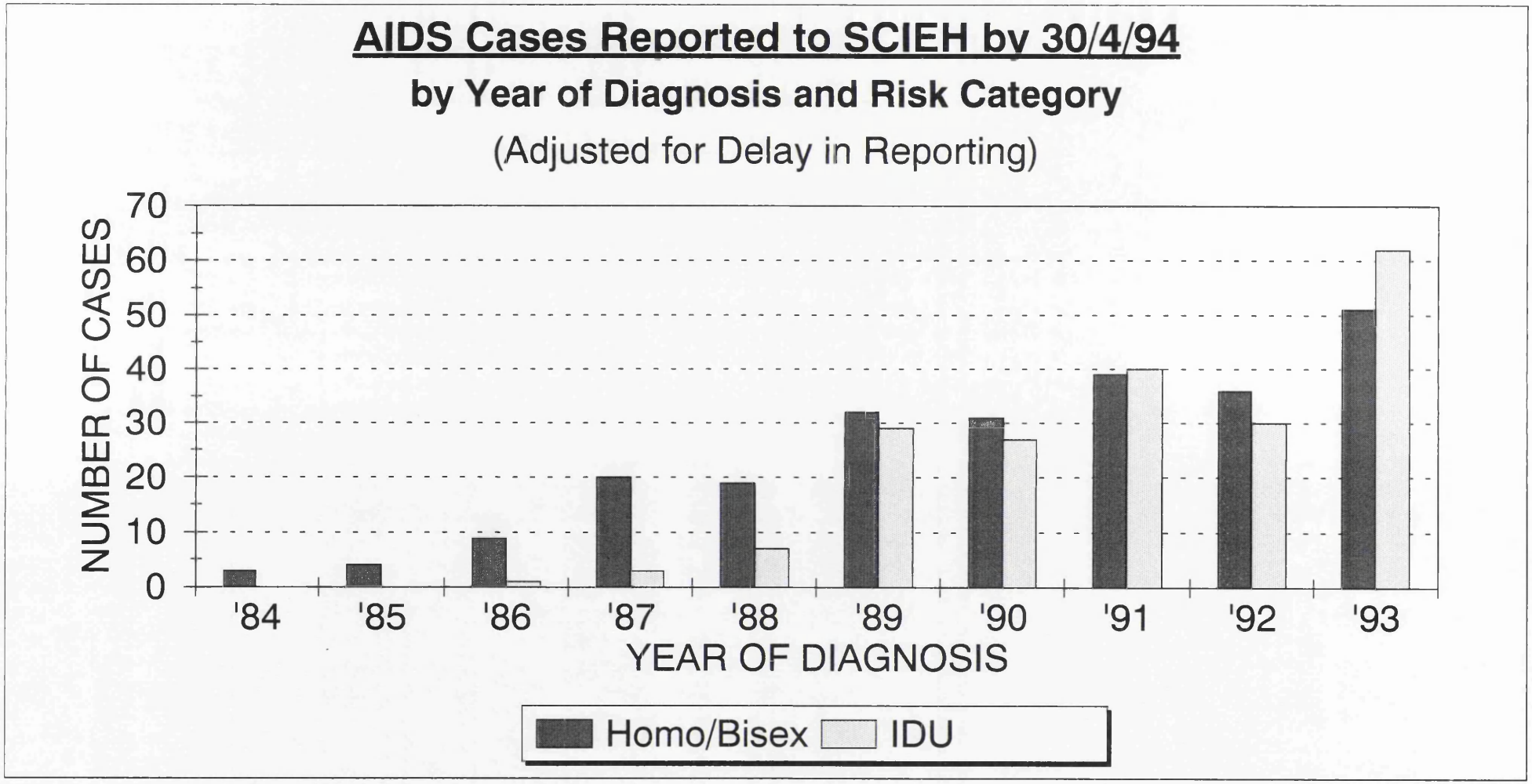
AIDS Cases Reported to SCIEH by 30/4/94
by Year of Diagnosis and Risk Category
(Adjusted for Delay in Reporting)
NUMBER OF CASES
70
60
50
40
30
20
10
0
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF DIAGNOSIS
Homo/Bisex
IDU

Figure 2.08

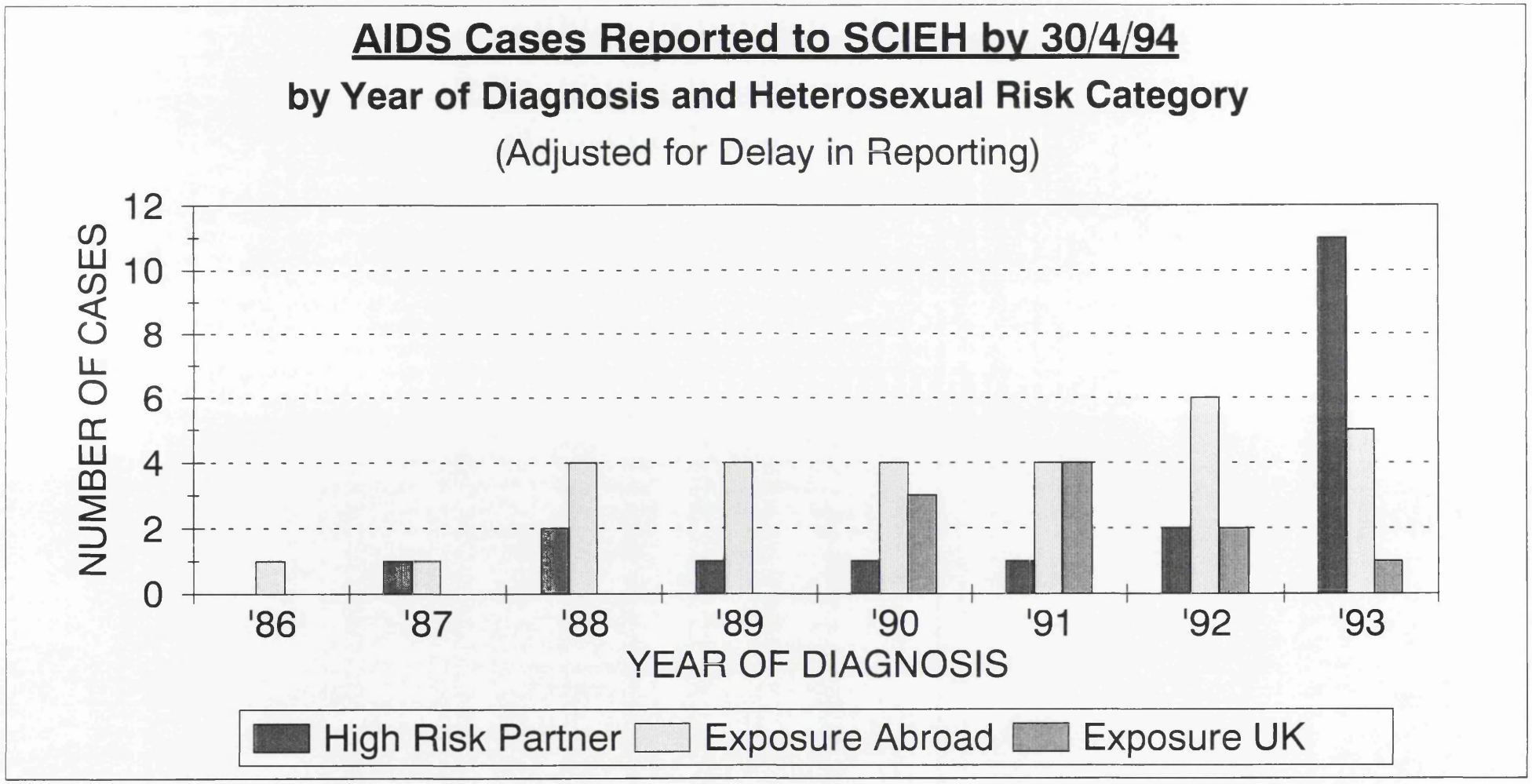
AIDS Cases Reported to SCIEH by 30/4/94
by Year of Diagnosis and Heterosexual Risk Category
(Adjusted for Delay in Reporting)
NUMBER OF CASES
12
10
8
6
4
2
0
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF DIAGNOSIS
High Risk Partner
Exposure Abroad
Exposure UK

Figure 2.09

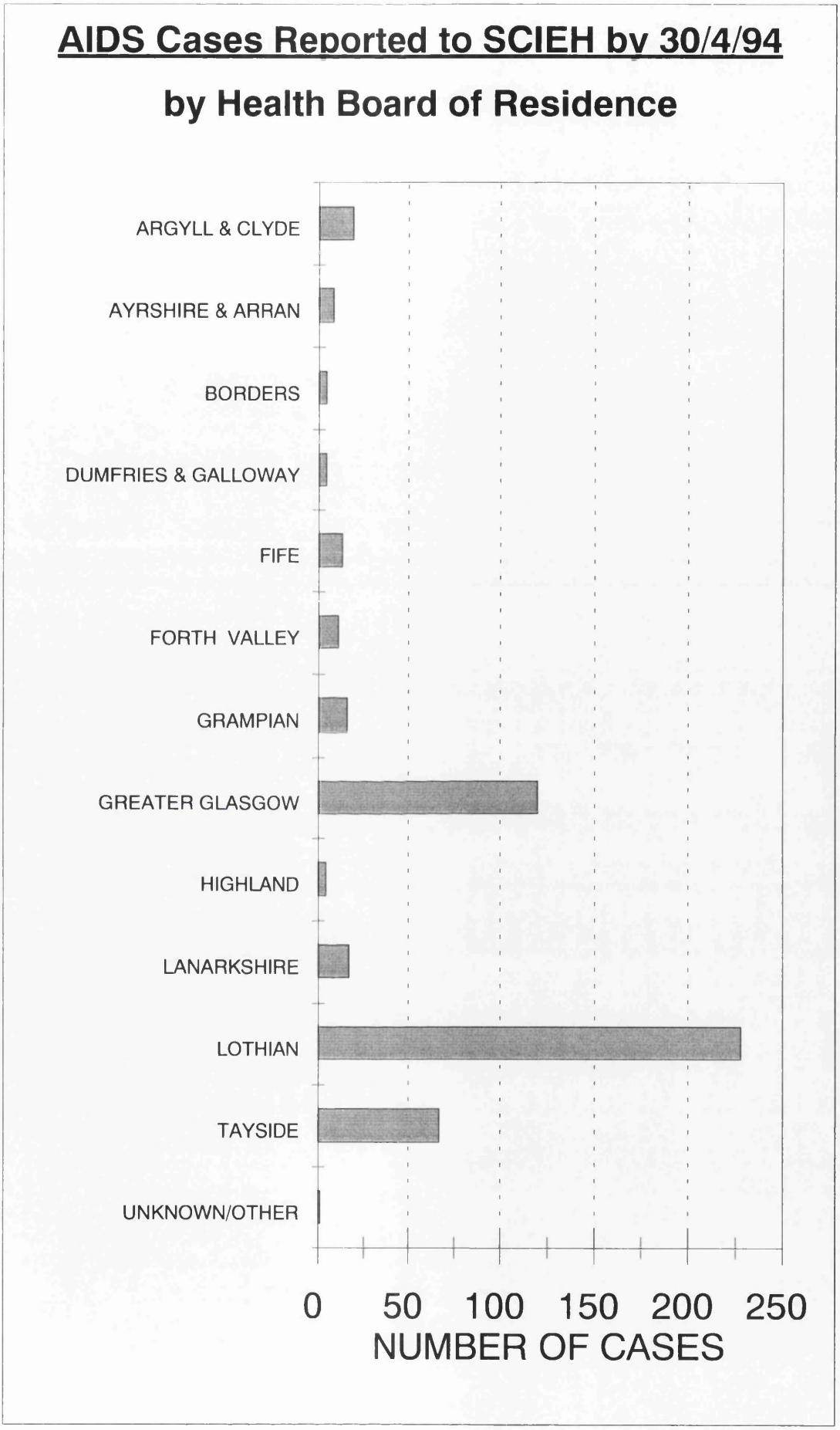
AIDS Cases Reported to SCIEH by 30/4/94
by Health Board of Residence
ARGYLL & CLYDE
AYRSHIRE & ARRAN
BORDERS
DUMFRIES & GALLOWAY
FIFE
FORTH VALLEY
GRAMPIAN
GREATER GLASGOW
HIGHLAND
LANARKSHIRE
LOTHIAN
TAYSIDE
UNKNOWN/OTHER
0
50
100
150
200
250
NUMBER OF CASES

Figure 2.10

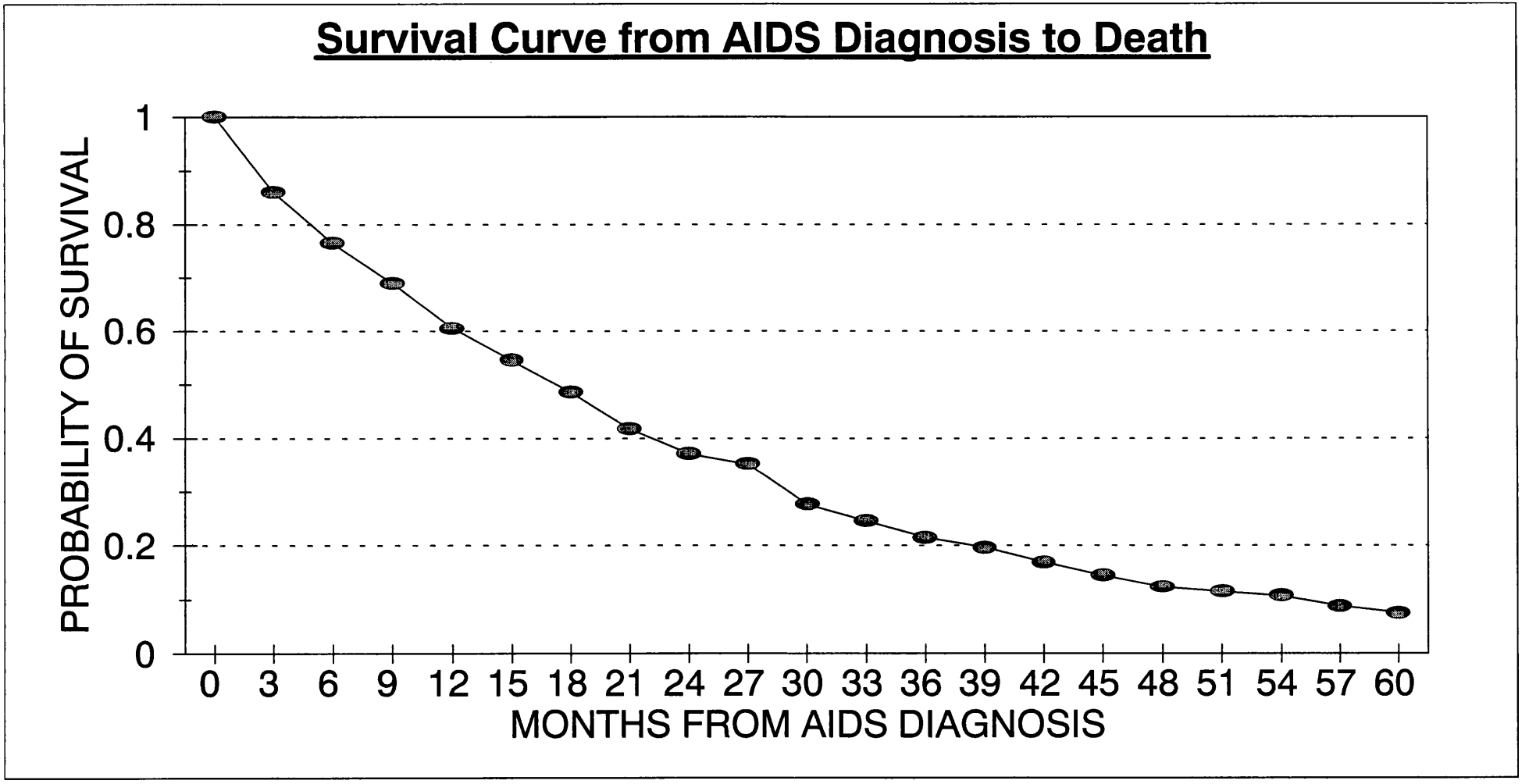
Survival Curve from AIDS Diagnosis to Death
PROBABILITY OF SURVIVAL
1
0.8
0.6
0.4
0.2
0
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45 48 51 54 57 60
MONTHS FROM AIDS DIAGNOSIS

Figure 2.11

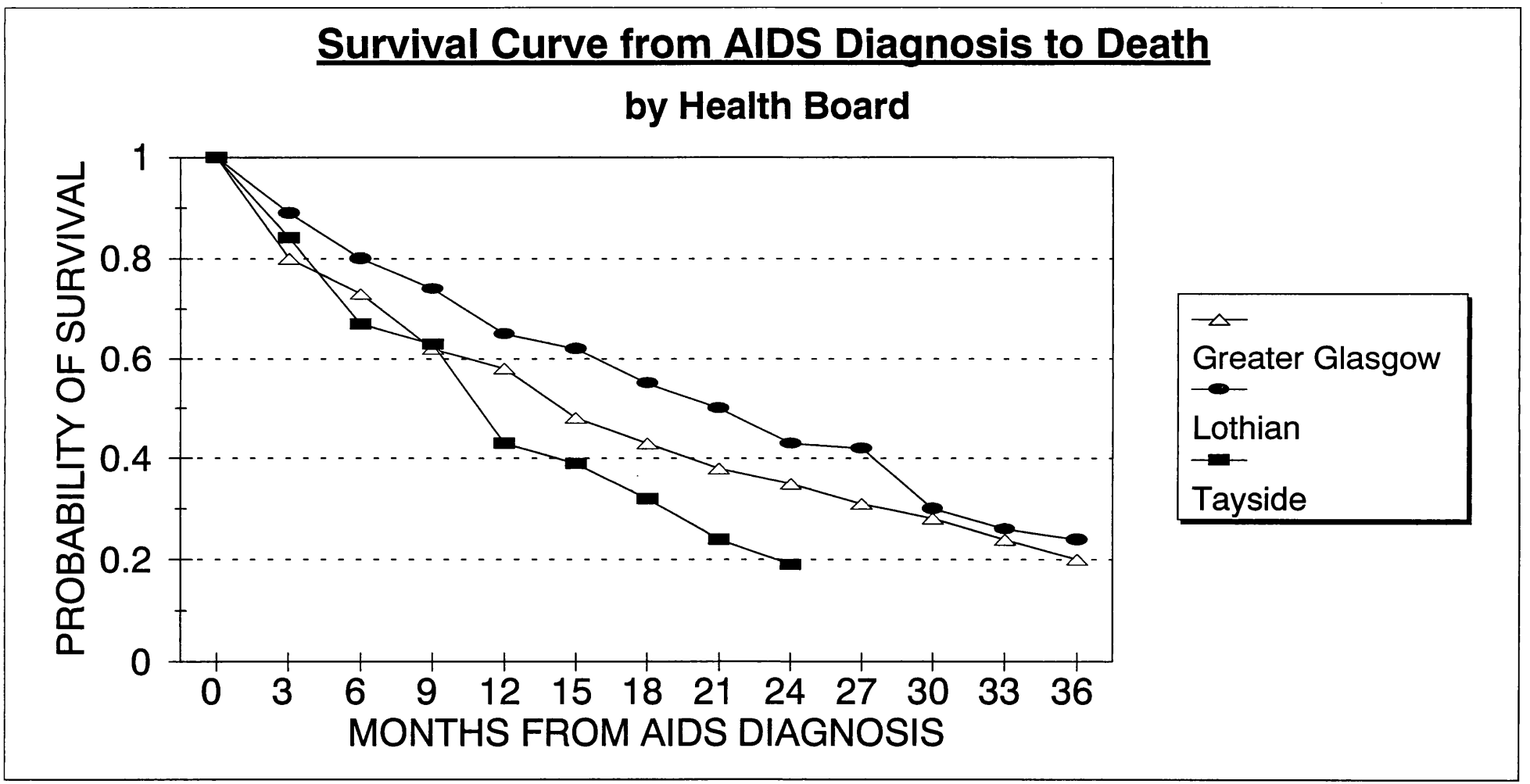
Survival Curve from AIDS Diagnosis to Death
by Health Board
PROBABILITY OF SURVIVAL
1
0.8
0.6
0.4
0.2
0
0 3 6 9 12 15 18 21 24 27 30 33 36
MONTHS FROM AIDS DIAGNOSIS
Greater Glasgow
Lothian
Tayside

Figure 2.12

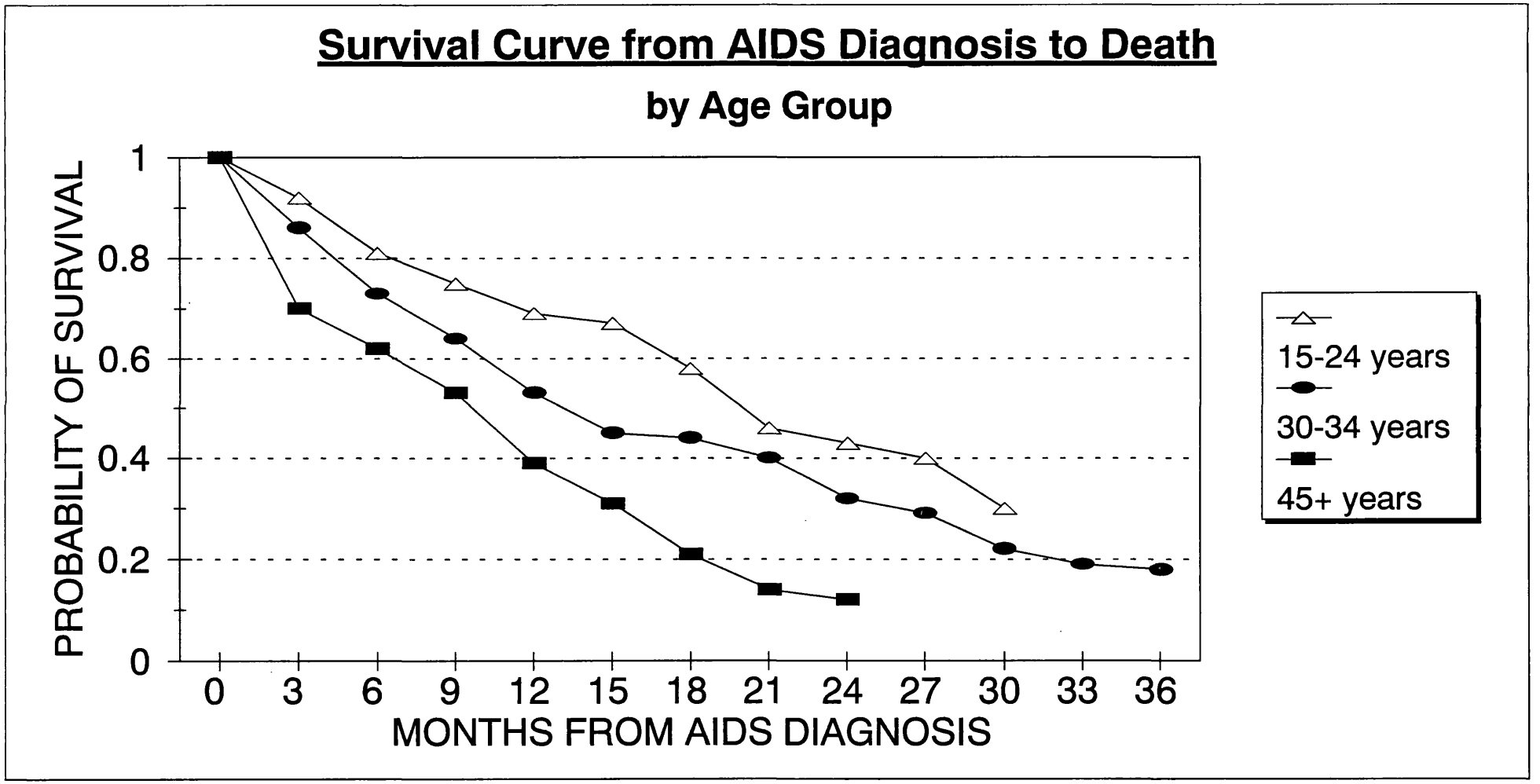
Survival Curve from AIDS Diagnosis to Death
by Age Group
PROBABILITY OF SURVIVAL
1
0.8
0.6
0.4
0.2
0
0 3 6 9 12 15 18 21 24 27 30 33 36
MONTHS FROM AIDS DIAGNOSIS
15-24 years
30-34 years
45+ years

Figure 2.13

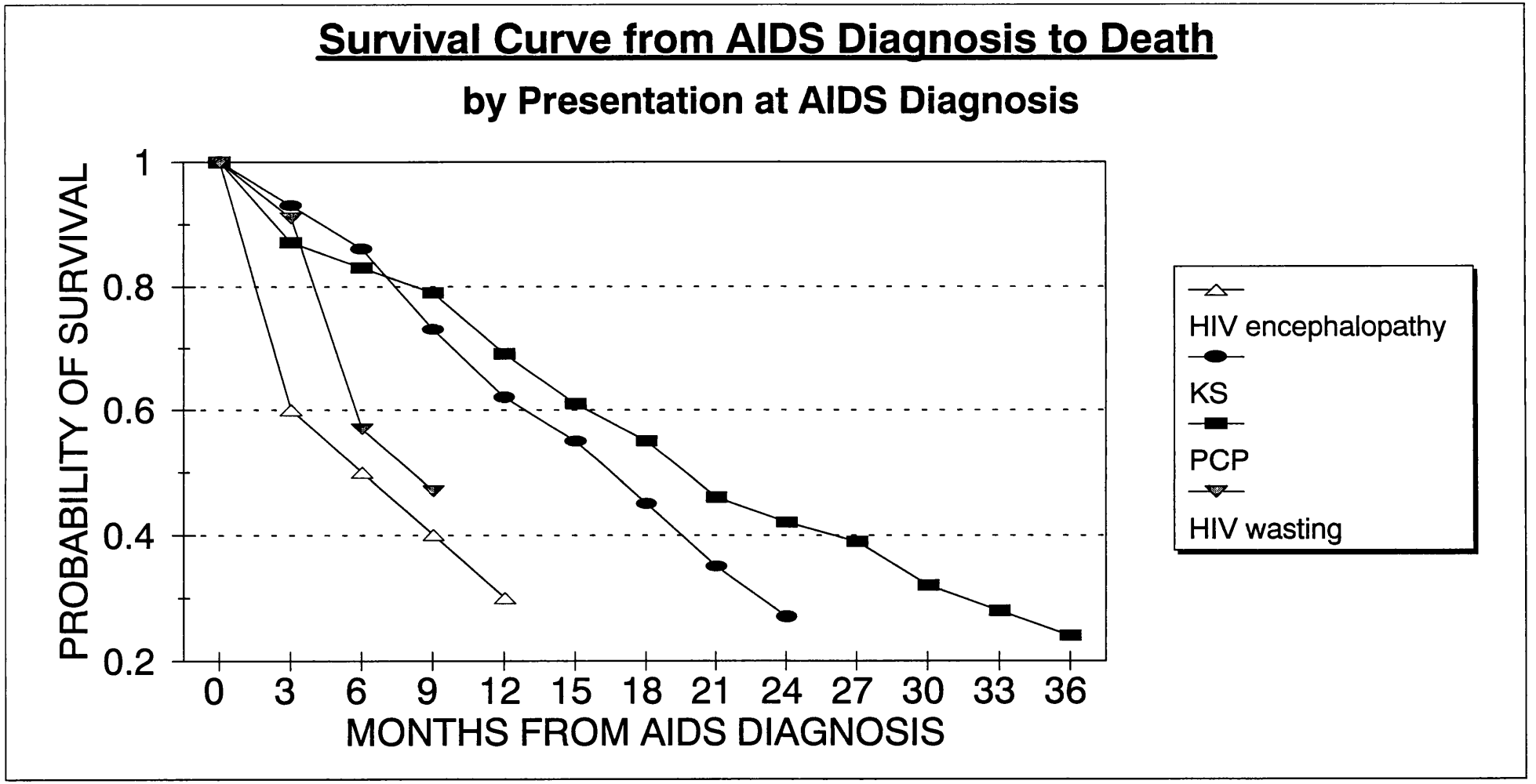
Survival Curve from AIDS Diagnosis to Death
by Presentation at AIDS Diagnosis
PROBABILITY OF SURVIVAL
1
0.8
0.6
0.4
0.2
0
3
6
9
12
15
18
21
24
27
30
33
36
MONTHS FROM AIDS DIAGNOSIS
HIV encephalopathy
KS
PCP
HIV wasting

Figure 2.14

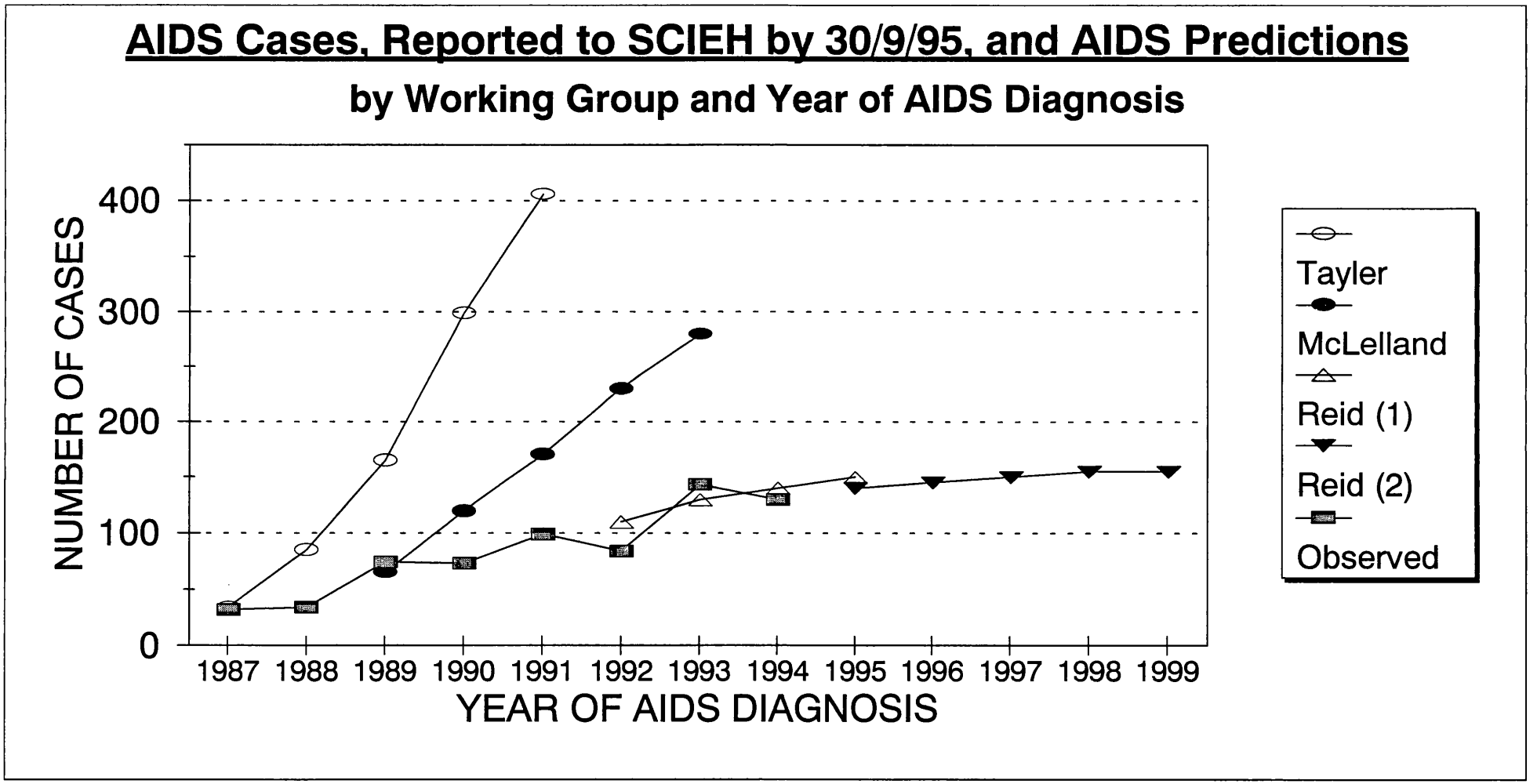
AIDS Cases, Reported to SCIEH by 30/9/95, and AIDS Predictions
by Working Group and Year of AIDS Diagnosis
NUMBER OF CASES
400
300
200
100
0
1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999
YEAR OF AIDS DIAGNOSIS
Tayler
McLelland
Reid (1)
Reid (2)
Observed

Figure 2.15

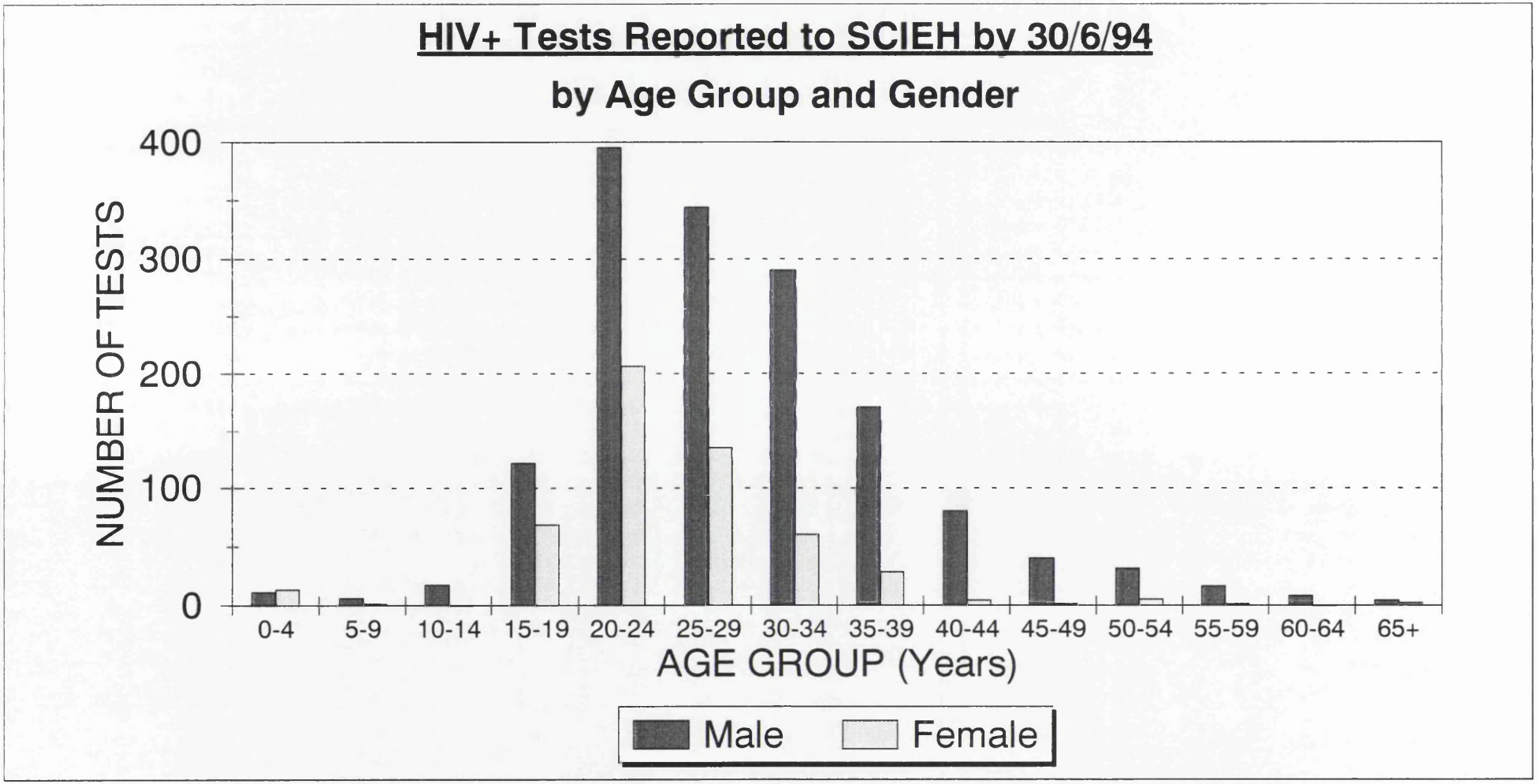
HIV+ Tests Reported to SCIEH by 30/6/94
by Age Group and Gender
NUMBER OF TESTS
400
300
200
100
0
0-4
5-9
10-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65+
AGE GROUP (Years)
Male
Female

Figure 3.01

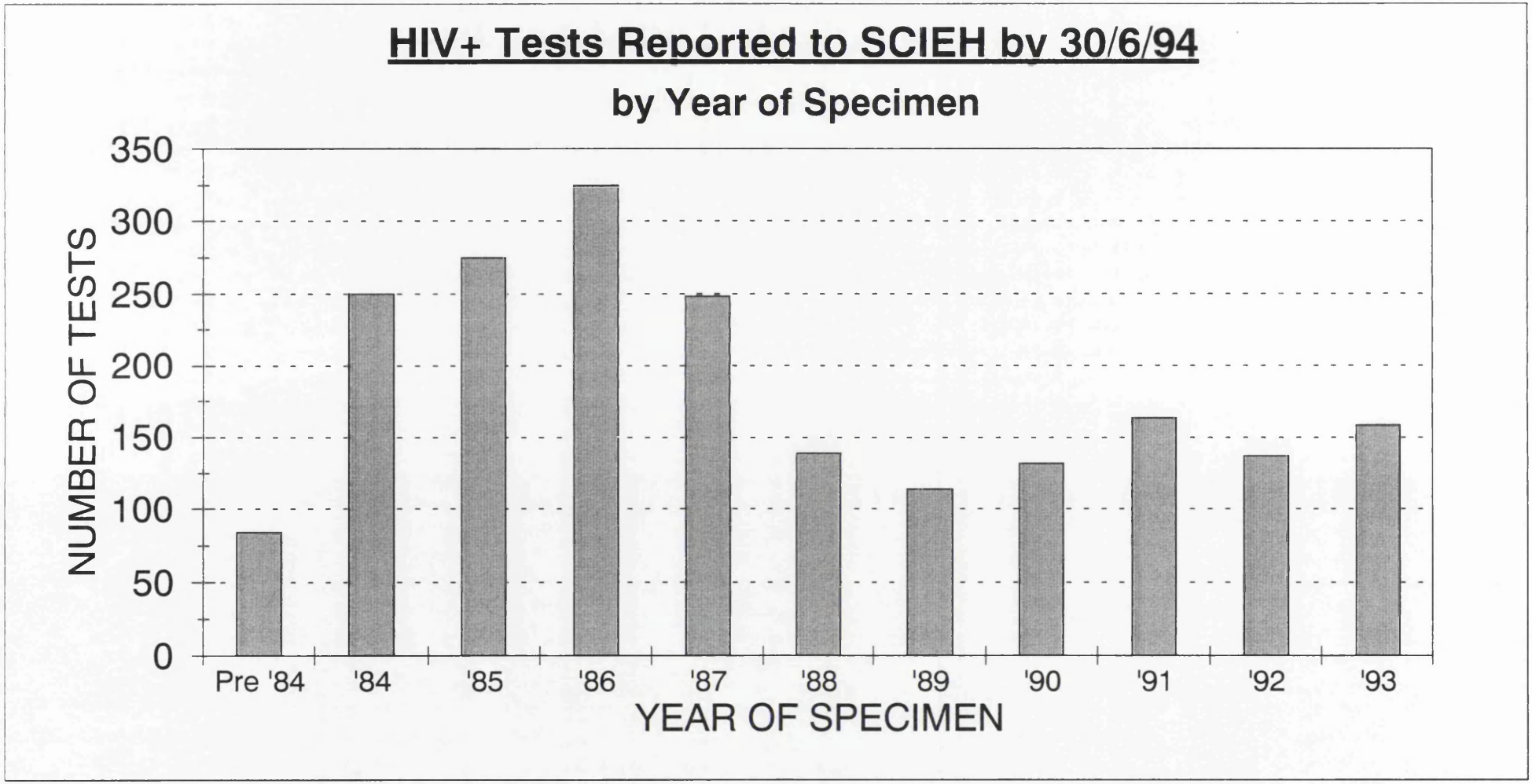
HIV+ Tests Reported to SCIEH by 30/6/94
by Year of Specimen
NUMBER OF TESTS
350
300
250
200
150
100
50
0
Pre '84
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF SPECIMEN

Figure 3.02

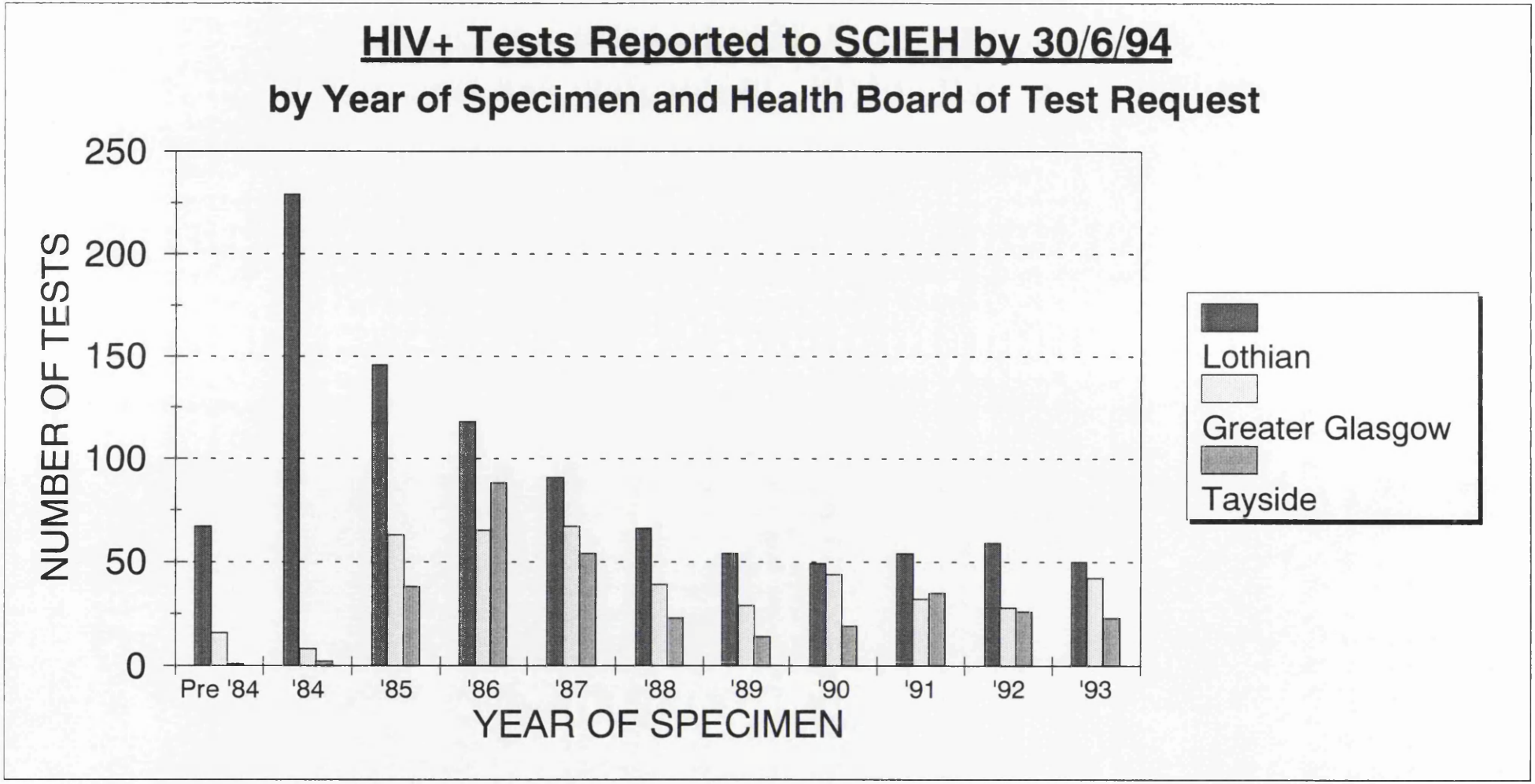
HIV+ Tests Reported to SCIEH by 30/6/94
by Year of Specimen and Health Board of Test Request
NUMBER OF TESTS
250
200
150
100
50
0
Pre '84
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF SPECIMEN
Lothian
Greater Glasgow
Tayside

Figure 3.03

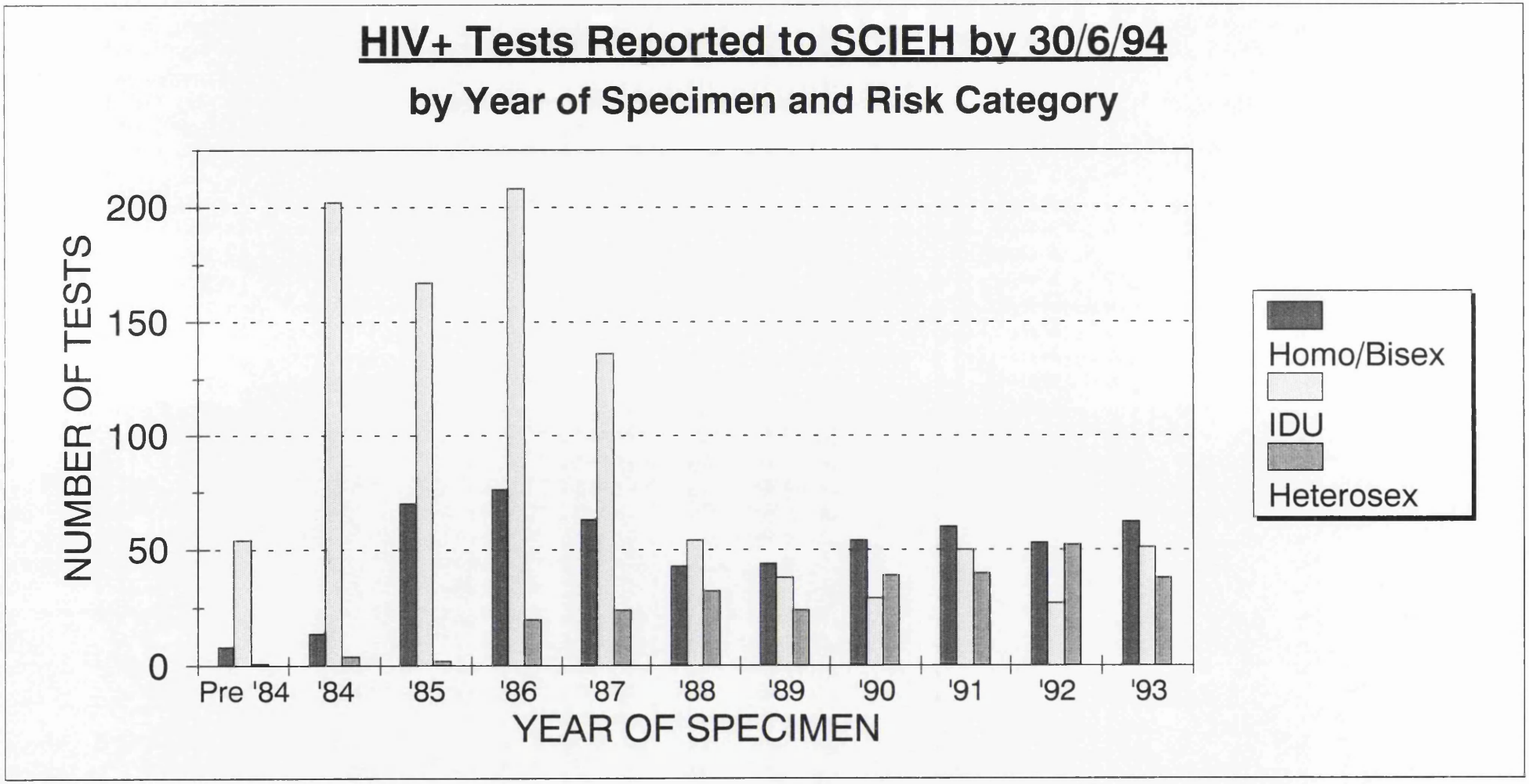
HIV+ Tests Reported to SCIEH by 30/6/94
by Year of Specimen and Risk Category
NUMBER OF TESTS
200
150
100
50
0
Pre '84
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF SPECIMEN
Homo/Bisex
IDU
Heterosex

Figure 3.04

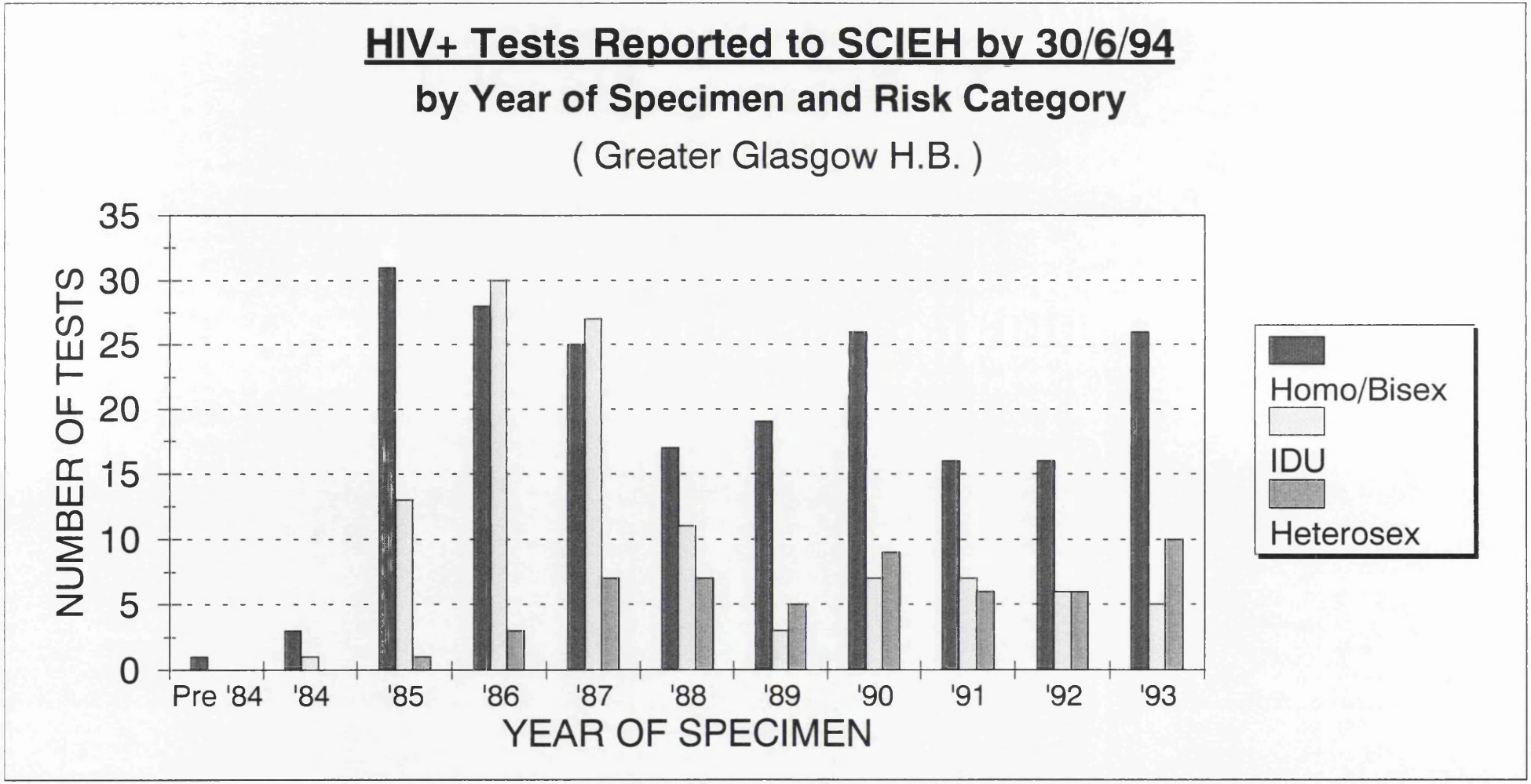
HIV+ Tests Reported to SCIEH by 30/6/94
by Year of Specimen and Risk Category
(Greater Glasgow H.B.)
NUMBER OF TESTS
35
30
25
20
15
10
5
0
Pre '84
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF SPECIMEN
Homo/Bisex
IDU
Heterosex

Figure 3.05

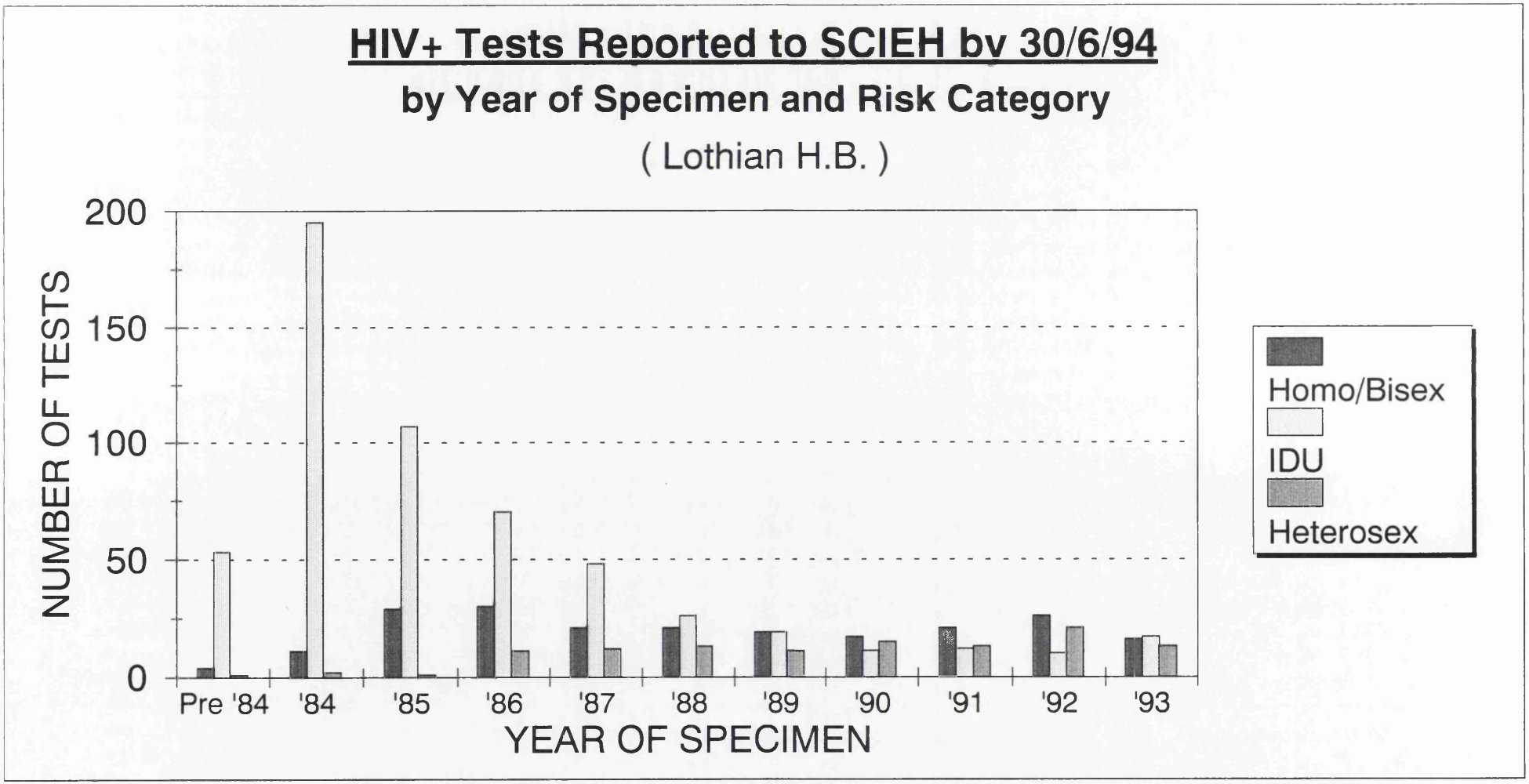
HIV+ Tests Reported to SCIEH by 30/6/94
by Year of Specimen and Risk Category
(Lothian H.B.)
NUMBER OF TESTS
200
150
100
50
0
Pre '84
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF SPECIMEN
Homo/Bisex
IDU
Heterosex

Figure 3.06

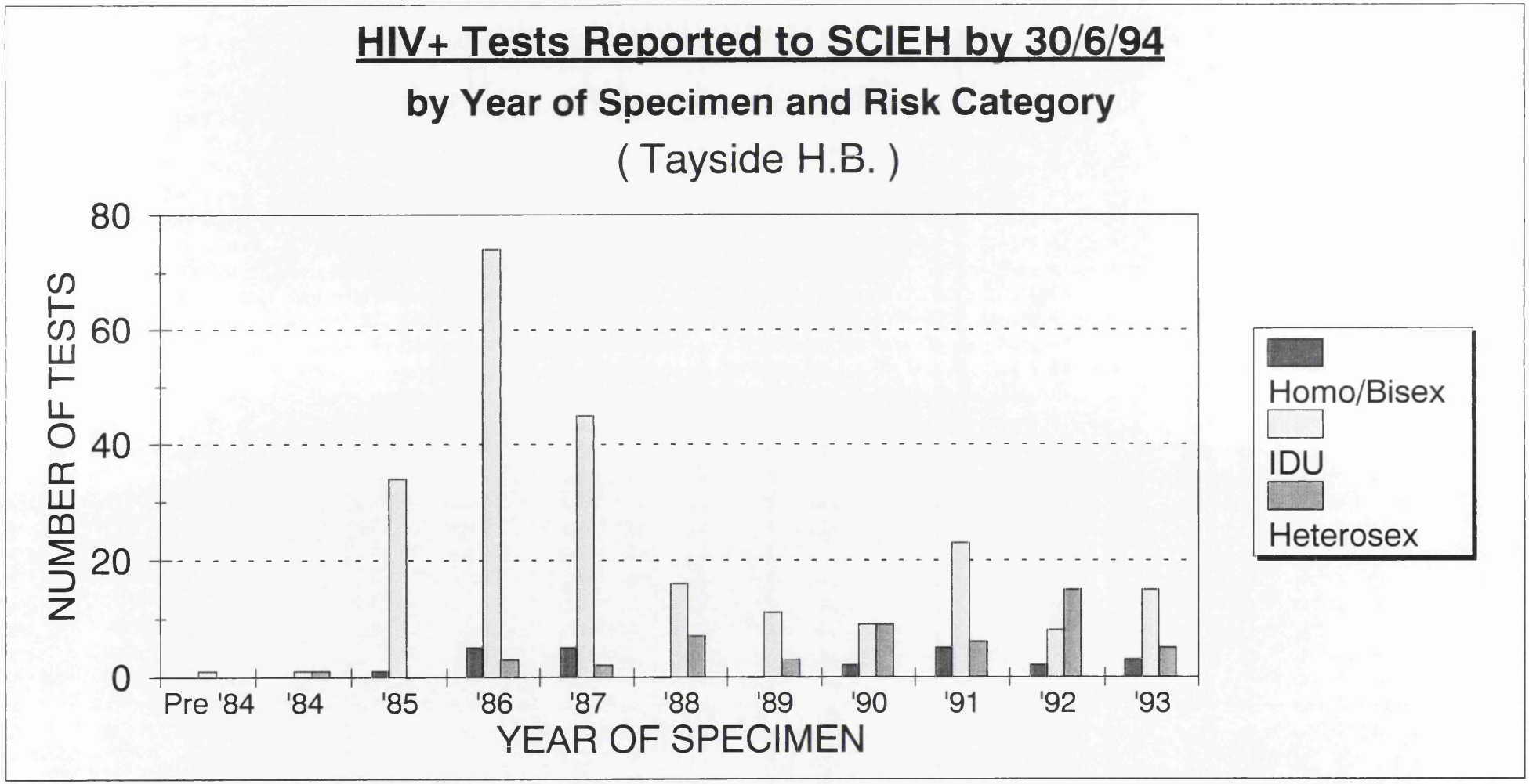
HIV+ Tests Reported to SCIEH by 30/6/94
by Year of Specimen and Risk Category
(Tayside H.B.)
NUMBER OF TESTS
80
60
40
20
0
Pre '84
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF SPECIMEN
Homo/Bisex
IDU
Heterosex

Figure 3.07

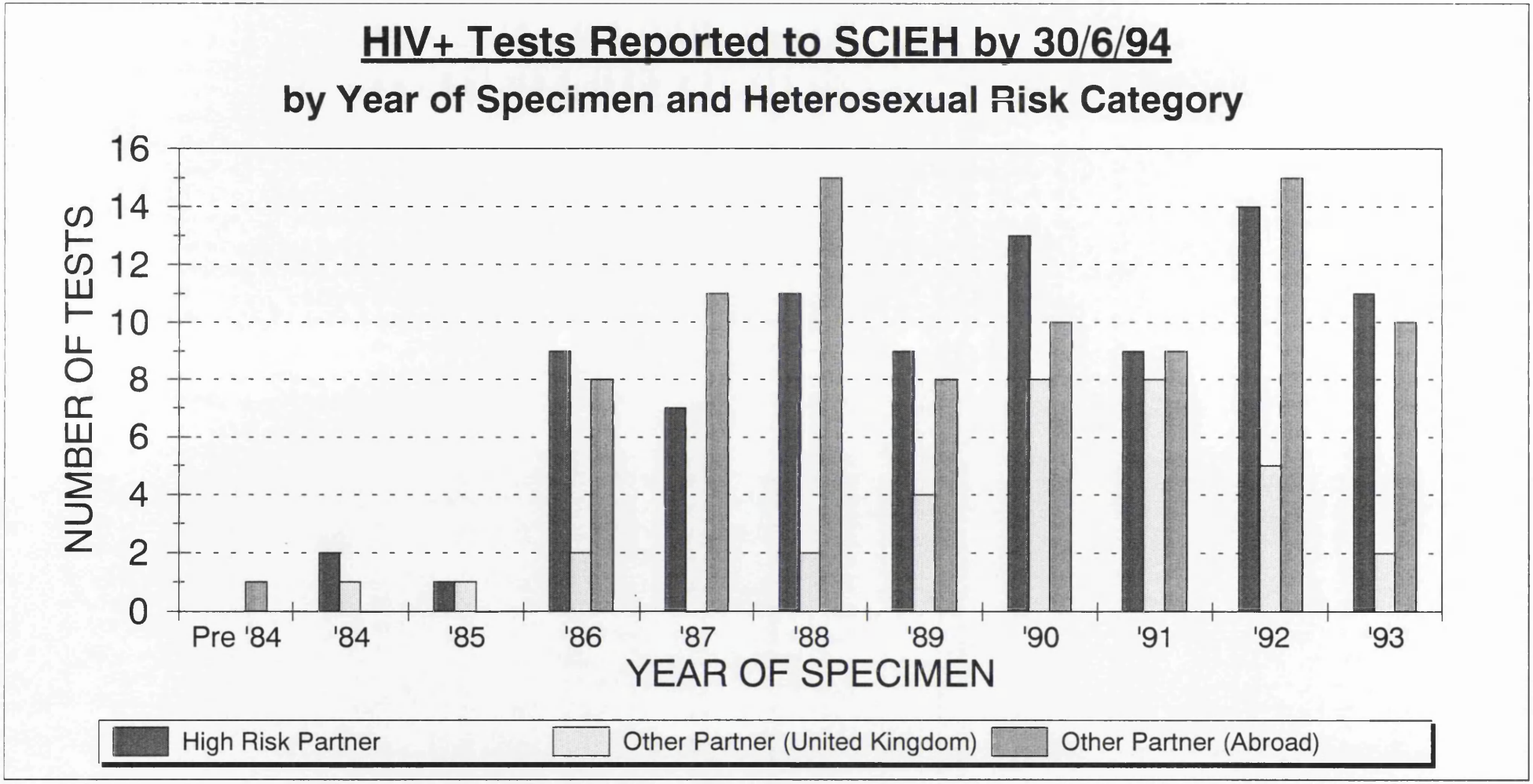
HIV+ Tests Reported to SCIEH by 30/6/94
by Year of Specimen and Heterosexual Risk Category
NUMBER OF TESTS
16
14
12
10
8
6
4
2
0
Pre '84
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF SPECIMEN
High Risk Partner
Other Partner (United Kingdom)
Other Partner (Abroad)

Figure 3.08

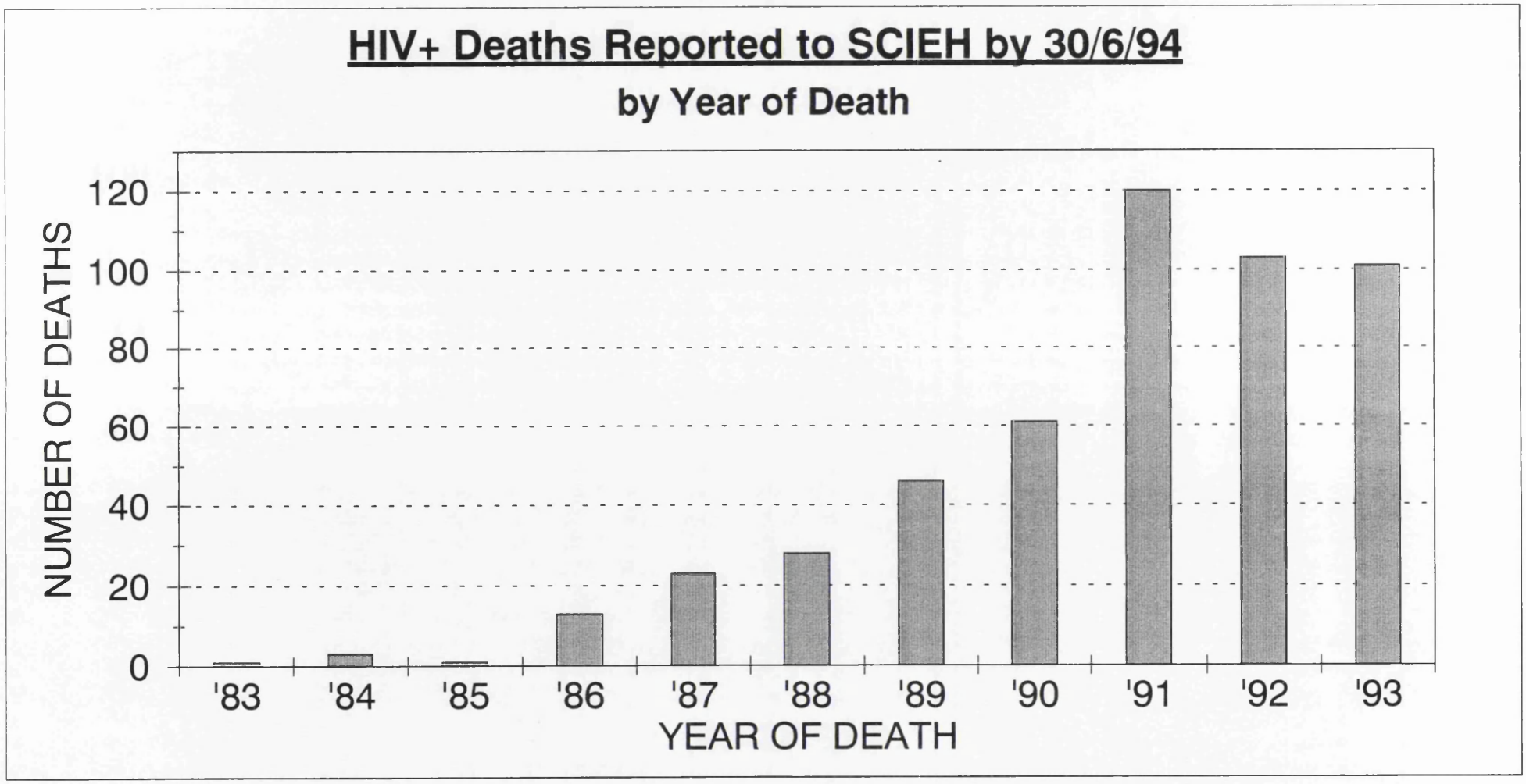
HIV+ Deaths Reported to SCIEH by 30/6/94
by Year of Death
NUMBER OF DEATHS
120
100
80
60
40
20
0
'83
'84
'85
'86
'87
'88
'89
'90
'91
'92
'93
YEAR OF DEATH

Figure 3.09

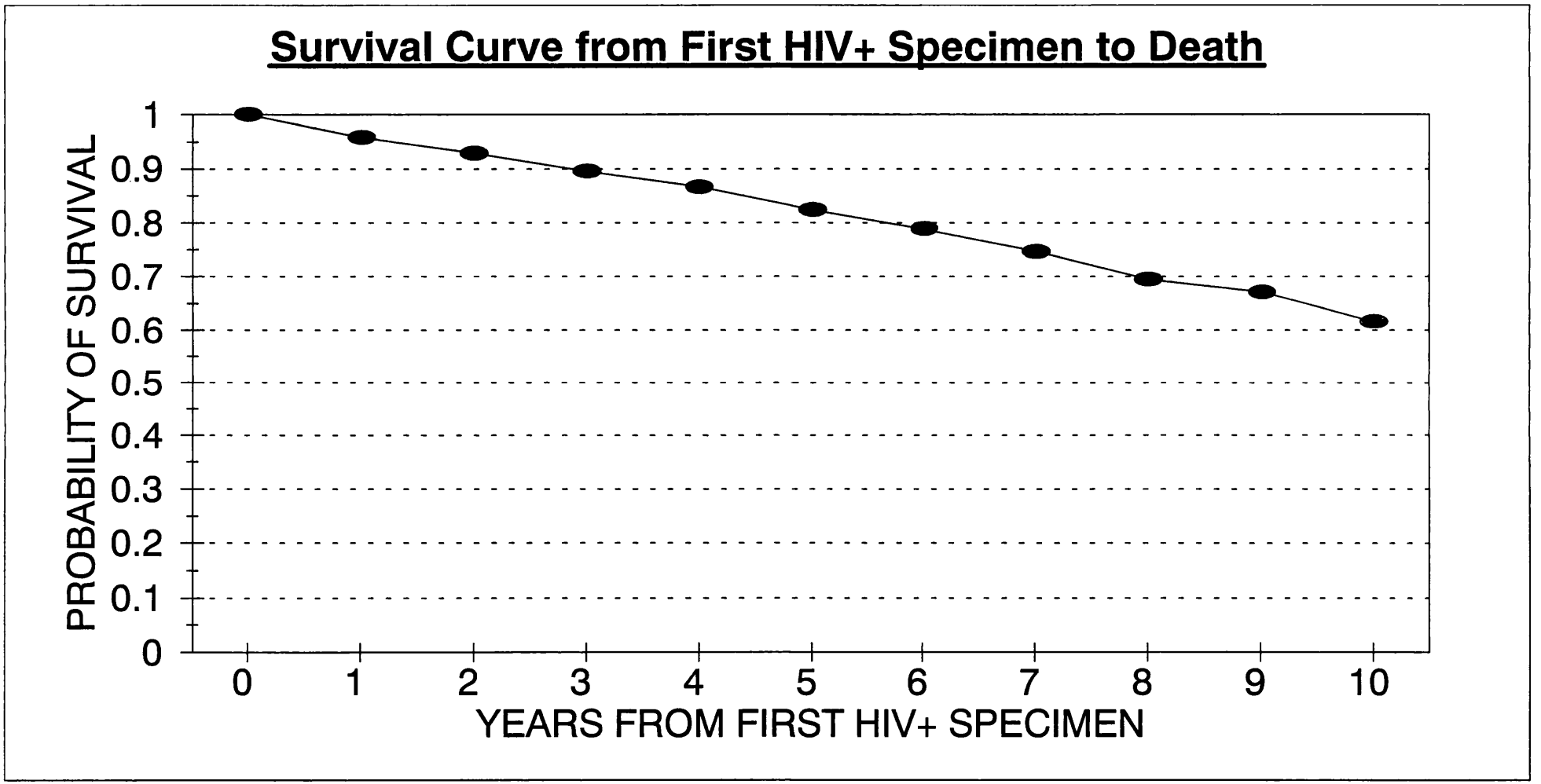
Survival Curve from First HIV+ Specimen to Death
PROBABILITY OF SURVIVAL
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
1
2
3
4
5
6
7
8
9
10
YEARS FROM FIRST HIV+ SPECIMEN

Figure 3.10

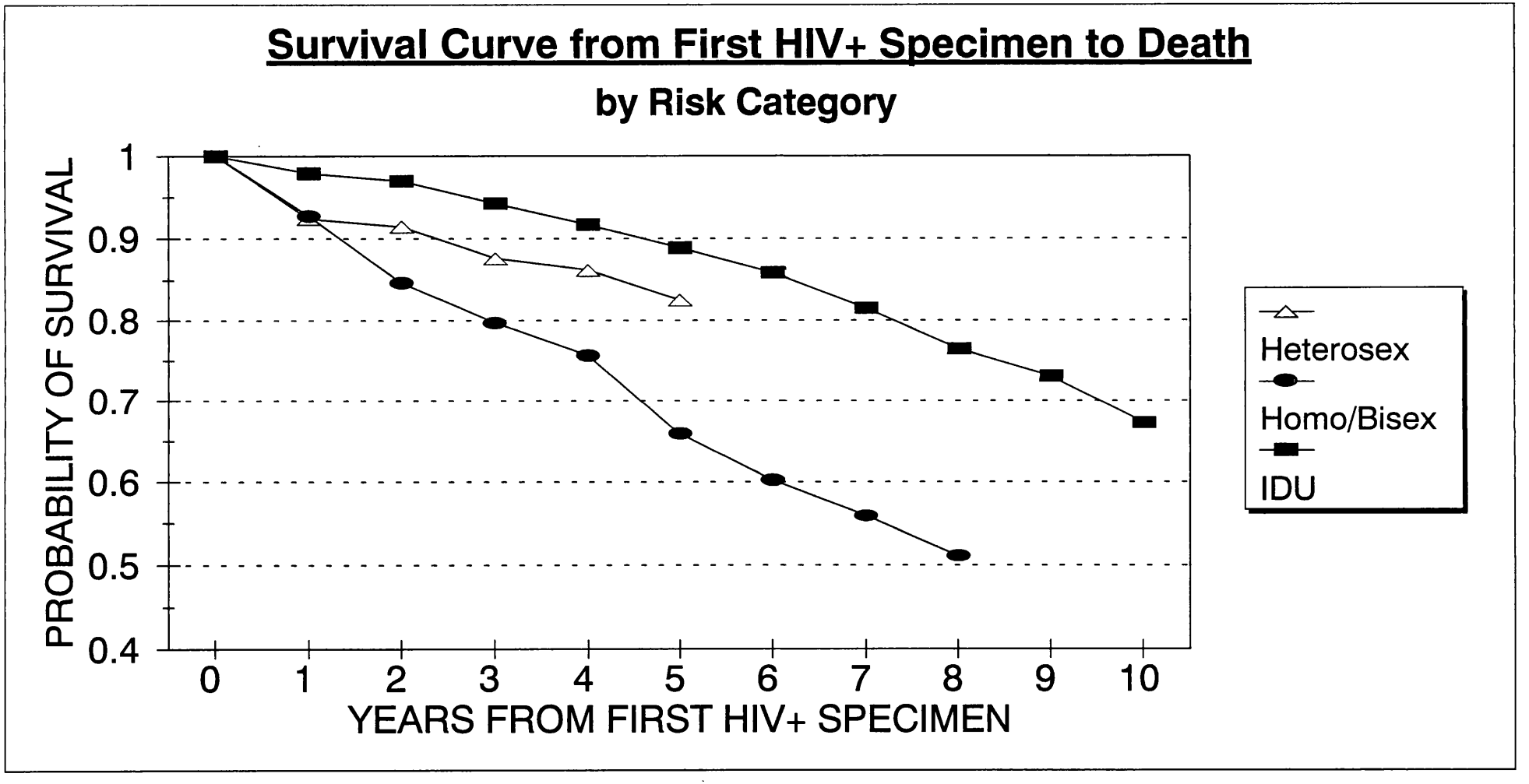
Survival Curve from First HIV+ Specimen to Death
by Risk Category
PROBABILITY OF SURVIVAL
1
0.9
0.8
0.7
0.6
0.5
0.4
0
1
2
3
4
5
6
7
8
9
10
YEARS FROM FIRST HIV+ SPECIMEN
Heterosex
Homo/Bisex
IDU

Figure 3.11

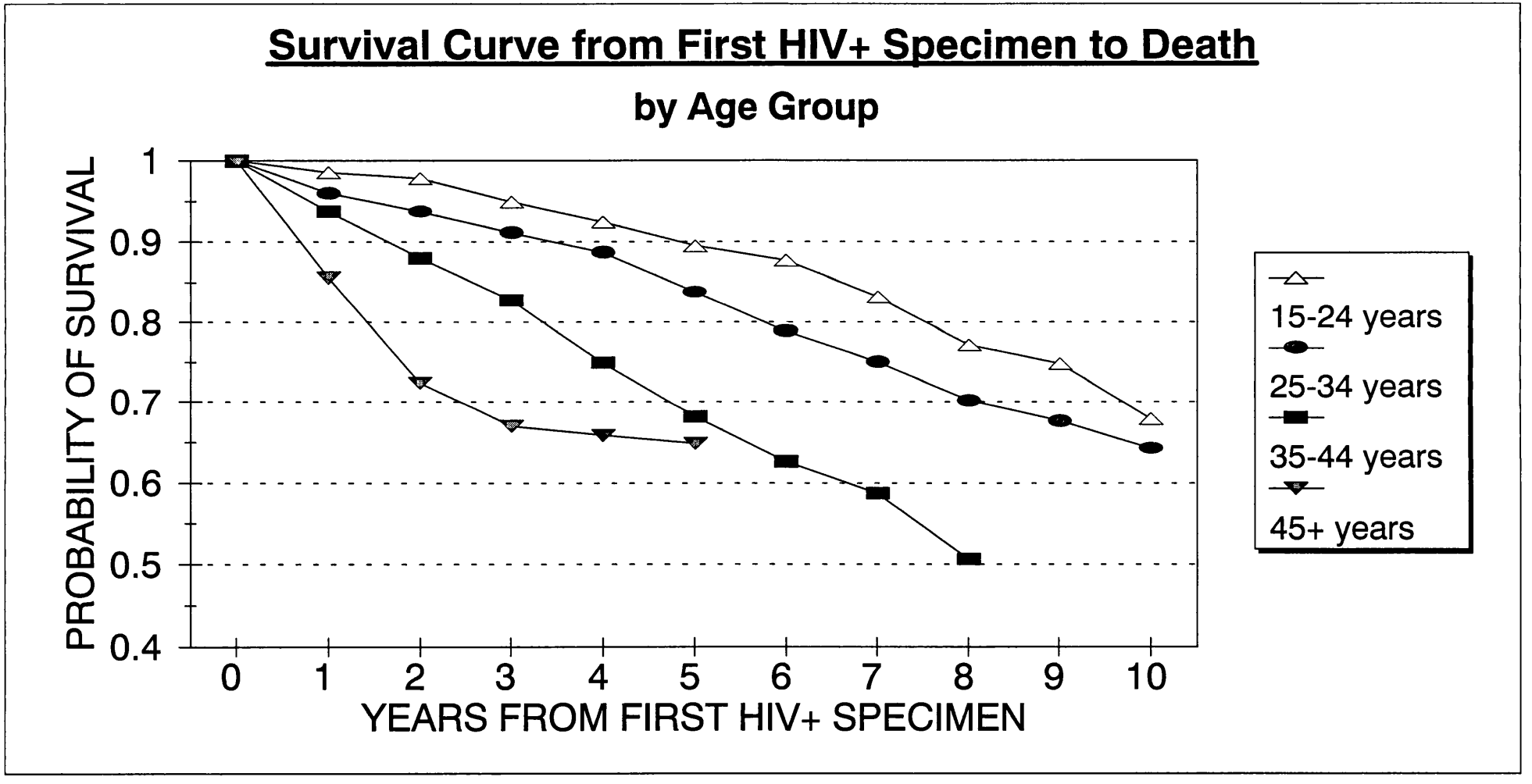
Survival Curve from First HIV+ Specimen to Death
by Age Group
PROBABILITY OF SURVIVAL
1
0.9
0.8
0.7
0.6
0.5
0.4
0
1
2
3
4
5
6
7
8
9
10
YEARS FROM FIRST HIV+ SPECIMEN
15-24 years
25-34 years
35-44 years
45+ years

Figure 3.12

Location of HIV Testing Laboratories

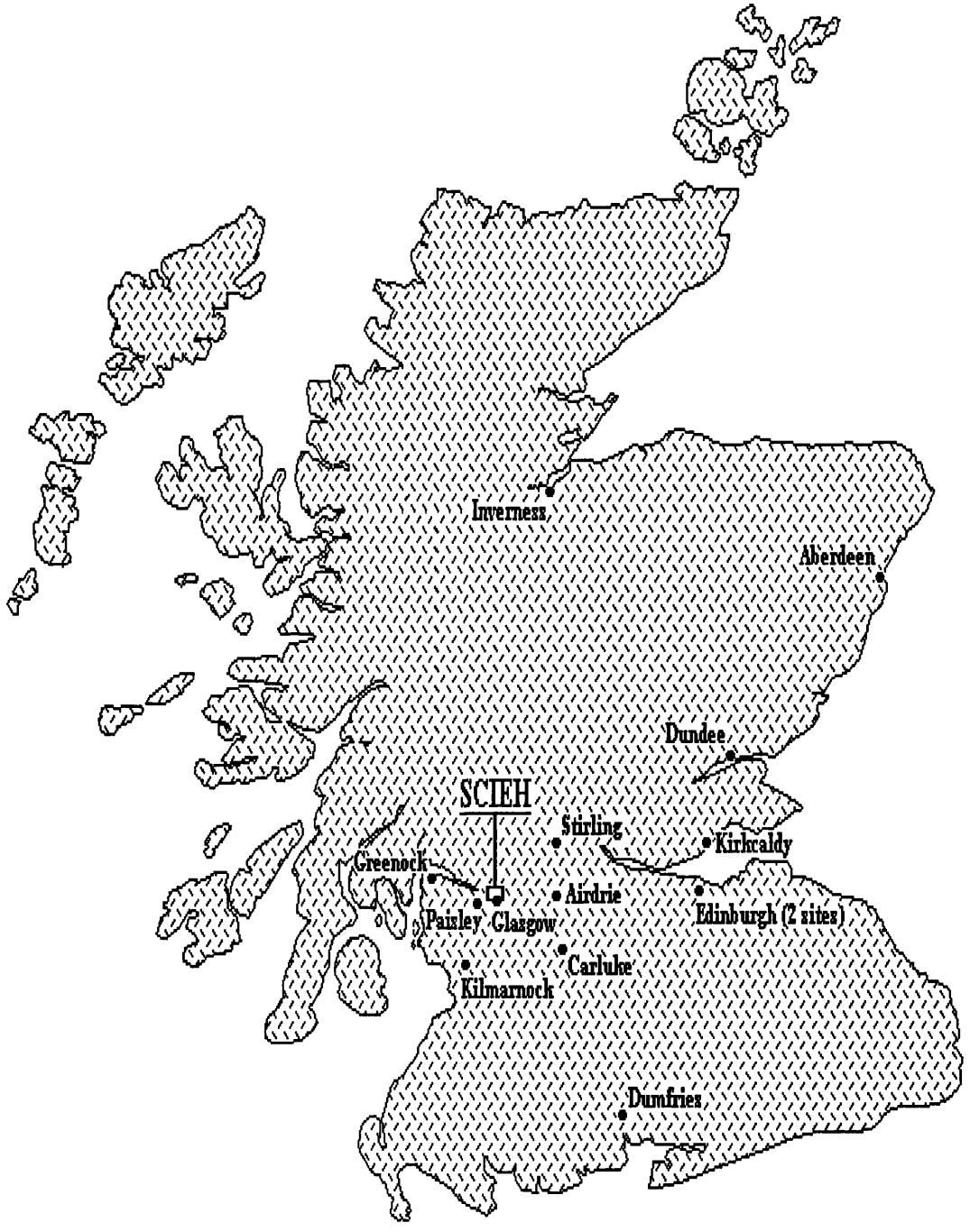

Figure 4.01

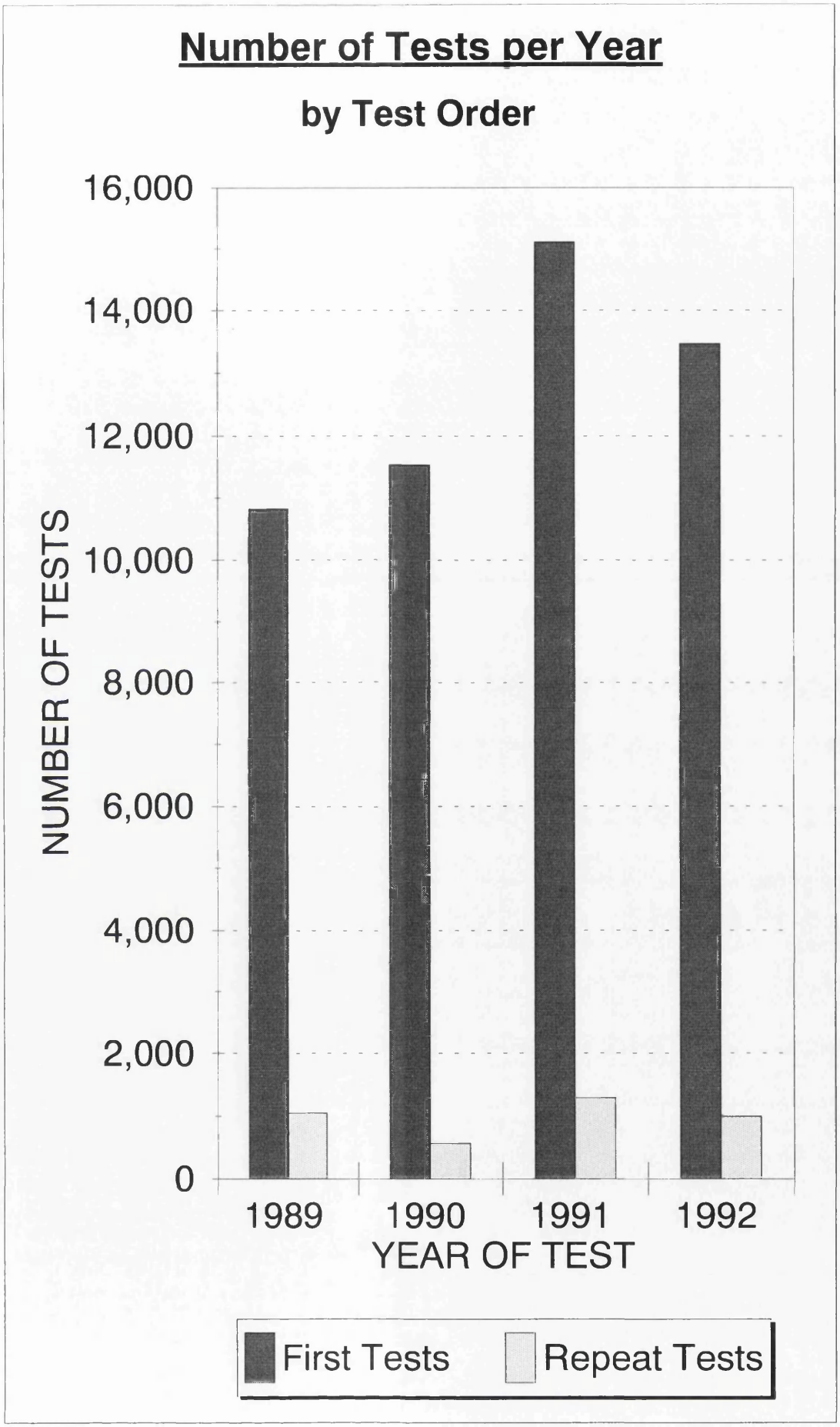
Number of Tests per Year
by Test Order
16,000
14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
NUMBER OF TESTS
1989
1990
1991
1992
YEAR OF TEST
First Tests
Repeat Tests

Figure 4.02

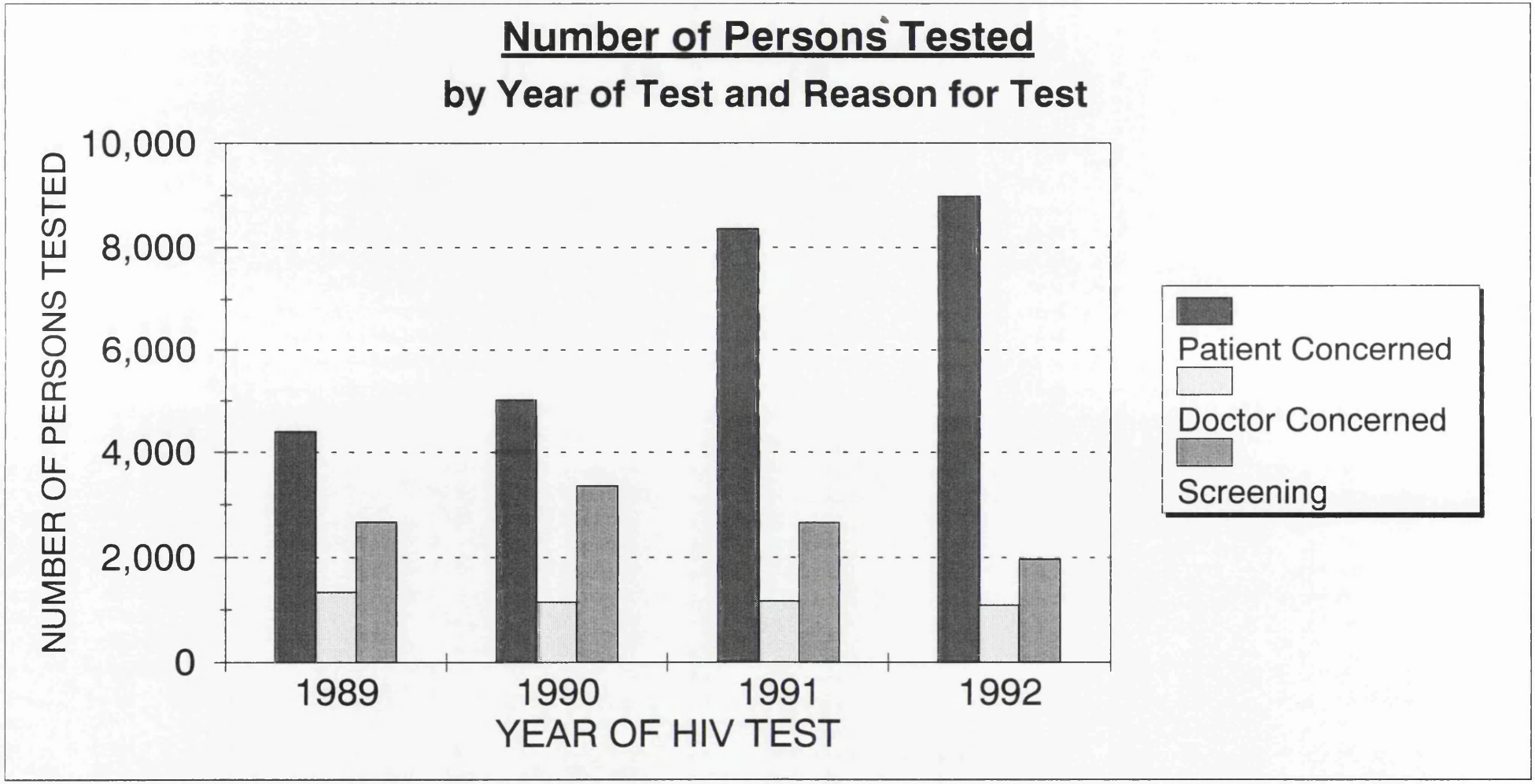
Number of Persons Tested
by Year of Test and Reason for Test
NUMBER OF PERSONS TESTED
10,000
8,000
6,000
4,000
2,000
0
1989
1990
1991
1992
YEAR OF HIV TEST
Patient Concerned
Doctor Concerned
Screening

Figure 4.03

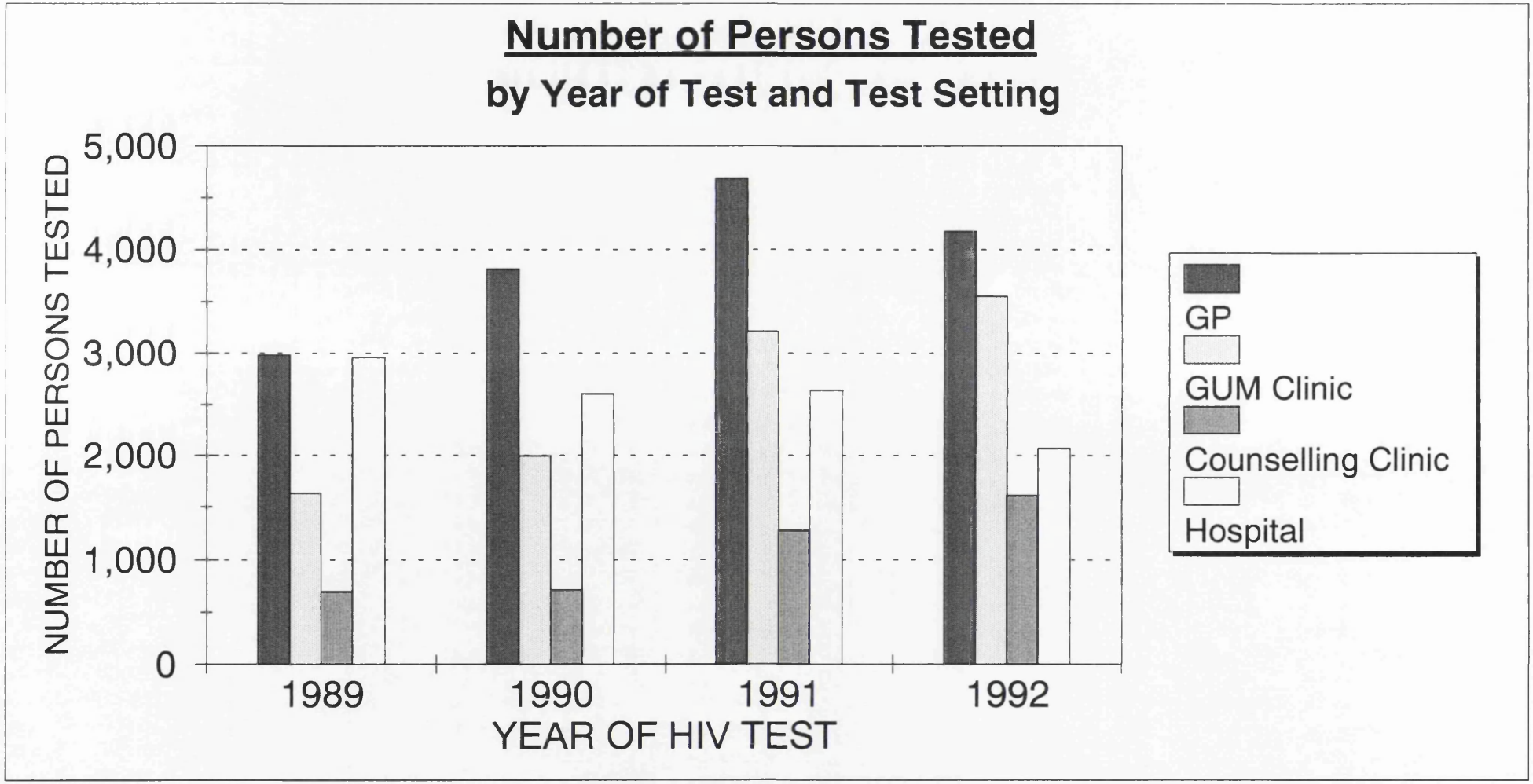
Number of Persons Tested
by Year of Test and Test Setting
NUMBER OF PERSONS TESTED
5,000
4,000
3,000
2,000
1,000
0
1989
1990
1991
1992
YEAR OF HIV TEST
GP
GUM Clinic
Counselling Clinic
Hospital

Figure 4.04

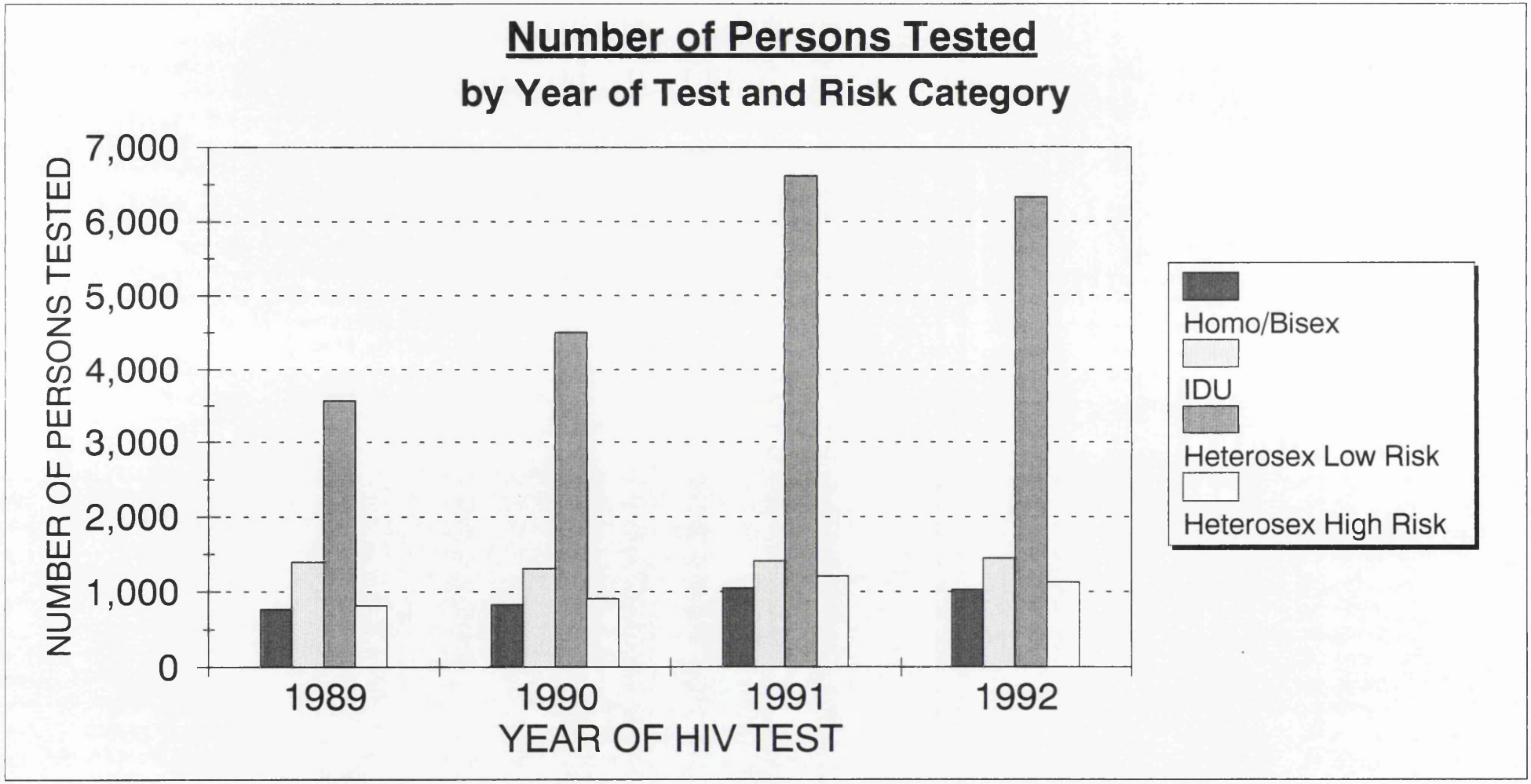
Number of Persons Tested
by Year of Test and Risk Category
NUMBER OF PERSONS TESTED
7,000
6,000
5,000
4,000
3,000
2,000
1,000
0
1989
1990
1991
1992
YEAR OF HIV TEST
Homo/Bisex
IDU
Heterosex Low Risk
Heterosex High Risk

Figure 4.05

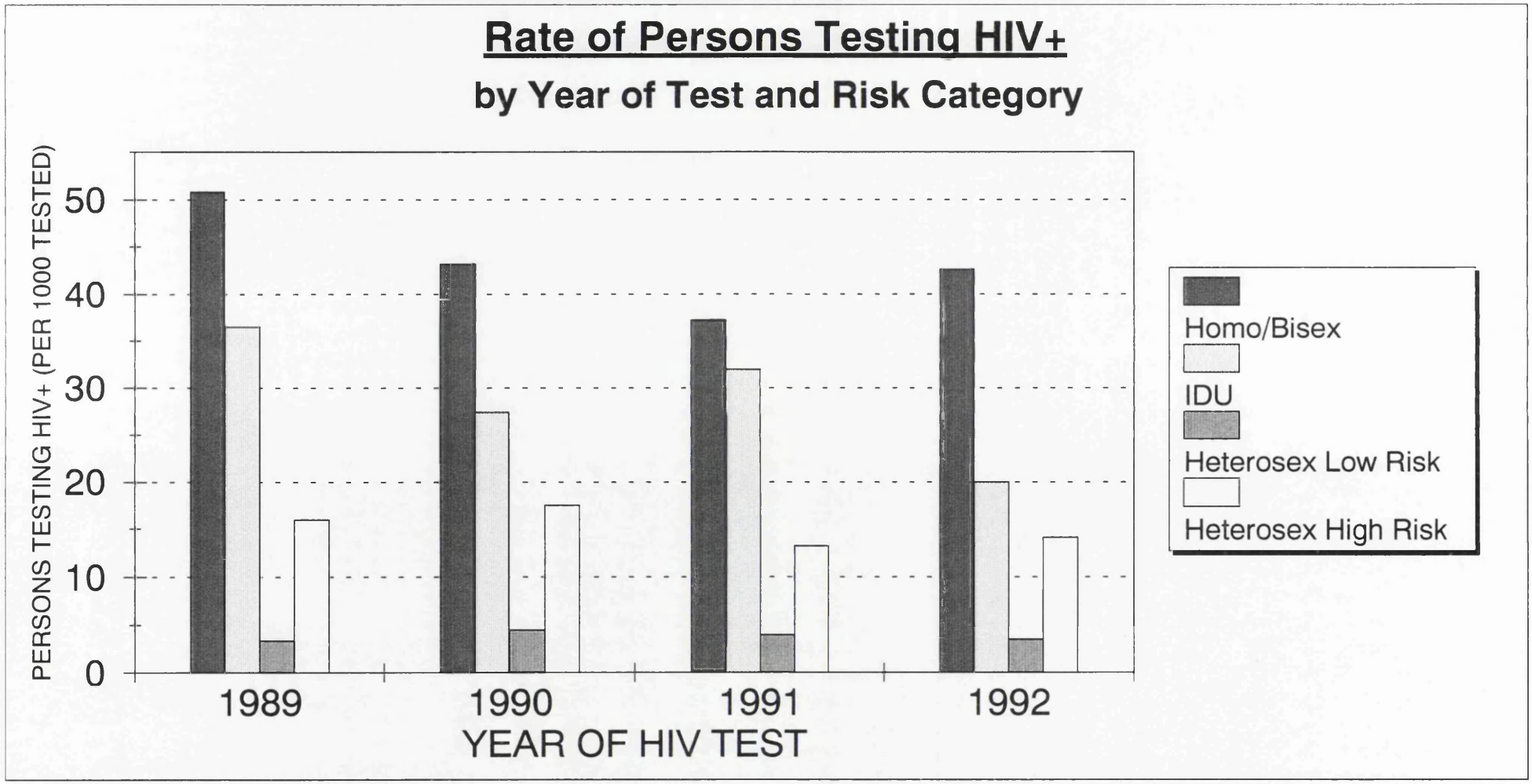
Rate of Persons Testing HIV+
by Year of Test and Risk Category
PERSONS TESTING HIV+ (PER 1000 TESTED)
50
40
30
20
10
0
1989
1990
1991
1992
YEAR OF HIV TEST
Homo/Bisex
IDU
Heterosex Low Risk
Heterosex High Risk

Figure 4.06

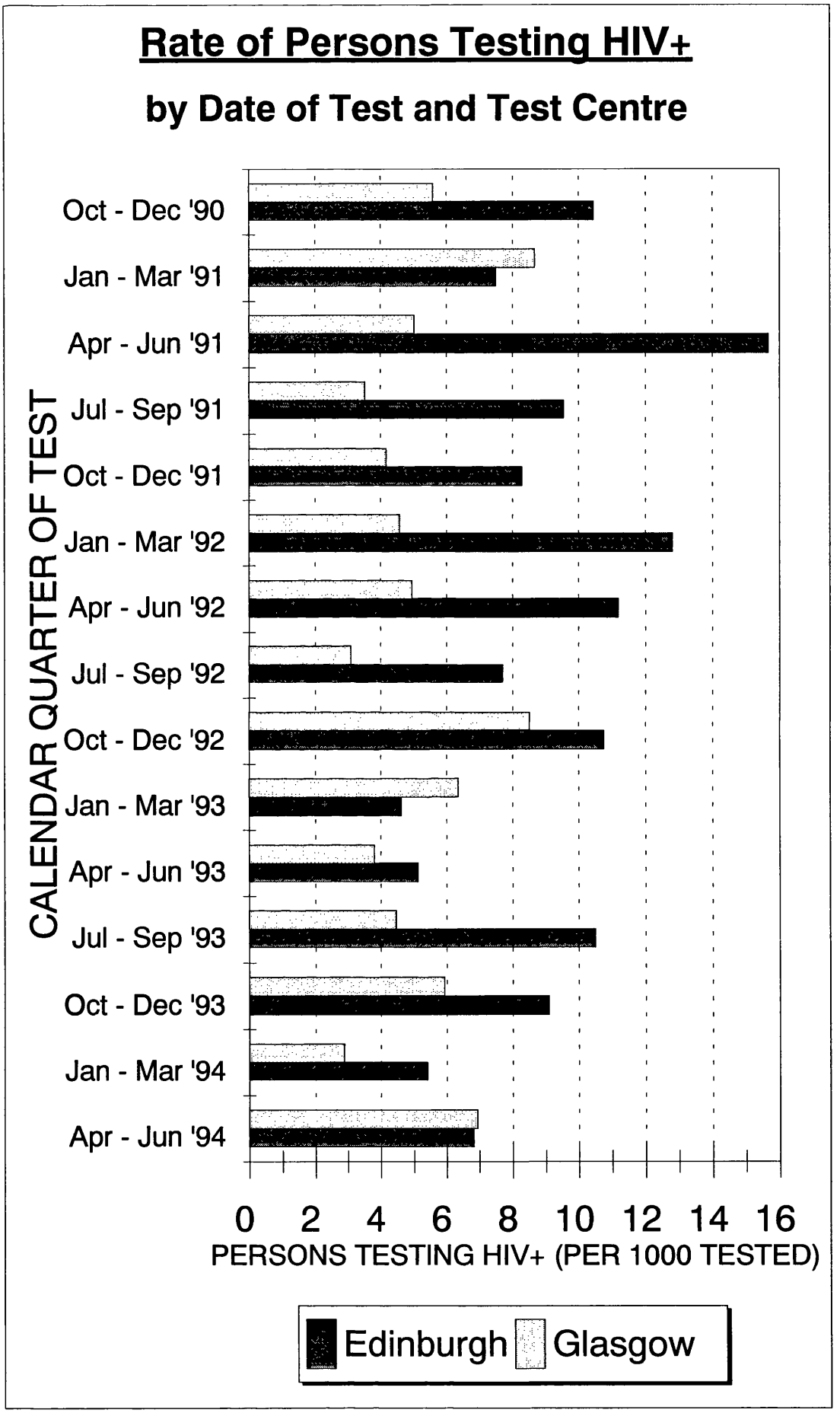
Rate of Persons Testing HIV+
by Date of Test and Test Centre
CALENDAR QUARTER OF TEST
Oct - Dec '90
Jan - Mar '91
Apr - Jun '91
Jul - Sep '91
Oct - Dec '91
Jan - Mar '92
Apr - Jun '92
Jul - Sep '92
Oct - Dec '92
Jan - Mar '93
Apr - Jun '93
Jul - Sep '93
Oct - Dec '93
Jan - Mar '94
Apr - Jun '94
0 2 4 6 8 10 12 14 16
PERSONS TESTING HIV+ (PER 1000 TESTED)
Edinburgh
Glasgow

Figure 5.01

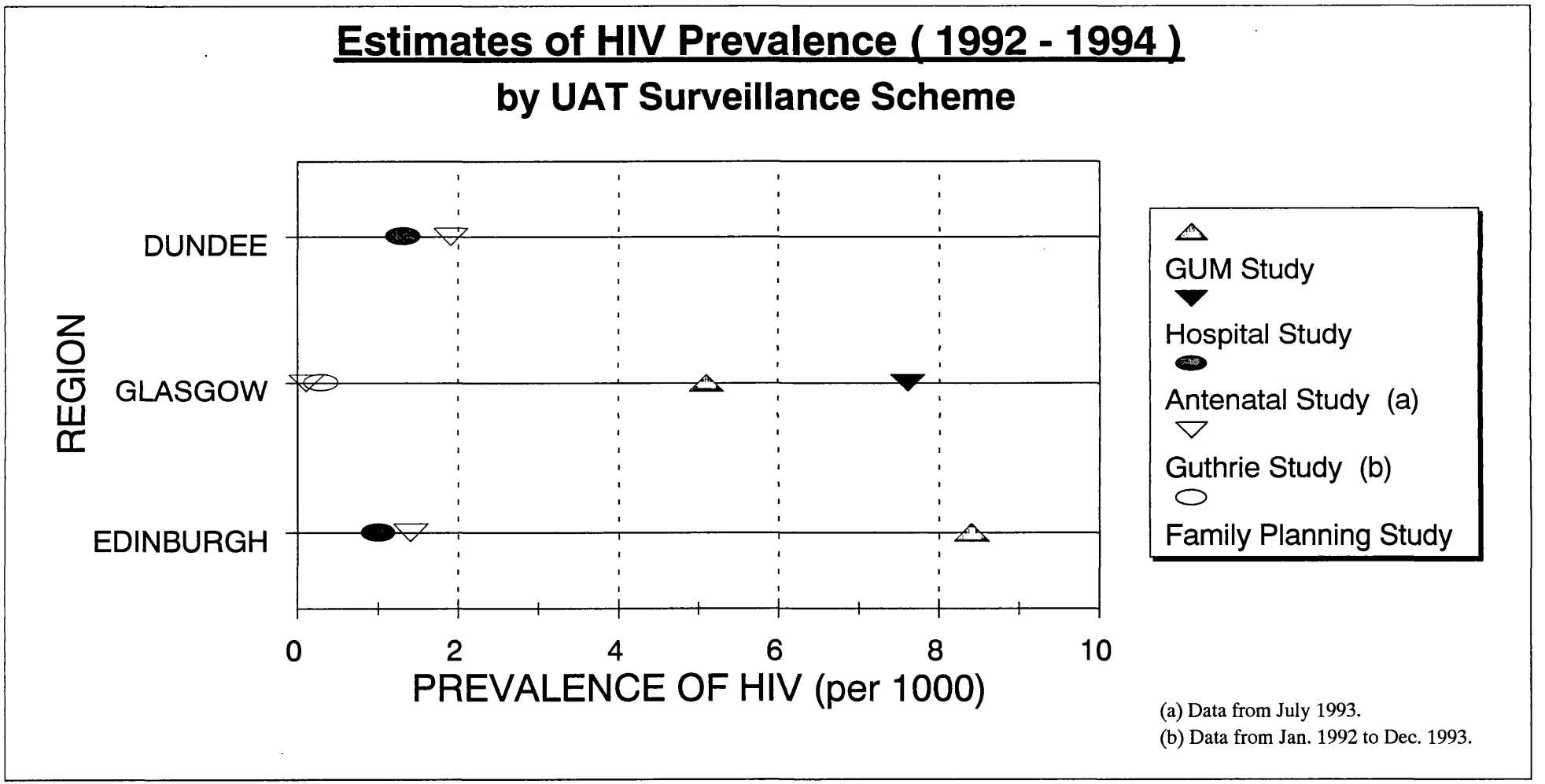
Estimates of HIV Prevalence (1992 - 1994)
by UAT Surveillance Scheme
REGION
DUNDEE
GLASGOW
EDINBURGH
0
2
4
6
8
10
PREVALENCE OF HIV (per 1000)
GUM Study
Hospital Study
Antenatal Study (a)
Guthrie Study (b)
Family Planning Study
(a) Data from July 1993.
(b) Data from Jan. 1992 to Dec. 1993.

Figure 5.02

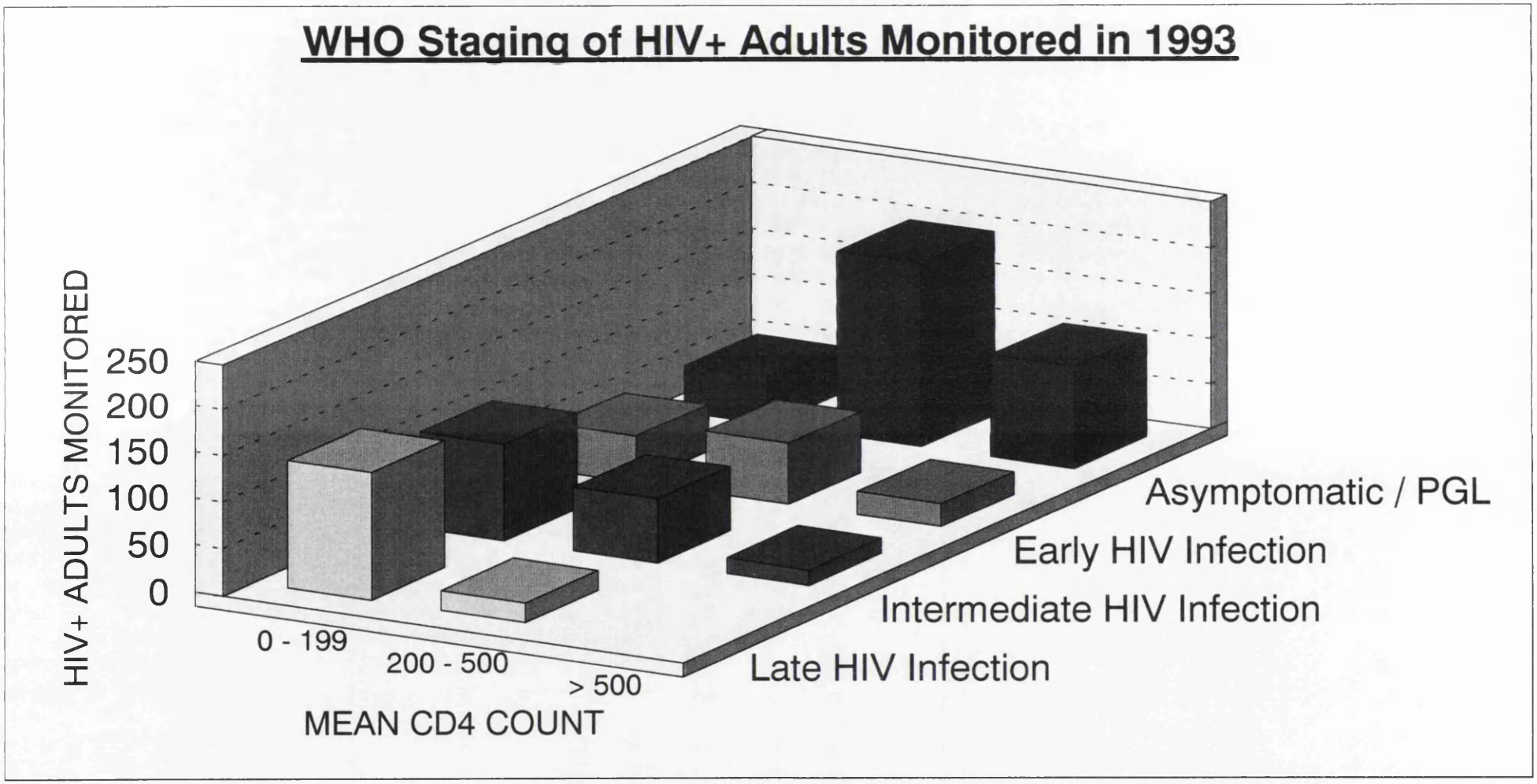
WHO Staging of HIV+ Adults Monitored in 1993
HIV+ ADULTS MONITORED
250
200
150
100
50
0
0 - 199
200 - 500
> 500
MEAN CD4 COUNT
Asymptomatic / PGL
Early HIV Infection
Intermediate HIV Infection
Late HIV Infection

Figure 6.01

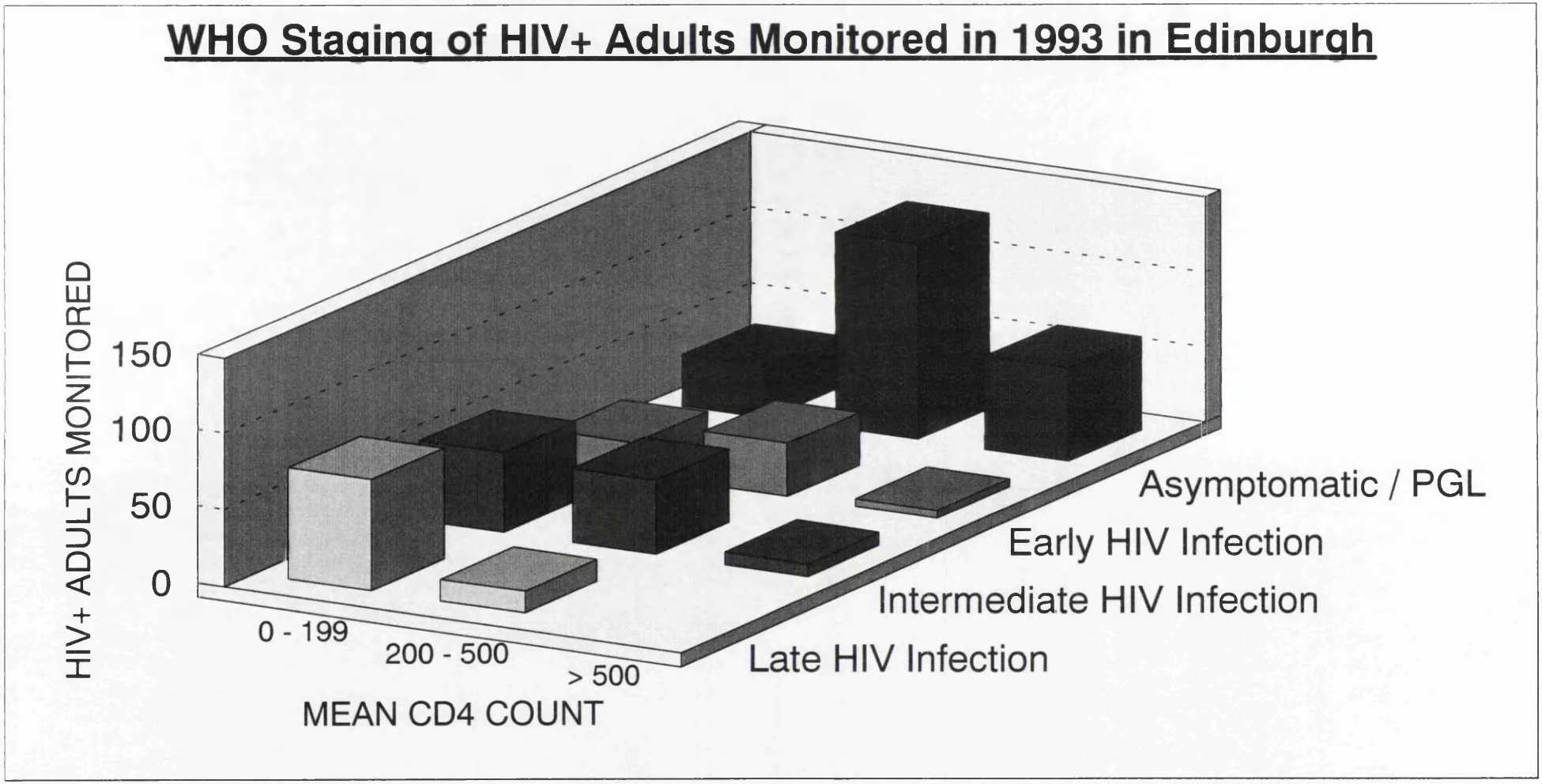
WHO Staging of HIV+ Adults Monitored in 1993 in Edinburgh
HIV+ ADULTS MONITORED
150
100
50
0
0 - 199
200 - 500
> 500
MEAN CD4 COUNT
Asymptomatic / PGL
Early HIV Infection
Intermediate HIV Infection
Late HIV Infection

Figure 6.02

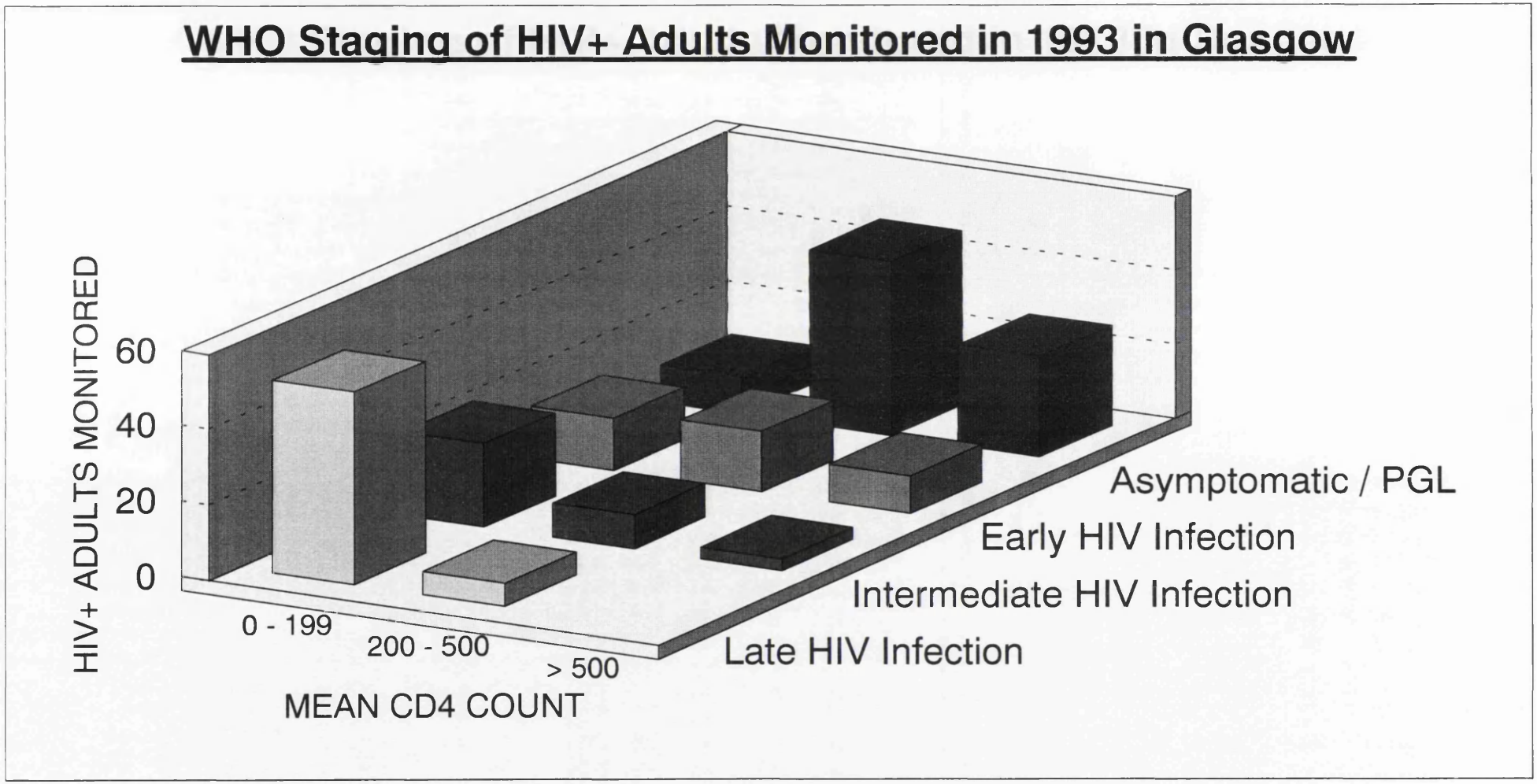
WHO Staging of HIV+ Adults Monitored in 1993 in Glasgow
HIV+ ADULTS MONITORED
60
40
20
0
0 - 199
200 - 500
> 500
MEAN CD4 COUNT
Asymptomatic / PGL
Early HIV Infection
Intermediate HIV Infection
Late HIV Infection

Figure 6.03

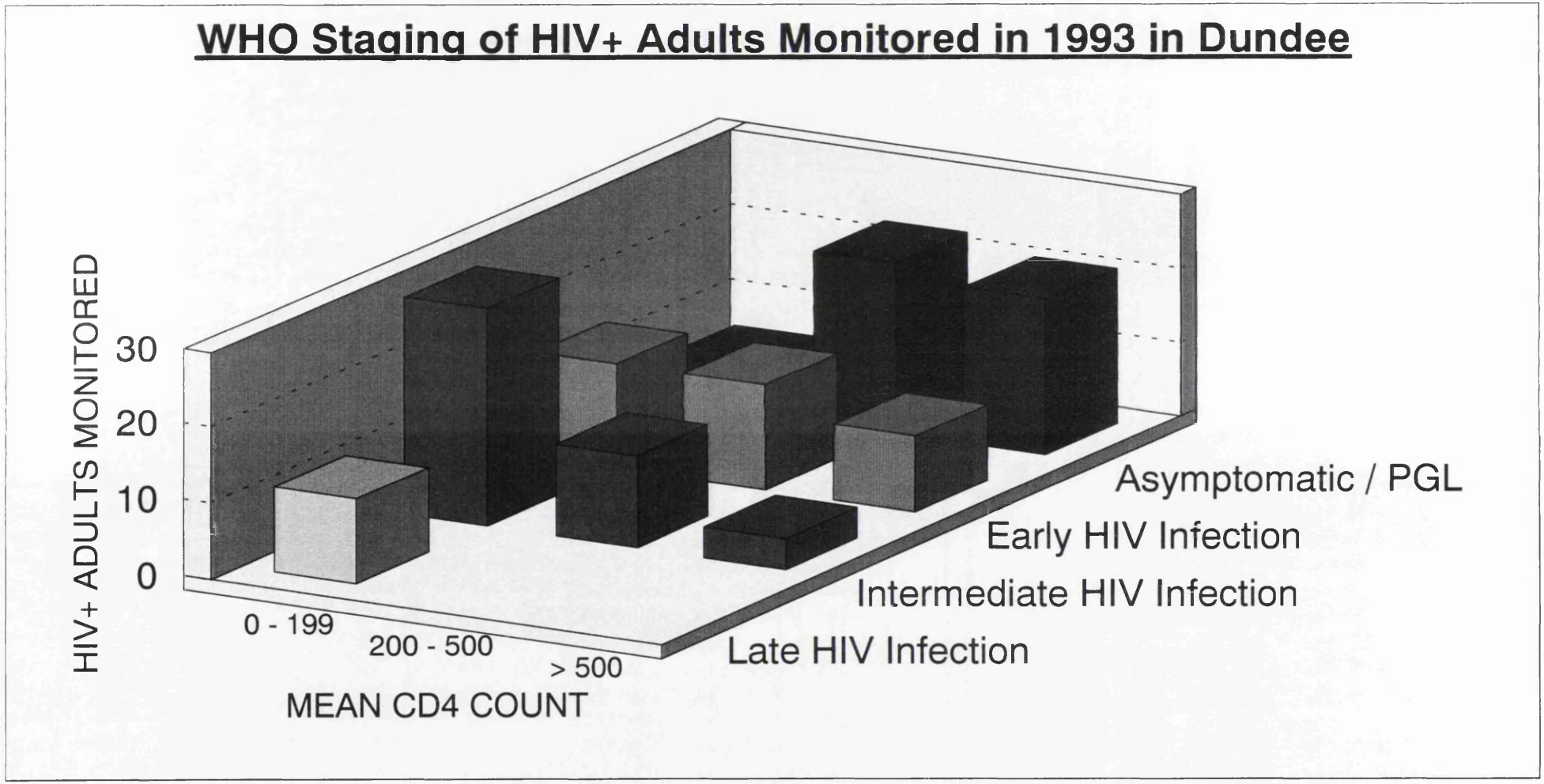
WHO Staging of HIV+ Adults Monitored in 1993 in Dundee
HIV+ ADULTS MONITORED
30
20
10
0
0 - 199
200 - 500
> 500
MEAN CD4 COUNT
Asymptomatic / PGL
Early HIV Infection
Intermediate HIV Infection
Late HIV Infection

Figure 6.04

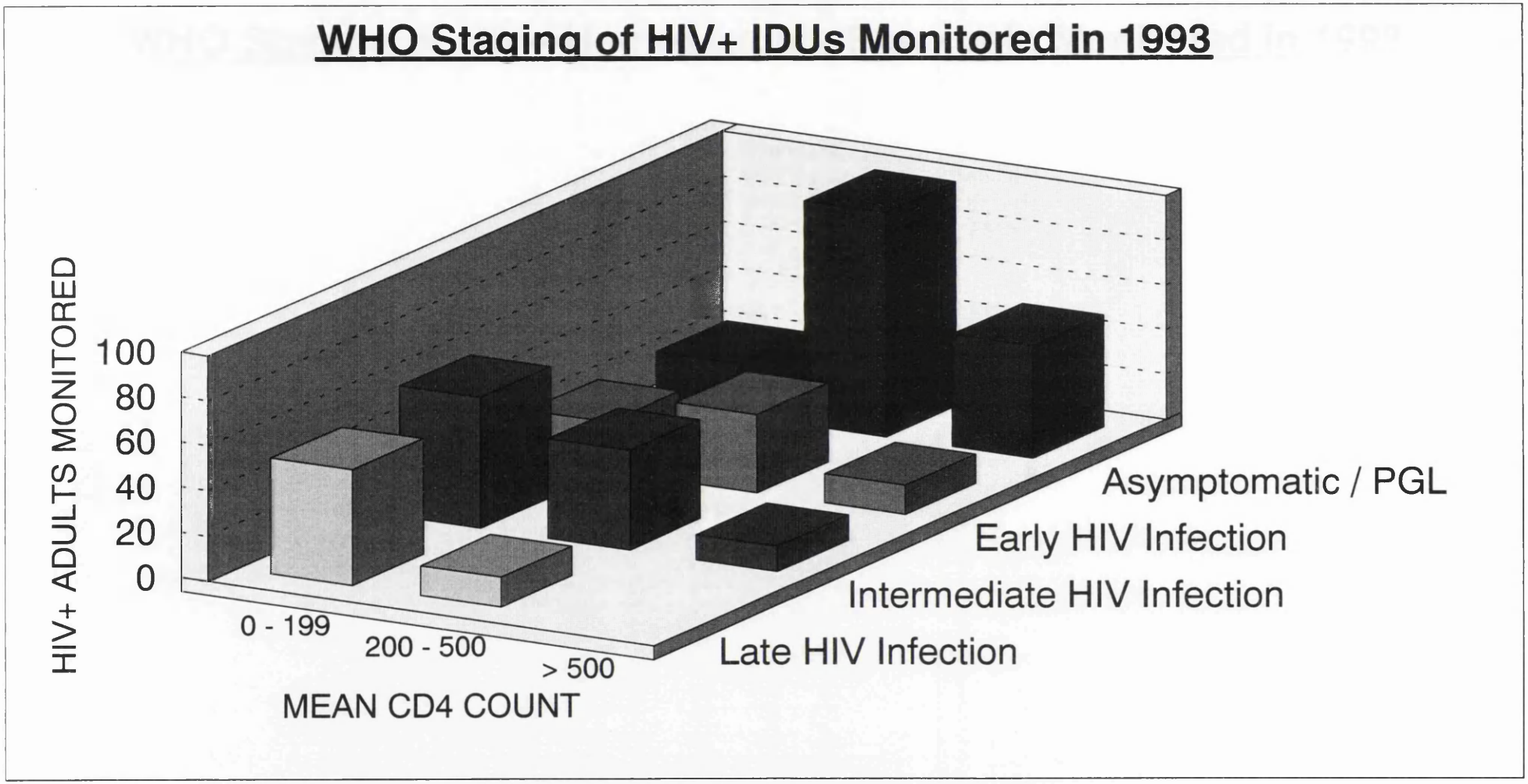
WHO Staging of HIV+ IDUs Monitored in 1993
HIV+ ADULTS MONITORED
100
80
60
40
20
0
0 - 199
200 - 500
> 500
MEAN CD4 COUNT
Asymptomatic / PGL
Early HIV Infection
Intermediate HIV Infection
Late HIV Infection

Figure 6.05

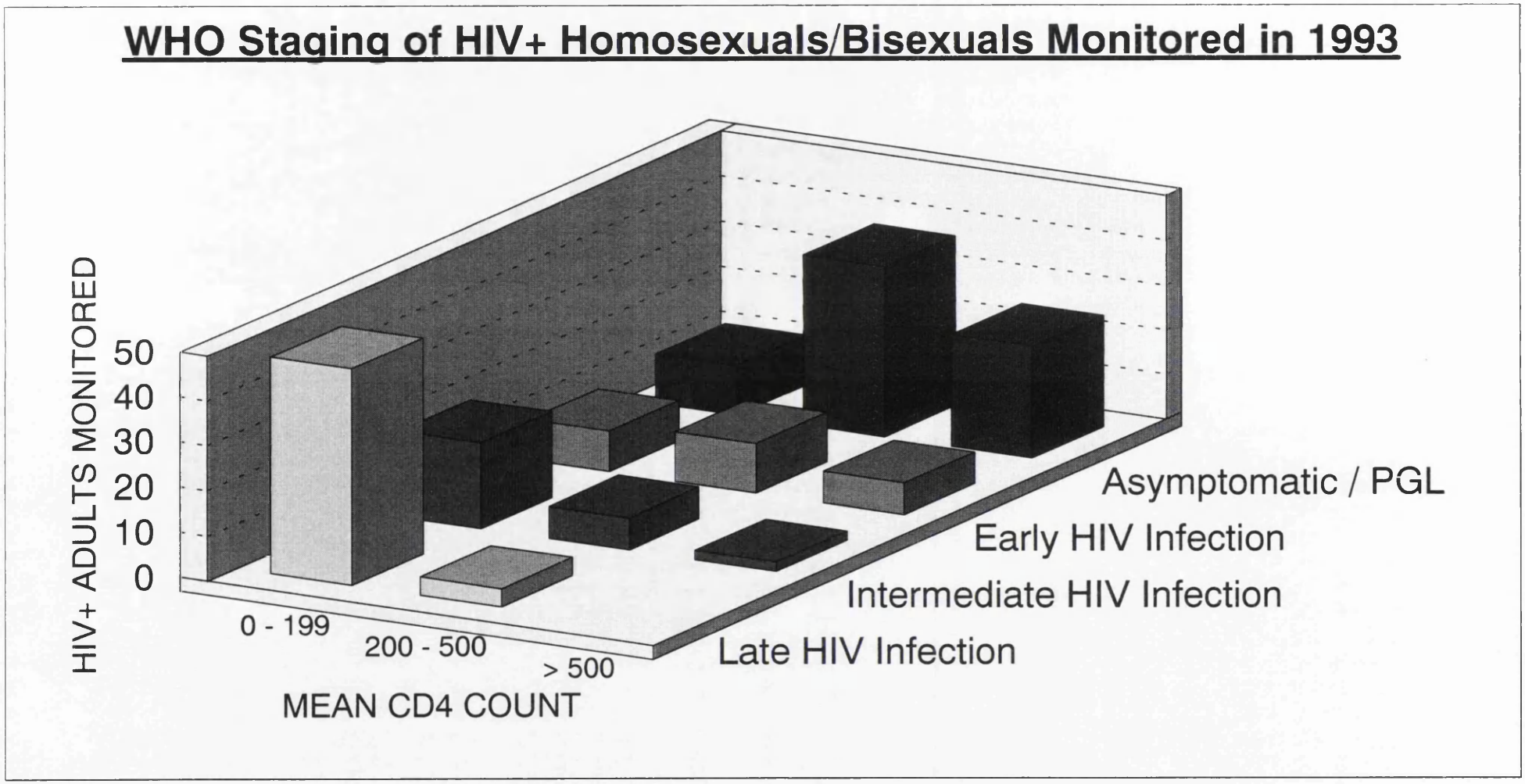
WHO Staging of HIV+ Homosexuals/Bisexuals Monitored in 1993
HIV+ ADULTS MONITORED
50
40
30
20
10
0
0 - 199
200 - 500
> 500
MEAN CD4 COUNT
Asymptomatic / PGL
Early HIV Infection
Intermediate HIV Infection
Late HIV Infection

Figure 6.06

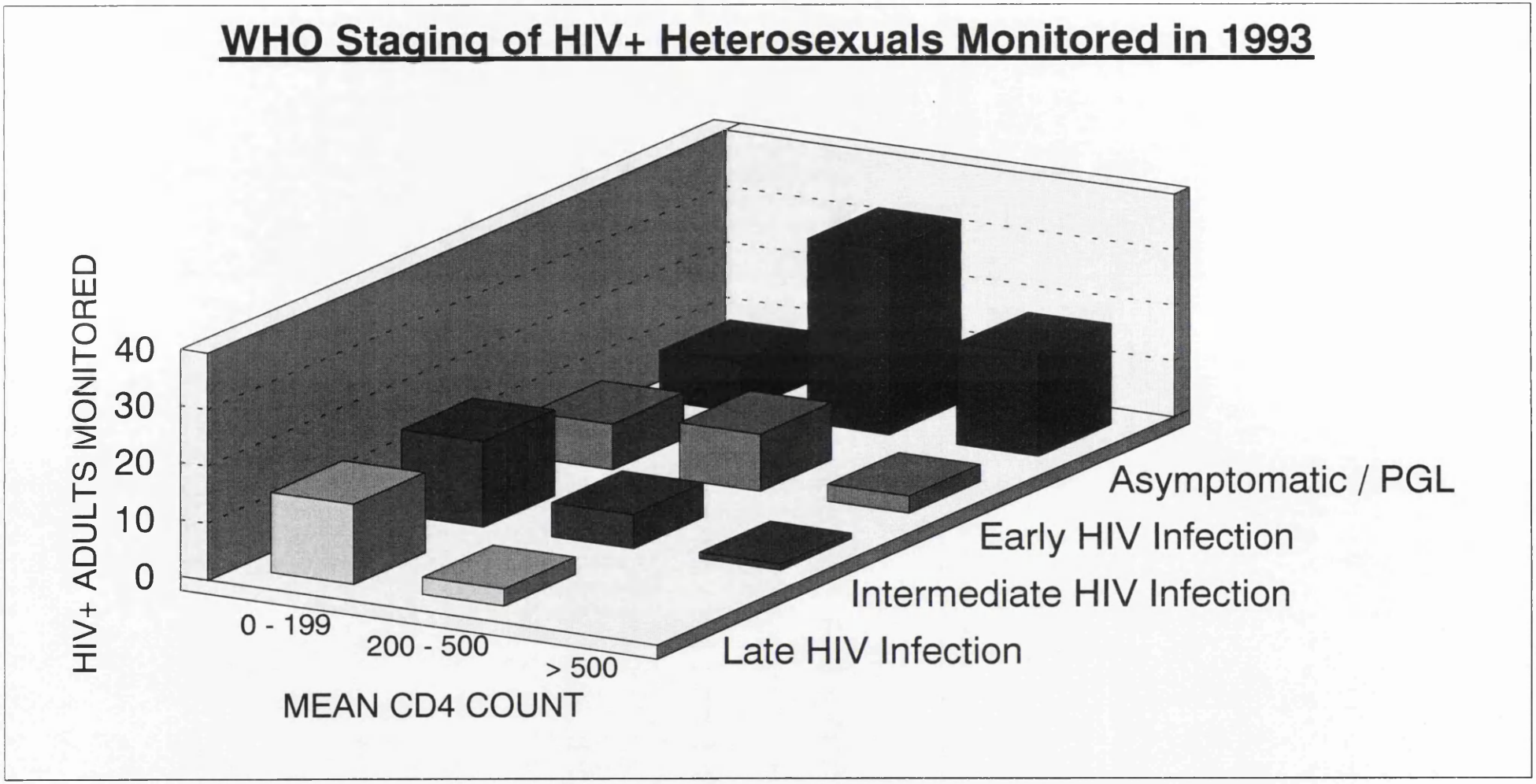
WHO Staging of HIV+ Heterosexuals Monitored in 1993
HIV+ ADULTS MONITORED
40
30
20
10
0
0 - 199
200 - 500
> 500
MEAN CD4 COUNT
Asymptomatic / PGL
Early HIV Infection
Intermediate HIV Infection
Late HIV Infection

Figure 6.07

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Glossary

AIDS	acquired immune deficiency syndrome
ANSWER	AIDS news supplement to the weekly report
APPGA	All-Party Parliamentary Group on AIDS
BMDP	a computer package for statistical analysis
BPASU	British Paediatric Associated Surveillance Unit
BTS	Blood Transfusion Service
CD4 count	the number of CD4 T-lymphocyte cells per cubic millimetre of blood
CDC	Centers for Disease Control
CDEH(S)U	Communicable Diseases and Environmental Health (Scotland) Unit
CDSC	Communicable Disease Surveillance Centre
CD(S)U	Communicable Diseases (Scotland) Unit
CI	confidence interval (statistical term)
DATAEASE	a computer package for data processing
DNA	deoxyribonucleic acid
EH(S)U	Environmental Health (Scotland) Unit
ELISA	enzyme linked immunosorbent assay
FOP	form of particulars
FORTRAN	a computer language compiler
GP	general practitioner
GUM	genito-urinary medicine
HBV	hepatitis B virus
HEBS	Health Education Board for Scotland
HEALS	HIV Epidemiology and Laboratory Sub-committee
HIV	human immunodeficiency virus
HTLV-I	human T-cell leukaemia virus - type one
HTLV-III	human T-cell leukaemia virus - type three
ICH	Institute of Child Health
IDU	injecting drug user
KS	Kaposi's sarcoma
LAV	lymphadenopathy associated virus
MMWR	Morbidity and Mortality Weekly Report
MRC	Medical Research Council
NHS	National Health Service

Glossary (contd.)

OOI	other opportunistic infection
OR	odds ratio (statistical term)
PCP	pneumocystis carinii pneumonia
PCR	polymerase chain reaction
PHLS	Public Health Laboratory Service
PML	progressive multifocal leukoencephalopathy
RGS	Registrar General for Scotland
RNA	ribonucleic acid
RR	relative risk (statistical term)
SAM	Scottish AIDS Monitor
SAS	a computer package for statistical analysis
SCIEH	Scottish Centre for Infection and Environmental Health
SMR	Scottish morbidity record
SPSSPC+	a computer package for statistical analysis
STD	sexually transmitted disease
UAT	unlinked anonymous testing
UK	United Kingdom
USA	United States of America
WCC	white cell count
WHO	World Health Organization