The role of physical and mental health multimorbidity in the risk of suicidal thoughts and behaviours

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Abstract

Background

The effects of physical illness and psychiatric disorders have been extensively investigated in fatal and non-fatal suicidal behaviour. Although different study designs have focused on the independent roles of physical and mental illness in suicidality, few studies have examined the relationship between co-occurring physical and mental health conditions (multimorbidity) and suicide risk. Considering the paucity of research, the present doctoral programme of research aimed to investigate if populations with physical/mental multimorbidity have an increased risk of suicidal thoughts and behaviours, compared to those with neither physical nor mental health conditions, and further investigate if this effect is stronger than either of the health conditions alone.

Methods

Based on the well-established terms of comorbidity and multimorbidity, the effect of co-occurring health conditions in the risk of suicidality was investigated by undertaking an overview of reviews and a systematic review. Four empirical studies of existing datasets were conducted in order to explore if suicidality (suicidal thoughts and suicide attempts) varies as a function of physical/mental multimorbidity. Two national mental health surveys from the United Kingdom (National Psychiatric Morbidity Survey 2000, n = 8575; Adult Psychiatric Morbidity Survey 2007, n = 7389) and one cohort study carried out in Scotland (West of Scotland Twenty-07 study, n = 4510) were used and both cross-sectional and prospective study designs were employed.

Results

Findings indicated that those with physical/mental multimorbidity are more likely to have suicidal thoughts and attempt suicide, compared

to those with neither physical nor mental health conditions. The results were consistent: having both physical and mental health conditions did not increase risk of suicidal thoughts or attempts, beyond the risk conferred by mental illness alone. Having only physical health conditions was not associated with either suicidal thoughts or suicide attempts.

Conclusions

Overall, the findings suggest a potential risk of suicidality for populations with physical/mental multimorbidity. Although multimorbidity was a predictor of suicidality, it did not increase the risk of any suicide-related outcome more than mental health conditions alone. The current findings highlight that health care professionals should focus on populations who have reached services for non-mental health issues, but subsequently develop mental illness, as this pattern of multimorbidity could potentially be a risk factor for suicidal thoughts and behaviours. Further research is needed to better understand the risk of suicide in individuals with physical/mental multimorbidity.

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List of Publications Arising from this Thesis

Kavalidou, K., Smith, D.J., O'Connor R. C. (2016). The role of physical and mental health multimorbidity in suicidal ideation. *Journal of Affective Disorders,* 209, 80-85.

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"Keep Ithaca always in your mind. Arriving there is what you are destined for. But do not hurry the journey at all. Better if it lasts for years, so you are old by the time you reach the island, wealthy with all you have gained on the way, not expecting Ithaca to make you rich".

C. P. Cavafy

Before reaching the starting point of my PhD journey, I have met a tremendous number of people, who in their own way made me more passionate in working towards suicide research and prevention. To the lives lost and the pain felt by the people I have met, I dedicate my PhD journey.

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Aikaterini Kavalidou
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Author's Declaration

"I hereby declare that I am the sole author of this thesis, except where the assistance of others has been acknowledged.

It has not been submitted in any form for another degree or professional qualification."

Aikaterini Kavalidou
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Chapter 1: Introduction

Although the wider research literature indicates that a proportion of individuals with physical illness also have psychiatric disorders, and that those with mental illness are at risk of developing physical health conditions, studies focused on those with physical/mental co-occurring (multimorbid) conditions seems to have been largely neglected in suicide-related research.

This chapter presents the sociodemographic characteristics associated with increased suicide risk and synthesises the literature on the relationship between mental disorders, physical health conditions and suicide risk. Based on the lack of evidence on mental/physical co-occurrence in suicidal behaviours and suicide, in the final section of this chapter, the structure of the current PhD thesis is presented, which aimed to investigate if and to what extent suicide risk varies as a function of mental/physical multimorbidity.

1.1 Background

According to the World Health Organisation (WHO 2014a), around 804,000 people die by suicide worldwide every year. While this number of deaths translates into one person dying every 40 seconds, the frequency of suicide attempts is at least 20 times more than the deaths by suicide (WHO 2014a). The prevalence of suicide-related outcomes (self-harm with or without suicidal intent, suicidal thoughts, suicide attempts and suicide), often referred to as suicidality, differs between sub-populations (Meyer et al., 2010; Mościcki, 2001). Some studies indicate that those with mental and physical health conditions exhibit a higher suicide risk compared to those without; indeed many suicide prevention strategies highlight health care services as a key intervention point (Luoma, Martin & Pearson 2002; WHO 2014a).

Research based on psychology and psychiatric epidemiology has indicated that risk of suicidal behaviours and suicide is elevated in those with mental illness as well as those with a history of suicide attempts and those experiencing negative life events (Hawton et al., 2012; Hawton, Casañas i Comabella, Haw, & Saunders, 2013; Mendez-Bustos, de Leon-Martinez, Miret, Baca-Garcia, & Lopez-Castroman, 2013). Major depression and substance abuse have been shown to be the main psychiatric conditions with the strongest relationships with suicide-related outcomes (in some populations at least 80% of those dying by suicide do so during an episode of major depression) (Bertolote & Fleischmann, 2002; Hawton et al., 2013; Roy, 2003; Sher, 2006). There is also considerable evidence that adverse life events, physical illness, traumatic experiences and socioeconomic changes increase the likelihood of suicidal behaviours and deaths by suicide (Foster 2011; Townsend et al. 2016; Tsai, Lucas & Kawachi 2015). Considering that populations with adverse life events have a high prevalence of health issues, mainly mental disorders, the need for targeted heath care interventions for these populations is clear (Dube et al. 2003; Foster 2011; Mann et al. 2005).

The role of primary care services in suicide prevention has also received much research attention due, in part, to the evidence that high-risk populations make contact with GPs in the months before death (Kavalidou,

Mcphedran & De Leo 2015; Luoma, Martin & Pearson 2002) and because of the relative lack of training in using suicide risk assessments in these settings (Lemieux, Saman & Lutfiyya 2014; Saini et al. 2014). In Luoma and colleagues' review (2002), people aged 35 years and younger have more frequent contact with mental health care services than those 55 and older, with the latter having more contact with primary care services before suicide. A variety of studies of clinical populations have found significant associations between multiple mental disorders and high suicide risk, with some authors reporting that multiple physical conditions are additionally associated with suicide-related outcomes (Henriksson et al. 1993; Lecrubier 2001; Webb et al. 2012b). Although it is known that the number of health conditions increases by age, there is a lack of clarity on which patterns of illness co-occurrence elevate suicide risk (Druss & Walker, 2011; Sauver et al., 2015).

Some work has also addressed the use of risk scales in the prediction of suicide, based on populations reached by or in need of health care services (Carter et al. 2017; Chan et al. 2016; Quinlivan et al. 2017). Specifically, a recent review of studies of self-harm highlighted that although poor health is a strong predictor of suicide, risk scales do not predict suicidal behaviours (Chan et al. 2016). Given the established relationship between poor physical health and suicidal behaviour, considerable research interest has been directed at the high rate of primary care contact of physically ill people before ending their life (NCISH, 2014; Luoma et al., 2002). As there is no suicide risk assessment tool specifically for those hospitalised due to physical illness, a predictive model of future suicidal behaviours based on the somatic conditions among mental health patients has been developed (Karmakar et al. 2016). Based on patient suicide risk assessments conducted during hospitalisation, and their history of physical conditions, Karmakar and colleagues (2016) found that the number of mental health patients with co-occurring physical illness was higher in the suicide risk group compared to the control group (mental health patients without suicide attempts). Indeed, these authors concluded that similar models should be incorporated into clinical assessments of suicide risk within hospital settings (Karmakar et al. 2016).

Overall, both physical and psychiatric disorders are associated with increased suicide risk and populations with either conditions are considered the most vulnerable sub-groups in terms of suicide risk. However, given the high prevalence of mental disorders among physically ill populations and *vice versa* (Doherty & Gaughran, 2014; Druss & Walker, 2011), the effect of physical/mental illness co-occurrence on suicidality has not been clearly established. Although the WHO's recent report suggests (2014b) that those with mental health comorbidity have an increased risk of suicidal behaviours and suicide, no clear evidence exists for the types of mental and/or physical health co-occurring conditions that may increase suicide risk. Considering that risk scales and proposed models on the prediction of suicide have so far only been tested in vulnerable populations in contact with health care services, the need to investigate the nature and effect of multiple health conditions on suicide-related outcomes in general population samples, is important.

This chapter reviews evidence on suicide risk factors and focuses on the role of mental and physical health conditions. The last section of this chapter presents the research questions and structure of the thesis.

1.2 Suicide risk factors

As suicide is a complex phenomenon, involving the interaction of genetic, neurobiological, behavioural and environmental factors, the vulnerability to suicide is defined through distal or predisposing and proximal/environmental risk factors (Van Heeringen & Mann 2014; O'Connor 2011; O'Connor & Nock 2014). While sociodemographic characteristics differentiate those at risk of suicide, psychiatric conditions and physical illness, as predisposing factors, have been widely investigated. The following subsections provide a narrative review of the research evidence on the role of sociodemographic characteristics, mental illness and physical conditions in all suicide-related outcomes.

1.2.1 Sociodemographic characteristics

Overall, gender, age, marital and socio-economic status have been associated with a high risk of suicide (Hawton, 2000). More specifically, males are at an increased risk of suicide compared to females, this gender difference is explained, in part, because men tend to use more lethal methods of suicide and they are less likely to seek help (Callanan & Davis, 2012; Hawton, 2000; Mergl et al., 2015; Michelmore & Hindley, 2012).The overrepresentation of females in non-fatal suicidal behaviours (self-harming, suicide attempts), has been described as the "gender paradox" (Canetto & Sakinofsky 1998); a review by Schrijvers and colleagues (2012) highlighted that gender differences are presented in terms of psychopathology and suicide risk (higher prevalence of internalising disorders in women and higher prevalence of externalising disorders in men). The lack of coping strategies for men, when experiencing social life stressors like separation and financial difficulties, may also result in the 'gender-gap' differences in suicidality.

The gendered pattern of suicide risk is consistent across age-groups; epidemiological findings show young, middle-aged and older male adults as having a higher rate of death by suicide, compared to females (Fung & Chan 2011; Gould, Greenberg & Velting 2003; Mcloughlin, Gould & Malone 2015; WHO 2014a). Starting in adolescence and young adulthood, reviews have systematically found that psychopathology and previous suicide attempts significantly increase the risk of subsequent suicide (Gould, Greenberg & Velting 2003; Mcloughlin, Gould & Malone 2015). While suicide is the second leading cause of death for those 15 to 29 years of age globally, when comparing young adults from high-income countries to those from low and middle-income areas, the latter group of youths have much higher suicide rates (WHO 2014a). More specifically, Kõlves and De Leo (2016) recently analysed the global suicide rate for the ages of 15-19, between 1990 and 2009. Although they reported a decline in the rates worldwide, they presented a decrease in the European rates (males:13.13 to 10.93 and females: 3.88 to 3.34) but an increase in South American countries mainly for males, 7.36 to 11.47 (females: 5.59 to 7.98, p=0.053; Kõlves & De Leo, 2016).

Although suicide is rare among adolescents, especially for those younger than 12 years old, self-harming behaviours like self-cutting and self-poisoning are highly prevalent, especially for females (Hawton, Saunders, & O'Connor,

2012). Considering that self-harm is an important risk factor for subsequent suicidal behaviour, its role has been shown to be as important as other major suicide risk factors, like history of psychiatric treatment (Townsend 2014). Specifically, in a UK study based on data from the Multicentre Study of Self-harm in England and national suicide statistics, self-cutting predicted suicide (HR = 2.1 95% CI 1.1–3.4, $p < 0.05$), along with previous psychiatric treatment (HR = 4.2, 95% CI 1.7–10.5, $p < 0.01$) and being male (HR) = 2.4, 95% CI 1.2–4.8, $p < 0.05$). Despite the high rates of adolescent self-harm, the frequency of hospital contact due to adolescent self-harming behaviours is low but there is some evidence that it has increased in recent decades in the UK (Hawton, Saunders, & O'Connor, 2012). In terms of sociodemographic differences in self-harm within UK, a systematic review of the ethnic differences in self-harm rates highlighted that Asian males have the lowest rates and Black women are more likely to self-harm than White males and females (Al-Sharifi, Krynicki & Upthegrove 2015).

Even though suicide is the second leading cause of death for those 15 to 29 years of age globally, older adults also have a persistent suicide risk (WHO 2014a). Fung and Chan (2011)'s systematic review on gender differences in suicidal behaviours among old people found that oldest old males (>80 years old) had the highest proportion of deaths by suicide, compared to females in the same age category. While depression, alcohol dependence and physical conditions were associated with suicide risk in older people, Fung and Chan suggested that as half of suicides in this age group had contact with health care professionals before their death, health care services should be considered as key opportunities for suicide prevention interventions (Fung & Chan 2011).

Other studies of sociodemographic risk factors have highlighted the importance of livings conditions and financial difficulties (Knipe et al. 2015; Meltzer et al. 2011; Pitman et al. 2012; Yamauchi et al. 2013). It has also been well documented that being single, separated or widowed are significant suicide risk factors, especially for middle-aged and older men, whilst being married acts as a protective factor against suicide (Hawton, 2000). Although the majority of studies present cohabitation as a protective factor, a few empirical studies suggest that its protective function may

decrease with increasing age, as Fung and Chan (2011) presented in their review.

Research into the role of socioeconomic factors in suicidality has increased in recent years, in part, as a result of the post-2007 global recession (Haw et al. 2015; Knipe et al. 2015; Meltzer et al. 2011; Oyesanya, Lopez-Morinigo & Dutta 2015). While debt, job loss and prolonged unemployment have been linked to suicidal behaviour and specifically to male suicide mortality, psychological distress and feelings of hopelessness related to financial difficulties have long been recognised as contributory factors in suicidality (Haw et al. 2015). In addition to the association between socioeconomic status and suicidality, low professional skill occupations (i.e. labourers, machine operators) have been additionally associated with an increased risk of suicide (Milner et al. 2013; Milner, Niven & LaMontagne 2014). Other socioeconomic indicators including social rank have also been found to be associated with suicide risk. For example, perceived lower social class and social ranking have been shown to be significantly associated with suicidality (Kim, Park & Yoo 2015; Wetherall et al. 2015). More specifically, when the Adult Psychiatric Morbidity Survey of England 2007 (APMS) was analysed, *perceived relative* income ranking was more strongly associated with suicidal behaviours than actual or absolute income (Wetherall et al. 2015). This finding is noteworthy as it highlights the importance of social comparisons in suicide risk.

Overall, several sociodemographic characteristics have significant associations with an increased risk of suicidal behaviours and suicide in non-clinical and clinical populations.

1.2.2 The role of mental illness

Psychiatric illness has been identified as the most important contributory factor to risk of suicidal behaviours and suicide, with psychological autopsy studies indicating that 90% or even up to 98% of people who die by suicide have a diagnosable mental condition (Bertolote & Fleischmann, 2002; Cavanagh, Carson, Sharpe, & Lawrie, 2003; Hawton et al., 2013). It is worth noting that a more recent meta-analysis on the presence of mental illness in

suicides, has suggested that the prevalence of mental disorders in suicide cases has been decreasing with the most recent mean prevalence of psychiatric illness estimated to be 80.8% (95% CI=76.1-84.8; (Cho et al. 2016). Overall, depression, alcohol abuse, personality and anxiety disorders are the most common psychiatric disorders associated with suicidality (Hawton & Heeringen, 2009).

While much work has been carried out on the mental illness and suicidality association, attention has also been given to the minority of suicides that occur in the absence of mental disorders (Cho et al. 2016; Milner, Sveticic & De Leo 2013; O'Connor & Nock 2014). Along with studies criticising psychological autopsy studies (suggesting that around 90% of people dying by suicide have a mental condition), arguing that they over-represent mental illness as a suicide risk factor, a recent review has highlighted that psychological autopsy studies fail to report the number of suicides with no mental illness; hence, there is no clear indication of the proportion of suicide cases with no psychiatric disorders (Hjelmeland & Knizek, 2017; Milner et al., 2013). To that end, psychological models view suicide as a behaviour and not simply as an epiphenomenon of psychiatric illness, where feelings of burdensomeness, entrapment, defeat and hopelessness (which may be related to psychiatric disorder) are posited to be key in the aetiology of suicidal ideation and behaviour (Joiner, 2005; O'Connor, 2011; O'Connor & Nock, 2014).

Depression and mood disorders, more generally, are the most common mental conditions diagnosed in populations who have either attempted or died by suicide (Bertolote & Fleischmann, 2002; Hawton et al., 2013; WHO, 2014b; Wolfersdorf, 1995). Nonetheless, attention has also been given to other mental conditions co-occurring with depression, with studies indicating that the risk of suicidal behaviours and death increases when depression is present among patients with other mental health conditions (Batterham, Christensen & Calear 2013; Bronisch & Wittchen 1994; Zalpuri & Rothschild 2016). The results from the Munich Follow-up prospective study, highlighted that although depression is associated with suicide attempts, its association is not significantly stronger than that for not having any psychiatric diagnosis;

however, the coexistence of lifetime anxiety disorder with depression elevates suicide risk (Bronisch & Wittchen 1994).

A US study investigating the co-occurrence of depression and alcohol disorder (AUD) in relation to suicide attempts, found that the severity of depression plays the most significant role in suicide attempts, regardless of whether alcohol disorder was also present as a secondary diagnosis [primary depression with secondary AUD [AHR (95% CI):1.41 (1.04, 1.92)] and without secondary AUD [AHR (95% CI):1.30 (1.00, 1.71); Britton et al., 2015]. Furthermore, a review of empirical studies on alcohol abuse, depression and suicidality among adolescents, suggested that when depression and alcohol abuse coexist the risk of suicide is high; however, the authors highlighted that there is a lack of studies on causality between the disorders and more studies are required to unravel the association between these conditions and suicidality (Galaif et al. 2007).
As Gonda and colleagues (2012) note in their review, bipolar disorder is the affective disorder with the highest rate of suicidal behaviours, conferring up to a 60-fold higher suicide rate compared to the general population. Overall, this review found depressive episodes (specifically first episodes at the onset of the disorder), rapid cycling, childhood abuse, diagnosis at young age (before 25 years of age), impulsivity and psychiatric comorbidity as disease-specific risk factors for suicidal behaviours in bipolar disorder (Gonda et al. 2012). However, a more recent meta-review, while recognising the increased suicide rates among patients with bipolar disorder, additionally found that borderline personality disorder, depression and anorexia were also associated with a high suicide risk (Chesney, Goodwin & Fazel 2014).

Alcohol abuse is also highly associated with suicide-related outcomes, with the association between alcohol and suicidal behaviours being stronger among patients hospitalised because of alcohol dependence (Harris & Barraclough 1997; Innamorati et al. 2010; Sher 2006). Taking the wider literature as a whole, the evidence suggests that the co-occurrence of alcohol abuse/dependence with affective disorders, confers the highest risk of suicide compared to other co-occurring mental health conditions (Bertolote & Fleischmann, 2002; Carra, Bartoli, Crocamo, Brady, & Clerici, 2014; Sher, 2006; Sullivan, Fiellin, & O'Connor, 2005). While this comorbidity

often includes multiple other conditions, like post-traumatic disorder, its effect has mostly been studied in relation to suicide attempts and deaths by suicide (Bertolote & Fleischmann, 2002; Dore, Mills, Murray, Teesson, & Farrugia, 2012).

While people with personality disorders (PD) have an increased suicide risk, often due to comorbid psychiatric disorders, research suggests that borderline personality disorder is highly prevalent among those who attempt suicide and those who self-harm (Black et al. 2004; Fyer et al. 1988; Kulkarni, Rao & Begum 2013; Maddock et al. 2010; Zaheer, Links & Liu 2008). For example, Björkenstam and colleagues followed up 25,217 patients who were hospitalised between 1987-2013 and had a primary PD diagnosis. This Swedish study also aimed to investigate if a PD diagnosis, along with a psychiatric and somatic comorbidity, was associated with choice of suicide method (Bjorkenstam et al. 2016). The authors found that being hospitalised for PD was associated with a higher suicide risk, compared to the general population and that the elevated suicide risk was related to psychiatric and somatic comorbidities (Bjorkenstam et al. 2016).The risk of suicide was higher in women and poisoning and hanging were the most common suicide methods, similar to the general Swedish population. Differences were found between PD clusters (cluster A=paranoid, schizoid; cluster B=antisocial/dissocial, emotionally unstable/explosive/borderline, histrionic; and cluster C=anankastic, anxious/avoidant, dependent) and gender: specifically, men had higher standardised mortality ratios (SMR), with jumping from heights as the method in all clusters, while women in cluster A had highest SMR for drowning and in cluster B the highest SMR was for cutting.

Anxiety has also been associated with a high suicide risk (Batterham, Christensen & Calear 2013; Bronisch & Wittchen 1994; Sareen et al. 2005) (Baterham et al., 2013; Bronisch and Wittchen, 1994; Sareen et al., 2005). For example, an Australian cohort study found that a larger proportion of suicidal thoughts incidence was explained by anxiety disorder (24.3%) than depression (16.1%; Batterham et al., 2013). A recent meta-analytic review of anxiety and related disorders [i.e. obsessive-compulsive disorder, post-traumatic stress disorder (PTSD)] as predictors of suicidality, highlighted that anxiety was a weak predictor of suicide, but a significant predictor of suicidal

ideation and attempts (Bentley et al. 2016). Although PTSD had the largest statistical relationship with suicide attempts, the authors suggested that this is not practically helpful for clinicians as it was associated with only a 0.9% probability of attempting suicide in a year (Bentley et al. 2016).

Recent research has also identified people with autism and attention deficit hyperactive disorder (ADHD) as populations with increased risk of suicidality (Allely 2014; Furczyk & Thome 2014). Those with psychosis spectrum disorder or schizophrenia, have also been shown to have a reduced life expectancy of between 15 and 25 years (Hawton, Sutton, Haw, Sinclair, & Deeks, 2005). In terms of suicide risk in schizophrenia, a systematic review from 2010 (Hor & Taylor, 2010) reported that depressive episodes, suicide attempt history, active hallucinations and physical illness comorbidity are significant factors for suicide deaths (Hawton et al., 2005; Lyu & Zhang, 2014).

In sum, psychiatric conditions are predictors of all suicide-related outcomes, with the strongest relationships for affective disorders, alcohol abuse, anxiety and borderline personality disorder. The co-occurrence of mental health conditions, mainly depression comorbidities, increase the risk of suicidality, with some literature also indicating that co-existing physical conditions, among populations with mental illness, have an additional effect.

1.2.3 The effect of physical illness on the risk of suicidal behaviour

The relationship between physical and mental illness is much discussed and research indicates that medical conditions often co-occur with mental disorders (Doherty & Gaughran, 2014; Druss & Walker, 2011; Vigo, Thornicroft, & Atun, 2016). Although the additional burden of mental conditions in somatic illness impacts on one's quality of life, those with either mental and/or physical multimorbidity (having two or more co-occurring conditions) clearly represent a cost increase in primary care (Brilleman et al. 2013).

Much work has been conducted on the effect of physical conditions on the risk of suicidal behaviour and suicide, although it is not yet clear whether physical illness on its own increases the risk of suicide or if this relationship is

mediated by other factors like other comorbid psychiatric conditions (Harris & Barraclough, 1994; Ratcliffe, Enns, Belik, & Sareen, 2008; Scott et al., 2010; Webb et al., 2012a, 2012b). In one large scale study, data from 14 World Mental Health surveys, including both high and low-income countries, were used to examine the association between physical illness and suicidal ideation/suicide attempts (Scott et al., 2010). The illnesses investigated were cancer, epilepsy, cardiovascular disease, ulcers, musculoskeletal and respiratory conditions and the study sample comprised of 37,915 participants. The findings were clear: physical illness had a direct effect on suicidal ideation and attempts, independently of mental disorders; cancer, heart attack/stroke and epilepsy were associated with suicide plans before adjusting for mental disorders. After adjustment only epilepsy remained significant (Scott et al., 2010). Overall, the association between physical illness and suicidality was stronger in the younger age groups and the only condition that was more strongly associated with ideation/attempts, when comparing high and low-income countries, was arthritis in lower income countries [lower income countries: ideation (OR, 2.3; 95% CI, 1.6-3.3), attempts (OR, 3.4; 95% CI, 2.1-5.7); high income countries: ideation (OR, 1.4; 95% CI, 1.2-1.7), attempts (OR, 1.2; 95% CI, 0.8-1.7)].

In addition to Scott and colleagues finding that epilepsy is independently associated with suicide plans (after adjusting for mental conditions), further research indicates that the risk of suicide is increased after an epilepsy diagnosis (SMR 2-3.5), highlighting that the 6 months post-diagnosis period is associated with suicide regardless of having a comorbid mental disorder (Bagary, 2011; Bell & Sander, 2009; Scott et al., 2010). Other neurological conditions studied within the suicide mortality domain are multiple sclerosis and Parkinson's disease (Bagary, 2011; Bell & Sander, 2009; Klaassen et al., 2015; Lewis, Anderson, & Feuchtinger, 2014; Pompili et al., 2012). Although Parkinson's disease has been mostly associated with suicidal thoughts, a recent Korean study reported that those with Parkinson's disease had twice the suicide rate compared to the general population, noting that males, those with co-occurring mental disorders and those taking high levodopa dosages, were more at risk (Lee et al. 2018; Lewis, Anderson & Feuchtinger 2014). Multiple sclerosis (MS) is another physical health condition associated with a high prevalence of suicide-related outcomes (Chwastiak & Ehde, 2007;

Pompili et al., 2012). Indeed, an increased risk of suicidality among MS populations was evident in Pompili et al.'s (2012) systematic review. In the latter review, the authors pinpointed the severity of depression and pre-existing suicidal behaviour before MS diagnosis as significant factors in the relationship that should be considered when assessing suicide risk. A recent meta-analysis on mortality in those with MS demonstrated that although cancer deaths in MS populations has decreased in the last 50 years, suicide, among other causes of death, had more than doubled (increased by 2.13 times), compared to the general population (Manouchehrinia et al. 2016).

Several studies have explored the effects of headache and migraine on suicidality, with a number of empirical investigations coming from the pain research field (Breslau et al. 2012; Ilgen et al. 2013; Nović et al. 2016; Ratcliffe et al. 2008)). Overall, there is an increased risk of suicidality, specifically for those who report migraine auras and some studies indicate that migraine can have an independent association with suicidal behaviours, regardless of mental illness (Nović et al. 2016). Diabetes has also attracted a lot of interest in relation to suicidality, with a recent meta-analysis of 3 million participants, showing that having diabetes is not associated with an increased risk of death by suicide (Sarkar & Balhara, 2014; Wang et al., 2016).

Cancer and stroke, conditions with the highest mortality among other causes of death (GBD 2016; WHO 2014b), have also been explored in suicide research. Taking cancer, initial reviews have found that cancer patients have double the risk of suicide compared to general population samples, with the first-year post-diagnosis period representing the highest risk period (Anguiano et al. 2012). Some studies have also found that having an advanced cancer status, especially for pancreatic cancer, is a significant suicide risk factor (Anguiano et al. 2012; Costantini et al. 2014). While being male and older provide an increased risk of suicide among populations with cancer, those with additional mental conditions have a much higher risk compared to those without a mental comorbidity (Anguiano et al. 2012; Costantini et al. 2014; Robson et al. 2010). Stroke has also been shown to be a risk factor for suicidal thoughts and deaths and although the suicide rates in older adult stroke patients have been decreasing in recent years, among younger

patients with co-occurring depression the suicide rates have been increasing (Pompili et al., 2012, 2015). In a Swedish cohort study, younger age, male gender and post-stroke depression were risk factors for people who attempted suicide and the period with the highest risk of suicide was 2 years after the stroke (Eriksson et al. 2015).

Although not consistent, most of the literature indicates that physical illness is associated with suicidal behaviours and suicide, with psychiatric disorders, mainly depression, mediating this relationship. Most of the focus in suicide prevention interventions for physically ill populations seems to be given to the post-diagnosis periods, as these have been associated with a high suicide risk, while a few studies, specifically for cancer, have additionally indicated that the advanced state of the disease is significant risk factor for suicidality.

1.2.4 The association between co-occurring health conditions and suicidal behaviours and suicide

Suicide-related research has investigated the effect of co-occurring conditions on suicidality. The majority of the research has focused on the increasing number of health conditions found in high risk populations, such as mental health patients and older adults (Hawton & Heeringen, 2009; Juurlink, Herrmann, Szalai, Kopp, & Redelmeier, 2004; Kulkarni et al., 2013; Lapierre et al., 2011).

In a British study, contact with mental health services prior to death was investigated in depressed older adults with and without anxiety comorbidities (Oude Voshaar et al. 2016). Among the 1909 patients with depression receiving mental health care, 17.4% had anxiety (Oude Voshaar et al. 2016). The authors highlighted that although the prevalence of the anxiety comorbidity was low, in contrast to the results from population-based studies, clinicians should give further attention to patients presenting with such a co-occurrence, in terms of risk of subsequent suicidality (Oude Voshaar et al. 2016).

With further studies focusing on older age groups, some findings indicate that the number of physical conditions is an additional risk factor, often mediated

by depressive symptomatology (Bartels et al. 2002; Conwell, Van Orden & Caine 2011; Juurlink et al. 2004; Webb et al. 2012b). Depression has been widely investigated as a co-existing disorder in the context of physical conditions like chronic obstructive pulmonary disease (COPD), cardiovascular disease and chronic kidney disease (Hawkins et al. 2018; Hegerl & Mergl 2014; Macaron et al. 2014; Palmer et al. 2013). Overall, it is suggested that each of these somatic conditions provides an increased risk of suicidality when depression is a comorbid disorder; although the effect of COPD is unclear as many authors suggest that depression and COPD symptoms often overlap; nonetheless it has been suggested that COPD should be seen as a risk factor on its own (Goodwin 2011; Hegerl & Mergl 2014).

Many studies of suicidality and co-occurring conditions have focused on the presence of multiple psychiatric disorders, which have been indicated as strong predictors of subsequent suicidal behaviours and suicide. Depression seems to have a role as a comorbid psychiatric disorder in both out- and inpatients: specifically, for outpatients with panic disorder, comorbid depression increases the risk of a suicide attempt, whereas when absent, panic disorder is less likely to be associated with suicidal behaviour; for inpatient veterans hospitalised for alcohol abuse and/or depression, when the primary diagnosis was depression and alcohol was secondary, there was no additive risk of subsequent suicide due to alcohol abuse (Britton et al. 2015; Diaconu & Turecki 2007). At the same time, for adolescent outpatients with depression, alcohol use and comorbid Axis I disorders have been found to be significant clinical factors for predicting future suicidality (Tuisku et al. 2012).

Based on studies of those with bipolar and borderline disorders, medical outpatients in the US with both diagnoses had four times higher risk of suicide attempts compared to outpatients with neither of these disorders (Zimmerman et al. 2014). Nock and colleagues also investigated the additive role of multiple mental health conditions in suicide risk, highlighting that some disorders are associated with suicidality because of their comorbid conditions and not due to their own significant direct effect (Nock, Hwang, Sampson, & Kessler, 2010).

In sum, it is evident that multiple health conditions have an effect on suicidality, with some studies suggesting that co-occurring conditions, mainly psychiatric, have an additive role in increasing suicide risk.

1.3 Current thesis and aim

A high prevalence of co-existing psychiatric diagnoses has been repeatedly found among those who attempt or die by suicide, with studies finding that the number of co-occurring physical health conditions increases the risk of suicidality (Henriksson et al., 1993; Nock et al., 2010; Scott et al., 2010; Suominen et al., 1996; Webb et al., 2012b). Although the wider literature indicates that the majority of those with physical illness have additional psychiatric disorders and those with mental illness are at risk of developing medical conditions, the study of those with physical/mental co-occurring health conditions, regardless of temporality, has been neglected in suicide-related research. The terminology coming from the wider literature indicates that, having two or more conditions without reference to an index condition, is called multimorbidity (Almirall & Fortin 2013). As elaborated later on this thesis (Chapter 4), multimorbidity covers both physical and mental co-occurrence. Considering that this physical/mental co-occurrence has been overlooked as a suicide risk factor, the current thesis seeks to answer the following research questions:

1) Does suicide risk vary as a function of mental/physical multimorbidity?
2) Does mental/physical multimorbidity confer a higher suicide risk beyond the independent effects of mental and physical conditions on their own?

The following subsection outlines the structure of the current doctorate thesis.

1.4 Thesis structure

Chapter 1 provides a brief overview of the independent and co-occurring role of physical and mental conditions in the aetiology of suicidal behaviours and

suicide. In the final section of Chapter 1, the research questions and structure of the thesis are presented. The second chapter (Chapter 2) presents an overview of reviews of the well-established term comorbidity, which refers to having a co-occurring condition in addition to an index disease, and its role in suicidal behaviours and suicide. Then, in Chapter 3, a systematic review of multimorbidity (having two or more conditions without a reference to an index disease) and suicide risk is conducted, while Chapter 4 summarises the methodology employed in the subsequent empirical studies. Chapters 5 to 7 describe the four PhD empirical studies that were conducted to answer the main research questions of the current thesis. The thesis ends (Chapter 8) with a discussion of the empirical studies' results, conclusions, limitations and further research suggestions.

Chapter 2: Comorbidity and suicide risk: An overview of reviews

Background

In recent decades, the role of comorbidity (defined as having another distinct clinical illness in addition to an index condition) in suicidal behaviour and suicide has attracted a lot of research interest. However, it is not yet clear to what extent the type of illness comorbidity elevates suicide risk.

Methods

As comorbidity is a well-established and widely used term referring to one or more conditions that co-occur with a primary disease, an overview of reviews investigating its relationship with suicide risk was conducted. A title search of English language reviews was performed in Medline, Embase, Web of Science and PsychINFO, using the keywords “comorbid*” and “suicid*” for the years 1966 to March 2017.

Results

The initial records search yielded 29 potential reviews. After removing duplicates (9 records) and applying the inclusion and exclusion criteria, 6 records were included in the final list of studies. All reviews focused on psychiatric comorbidities, with two reviews including the role of physical injuries/illness comorbidity. Major disorders, like depression, anxiety and PTSD, that co-exist with further conditions, seem to provide a higher prevalence of suicidality (defined as either suicidal ideation, suicide attempts or suicide) compared to other patterns of comorbidity.

Conclusions

Although empirical studies into the role of psychiatric comorbidities in suicide risk have been conducted, very limited attention has been given to physical/mental co-occurrence in suicide-related studies. More research is

needed into the role of specific comorbid conditions in suicide risk, in order to inform the development of effective suicide prevention strategies for vulnerable populations.

2.1 Introduction

A lot of studies have been conducted in regard to the impact of either physical or mental health illness on the well-being and social functioning of patients and their carers (Connell et al. 2012; Whitehead et al. 2017; Yueh-Juen 2012). Quality of life (QoL), as defined by the World Health Organisation in late 50s'(WHO 1958), includes the mental, psychological and social well-being of a person. Researchers also use health-related quality of life (HRQoL) to describe how one's life is modified through the effect and duration of a disease, injury or treatment (Megari 2013). Studies focusing on the impact of chronic conditions have highlighted that as the number of co-occurring diseases increases these adversely affect QoL and they increase health care costs (Bayliss et al. 2004; Hutter, Schnurr & Baumeister 2010; Kedote, Brousselle & Champagne 2008; Megari 2013).

To that end, the health care needs and health-service utilization of those with multiple chronic health issues have been the focus of primary care services and clinical epidemiology since the 1970s (Feinstein, 1970; Salive, 2013; Valderas, Starfield, Sibbald, Salisbury, & Roland, 2009). The importance of comorbidity was introduced by Feinstein, with the term referring to having another distinct clinical entity in addition to an index condition (Feinstein, 1970). Focusing on the different therapeutic outcomes for patients with the same diagnosis and sociodemographic characteristics, Feinstein suggested that comorbidities may possibly explain the significant prognostic differences in patients with the same index disease (Feinstein 1970). In short, omitting the additional health issues associated with an index condition was providing misleading mortality rates for the general population as well as under-estimating the fatality rates of the condition under study.

In recent decades, the role of comorbidity in suicidal behaviour and suicide mortality has been extensively investigated (Gallo et al., 2016; Henriksson et al., 1993; Nock et al., 2010; Oquendo et al., 2005; Suominen et al., 1996; Walker, McGee, & Druss, 2015). Although it is well recognised that a psychiatric disorder increases suicide risk and more than 90% of those who die by suicide have a mental disorder, comorbidity of mood and substance abuse disorder has also been found to be the most frequently co-occurring

diagnoses, among those who die by suicide (Bertolote, 2004; Bertolote & Fleischmann, 2002; Galaif et al., 2007). Similarly, data from psychological autopsy studies also suggest that the co-occurrence of depressive disorder and alcohol dependency is the most common diagnosis followed by the comorbidity of mood and anxiety-related disorders (Henriksson et al. 1993; Lesage et al. 1994).

Although suicide is difficult to predict as it is a statistically rare event, a past history of suicide attempts is one of strongest predictors of future suicidal behaviours (Beautrais 2004; Karasouli et al. 2011). Carrà and colleagues (2014) concluded that the co-occurrence of bipolar disorder (BD) with alcohol and other substance use disorders (AUD/SUD) is associated with a suicide attempt risk. The same meta-analysis found that although sex and age were not associated with the risk of suicide attempts for those with BD and the specific comorbidities, having prolonged and lifetime comorbidity was associated with a higher suicide attempt risk (Carra et al. 2014). While both males and females with comorbid personality disorders and psychiatric disorders constitute a high-risk group for suicide attempts, when AUD is comorbid with depression, AUD does not indicate an additional risk (Britton et al., 2015; Hawton, Houston, Haw, Townsend, & Harriss, 2003). Furthermore, Britton and colleagues (2015) noted that for veterans hospitalised in an acute setting due to alcohol use disorder or depression, the latter was the strongest predictor of further suicide attempts and that although AUD should be taken into account for treatment planning, AUD comorbidity does not increase suicide attempt risk further.

To determine the prevalence of physical and mental illness comorbidity among those who die by suicide, a variety of studies have been conducted (Rockett et al. 2009; Ruzicka, Choi & Sadkowsky 2005; Séguin et al. 2006). Based on a multiple cause of death analysis for a period of five years, an Australian study presented all the health conditions recorded in death certificates (Ruzicka, Choi & Sadkowsky 2005). The findings highlighted that somatic illness is more frequent in suicides of those 60 years of age and over and mental illness is more prevalent among those below 60 years old; the authors found that 22.6% of males (n=3882) and 23% of females (n=1311) had two health conditions recorded in their certificates (Ruzicka, Choi &

Sadkowsky 2005). The same multiple cause of death analysis for a similar time period was further replicated in the US, with Rockett and colleagues (2007) finding that 4% of males (n=121.479) and 6% of females (n=29.704) had two or more comorbidities registered on their death certificates (Rockett et al., 2007). Rockett et al. (2007) additionally noted that females who died by suicide were more likely to have physical and mental comorbidities than males. A high prevalence of mental comorbidity was also reported in a Canadian study employing a psychological autopsy methodology for 102 suicide deaths (Séguin et al., 2006). The authors reported that 42% of those who died by suicide had a mood and substance use disorder comorbidity and concluded that suicide prevention interventions in clinical settings should specifically focus on the presence of substance use related disorders for suicide risk (Séguin et al., 2006).

The number of co-occurring physical conditions in one person has been explored in relation to suicidal behaviours and suicide, with (unsurprisingly) a greater number of conditions being associated with an increased risk of suicide (Ratcliffe et al., 2008; Rollman & Shear, 2003; Scott et al., 2010). Although contradictory findings have been reported in the literature in relation to the role of a single physical condition in suicide risk, the majority of the literature suggests that comorbid mental health conditions may have a mediating role in the risk of suicidality among those with a single physical illness (Barker, Kölves, & De Leo, 2015; Fassberg et al., 2016; Feinstein & Pavisian, 2017; Harris & Barraclough, 1994; Kalson-Ray, Edan, & Leray, 2017; Pompili, Forte, Berman, & Lamis, 2016). Specifically depression, as the most common comorbid diagnosis in primary care patients with one physical condition, seems to play a role and is associated with an increased risk of suicide (Carson, Best, Warlow, & Sharpe, 2000; Feinstein & Pavisian, 2017; Pompili et al., 2016; Robson et al., 2010).

Although comorbid conditions or disorders have an effect on suicidal behaviours and suicide, no clear research evidence exists on the type of illness comorbidity that elevates suicide risk.

2.2 Aim of the current overview

Given that comorbidity is: a) a well-established term referring to one or more conditions that co-occur with a primary disease, and b) it has been extensively investigated in a number of empirical suicide-related studies, a narrative overview of existing reviews was performed. Considering that the role of multimorbidity in suicidality is the primary research focus of this PhD and taking into account the variety of reviews conducted to date on comorbidity and its association with suicidality, an overview of reviews only was performed. Hence, the aim of the current overview was to map evidence from reviews about the nature and extent of the relationship between comorbidity and suicidality.

2.3 Methods

2.3.1 Data-sources and eligibility criteria

A title search of English language reviews was performed in Medline, Embase, Web of Science and PsychINFO, using the keywords “comorbid*” and “suicid*” for the years 1966 to March 2017. Further to the language and time-period criteria, eligible review studies met the following inclusion criterion: they reported a) literature or/and a systematic review evaluating the impact of either psychiatric or physical health comorbidity (or both) on suicidality (suicidal ideation, suicide attempts or suicides). There were two exclusion criteria: a) review with no description of the literature search methodology and, b) review with no quantitative or qualitative evaluation of the findings. Additional reviews of comorbidity and suicidal behaviour found in the reference lists of the eligible studies, that did not appear in our web-sources search, were included.

2.4 Results

The initial records search yielded 29 potential reviews. After removing duplicates (9 records) and applying the inclusion and exclusion criteria, 6 records were included in the final list of studies. More specifically, excluded studies were: 1 review written in German (Nitkowski & Petermann 2011); 2

case-report studies (Kiraly & Sher 2015; Singer 2006); 3 original empirical studies (Baldassano 2006; Borges et al. 2005; Tondo et al. 1999); 2 reviews not presenting a literature search methodology (Lecrubier, 2001; Pompili et al., 2009); 1 study not presenting an evaluation method of the reviewed studies (Pompili et al., 2010); 4 reviews presenting neither a literature search methodology nor an evaluation method of the reviewed studies (Ganz & Sher 2009; Juang & Yang 2014; Runeson & Rich 1992; Saitta et al. 2011).

The synthesis of results is based on the comorbidity patterns of all the conditions included in the six reviews. The characteristics of the studies included in this overview are summarised in Table 1.

Table 2. 1 Characteristics of reviews on the role of comorbidity in suicidality

Author(s)/year published	**Aim & Methodology**	**Number of studies included**	**Type of comorbidity**	**Type of suicidality**	**Results & Limitations**
Barzilay and Apter (2014)	**Aim:** Summarize the established and most recent research findings on suicide risk factors in individuals (adults and adolescents) with mood and common comorbid disorders. **Methodology**: Review with narrative synthesis. **Web-sources**: Pubmed, Medline and PsychINFO. **Language**: English. **Time-period**: 1990-2014	Not mentioned	Psychiatric comorbidities of mood disorders	Suicide ideation, suicide attempt, suicide	**Results**: When mood disorders co-occur with either substance/alcohol abuse, disruptive disorder, eating disorder and borderline personality disorder, significantly increase the risk of suicide attempts and suicide. **Limitations**: None reported
Blasco-Fontecilla et al. (2016)	**Aim:** Review patterns of comorbidity in SB with a focus	Not mentioned	All patterns of comorbidity,	Suicidal behaviour and suicide	**Results**: The authors concluded that

Author(s)/year published	Aim & Methodology	Number of studies included	Type of comorbidity	Type of suicidality	Results & Limitations
	on how suicide attempts are more likely in those with accompanying comorbid disorders. **Methodology**: Narrative review. **Web-sources**: Pubmed, manual search and inclusion of studies conducted from the authors of the review. **Time-period:** 2012-2016		psychiatric or/and physical		comorbidity among subjects with mood disorders increases the risk of suicidal behaviour. Furthermore, comorbidity of Axis II, personal injury and physical illness in suicide attempters increase the repetition of suicidal behaviours. **Limitations**: The inclusion of original studies conducted by the authors of the review.
Hawgood and De Leo (2008)	**Aim:** 1) Understanding the relationship between anxiety disorders and suicidal	41 studies	Conditions that comorbid with anxiety disorders.	Self-harm, suicidal behaviour and suicide	**Results**: Comorbid anxiety disorders significantly contribute

Author(s)/year published	Aim & Methodology	Number of studies included	Type of comorbidity	Type of suicidality	Results & Limitations
	behaviour and 2) present critical comments on methodological issues, and highlight areas for future research. **Methodology**: Review. **Web-sources**: Medline. **Time-period:** January 2006 - May 2007.				to suicidal behaviour risk among patients with bipolar disorder, major depression and schizophrenia. Social phobia is related to suicidal behaviour in individuals with bipolar disorder, both for adults and child/adolescents. Symptoms of anxiety were associated with suicide attempts in depressed adolescents, while anxiety disorder increase the risk of suicide ideation and attempts in depressed

Author(s)/year published	Aim & Methodology	Number of studies included	Type of comorbidity	Type of suicidality	Results & Limitations
					elderly. Overall anxiety disorders when co-occur with other mental conditions, influence suicidal behaviour. **Limitations**: Findings should be interpreted with caution due to the methodological limitations of the studies reviewed
Kilbane et al. (2009)	**Aim:** evaluates suicide in bipolar disorder populations across all age groups who present with comorbid panic symptoms. **Methodology**: Review of literature. **Web-**	26 original studies	Comorbidity of panic in bipolar disorder	Self-harm, suicide attempts and suicide	**Results**: 4 papers support increased risk, 9 papers do not support increased risk, and 3 papers are inconclusive. **Limitations**: The

Author(s)/year published	Aim & Methodology	Number of studies included	Type of comorbidity	Type of suicidality	Results & Limitations
	sources: Medline and PsycINFO. **Time-period:** 1950 - August 2007				methodological limitations of the studies included
Panagioti et al. (2012)	**Aim:** 2-fold aim: 1) to examine the association between PTSD and suicidality and, 2) to investigate the impact of depression on the association between PTSD and suicidality. **Methodology**: Meta-analysis. **Web-sources**: EMBASE, PILOT, Medline, PsycINFO and Web of Science. **Time-period:** 1966 – June 2010.	63 studies	Comorbidity of depression in PTSD	Suicidal behaviour and suicide	**Results**: Higher levels of comorbid depression in PTSD participants, heightened the risk of suicide in PTSD participants (compared with controls who had only depression). **Limitations**: Publication bias and methodological quality of the original studies included; effect sizes provided were based on cross-sectional

Author(s)/year published	Aim & Methodology	Number of studies included	Type of comorbidity	Type of suicidality	Results & Limitations
					designs, therefore no causal could be provided; different definitions of PTSD along the 30 years of literature included; results about the relationship of depression-PTSD with suicidality was based on less than a quarter of the total studies reviewed.
Panagioti et al. (2009)	**Aim:** 2 broad aims: 1) The first was to assess the extent to which PTSD is associated with suicide, and 2) to determine the effects of co-morbid disorders on PTSD-	65 studies	Comorbidity of psychiatric disorders in PTSD	Any measure of suicidality (suicidal thoughts, suicide attempts, suicide)	**Results**: a) Those with PTSD and depression comorbidity have an increased frequency of suicidal behaviour, regardless which

Author(s)/year published	Aim & Methodology	Number of studies included	Type of comorbidity	Type of suicidality	Results & Limitations
	suicidality relationship. **Methodology**: Narrative review. **Web-sources**: Medline, EMBASE, PsycINFO and Web of Science. **Time-period:** 1966 – October 2008.				condition is the primary diagnosis; b) Comorbid PTSD among individuals with substance use disorders, increases risk of suicidal behaviour; c) Increased rates of suicidality among those with psychosis and comorbid PTSD; d) Serious mental illness (Axis I and II) that co-occur with PTSD escalate suicidal ideation and risk of suicide attempts. **Limitations**: None reported.

2.5 Description of included studies

The majority of papers were narrative reviews (5/6), with only one performing a meta-regression analysis, and all of the studies were published between 2008 and 2016 (see Table 1; (Barzilay & Apter 2014; Blasco-Fontecilla et al. 2016; Hawgood & De Leo 2008; Kilbane et al. 2009; Panagioti, Gooding & Tarrier 2009, 2012). All reviews focused on psychiatric comorbidities; in addition, the Blasco-Fontecilla et al. (2016) and Hawgood and De Leo (2008) reviews included the role of physical injuries/illness comorbidity. All measures of suicidality (suicidal ideation, suicide attempts, suicide) were included in each review (Barzilay & Apter, 2014; Blasco-Fontecilla et al., 2016; Hawgood & De Leo, 2008; Kilbane et al., 2009; Panagioti et al., 2012, 2009).

2.5.1 Suicide risk in individuals with mood disorder comorbidities

When focusing on the contributory factors that elevate suicide risk in mood disorders, Barzilay and Apter (2014) have summarised evidence on the comorbidities of both depression and bipolar disorder. While the studies they reviewed provided contradictory evidence regarding the role of comorbid anxiety disorders for adults, the authors noted that for adolescents the co-occurrence of depression and generalised anxiety disorder provides increased suicide risk (Barzilay & Apter, 2014). At the same time, the review found that in both adult and adolescent populations, when mood disorders are comorbid with alcohol abuse, disruptive disorder, eating disorder and borderline personality disorder, there is an increased risk of suicide attempts and deaths by suicide (Barzilay & Apter, 2014).

Bipolar disorder (BD) comorbidities were further reviewed by Kilbane and colleagues (2009). Although the majority of studies reviewed presented a non-significant or negative association between panic disorder and suicidality in BD individuals (see Table 1), few studies presented an increased risk of suicide attempts or suicide for panic disorder and BD comorbidity. Kilbane et al. concluded that the contradictory findings for the role of panic disorder and BP comorbidity in suicidality are related to the methodological differences between the studies' samples and designs.

The role of unipolar depression comorbid with PTSD (as the primary diagnosis) was examined by Panagioti et al. (2012). Employing meta-regression analysis they showed that when the levels of depression among individuals with PTSD were higher, compared to controls (i.e., those with depression only), then the levels of suicidality in the PTSD group were also higher (Panagioti et al., 2012). Furthermore, the authors noted that PTSD increases suicide risk regardless of whether it is the primary or secondary psychiatric diagnosis (Panagioti et al., 2012).

Blasco-Fontecilla and colleagues (2016) summarised evidence on different patterns of comorbidity and their role in suicide risk. They reported that for comorbidity of Axis I and Axis II disorders, the presence of depression increased the risk of suicidal behaviours when it co-occurred with anxiety or panic-related disorders, substance/alcohol abuse or borderline personality disorder (BPD). These authors concluded that although the above comorbidities seem to increase the risk of suicidal behaviours, the severity of co-occurring mood disorders has the most important role in differentiating those at higher versus lower suicide risk (Blasco-Fontecilla et al., 2016).

2.5.2 Suicide risk among those with PTSD and anxiety disorder comorbidities

Considering the extensive research into the relationship between anxiety disorders and suicidal behaviours, Hawgood and De Leo (2008) reviewed studies that presented any anxiety disorder co-occurring with other psychiatric disorders. While anxiety disorder is an established suicide risk factor, Hawgood and De Leo (2008) suggest that a positive association between anxiety and suicidality is more common when the disorder co-exists with further comorbid conditions. While bipolar disorder, major depression, substance abuse and schizophrenia were associated with an increased risk of suicidal behaviour among adults with an anxiety disorder, features or symptoms related to anxiety significantly increase the risk of suicide attempts in adolescents and young adults. The authors concluded that although anxiety disorders (panic disorder, OCD, social phobia) are associated with suicidality, especially when they are comorbid with other disorders,

more evidence is needed and findings must be interpreted with caution (Hawgood & De Leo, 2008).

Focusing on the relationship between PTSD and suicidal behaviours, Panagioti et al. (2009) reviewed original studies to determine the effect of PTSD on suicide risk. Among individuals with PTSD following the experience of trauma, abuse and natural disasters, specific comorbid psychiatric disorders were found to be associated with increased suicidal thoughts and behaviours (Panagioti et al., 2009): comorbid depression, psychosis, substance abuse and personality disorders increased risk of suicidal behaviours among individuals with PTSD, with the authors highlighting that some patterns of PTSD comorbidities differentiated suicide risk (based on the type of the pre-existing condition). More specifically, when depression or psychosis was the primary diagnosis, PTSD seems to heighten the risk of suicidal thoughts and attempts compared to those having PTSD as the primary condition. Although something similar in regard to the timing of a diagnosis was not evident for those with co-occurring PTSD and substance use disorders, the risk of suicidal behaviours was predicted more specifically from PTSD symptoms rather than features of substance abuse. Likewise when PTSD was co-existing with serious mental illness like BPD, Panagioti and colleagues concluded that this pattern of comorbidity escalates suicide risk.

2.5.3 Suicide risk among physical and psychiatric comorbidities

The narrative review from Blasco-Fontecilla and colleagues included studies investigating the somatic and mental disorder co-occurrence in regard to suicide risk. Based on six studies the authors concluded that suicidal behaviours are frequent among patients with physical illness, highlighting the role of comorbid psychiatric disorders. Moreover, Blasco-Fontecilla and colleagues suggested that the risk of suicide attempts may probably be either age or gender dependent. More specifically for age, they found that physical illness plays a significant role in the development of suicidal behaviours among the elderly. In addition, lethality of suicide attempts was shown to be significantly associated with having more physical health conditions and being over 65 years of age (Blasco-Fontecilla et al., 2016). For the importance of physical illness in suicide attempts, the authors presented one study, where

men rated a personal injury or illness as an important life event related to a suicide attempt (i.e., 6th life event) (Blasco-Fontecilla et al., 2016).

Hawgood and De Leo (2008) briefly summarised the findings from two studies on the role of anxiety disorders among patients with multiple sclerosis (MS) and coronary artery disease who had a history of suicidal behaviour. Specifically, outpatients with MS and anxiety comorbidity were more likely to have a history of suicide attempts and suicidal thoughts, while those with coronary artery disease co-occurring with anxiety and depression were likely to have made suicide attempts.

2.6 Discussion

Overall, the findings from the reviews provide evidence that psychiatric comorbidities increase the risk of suicidal behaviours. Major disorders, like depression, anxiety and PTSD, that co-exist with further conditions, seem to convey a higher prevalence of suicidality compared to other patterns of comorbidity. It was consistent across the reviews that depression comorbidities specifically are associated with increased suicide risk, regardless of whether they are primary or secondary diagnoses, with some authors highlighting the severity of depression as a key factor in the differentiation of risk of suicidal behaviours. Even though there are inconsistencies in studies regarding the independent effect of anxiety disorder in suicidality, the reviews highlighted the mediating effect of anxiety on mood disorders to increase risk of suicidal behaviour. With previous studies reporting high prevalence of AUD and depression comorbidity among those who have died by suicide (Bertolote & Fleischmann, 2002) alcohol abuse was found to be a risk factor for suicidality in individuals with psychiatric comorbidities.

In the wider literature comorbidity has been extensively studied, mostly in regard to psychiatric co-occurring conditions, having major physical conditions has been additionally explored mostly due to their co-existence with further mental illness (Abramovitch, Dar, Mittelman, & Wilhelm, 2015; Amerio, Odone, Tonna, Stubbs, & Ghaemi, 2015; Kang et al., 2015; Marrie et al., 2015; Melton, Croarkin, Strawn, & Mcclintock, 2016; Šprah, Dernovšek,

Wahlbeck, & Haaramo, 2017; van den Brink, Gerritsen, Oude Voshaar, & Koopmans, 2014; van den Brink, Gerritsen, Voshaar, & Koopmans, 2013; van Ool et al., 2016). Although some empirical studies into the role of psychiatric comorbidities in suicide risk have been conducted, very limited attention has been given to physical/mental co-occurrence in suicide-related studies. Given that the conclusions of Blasco-Fontecilla et al. (2016) and Hawgood and De Leo (2008) (i.e., the increased risk of suicidal behaviour among those with physical illness and comorbid mental conditions) are based on limited exploratory studies, more research is needed to identify the specific pattern of comorbidity that is associated with elevated risk of suicidality (2016).

Although the severity of a condition and the timing of a diagnosis in comorbidity may differentiate suicide risk, the limitations of each review should be taken into account in terms of the generalisability of the findings (see Table 1). The quality of methodology in the exploratory studies included in the reviews did not provide clear evidence on the patterns of comorbidity in suicidal behaviour and suicide, with some authors suggesting that due to inconsistencies in findings, their results should be interpreted with caution. However, as concluded and suggested by the reviews, more research is needed into the role of specific comorbid conditions in suicide risk, in order to inform the development of effective suicide prevention strategies for vulnerable populations.

2.7 Limitations of this overview

The aim of this overview was to summarise the evidence on the role of different types of comorbidity in suicide risk. Due to the differences in the methodological design of the reviews under study and the empirical studies that may have been duplicated across the reviews, only a narrative presentation of evidence on the relationship between comorbidity and suicidality could be provided. Although a quality assessment of the eligible reviews is not within the scope of this overview, there was a dearth of studies that systematically investigated the role of comorbidity in suicidality. A further limitation of this overview was (because of limitations in time) it was only possible to include reviews that had used comorbidity in their title,

therefore relevant studies that used other terms for co-occurring conditions in their title may have been excluded.

Chapter 3: Multimorbidity and suicide risk: A systematic review

Background

Physical illness and mental disorders play a significant role in fatal and non-fatal suicidal behaviour. However, there is no clear evidence for the additional effect of multiple health conditions in suicidality. The aim of the current review was to critically appraise the existing research literature and investigate whether multimorbidity, defined as the co-existence of two or more health conditions, was associated with increased risk of suicidal ideation, suicide attempts or suicide.

Methods

We searched four databases (Web of Knowledge, Embase, Medline Ovid, and PsychINFO) for empirical studies published between 1966 and June 2017 and written in English. Studies that assessed the relationship between multimorbidity and suicidality were considered for inclusion in the review.

Results

Following title and abstract screening, 22 articles were assessed for eligibility and a total of 14 studies were included in the final synthesis. Due to the heterogeneity of study designs and samples, meta-analyses could not be performed. Multimorbidity was associated with suicidal ideation, suicide attempts and suicide. However, most of the evidence was for an association with suicide. The majority of studies investigated psychiatric multimorbidity (six out of fourteen studies), two studies reported on physical/mental health multimorbidity, one included the cumulative number of all types of conditions (mental and/or physical), while the remainder (n=5) explored physical health multimorbidities with mental illness included as a confounder.

Conclusions

Although the co-existence of two or more health conditions was associated with suicidal behaviour and suicide, further studies are needed to clarify the strength of the association between multimorbidity and suicide risk. Suicide prevention strategies may need to consider multimorbidity as a target for intervention.

3.1 Introduction

Research into fatal and non-fatal suicidal behaviour has identified a wide range of predisposing and proximal risk factors (Klonsky, May, & Saffer, 2016; Mościcki, 1997; O'Connor, 2011). Specifically, psychiatric disorders, socio-demographic characteristics, negative life events and physical health problems have been identified as factors that may elevate the risk of suicide. As discussed in Chapter 2, there is considerable evidence that major mental disorders from axis I and II contribute to deaths by suicide, with studies highlighting that psychiatric comorbidity also elevates the risk of suicide attempts and ideation (Hawton et al., 2003; Henriksson et al., 1993; Marttunen, Aro, Henriksson, & Lönnqvist, 1991; Nock et al., 2010; Ramsawh et al., 2014). While psychiatric disorders are additionally associated with chronic physical health issues and premature mortality, somatic illness has also been identified as a suicide risk factor in its own right (Doherty & Gaughran, 2014; Martin et al., 2014; Osborn, Levy, Nazareth, & King, 2018; Robson et al., 2010; Stenager & Stenager, 2008). Considering that the severity level of a condition may differentiate the risk of suicide, Qin and colleagues highlighted that suicide risk is significantly associated with inpatient treatment regarding allergy (allergic rhinitis without bronchial asthma, allergic rhinitis with bronchial asthma, and atopic dermatitis), which meant a severe level of the condition, but not with outpatient treatment (Qin, Mortensen, Waltoft, & Postolache, 2011). The striking finding from this study was that the co-occurring mood disorder of those who have been hospitalised for allergy eliminated suicide risk and that allergy increased suicide risk only for individuals with no history of mood disorder (Qin et al., 2011).

More recently, research attention has also been directed at physical comorbidities, as there may be an association between multiple co-occurring somatic illnesses and suicide risk (Scott et al., 2010). Studies on the role of physical pain conditions in the risk of suicidal behaviours have additionally found significant associations with any suicidality outcome, with people having multiple pain conditions being three times more likely to report a suicide attempt compared to those without chronic pain (Hassett, Aquino & Ilgen 2014; Ilgen et al. 2008, 2013).

In addition to the dose–response relationship between the number of physical health problems and suicidal behaviour, some studies also suggest that the relationship between chronic physical illness and suicide risk may vary as a function of subsequent mental disorders (Bolton, Gunnell, & Turecki, 2015; Goodwin, Kroenke, Hoven, & Spitzer, 2003; Qin, Hawton, Mortensen, & Webb, 2014). Past reviews have found that chronic conditions like cancer, multiple sclerosis, and migraine are associated with increased suicide risk, with depression reported to be the most common psychiatric diagnosis among such physically ill populations (Anguiano et al., 2012; Nović et al., 2016; Pompili et al., 2016).

3.2 Aim

While the effects of single conditions, either mental or physical ill-health, on suicidality have been reported, the role of multimorbidity, defined as the co-occurrence of more than two health conditions (with no reference to an index condition), has not been extensively studied (Valderas et al. 2009). Considering this, the aim of the current review was to establish the nature and extent of the association between multimorbidity and suicidality outcomes (classified as suicidal thoughts, suicide attempts and suicides).

3.3 Methods

3.3.1 Definitions and keywords

Multimorbidity was defined as the co-occurrence of two or more physical or mental health conditions. Keywords used in our systematic literature search were “multimorbid*” OR “multi-morbid*” AND “suicid*”.

3.3.2 Data sources and eligibility criteria

We searched four databases (Web of Knowledge, Embase, Medline Ovid, and PsychINFO) for original journal articles, published between January 1966 and June 2017 and written in English. Additional records of multimorbidity and

suicidality were identified through the reference lists of the selected publications and personal contact with key authors of relevant studies. Besides the language and time-period limitations imposed, we included studies based on the following criteria: a) empirical studies in which multimorbidity and suicidality were assessed, and b) studies presenting an analysis of a direct possible association between multimorbidity and suicidality. Studies that did not report a direct association between multimorbidity and suicidality were excluded.

3.3.3 Quality assessment

In order to stratify the reviewed studies into those with higher and lower quality, a rating assessment tool was designed by the authors based on the quality assessment framework used by O'Connor et al. (2016). The quality rating for each quantitative study (maximum score 8) was based on the following: a score of 0-2 each for study design and cofounding variables including in analyses; a score of 0-1 for statistical analyses, suicidality assessment, multimorbidity assessment and inclusion of study comparison group (see Table 1). The quality assessment scores for each study are summarised in the results section and in Table 2.

Table 3. 1 Quality assessment tool for eligible studies included within this systematic review

Criteria	0	1	2
Design	Cross-sectional	Case-control	Prospective
Statistical analyses	Descriptive statistics	Linear regression model; univariate logistic regression model; multinomial regression model	
Suicidality assessment (including suicidal thoughts, suicide attempts, suicides)	Questionnaire; self-reported information; single question	Validated scale (e.g. BSSI, C-SSRS, HRSD); clinical interview of a diagnostic assessment tool; hospital registries; death registries	
Multimorbidity assessment	Questionnaire; self-reported information; single question	Validated scale (e.g. CIRS, SCID-I, ICED); clinical interview of a diagnostic assessment tool; clinical interview of international classification tool; hospital registries; death registries	
Study comparison group	No comparison group	Comparison group with no multimorbidity issues; comparison group with no suicidality reported (including suicidal thoughts, suicide attempts, suicides)	
Confounding variables in analyses	Analyses did not include adjustment for any confounding factors	Basic sociodemographic variables were adjusted in the analyses	Basic sociodemographic variables and additional confounding variables were included in the analyses e.g. prescribed medication, hazardous drinking, drug dependency

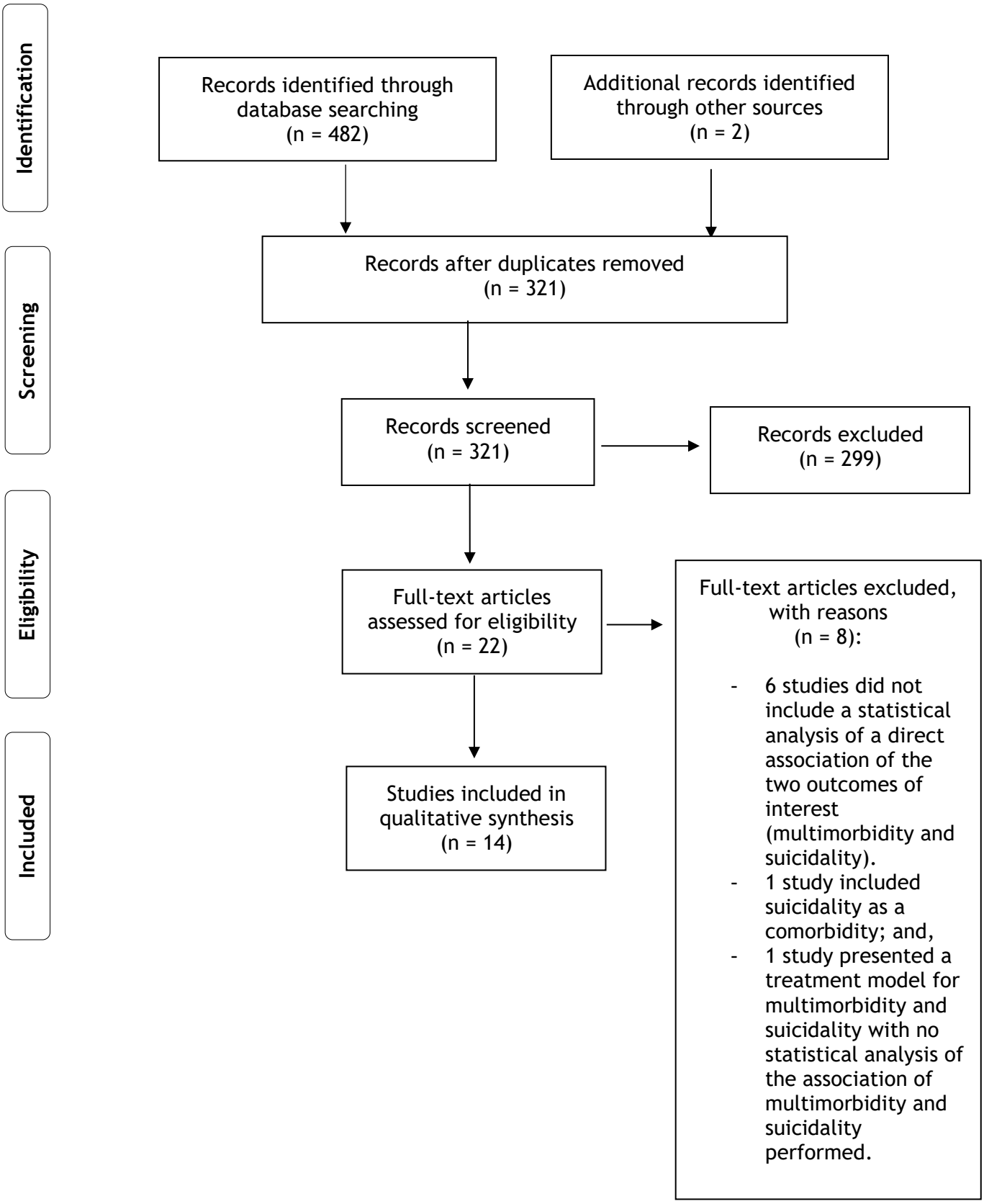
3.4 Results

The search strategy identified 484 records and after 163 duplicates were removed, 321 articles were assessed for eligibility (Figure 1). The reference lists of the included papers that used the term multimorbidity or multi-morbidity in their titles were also hand-searched. The search yielded a total of 14 empirical articles that were included in the qualitative synthesis of the review (Table 2).

3.4.1 Quality assessment scoring of reviewed studies

The quality assessment scores for the fourteen studies ranged from 3 (lowest) to 7 (highest). Five out of the fourteen reviewed studies attained a score of 7 (Ahmedani et al., 2017; Qin, Webb, Kapur, & Sørensen, 2013; Qin et al., 2014; Webb et al., 2012a, 2012b). The quality rating outcomes for each study are summarised in Table 2.

Figure 3. 1 Systematic review process of studies investigating multimorbidity and suicidality



3.4.2 Characteristics of included studies

The fourteen studies were published between 1998 and 2017 (see Table 2). Three studies each originated from the United Kingdom (Kavalidou, Smith & O'Connor 2017; Webb et al. 2012a, 2012b), and from Germany (Bischof et al. 2015; Lossnitzer et al. 2009; Wunderlich, Bronisch & Wittchen 1998), two from Denmark (Qin et al., 2013; Qin et al., 2014), with the rest of the studies conducted in Ireland (Kelleher et al. 2013), United States (Ahmedani et al., 2017; Calabrese et al., 2011; Nock et al., 2017), Switzerland (Angst, Sellaro & Merikangas 2002) and Canada (Juurlink et al. 2004). The majority of studies were case-control studies (N=7) (Ahmedani et al., 2017; Bischof et al., 2015; Juurlink et al., 2004; Qin et al., 2013; Qin et al., 2014; Webb et al., 2012a, 2012b) or prospective cohort studies (N=4) (Angst, Sellaro & Merikangas 2002; Calabrese et al. 2011; Kelleher et al. 2013; Wunderlich, Bronisch & Wittchen 1998). In thirteen out of the fourteen studies the findings were expressed through odds ratios and included multinomial, conditional, and univariate regression models, while one included a more descriptive presentation of the outcomes of interest.

3.4.3 Populations

In seven studies clinical population data were extracted from primary care registries, mental health facilities and mortality records (Ahmedani et al., 2017; Juurlink et al., 2004; Nock et al., 2017; Qin et al., 2013; Qin et al., 2014; Webb et al., 2012a, 2012b). The Danish studies used the same clinical sample for both of the studies included in this review (Qin et al., 2014, 2013). Adolescents and young adults from the general population, ranging from 13 to 24 years old, were included in four studies, while two studies investigated adults from the military services (Angst et al., 2002; Calabrese et al., 2011; Kavalidou et al., 2017; Kelleher et al., 2013; Nock et al., 2017; Wunderlich et al., 1998). All studies contained descriptive data for both sexes. In considering the association between multimorbidity and suicidality per se, four studies adjusted their analyses for gender [presented as odd ratios (OR) and relative risk ratios (RRR)], while both of the Webb et al. studies presented gender-specific risk ratios (Bischof et al., 2015; Kelleher et

al., 2013; Qin et al., 2014, 2013, Webb et al., 2012a, 2012b). Webb and colleagues concluded that increasing multimorbidity was linked with increased suicide risk in women but not in men (2012b), and that the effect of physical multimorbidity on the relative risk of self-harm (defined as non-fatal self-harm episodes) was large in women, independently of depression (2012a).

3.4.4 Definitions and measurement of multimorbidity

Multimorbidity was used as a term to describe the co-occurrence of multiple health conditions in nine studies, although this included two studies conducted within the same research group (Ahmedani et al., 2017; Angst et al., 2002; Calabrese et al., 2011; Juurlink et al., 2004; Kavalidou et al., 2017; Kelleher et al., 2013; Nock et al., 2017; Webb et al., 2012a, 2012b). Four studies used comorbidity to describe the co-occurrence of multiple health conditions, with two studies originating from the same research group (Bischof et al., 2015; Qin et al., 2014, 2013; Wunderlich et al., 1998).

Psychiatric multimorbidity was explored in six studies, whereas five studies investigated physical multimorbidity but included the confounding role of psychiatric diagnoses in their adjusted regression analyses. While the study by Lossnitzer and colleagues (2009) explored the burden of all types of illness (physical and/or mental) on suicide risk, only two studies, one conducted in United Kingdom and the other in Denmark, examined the interaction between physical and psychiatric illness per se (Kavalidou et al., 2017; Qin et al., 2014). In addition, the Danish study assessed the temporal nature of physical/mental multimorbidity effect on suicide risk (Qin et al., 2014).

While multimorbidity was the primary study outcome explored in relation to suicidality for all the reviewed studies, only Kelleher et al. investigated multimorbidity as a secondary predictor in their analyses (Kelleher et al., 2013). For the same study it should also be noted that although the findings indicated the significant role of multimorbidity in suicide attempt history among those with psychopathology, when controlling for psychotic symptoms the multivariate analyses did not yield a significant effect for multimorbidity (Kelleher et al., 2013).

As described in Table 2 the measurement and assessment of all types of health conditions varied across the studies with only two out of fourteen using the same instrument for assessing psychiatric illness, the Munich version of the Composite International Diagnostic Interview (M-CIDI) (Bischof et al., 2015; Wunderlich et al., 1998). In the studies of clinical populations, health conditions were coded according to standardised international diagnostic tools such as the International Classification of Diseases (ICD) (Ahmedani et al., 2017; Qin et al., 2014, 2013) and the Diagnostic and Statistical Manual of Mental Disorders (DSM) (Angst et al., 2002; Bischof et al., 2015; Calabrese et al., 2011). Furthermore, six studies assessing the number of multiple health conditions among clinical populations used medical health records (Ahmedani et al., 2017), prescription medical records (Juurlink et al., 2004), hospital registries (Qin et al., 2014, 2013) and primary care data sources (Webb et al. 2012a, 2012b).

3.4.5 Suicidal ideation, attempt history and deaths by suicide

Studies included assessment of suicidal ideation, suicide attempts as well as death by suicide. Thirteen out of the fourteen reviewed studies found a significant association between multimorbidity with at least one assessment of suicidality (Table 2). In the study that did not find an association between multimorbidity and suicidality, Lossnitzer and colleagues (2009) noted that physical comorbidities of congestive heart failure (CHF) do not increase the risk of suicidal thoughts, however those with depression and CHF had a higher suicide risk compared to those with no co-occurring depression.

Furthermore, significant associations were found with multimorbidity in the three studies exploring both suicidal ideation and previous suicide attempts (Bischof et al., 2015; Wunderlich et al., 1998; Kelleher et al., 2013). In three studies where suicidal ideation only was assessed, there was a significant effect of co-occurring conditions on suicidal ideation (Calabrese et al., 2011; Kavalidou et al., 2017; Lossnitzer et al., 2009). In Nock and colleagues' study (2017), the only reviewed study including two suicidality outcomes (suicide cases, suicide ideators) and one matched control group, having 2 or more mental conditions differed significantly between suicide cases and propensity

matched controls, with no significant differences found between suicide cases and suicide ideators. The authors noted that this latter finding provides evidence that known factors that increase suicide risk, like mental conditions, may be predictive of suicidal ideation as well (Nock et al., 2017).

The two studies that explored suicide attempt history only found an increased risk among their multimorbid sample, while the five remaining studies examining the relationship between multimorbidity and suicide deaths reported elevated odds and relative risk ratios (Ahmedani et al., 2017; Angst et al., 2002; Juurlink et al., 2004; Qin et al., 2014, 2013, Webb et al., 2012a, 2012b).

Only three studies assessed recent suicidal thoughts and/or attempts (Kelleher et al., 2013: suicidal thoughts and attempts occurring within the past 2 weeks; Kavalidou et al., 2017: suicidal thoughts in past year; Nock et al., 2017: suicidal thoughts in the past 30 days), whereas all of the other studies investigated lifetime suicidality. The assessment of suicidal ideation and attempts was extremely heterogeneous, with the Munich version of the Composite International Diagnostic Interview (M-CIDI) used in two studies (Bischof et al., 2015; Wunderlich et al., 1998), with the Patient Health Questionnaire (PHQ) used in two further studies (Calabrese et al., 2011; Lossnitzer et al., 2009).

Table 3. 2 Characteristics of reviewed studies investigating the association of multimorbidity and suicide risk.

Author/Country & Quality Assessment Score (QA)	**Population**	**Description of multimorbidity**	**Type of suicidality**	**Study design**	**Main findings**	**Limitations**
Ahmedani et al., 2017 USA QA = 7	2,674 adult participants	Physical multimorbidity of 19 physical conditions were derived from health care records, according to ICD-9 codes	Deaths by suicide identified through the electronic health records of Virtual Data Warehouse (VDW), matched with official mortality records	Case-control study	38.2% (n=1.020) of those who died by suicide had multimorbidity issues. Having 2 or more conditions was associated with an increased suicide risk (OR=4.12, p<0.0001), even after adjusting for age, sex and any adjusted psychiatric condition (OR=1.70, p<0.001)	Results should be interpreted with caution as: a) the health records analysed belonged to well-insured individuals, leaving those with no insurance excluded; b) not all US health care settings were represented; c) data on ethnicity/race were not available and were not used in the adjusted analysis; d) the authors noted that the coding of

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
						conditions may be inaccurate, as they were given by the insurance providers.
Angst et al., 2002 Switzerland QA = 5	591 adult participants	Psychiatric multimorbidity according to: DSM-III criteria and the Structured Psychopathological Interview and Rating of the Social Consequences for Epidemiology (SPIKE).	History of suicide attempts Assessed through the diagnostic interview of SPIKE.	Prospective cohort study	The clinical severity - suicide attempts (%) - increased by the comorbid number of psychiatric DSM-III axis I disorders (0–10). More specifically: No disorder 2%; 1 disorder 7.8%; 2 disorders 17.8%; 3 disorders 23.2%; 4 disorders 21.7%; 5+ disorders 57.1%, *p*=0.001.	Some disorders were excluded from the analyses due to the availability of diagnostic criteria across the three waves of interviews of the study.
Bischof et al., 2015 Germany QA = 6	442 adult participants	Psychiatric comorbidity of gambling behaviour and psychiatric disorders. according to: DSM-	Suicidal ideation and suicide attempts	Cross sectional	Comorbidity of: a) mood disorders with gambling disorder and b) Cluster B personality disorders with gambling disorder were the predominant risk factors for suicidal events,	Exclusion of individuals who did not report depressive symptoms in CIDI, as assumed to be non suicidal, was reported

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
		IV, Gambling Section of the Composite International Diagnostic Interview (CIDI), Munich Composite International Diagnostic Interview (M-CIDI), and Structured Clinical Interview for DSM-IV, Axis II (SCID II)			independently from the severity of the gambling disorder. Specifically, for suicidal ideation there was a significant association with mood disorders (RRR=5.14, 95% CI: 2.91-9.07, p< 0.001) and substance use disorders exc. tobacco (RRR=1.73, 95% CI: 1.02-2.94, p= 0.042). Suicide attempts were significantly associated with mood disorders (RRR=11.92, 95% CI: 4.70-30.26), anxiety disorders (RRR=2.24, 95% CI: 1.16-4.34, p=0.017) and cluster B personality disorders (RRR=2.40, 95% CI: 1.13-5.10, p=0.023). Cluster B personality disorders were the only psychiatric comorbidity with gambling	as a limitation from the authors Recruitment was based on different channels including as well some participants from treatment centres (11%).

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
					behavior that gave a three-fold risk for attempting suicide when participants with suicidal ideation were compared to those with suicide attempts (RRR=3.08, 95% CI: 1.48-6.40, p= 0.003).	
Calabrese et al., 2011 USA QA = 6	2,616 National Guard soldiers	Psychiatric multimorbidity according to: DSM-IV criteria, PTSD Checklist-Civilian Version, Patient Health Questionnaire-9 (PHQ-9), GAD-7 and the Mini-International Neuropsychiatric Interview.	Suicidal ideation, assessed through the Patient Health Questionnaire-9 (PHQ-9)	Prospective cohort study	Among those with current PTSD, comorbidity with more than 1 disorder was associated with a higher risk for suicidal ideation (OR=2.1, 95% CI: 1.0-4.6). Those with PTSD and 2 additional disorders were 7.5 times more likely to have ever experienced suicidal ideation as compared to those with PTSD only (OR= 7.5, 95% CI: 3.0-18.3).	The psychopathologies were self-reported, which may lead to misdiagnosis given the retrospective and non-clinical nature of the data Although PTSD diagnosis was current, suicidal ideation was lifetime. Therefore the analyses can not provide evidence of a direct effect of

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
						current PTSD on suicidal thoughts.
Juurlink et al., 2004 Canada QA = 5	1354 adults, 66 years or older.	Multimorbidity was defined as the total number of either mental or physical conditions per patient. Data on 17 health conditions were assessed through the prescription medication records of the Ontario Drug Benefit program.	Deaths by suicide identified from the Office of the Chief Coroner for Ontario.	Case-control study.	Compared with patients with no illness, those with 3 illnesses had a 3-fold increase in the estimated relative risk of suicide and those with 5 illnesses had a 5-fold increase in suicide risk (OR=3.5; 95% CI 2.9-4.2 and OR=5.7; 95% CI, 4.4-7.4 respectively). Overall, a strong association was found between the cumulative number of conditions and the estimated relative risk of suicide.	The use of prescription records for classifying illnesses has been identified as a limitation. Lack of data on malignancies, alcohol abuse, bereavement and isolation were also seen as limitations. Furthermore, authors mention that the identification of deaths by suicide is prone to multiple biases and that misclassification of

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
						the medical illnesses explored may bias the association of illness and suicide risk.
Kavalidou et al., 2017 UK QA = 6	7389 participants, aged 16 and over.	Mental/physical multimorbidity assessed through the Clinical Interview Schedule (CIS-R) and a show card of 22 health conditions.	Past year suicidal thoughts, assessed through the Clinical Interview Schedule (CIS-R).	Cross-sectional study.	Compared to those with neither physical nor mental conditions physical/mental multimorbidity was significantly associated with suicidal thoughts (OR= 26.857; 95% CI, 16.287–44.286, p < 0.001). The effect of multimorbidity on suicidal thoughts was significant after the adjustment for demographics (OR= 24.053; 95% CI,14.505–39.885, p < 0.001) and followed the same significance even after adjusting for demographics, negative life events, prescribed medication, hazardous drinking and drug dependency (OR=	Listed limitations from authors: a) Secondary analysis of cross-sectional data; b) no possibility in investigating the temporal relationship between the onset of physical/mental health conditions and suicidal thoughts; c) lack of information regarding the severity of either physical or mental conditions; d) suicidal thoughts were not assessed through a

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
					15.632; 95% CI, 9.274–26.349, p < 0.001). Overall, multimorbidity was associated with suicidal thoughts, but it did not appear to elevate risk beyond the independent effects of common mental disorders.	suicide risk assessment but through a clinical diagnostic instrument (CIS-R).
Kelleher et al., 2013 Ireland QA = 5	1112 school-based adolescents (aged 13-16 years).	Psychiatric multimorbidity of emotional, conduct and hyperkinetic disorders measured with: Strengths and Difficulties Questionnaire (SDQ). Psychotic symptoms were assessed with the Adolescent Psychotic	Suicidal thoughts and suicide attempts (measured at 3 time-points), assessed with the Paykel Suicide Scale.	Prospective cohort study.	Participants with psychopathology who had a history of attempting suicide were significantly more likely to have multimorbidity across the 3 SDQ disorder list (emotional, conduct, hyperkinetic), than those who did not have such a history (OR=1.50; 95% CI: 1.10-2.04). In the multivariate model to control for the effect of psychotic symptoms, multimorbidity was no longer	Only the wide CIs for acute suicide attempts, was reported by the authors as a limitation of the study.

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
		Symptoms Screener.			significantly associated with suicide attempts (OR= 1.26; 95% CI: 0.92-1.75).	
Lossnitzer et al., 2009 Germany QA = 3	294 patients with congestive heart failure (CHF).	Multimorbidity was measured with the German version of the Modified Cummulative Illness Rating Scale (CIRS-G), which assess impairment severity of 14 organs (heart and mental disorders were not assessed with CIRS-G). Depression of those with CHF was assessed separately, using	Suicidal ideation and ideas of self-harm assessed with the German version of the Patient Health Questionnaire (PHQ-9).	Cross-sectional study.	Among patients with CHF, multimorbidity (summary score of the CIRS-G scale) was not associated with suicidal ideation and/or ideas of self-harm (CHF with suicidal ideation and/or ideas of self-harm: M=8.5, SD=7.3, CHF without suicidal ideation and/or ideas of self-harm: M=8.5, SD=6.7, p= 0.99). When comparing CHF patients with depression to CHF patients without depression, both lifetime and first-episode depression increased the risk of suicidal ideation and ideas of self-harm (lifetime depression:	Limitations mentioned from the authors: a) Cross-sectional study design; b) Large confidence intervals (CIs) for the odd ratios (OR) of depression; c) using SCID and PHQ-9 (that both assess suicidal ideation) may imply a cofound between the dependent and independent variables of the analysis.

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
		the Structured Clinical Interview for DSM-IV (SCID) and the Patient Health Questionnaire (PHQ-9).			OR=10.89, CI: 2.49–47.72; first-episode depression: OR= 3.92, CI: 1.16–13.22).	
Nock et al., 2017 USA QA = 5	US Army population: 135 of soldiers who died by suicide; 137 control soldiers (matched for sociodemographic factors); and 118 control soldiers who reported suicide ideation in the past year.	The total number of mental disorders were assessed with a combination of the screening version of the PTSD Checklist and the Composite International Diagnostic Interview-Screening Scales.	Suicide deaths were derived from the Army Casualty and Mortuary Affairs Operation Center (CMAOC). The suicidal behaviour of the control group was assessed using the Columbia-Suicide Severity Rating Scale (C-SSRS).	Psychological autopsy study employing propensity score-matching.	As reported by next of kin, there was a dose-response relationship between the number of lifetime mental conditions and suicide (x2= 17.4, p< 0.05). Having 2 and 3+ lifetime disorders were significantly associated with suicide (OR= 2.9, 95% CI: 1.1-7.5; OR= 5.1, 95% CI: 2.3-11.2, respectively). For the past 30 days prevalence of mental disorders, having 2 and 3+ disorders significantly increased the risk of suicide deaths (OR=	Limitations mentioned by authors: a) Over and under-reporting of information, based on the retrospective nature of a psychological autopsy study; b) representativeness of sample as only 1/3 of all suicides during the study period were included; c) small sample which limited

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
			The characteristics of the soldiers who died by suicide were assessed with a modified version of the Suicide Intent Scale.		14.1, 95% CI: 4.8-41.1; OR=98.7, 95% CI: 25.8-377.4, respectively). When suicide cases where compared with suicide ideators, having 3+ disorders provided increased risk of suicidal ideation (OR= 31.3, 95% CI: 1.7-588.1). As reported by next of kin, there was a dose-response relationship between the number of lifetime mental conditions and suicide (x2= 17.4, p< 0.05). Having 2 and 3+ lifetime disorders were significantly associated with suicide (OR= 2.9, 95% CI: 1.1-7.5; OR= 5.1, 95% CI: 2.3-11.2, respectively). According to soldiers supervisors, the prevalence of both lifetime and 30 past days of mental	the power of detecting small to medium effects or examining the interactions between risk factors; and, d) limited number of risk factors examined in the study.

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
					conditions had a significant association with suicide deaths (2 lifetime disorders: OR=5.8, 95% CI: 2.5-13.4; 3+ lifetime disorders: OR=4.8, 95% CI: 2.0-11.5; 2 disorders in the past 30 days: OR= 32.6, 95% CI: 6.8-157.0; 3+ disorders in the past 30 days: OR= 22.4, 95% CI: 3.7-135.9).	
Qin et al., 2013 Denmark QA = 7	27 262 suicide cases and 468 007 live controls matched for sex and date of birth.	Multimorbidity of physical illnesses assessed through the Danish National Hospital Register (ICD-10 categories).	Definite suicides through the Cause of Death Register.	Nested case-control study.	Multiple comorbidities were associated with a progressive increase in suicide risk for both sexes (2 physical illn. IRR=2.43, 95% CI: 2.34 - 2.52; 3 physical illn. IRR=3.35, 95% CI: 3.20 - 3.52; 4 physical illn. IRR=4.24, 95% CI: 3.98 - 4.53; 5 physical illn. IRR= 5.30, 95% CI: 4.84 - 5.80, >5 physical illn. IRR=7.07, 95% CI: 6.34 - 7.89).	Authors considered only serious physical illnesses resulting in hospitalization and results can not be generalised for those with physical illness not hospitalised. Regarding psychiatric history they used psychiatric service

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
					The elevated risks were reduced after adjusting for psychiatric history and socio-economic status (2 physical illn. IRR=1.76, 95% CI: 1.69 -1.83; 3 physical illn. IRR=2.07, 95% CI: 1.97 – 2.19; 4 physical illn. IRR=2.21, 95% CI: 2.06 – 2.38; 5 physical illn. IRR= 2.35, 95% CI: 2.12 – 2.61; >5 physical illn. IRR= 2.71, 95% CI: 2.40 – 3.07).	contact as a proxy for psychiatric status and this may reflect only serious/severe disorders. Data on physical illness do not represent the lifetime of older subjects and can not be applied to all age-groups.
Qin et al., 2014 Denmark QA = 7	The study included 27 262 suicide cases, and 468 007 live controls matched for sex and date of birth.	Physical illness and psychiatric multimorbidity, assessed through the Danish National Hospital Register (ICD-10 categories) and the Danish	Definite suicides through the Cause of Death Register.	Nested case-control study.	People with both physical and psychiatric disorders were prone to die by suicide when compared to the control group. More specifically suicide risk was significantly associated with: Psychiatric disorder before physical illness [Crude IRR (adjusted for gender and age) =	Authors considered only serious physical illnesses resulting in hospitalization (not milder physical illnesses) and results can not be generalised for those with physical illness not hospitalised

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
		Psychiatric Central Register.			18.47, 95% CI: 17.56–19.43; Adjusted IRR (additionally for sociodemographics)= 14.05, 95% CI: 13.33–14.80]. Psychiatric disorder after physical illness [Crude IRR (adjusted for gender and age) = 30.10, 95% CI: 28.70 – 31.56; Adjusted IRR (additionally for sociodemographics) = 24.16, 95% CI: 23.00 – 25.36].	Regarding psychiatric history they used psychiatric service contact as a proxy for psychiatric status and this may reflect only serious/severe disorders.
Webb et al., 2012a UK QA = 7	A total of 873 adult suicide cases and 17 460 living controls matched on age and sex were studied.	Physical multimorbidity was measured as the number of physical illnesses from a list of 11 conditions. Primary care records were taken from the General	National mortality records for suicides (including open verdicts).	Nested case-control study.	Overall the study indicated that clinical depression is a strong confounder of increased suicide risk among physically ill people. Gender had an effect on the association of physical multimorbidity and suicide risk, with women having 3 or more physical illnesses providing an increased risk compared to those	The reference group consisted of patients without any of the assessed physical illnesses but could have had other medical conditions. Adjustments for clinical depression were not fully

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
		Practice Research Database (GPRD).			without any of the examined conditions (1 physical illn.: OR=1.27, 95% CI: 0.89-1.79; 2 physical illn.: OR=1.42, 95% CI: 0.88-2.30; ≥ 3 physical illn.: OR= 2.27, 95% CI: 1.35-3.84, x=8.6, p=0.003). The risk was higher for women 50 years or older, which was partially explained by clinical depression (adjusted OR=1.53, 95% CI: 0.90-2.59). The point estimate was large for younger women with 3 or more illnesses as well (OR, 9.51; 95% CI, 2.32-39.01). Due to the limited cases in the younger age groups though (4 female cases younger than 50 years with 2 physical illnesses and 3 younger cases with 3 or more conditions) the increased	comprehensive because they could not assess depression among people who did not seek treatment.

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
					ORs should be viewed with caution.	
Webb et al., 2012b UK QA = 7	2306 self-harm cases and 46,120 age and gender-matched controls	Physical multimorbidity was measured as the number of physical illnesses from a list of 11 conditions. Primary care records were taken from the General Practice Research Database (GPRD).	Recorded episodes of self-harm among patients registered at GPRD practices.	Nested case-control study	A dose–response relationship with increasing number of physical illnesses and risk of self-harm was found for both men and women when compared to those with no physical illness (1 illn. only: OR= 1.41, 95% CI: 1.27–1.56; 2 or more illn.: OR= 1.77, 95% CI: 1.49–2.10, x^2= 66.3, p<0.001). The association remained significant after controlling for clinical depression (for both men and women): (1 illn. only: OR= 1.20, 95% CI: 1.08–1.34; 2 or more illn.: OR= 1.22, 95% CI: 1.02–1.46, x^2= 11.2, p<0.001).	The reference group that consisted of patients with none of the 11 assessed physical illnesses may have had conditions that the authors did not examine. The study dataset contained no standardised information to indicate the severity of each self-harm episode and diagnosis of physical illness or depression.

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
					In the analysis run for males and females separately the multimorbidity effect was found significant for both sexes. However, in the adjusted model for clinical depression, the dose response pattern was not explained by the presence of clinical depression in women only (1 physical illn. only: OR= 1.27, 95% CI: 1.09–1.48; 2 physical illn. or more: OR= 1.48, 95% CI: 1.15–1.92, x^2= 14.0, p< 0.001).	Lastly the authors could not identify all completed suicide cases and remove them from the analysis.
Wunderlich et al., 1998 Germany QA = 6	3021 young adults aged 14–24 years.	Psychiatric multimorbidity of diagnostic groups based on: the Munich version of the Composite International	Suicide attempt history and suicidal thoughts, assessed through the Munich version of the Composite International	Survey was part of a prospective longitudinal study.	91% of all suicide attempters had at least one mental disorder with the vast majority being comorbid or multimorbid (79%). The risk for suicide attempt was: 3.5 times higher for subjects with 2 DSM-IV diagnoses than for	The assessment of DSM-IV disorders and suicide attempts were lifetime but the suicide attempts may not have occurred at the same time as the

Author/Country & Quality Assessment Score (QA)	Population	Description of multimorbidity	Type of suicidality	Study design	Main findings	Limitations
		Diagnostic Interview (M-CIDI).	Diagnostic Inter-view (M-CIDI).		subjects with no diagnosis (OR=3.5, 95% CI: 1.3–9.1) 6.4 times higher for those with 3 DSM-IV diagnoses (OR=6.4, 95% CI: 2.4–16.9) and 18 times higher for those with more than 3 DSM-IV diagnoses (OR=18.4, 95% CI: 7.8–43.6). In addition, the authors examined 5 diagnostic groups of comorbid DSM-IV diagnoses and reported that when anxiety and depressive disorders were involved, comorbidity was associated with the highest risk for suicide attempt.	disorder in question. This may lead in inconclusive results and can not provide evidence of the disorder-suicidality association.

3.5 Discussion

Overall, the findings yield some support for the overarching hypothesis that multimorbidity is associated with increased risk of suicidality. Although the number of studies was limited, multimorbidity of either physical, psychiatric or physical and psychiatric illnesses was associated with higher levels of suicidal ideation, suicide attempts and suicide compared to no multimorbidity. However, the majority of the reviewed studies explored psychiatric multimorbidity (six out of fourteen studies) and the studies that explored physical multimorbidity (five out of fourteen) had additionally included the role of mental illness as a cofounder or a comorbid condition among those with physical health issues. Although it is well established that mental illness has a primary role in the aetiology of suicide risk, its role as a mediator of physical illness–suicidality relationship remains unclear, with research yielding contradictory findings (Bertolote, 2004; Chesney et al., 2014; Goodwin et al., 2003; Harris & Barraclough, 1997; Ramsawh et al., 2014; Wang, Tang, Xu, Weng, & Liu, 2016).

With regard to the different indices of suicidality, suicide was the outcome most commonly investigated [(n=6/14); (see Table 1)]. All 6 studies found evidence of an increased risk of suicide among those individuals with two or more health conditions. However, due to the heterogeneity of the populations studied, the generalisability of these findings is likely to be limited.

A major challenge when trying to integrate the findings from across the studies is the inconsistent use of terminology regarding the co-occurrence of two or more physical or mental health conditions. Specifically, 'multimorbidity' and 'comorbidity' were often used interchangeably, making the comparison of studies difficult (Valderas et al., 2009). In addition, comorbidity (which refers to the presence of one or more diseases co-occurring with a primary disease) and multimorbidity (which refers to the presence of two or more conditions but does not prioritise which health issue is more important than another), are conceptualised differently in the wider chronic illness literature (Valderas et al., 2009). This operationalization

regarding the terminology used has not been consistently applied in the studies reviewed here.

Although we present some evidence in support of a possible association between multimorbidity and suicidality (Table 1), study limitations and risk of bias should be considered. First, the term multimorbidity is not yet used routinely in suicide-related studies, therefore we may have excluded studies that assessed multimorbidity but did not describe it as such. Second, half of the studies were based on self-reported information, surveys and interviews, and may therefore have excluded participants deemed ineligible based on the assessment tools used; plus some health conditions may have been over- or under-reported. Some studies included lifetime conditions and current suicidal behaviours or *vice versa*, which cannot provide evidence about the effect of current/recent multimorbidity issues on current suicidal behaviour (Calabrese et al. 2011; Wunderlich, Bronisch & Wittchen 1998). Furthermore, there were inconsistencies in terms of the nature of how severe a health condition had to be before being recorded in the studies. Some studies obtained patients' health information from primary care datasets, so this may have introduced a systematic bias as these datasets may only record conditions that require medical treatment (Qin et al., 2014, 2013, Webb et al., 2012a, 2012b). Whereas other studies may have recorded less severe chronic conditions which did not require contact with health care facilities.

In respect of reporting and publication bias, unpublished and non-English language studies were not included in this review. Furthermore "within study" selection bias should also be noted, for example in Bischof and colleagues' study their sample included participants from both general and clinical settings, something that may have influenced their results. Specifically, participants from the general population recruited through telephone contact may have over-reported suicidal behaviours while participants from treatment services may have only reported suicidal history resulting in medical care. This mixed sample methodology may not provide a clear indication of suicide risk among those with gambling behaviour (their target population) and comorbid psychiatric disorders either in general or clinical settings.

Given that all of the studies found at least some evidence of an association between multimorbidity and suicide risk, it is important to note that, there must be studies which did not find an association but were not published because they were reporting null effects. Given the restricted range in study quality scores, it is not possible to make any reliable judgment about the relationship between study quality, multimorbidity and suicide risk.

3.6 Exclusion of studies

We would like to highlight three studies that were excluded from our review, based on our aim of reviewing studies which presented an analysis of the association between multimorbidity and suicidality. These studies were excluded because either they only adjusted for multimorbidity or because they defined suicidality as a comorbid condition in their analysis.

First, Gallo and colleagues (2016) found that suicidal ideation was associated with all-cause mortality among patients with depression and when medical illness comorbidity [measured with the Charlson Comorbidity Index (CCI)] was considered, suicidal ideation significantly differed across the CCI scoring range (p= 0.049, HR: 1.07, 95% CI: 0.85-1.35). Second, in their adjusted analyses Kelleher and colleagues (2013b) found that psychiatric multimorbidity (more than one diagnosis) could not explain the relationship between psychotic experiences and suicide plans and attempts among adolescents (suicide plans: OR=3.25, 95% CI: 1.27-8.33; suicide attempts: OR=3.13, 95% CI: 1.11-8.79). Lastly, Sacco et al., found that suicidality (defined as a comorbidity in their study) was higher in those who had depression with alcohol comorbidity compared to those with depression only (depression without alcohol comorbidity: M:1568, SE:20.35 vs depression with alcohol comorbidity: M:266, SE:36.21, p< 0.001).

3.7 Conclusions

Based on non-clinical and clinical population studies reviewed herein we found some support for a potential association between multimorbidity and

suicidality, particularly with respect to suicide. Given the different types of multimorbidity, taken as whole, our findings suggest that psychiatric multimorbidity increases suicide risk in both non-clinical and clinical populations. Even though the role of physical multimorbidity in suicide risk has not been extensively studied, the current review points tentatively to an association between physical multimorbidity and suicide risk, beyond the confounding effect of mental illness among those who are physically ill. However, the risk of suicide and suicidal ideation among those with mental and physical illness multimorbidity was only investigated in Qin et al. and Kavalidou et al. studies. In the former, Qin and colleagues (2014) found that suicide risk varied as a function of the timing of onset of the two types of illness. More specifically these authors noted that people with multimorbid physical/mental illness were at increased risk of dying by suicide if the two types of illness were diagnosed close in time to each other, regardless of which was diagnosed first. In addition, even if the onset of psychiatric disorder developed some years after the diagnosis of physical illness it exacerbated the risk substantially (Qin et al., 2014). In Kavalidou and colleagues' study (2017), although mental/physical multimorbidity was significantly associated with suicidal thoughts, it did not convey additional risk beyond the independent effects of common mental disorders or physical health conditions.

While the co-existence of two or more health conditions appears to be associated with suicidal ideation, suicide attempts and suicide, further studies are needed to clarify the strength of the association between multimorbidity and suicidality. Future research should investigate the type and nature of conditions within multimorbid populations that significantly increase suicide risk. Detailed research into the effect of multimorbidity on suicide risk could guide physicians and clinicians in assessing their patients' suicide risk. Indeed, tailor-made suicide risk assessments for these vulnerable populations may be required.

Chapter 4: Methodology

Background

Literature indicates that having multiple diseases increases the risk of suicidality, more than having none or one single disease alone. However, most of the research on suicide risk factors has focused either on the role of psychiatric disorders or physical conditions, while the co-occurrence of physical and mental illness within a person, with no reference to the index condition, has been overlooked. Indeed, limited studies explore the specific co-occurrence, with no studies conducted on population-based surveys.

Methods

The current chapter presents the overall methodology followed in the four PhD empirical studies, which aimed to investigate if populations with physical/mental co-occurrence (multimorbidity) exhibit higher risk of suicidal thoughts and suicide attempts, compared to those with neither physical nor mental conditions. Cross-sectional and prospective analyses were conducted utilising three different databases: a) the National Psychiatric Morbidity Survey of Great Britain 2000, b) the Adult Psychiatric Morbidity Survey 2007, and c) the West of Scotland Twenty-07 Cohort study.

Conclusions

The secondary analysis of population-based survey and cohort studies will help us better understand the role of multiple health conditions, involving both physical and mental health issues, in suicidal behaviours.

4.1 Introduction

In the reviews presented in chapters 2 and 3, it was evident that the co-occurrence of multiple health conditions increases the risk of suicidality more than having no health conditions or having one single disease alone. However, the majority of studies have focused on populations that have psychiatric disorders as a primary diagnosis, with limited research conducted on the effect of comorbid physical conditions among those with a mental health disorder experiencing suicidal behaviours (Karmakar et al. 2016). Furthermore, those with a somatic illness as a primary diagnosis have been additionally investigated in terms of their suicidality, with most of those studies also controlling for mental illness. Overall, clinical populations of patients with either psychiatric or physical conditions have been investigated in terms of their risk of suicidal behaviours and suicide; however, the co-occurrence of physical and mental illness within a person, with no reference to an index condition, has been overlooked as a suicide risk factor.

Considering the lack of studies into the relationship between the co-occurrence of physical and mental illness and the risk of suicidal behaviours, the current doctorate thesis aimed to explore if: a) the risk of suicidal behaviours varies as a function of physical/mental co-occurrence and b) if physical/mental co-occurrence increases the risk of suicidal behaviours more than either condition alone. The current chapter presents the overall methodology of the empirical studies presented in this PhD thesis and is organised in the following sections: the terminology used, number and type of study designs employed, participants, measures used and statistical analysis.

4.2 Key terminology used throughout this PhD thesis

In the literature, the most common terms used in regard to disease co-occurrence are comorbidity and multimorbidity, leaving aside multi-word expressions that describe populations with multiple diseases (Almirall & Fortin 2013). Almirall and Fortin (2013) summarised the differences between *disease* and *condition* in their review and indicated that the latter term does

not indicate the pathology included in the disease model and that either of the terms are appropriate to use for coexisting health issues. In the following sections of this thesis, the term *condition* will be used to refer to any health issue among our study participants. Only to avoid the repetition of *condition*, the terms *issue*, *illness*, or *disorder* will be additionally used. Further to avoiding the repetition of the key terms in this thesis, the use of psychiatric condition instead of mental health condition, and the use of somatic condition instead of physical health condition, are used interchangeably.

As previously discussed (in Chapter 3), multimorbidity refers to having two or more conditions, with no reference to a primary one (Almirall & Fortin, 2013; Le Reste et al., 2013; Van Den Akker, Buntinx, & Knottnerus, 1996). Although there is no general consensus on multimorbidity, regarding the type of conditions covered (physical health only or mental health only), it has been presented that multimorbidity, as a term, covers both physical and mental health conditions (Almirall & Fortin 2013; Fortin et al. 2005; Lefèvre et al. 2014; Le Reste et al. 2013). In terms of the chronicity of the conditions covered by the term multimorbidity, previous research mainly refers to long-term or chronic; however, with more recent studies additionally covering acute conditions, no restrictions on chronicity are given for the health issues covered by the term multimorbidity (Almirall and Fortin, 2012; Fortin et al., 2005; Lefèvre et al., 2014; Le Reste et al., 2013).

The present thesis, which aims to explore if physical and mental condition co-occurrence is associated with suicidal behaviours, uses the term multimorbidity to refer to multiple conditions where no specific condition is used as an index one. Henceforth, multimorbidity refers to having at least one physical health plus at least one mental health condition (however, to avoid repetition of this term, periphrastic terms will also be used (i.e. co-occurrence, co-existence)).

In the field of suicide research there is no agreed-upon terminology used to describe all aspects of the suicidal process and there is an ongoing debate about what constitutes self-harm, suicide attempts and non-suicidal self-injury (Kapur et al. 2013; Silverman & De Leo 2016). In this thesis, suicidal

thoughts, defined as thoughts of killing one's self and suicide attempts, defined as attempts to kill one's self, are assessed and analysed.

Within suicide research, as outlined in Chapter 1, the term suicidality is used routinely to summarise all suicide-related thoughts and behaviours. Based on that and in order to avoid the repetitive use of any suicide-related behaviour, suicidality is used in the current thesis. It is important to note that given the statistical rarity of suicide (and related behaviours), some authors have also operationalized suicidality as being comprised of the combination of a number of suicide-related items, i.e. suicidal ideation, suicide attempts, self-harm, deaths by suicide. In the current thesis, the variable of suicidality is also computed for each empirical study and combines the items of both suicidal thoughts and suicide attempts.

4.3 Study design

The empirical studies included in this PhD thesis employed both cross-sectional (Chapters 5, 6, first part of Chapter 7) and prospective study designs (second part of Chapter 7), to assess the role of physical and mental health multimorbidity in the risk of suicidal behaviours. The key hypothesis for the cross-sectional design studies was that people with physical/mental multimorbidity, within the past year, will exhibit higher risk of past year suicidal thoughts and behaviours, compared to those with neither physical nor mental conditions. In terms of the prospective study design, the association of physical/mental multimorbidity and suicidality will be investigated across four follow-up waves. More specifically, current multimorbidity conditions of each wave will be paired with subsequent suicidality items (suicidal thoughts and suicide attempts) of the following wave. This methodology will demonstrate if physical/mental multimorbidity can predict suicidality.

In both study designs (cross-sectional and prospective), physical and mental health conditions, and measures of suicidal thoughts and suicide attempts are

assessed. The following subsections summarise the sample selections and statistical analysis employed in all empirical studies.

4.3.1 Sample selection

In order to investigate the relationship between mental and physical conditions, and suicidality (suicidal thoughts and suicide attempts) in the general population, the sample data in the current thesis were drawn from two national mental health surveys of United Kingdom (UK) and one cohort study carried out in Scotland. Specifically, the secondary analysis of datasets explored in the current thesis were: the National Psychiatric Morbidity Survey of Great Britain 2000 (NPMS; Office for National Statistics., 2003), the Adult Psychiatric Morbidity Survey 2007 (APMS; McManus, Meltzer, Brugha, Bebbington, & Jenkins, 2009) and the West of Scotland Twenty-07 study (Twenty-07; Benzeval et al., 2009).

In terms of the surveys, NPMS and APMS are the second and third in a series of surveys conducted in English households, aiming to describe the prevalence of both treated and untreated mental illness, based on self-reported information (McManus et al. 2016). Using the same methodology to assess mental health conditions across all national surveys from 1993 until 2014, this English study is one of the most consistent series of surveys globally (McManus et al., 2016). With respect to the Scottish cohort study, Twenty-07 was established in 1986 in order to investigate health inequalities among Scottish residents, based on their socioeconomic characteristics. Including three cohort groups (those in cohort 1 were born in 1932, those in cohort 2 were born in 1952 and the final cohort comprised residents born in 1972) it is a very comprehensive dataset in which to investigate health changes across the lifespan (Benzeval et al., 2009).

While the details of the data collection process for each survey are presented separately in each empirical chapter, it is worth noting that stratification sampling was employed across all datasets. All data were weighted in order to be representative of each study's national population.

4.3.2 Measures

The outcomes of interest in all of the empirical studies were suicidal thoughts, suicide attempts and suicidality (combination of suicidal thoughts and suicide attempts). All of the suicide-related items were self-reported and based on single questions with yes/no replies. While the timing of both suicidal thoughts and attempts were assessed (lifetime and past year time periods), only the responses related to the past year were selected for all of our analysis. Choosing past year periods for both suicidal thoughts and attempts was based on the timing of assessment for the physical and mental health conditions given in the datasets explored. Considering that the mental and physical conditions were seen as current or present during the surveys' interviews (details on the assessment periods included in each study-chapter), only past year suicidal thoughts and suicide attempts could be taken into account, in order to present the effect of current multimorbidity conditions on suicidality.

As the aim of the current research was to investigate the effect of physical/mental multimorbidity in the risk of suicidal behaviours, both somatic and mental health conditions were assessed in all datasets. While the response for having or not having any physical health issue was based on (i) show cards or (ii) single questions for specific physical conditions (yes/no replies), mental disorders were assessed through clinical diagnostic instruments. The type of physical and mental health conditions investigated in every dataset are presented in the respective empirical chapter.

In terms of covariates known to have an effect on suicidal behaviours and suicide risk (as described in chapter 1), sociodemographic and clinical information were collected and analysed in all of the empirical studies. With regard to sociodemographic information, gender, age, living conditions/marital status, education level and variables related to socioeconomic status, like employment and/or social class by occupation were collected in all datasets and used in our analysis. In each study, the sociodemographic information was dichotomised in advance of the analysis. In addition, psychiatric medication was also explored in both the UK surveys

and the Scottish cohort study. The assessment of clinical covariates and sociodemographic variables is described in each empirical chapter. Negative or stressful life events, which are found to have an association with suicidal behaviours (Foster 2011; Zhang et al. 2015), were explored in two out of the three datasets, namely the NPMS 2000 and the APMS 2007. The presence of any negative event during the past year was computed as a binary variable in both UK datasets and used in the analysis.

4.3.3 Statistical analysis

Based on their physical and mental health conditions, participants in each dataset were grouped into mutually exclusive health groups. Specifically, participants were classified as having: a) one or more physical health condition, b) one or more mental health condition, c) at least one physical health plus one mental health condition, and d) neither mental nor physical health condition. The suicide-related variables were: suicidal thoughts, suicide attempts and suicidality (combination of suicidal thoughts and attempts).

For the cross-sectional analyses of the first two studies (NPMS 2000; APMS 2007) multinomial logistic regression models were run in order to investigate if physical and mental disorder multimorbidity increases the risk of suicidal thoughts, suicide attempts, and suicidality, compared to having neither of conditions. Binary logistic regression was performed in order to explore if the physical by mental health conditions interaction was associated with increased risk of suicidal behaviours beyond the independent effects of having either condition alone.

For the third cross-sectional analysis, using data from the Twenty-07 study, logistic regressions were conducted to explore if those with physical/mental multimorbidity have an elevated risk of suicidal thoughts and suicide attempts, compared to those who do not have such multimorbidity. The physical health by mental health condition interaction effect was also tested using binary regression.

For the fourth empirical study of this thesis, which involved a prospective analysis, the twenty-07 dataset was once again explored. In order to determine whether physical/mental health multimorbidity increases the risk of suicidal thoughts and suicide attempts longitudinally, a generalised estimating equation model (GEE) was performed. Estimated marginal means were further used in order to test whether the effect of physical/mental multimorbidity was stronger than either of health conditions alone.

The sociodemographic and clinical variables were used as covariates in the regression models and in the generalised estimating equation analyses. For all four empirical studies odds ratio (OR) and 95% CIs are reported, and the significance level was set at $p < 0.05$. The Statistical Package for Social Sciences SPSS version 24 was used for all analyses (SPSS Inc., Chicago, IL, USA).

4.4 Ethical issues

The empirical studies contained in the current PhD thesis included secondary analyses of cross-sectional and longitudinal data. As each survey and cohort study received ethical clearance from the appropriate committees, no further ethical approval was required for our secondary analysis. The ethical clearance for each study is as follows:

a) National Psychiatric Morbidity Survey 2000 (NPMS): Ethical approval was taken from the London Multi-Centre Research Ethics Committee and the 149 local research ethics committees (LRECs) which were responsible for the addresses selected in the sampling process.
b) Adult Psychiatric Morbidity Survey 2007 (APMS): Ethical clearance was obtained from the Royal Free Hospital and Medical School Research Ethics Committee (Ethical approval reference number: 06/Q0501/71).
c) West of Scotland Twenty-07 study: Ethical approvals were given from the Ethical subcommittee of the West of Scotland Medical Committee and the Ethics Committee for Non-Clinical Research Involving Human Subjects of University of Glasgow.

4.5 Summary

To test the hypothesis that people with physical/mental multimorbidity may have higher risk of suicidal thoughts and suicide attempts, compared to those with neither physical nor mental conditions, a series of empirical studies on population data were analysed in the current PhD thesis. This chapter presented the terminology, the overall study design and analysis strategy followed in each of the four studies. The next section describes the first empirical study, on the role of physical/mental multimorbidity in suicidality among participants of the National Psychiatric Morbidity Survey of Great Britain, conducted in 2000.

Chapter 5. The role of physical and mental multimorbidity in the risk of suicidal behaviours: analysis of the Psychiatric Morbidity Survey 2000 of Great Britain

Background

Previous research has focused on the separate roles of mental illness and physical conditions in the aetiology and course of suicide risk, with relatively few studies investigating the importance of the co-occurrence of physical and psychiatric disorders (multimorbidity). We aimed to investigate whether suicide risk might be influenced by physical and mental health multimorbidity.

Methods

Data from the National Psychiatric Morbidity Survey of Great Britain were analysed. Participants who responded to the suicidality and physical health conditions and mental health disorder questions were grouped into four distinct categories based on their health conditions: a) common mental disorders (CMD) only, b) physical health conditions only, c) CMD/physical health multimorbidity and d) a control group with neither physical nor CMDs. Multinomial and binary logistic regression analyses were conducted and odds ratios (OR) and 95% CIs are presented.

Results

In the fully adjusted analyses, multimorbidity had a significant association with suicidal thoughts and attempts (suicidal thoughts: OR = 6.30, 95% CI: 4.45-8.92, p< 0.001; suicide attempts: OR = 4.02, 95% CI: 1.67-9.67, p= 0.002). While having CMDs only increased the risk of suicidality, analysis did not confirm previous findings on the effect of physical illness on suicidality, as there was no evidence of an association between the latter and either suicidal thoughts or suicide attempts (suicidal thoughts: OR = 0.93, 95% CI: 0.62-1.41, p=0.75; suicide attempts: OR = 0.36, 95% CI: 0.07-1.72, p=0.20). Furthermore, the interaction between physical health and CMD conditions

was not associated with increased risk of either suicidal thoughts (b=-0.04, SE= 0.24, OR= 0.95, p=0.86) or suicide attempts (b=-0.83, SE= 0.74, OR= 0.43, p=0.26), beyond the independent effect of common mental disorders.

Limitations

Secondary analysis of an existing dataset which was not specifically designed to address this research question.

Conclusions

Although our findings indicate that physical/mental multimorbidity is associated with suicidal behaviours, it does not appear to confer additional risk beyond the independent effects of common mental disorders.

5.1 Introduction

In Chapter 3 the research evidence on the role of multimorbidity in suicide risk was discussed extensively. The existing evidence suggests that, those with multimorbidity of physical or mental health conditions are at an increased risk of suicidal behaviours and suicide, relative to those who are not multimorbid (Ahmedani et al., 2017; Angst et al., 2002; Bischof et al., 2015; Calabrese et al., 2011; Juurlink et al., 2004; Nock et al., 2017; Qin et al., 2013; Webb et al., 2012a, 2012b; Wunderlich et al., 1998). However, although the co-occurrence of physical and mental conditions in relation to suicidality has been investigated in a few previous studies, the majority of literature has focused on the effect of a primary psychiatric condition and additional mental disorders, as summarised in chapters 2 and 3. Very few studies of the effect of physical/mental multimorbidity on suicidality have been largely conducted and these have tended to be restricted to primary care datasets (Qin et al., 2014), with national mental health surveys largely under-utilised for this purpose (Kavalidou, Smith & O'Connor 2017). Considering that population-based surveys include participants who may not be in contact with health care services (McManus et al., 2016), the use of survey data seems to be an important source of data for research in this area.

5.2 The role of large-scale surveys to estimate the prevalence of mental illness and suicidal ideation and behaviour

Considering the importance of the epidemiological data emerging from mental health surveys, the current section describes the prevalence of suicidal ideation behaviour and its association with chronic conditions, as investigated in worldwide health surveys.

As mental illness is one of the leading causes of death worldwide (Whiteford et al. 2013), national population surveys serve an important function to investigate the health-related behaviours of those who may not be referred to care (Jenkins 2003). Hence, the evidence on which mental health policies

are predicated is often based on a variety of mental health surveys that have been conducted worldwide (Jenkins 2003; McManus et al. 2016).

To estimate and monitor the prevalence of psychiatric disorders and suicidal behaviours, the World Health Organisation (WHO) established standard clinical severity measures based on the International Classification of Diseases (ICD) and the Diagnostic and Statistical Manual of Mental Disorders (DSM), (Kessler et al. 2006). From such monitoring, we know that the global burden of mental illness accounts for 32·4% of years lived with disability (YLDs; Vigo et al., 2016). There is also evidence from WHO mental health surveys that depression is associated with suicidal ideation in developed countries, while in developing countries anxiety and impulse-control disorders are more common in the context of suicide attempts (Nock et al., 2009). Moreover, a dose-response association has been found regarding mental health comorbidities for all countries included in the World Mental Health surveys, with a greater number of conditions predicting increased risk of suicidal behaviours.

In light of the research evidence indicating the poor physical health and excess mortality among those with somatic illness and mental conditions, the WHO and other mental health surveys include the assessment of chronic physical conditions (De Hert et al. 2011; Kessler et al. 2006; McManus et al. 2016; Slade et al. 2009; Vigo, Thornicroft & Atun 2016). As a result, there is considerable evidence from cross-sectional analyses of psychiatric morbidity surveys that mood and substance abuse disorders are significantly associated with chronic physical health conditions such as arthritis, chronic obstructive pulmonary disease (COPD), and stroke; this evidence also highlights the association between increasing numbers of co-occurring mental disorders and elevated risk of chronic physical conditions (Kessler et al. 2006; Vigo, Thornicroft & Atun 2016). Further evidence of comorbidity was also found in a mental wellbeing household survey of 8,841 Australian residents aged between 16 and 85 years: the highest rates of comorbidity were observed between anxiety and affective disorders (58.5% of those with affective disorders had a comorbid anxiety disorder) and 28% of participants who had a

chronic physical condition also had a mental disorder (Teesson, Slade & Mills 2009).

Household surveys have also been used to estimate the prevalence of suicidality in the general population among those not attending health care services (ABS, 2008) and for the prediction of subsequent suicidal behaviours (Nock et al., 2009). In an Australian survey with an estimated population count of 16 million persons aged 16-85 years, 368,100 people reported suicidal thoughts in the past 12 months and almost three-quarters (72%) of them met the criteria for a mental disorder in the past 12 months; affective disorder was associated with a greater risk of suicidality (17.4%) than substance use disorder (10.9%) and anxiety disorder (9.1%) (ABS, 2008). In another US study, a national representative household survey of 9,282 adults, reported that depression predicted those who will develop suicidal thoughts, but will not engage in suicidal behaviours; however, post-traumatic stress disorder, conduct disorder or substance use disorders predicted the suicide ideators who will further plan or attempt suicide (Nock et al., 2010).

Since 1993 the monitoring of mental illness and treatment access in England has been provided through the Psychiatric Morbidity Surveys (McManus et al. 2016). The four surveys conducted to date (1993, 2000, 2007, 2014[1]) have recorded the prevalence of both treated and untreated mental health and physical health conditions, with the last three focusing on the prevalence of suicidal ideation and suicide attempts in the general population. As this series of surveys has adopted the same methodological approach and screening assessments throughout, it is considered the most consistent programme in the world (McManus et al. 2016).

In each UK psychiatric survey around one adult in six has a common mental disorder (CMD), with the highest rates reported among women (1 woman in 5 have a CMD (20.7%)) compared with about 1 man in 8 (13.2%). In the most recent report, the Adult Psychiatric Morbidity Survey 2014, additional focus was given to the comorbidity of chronic physical health conditions (namely

[1] The data of the Adult Psychiatric Morbidity Survey conducted in 2014 were not publicly available during the writing of this PhD thesis.

asthma, cancer, diabetes, epilepsy, and high blood pressure) and mental illness, with the results indicating that those with a physical health condition had at least one comorbid mental disorder (McManus et al., 2016). The prevalence of suicidal behaviours appears to be increasing. For example, the lifetime prevalence of self-harm (2.4% in 2000, 3.8% in 2007, to 6.4% in 2014) and past year suicide thoughts (3.8% in 2000, 5.4% in 2014) has changed considerably in recent years. While age did not significantly predict the prevalence of suicidal attempts in men and women, the latter group had a higher rate (8.0% of women compared with 5.4% of men). Overall, in the most recent APMS conducted in 2014, there was an increase in self-harming behaviours in young women and increased risk of suicidal thoughts for those who were unemployed, economically inactive, or receiving out-of-work disability, and among men aged between 55 to 64 (McManus et al., 2016).

5.2.1 National Psychiatric Morbidity Survey 2000

As noted above, the national psychiatric morbidity surveys have been conducted since 1993 and repeated every seven years in the UK. The second of this series, the National Psychiatric Morbidity Survey (NPMS) was conducted in 2000, and it aimed to explore the prevalence of mental disorders among adults living in private households in Great Britain (Singleton et al. 2001). The age range of the survey's participants was 16 to 74 years of age, which was different from the first survey in 1993 that focused on those aged between 16 and 64 years old. The sampling process was based on the postcode address file (PAF) and stratification was based on socio-economic status within NHS region. The regions covered were England, Scotland (including Highlands and Islands region) and Wales.

A two-stage process of assessing mental illness was adopted. This included the use of screening instruments and structural assessments, through face-to-face interviews and self-completion methodology. Overall, the mental health conditions investigated were neurotic disorders, substance misuse and dependency. A sub-sample from the first stage of completion were asked to participate in a second interview stage, which focused on the assessment of psychosis and personality disorders. Beside the prevalence of psychiatric

disorders, the survey aimed to investigate the circumstances associated with mental illness, like health care service use, employment, accommodation, income and debt, and lifetime stressful events. Items assessing suicidal thoughts and attempts were included in the 2000 for all participants for the first time, whereas in the original survey in 1993, suicidal behaviours were only assessed among those responding positively to depressive symptoms. As a result, the 2000 NPMS was the first national survey of suicidality in the general population of Great Britain (Singleton et al. 2001).

5.2.2 Prevalence of mental illness and suicidal behaviours among NPMS 2000 participants

The neurotic disorders assessed in NPMS were mixed anxiety and depression, generalised anxiety, depressive episode, obsessive-compulsive disorder, phobias and panic. While one in six people reported having one neurotic disorder in the week prior to the interviews, the most common disorder was mixed anxiety and depression (88 cases per 1,000), leaving generalised anxiety as second most prevalent (44 people per 1, 000). The diagnosis of a probable psychotic disorder was prevalent in 5 adults per 1,000. While a quarter of NPMS participants were classified as being at a hazardous level of drinking the year prior the interviews, alcohol dependence was quite prevalent (74 people per 1,000) and drug dependency was found evident in 37 per 1,000 participants (Singleton et al., 2001). In terms of the sociodemographic characteristics of those with a neurotic disorder, 59% were women; the most prevalent age-group was the 35 to 54 years old age group and those who were divorced or separated, a single parent/one person family unit (Singleton et al., 2001) were also over-represented. Physical health complaints were also quite prevalent, with half of those with a neurotic disorder reporting one physical health issue and 67% of those with psychosis also reporting a longstanding physical health condition.

With respect to suicidal behaviours, 14.9% of the NPMS participants reported lifetime suicidal thoughts and 3.9% past year thoughts. Past year suicide attempts were reported by 0.5% of participants, while 4.4% of the entire sample mentioned lifetime attempts (O'Brien et al. 2002). Self-harming

behaviours without suicidal intent were reported by 2% of respondents. Self-harm was more common among young participants than older participants (present in 5% of the youngest age groups and in only 0.2% of those aged 65-74 years. Overall, being a woman, unemployed, divorced and being a lone parent were each associated with suicidal thoughts and attempts.

In terms of the psychiatric disorders correlated with the suicide-related outcomes psychosis and alcohol dependence were consistently associated with all outcomes. While having an OCD diagnosis and experiencing a depressive episode were highly prevalent among those with suicidal thoughts (62% and 52% respectively), self-harm was more prevalent among those with panic and phobic symptoms (16% and 13%, respectively). The effect of being homeless, sexually abused, going through a financial crisis, experiencing a severe problem with a close friend and having a severe lack of social support, were associated with suicidal thoughts, suicide attempts and self-harming behaviours. Those who reported three or more stressful events were more likely to have attempted suicide, while a quarter of those with a high number of events reported suicidal thoughts (O'Brien et al., 2002).

5.3 Aim of current study

International studies have systematically reported high suicide mortality ratios based on different psychiatric illnesses, with a history of suicide attempts being a key risk factor (Harris & Barraclough, 1997; Hawton et al., 2013; Mann et al., 2005; O'Connor & Nock, 2014; WHO, 2014b). At the same time, physical health conditions have also been shown to be associated with an increased risk of suicidal behaviour, even in the absence of a psychiatric condition (Pompili et al., 2016; Scott et al., 2010).

Despite the growing evidence that both mental and physical health disorders contribute to suicide risk, very few studies have investigated the extent to which their co-occurrence (multimorbidity) is associated with suicide risk (Kavalidou et al., 2017; Qin et al., 2014; Singhal, Ross, Seminog, Hawton, & Goldacre, 2014). Most of the extant research has focused on comorbidity and suicide risk, with comorbidity defined as a further diagnosis which is

secondary to an index condition (Blasco-Fontecilla et al., 2016; Feinstein, 1970). To address this gap in knowledge, we aimed to investigate the extent to which suicidality varies as a function of multimorbidity defined as having at least one physical health plus at least one mental health condition (with no index condition specified). We hypothesized that individuals with physical/mental health multimorbidity would have a higher risk of suicidal thoughts and suicide attempts compared to individuals with neither physical nor mental health conditions.

5.4 Materials and methods

5.4.1 Settings and participants

Secondary analysis of the National Psychiatric Morbidity Survey of Great Britain (NPMS) 2000 was performed. NPMS 2000 is the second in a series of surveys conducted in private households for adults of 16 to 74 years of age. The main aim of this survey was to report the prevalence of mental disorders, their association with life events and social disadvantage, and the health care use of those with a mental illness. A stratified multi-stage probability sample was collected and data were weighted by age, sex and region to be representative of the national population (Singleton et al., 2002). A total of 8,580 participants were interviewed (see technical report by Singleton et al., 2002 for full details).

5.4.2 Measures

5.4.2.1 Mental health and physical health conditions

The revised version of the Clinical Interview Schedule (CIS-R) was used to assess the presence of neurotic disorders in the week prior to the interviews. Individuals were assessed to determine the presence of any of the following disorders: generalised anxiety disorder (GAD), mixed anxiety and depression (MAD), panic disorder, phobia, obsessive-compulsive disorder (OCD) and depressive episodes. These were classified as common mental disorders (CMD). In regard to physical health complaints/conditions, participants were

asked if they had any current longstanding health condition, with their replies coded and keyed in by the interviewers. Participants' physical health complaints and CMDs are presented in Table 1.

5.4.2.2 Suicidal thoughts and behaviours

The CIS-R was also used to assess participants' suicidal thoughts, suicide attempts and self-harming behaviours, with a Yes/No response (O'Brien et al., 2002). The suicidality related-questions asked by NPMS 2000 interviewers were: "Have you ever thought of taking your life, even though you would not actually do it?"; "Have you ever made an attempt to take your life, by taking an overdose of tablets or in some other way?" and "Have you deliberately harmed yourself in any way but not with the intention of killing yourself?". Those who replied yes to the suicidal thoughts and suicide attempts questions, were further asked about the timing of behaviours, specifically if they occurred during past week, past year or lifetime. Self-harming items were not followed up with a question regarding time-periods, hence considered as lifetime. As the current study is focusing on the presence of CMDs and physical complaints *at the time of the interviews*, only past year suicidal thoughts and suicide attempts were considered for the current analysis. Furthermore, the suicidal thoughts and attempts items were combined and a derived variable of "past year suicidality" (Yes/No) was computed and used in the present study.

To determine whether the risk of suicidal behaviours varies as a function of physical/mental health multimorbidity, NPMS participants were divided into four mutually exclusive health groups and were analysed in relation to the three outcomes of interest, i.e., suicidal thoughts, suicide attempts and suicidality. Specifically, the health groupings were: a) neither CMD nor physical complaints, b) CMD only, c) physical conditions only, and d) multimorbidity. As in the literature, multimorbidity refers to having two or more co-occurring health conditions (Valderas et al. 2009), in the present study participants with one or more CMD plus one or more physical health condition, were identified as having physical/mental multimorbidity. The numbers of NPMS participants in each health group are presented in Figure 1.

5.4.2.3 Clinical covariates

Stressful life events and substance abuse and dependency were further assessed in NPMS 2000 and analysed in the current study. A set of cards listing 18 life events were shown to participants, who were asked to reply if they had experienced any of them at any point in their life and during the past 6 months. Overall, the events were around serious illness, death, separation, serious problems with close friend/relative, financial crisis, work-related issues, violence, bullying and homelessness. Considering that all health issues and suicidality variables used in our study were identified as current and within the past year, only the life events occurring the past 6 months were analysed. The dichotomous variable "stressful life events within the past 6 months" (Yes/No) was further computed and used in the analysis as a covariate.

Past year hazardous drinking was assessed with the Alcohol Use Disorders Identification Test (AUDIT), which covers a scoring range of 0-40. For those scoring 10 or more and identified with hazardous alcohol use, the Severity of Alcohol Dependence Questionnaire (SAD-Q) referring to a past 6 month period, was also administered. AUDIT, as an indicator of hazardous drinking, and SAD-Q, used for assessing the prevalence of alcohol dependence, were combined in NPMS and provided the following hazardous drinking groups: a) no hazardous drinking, b) hazardous drinking but no dependency, and c) alcohol dependency. This derived variable was further computed as an "alcohol dependency" binary item (Yes/No) and used in our analysis. Through a computer-assisted questionnaire completion, NPMS participants were asked if they have used any type of drug during their lifetime and in the past year. For drugs like cannabis, opiates, amphetamines, cocaine, crack, ecstasy, glue and tranquillisers, further questions were asked focusing on the past month. Based on the frequency of use and issues related to not being able to cut-down, a "drug dependency" indication was given as a binary variable (Yes/No) in NPMS and was further used in the current study.

In terms of service use and treatments followed, NPMS participants were asked about any medication taken by mouth or injection, including among others, central nervous system-related medications, analgesics and antiepileptics. Specifically, for mental illness medication taken by mouth, participants were asked about the following drug types: hypnotic, anxiolytic, barbiturate, antipsychotic, antimanic, tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), other antidepressants and central nervous system (CNS) medication. Based on the specific psychiatric medication list of drugs taken by mouth, the "any psychiatric medication" (Yes/No) variable was computed and use in the current study.

The sociodemographic characteristics of NPMS participants, namely age, sex, living conditions, ethnic origin, employment status, any higher education (having a university degree), social class (via occupation), were further used and presented in Table 2 for each health group.

5.4.3 Statistical analysis

Descriptive statistics, Chi squares and one way ANOVAs were used to investigate the association between sociodemographic characteristics and health group and to explore any association with past year items on suicidality (Health groups: neither CMD nor physical conditions, CMD only, physical conditions only, and multimorbidity). In order to investigate the association between physical/mental multimorbidity and past year suicidal thoughts, attempts and suicidality, multinomial logistic regression analyses were run. Odds ratios (OR) and 95% CIs are reported. As sociodemographic, clinical and stressful life factors have an effect on suicide-related outcomes, a series of multinomial logistic regression models were conducted, adjusting for: a) sociodemographic characteristics only and; b) sociodemographic characteristics, stressful life events, hazardous drinking, drug dependency and any psychiatric medication. To test if the effect of physical/CMD multimorbidity increases the risk of suicidal behaviours more than the independent effects of either conditions, binary logistic regression analyses including the conditions interaction effect were performed. The significance

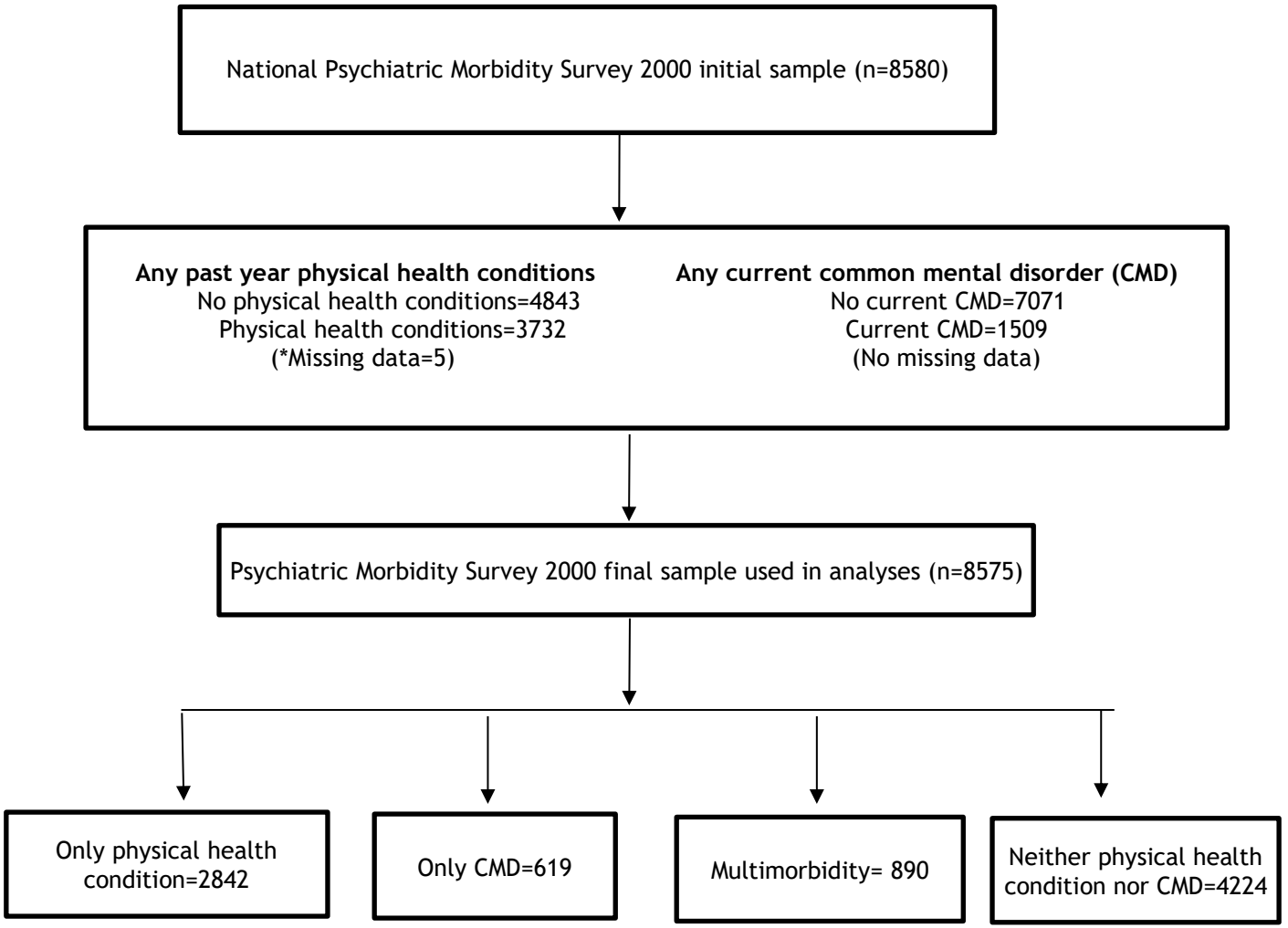
level was set at $p < 0.05$ and the statistical analysis was performed with the Statistical Package for Social Sciences SPSS version 22 (SPSS Inc., Chicago, IL, USA).

Table 5. 1 Proportion with physical health conditions and common mental disorders among the National Psychiatric Morbidity Survey (NPMS) 2000 respondents

Physical health conditions				Common mental disorders	
Arthritis	864 (10.1%)	Large & small intestine	201 (2.3%)	Any phobia	176 (2.1%)
Asthma	495 (5.8%)	Migraine/headaches	119 (1.4%)	Depressive episode	255 (3%)
Back & neck	656 (7.7%)	Muscle-skeletal	1762 (20.5%)	Generalised anxiety disorder	431 (5%)
Blood pressure	420 (4.9%)	Neoplasms	121 (1.4%)	Mixed anxiety/depressive disorder	769 (9%)
Blood vessel	109 (1.3%)	Nervous system	411 (4.8%)	Panic disorder	69 (0.8%)
Blood disorders	45 (0.5%)	Respiratory system	674 (7.9%)	Obsessive compulsive disorder	114 (1.3%)
Bronchitis/emphysema	59 (0.7%)	Reproductive system	119 1.4%)		
Deafness/poor hearing	82 (1%)	Skin complaints	129 (1.5%)		
Diabetes	239 (2.8%)	Stomach & ulcer	169 (2%)		
Digestive system	451 (5.3%)	Stroke & heart	463 (5.4%)		
Endocrine disorders	447 (5.2%)	Other nervous system	297 (3.5%)		
Ear complaints	167 (1.9%)	Other respiratory	93 (1.1%)		
Eye complaints	130 (1.5%)	Other digestive	111 (1.3%)		
Genito-urinary system	216 (2.5%)	Other ear	88 (1%)		
Hay fever	65 (0.8%)	Other bone/joint/muscle	434 (5.1%)		
Heart & circulating system	916 (10.7%)	Other endocrine/metabolic	221 (2.6%)		
Infectious & paracitic disorder	29 (0.3%)	UT/bladder kidney	102 (1.2%)		

*The number of conditions may not add up to that total number of the PMS sample (n=8580), as participants had one or more of the indexed conditions.

Figure 5. 1 Flowchart of the National Psychiatric Morbidity Survey 2000 sample



*missing data include: No answer.

Table 5. 2 Sociodemographic characteristics of NPMS participants with multimorbidity, CMD only, physical health complaints only and neither physical nor CMD (n=8575)

	Multimorbidity	**Common mental disorders only (CMD)**	**Physical health problems only**	**Neither physical nor CMD**
Characteristics*	**n=890**	**n=619**	**n=2842**	**n=4224**
Age *M (SD)*	47.76 (14.1)	37.99 (12.3)	51.73 (15.3)	41.67 (14.9)
Sex *n (%)*				
Male	327 (36.7)	222 (35.9)	1293 (45.5)	2007 (47.5)
Female	563 (63.3)	397 (64.1)	1549 (54.5)	2217 (52.5)
Living conditions *n (%)*				
Living with someone	456 (51.2)	319 (51.5)	1785 (62.8)	2532 (59.9)
Not living with someone	434 (48.8)	300 (48.5)	1057 (37.2)	1692 (40.1)
Ethnic groups *n (%)*				
White	831 (94.2)	564 (92)	2718 (96.2)	3915 (93.5)
Non-white	51 (5.8)	49 (8)	107 (3.8)	274 (6.5)
Employment status n *(%)*				
Currently employed	352 (39.9)	423 (69)	1438 (50.9)	3054 (72.9)
Not currently employed	530 (60.1)	190 (31)	1387 (49.1)	1137 (27.1)
Any higher qualifications n *(%)*				
Yes	518 (58.7)	484 (79)	1814 (64.2)	3255 (77.7)
No	364 (41.3)	129 (21)	1012 (35.8)	935 (22.3)
Social class n (%)				
Professional	26 (3)	23 (3.9)	131 (4.7)	238 (5.9)
Intermediate occupations	201 (23.6)	203 (34.1)	771 (27.9)	1262 (31.1)
Skilled occupations (non-manual)	199 (23.3)	155 (26)	681 (24.7)	986 (24.4)
Skilled occupation (manual)	169 (19.8)	86 (14.4)	525 (19)	723 (17.9)
Partly-skilled	164 (19.2)	98 (16.4)	477 (17.3)	626 (15.5)
Unskilled occupations	93 (10.9)	31 (5.2)	172 (6.2)	194 (4.8)
Armed forces	1 (0.1)	-	5 (0.2)	7 (0.2)

Past year suicidality n (%)				
Yes	135 (15.2)	106 (17.1)	39 (1.4)	71 (1.7)
No	752 (84.8)	513 (82.9)	2800 (98.6)	4150 (98.3)
Past year suicidal thoughts n (%)				
Yes	134 (15.1)	106 (17.1)	39 (1.4)	70 (1.7)
No	753 (84.9)	513 (82.9)	2801 (98.6)	4151 (98.3)
Past year suicide attempts n (%)				
Yes	22 (2.5)	15 (2.4)	3 (0.1)	10 (0.2)
No	865 (97.5)	604 (97.6)	2836 (99.9)	4211 (99.8)

*percent (%) is based on the omission of missing values.

5.5 Results

5.5.1 Sociodemographic characteristics of NPMS participants reporting suicidality

Out of the total NPMS sample (n=8575), 10.4% were classified as being multimorbid, with the majority being female (63.3%), of a White ethnic origin (94.2%) and not currently employed (60.1%; Table 2). The remaining health groups similarly had more women than men (CMD: 64.1%; physical only: 54.5%; and neither physical nor mental health: 52.5%) and of White ethnic origin (CMD: 92%; physical health only: 96.2%; and, neither physical nor mental health: 93.5%; Table 2). In contrast with multimorbidity, the majority of the rest of the health groups were currently employed (CMD: 69%; physical health only: 50.9%; and, neither physical nor mental health: 72.9%). Similar to the other health groups, more than half of those with multimorbidity had a high level of education (58.7%) and were living with someone (51.2%; Table 2). Past year suicidal behaviours differed between the health groups (suicidal thoughts: x^2= 662.118, df=3, p< 0.001; suicide attempts: x^2 = 111.005, df=3, p< 0.001). Specifically, 15.1% of the multimorbidity group had past year suicidal thoughts, 17.1% of the CMD only group and 1.4% of those with physical health conditions only group. Further to suicide attempts, 2.5% of the multimorbidity group attempted suicide in the previous year, 2.4% of the CMD group and 0.1% of the physical health conditions group.

Based on those reporting past year suicidality, a number of chi square analyses were run in order to investigate if there were any differences in the associations between sociodemographic characteristics and each health group. While sex, ethnicity and living conditions did not differ between groups, employment status (x^2 = 36.185, df=3, p< 0.001), education level (x^2 = 32.807, df=3, p< 0.001), and social class (x^2 = 30.251, df=15, p= 0.001) differentiated the groups. More specifically, as the positive adjusted residual of 5.0 indicated (adjusted for sample size), most of those with multimorbidity were not currently employed (multimorbidity: 51.8%, CMD only: 27.6%, physical only: 11.2%, neither physical nor CMD:9.4%). In respect of education, a positive adjusted residual of 4.6 showed that most of the multimorbidity participants did not have any high qualification (multimorbidity: 56%, CMD

only: 32.1%, physical only: 3,7%, neither physical nor CMD: 8.3%). In terms of social class, a positive adjusted residual of 2.7 indicated that most people with multimorbidities were unskilled (60%). In the physical only and control groups, the positive adjusted residuals indicated that these groups had more participants from skilled non-manual occupations (physical only: 18.1%, neither physical nor CMD: 27.7%), with 37% of those with CMD only, having an intermediate occupation status. Age additionally differentiated the health groups [F(3)=7.566, p< 0.001, multimorbidity M=42.01 (SD:14.29); CMD M= 35.46 (SD: 12.10); physical only M=43.15 (SD: 15.31), neither physical nor CMD M=35.46 (SD: 12.51).

5.5.2 Unadjusted multinomial logistic regression for the relationship between physical/mental multimorbidity and past year suicidal thoughts and behaviour

To investigate the relationship between the different health groups and their association with past year suicide related outcomes, three unadjusted multinomial regression analyses were performed (Table 3). The results indicated that those with physical/mental multimorbidity had significantly increased odd ratios of past year suicidal thoughts and behaviour, compared to those with neither conditions (reference group). Analyses showed that those with CMDs were also more likely to report suicidal thoughts and behaviours, compared to the reference group (suicidal thoughts: OR= 12.25; 95% CI, 8.93-16.798, *p<0.001*; suicide attempts: (OR= 10.45; 95% CI, 4.67-23.38, *p<0.001*). There was no association between presence of any physical health condition and risk of either suicidal thoughts or attempts (suicidal thoughts: OR= 0.826; 95% CI, 0.55-1.22, *p<0.341*; suicide attempts: OR= 0.44; 95% CI, 0.12-1.62, *p<0.445*).

5.5.3 Adjusted multinomial logistic regression analyses for sociodemographic characteristics

After adjusting for sex, age, living conditions, ethnic group, any education qualifications, employment status, and social class by occupation, the presence of multimorbidity and CMDs were associated with all indices of

suicidality, while physical conditions were not found to have any association with past year suicidal thoughts and attempts (OR= 0.99; 95% CI, 0.66-1.49, *p*=0.976; Table 4).

5.5.4 Fully adjusted regression analyses including all covariates

After the adjustment for sociodemographics, stressful life events, hazardous drinking, drug dependency and any psychiatric medication, multimorbidity was significantly associated with both suicidal thoughts (OR= 6.30, 95% CI, 4.45-8.92, *p<0.001*) and suicide attempts (OR= 4.02, 95% CI, 1.67-9.67, *p*=0.002). While having CMD only was additionally associated with suicidal thoughts (OR= 7.39, 95% CI, 5.21-10.49, *p<0.001)* and suicide attempts (OR= 3.49, 95% CI, 1.38-8.77, *p=0.008),* in the same fully adjusted model physical health conditions did not have any association with either suicidality, suicidal ideation or suicide attempts (Table 5).

5.5.5 Binary logistic regression for the interaction effect of physical and mental illness in suicidal behaviours

In order to test if having physical and CMD multimorbidity increases the risk of suicidal behaviour more than each condition does alone, two logistic regression analyses for suicidal thoughts and suicide attempts, including the interaction effect of physical and CMD conditions, were performed. Although having CMD-only increased the risk of suicidal thoughts (*b*=-2.52, SE= 0.12, OR= 0.08, p<0.001) and suicide attempts (*b*=-2.64, SE= 0.32, OR= 0.07, p<0.001), having both physical and CMD conditions did not increase the risk of either suicidal thoughts (*b*=-0.04, SE= 0.24, OR= 0.95, p=0.86) or suicide attempts (*b*=-0.83, SE= 0.74, OR= 0.43, p=0.26).There was no effect of physical conditions on suicidal thoughts (*b*=0.16, SE= 0.11, OR= 1.17, p=0.15) or suicide attempts (*b*=0.17, SE= 0.29, OR= 1.18, p=0.55).

Table 5. 3 Unadjusted multinomial regression analyses investigating the relationship of past year suicidality, suicidal thoughts and suicide attempts with physical and common mental health disorders among NPMS 2007 participants

	Suicidality			Suicidal thoughts			Suicide attempts		
	n (%)	OR	95% CI	n (%)	OR	95% CI	n (%)	OR	95% CI
Neither physical nor CMD	71 (1.7)	-	-	70 (1.7)	-	-	10 (0.2)	-	-
One or more CMD	106 (17.1)	**12.078***	8.821-16.537	106 (17.1)	**12.253**	8.938-16.798	15 (2.4)	**10.458**	4.677-23.383
One or more physical illness	39 (1.4)	0.814	0.549-1.207	39 (1.4)	0.826	0.556-1.225	3 (0.1)	0.445	0.122-1.620
Multimorbidity[a]	135 (15.2)	**10.493**	7.792-14.131	134 (15.1)	**10.553**	7.823-14.235	22 (2.5)	**10.710**	5.054-22.698

[a]One or more CMD and one or more physical illness in the same person

*Significance of bold value is $p < 0.001$

Table 5. 4 Adjusted multinomial regression analyses for sociodemographic characteristics investigating the relationship of past year suicidality, suicidal thoughts and attempts with physical and common mental health disorders among NPMS 2007 participants

	Suicidality[1]		Suicidal thoughts[1]		Suicide attempts[1]	
	OR	95% CI	OR	95% CI	OR	95% CI
Neither physical nor CMD	-	-	-	-	-	-
One or more CMD	**10.176***	7.324-14.138	**10.344**	7.435-14.390	**7.178**	3.014-17.092
One or more physical illness	0.977	0.650-1.468	0.994	0.661-1.495	0.413	0.088-1.942
Multimorbidity[a]	**9.313**	6.742-12.865	**9.385**	6.782-12.987	**7.553**	3.843-18.191

[1]Adjusted for sociodemographic characteristics: sex, age, living conditions, ethnic group, any high educational qualification, employment status, social class by occupation.

[a]One or more CMD and one or more physical illness in the same person

*Significance of bold value is $p < 0.001$.

Table 5. 5 Adjusted multinomial regression analyses for all covariates, investigating the relationship of past year suicidality, suicidal thoughts and attempts with physical and common mental health disorders, among NPMS 2007 participants

	Suicidality[1]		Suicidal thoughts[1]		Suicide attempts[1]	
	OR	95% CI	OR	95% CI	OR	95% CI
Neither physical nor CMD	-	-	-	-	-	-
One or more CMD	**7.283****	5.143-10.312	**7.399****	5.218-10.492	**3.490***	1.389-8.771
One or more physical illness	0.920	0.609-1.390	0.937	0.620-1.417	0.365	0.077-1.729
Multimorbidity[a]	**6.263****	4.431-8.852	**6.305****	4.452-8.929	**4.028***	1.677-9.677

[1]Adjusted for all covariates: sex, age, living conditions, ethnic group, any high educational qualification, employment status, social class by occupation, negative life events, any psychiatric medication, alcohol and drug dependency.

[a]One or more CMD and one or more physical illness in the same person

* The significance of bold value is $p < 0.05$

**The significance of bold value is $p < 0.001$

5.6 Discussion

The Psychiatric Morbidity Survey of Great Britain conducted in 2000 was analysed, in order to explore the role of physical and mental illness multimorbidity in the risk of suicidal behaviours. Physical/mental multimorbidity was associated with an increased risk of suicidal thoughts and suicide attempts, compared to those with neither physical nor mental disorders. While those with CMDs only also had an elevated risk for all suicide-related behaviours, compared to the control group, there was no such risk among those who only reported physical health conditions. The results of the current study indicate that although physical/CMD multimorbidity could act as a suicide risk factor, the disease co-occurrence does not appear to increase the risk of suicidal thoughts and attempts beyond having CMDs alone.

As hypothesised, the NPMS participants with multimorbidity exhibited higher risk of suicidality compared to those with neither physical nor CMD conditions and in terms of the history of suicide attempts reported in the survey, the multimorbidity group reported the highest absolute number of attempts (although not statistically the highest number; Table 3). As such, our results lend some support to earlier research on the interaction between mental and physical illness in the risk of suicidal thoughts and attempts (Christiansen & Stenager, 2010; Goodwin et al., 2003; Qin et al., 2014; Webb et al., 2012a). Regarding suicidal thoughts, a US study on primary care patients found that patients with pulmonary disease and co-occurring depression had the highest risk of suicidal ideation, compared to those who had either or neither of the two conditions (Goodwin et al., 2003).

In terms of previous findings on suicidal attempts and physical/mental co-occurrence, Christiansen and Stenager's (2010) work on Danish children and adolescents, highlighted that epilepsy increased the risk of suicidal attempts when it was co-occurring with a psychiatric history. In another study focused on the role of specific physical conditions in suicidality, findings suggested that certain diagnoses like cancer, osteoporosis and COPD are specifically associated with a high suicide risk, identifying depression as a strong confounder of increased suicide risk among physically ill populations (Webb

et al. 2012b). It should be noted that in our study we did not focus on the effect of specific physical conditions on suicidal behaviours but on the presence of any self-reported somatic condition. This was a pragmatic decision informed by the size of our sample; our approach aimed to maximise statistical power. Furthermore, investigating the risk of suicide, Qin and colleagues (2014) presented the interaction between physical and psychiatric illness, taking temporality of conditions into account, and found that suicide risk is increased when the two types of illness co-occur, regardless of which one was diagnosed first.

The multimorbidity group in the current study had a higher risk of suicide attempts, compared to the control group. Although the method of suicide attempts was not assessed in the survey, one possible explanation for the increased risk of suicide attempts in this group, may be the easier access to multiple medications among those with physical and mental health issues. Consistent with this conjecture, a study of self-poisoning among older adult patients admitted to a general hospital found that the most common attempt suicide attempt method was an overdose of prescribed medication for existing medical and/or psychiatric conditions (Gavrielatos et al. 2006). It is worth noting that there is no evidence to date, into whether those with multimorbidity kill themselves using prescribed medication or other methods, as this population group has been overlooked in studies exploring suicide methods.

Although polypharmacy is one mechanism by which multimorbidity may possibly increase risk of suicide, psychological mechanisms additionally require exploration. For example, further studies should investigate the extent to which entrapment and acquired capability (Joiner 2005; O'Connor et al. 2016) are elevated in multimorbid populations. As the increasing number of health conditions, which in the given study are both physical and mental disorders in one person, could probably affect coping strategies and increase the sense of entrapment, suicidal behaviours among multimorbid populations could be motivated by a desire to escape from stressful and painful situations (Fegg, Kraus, Graw, & Bausewein, 2016; O'Connor, 2003; O'Connor & Nock, 2014).

Our findings on the association of CMDs with suicidal thoughts and attempts are in line with previous results, which as described in chapters 2 and 3, suggest that having one or more mental disorders increases suicide risk. Franklin and colleagues (2016) recently highlighted that suicide research has not progressed enough in the last 50 years and significant risk factors found to date cannot predict subsequent suicidal behaviours more than chance alone. In addition to that, it is quite clear from the studies reviewed in chapters 2 and 3, that although co-occurring mental illnesses confer a high risk of suicidality (compared to having one mental disorder or none), this co-occurrence probably isn't specific enough to be helpful when implementing a safety plan or assessing risk of future suicidal behavior (Batterham et al., 2013; Bronisch & Wittchen, 1994; Nock et al., 2010). Further studies, therefore, using linkage data from mental health services and suicide registries, are required to explore which CMD co-occurrence is associated with a higher suicide risk.

Interestingly, when exploring the relationship between physical illness and suicidality, our findings indicate no increased risk of either suicidal thoughts or suicide attempts, which is in contrast with the majority of the extant literature. Overall, previous research has consistently reported an association between physical illness and suicidal ideation and behaviour (Lin et al., 2016; Scott et al., 2010; Webb et al., 2012a). However, in most cases psychiatric comorbidities have mediated the relationship between physical illness and suicidal behaviour and suicide. One possible explanation for the absence of a relationship between physical illness and suicidality in our study could be due to the self-reported nature of the physical health conditions in NPMS 2000. While previous studies which found that single or multiple somatic conditions had an effect on suicidality had used data from health care settings, the self-reported information regarding physical illness in NPMS may not represent similarly serious conditions that need regular medical care or hospitalisation. Hence, the association between physical illness and suicidality, based on administrative data, may indicate the severity or chronicity of physical illness as a suicide risk factor, and not the physical illness per se. Further studies should consider the severity of any physical health condition examined in

relation to suicide risk and attention should be given to the use of self-reported information, as this latter type of information may not be sufficient for exploring the illness severity-suicidality relationship.

It is also worth noting that in the current analysis, the health groupings were mutually exclusive, indicating that those with physical conditions did not have any co-occurring CMDs. In the research literature, when a single physical health condition is explored in relation to suicidality, the role of co-occurring mental illness is also taken into consideration, usually by applying statistical models adjusted for psychiatric disorders (Pompili et al., 2016). Considering that in our current study design we excluded any CMD co-occurring with physical illness, this may account, in part, for the non-significant relationship between physical illness and suicidal behaviours. Indeed, Nock and colleagues (2010) have suggested that conditions that are thought to increase suicide risk may do so due to their association with a co-occurring condition that independently increases the risk of suicide (e.g., Nock reported that dysthymia had a low but significant association with suicide attempts, but in the presence of comorbid disorders, this association was lost). Based on their suggestion and our findings, it is important to highlight that the lack of well-defined groups of those who only have a physical health condition (with no comorbid common mental disorders), may contribute to misleading results in respect of the effect of somatic illness on suicidality. To that end, the methodology followed in the current study, regarding grouping participants into distinct groups, could be beneficial for future suicide-related studies that aim to explore the role of physical illness per se.

In terms of having both physical and mental conditions compared to having either and their relationship with suicidality, our NPMS results provide evidence that the interaction between somatic and CMD conditions does not increase suicide risk more than each condition alone. Although to the best of our knowledge there is no previous study presenting a similar physical/mental interaction model in the statistical prediction of suicidal behaviours, this finding would seem to suggest that physical/CMD multimorbidity does not act additively to increase the risk of non-fatal suicidal behaviours. Furthermore,

our finding that multimorbidity has an effect on suicidality indicate that this finding is CMD driven, considering that physical conditions on their own do not increase suicide risk in our analysis. Future population-based studies investigating whether physical/mental multimorbidity increases suicide risk, should further examine if this co-occurrence increases the risk beyond the independent effect of either condition. In addition, it would be important to investigate specific physical ill-health populations and perhaps limit analyses to those conditions which have a minimum level of severity.

5.7 Strengths and Limitations

The National Psychiatric Morbidity Survey (NPMS) 2000 is part of a series of surveys utilizing the same methodological approach since 1993 and it is a unique dataset recording the prevalence of mental conditions in private households (McManus et al., 2016). Although this is a self-report survey, a strength of the NPMS methodology is that it uses structured assessments and screening instruments based on diagnostic criteria, thereby rendering the survey comparable with other global mental health surveys (Kessler et al., 2009; McManus et al., 2016; Slade et al., 2009). Based on previous mental health surveys, 1 in 5 people experience a CMD within a 12- month period, which is not inconsistent with the NPMS results, where about 1 in 6 people reported at least one CMD in the week prior to the survey (Singleton et al. 2001; Slade et al. 2009; Steel et al. 2014). Further to that, exploring suicidal thoughts/behaviours in a survey like NPMS provides a prevalence estimate of suicidality among the general population who may not be in contact with health care services.

A main limitation of the present study is that we conducted secondary analyses of cross-sectional data. The study itself did not provide further information on the exact timing or nature of past year physical/mental conditions' diagnoses and suicidal behaviours; therefore, it was not possible to investigate the temporal relationship between the onset of physical/mental health conditions and suicidal thoughts. It is also worth noting that the presence of any of the physical conditions may have been over- or under-reported and that some of the conditions may not reflect

serious illness requiring hospitalisation. However, we were unable to find any studies to compare the rates of each past year physical conditions in other survey samples and therefore cannot comment directly on any under- or over-reporting. Furthermore, as we could not assess the severity of each condition we did not exclude any physical health condition when creating the physical health and multimorbidity groupings. Further studies should investigate the type and severity of physical health conditions, as this could moderate the relationship between multimorbidity and suicidal ideation and behaviour.

Although CMD severity scores were used to classify individuals into diagnostic categories, future research should explore the severity of mental illness in the context of multimorbidity in more detail. A further limitation is that the suicidal thoughts and suicide attempt items in the NPMS were not based on a specific suicide risk assessment scale but were measured through a clinical diagnostic instrument (CIS-R). Nonetheless, such methods of assessment of suicidal thoughts and behaviours are thought to be reliable and valid and are widely used (O'Connor & Nock, 2014).

5.8 **Conclusions**

Studies on the risk of self-harm and suicidal behaviour tend to focus on clinical populations with either primary psychiatric or physical conditions, with fewer studies exploring the effect of mental/physical multimorbidities within individuals. We report elevated risk of suicidal ideation and attempts among people who had co-occurring physical and common mental disorders in the past year, relative to individuals without these conditions. Although our findings indicate that multimorbidity is associated with suicidal thoughts and suicide attempts, it does not appear to confer additional risk beyond the independent effects of common mental disorders.

As suicide is a major public health issue and multimorbidity within aging populations increase, both primary care and mental health clinicians should focus on effectively assessing suicide risk among patients with multimorbid physical/mental conditions. Further studies on which physical and mental

conditions within multimorbid populations exhibit increased risk are required for the development of targeted suicide prevention strategies for this vulnerable population.

The present cross-sectional analysis of a mental health survey provided evidence for the role of multimorbidity in the risk of suicidal behaviours. Considering that NPMS is the first UK psychiatric survey investigating suicidal behaviours in the general population, the following UK survey conducted in 2007 (Adult Psychiatric Morbidity Survey, APMS) was further employed in the present thesis. Within psychological science, attention has been given to the lack of direct replication studies, which is further associated with the reproducibility of previous findings based on new data (Lindsay 2015; Open Science Collaboration 2015). Hence, in order to attempt to replicate the findings of the current study and determine whether suicide risk varies based on physical and mental illness co-occurrence, the NPMS study methodology and analyses was further performed based on the APMS 2007 dataset. Consequently, the following chapter is a cross-sectional study investigating the role of physical and mental illness multimorbidity in suicidality, among the participants of the Adult Psychiatric Morbidity Survey (APMS) 2007.

Chapter 6: The role of physical and mental health multimorbidity in suicidal thoughts and behaviour: results from the Adult Psychiatric Morbidity Survey of England (2007)

Background

Increasing attention has been given to people with somatic and mental disorders in suicide research, with few studies exploring the extent to which suicide risk varies as a function of physical and mental co-occurrence. We aimed to investigate whether people with a mental and physical illness multimorbidity have elevated risk of suicidal behaviours, compared to those without this multimorbidity.

Methods

Data from the Adult Psychiatric Morbidity Survey of England 2007 were analysed. Participants who responded to the suicidality questions were grouped into four distinct categories based on their health conditions [common mental disorders (CMD) only, physical health conditions only, CMD/physical health multimorbidity and a control group with neither physical nor CMDs]. Multinomial logistic regression analyses were conducted and odds ratios (OR) and 95% CIs are presented.

Results

In the fully adjusted model, multimorbidity had a significant effect on suicidal ideation and suicide attempts, compared to the control group (suicidal ideation OR= 15.63, 95% CI: 9.27-26.34; suicide attempts OR= 23.16, 95% CI: 3.06-175.00). There was also an increase within the CMD-only group (suicidal ideation OR= 16.64, 95% CI: 8.88-31.19; suicide attempts OR= 15.59, 95% CI:1.68 -144.27), but not for the physical illness-only group (suicidal ideation OR= 1.49, 95% CI: 0.86 - 2.591; suicide attempts OR= 2.48, 95% CI: 0.29 - 20.69).

Limitations

Secondary analyses of cross-sectional data.

Conclusions

Multimorbidity may act as a marker of risk for suicidal ideation and suicide attempts but not beyond the independent effects of physical illness and common mental disorders. Primary care and mental health clinicians should consider suicide risk among patients with multimorbid physical/mental health conditions.

6.1 Introduction

In Chapter 5 the effect of physical/mental multimorbidity in suicidal behaviours among British mental health survey participants was presented. Both suicidal thoughts and suicide attempts, taking place in the past year, were significantly associated with a physical and mental co-occurrence; however, this co-occurrence did not increase the risk of suicidality beyond the independent effect of mental illness alone. Considering the lack of studies on the role of multimorbidity in suicidal behaviours explored in survey designs, the third of the national psychiatric morbidity surveys conducted in Britain was further investigated. Hence, the current chapter replicates the methodology followed in NPMS 2000 (chapter 5) using the Adult Psychiatric Morbidity Survey 2007 (APMS), aiming to determine whether those with a physical health and CMD multimorbidity exhibit a higher risk of suicidal thoughts and suicide attempts, compared to others without such multimorbidity.

6.1.1 The Adult Psychiatric Morbidity Survey 2007

The Adult Psychiatric Morbidity Survey (APMS) 2007 is the third in a series of surveys administered in English households for adults, aged 16 and over. The aim of the survey was to investigate the prevalence of both treated and untreated mental illness based on self-reported information from 7,403 participants. The sampling frame was the small user Postcode Address File (PAF) and one adult (<16 years old) was selected for interview in each household (McManus et al., 2009). Population-based multiphase probability sampling was performed and both face-to-face and self-completion methodologies were employed (McManus et al., 2009). Information was collected on general health, service use, risk factors, demographics, suicidal behaviours and assessment of a range of mental disorders. While marital status was coded based on self-reports, data on ethnicity, equivalised household income, health conditions, and mental health related medication were established through show cards. The use of health care services and the assessment of current mental health conditions were ascertained in the face-to-face interviews (McManus et al., 2009). In addition, suicidal behaviours

were assessed both in the self-completion and interview phases (McManus et al., 2009). For the results to be representative of the 16 years and over population, the survey data were weighted to take account of non-response (McManus et al., 2009).

6.1.2 Sociodemographic differences of suicidal behaviours in APMS 2007

Official mortality statistics have been used to identify the characteristics of people exhibiting high suicide risk (Jenkins 2003). In addition, household surveys have advanced our understanding of risk by recording the sociodemographic characteristics of those who experience suicidal behaviours but who tend not to seek mental health care (Jenkins 2003; McManus et al. 2009). As noted by MacManus and colleagues (2009), another strength of population-based surveys is that they capture the group of patients who present to primary care services with non-fatal self-harm (with or without suicidal intent) but who are not identified as suicidal, therefore they are missing in administrative health datasets of the epidemiology of suicidal behaviours.

Overall in the 2007 national survey, lifetime suicidal ideation was self-reported by 16.7% of APMS participants, 5.6% had made a suicide attempt since the age of 16 and 4.9% reported lifetime self-harming behaviours. Both thoughts of suicide and suicide attempts were more common in women (suicidal thoughts:19.2% of women, 14.0% of men; suicide attempts: 6.9% of women, 4.3% of men) and in younger adults (suicidal thoughts: 20.6% of those aged 16-24 years, 10.0% of those aged 65-74 years and 3.5% of those aged 75 years or over; suicide attempts: 7.3% of those aged 16-24 years, 2.7% of those aged 65-74 years and 1.3% of those aged 75 or over). Self-harm followed the same pattern, being more prevalent in younger women than men (17.0% of women aged 16-24 years, compared with 7.9% of men in the same age group), but no sex differences were observed in the older age groups (McManus et al., 2009).

In respect of further sociodemographic differences, the rates of lifetime suicidal behaviours varied as a function of marital status, ethnicity and

equivalised household income. Both male and female participants who were divorced reported lifetime suicidal thoughts more often compared to those who were married (men: 31.0% of divorced, compared with 10.4% of married; divorced women: 33.5%, compared with married women 15.3%), while the same marital status pattern was found for suicide attempts (14.2% of divorced men and women; 3.0% of married men and 5.0% of married women).

The prevalence of suicide attempts did not differ across the ethnic groups of "White", "Black" and "South Asian", while the highest prevalence of suicidal thoughts was observed for White males and females (15.0% and 20.0% respectively). Men within the lowest household income groups were also found to have an increased risk of suicidal thoughts and even more so, when the highest and lowest income quintiles were compared. The strongest pattern was found for the risk of suicide attempts in both men and women (9.0% of men and 12.2% of women from the lowest income quintile, compared with 1.8% of men and 3.8% of women from the highest quintile; McManus et al., 2009).

The help seeking behaviour of the 2007 APMS participants who reported suicide attempts appears to have increased in comparison with the findings from the 2000 APMS survey, with 60% of the respondents seeking help mainly from psychiatric services or hospital, GPs and friends, family and neighbours in 2007, compared to 52% in 2000. There was no difference between males and females in the source of help-seeking behaviour (McManus et al., 2009).

6.1.3 Lifetime health issues and suicidal behaviours in APMS 2007

In face-to-face interviews, participants were asked about their general health issues after the age of 16. Twenty-two health conditions were presented on show cards with a further question on the timing of conditions, namely lifetime and past year periods. In the same interview phase, participants were asked if they ever thought of taking their own life (suicidal thoughts) and if they had ever attempted to take their own life (suicide attempts), covering the time periods of lifetime, past year and past week.

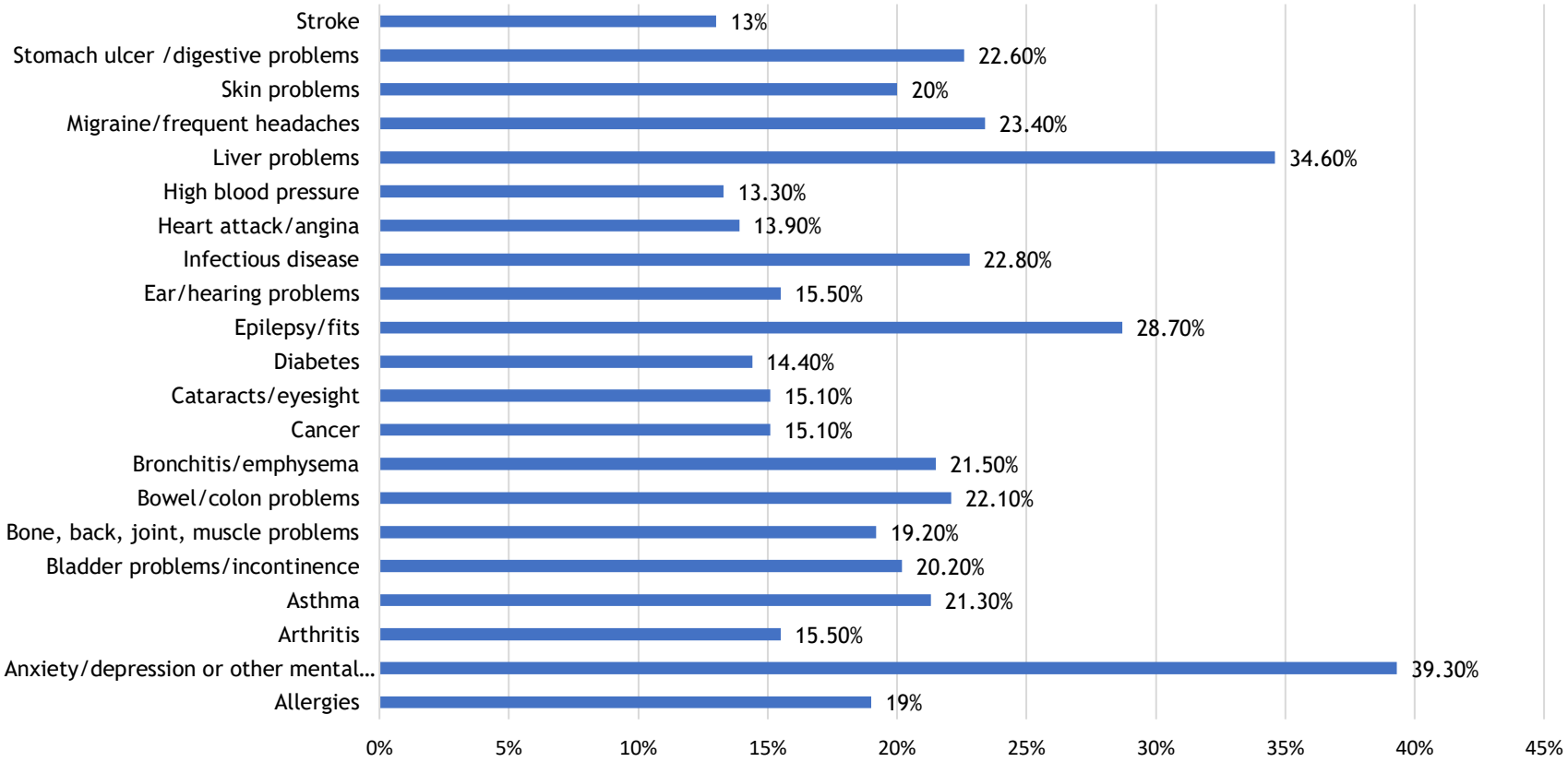
When inspecting the proportion of those with lifetime conditions who reported suicidal thoughts and attempts, those with mental health issues, liver problems and epilepsy were the condition-groups with high risk of suicidality (thoughts and attempts), preceding those with migraine and infectious conditions (Figure 1 & 2). This finding is consistent with previous mental health surveys that have shown an increased risk of suicidal behaviours for participants experiencing the same lifetime conditions (Le Strat, Le Foll, & Dubertret, 2015; Nock et al., 2010; Scott et al., 2010). More specifically, the WHO survey which included worldwide data, described high blood pressure, heart attack/stroke, arthritis, chronic headache and respiratory conditions significantly associated with suicide attempts, with epilepsy being the only condition strongly associated with any suicidal outcome (suicidal ideation, suicide plan, suicide attempt) when compared to other physical health issues (Scott et al., 2010).

Considering the differences between case control studies using primary care data and cross-sectional analysis of self-reported information, the pattern of findings related to the increased suicide risk among lifetime health conditions, like mental disorders, epilepsy, diabetes, asthma and migraine is constant (Druss & Pincus, 2000; Goodwin & Eaton, 2005; Mościcki, 1997; Pompili et al., 2016; Singhal et al., 2014). Studies based on administrative registries, surveys, hospital admission or coroner data, regarding self-harm, have similarly reported an increased risk of suicide among patients with chronic health conditions, with mental disorders being the strongest predictor of suicide attempts (Christiansen & Stenager, 2010; Hawton, Fagg, & Marsack, 1980; Nilsson, Ahlbom, Farahmand, Åsberg, & Tomson, 2002; Webb et al., 2012b).

However, contradictory findings have been found for the effect of physical conditions per se on the risk of suicidal behaviours. Based on our results on NPMS 2000 (chapter 5), physical illness seemed not to have any effect in either suicidal thoughts or suicide attempts. It should be noted that our physical only health group did not have any co-occurring mental health condition. A variety of studies report that the elevated risk of suicide among physically ill populations varies as a function of subsequent mental disorders,

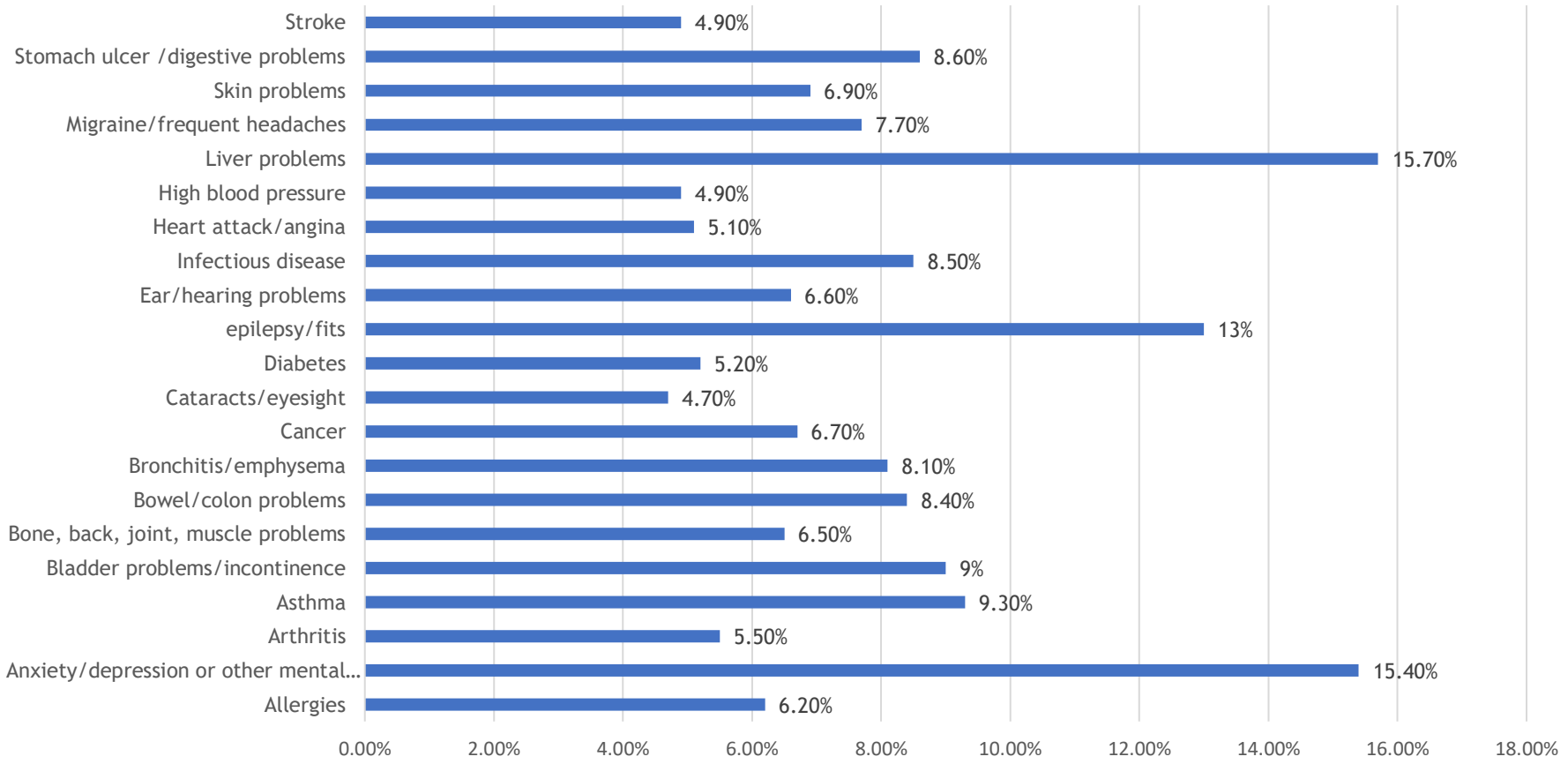
whereas other studies report that a disease of any organ increases the risk, even in the absence of mental illness (Bolton, Walld, Chateau, Finlayson, & Sareen, 2015; Qin et al., 2013; Webb et al., 2012a). While having psychiatric illness is seen as a confounding or mediating factor in the link between chronic conditions and risk of suicide, limited studies to date have investigated the effect of physical comorbidities among those with mental conditions who engage in suicidal behaviours.

Figure 6. 1 Lifetime suicidal thoughts among APMS participants experiencing health conditions since the age of 16



Proportion of participants with lifetime health conditions who had lifetime suicidal thoughts

Figure 6. 2 Lifetime suicide attempts among APMS participants experiencing health conditions since the age of 16



Proportion of participants with lifetime health conditions who had lifetime suicide attempts

6.2 Aim of current study

Previous research has found that mental disorders are significantly associated with suicide-related outcomes, while somatic conditions on their own have been found to have a relationship with suicidality (Hawton et al., 2003; O'Connor & Nock, 2014; Pompili et al., 2016; Scott et al., 2010; Singhal et al., 2014). Although previous studies have focused on the separate role of psychiatric and physical conditions in suicide risk, limited studies have explored the effect of physical and mental illness co-occurrence (multimorbidity) on suicidal behaviours. In Chapter 5, we found that physical/mental multimorbidity has an effect on both suicidal thoughts and suicide attempts; however, this multimorbidity did not provide any risk beyond having mental illness alone. Nonetheless, considering the paucity of research, the aim of the current study was to investigate again the extent to which suicide risk varies as a function of physical/mental multimorbidity. Based on the extant literature, the key hypothesis of this study is that an individual with at least one physical illness plus at least one mental disorder will exhibit higher risk of suicidal behaviours compared to those without those co-occurring conditions.

6.3 Materials and Methods

6.3.1 Setting and participants

Secondary analyses of data from the Adult Psychiatric Morbidity Survey (APMS) 2007 of England were conducted. APMS 2007 is the third in a series of surveys administered in English private households for adults, aged 16 and over. In order for the results to be representative of the national population, data were weighted based on age, sex and region. Data were additionally weighted to take into account of non-response. The survey's aim was to describe the prevalence of both treated and untreated mental illness based on self-reported information of 7403 participants. Population-based multiphase probability sampling was performed and both face-to-face and self-completion methodologies were employed. Both first and second phase

interviews from the APMS were used for the data analysed in the current study (McManus et al. 2009).

6.3.2 Measures

Mental health conditions, including non-psychotic symptoms in the week prior to interview, were assessed through the revised Clinical Interview Schedule (CIS-R). Participants who met the criteria for a depressive episode, generalised anxiety disorder (GAD), mixed anxiety and depressive disorder (MAD), panic disorder, phobia, and obsessive compulsive disorder (OCD) were considered to have a 'common mental disorder' (CMD). With respect to health conditions, a show card of 22 health conditions was provided to participants. With the exception of "anxiety, depression or other mental health issue", all of the other conditions asked about were physical health conditions. If a positive response to a health condition was indicated, this was followed up with a question asking whether the condition had been experienced in the past year or lifetime. Given that the timeline for CMDs was current the time-frame used for physical health condition was past year. Physical health conditions experienced in the past year and current CMDs are presented in Table 1.

Items related to suicidal thoughts, suicide attempts and self-harm were assessed through the CIS-R. Participants were asked the following questions: "Have you ever thought of taking your life, even though you would not actually do it?"; "Have you ever made an attempt to take your life, by taking an overdose of tablets or in some other way?" and "Have you ever deliberately harmed yourself in any way but not with the intention of killing yourself?". A positive response on these items was followed up with a further question on whether the thoughts/behaviours occurred during the past week, the past year or whether they were lifetime responses. No further question about the timing was asked for self-harming behaviours (i.e., cutting, burning); as a result, those behaviours were considered as lifetime occurrence. Based on the selection of past year physical health conditions and current CMD in the present study, only past year suicidal thoughts and suicide attempts were included in the analyses. The items assessing past year

suicidal thoughts and attempts were combined and the derived variable of "presence of past year suicidality" was computed. Suicidality was included in the analyses as a further outcome of interest.

In order to investigate the extent to which suicide risk varies as a function of physical and mental health multimorbidity, participants were grouped into four mutually exclusive categories: those with (1) one or more CMDs; (2) one or more physical health conditions; (3) both CMD and physical health conditions (multimorbidity) and; (4) neither physical health conditions nor CMD (controls). As with the previous empirical study in chapter 5, for the present analysis multimorbidity was defined as the co-occurrence of at least two health conditions, at least one physical plus at least one mental within the same person. The frequencies of participants as a function of physical and mental health conditions are presented in Figure 3.

Hazardous drinking, drug dependency and prescribed medication were also recorded in the current study. Hazardous drinking and alcohol dependency levels were assessed using the Alcohol Use Disorders Identification Test (AUDIT). For participants who had an AUDIT score of more than 10 (range 0-40), indicating hazardous drinking, the Severity of Alcohol Dependence Questionnaire (SADQ-C, with reference to drinking in the past 6 months) was administered in order to assess alcohol dependency. The scoring combination of AUDIT +10 and SADQ-C was selected for high hazardous drinking in the present study and was computed as a binomial variable (Yes/No). Drug use was also assessed via a computer-assisted self-completion interview (CASI). The computed past year drug dependency item (Yes/No) was selected for our analyses. Furthermore, APMS participants were questioned about different types of current prescribed psychiatric medication and the derived variable of assessing any current prescribed medication (Yes/No) was used.

The participants were additionally asked about 18 negative life events including serious illness, death, abusive relationships, work problems, financial stress and homelessness. The experience of negative life events was reported for either lifetime (more than 6 months ago but since or before the age of 16 years) or for the past 6 months. The derived variable entitled the

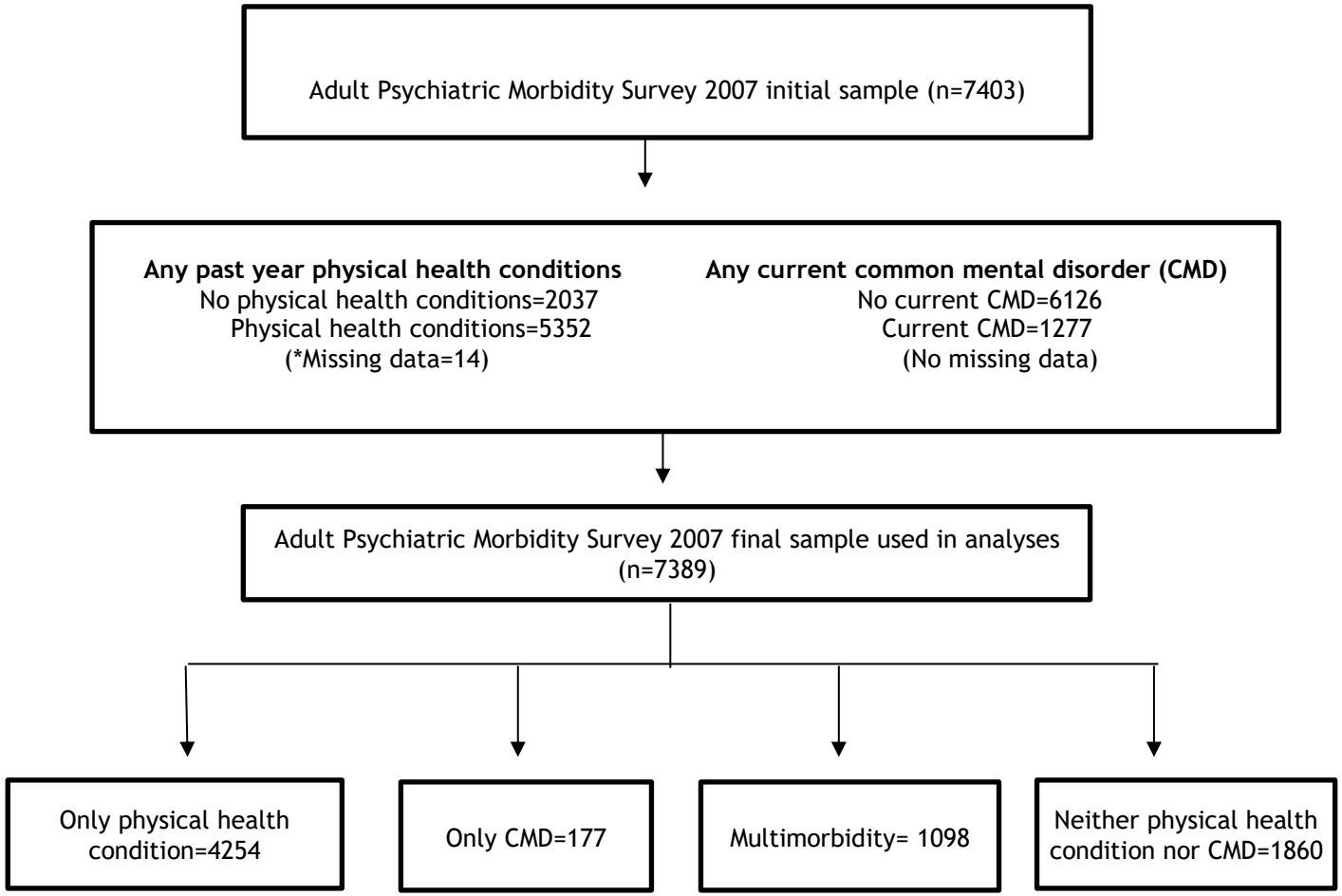
"presence of negative life events within the past 6 months" (Yes/No) was computed and used in the analyses.

Sociodemographic information regarding living conditions (de facto status), ethnic origin, employment status and deprivation index were computed as binomial variables. Standard sociodemographic characteristics per health condition group are presented in Table 2.

6.3.3 Statistical analyses

Descriptive statistics were used for the demographic characteristics of the four different physical/mental health condition groups (i.e., CMD only, physical health condition only, multimorbidity, neither physical health condition nor CMD). Chi squares and one-way ANOVAs were carried out to investigate any sociodemographic differences across the health groupings who reported past year suicidality. Multinomial logistic regression analyses were conducted to investigate the association between past year suicidality, suicidal thoughts, suicide attempts and multimorbidity. In order to investigate if the effect of multimorbidity increases the risk of suicidal behaviours more than the independent effects of CMD and physical illness, two binary logistic regression analyses including the conditions interaction effect were performed. The reference category for the multinomial regressions was those with "neither physical health condition nor CMD" (group 4) and odds ratios (OR) and 95% CIs are reported. With previous research indicating a differentiation in suicide risk based on demographic, clinical characteristics and traumatic events (Belik, Cox, Stein, Asmundson, & Sareen, 2007; Foster, 2011; Pompili et al., 2014) a series of multinomial logistic regression models were conducted adjusting for: a) sociodemographic characteristics and; b) sociodemographic characteristics, negative life events, hazardous drinking, drug dependency and prescribed medication. The significance level was set at $p < 0.05$ and the statistical analysis was performed with the Statistical Package for Social Sciences SPSS version 22 (SPSS Inc., Chicago, IL, USA).

Figure 6. 3 Flowchart of the Adult Psychiatric Morbidity Survey 2007 sample



*missing data include: No answer/refused, Don't know.

Physical health conditions n (%)*				Common mental disorders n (%)	
Allergies	757 (10.2%)	Epilepsy/fits	44 (0.6%)	Any phobia	160 (2.2%)
Arthritis	1309 (17.7%)	Ear/hearing problems	43 (10.0%)	Depressive episode	255 (3.4%)
Asthma	679 (9.2%)	Infectious disease	39 (0.5%)	Generalised anxiety disorder	363 (4.9%)
Bladder problems/incontinence	353 (4.8%)	Heart attack/angina	216 (2.9%)	Mixed anxiety/depressive disorder	641 (8.7%)
Bone, back, joint and muscle problems	2047 (27.7%)	High blood pressure	1514 (20.5%)	Panic disorder	83 (1.1%)
Bowel/colon problems	455 (6.1%)	Liver problems	68 (0.9%)	Obsessive compulsive disorder	86 (1.2%)
Bronchitis/emphysema	216 (2.9%)	Migraine or frequent headaches	1019 (13.8%)		
Cancer	116 (1.6%)	Skin problems	819 (11.1%)		
Cataracts/eyesight problems	1280 (17.3%)	Stomach ulcer or digestive problems	522 (7.1%)		
Dementia or Alzheimer's	7 (0.1%)	Stroke	42 (0.6%)		
Diabetes	386 (5.2%)				

Table 6. 1 Proportion of past year physical health conditions and current common mental disorders (CMD) among APMS 2007 participants

*The number of conditions may not add up to that total number of the APMS sample (n=7389), as participants had one or more of the indexed conditions.

Table 6. 2 Sociodemographic characteristics of APMS participants with multimorbidity, CMD only, physical health conditions only and neither physical nor CMD (n=7389)

	Multimorbidity	**Common mental disorders only (CMD)**	**Physical health conditions only**	**Neither physical nor CMD**
Characteristics*	**n=1098**	**n=177**	**n=4254**	**n=1860**
Age *M (SD)*	48.73 (16.6)	36.90 (15.1)	55.62 (18.3)	43.58 (17.1)
Sex *n (%)*				
Male	353 (32.1)	66 (37.3)	1834 (43.1)	933 (50.2)
Female	745 (67.9)	111 (62.7)	2420 (56.9)	927 (49.8)
Living conditions *n (%)*				
Living with someone	508 (46.3)	67 (37.9)	2475 (58.2)	1078 (58)
Not living with someone	590 (53.7)	110 (62.1)	1779 (41.8)	782 (42)
Ethnic groups *n (%)*				
White	993 (91.9)	144 (83.7)	4015 (94.8)	1642 (88.8)
Non white	88 (8.1)	28 (16.3)	221 (5.2)	208 (11.2)
Employment status n *(%)*				
Currently employed	485 (44.2)	95 (53.7)	2113 (49.7))	1265 (68)
Not currently employed	613 (55.8)	82 (46.3)	2141 (50.3)	595 (32)
Any higher qualifications n *(%)*				
Yes	720 (66.4)	129 (75.4)	2916 (68.9)	1462 (79.1)
No	365 (33.6)	42 (24.6)	1319 (31.1)	387 (20.9)
Index of Multiple Deprivation *n (%)*				
0.59->8.35 (least deprived)	139 (12.7)	22 (12.4)	889 (20.9)	366 (19.7)
8.35->86.36 (most deprived])	959 (87.3)	155 (87.6)	3365 (79.1)	1494 (80.3)
Past year suicidality n (%)				
Yes	218 (19.9)	38 (21.5)	67 (1.6)	17 (0.9)
No	880 (80.1)	139 (78.5)	4187 (98.4)	1843 (99.1)
Past year suicidal ideation n (%)				
Yes	217 (19.9)	38 (21.7)	67 (1.6)	17 (0.9)
No	875 (80.1)	137 (78.3)	4185 (98.4)	1841 (99.1)
Past year suicide attempts n (%)				
Yes	39 (3.6)	5 (2.9)	7 (0.2)	1 (0.1)
No	1058 (96.4)	170 (97.1)	4245 (99.8)	1858 (99.9)

* percent (%) is based on the omission of missing values

6.4 Results

6.4.1 Sociodemographic characteristics of APMS participants with multimorbidity

Of the 1098 APMS participants with physical and common mental disorder multimorbidity, 67.9% were women (see Table 2). The majority of the multimorbidity group belonged to the most deprived category (87.3%), while 613 participants from the same health group were not currently employed. Similar to the other health groups, the majority of those with multimorbidity were White (ethnic group category) and had a high educational qualification. Regarding the responses to the suicidal ideation and attempts items, the highest proportion of people who reported suicide attempts was in the multimorbidity group (3.6%, n=39), while 19.9% and 21.7% of those within the multimorbidity and CMD groups, respectively, reported past year suicidal thoughts.

The participants with past year suicidality who belonged to each of the health groupings (i.e., the CMD, physical, multimorbidity, neither physical nor CMD groups) did not differ with regard to sex, employment status, living conditions. However, there was a significant difference between groups regarding age [$F(3)=11.229$, $p< 0.001$]. Those with multimorbidity experiencing suicidality were also more likely to have higher education compared to the rest of groups (multimorbidity 59.7% vs physical 22.7% vs CMD 10.7% vs neither physical nor CMD group 6.9%, $p= 0.015$). In addition, 65.4% of the White ethnic group was multimorbid ($p= 0.01$), with 50% of the non-White ethnic group being multimorbid compared to the CMD group (30.8%), physical only group (7.7%) and neither group (11.5%). While all participants who reported previous suicidal thoughts/attempts from the neither group were most deprived (100%, $p=0.037$), 65% of those with the lowest deprivation index level were multimorbid, 11.7% had CMD, and 17.7% physical conditions.

6.4.2 Unadjusted analyses of the relationship between physical and mental health conditions, past year suicidality, suicidal thoughts and attempts

Three separate unadjusted multinomial regression analyses were performed for the different illness groupings and past year suicidal history items (Table 3). The unadjusted model for suicidality showed that participants with either CMD only, any physical health condition only and multimorbidity were more likely to experience suicidality compared to those with neither physical health condition nor CMD (OR= 29.63; 95% CI, 16.30-53.85, *p<0.001*; OR= 1.73; 95% CI, 1.01-2.96, *p=0.044*; OR= 26.85; 95% CI, 16.28-44.28*, p<0.001*, respectively). A similar pattern of findings was found for suicidal thoughts; the unadjusted model for suicide attempts, however, indicated that only those with one or more CMDs and multimorbidity had significantly increased odds ratios, compared to those with neither illness. The presence of any physical health problems did not provide any significant increased risk of suicide attempts (OR= 3.06; 95% CI, 0.37-24.92, *p=0.295*).

6.4.3 Adjusted multinomial logistic regression analyses for sociodemographic characteristics

Following adjustment for sociodemographic characteristics (sex, age, living conditions, ethnic group, education qualifications, employment status, and deprivation index), the presence of any physical health condition, CMDs and multimorbidity were associated with all indices of suicidality (OR= 1.95; 95% CI, 1.13-3.35, *p*=0.015; OR= 21.71, 95% CI, 11.74-40.13, *p*<0.001; OR= 23.98, 95% CI, 14.46-39.76, *p*<0.001) and suicidal thoughts (OR= 1.94, 95% CI, 1.13-3.34, *p*=0.016; OR= 22.01, 95% CI, 11.90-40.71, *p*<0.001; OR= 24.05, 95% CI, 14.50-39.88, *p*<0.001) with the exception of the association between physical health condition and suicide attempts (OR= 4.143; 95% CI, 0.506-33.888, *p*=0.185; Table 4).

6.4.4 Adjusted multinomial logistic regression analyses for all covariates

After the adjustment for sociodemographics, negative life events, hazardous drinking, drug dependency and any prescribed medication, multimorbidity and CMDs were significantly associated with both suicidal thoughts (OR= 15.63, 95% CI, 9.27-26.34, *p<0.01*; OR= 16.64, 95% CI, 8.88-31.19, *p<0.001*) and suicide attempts (OR= 23.16, 95% CI, 3.06- 175.00, *p*=0.002; OR= 15.59, 95% CI, 1.68-144.27, *p*=0.016). In the same fully adjusted model physical health conditions did not have any association with either suicidality, suicidal ideation or suicide attempts (Table 5).

6.4.5 Binary logistic regression and the interaction effect of multimorbidity

The interaction effect of physical/CMD multimorbidity was investigated through two separate logistic regression models, with past year suicidal thoughts and suicide attempts as outcome variables. Although having CMD-only and physical-only conditions increased the risk of suicidal thoughts (CMD: *b*=2.78, SE= 0.141, OR= 16.21, p<0.001; Physical: *b*=0.62, SE= 0.269, OR= 1.86, *p*= 0.020), having both conditions did not significantly increase the risk of suicidal thoughts more than the sum of their independent effects (*b*=0.709, SE= 0.608, OR= 2.03, *p*=0.244). Similarly, the interaction effect of physical and CMD conditions did not increase the risk of suicide attempts (*b*=-0.19, SE= 1.297, OR= 0.827, *p*=0.884), while only CMD was found to significantly increase the risk of attempts (CMD: *b*=3.08, SE= 0.390, OR= 21.94, p<0.001; Physical: *b*=0.34, SE= 0.604, OR= 1.40, *p*=0.570).

Table 6. 3 Unadjusted multinomial regression analyses investigating the relationship of past year suicidality, suicidal thoughts and suicide attempts with physical and common mental health disorders among APMS 2007 participants

	Suicidality			Suicidal thoughts			Suicide attempts		
	n (%)	OR	95% CI	n (%)	OR	95% CI	n (%)	OR	95% CI
Neither physical nor CMD	17 (0.9)	-	-	17 (0.9)	-	-	1 (0.05)	-	-
One or more CMD	38 (21.4)	**29.638****	16.309 - 53.858	38 (21.7)	**30.038****	16.524 - 54.604	5 (2.8)	**54.647****	6.348 - 470.438
One or more physical illness	67 (1.6)	**1.735***	1.016 - 2.962	67 (1.6)	**1.734***	1.015 - 2.961	7 (0.16)	3.064	0.377 - 24.920
Multimorbidity[a]	218 (19.8)	**26.857****	16.289 - 44.281	217 (19.9)	**26.857****	16.287 - 44.286	39 (3.5)	**68.490****	9.396 - 499.221

[a]One or more CMD and one or more physical illness in the same person
*Significance of bold value is p< 0.05
**Significance of bold value is p < 0.001

Table 6. 4 Adjusted multinomial regression analyses for sociodemographic characteristics investigating the relationship of past year suicidality, suicidal thoughts and attempts with physical and common mental health disorders among APMS 2007 participants

	Suicidality[1]		Suicidal thoughts[1]		Suicide attempts[1]	
	OR	95% CI	OR	95% CI	OR	95% CI
Neither physical nor CMD	-	-	-	-	-	-
One or more CMD	**21.710*** **	11.744 - 40.134	**22.012*** **	11.901 - 40.716	**28.131****	3.098 - 255.448
One or more physical illness	**1.952***	1.136 - 3.353	**1.949***	1.134 - 3.348	4.143	0.506 - 33.888
Multimorbidity[a]	**23.983*** **	14.464 - 39.767	**24.053*** **	14.505 - 39.885	**51.624*** **	7.031 - 379.019

[1]Adjusted for sociodemographic characteristics: sex, age, living conditions, ethnic group, any high educational qualification, employment status, deprivation index.

[a]One or more CMD and one or more physical illness in the same person

* Significance of bold value is p< 0.05

** Significance of bold value is p< 0.01

*** Significance of bold value is p < 0.001

Table 6. 5 Adjusted multinomial regression analyses for all covariates, investigating the relationship of past year suicidality, suicidal thoughts and suicide attempts with physical and common mental health disorders among APMS 2007 participants

	Suicidality[1]		Suicidal thoughts[1]		Suicide attempts[1]	
	OR	95% CI	OR	95% CI	OR	95% CI
Neither physical nor CMD	-	-	-	-	-	-
One or more CMD	**16.548*** **	8.834- 30.998	**16.644*** **	8.881- 31.193	**15.594***	1.686- 144.276
One or more physical illness	1.498	0.865- 2.595	1.496	0.863 - 2.591	2.487	0.299 - 20.695
Multimorbidity[a]	**15.594*** **	9.252- 26.284	**15.632*** **	9.274- 26.349	**23.168** **	3.067- 175.001

[1]Adjusted for all covariates: sex, age, living conditions, ethnic group, any high educational qualification, employment status, deprivation index, negative life events, any prescribed psychiatric medication, high hazardous drinking, and drug dependency

[a]One or more CMD and one or more physical illness in the same person

* The significance of bold value is p< 0.05

** The significance of bold value is p< 0.01

*** The significance of bold value is p < 0.001

6.5 Discussion

Overall, within a general population sample, we identified a possible association between mental/physical multimorbidity and suicidal behaviours. As previous studies on mental and physical co-occurrence have suggested an increased risk of suicidality, our current findings provide further evidence of the role of coexisting mental and physical conditions in suicidality (Goodwin et al., 2003a; Goodwin, Marusic, & Hoven, 2003; Jones et al., 2004; Pompili et al., 2016; Qin et al., 2014). Multimorbidity was found to be significantly associated with a risk for suicidal thoughts, however it does not appear to confer a higher risk beyond the independent effects of CMD and physical-only. Although an association was further found for multimorbidity and past year suicide attempts, caution should be held when interpreting the results, due to the wide CIs presented.

Our secondary analysis of the APMS 2007 data confirms the results reported in chapter 5 on the significant effect of multimorbidity in suicidal behaviours found in the NPMS 2000 study and overall our findings seem to be in line with previous studies on the importance of mental and physical conditions as co-existing diagnoses in suicidality (Bolton et al., 2015; Lossnitzer et al., 2009; Qin et al., 2014; Webb et al., 2012b). In a population-based study in Canada, Bolton and colleagues concluded that when mental illness was taken into account, cancer patients compared to patients with other chronic illness had an increased suicide risk, 3 months following cancer diagnosis (Bolton et al., 2015). The same study found that asthma, chronic obstructive pulmonary disease (COPD) and multiple sclerosis are also associated with an increased risk of suicide (Bolton et al., 2015). A further study on the role of physical and mental illness co-occurrence conducted in Germany, reported that both current and lifetime depression among patients with congestive heart failure (CHF) increase the risk of suicidal thoughts and ideas of self-harm, compared to CHF patients without depression (Lossnitzer et al., 2009).

Although limited research has investigated the role of physical illness and suicide risk among populations with a pre-existing mental illness, a Danish study found that suicide risk was high when the onset of physical and mental

illness occurred close in time, especially when the physical illness preceded the mental illness (Qin et al., 2014). The authors concluded that the timing of psychiatric diagnosis before or after a physical illness can differentiate the suicide risk (Qin et al., 2014). As we reported in chapter 5, in our study it was not feasible to address the timing of physical and mental diagnoses within the past year, as there was no related information provided in the APMS dataset.

When all health groups were compared to those with neither mental or physical health conditions, the multimorbidity group was found to have the highest risk for suicide attempts (Table 3). However, given the large and overlapping confidence intervals and the very small number of cases our results should be interpreted with caution, as suicide (and suicide attempts) is a rare event and the investigation of the effect of multimorbidity on suicidality should be explored in a larger sample of suicide cases. Nonetheless, in our study the multimorbidity group included the largest number of suicide attempts (n=39) compared to the other health groups and this trend highlights the potential importance of multimorbidity on suicide attempts. As mentioned in the previous chapter, the easy access of patients with physical and mental multimorbidity to multiple medications, could possibly explain the high number of attempts in our results. In a German study investigating the reason for killing oneself mentioned in suicide notes of people with mental and physical illness, both groups of patients were found to have several comorbid diseases (those with mental disorders had comorbid physical illness and vice versa; Fegg et al., 2016). Due to intoxication being the most common suicide method for both patients' groups in the same study, Fegg and colleagues suggested that this death outcome could be related to the drug accessibility of those patients (Fegg et al. 2016).

Given the elevated risk of suicidal ideation among the multimorbid group in our study and the importance of the risk of transition from suicidal ideation to suicide attempts, the role of physical/mental multimorbidity needs to be further investigated (Nock et al., 2009; O'Connor, 2011; O'Connor & Nock, 2014). Findings from pain studies indicate that conditions like arthritis and migraine, which are also examined in our study, have an association with lifetime and past year suicidality (Braden & Sullivan 2008; Ratcliffe et al.

2008). Based on the indications that pain related conditions increase suicidality when they co-occur with mental disorders, this association could partially explain the risk of suicidal thoughts found among the APMS participants with multimorbidity and not among the physical only group (Newton-John 2014; Ratcliffe et al. 2008). Further population-based studies should investigate if non-pain and pain related conditions differ in terms of their suicidality risk and whether comorbid mental illness has an additional effect in this relationship.

While the prevalence of multimorbidity increases with age and a variety of studies have focused on young and old age groups with co-occurring conditions, future studies should explore the risk of suicidality in relation to the different multimorbid age groups (Barnett et al. 2012; McCloughen et al. 2012; Salive 2013). Based on psychiatric multimorbidity, Moor and colleagues (2012) explored the effect of bipolar disorder comorbidities in adolescents and young adults (15 to 36 years of age). They found that suicide attempts were predicted by a greater number of co-occurring disorders and specifically self-harming behaviours were predicted by the co-occurrence of panic and borderline personality disorder (Moor et al. 2012). Overall, this study from New Zealand highlighted that the onset of bipolar disorder during childhood was significantly associated with self-harming behaviours but not with suicide attempts.

In terms of physical and mental illness multimorbidity, a Finnish study on 229 cases of suicide, found that hospital treated mental illness was more common among male adults aged 25 or younger with physical illness, than among men without physical illness (27% vs 7% respectively). Based on their findings, Viilo et al (2005) indicated that because physical illness is highly prevalent among populations with mental health conditions, physical illness resulting in hospitalisation should be seen as a suicide risk factor among young adults. A review by McCloughen et al. (2012) that found a high prevalence of physical/mental illness co-occurrence, among young adults aged 16 to 24, has highlighted that physical/mental multimorbidity may reflect a common aetiology rather than a causal association. Considering that suicide is a significant cause of death in this young age group, McCloughen and colleagues

pointed out that since mental/physical co-occurrence affects one's quality of life, consequently it affects one's sense of hope; taking into account that the latter, hence lack of, is highly associated with suicidality, the authors propose more attention be given to the ways young adults experience their health conditions.

In addition, those with common mental disorders (CMD) in the APMS survey appear to have an elevated risk on all suicidal items compared to those with neither physical nor CMD conditions. As mentioned earlier, our findings are consistent with previous research and indicate a strong association between CMD and risk of suicidal behaviours. Although the presence of CMD had a persistent effect even when sociodemographic and clinical variates were controlled for, physical health conditions on the other hand were not associated with suicidality when all covariates were taken into account. More specifically our findings indicate that having physical conditions is significantly associated with past year suicidal thoughts and attempts (unadjusted and adjusted for sociodemographic), however further factors like negative life events, prescribed psychiatric medication, alcohol and drug abuse reduce the effect of somatic illness on suicidality. It should be noted that some of the physical conditions assessed in the APMS may not represent serious somatic conditions that needed chronic medical treatment, hence accounting for the reduced effect on either suicidality assessments.

6.6 Strengths and Limitations

Given that the current study replicates the same study design included in chapter 5, which was based on the previous National Psychiatric Morbidity Survey conducted in Great Britain (2000) employing the same methodology, similar strengths and limitations are noted below.

The Adult Psychiatric Morbidity Survey (APMS) 2007 is the third in a series of surveys administered in English private households, investigating the prevalence of mental conditions in adults and following a similar methodological approach since 1993 (McManus et al., 2016). One of the strengths of APMS is the use of structured assessment tools, based on diagnostic criteria, which can assist in identifying people with sub-threshold

psychiatric symptoms (McManus et al., 2016). Further to the screening instruments used for mental disorders, one of the strengths of APMS is the investigation of the prevalence of suicidality among the general population, by employing questions regarding suicidal thoughts and behaviour in the computerised self-reported parts of interview, to avoid underreporting of suicidality due to feelings of discomfort that may be experienced in face-to-face interviews (McManus et al., 2016).

One of the limitations of the current study is that we could not investigate the temporal relationship between physical and mental illness due to lack of information regarding the timing of conditions in APMS. Furthermore, the cross-sectional nature of the current study cannot provide any insight into the causal (or otherwise) relationship between multimorbidity and suicidality; further prospective studies testing this association are needed. Similar to the NPMS study limitations, the self-reported physical health conditions in APMS 2007 could be over or under-reported among the respondents. It should also be noted that the control group with neither physical nor CMDs may have had other somatic or mental health conditions that we did not control for in our analysis. Moreover, the severity of either physical or CMD which was not investigated in both the current and previous chapter, should be explored in future studies, as severity of either conditions may moderate the association between physical/mental multimorbidity and suicidality.

As noted earlier, replication is also required and caution is urged when interpreting the wide CIs in the multinomial logistic regression analyses. A further limitation of APMS was that items related to lifetime and past period suicidal behaviours were not measured through a suicide risk assessment scale but were measured through a clinical diagnostic instrument (CIS-R).

6.7 Conclusions

An increasing number of studies in suicide-related research has explored the risk factors that increase suicidality, specifically in regard to primary care patients. However, limited focus has been given to those having either a

physical or a mental disorder as an index condition, leaving populations who present with co-occurring somatic and psychiatric disorders, understudied. In the current analysis of a national mental health survey, we found elevated risk of suicidal ideation among participants identified as having physical/mental multimorbidity, compared to those without any of these conditions. Even though we additionally report a high risk of suicide attempts for multimorbid populations, due to the small number of attempt cases in APMS, those findings should be interpreted with caution. Whilst multimorbidity was associated with increased risk of suicidal behaviours, interestingly there was no additional risk over and above the separate effect of having either CMD or physical illness alone.

As multimorbidity affects all age groups, primary health care professionals should focus on people presenting with co-occurring physical and mental disorders, as they could exhibit high suicide risk compared to patients with single conditions (although their risk is no greater than those with CMD).

In terms of further studies, the impact of austerity upon populations with multimorbid conditions may additionally moderate the association of multimorbidity and suicidality and this should be considered. It should also be noted that it was not feasible to assess the impact of austerity in our study, as the survey was conducted before the global economic recession. Furthermore, while most of the previous studies on the role of physical illness in suicidality additionally adjust for mental illness in their analysis, it is likely that those with physical/mental multimorbidity being already indicated as a suicide risk group in those studies but not defined as such. Hence, in order to avoid similar methodological issues that overlook this specific study-population, well defined health groups of physical/mental multimorbidity, as indicated in the current study, should be investigated for suicide risk and compared to those with no such multimorbidity. Findings on the role of physical/mental multimorbidity in suicidality could help in formulating specific suicide risk assessments for this vulnerable population.

The present cross-sectional study contributes to the literature around the relationship between multimorbidity and suicidal behaviour, which, to date,

has not extensively investigated in the context of the co-occurrence of physical and mental health conditions. Based on the cross-sectional analyses of the current and previous chapter, a further dataset focusing on Scottish participants, was used in order to replicate the same study methodology and determine the role of multimorbidity in the risk of suicidal behaviours. Specifically, the following chapter aims to address the thesis' research questions, based on participants who took part in the West of Scotland Twenty-07 Cohort study (Twenty-07). Considering in addition, that multimorbidity increases within different age-groups (Sauver et al. 2015), its effect on suicidal behaviour across the lifespan should be investigated. Therefore, a prospective analysis aiming to provide evidence of whether multimorbidity predicts subsequent suicidal behaviours, was further conducted based on the Scottish follow-up study. Taking into account the limitation of employing cross-sectional analyses, which cannot help us determine causality between the physical/mental illness co-occurrence and risk of suicidal behaviours, we find that the longitudinal study design further employed, will address this limitation and demonstrate the predictability of multimorbidity in suicidality.

Hence, by employing both cross-sectional and prospective analyses, the following chapter on the Twenty-07 cohort participants, will help us appreciate the progress of suicidal thoughts and self-harming behaviours among vulnerable populations through the lifespan.

Chapter 7: The role of physical and mental health multimorbidity in suicidal thoughts and behaviours in a Scottish population cohort

Background

Longitudinal studies have been used to predict suicidal thoughts and behaviours as outcomes based on a variety of clinical and sociodemographic risk factors. However, studies of co-occurring physical and mental health disorders (multimorbidity) as possible risk factors for suicidality are relatively uncommon. The aim of the current study was to analyse longitudinal data and investigate within a population cohort: a) whether suicidal ideation and suicide attempts varied as a function of levels of physical/mental health multimorbidity, and b) whether physical/mental health multimorbidity predicted suicidal thoughts and behaviours as outcomes.

Methods

Data from the West of Scotland Twenty-07 prospective cohort study were analysed. Twenty-07 is a multiple cohort study following people from Greater Glasgow and the West of Scotland for 20 years, through five waves of data collection. Participants who responded to past-year suicidal thoughts and suicide attempt items in each wave were grouped into four distinct health-groups based on having: a) one or more physical health conditions, b) one or more mental health conditions, c) at least one physical plus one mental health condition (multimorbidity), and d) neither physical nor mental health conditions (control-group). The predictive role of multimorbidity in suicidality was tested with a generalised estimating equation (GEE) model and odds ratios (ORs) and 95% CIs are presented. Whether the effect of physical/mental multimorbidity was stronger than either of health conditions alone was also assessed.

Results

Within fully adjusted models multimorbidity had a significant effect on suicidal thoughts and suicide attempts, compared to the control-group. An increased risk was found for the mental health group and both indices of suicidality, but not for the physical health group. Multimorbidity was not found to increase the risk of suicidality, more than mental illness alone.

Limitations

The small number of suicide attempt cases resulted in wide CIs and precluded a number of adjusted prospective analyses.

Conclusions

In a representative sample of the Scottish population, we identified an effect of physical/mental multimorbidity on risk of suicidal thoughts and suicide attempts. Although this pattern of multimorbidity was associated with suicidality, it was not more strongly associated than for mental or physical health conditions alone. Future studies should employ a prospective analysis/design on the role of multimorbidity in suicidality, based on larger datasets.

7.1 Introduction

As previously discussed (see Chapters 5 & 6), mental and physical multimorbidity may confer increased risk of suicidal thoughts and behaviours within the general population. Based on our findings in Chapters 5 & 6, having co-occurring mental and physical health conditions increased risk of suicidal thoughts and attempts, when compared to those with neither condition. However, this risk was not significantly greater than the independent effect of common mental health conditions. Moreover, our findings related to the risk of suicide attempts must be interpreted with caution, given the wide 95% confidence intervals (CIs) and the small case numbers.

While the previous empirical studies within this thesis investigated the potential role of mental/physical multimorbidity in the risk of suicidality among British survey participants, the current chapter examines the presence of the same pattern of multimorbidity in a Scottish cohort study. Along with replicating the cross-sectional analyses of the previous thesis studies, we further aimed to investigate suicidal behaviours among multimorbid populations prospectively at different time-points. Hence, this chapter describes findings from both a cross-sectional and a longitudinal design.

7.1.1 Longitudinal studies on suicidal behaviours and suicide

A variety of study designs have been used to investigate risk factors that might increase suicidal behaviours and suicide, with most research employing a quantitative methodology (Mościcki, 2001; Mugisha, Knizek, Kinyanda, & Hjelmeland, 2011; WHO, 2014b). Cohort studies have been widely used, with a variety of studies yielding evidence for psychiatric disorder, marital status, adolescence, workplace bullying, smoking, and partner violence as key risk factors for suicidal behaviour (Devries et al., 2013; Junker, Bjørngaard, & Bjerkeset, 2017; Kposowoa, 2000; Large et al., 2016; Nielsen, Nielsen, Notelaers, & Einarsen, 2015; Scott, Pilkonis, Hipwell, Keenan, & Stepp, 2015).

Recently, Christiansen and colleagues (2014) reviewed and ranked studies of youth suicidal behaviour in terms of their level of evidence (LoE). The highest LoE for the risk of suicide and suicide attempts was found in cohort and large sample studies. Conversely, cross-sectional studies yielded the lowest LoE (Christiansen, Larsen, Agerbo, Bilenberg, & Stenager, 2014). The authors concluded that in order to provide evidence on causality, suicide-related studies should follow a clear longitudinal structure, based either on registries or on populations that have been repeatedly followed over time (Christiansen et al., 2014).

With research indicating that previous self-harming behaviours are strong predictors of future suicidal thoughts, attempts and suicide, a meta-analysis of longitudinal studies investigating prior and subsequent suicidal behaviours was performed by Ribeiro and colleagues (2016). Based on 172 longitudinal studies, the authors found that prior thoughts of self-injury and behaviours (SITB) were significant risk factors for future suicidal behaviour and suicide. More specifically, a history of suicide attempts and non-suicidal self-injury increased the risk of future suicide attempts, with previous suicidal thoughts and suicide attempts the strongest predictors of suicide deaths (Ribeiro et al. 2016). However, the effects of prior SITBs were weak, with Ribeiro and colleagues noting that prior self-injurious and suicidal behaviours cannot improve prediction of future suicidality beyond chance levels (Ribeiro et al., 2016).

Some cohort studies have been further meta-analysed, stratified by suicide risk categorisation (i.e., high versus low), aiming to distinguish high-risk and lower-risk patients based on their history of suicide attempts (Large et al., 2016). Unsurprisingly, Large and colleagues found a strong association between membership of a high-risk population (i.e., suicide attempt history) and death by suicide. However, the meta-analysis found that half of suicides were likely to occur in low-risk groups and the positive predictive value analysis suggested that 95% of those in the high-risk groups will not die by suicide. The authors concluded that despite the research progress on suicide studies, no satisfactory statistical model distinguishing high-risk and low-risk patients has so far been described (Large et al., 2016).

In recent decades, there has been growing interest in the relationship between bullying and suicidality. Indeed, a meta-analysis of cross-sectional and longitudinal studies investigating the relationship between bullying and suicide risk in young adult and adolescent populations has been conducted (Klomek, Sourander & Gould 2010). While the authors highlighted the lack of longitudinal research, the cross-sectional findings indicated an association between bullying and risk of suicidal ideation and attempts, with (the limited) longitudinal research confirming the association but finding that the relationship was moderated by sex (Klomek, Sourander & Gould 2010). Specifically, females who have been peer victimised were at risk of suicidality, whereas males who have been bullied were only at increased risk when psychopathology, like conduct disorder, was present (Klomek et al., 2010). The authors concluded that bullying in children and adolescents is clearly associated with suicidality and conduct disorder among males; they stressed the importance of addressing bullying in violence reduction and suicide prevention programmes (Klomek et al., 2010).

Psychopathology and a history of suicide attempts are among the strongest risk factors for suicide (Bertolote & Fleischmann, 2002; Hawton & Heeringen, 2009; Mościcki, 2001; O'Connor & Nock, 2014) although the risk of suicide varies as a function of type of psychopathology. For example, in a large Swedish cohort study following 39,685 patients discharged after a suicide attempt, Tidemalm et al. (2008) aimed to investigate the effect of specific mental disorders on the risk of suicide. In this 31 year follow-up study, schizophrenia or unipolar and bipolar disorder exhibited the highest suicide risk in the short-term (i.e., in the first year after being hospitalised for a suicide attempt) and across the entire follow-up period (Tidemalm et al. 2008). Although other psychiatric diagnoses (other depressive disorder, anxiety disorder, adjustment or post-traumatic stress disorder, alcohol abuse or dependence, drug abuse or dependence and personality disorder) were significantly associated with a risk of suicide, the risks were lower. Overall, this Swedish study highlighted that specific types of psychiatric diagnoses, alongside a suicide attempt hospitalisation, have a strong impact on the risk of future deaths by suicide (Tidemalm et al., 2008). Based on their findings,

Tidemalm and colleagues (2008) proposed that those with a suicide attempt history and who are diagnosed with schizophrenia or bipolar and unipolar disorders, especially within the first two years of a suicide attempt should receive a detailed care plan.

Few studies have explored the risk of suicidality of hospital-admitted patients, by grouping them in categories based on having either physical illness or psychiatric disorders (Junker, Bjørngaard & Bjerkeset 2017; Singhal et al. 2014). Exceptions include a retrospective cohort study using English hospital admission data on self-harm, for a period of 3 years, to determine the relative risk (RR) of self-harm and suicide for specific psychiatric and physical conditions (Singhal et al., 2014). Consistent with previous studies, the relative risk of self-harm among those with mental disorders (depression, bipolar disorder, alcohol abuse, anxiety disorders, eating disorders, schizophrenia and substance abuse) was increased, compared to patients who were admitted to hospital for other medical or surgical reasons (Singhal et al., 2014). An increased risk for self-harm was additionally found for those with epilepsy, asthma, migraine, psoriasis, diabetes mellitus, eczema and inflammatory polyarthropathies diagnoses; for suicide risk, all psychiatric conditions provided increased RRs, with only asthma, epilepsy, eczema and cancers among the physical conditions yielding moderately increased RRs, compared to the reference group (Singhal et al., 2014). In addition, Singhal and colleagues suggested that monitoring the mental distress component of those with physical conditions would improve the integration of psychiatric and primary care services for suicide prevention purposes (Singhal et al., 2014).

In contrast to the large numbers of longitudinal studies investigating the effect of mental illness on subsequent suicidal behaviours and suicide (Beckman et al. 2016; Cooper et al. 2005; Large et al. 2016), the effect of physical conditions per se on future suicidality has not been extensively investigated in cohort studies (Erlangsen, Stenager & Conwell 2015; Goodwin & Eaton 2005; Kam et al. 2015; Klaassen et al. 2015). However, a few cohort studies have found cancer, asthma and migraine to be predictive of future suicide (Breslau et al. 2012; Goodwin & Eaton 2005; Kam et al. 2015). When

focusing on the effect of physical illness on suicidality among older age populations, the oldest old (80 years and over) seem to have twice the risk of suicide, compared to the younger old (65-79 years of age). In the past decade, attention has also focused on the association of chronic pain conditions with suicidal behaviours and suicide (Hassett et al., 2014; Luntamo et al., 2014; Stenager, Christiansen, Handberg, & Jensen, 2014; Woolley, Fredman, Goethe, Lincoln, & Heeren, 2008). Overall, the evidence suggests that pain severity, psychiatric comorbidities (mainly depression and substance abuse), and type of pain condition are all associated with an increased suicide risk (Calati et al. 2015; Hassett, Aquino & Ilgen 2014).

7.2 Aim of current study

Although longitudinal studies have been used to predict suicidal behaviours from clinical and sociodemographic risk factors (Erlangsen, Stenager & Conwell 2015; Goodwin & Eaton 2005; Klaassen et al. 2015; Klomek, Sourander & Gould 2010; Singhal et al. 2014; Tidemalm et al. 2008), studies of physical and mental health co-occurrence as a risk factor for future suicidality are scarce. Given this gap in knowledge, the aim of the current study was to analyse longitudinal data from Scottish participants who have been followed up for 20 years and investigate, a) whether suicidal ideation and suicide attempts vary as a function of physical/mental multimorbidity, and b) whether physical/mental health multimorbidity predicts suicidal thoughts and behaviours. Specifically, we hypothesised that in comparison to those with no physical or mental health conditions, those with physical/mental health conditions would have: a) higher suicide risk (risk of suicidal thoughts and suicide attempts) at each follow up time-point (cross-sectional), and b) higher suicide risk over the course of the follow-ups (longitudinal).

7.3 Methods

7.3.1 Setting and participants

Secondary analyses of The West of Scotland Twenty-07 Cohort Study (Twenty-07). Twenty-07 was established in 1986 at the MRC Social and Public Health Sciences Unit, University of Glasgow (Benzeval et al. 2009). The aim of the twenty-07 was to follow study participants from the Central Clydeside Conurbation (Glasgow city and environs) across five waves and to investigate the progress of inequalities in health, based on the social factors of gender, age, marital status, social class and area of residence (Benzeval et al., 2008). Twenty-07 involves three cohorts 20 years apart (n=4,510) of participants born around 1932, 1952 and 1972. In the baseline study year (1987/88) participants were approximately 15, 35 and 55 years old. As presented in Figure 1, they were followed up at 1990/92 (Wave 2), at 1995/97 (Wave 3), at 2000/04 (Wave 4) and 2007/08 (Wave 5). Regional and locality samples were included: regional samples were collected by stratifying local districts by census data on socioeconomic groups and unemployment, along with 52 postcode sectors selected; locality samples were taken from postcode sectors from two areas in Glasgow (Benzeval et al., 2008). For both samples, an enhanced electoral register was used in order to select residents from target age groups. Further information on data collection, type of data and collecting process can be found here http://2007study.sphsu.mrc.ac.uk/.

7.3.2 Measures

The presence of long-standing chronic conditions was enquired about during interviews. Initially participants were asked: “Do you have any long-lasting illness, disability or infirmity? By long-standing I mean anything that has troubled you over a period of time or that is likely to affect you over a period of time?” As an additional prompt, show cards with common conditions were shown, for which they provided a yes/no reply (see Figure 2). Mental health conditions were specifically asked about: “Do you suffer from anxiety or depression, or do you have any mental problems, phobias, panics or nervous disorders which you haven't already told me about?”. A further question asked about doctor consultation, within the last 12 months. While all twenty-07 participants (regardless of whether they replied positively to the long-standing question) were asked about any type of prescribed or non-prescribed medication, those who had a chronic condition were further asked about any

medication taken for their condition. All the questions regarding long-standing illness and medication were repeated at each follow-up wave.

The data for all chronic conditions were cross-checked and after combining further information on medication use and verbatim responses, Katikireddi and colleagues computed variables for current health conditions, for each participant at each wave (Katikireddi et al. 2017). The derived variables of the physical health conditions computed by Katikireddi and colleagues were used in our analysis.

After data cleaning and coding, eight variables covering mental health conditions were computed by Katikireddi and colleagues (2017) and used in our study. The proportions of twenty-07 participants with physical and mental health conditions at baseline and at each follow-up wave are given in Table 1.

Questions about suicidal behaviours were asked at the first follow-up period (wave 2). Participants were asked: “Have you ever seriously thought about taking an overdose of drugs or injuring yourself deliberately?” Those replying yes were further asked: “Have you ever actually taken an overdose of drugs or injured yourself deliberately?” In the subsequent follow-up waves (3-5), participants were asked if they had suicidal thoughts and if they had attempted suicide since the last time they were contacted. Specifically, the questions were: “Since we last visited you in (last wave) have you ever seriously thought about taking an overdose of drugs or injuring yourself deliberately?” and "Since we last visited you in (last wave) have you ever actually taken an overdose of drugs or injured yourself deliberately?”. The following additional questions were asked regarding the specific date/year of their suicidal thoughts and suicide attempt, respectively:
“When was the last time you felt like that?” and “When was the last time that happened?”

As the physical and mental health conditions of participants were considered ‘as current’ at each wave, only suicidal behaviours within the past year were used in the present analyses. Based on the date of interview and the dates

given by the participants regarding their own suicidal thoughts and suicide attempts, “past year suicidal thoughts” and “past year suicide attempts” (Yes/No) were computed. Participants who reported suicidal thoughts and attempts within 12[2] months of their interview were considered as having suicidal thoughts/attempts within the past year. The items assessing suicidal thoughts and attempts were also combined to yield the derived variable of “past year suicidality”. Table 2 presents the number of twenty-07 participants reporting past year suicidal ideation, suicide attempts and suicidality for waves 2 to 5.

In order to explore if suicide risk varies as a function of physical/mental multimorbidity, participants were grouped into four mutually exclusive categories at each wave: those with (1) neither physical nor mental health condition (controls) (2) one or more physical health condition; (3) one or more mental health condition and; (4) multimorbidity. As in the previous NPMS 2000 and APMS 2007 analyses, multimorbidity was defined as the co-occurrence of at least one physical condition and at least one mental health condition. Since the suicidal behaviours items were introduced in wave 2, our analysis of the role of mental/physical multimorbidity in the risk of suicidal thoughts and suicide attempts is restricted to waves 2 to 5.

As previous studies indicate the significant effect of sociodemographic characteristics in the prediction of suicidal behaviour, a number of logistic regressions were adjusted for sociodemographic characteristics. After computing the categorical variables of marital status and education levels into the binary variables of “living conditions” (Yes/No) and “higher education” (Yes/No), respectively, the sociodemographic characteristics used in the current study were: age, marital status, education level and economic status. The sociodemographic characteristics of each health condition group and for all waves (1-5), are presented in Table 3.

7.3.3 Statistical analysis

[2] We used 366 days to compute all past year suicide-related variables.

7.3.3.1 Data preparation

The analyses of the twenty-07 cohort in this chapter, included a cross-sectional and a prospective design. While the original dataset (wide-version)[3] was used for the cross-sectional part, twenty-07 was further restructured and its long-version was used for the prospective analyses. All the statistical analysis was performed with the Statistical Package for Social Sciences SPSS version 24 (SPSS Inc., Chicago, IL, USA).

7.3.4 Cross-sectional analysis

The wide-version of twenty-07 was used for the cross-sectional analysis. A number of logistic regressions were run for each wave separately (waves 2 to 5), in order to investigate the relationship between suicidal thoughts, suicide attempts, suicidality and multimorbidity. The reference category for the regression analysis was those with "neither physical nor mental health conditions". Furthermore, the regressions were adjusted for the sociodemographic characteristics of: sex, age, living conditions, employment status, higher education, and social class. A series of binary logistic regression models were run for waves 2 to 5, in order to explore the interaction effect of physical and mental health conditions on every suicide-related outcome. Specifically, we investigated if the co-occurrence of physical and mental health conditions increases the risk of suicidal thoughts, suicide attempts and suicidality, more than having physical health or mental health conditions alone. The significance level was set at $p < 0.05$ and odd ratios (ORs) and 95% CIs were presented.

7.3.5 Prospective analysis

The long-version of the dataset was used for a longitudinal analysis using a generalised estimating equation (GEE) model. In the long version of the dataset repeated measurements over time are represented by separate

[3] As Wickham (2014) presents, in data-analysis the version of a dataset that includes its variables in columns, is usually referred to as a wide-version. When the dataset from a wide-version is restructured, and the columns are turned into rows, the version is called long.

observations and so tend to be correlated. The GEE model allows for these correlations. Hence, a GEE model, based on the repeated twenty-07 measurements of health conditions and suicide-related items, was used in order to investigate if multimorbidity, physical health conditions only, and mental health conditions only predict suicidal thoughts, suicide attempts and suicidality. The reference category for the GEE was those with "neither physical nor mental health conditions" and the effect sizes are presented through ORs and 95% CIs. Estimated marginal means are utilized to test for differences between multimorbidity and either physical or mental health conditions alone.

7.3.6 Missing data

As there were few missing data, regarding the dates reported for previous suicidal thoughts and behaviours, the computed items of "past year suicidal thoughts" and "past year suicide attempts", were expanded into three versions and sensitivity analyses were conducted. More specifically, in the main version (Table 2), when the dates of last having either suicidal thoughts or attempted suicide were missing, the derived variables of "past year suicidal thoughts" and "past year suicide attempts" did not include the cases with those missing replies. Within the sensitivity analysis and in the second version, all missing replies were treated as a past year suicidal behaviour (within 12 months of the interview). For the third version, missing replies were treated as taking place more than a year ago (more than 12 months since the interview). Appendix A (Tables 1 & 2) include the sensitivity analyses conducted based on the second and third modified versions.

Figure 7. 1 Twenty-07 sample and measurements for baseline and follow-up waves

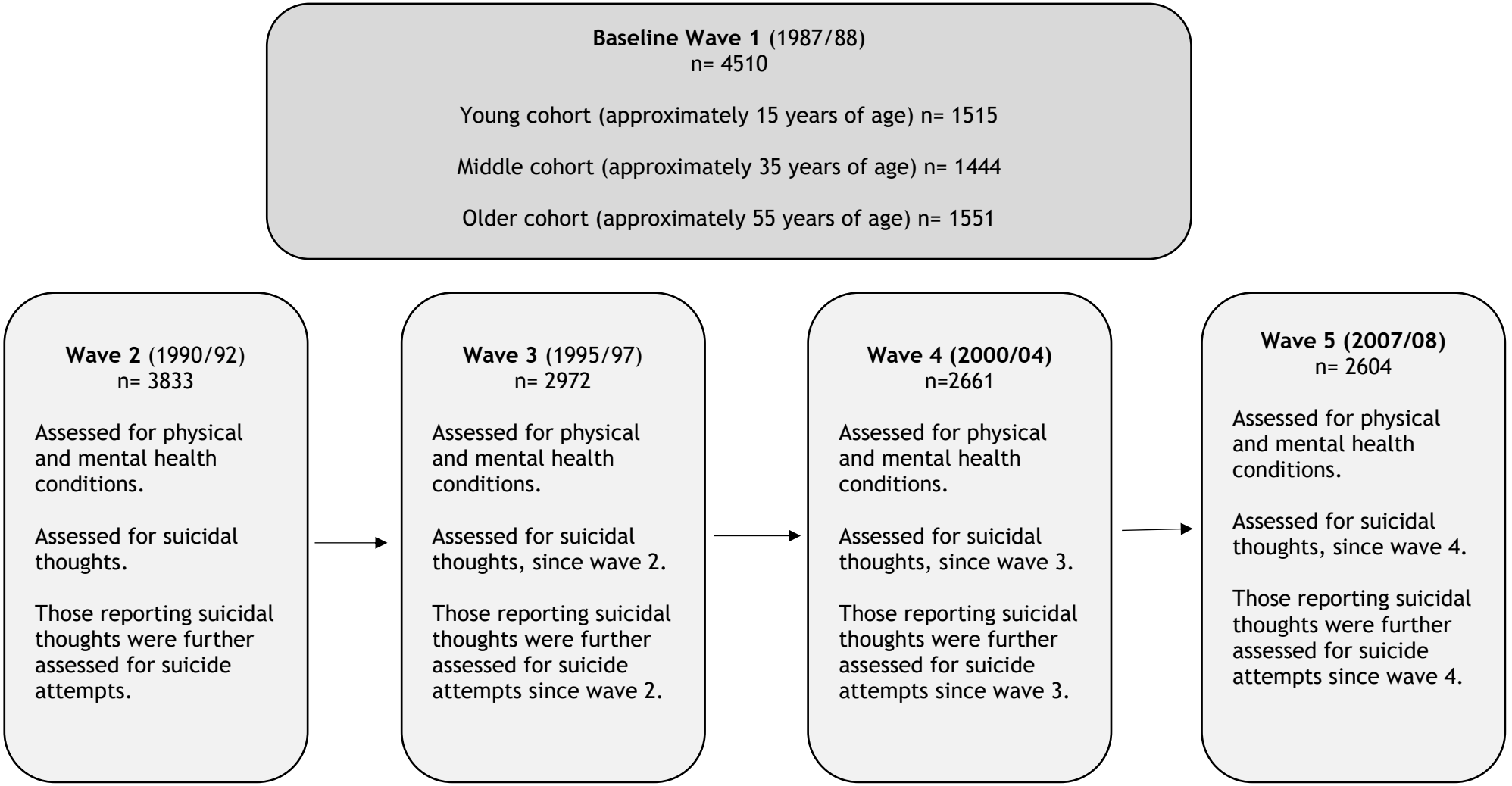


Figure 7. 2 List of common long-standing conditions presented to twenty-07 participants

- Bronchitis and respiratory disease
- Arthritis and rheumatism
- Cancer
- Asthma
- Stomach ulcers and gastric problems
- Gall bladder problems
- Hernias
- Epilepsy
- High blood pressure
- Angina
- Other heart trouble
- Stroke
- Circulatory problems e.g. 'hardening of the arteries'
- Liver problems
- Migraine
- Thyroid problems
- Diabetes
- Problems with the nervous system (e.g. Multiple Sclerosis or Parkinson's Disease)
- Spondylitis
- Sciatica
- Other back problems
- Colitis
- Diverticulitis
- Hay fever
- Sinusitis
- Anaemia
- Cystitis
- Other kidney, urinary or prostate problems
- Skin problems
- Allergy
- Tinnitus
- Other problems with ears or hearing
- Problems with eyes or sight
- Problems with alcohol
- Anxiety or depression

Table 7. 1 Proportion of twenty-07 participants with current physical and mental health conditions at each wave

Conditions	Baseline (n=4510) n (%)	Wave 2 (n=3833) n (%)	Wave 3 (n=2972) n (%)	Wave 4 (n=2661) n (%)	Wave 5 (n=2604) n (%)
Mental health conditions					
Alcohol	14 (0.3)	26 (0.7)	25 (0.8)	40 (1.5)	40 (1.5)
Drunkenness	1 (0)	2 (0.1)	-	1 (0)	1 (0)
Anorexia	2 (0)	3 (0.1)	3 (0.1)	3 (0.1)	2 (0.1)
Anxiety	152 (3.4)	226 (5.9)	201 (6.8)	199 (7.5)	310 (11.9)
Dementia	2 (0)	-	-	-	7 (0.3)
Depression	235 (5.2)	278 (7.3)	185 (6.2)	240 (9)	339 (13)
Learning disability	7 (0.2)	7 (0.2)	6 (0.2)	5 (0.2)	6 (0.2)
Schizophrenia	9 (0.2)	10 (0.3)	11 (0.4)	15 (0.6)	24 (0.9)
Substance abuse	3 (0.1)	3 (0.1)	5 (0.2)	5 (0.2)	7 (0.3)
Physical health conditions					
Asthma	160 (3.5)	158 (4.1)	156 (5.2)	181 (6.8)	190 (7.3)
Atrial	2 (0)	2 (0.1)	4 (0.1)	11 (0.4)	19 (0.7)
Blind	17 (0.4)	21 (0.5)	23 (0.8)	24 (0.9)	38 (1.5)
Bronchitis	3 (0.1)	2 (0.1)	2 (0.1)	3 (0.1)	3 (0.1)
Cancer	29 (0.6)	37 (1)	44 (1.5)	58 (2.2)	93 (3.6)
Coronary Heart Disease	141 (3.1)	171 (4.5)	172 (5.8)	181 (6.8)	213 (8.2)

Constipation	24 (0.5)	40 (1)	12 (0.4)	2 (0.1)	4 (0.2)
Chronic Obstructive Pulmonary Disease	48 (1.1)	49 (1.3)	45 (1.5)	40 (1.5)	66 (2.5)
Diabetes	41 (0.9)	48 (1.3)	64 (2.2)	99 (3.7)	156 (6)
Dyspepsia	200 (4.4)	191 (5)	130 (4.4)	135 (5.1)	145 (5.6)
Epilepsy	37 (0.8)	39 (!)	32 (1.1)	29 (1.1)	27 (1)
Glaucoma	11 (0.2)	13 (0.3)	18 (0.6)	22 (0.8)	41 (1.6)
Heart failure	11 (0.2)	12 (0.3)	10 (0.3)	13 (0.5)	25 (1)
Hepatitis	1 (0)	-	1 (0)	2 (0.1)	-
Hypertension	228 (5.1)	295 (7.7)	299 (10.1)	448 (16.8)	641 (24.6)
Inflammatory Bowel Disease (IBD)	20 (0.4)	22 (0.6)	23 (0.8)	27 (1)	31 (1.2)
Irritable Bowel Syndrome	19 (0.4)	39 (1)	59 (2)	64 (2.4)	73 (2.8)
Intestine	18 (0.4)	27 (0.7)	42 (1.4)	61 (2.3)	90 (3.5)
Kidney	3 (0.1)	4 (0.1)	7 (0.2)	4 (0.2)	17 (0.7)
Liver	3 (0.1)	4 (0.1)	2 (0.1)	6 (0.2)	11 (0.4)
Migraine	191 (4.2)	201 (5.2)	161 (5.4)	193 (7.3)	201 (7.7)
Multiple sclerosis	8 (0.2)	9 (0.2)	12 (0.4)	10 (0.4)	15 (0.6)
Parkinson	3 (0.1)	2 (0.1)	1 (0)	2 (0.1)	21 (0.8)
Prostate	13 (0.3)	28 (0.7)	34 (1.1)	42 (1.6)	52 (2)
Psoriasis	127 (2.8)	169 (4.4)	149 (5)	216 (8.1)	226 (8.7)
Sinusitis	7 (0.2)	11 (0.3)	16 (0.5)	9 (0.3)	16 (0.6)
Stroke	21 (0.5)	23 (0.6)	39 (1.3)	52 (2)	80 (3.1)

Thyroid	46 (1)	58 (1.5)	65 (2.2)	93 (3.5)	154 (5.9)
Vascular disease	30 (0.7)	46 (1.2)	55 (1.9)	78 (2.9)	103 (4)
Hearing problems	72 (1.6)	184 (4.8)	193 (6.5)	236 (8.9)	284 (10.9)
Inflammatory problems	40 (0.9)	86 (2.2)	66 (2.2)	88 (3.3)	116 (4.5)
Pain	700 (15.5)	821 (21.6)	785 (26.6)	777 (29.3)	875 (33.6)

Table 7. 2 Past year suicidal thoughts, suicide attempts and suicidality in Twenty-07 follow-up waves

	Suicidal thoughts* Yes/No	Suicide attempts* Yes/No	Suicidality* Yes/No
Wave 2	Yes = 41 / No = 2427	Yes = 5 / No = 2465	Yes = 42 / No = 2425
Wave 3	Yes = 37 / No = 2109	Yes = 9 / No = 2137	Yes = 38 / No = 2107
Wave 4	Yes = 49 / No = 2598	Yes = 7 / No = 2647	Yes = 49 / No = 2598
Wave 5	Yes = 56 / No = 2498	Yes = 9 / No = 2550	Yes = 54 / No = 2498

*Missing replies omitted.

Table 7. 3 Sociodemographic characteristics of twenty-07 participants with physical only, mental only, multimorbidity and neither physical nor mental health conditions, at follow-up waves 2-5

	Physical health conditions only	Mental health conditions only	Multimorbidity	Neither physical nor mental health conditions
Characteristics*	**Wave 2**			
Age M (SD)	49.6 (12.8)	30.8 (14.6)	50 (12.5)	30.4 (14.9)
Sex n (%)				
Male	643 (45.6%)	66 (33.5%)	125 (39.7%)	932 (48.8%)
Female	768 (54.4%)	131 (66.5%)	190 (60.3%)	978 (51.2%)
Marital status n (%)				
Never married	206 (14.6%)	119 (60.4%)	56 (17.8%)	1172 (61.4%)
Married	996 (70.7%)	53 (26.9%)	178 (56.5%)	625 (32.8%)
Divorced/separated	113 (8%)	21 (10.7%)	43 (13.7%)	78 (4.1%)
Widowed	93 (6.6%)	4 (2%)	38 (12.1%)	33 (1.7%)
Education level achieved[4] n (%)				
None	12 (10.6%)	11 (10.2%)	3 (13%)	86 (7.8%)
Standard education or equivalent	101 (89.4%)	97 (89.8%)	20 (87%)	1011 (92%)

[4] The item related to the level of education achieved at each follow-up, refers to the period from last wave until the current one questioned

Higher education	-	-	-	2 (0.2%)
Economic status n (%)				
Not in the labour force	388 (27.9%)	62 (31.8%)	90 (29.5%)	534 (28.1%)
Employed	757 (54.5%)	91 (46.7%)	103 (33.8%)	1156 (60.8%)
Unemployed	90 (6.5%)	31 (15.9%)	37 (12.1%)	201 (10.6%)
Not working on account of illness/disability	155 (11.2%)	11 (5.6%)	75 (24.6%)	9 (0.5%)
	Wave 3			
Age M (SD)	54.8 (12.1)	38.5 (14.6)	55.7 (11.7)	37.5 (14.5)
Sex n (%)				
Male	582 (43.9%)	39 (37.9%)	98 (34.9%)	606 (48%0
Female	744 (56.1%)	64 (62.1%)	183 (65.1%)	656 (52%)
Marital status n (%)				
Never married	213 (20.9%)	32 (36.8%)	57 (21.6%)	362 (46.4%)
Married	649 (63.8%)	39 (44.8%)	142 (53.8%)	357 (45.7%)
Divorced/separated	75 (7.4%)	14 (16.1%)	29 (11%)	39 (5%)
Widowed	80 (7.9%)	2 (2.3%)	36 (13.6%)	23 (2.9%)
Education level achieved n (%)				

None	-	-	-	-
Standard education or equivalent	160 (46%)	23 (51.1%)	36 (48.6%)	195 (41.1%)
Higher education	188 (54%)	22 (48.9%)	38 (51.4%)	280 (58.9%)
Economic status n (%)				
Not in the labour force	521 (40.5%)	19 (19.4%)	87 (32.2%)	256 (20.7%)
Employed	595 (46.3%)	57 (58.2%)	101 (37.4%)	915 (74%)
Unemployed	58 (4.5%)	11 (11.2%)	19 (7%)	49 (4%)
Not working on account of illness/disability	111 (8.6%)	11 (11.2%)	63 (23.3%)	17 (1.4%)
	Wave 4			
Age M (SD)	59.1 (11.9)	41.9 (14.1)	58.5 (11.7)	42.3 (14.1)
Sex n (%)				
Male	618 (45%)	41 (39%)	119 (34.8%)	420 (49.9%)
Female	755 (55%)	64 (61%)	223 (65.2%)	421 (50.1%)
Marital status n (%)				
Never married	209 (15.3%)	40 (38.1%)	69 (20.4%)	273 (32.9%)
Married	896 (65.7%)	54 (51.4%)	172 (50.7%)	480 (57.9%)
Divorced/separated	102 (7.5%)	7 (6.7%)	54 (15.9%)	52 (6.3%)
Widowed	157 (11.5%)	4 (3.8%)	44 (13%)	24 (2.9%)

Education level achieved n (%)				
None	64 (26%)	20 (33.9%)	21 (26.9%)	81 (20.4%)
Standard education or equivalent	62 (25.2%)	21 (35.6%)	23 (29.5%)	105 (26.4%)
Higher education	120 (48.8%)	18 (30.5%)	34 (43.6%)	212 (53.3%)
Economic status n (%)				
Not in the labour force	619 (45.5%)	14 (13.7%)	136 (40.5%)	110 (13.3%)
Employed	668 (49.2%)	73 (71.6%)	136 (40.5%)	680 (82.3%)
Unemployed	31 (2.3%)	4 (3.9%)	14 (4.2%)	30 (3.6%)
Not working on account of illness/disability	41 (3%)	11 (10.8%)	50 (14.9%)	6 (0.7%)
	Wave 5			
Age M (SD)	64.2 (12.7)	48 (13.5)	63.4 (12.5)	47.9 (13.7)
Sex n (%)				
Male	596 (43.9%)	44 (40.4%)	183 (37.7%)	337 (51.7%)
Female	762 (56.1%)	65 (59.6%)	302 (62.3%)	315 (48.3%)
Marital status n (%)				
Never married	174 (12.8%)	34 (31.5%)	107 (22.1%)	139 (21.5%)
Married	859 (63.3%)	52 (48.1%)	219 (45.2%)	422 (65.3%)
Divorced/separated	131 (9.7%)	19 (17.6%)	80 (16.5%)	61 (9.4%)
Widowed	192 (14.2%)	3 (2.8%)	78 (16.1%)	24 (3.7%)

Education level achieved n (%)				
None	277 (21.7%)	17 (16%)	152 (33.5%)	61 (10%)
Standard education or equivalent	539 (42.3%)	60 (56.6%)	164 (36.1%)	226 (37.1%)
Higher education	459 (36%)	29 (27.4%)	138 (30.4%)	322 (52.9%)
Economic status n (%)				
Not in the labour force	559 (42%)	12 (12%)	186 (39.7%)	70 (11.2%)
Employed	711 (53.4%)	68 (68%)	177 (37.7%)	544 (86.9%)
Unemployed	18 (1.4%)	12 (12%)	20 (4.3%)	9 (1.4%)
Not working on account of illness/disability	43 (3.2%)	8 (8%)	86 (18.3%)	3 (0.5%)

* percent (%) is based on the omission of missing values

7.4 Results

7.4.1 Demographic characteristics and suicidality of participants with multimorbidity across waves

As presented in Table 3, half of the multimorbidity group in each wave were female and most of the participants in this group were married. While in waves 2 and 3 a considerable proportion of those with multimorbidity were employed (34% and 37.5% respectively), at waves 4 and 5 around 40% of those with multimorbidity were not in the labour force, partly due to members of the older cohorts being retired by the last follow-up periods (Table 3). In terms of education level, the highest level of education of those with multimorbidity issues was achieved by waves 3 and 4.

With regard to suicidality, the largest proportion of participants having thoughts about suicide were those identified as multimorbid. More specifically, people with multimorbidity accounted for 53.7% of those reporting suicidal thoughts at wave 2, 62.2% of those having past year suicidal thoughts at wave 3, 63.3% of those in wave 4 and 66.1% of those in wave 5. For past year suicide attempts overall, the number of cases was low, with 5 people reporting suicide attempts at wave 2, 9 participants at wave 3, 7 participants at wave 4 and 9 participants at wave 5.

7.4.2 Cross-sectional results

7.4.2.1 Unadjusted analyses of the relationship between health groups, suicidal thoughts, suicide attempts and suicidality

Three separate unadjusted logistic regression analyses were performed for the health groupings and past year suicide-related items for all waves (Table 4). The unadjusted model for suicidal thoughts showed that participants with multimorbidity were more likely to experience past year suicidal thoughts compared to those with neither physical nor mental health conditions, at all waves (wave 2: OR= 16.29; 95% CI, 5.56-47.71, $p<0.001$; wave 3: OR= 12.34;

95% CI, 4.96-30.67, *p<0.001*; wave 4: OR= 27.91; 95% CI, 8.47-91.96, *p<0.001*; wave 5: OR= 52.70; 95% CI, 7.20-385.54, *p<0.001*). A similar pattern of findings was found for suicidality (Table 4); the unadjusted model for suicide attempts indicated that those with multimorbidity at wave 4 had significantly increased odds ratios, compared to the control group (OR= 9.88; 95% CI, 1.10-88.73, *p=0.041*). Due to the small number of suicide attempt cases, a regression analysis could not be performed for waves 2,3 and 5.

For the rest of the health groups, those with only mental health conditions were also more likely to experience past year suicidal thoughts, compared to those with neither physical nor mental health conditions (wave 2: OR= 14.39; 95% CI, 3.96-51.87, *p<0.001*; wave 3: OR= 9.54; 95% CI, 3.00-30.27, *p<0.001*; wave 4: OR= 23.60; 95% CI, 6.15-90.49, *p<0.001*; wave 5: OR= 79.27; 95% CI, 10.19-616.73, *p<0.001*). Although at waves 3 and 4 significance was found between suicide attempts and the mental health group, due to the small numbers and wide CIs, caution is urged when interpreting these findings (wave 3: OR= 6.08, 95% CI, 1.00-36.93, *p=0.05;* wave 4: OR= 16.21, 95% CI, 1.45-180.37, *p=0.023*). Having physical health conditions was not associated with suicidal thoughts and behaviour in any wave (Table 4).

7.4.2.2 Adjusted analyses for sociodemographic characteristics

Following adjustment for the sociodemographic characteristics of sex, age, living conditions, education level, employment status and current social class, the presence of physical/mental multimorbidity remained significantly associated with suicidal thoughts at all follow-up periods, with waves 2 and 5 providing reduced effect sizes (wave 2: OR= 12.97; 95% CI, 3.94-42.73, *p<0.001*; wave 3: OR= 17.80; 95% CI, 5.81-54.52, *p<0.001*; wave 4: OR= 33.69; 95% CI, 9.46-119.92, *p<0.001*; wave 5: OR= 19.20; 95% CI, 2.35-156.37, *p=0.006*) and suicidality (wave 2: OR= 13.20; 95% CI, 4.01-43.43, *p<0.001*; wave 3: OR= 18.39; 95% CI, 6.02-56.19, *p<0.001*; wave 4: OR= 33.69; 95% CI, 9.46-119.92, *p<0.001*; wave 5: OR= 17.46; 95% CI, 2.11-143.99, *p=0.008*). Due to small numbers of cases for past year attempts, adjusted analyses could not be performed. Furthermore, in respect of the other health groups, while having only mental health conditions was associated with suicidal thoughts

and suicidality (Table 5), no significance was found for the role of physical health conditions in any suicide-related item.

Unadjusted and adjusted logistic regressions were additionally conducted based on the sensitivity analyses. Results indicated the same significant association of both multimorbidity and mental health conditions with suicidal thoughts, while physical health conditions were not associated with any suicide-related outcome (Appendix A, Tables 3 – 6). Due to the small of suicide attempts, no adjusted analyses could be performed.

7.4.2.3 The interaction effect of physical and mental health co-occurrence on suicidal thoughts, suicide attempts and suicidality

In order to investigate the role of multimorbidity in suicidality not only compared to the reference group (neither physical nor mental health conditions) but to the other health categories (physical health conditions only; mental health conditions only), the interaction effect of physical and mental health conditions on suicidality was investigated through two separate logistic regression models for each wave. Past year suicidal thoughts and suicide attempts were set as the outcome variables. As presented in Table 6, only mental health conditions had an effect on suicidal thoughts, in all waves analysed, with no significance found with physical health conditions. Having both physical and mental health conditions (multimorbidity) did not increase risk of suicidal thoughts more than having mental health conditions alone, in any wave.

Due to the small number of suicide attempt cases, only wave 3 was analysed with past year suicide attempts as outcome variable; while only mental illness was associated with suicide attempts, but not physical illness (mental health conditions: *b*=2.07, SE= 0.689, OR= 7.93, *p=0.003*; physical health conditions: *b*=-0.97, SE= 0.690, OR= 0.37, *p*= 0.156), after testing for the effect of mental/physical interaction, a borderline significance was found and mental illness proved to have a stronger effect on suicidal behaviour than physical/mental multimorbidity (mental health conditions: *b*=1.80, SE= 0.920, OR= 6.08, *p=0.05*; physical health conditions: *b*=-1.36, SE= 1.156, OR= 0.25,

p=0.236; mental health conditions*physical health conditions: *b*=-0.65, SE= 1.478, OR= 1.92, *p*=0.657).

Table 7. 4 Unadjusted logistic regression investigating the relationship of past year suicidal thoughts, suicide attempts and suicidality with health groupings among twenty-07 participants

	Suicidal thoughts				**Suicide attempts**				**Suicidality**			
	n	**OR**	**95% CI**	***p***	**n**	**OR**	**95% CI**	***p***	**n**	**OR**	**95% CI**	***p***
Neither physical nor mental												
Wave 2	4	1 (ref)	-	-	-	1 (ref)	-	-	4	1 (ref)	-	-
Wave 3	6	1 (ref)	-	-	3	1 (ref)	-	-	6	1 (ref)	-	-
Wave 4	3	1 (ref)	-	-	1	1 (ref)	-	-	3	1 (ref)	-	-
Wave 5	1	1 (ref)	-	-	-	1 (ref)	-	-	1	1 (ref)	-	-
One or more physical condition												
Wave 2	9	1.394	0.428-4.540	0.582	1	-	-	-	9	1.395	0.428-4.544	0.581
Wave 3	2	0.254	0.051-1.262	0.094	1	0.255	0.026-2.452	0.236	3	0.382	0.095-1.530	0.174
Wave 4	7	1.423	0.367-5.519	0.610	-	-	-	-	7	1.423	0.367-5.519	0.610
Wave 5	6	2.766	0.332-23.025	0.347	-	-	-	-	6	2.766	0.332-23.025	0.347
One or more mental condition												
Wave 2	6	**14.349**	3.969-51.878	<0.001	2	**-**	-	-	7	**16.945**	4.858-59.105	<0.001
Wave 3	6	**9.543**	3.008-30.275	<0.001	2	**6.086**	1.003-36.936	0.050	6	**9.543**	3.008-30.275	<0.001
Wave 4	8	**23.603**	6.156-90.495	<0.001	2	**16.214**	1.457-180.371	0.023	8	**23.603**	6.156-90.495	<0.001
Wave 5	12	**79.277**	10.190-616.734	<0.001	3	**-**	-	-	12	**79.277**	10.190-616.734	<0.001
Multimorbidity[a]												
Wave 2	22	**16.295**	5.565-47.711	<0.001	2	**-**	-	-	22	**16.295**	5.565-47.711	<0.001
Wave 3	23	**12.347**	4.969-30.675	<0.001	3	2.985	0.599-14.879	0.182	23	**12.347**	4.969-30.675	<0.001
Wave 4	31	**27.913**	8.473-91.962	<0.001	4	**9.882**	1.100-88.733	0.041	31	**27.913**	8.473-91.962	<0.001
Wave 5	37	**52.700**	7.203-385.543	<0.001	6	**-**	-	-	35	**49.851**	6.804-365.246	<0.001

[a] One or more mental and one or more physical illness in the same person

Table 7. 5 Adjusted logistic regression analyses for sociodemographic characteristics, investigating the relationship of past year suicidal thoughts and suicidality with physical and mental health conditions among twenty-07 participants

	Suicidal thoughts[1]			**Suicidality**[1]		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***
Neither physical nor mental						
Wave 2	1 (ref)	-	-	1 (ref)	-	-
Wave 3	1 (ref)	-	-	1 (ref)	-	-
Wave 4	1 (ref)	-	-	1 (ref)	-	-
Wave 5	1 (ref)	-	-	1 (ref)	-	-
One or more physical illness						
Wave 2	1.232	0.338-4.493	0.752	1.245	0.342-4.534	0.740
Wave 3	0.275	0.032-2.393	0.242	0.563	0.107-2.955	0.497
Wave 4	1.917	0.423-8.689	0.399	1.917	0.423-8.689	0.399
Wave 5	2.241	0.230-21.852	0.488	2.212	0.227-21.583	0.495
One or more mental						
Wave 2	**7.431**	1,589-34.743	0.011	**10.239**	2.439-42.990	0.001
Wave 3	**7.825**	1.775-34.498	0.007	**7.912**	1.792-34.927	0.006
Wave 4	**19.137**	4.695-78.003	<0.001	**19.137**	4.695-78.003	<0.001
Wave 5	**53.822**	6.560-441.577	<0.001	**54.700**	6.678-448.041	<0.001

Multimorbidity[a]						
Wave b	**12.978**	3.941-42.736	<0.001	**13.205**	4.015-43.431	<0.001
Wave c	**17.802**	5.812-54.529	<0.001	**18.395**	6.021-56.196	<0.001
Wave d	**33.693**	9.466-119.929	<0.001	**33.693**	9.466-119.929	<0.001
Wave e	**19.207**	2.359-156.378	0.006	**17.468**	2.119-143.997	0.008

[1] Adjusted for sociodemographic characteristics: sex, age, living conditions, employment status, any standard/high educational qualification, social class
[a] One or more mental and one or more physical illness in the same person

Table 7. 6 The interaction effect of current physical and mental health conditions on past year suicidal thoughts among the twenty-07 cohort study participants

	Wave 2			Wave 3			Wave 4			Wave 5		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Before the interaction effect analysis												
Physical health conditions only	1.231	0.590-2.571	0.579	0.831	0.403-1.714	0.616	1.244	0.619-2.498	0.540	0.810	0.422-1.553	0.525
Mental health conditions only	**12.376**	**6.305-24.292**	**<0.001**	**20.916**	**9.351-46.783**	**<0.001**	**20.674**	**10.179-41.991**	**<0.001**	**26.781**	**11.987-59.833**	**<0.001**
After the interaction effect analysis												
Physical health conditions only	1.394	0.428-4.540	0.582	0.254	0.051-1.262	0.094	1.423	0.367-5.519	0.610	2.766	0.332-23.025	0.347
Mental health conditions only	**14.349**	**3.969-51.878**	**<0.001**	**9.543**	**3.008-30.275**	**<0.001**	**23.603**	**6.156-90.495**	**<0.001**	**79.277**	**10.190-616.734**	**<0.001**
Physical health conditions*Mental health conditions	0.815	0.181-3.677	0.790	5.091	0.797-32.537	0.085	0.831	0.171-4.031	0.818	0.240	0.026-2.231	0.210

7.4.3 Prospective results

7.4.3.1 Generalised estimating equation analyses of the predictive role of physical/mental multimorbidity in the risk of suicidality

Three separate generalised estimating equation (GEE) models were used in order to investigate the role of health groupings (multimorbidity, physical health conditions only, mental health conditions only) in the prediction of suicidal thoughts, suicide attempts and suicidality (Table 7). The GEE analysis included the health groupings and suicide-related items reported for waves 2 to 5. Multimorbidity had a significant association with all the suicidality indices investigated (suicidal thoughts: OR= 16.40, 95% 9.57-28.11, p<0.001; suicide attempts: OR= 8.27, 95% 2.73-25.06, p<0.001; suicidality: OR= 16.10, 95% 9.39-27.61, p<0.001).

While having physical health conditions was not associated with any suicide-related item (Table 7), having a mental health condition was a significant predictor of suicidal thoughts, suicide attempts and suicidality, compared to having neither physical nor mental health conditions (OR= 17.48, 95% 9.32-32.77, p<0.001; OR= 17.59, 95% 4.80-64.40, p<0.001; OR= 17.95, 95% 9.61-33.53, p<0.001, respectively).

7.4.3.2 Adjusted generalised estimating equation analyses of the predictive role of multimorbidity in suicidality

After adjustment for the sociodemographic characteristics of sex, age, living conditions, education level, employment status and social class, multimorbidity remained significantly associated with all suicide-related items (suicidal thoughts: (OR= 17.20, 95% 8.81-33.60, p<0.001; suicide attempts: (OR= 5.77, 95% 1.42-23.38, p<0.001; suicidality: (OR= 17.13, 95% 8.77-33.47, p<0.001). Although having only mental health conditions was additionally associated with suicidal thoughts, suicide attempts and suicidality (Table 8), the role of physical health conditions was not to found to be predictive of either suicide-related item.

7.4.3.3 The effect of physical/mental health multimorbidity in suicidality

In order to test whether the effect of physical/mental multimorbidity is stronger than either of the health conditions alone, we performed pairwise comparisons between multimorbidity, mental health conditions only, physical health conditions only and controls, using estimated marginal means. Our analyses on the 20 year follow-up period of twenty-07, indicated that multimorbidity does not increase the risk of suicidality, more than mental illness alone (suicidal thoughts p= 0.776; suicide attempts p=0.136).

Table 7. 7 Generalised estimating equation model on the predictive role of multimorbidity, physical and mental health conditions in the risk of suicidality among twenty-07 participants

	Suicidal thoughts			Suicide attempts			Suicidality		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Neither physical nor mental conditions	1 (ref)	-	-	1 (ref)	-	-	1 (ref)	-	-
Physical conditions only	0.987	0.534-1.826	0.967	0.309	0.058-1.644	0.169	1.030	0.559-1.898	0.923
Mental conditions only	**17.482**	9.324-32.778	<0.001	**17.593**	4.805-64.409	<0.001	**17.953**	9.612-33.534	<0.001
Multimorbidity [a]	**16.407**	9.574-28.116	<0.001	**8.279**	2.735-25.060	<0.001	**16.103**	9.392-27.611	<0.001

[a]One or more mental and one or more physical illness in the same person

Table 7. 8 Adjusted generalised estimating equation model on the predictive role of multimorbidity, physical and mental health conditions in the risk of suicidality among twenty-07 participants

	Suicidal thoughts[1]			Suicide attempts[1]			Suicidality[1]		
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Neither physical nor mental conditions	1 (ref)	-	-	1 (ref)	-	-	1 (ref)	-	-
Physical conditions only	1.172	0.551-2.497	0.680	0.364	0.039-3.417	0.377	1.264	0.599-2.668	0.538
Mental conditions only	**15.268**	7.389-31.550	<0.001	**14.187**	3.671-54.830	<0.001	**16.098**	7.844-33.039	<0.001
Multimorbidity [a]	**17.209**	8.814-33.603	<0.001	**5.776**	1.427-23.383	0.014	**17.135**	8.772-33.473	<0.001

[1] Adjusted for sociodemographic characteristics: sex, age, living conditions, any standard/high educational qualification, employment status, current social class

[a] One or more mental and one or more physical illness in the same person

7.5 Discussion

The West of Scotland Twenty-07 cohort study was analysed, in order to investigate if having at least one physical health plus one mental health condition (physical/mental multimorbidity) increases the risk of suicidal thoughts and behaviours, compared to having neither physical nor mental health issues. Our results indicated that having co-occurring physical and mental health conditions increases the risk of suicidality; specifically, we found that those with physical/mental health multimorbidity are more likely to have suicidal thoughts and attempt suicide, compared to people with neither physical nor mental health conditions. Furthermore, our findings indicated that physical/mental multimorbidity could be potentially used as a predictor of suicidal thoughts and behaviours. As the small number of cases of suicide attempts constrained our analyses (Table 4), the current findings mainly relate to the predictive role of multimorbidity on suicidal thoughts. Moreover, multimorbidity did not have a stronger effect than mental or physical health conditions alone; interestingly, physical health conditions were not associated with any suicide-related item. Overall, our findings suggest that the significant effect of multimorbidity on suicidality is predominantly driven by mental illness.

The current results, which are consistent in all of the twenty-07 waves analysed, confirm our earlier findings on the role of multimorbidity in suicidal thoughts and behaviours, among the participants of two British psychiatric morbidity surveys (Chapters 5 & 6). Specifically, in the National Psychiatric Morbidity Survey of 2000 (NPMS; Chapter 5), those with physical/mental multimorbidity were more likely to have past year suicidal thoughts (OR= 6.30, 95% CI, 4.45-8.92, p<0.001) and suicide attempts (OR= 4.02, 95% CI, 1.67-9.67, p=0.002), compared to those with neither of the health conditions investigated. Similarly, in the subsequent psychiatric morbidity survey of 2007, the Adult Psychiatric Morbidity Survey (APMS), multimorbidity was significantly associated with suicidal thoughts (OR= 15.63, 95% CI, 9.27-26.34, *p<0.01*) and suicide attempts (OR= 23.16, 95% CI, 3.06- 175.00, *p*=0.002), compared to the controls.

As reported earlier, the relationship between suicidality and multimorbidity, characterised by the co-presence of mental and physical illness, has not been extensively investigated in the wider literature (Chapter 3). One of the most relevant studies on the risk of suicidality among populations with health conditions (which has been extensively discussed in this thesis) indicated that the co-existence of a mental and a physical illness diagnosis, regardless of which one is given first, is a significant risk factor for suicide (Qin et al., 2014). These authors reported that the temporality of conditions is additionally important in clinical settings, as a psychiatric diagnosis coming years after a somatic condition provides higher risk of suicide, than having a somatic condition developed after a psychiatric diagnosis. Although our results are in accordance with the finding that the risk of suicidality is increased due to physical/mental multimorbidity, it was not feasible to investigate the onset of health conditions in our twenty-07 dataset and further exploration of the condition-timing is required.

While previous evidence on the role of multimorbidity is mainly about the risk of suicide attempts and deaths by suicide (Qin et al., 2014; Webb et al., 2012b), our findings shed more light on the risk of suicidal thoughts for those with multimorbidity issues and confirm previous findings. Based on previous research, a US study indicated that when pulmonary disease co-occurs with depression, the risk of suicidal thoughts is higher than having neither of the under-studied health conditions (Goodwin 2011); however, the same study further indicated that the risk of suicidal thoughts for pulmonary disease and depression co-occurrence is higher, compared to having either pulmonary disease or depression alone. Moreover, a Canadian population-based study found that among pain conditions (back problems, migraine, arthritis, fibromyalgia) only migraine co-occurring with multiple mental health conditions (3 or more) was the condition significantly associated with suicidal ideation (Goodwin, 2011; Ratcliffe et al., 2008).

In terms of the association of physical/mental health co-occurrence and the risk of suicide attempts, Fuller-Thomson and colleagues (2016) highlighted that among other factors (childhood adversities, current pain), those with arthritis, lifetime depression, anxiety or substance dependency have higher

odds of suicide attempts, compared to those without arthritis. However, as presented earlier, the small numbers of suicide attempts in twenty-07 limited our adjusted analyses and we cannot similarly suggest an association of the outcomes of interest, due to the wide CIs found.

Since there are limited studies on the effect of physical/mental multimorbidity in the risk of suicidality (Chapter 3), the lack of prospective studies is not surprising. With few exceptions, the majority of suicide-related cohort studies have investigated the predictive role of mental illness (Cooper et al. 2005; Crump et al. 2014; Large et al. 2016). A US study based on the Baltimore Epidemiologic Catchment Area follow-up, which included both a cross-sectional and longitudinal design similar to our study, aimed to investigate if asthma is associated with suicidal thoughts and behaviour and whether this health condition could be used as a predictor of suicidality (Goodwin & Eaton 2005). The associations between asthma and suicidal thoughts and attempts were significant, and when the authors included lifetime depression in their adjusted analyses, the association remained significant for suicidal thoughts (OR= 9.93, CI 95%: 6.37-14.27, $p<0.05$) and attempts (OR= 9.78, CI 95%: 5.9-16.21, $p<0.05$) in the following wave. Taking into account that lifetime depression did not reduce the predictive association of asthma with either suicidal thoughts or suicide attempts, the authors concluded that depression is not a key factor in the asthma-suicidality link (Goodwin & Eaton, 2005). Considering that the aim of our study did not include the investigation of specific physical or mental health conditions similarly with Goodwin and colleagues, further prospective studies should focus on the predictive role of depression in the physical illness-suicidality association.

Overall, our findings on the risk suicidality in multimorbid populations could be potentially related to the burden of multiple diseases that affect both physical and mental health. Although the co-existence of physical and mental illness is relatively prevalent, and it has an effect on mortality outcomes (Doherty & Gaughran, 2014; Martin et al., 2014; Osborn et al., 2018; Smith et al., 2014; Smith et al., 2013), it is not yet clear how the co-occurrence of these health conditions influences suicidal thinking and related behaviour. As

suggested earlier (Chapter 5; O'Connor, 2003; O'Connor and Nock, 2014), investigating feelings of entrapment in a stressful situation related to coping with multiple physical and mental health conditions, would help us understand the progress of suicidal thoughts in these vulnerable populations. Even though our findings on the risk of suicide attempts are weak due to the small numbers, further exploration is required to investigate whether having access to multiple medications, is a factor influencing the development of suicidal plans and behaviours.

It is evident in the literature that mental illness has a strong relationship with suicide-related outcomes and often its effect has been found to mediate the link between physical illness and suicidality (Hawton et al., 2013; O'Connor & Nock, 2014; Webb et al., 2012b). For the twenty-07 participants, mental health conditions were indeed associated with suicidal thoughts and behaviours and were found to be significant predictors of subsequent suicidality. Physical illness however, did not have any association with any of the suicidality outcomes explored. There are contradictory findings in the medical illness-suicidality literature, with some studies indicating a direct link of somatic illness with suicide-related outcomes and other findings presenting the mediating effect of psychiatric illness in this link (Pompili et al., 2016). Although our findings do not confirm a significant association of having only physical health conditions with risk of suicidality, potentially due to the small numbers found, further exploration is required based on larger datasets, like administrative health registries. Considering that the severity of physical health issues was not assessed in twenty-07, future studies should additionally investigate if the severity of a physical health condition differentiates risk of suicidality.

In regard to the second research question of this thesis, if physical/mental co-occurrence increases the risk of suicidal behaviours more than either condition alone, the interactive and separate effect of physical and mental health conditions in suicidality were investigated. The cross-sectional findings indicated that multimorbidity does not increase the risk of suicidality over and above mental illness alone. Consistent with all our cross-sectional findings on mental illness being a stronger factor than multimorbidity, our

longitudinal analyses additionally highlighted that multimorbidity is not a stronger predictor of suicidality, than mental illness alone. Taken together, our findings underline that physical and mental health conditions do not work additively in increasing the risk of suicidality. The work of Qin and colleagues (2014) presented earlier in this chapter, additionally indicated that mental illness alone provides a higher risk of suicide, than having physical/mental multimorbidity. However, in their study the comparison was made between those with mental illness and those with a specific onset of co-occurring conditions (developing a physical illness after a psychiatric diagnosis). As it was not feasible to investigate the temporality of health conditions in our study, further prospective studies investigating the risk of either suicidal thoughts, suicide attempts or suicide among multimorbid groups, should address the onset of physical and mental health conditions, as it can differentiate suicide risk.

7.6 Strengths and limitations

One of the major strengths of the current study is the use of longitudinal data that can advance our knowledge of the relationship between physical/mental health conditions and suicidality, over time. Considering the lack of longitudinal studies of suicidality in general population samples of people experiencing physical/mental illness co-occurrence, the twenty-07 cohort study is providing further evidence of this longitudinal association.

The results of the twenty-07 cohort should be viewed through its limitations. Consistent with the previous empirical studies' limitations, the secondary analysis of cross-sectional data must be noted, while attention should be given to the fact that twenty-07 was not designed to address the specific research questions given here. Given the self-reported nature of all health conditions, we cannot rule out that either the physical or the mental health conditions were over- or under-reported, and this may have influenced our findings. Furthermore, members of the reference group with neither physical nor mental health conditions could potentially have other health issues that were not reported or assessed for during the data collection. An additional

limitation that should be highlighted is the assessment of past suicidal thoughts and suicide attempts, which was based on single questions rather than a suicide risk assessment scale. However, it is worth noting that the twenty-07 cohort design did not focus on the investigation of suicidality per se, hence the lack of use of clinical instruments measuring suicidal thoughts and behaviours. As noted earlier, the small number of suicide attempt cases, yielded wide CIs in our findings, precluding a number of adjusted analyses. This latter limitation underlines the importance of further replication on larger datasets.

Furthermore, we were not able to investigate the temporality of physical and mental health conditions, due to the lack of information in regard to timing of conditions provided in the dataset. This would have been beneficial as previous research has pinpointed that the temporality of conditions may possibly moderate the association of multimorbidity and suicide-related behaviour (Qin et al., 2011). However, it was not feasible to address this issue due to the lack of related information in twenty-07. Lastly, it was not feasible to Investigate the predictive role of specific health conditions in the risk of suicidal thoughts and behaviours, as presented in previous studies (Webb et al., 2012a,2012b), due to the small number of cases in terms of suicidality.

7.7 Conclusions

To date, the majority of suicide-related literature has focused on the separate effects of either physical illness or mental disorders, with limited studies investigating the interaction between these health conditions in the general population. In the present study of a sample representative of the Scottish population, we found that physical/mental multimorbidity is a risk factor for suicidal thoughts and suicide attempts but not beyond the effects of mental illness. Given that cohort studies have not been explored in regard to the risk of suicidality for physical/mental multimorbid groups, our analyses make a useful contribution to the multimorbidity literature. Furthermore, as noted above, our results indicate that although multimorbidity is associated

with a risk of suicidal thoughts and behaviours, it is not associated with risk more than having mental or physical health conditions alone.

Although our cross-sectional findings confirm previous studies on physical/mental illness co-occurrence in suicide-related behaviour, prospective studies on this pattern of multimorbidity, in terms of suicidality, are scarce. Considering that suicide and related behaviour are rare events, future studies should employ a prospective analysis/design on the role of multimorbidity in suicidality, employing larger datasets. While suicide prevention strategies have been developed for different vulnerable populations at risk of suicide, no clear evidence exists for the risk of multimorbid patients. Our results potentially suggest that health professionals in primary and secondary care, should screen their patients with physical and mental illness co-occurrence for suicidal thoughts and behaviours. Considering the prevalence of physical/mental multimorbidity in primary care, further targeting and intervention is required.

Chapter 8: General discussion

Summary

The current chapter summarises the main findings of the empirical studies conducted within this thesis and focuses on future directions and clinical implications. Four studies were reported, based on data from two national mental health surveys of United Kingdom (UK) and one cohort study carried out in Scotland. They aimed to address the following research questions: a) does the risk of suicidal behaviours vary as a function of physical/mental multimorbidity? b) does physical/mental multimorbidity increase the risk of suicidal behaviours more than either condition alone? Findings indicated that those with physical/mental health multimorbidity are at risk of suicidal thoughts and behaviours. The results were consistent across all studies; those with mental health conditions were at elevated risk of suicidality, while having only physical health conditions did not have any association with any of the suicide-related outcomes. Interestingly, having both physical and mental health conditions did not increase risk of suicidal thoughts or attempts, beyond the risk conferred by mental illness alone.

Taken as a whole, the findings and the systematic review reported within this thesis highlight the need for further research into the relationship between multimorbidity and suicidal ideation and behaviour. Considering that cohort studies have not been explored in regard to the risk of suicidality for physical/mental multimorbid populations, our twenty-07 analyses make an important contribution to our understanding of multimorbidity and suicide-related outcomes. Although the literature indicates that multiple health conditions have an effect on suicidal behaviours and suicide, no clear research evidence exists on the type of illness co-occurrence that elevates suicide risk. More research into the effect of multimorbidity on suicide risk could guide physicians in assessing their patients' suicide risk and provide tailor-made suicide risk assessments for these vulnerable patient groups.

The current chapter summarises and synthesises the results of the four empirical studies, in order to address the research questions of this doctoral programme. Given the dearth of research into the relationship between co-occurring physical and mental health conditions and suicide risk, the following research questions were posed: a) do populations with physical/mental multimorbidity have an increased risk of suicidal thoughts and suicide attempts, compared to those with neither physical nor mental health conditions, and b) does physical/mental multimorbidity increases risk of suicidal thoughts and behaviours more than each condition alone?

The structure of this general discussion is divided in six sections: key findings, interpretation of results, strengths and limitations of studies, clinical implications, future directions and conclusions.

8.1 Key findings

In order to investigate whether the risk of suicidal behaviours varies as a function of physical/mental multimorbidity, three studies with a cross-sectional design and one with a prospective study design were employed, based on British (NPMS 2000; APMS 2007) and Scottish (Twenty-07 Cohort Study) population-based datasets. Overall, all studies indicated that physical/mental multimorbidity increases the risk of suicidality compared to having neither a physical nor mental health condition. A consistent finding across all studies is that although multimorbidity is associated with a risk of suicidality, it does not increase the risk of suicidal thoughts and behaviours beyond mental illness alone. Interestingly, having only physical health conditions was not associated with any suicide-related outcome.

8.1.1 Cross-sectional results

Studies 1 & 2 (Chapter 5; Chapter 6) used the national psychiatric morbidity surveys of Britain: the National Psychiatric Morbidity Survey (NPMS) conducted in 2000 and the Adult Psychiatric Morbidity Survey (APMS) published in 2007. Given that the assessment of all health conditions (mental

health conditions; physical health conditions) and suicidal behaviours followed a similar methodological approach across the two surveys, the same statistical analysis and design were applied across both studies.
Both British surveys' findings indicated that physical/common mental disorders (CMDs) multimorbidity increases the risk of suicidal thoughts and suicide attempts, compared to having neither physical nor CMDs alone. With regard to the interaction between physical and mental illness on the risk of suicidal behaviour, in both the NPMS and APMS, the results indicated that the co-occurrence of physical health conditions and CMDs did not increase the risk over and above CMDs alone.

When exploring the independent effects of mental and physical health conditions, having only CMDs was significantly associated with all the suicidality outcomes examined, and this was a consistent finding in both surveys. Furthermore, the analysis of the NPMS and APMS found little evidence of a physical health–suicidality association. In APMS, before applying the fully adjusted model with the clinical variables (drug dependence, alcohol abuse, negative life events and psychiatric medication), a significant association between physical health conditions and suicidal thoughts was found. It should be noted, however, that this association with suicidal thoughts was not found in the other empirical studies contained within this thesis.

The last cross-sectional thesis study (Chapter 7), the West of Scotland Twenty-07 Cohort Study, covered five waves of data collection and utilised a number of logistic regression models for each follow-up wave (waves 2-5). Considering that the measurement of all health conditions and suicidal behaviours were assessed with the same instruments/questions, for the baseline and follow-up periods, our statistical analysis and health grouping categorisations were the same for each wave. In respect of each wave, those with physical/mental multimorbidity had an increased risk of suicidal thoughts, compared to those having neither conditions. Although a similar pattern was found for the relationship of multimorbidity with suicide attempts in the unadjusted analyses, due to the small number of cases, the findings need to be interpreted with caution.

The separate effects of mental and physical conditions on the risk of suicidal thoughts and behaviours were further explored within this sample. Our results confirmed the previous findings reported in this thesis; they indicated that while mental illness had a significant association with suicidal thoughts and behaviours, physical illness alone did not have any significant role in the risk of suicidality.

In terms of the second thesis question, regarding the interaction of physical and mental health conditions in the prediction of risk of suicidal behaviour, the findings indicated that having both physical and mental health conditions did not increase the risk of suicidal thoughts more than having a mental illness alone. Due to the small numbers of suicide attempts, an analysis of the interaction between physical and mental health multimorbidity could not be performed.

8.1.2 Prospective analyses

Within Chapter 7, the longitudinal data from the twenty-07 cohort study were further analysed in order to investigate the predictive role of multimorbidity in the risk of suicidal thoughts and behaviours. Findings from the generalised estimating equation modelling confirmed the cross-sectional analyses as multimorbidity was associated with increased risk of suicidality. Due to the small number of suicide attempts some of the adjusted analyses were not performed. Nonetheless, our findings shed more light on the significant risk of suicidal thoughts, for those with physical/mental multimorbidity.

In terms of the separate role of mental and physical health in suicidality, mental health conditions were significant predictors of subsequent suicidality; however, physical health conditions did not have any association with either suicidal thoughts or suicide attempts. In terms of the interaction effect of physical and mental health conditions, although multimorbidity predicted suicidal thoughts, it did not have a stronger effect than mental health conditions alone.

Overall, the results of the twenty-07 prospective analyses confirm previous findings within this thesis and indicate that physical/mental multimorbidity is associated with increased risk of suicidality, but this association does not appear to confer additional risk beyond the independent effect of mental health conditions.

8.2 Interpretation of results

8.2.1 Risk of suicidal thoughts and behaviours in physical/mental multimorbidity

As elaborated on in the first 3 chapters of this thesis, the co-existence of physical and mental health conditions in one person has been overlooked in suicide-related research. The current thesis' findings highlight that physical/mental multimorbidity is associated with an increased risk of suicidal behaviours, compared to having neither physical nor mental health conditions. Surprisingly, having a physical and mental health co-occurrence does not work additively and our results indicate that multimorbidity does not increase the risk over and above mental illness alone. In addition, although most of our findings relate to suicidal thinking rather than suicide attempts because of small case numbers there was some tentative evidence (suicide attempts were highest in number), in all the multimorbidity groups investigated, that suicide attempt risk may also be elevated. Needless to say, these analyses need to be replicated in a much larger sample.

In terms of the sociodemographic characteristics of the multimorbidity groups in all datasets explored, it seems that more females than males had multimorbidity issues, the majority were living with someone, were not employed during the data collection phases, and had higher education degrees. Although the current thesis did not include any analyses stratified by age, our descriptive findings indicate that physical/mental health multimorbidity is quite prevalent in middle-aged populations, having a mean age close to 50 years of age in all the empirical studies explored (Chapters 5,6,7). Although studies on primary care data suggest that multimorbidity is prevalent in old populations (over 65 years of age), some findings pinpoint a

high prevalence of multimorbidity in younger age groups (Barnett et al. 2012). Specifically, in a Scottish study, using patients' data from primary care services (n=1751841), among those with multimorbidity, 36.0% (35.9-36.2) had a physical/mental illness co-occurrence and interestingly, this physical/mental multimorbidity was highly prevalent among patients younger than 65 years of age (Barnett et al., 2012). Consistent with this Scottish study, we found that people with physical and mental-ill health co-occurrence in a general population, belong to those younger than 65 years of age. As the group of younger patients with multiple conditions becomes more prevalent, medical-focused care similar to that which geriatric-related professionals provide for older multimorbid populations should be further considered (Barnett et al., 2012).

There are a few possible interpretations for our findings on the role of multimorbidity in the risk of suicidal thoughts and behaviours, based on the multiple illness-suicidality association and suicide-related psychological models. Previous studies on the burden of multiple conditions have suggested that having more than one health condition works cumulatively, affecting mental health and decreasing one's quality of life (Barnett et al. 2012; Megari 2013; Prince et al. 2007). Indeed, somatic and mental illness-related studies indicate a risk of suicidality for populations with two health conditions or more (Erlangsen et al., 2015; Hawton et al., 2003; Nock et al., 2010; Oquendo, Currier, & Mann, 2006; Scott et al., 2010; Webb et al., 2012a). Although current findings provide some additional support for the effect of multiple health conditions in suicidality, they differ significantly from previous studies, as they explored conjointly the presence of physical plus mental health condition in one person, compared to research to date exploring either multiple mental or multiple physical health conditions.

As elaborated on in chapters 2 and 3, when referring to psychiatric co-occurring conditions, the evidence that multiple mental disorders increase the risk of suicidality, compared to those with no mental health conditions, is quite well established. In terms of the medical illness-suicidality relationship, although some studies indicate that there is a dose-response effect of multiple physical health conditions on risk of suicidality, other studies

suggest that the risk of suicidality found in populations with somatic illness is due to the presence of psychiatric comorbidities (Pompili et al., 2016; Scott et al., 2010; Webb et al., 2012a). Our findings are consistent with such a view, as they could indicate that when suicidality is investigated among populations with physical health conditions, the significance of this association is likely to be mental illness-driven (significant risk of suicidality in physical/mental multimorbidity group vs no risk of suicidality in the physical only group). Considering that the research aim of this thesis was to explore the co-presence of any mental/physical health problems, we cannot comment on the risk of suicidal behaviours as a function of specific co-occurring mental/physical health conditions.

The current findings could also be interpreted through psychological mechanisms and models of suicidal behaviour. When focusing on physical/mental multimorbidity, Fegg and colleagues (2012) have suggested that these types of multiple conditions probably decrease one's coping strategies. Taking into account that poor coping skills are associated with suicidal behaviours, conditions related to both somatic and mental health, could lessen the capability of employing effective coping skills overall (Glazebrook, Townsend & Sayal 2016; Gooding et al. 2015; Tang, Xue & Qin 2015). Consistent with psychological models (O'Connor, 2011), the experience of physical/mental multimorbidity may increase the risk of suicidality via psychological mechanisms. The Integrated Motivational-Volitional model of suicidal behaviour (IMV) suggests that the emergence of suicidal thinking and enactment are, in part, related to coping and feelings of entrapment (O'Connor, 2011). In regard to our findings on suicidal thoughts, having both physical and mental illness related-pain, may increase feelings of entrapment and along with the lack of coping skills, could potentially result in the progression of suicidal thinking (O'Connor, 2011).

Furthermore, in relation to our results on suicide attempts, although we have stressed only a tentative association, it is likely that the impaired functionality of a multimorbid person, along with a probable easy access to multiple prescriptions, could potentially contribute to acting upon one's suicidal thoughts. To that end, a Danish study, concluded that people with

physical illness, were more likely to die by self-poisoning, due to their ready access to multiple medicines for either physical or mental disorders, compared to those dying by suicide without having a physical illness (Qin et al., 2014). Also, in an English study of primary care patients who died by suicide, Windfuhr and colleagues highlighted that being prescribed multiple psychotropic medication was associated with an increased risk of suicide (Windfuhr et al. 2016). Overall, coping with both physical and mental illness, combined with feelings of entrapment, poor functionality and easy medication access, could possibly explain the association between multimorbidity (or mental illness more generally) with the risk of suicidal thoughts and behaviour in our study findings.

The data from all of the empirical studies on the potential risk of suicidality for populations with physical/mental multimorbidity issues highlight the need for further investigation in these populations. To date, the majority of studies focus on the association between a single condition and subsequent risk of suicidal behaviours and suicide. It is quite evident from the studies reviewed in this thesis that in the wider suicide-related literature, physical and mental illness co-occurrence, is usually explored through statistical adjustments (e.g., including co-occurring illnesses as covariates). Considering, however, that a comorbid condition, along with the under-study illness, may actually form a specific health group, over-adjusting for the presence of any co-occurring health condition, could potentially result in overlooking an important and prevalent health group, like those with physical/mental multimorbidity issues. This overlooked health population was investigated in the current thesis and found to be a vulnerable health group, mainly in regard to the risk of suicidal thoughts. Although we did not further investigate which specific conditions of the physical/mental multimorbidity groups are associated with the risk of suicidality, future research is needed in order to determine whether there is a specific pattern of illness co-occurrence that increases this risk. As Salive (2012) has suggested, multimorbidity studies are important as they can help in detecting any underlying factors between health conditions that are often found to co-occur. Similarly, future studies should investigate whether there is a shared

pathophysiology between specific physical/mental multimorbidity patterns and risk of suicidality.

8.2.2 The independent effect of mental and physical health conditions in suicidality

As expected, our analysis demonstrated the strength of the mental illness-suicidality association. Similar to our findings, previous studies using administrative data, death registries and population-based surveys have demonstrated that the risk of suicidal thoughts, behaviours and suicide is heightened when mental illness is taken into consideration. All the empirical studies within this thesis highlighted the significant association between mental health conditions and both suicidal thoughts and suicide attempts. Specifically, in our prospective analyses, when we compared the effect of multimorbidity, on the risk of suicidality, with the effect of mental illness, findings indicated that mental illness had a stronger effect on the risk of suicidality. In other words, mental illness increases the risk of suicidal thoughts and behaviours, compared to having either physical/mental multimorbidity or neither mental nor physical health conditions. Similarly, in a study investigating the psychiatric comorbidities of patients with physical illness who have died by suicide, findings indicated that the risk of suicide was lower for those having co-occurring physical/mental health conditions (specifically for those who developed physical illness after a psychiatric disorder), compared to those with psychiatric disorder alone (Qin et al., 2014). Considering that the temporality of physical and mental conditions was not investigated in our studies, further research should explore if temporality of conditions in physical/mental multimorbidity differentiates risk of suicidality, compared to having mental illness alone.

In terms of our findings on the non-significant role that physical illness has in the risk of suicidal behaviours, the majority of studies on somatic conditions seem to suggest that when mental illness is controlled for, the effect of physical illness on the risk of suicidality is lost. Notwithstanding the difference in our methodology (not using mental conditions as statistical adjustment, rather categorising participants with physical and mental health

conditions into a distinct health group), the finding that physical illness has no role in suicidality beyond mental illness, confirms previous studies. The few suicide-related studies that have indicated that physical illness on its own as a significant risk factor of suicidality, are mostly based on severe conditions requiring hospitalisation (Qin et al., 2014; Qin et al., 2011; Webb et al., 2012b). As noted in the limitations sections of each empirical study, the self-reported nature of physical health conditions may reflect less severe conditions and the present study designs did not allow us to investigate how the severity of physical illness may affect the onset of suicidal behaviours. The lack of information on the severity of physical health conditions may have affected the analyses overall, by reducing the effect of physical conditions on either suicidal thoughts or suicide attempts. Hence, our finding that physical illness is not a unique risk factor for suicidal behaviour may potentially be limited to health conditions with low severity.

Taken together, the unique effect of mental illness on the risk of suicidal thoughts and suicide attempts was a consistent finding across the four empirical studies presented herein, while physical illness on its own, had no role in the risk of any suicide-related outcome.

8.3 Strengths and limitations of studies

The strengths of all of the current studies are that they are based on population-based surveys and potentially include people not in contact with health care professionals. As McManus and colleagues (2016) have indicated, the use of national mental health surveys extends our knowledge of the prevalence of psychiatric conditions, by detecting people not attending health care services. Moreover, the use of the UK surveys and a Scottish cohort study broaden our knowledge of the physical/mental health multimorbidity prevalence in general populations, as well as illustrating the association between mental/physical health multimorbidity and suicidality.

A strong point about all of the databases used is the provision of good quality information related to physical and mental health conditions and suicide-related outcomes (suicidal thoughts, suicide attempts). The NPMS 2000 and

APMS 2007 methodologies included the assessment of health conditions and suicidal behaviours, through the use of a structured diagnostic instrument (CIS-R). The methodologies in these British surveys ensured validity in terms of detecting common mental disorders and suicidal behaviours in a non-clinical environment. At the same time the use of the longitudinal Scottish study, Twenty-07, provided an opportunity to investigate the relationship between multimorbidity and suicidality across 20 years. Considering the lack of longitudinal studies exploring the effect of multimorbidity on suicidality, the use of the Scottish study was a major strength of this doctoral thesis.

Nevertheless, our findings should be viewed on context of their limitations. The cross-sectional analysis of secondary data has been viewed as the main limitation in each chapter. A further limitation noted is the self-reported nature of physical and mental health conditions, and suicidality. Although the UK surveys employed a computer-based section in regard to the questions of suicidality, in order to minimise under-reporting, suicide-related questions were not based on a suicide risk assessment scale. Furthermore, Twenty-07 did not use a suicide risk scale and employed two question-items for assessing the suicidal thoughts and behaviours of its participants.

Further, the severity of all physical health conditions could not be validated due to the nature of the information included in the datasets and this may have contributed to the reduced effect of physical health conditions on suicidality. Considering that research indicating a risk of suicidality for physical illness, is mostly based on populations that have been in contact with health care services, the inclusion of severity may have moderated the physical illness-suicidality relationship. Hence, the generalisability of findings should be viewed with caution, as they may not reflect people with conditions requiring hospitalisation or frequent primary care contact. Moreover, the reference groups with neither physical nor mental health conditions may have had other health issues that were not assessed during the assessment process of each survey.

The current studies were limited by the small number of cases regarding suicide attempts. Consequently, no firm conclusions can be arrived at about the role of multimorbidity in the risk of suicide attempts.

8.4 Clinical implications

A recent systematic review documenting health care contact before suicide indicated a large discrepancy in the contact rates between primary and mental health services (Stene-Larsen & Reneflot 2017). Indeed, the contact rate for primary health care, in the year before suicide, was 80%, while for mental health services it was 31% (Stene-Larsen & Reneflot, 2017). Given the potential role for primary care professionals in identifying patients at risk of suicide, our current findings highlight that multimorbid patients with physical and mental conditions, are highly likely to have been in contact with their GP in the year before their suicidal thinking or attempts. Although previous studies indicate a suicide risk for patients attending primary care for physical conditions (Bolton et al., 2015; Fassberg et al., 2016; Webb et al., 2012a), our findings more specifically indicate a risk of suicidality for those with both somatic and mental illness.

Given the nature of data used in the present studies, it was not possible to investigate the temporality of physical/mental conditions; nonetheless, previous studies have suggested its importance. Qin and colleagues (2014) pinpointed that the risk of suicide is exacerbated when psychiatric disorders are diagnosed some years after the physical illness (Qin et al., 2014). Their findings, along with our results, suggest that primary care professionals should focus on the follow-up screening of physically ill patients, regarding subsequent mental conditions, as these can be associated with subsequent suicidality.

The important role of mental health professionals in suicide prevention has already been highlighted in previous studies (Mann et al., 2005). The current thesis similarly indicates the importance of mental health professionals focusing on those with psychiatric disorders, and additionally suggests that attention should also be given to any physical illness developed among

mental health patients with no history of suicidality, as this comorbidity could be potentially associated with the emergence of suicidal thoughts and behaviours.

Overall, the main findings of this thesis highlight the importance of primary and secondary care as potential intervention points for suicide prevention, as patients with physical/mental multimorbidity frequently reach out to these health care services. Despite previous research highlighting the role of somatic illness alone, in terms of risk of suicidality, we underline that patients with physical health conditions, who regularly attend health care services, should be screened for any subsequent mental illness by primary care professionals, as a physical/mental multimorbidity may be associated with suicidal thoughts and behaviours.

8.5 Future directions

It is quite evident that the lack of consistent terminology in suicide-related studies, in regard to the co-occurrence of health conditions, has contributed to the lack of research evidence on the risk of suicidality among physical/mental health multimorbid populations. As Valderas and colleagues have noted (2009), the role of terminology, in regard to illness co-occurrence, is not necessarily problematic in clinical settings; in suicide-research however, the interchangeable use of comorbidity and multimorbidity result in some health groups who may have an increased risk of suicidality being overlooked. Furthermore, suicide-related studies need to be consistent with the use of terminology in the wider literature, which indicates that multimorbidity refers to having two or more conditions, while comorbidity is used only when we are exploring co-occurring conditions based on an index illness. By using proper and consistent terminology, future epidemiological studies have a better chance in robustly investigating the prevalence rate of suicidality among multimorbid populations.

Future studies should additionally investigate the role of multimorbidity in suicidality using patient registries that have been widely used as a tool to detect disease prevalence rates, health inequalities and mortality rates in

respect of other conditions. Due to the small number of cases, the current findings could not firmly conclude which type of suicidality (i.e., suicidal thoughts or suicide attempts) is better predicted by multimorbidity. The multimorbidity-suicidality association needs to be validated through large administrative and national patient registries which have sufficient numbers of cases of suicide attempts. Considering that suicide and related behaviours are rare events, linking population-based datasets with death registries will deepen our knowledge regarding the effect of multimorbidity in the risk of suicide.

In this thesis, we investigated whether current multimorbidity issues increase the risk of past year suicidal thoughts and behaviours. However, we cannot rule out that the current multimorbidity issues assessed by the interview periods were not chronic or lifetime. Previous studies found that prolonged or chronic illness is related to suicidality and that the chronic burden of multiple illnesses could possibly explain suicidal acts (Fegg et al. 2016; Karasouli, Latchford & Owens 2014). Therefore, future research designs should additionally employ a lifetime component of both types of illness (physical; mental) and suicidal behaviours, as chronicity of conditions could potentially predict subsequent suicidal behaviours and suicide.

Studies on severe somatic illness, such as advanced cancer or severe allergy, requiring hospitalisation, have reported an increased risk of suicidal thoughts and behaviours (Anguiano et al. 2012; Qin et al., 2011). Considering that the effect of physical illness severity on suicidality was not investigated in the empirical studies of this thesis, future studies should investigate whether the low, middle and high severity levels of different physical illnesses differentiate the risk of suicidal thoughts and behaviours. As frequent medical visits for a physical illness could indicate level of severity, further studies should explore medical visits data from administrative registries, in order to investigate the relationship of illness severity and suicide-related outcomes. In terms of using population-based surveys to explore the role of physical illness on suicidality without available information on severity, future study designs should consider using linkage data of prescribed medication, as a proxy for physical illness severity. A probable association of

a health condition severity with suicidality, could help in targeted suicide interventions in primary and secondary care.

Besides the chronicity of multimorbidity, as noted elsewhere, future studies should address the temporality of conditions, as there are few indications that the onset of mental and somatic conditions differentiates higher versus lower suicide risk. As mentioned earlier, having a psychiatric illness diagnosed years after the primary physical disease, seems to exacerbate suicide risk (Qin et al., 2014). Considering that the latter finding is based on linking national health care and death registries, future studies on physical/mental multimorbidity, should use similar linkage data. Indications that a physical illness precedes a mental diagnosis increases suicide risk could help in the application of suicide interventions and mental health promotion strategies during primary care contact.

The need for employing mixed-method study designs in the investigation of suicidality has also been highlighted in recent years (Kral, Links & Bergmans 2012). While quantitative prospective study designs based on population-based registries help us appreciate the effect of physical/mental multimorbidity in increasing risk of suicidality, qualitative research is required to understand how or why. In Fegg et al.'s study (2016) on suicide notes written by people experiencing multiple health conditions before death, it was evident that those with primary mental disorders had comorbid somatic illness and those with primary physical issues additionally had comorbid mental health conditions. In those suicide notes, the primary condition experienced or diagnosed by the deceased was mentioned as a reason to kill oneself consistently. This may indicate that the primary condition is the one that increases suicidal thoughts and feelings of entrapment among those with physical/mental multimorbidity. Qualitative studies focusing on people with psychiatric/physical multimorbidity who have a history of suicide attempts should be conducted in order to detect if the primary illness acts as a key determinant of suicidality. Such results will assist in providing proper suicide prevention interventions within health care and more accurately directing those interventions to those who most need help.

As reviewed in this thesis (Chapters 2 & 3), co-occurring depression, either as a primary or a secondary diagnosis, has a significant role in the risk of suicidal thoughts and behaviours. Interestingly, in a study examining the effects of allergy and co-occurring mood disorder, risk of suicide was higher in those with allergy alone, compared to those with allergy and comorbid mood disorder (Qin et al., 2011). The authors suggested that possibly patients with co-occurring conditions have better care and treatment, therefore their suicide risk in reduced. They further suggested that the treatment for a comorbid mood disorder, for allergic patients, may work protectively against suicide risk, as specific antidepressant medications additionally have an anti-inflammatory effect (Qin et al., 2011). Considering that physical illness alone exacerbated the risk of suicide in this latter study, future studies utilising hospital records, should investigate the risk of suicidality among those with different physical health conditions and comorbid depression, in order to understand the risk of suicidality based on the depression-physical illness clinical presentation.

8.6 Conclusions

The illness-suicidality association has been extensively investigated, with the majority of research focusing on the effect of either multiple psychiatric disorders or physical illness. Evidence on the role of co-occurring physical and mental illness (multimorbidity) on suicidality is limited and the group of patients with this pattern of multimorbidity is understudied. The studies presented within this thesis aimed to investigate if populations with physical/mental health conditions (multimorbidity) had an increased risk of suicidal thoughts and suicide attempts, compared to those with neither physical nor mental health conditions (controls). Overall, the findings suggest a potential risk of suicidality for populations with multimorbidity. Although multimorbidity was a predictor of suicidality, it did not increase the risk of either suicidal thoughts or suicide attempts more than mental health conditions alone. Hence, all of the thesis studies confirm previous findings on the substantial effect that mental health conditions have on the risk of suicidality.

Considering that suicide risk assessments have not been proven effective in regard to the prediction of suicidality, further studies are needed to determine which clinical populations are more at risk of suicide and when. The methodological approach followed in the current thesis indicated that grouping health populations with physical and mental health conditions into mutually exclusive categories was beneficial for presenting the risk of suicidality based on the separate and co-occurring (multimorbidity) effects of mental and physical illness. The current findings highlight that primary and secondary care professionals should focus on populations who have reached services for non-mental health issues, but subsequently develop mental illness, as this pattern of multimorbidity could potentially be a risk factor for suicidality. Further research is needed to better understand and intervene to reduce risk of suicide in individuals with multimorbidity.

Appendices

Appendix A

Table 1. Sensitivity analyses of past year suicidal thoughts, suicide attempts and suicidality for twenty-07 follow-up waves (version 2).

	Suicidal thoughts*	Suicide attempts	Suicidality
Wave b	Yes = 45 No = 2427	Yes = 6 No =2466	Yes = 47 No = 2425
Wave c	Yes = 38 No = 2109	Yes = 10 No = 2137	Yes = 39 No = 2107
Wave d	Yes = 56 No = 2598	Yes = 7 No = 2647	Yes = 56 No = 2598
Wave e	Yes = 64 No = 2498	Yes = 12 No = 2550	Yes = 64 No = 2498

* Missing replies treated as a past year behaviour (within the last 12 months).

Table 2. Sensitivity analyses of past year suicidal thoughts, suicide attempts and suicidality for twenty-07 follow-up waves (version 3).

	Suicidal thoughts*	Suicide attempts	Suicidality
Wave b	Yes = 41 No =2431	Yes = 5 No = 2467	Yes = 42 No = 2430
Wave c	Yes = 37 No = 2110	Yes = 9 No = 2138	Yes = 38 No = 2108
Wave d	Yes = 49 No = 2605	Yes = 7 No = 2647	Yes = 49 No = 2605
Wave e	Yes = 56 No = 2506	Yes = 9 No = 2553	Yes = 56 No = 2506

*Missing replies treated as taking place more than a year ago (not within the last 12 months).

Table 3. Unadjusted logistic regression investigating the relationship of past year suicidal thoughts, suicide attempts and suicidality with health groupings among twenty-07 participants (version 2).

	Suicidal thoughts			**Suicide attempts**			**Suicidality**		
Neither physical nor mental	n	OR	95% CI	n	OR	95% CI	n	OR	95% CI
Wave 2	6	1 (ref)	-	0	1 (ref)	-	6	1 (ref)	-
Wave 3	6	1 (ref)	-	3	1 (ref)	-	6	1 (ref)	-
Wave 4	4	1 (ref)	-	1	1 (ref)	-	4	1 (ref)	-
Wave 5	1	1 (ref)	-	0	1 (ref)	-	1	1 (ref)	-
One or more physical health condition									
Wave 2	11	1.135	0.418-3.082	2	-	-	12	1.240	0.463-3.316
Wave 3	2	0.254	0.051-1.262	1	0.255	0.026-2.452	3	0.382	0.095-1.530
Wave 4	7	1.067	0.312-3.65	0	-	-	7	1.067	0.312-3.657
Wave 5	8	3.685	0.460-29.530	0	-	-	8	3.685	0.460-29.530
One or more mental health condition									
Wave 2	6	**9.566**	3.017-30.332	2	-	-	7	**11.297**	3.709-34.411
Wave 3	6	**9.543**	3.008-30.275	2	**6.086**	1.003-36.936	6	**9.543**	3.008-30.275
Wave 4	11	**24.340**	7.599-77.961	2	**16.214**	1.457-180.371	11	**24.340**	7.599-77.961
Wave 5	13	**85.883**	11.106-664.125	3	-	-	13	**85.883**	11.106-664.125
Multimorbidity[a]									
Wave 2	22	**10.863**	4.359-27.076	22	**16.336**	5.579-47.831	22	**10.863**	4.359-27.076
Wave 3	24	**12.883**	5.205-31.886	23	**12.295**	4.949-30.547	24	**12.883**	5.205-31.886
Wave 4	34	**22.961**	8.081-65.238	31	**27.677**	8.401-91.179	34	**22.961**	8.081-65.238
Wave 5	42	**59.959**	8.221-437.290	37	**52.220**	7.138-382.030	42	**59.959**	8.221-437.290

[a]One or more mental and one or more physical condition in the same person

The significance of bold value is $p < 0.001$

Table 4. Adjusted logistic regression analyses for sociodemographic characteristics, investigating the relationship of past year suicidal thoughts and suicidality with physical and mental health disorders among twenty-07 participants (version 2).

	Suicidal thoughts		Suicidality	
Neither physical nor mental	OR	95% CI	OR	95% CI
Wave 2	1 (ref)	-	1 (ref)	-
Wave 3	1 (ref)	-	1 (ref)	-
Wave 4	1 (ref)	-	1 (ref)	-
Wave 5	1 (ref)	-	1 (ref)	-
One or more physical health condition				
Wave 2	1.362	0.433-4.280	1.373	
Wave 3	0.275	0.032-2.393	0.563	
Wave 4	1.356	0.334-5.501	1.356	
Wave 5	2.260	0.232-22.019	2.260	
One or more mental health condition				
Wave 2	**5.854***	1.338-25.621	**8.063****	2.063-31.506
Wave 3	**7.825****	1.775-34.498	**7.912****	1.792-34.927
Wave 4	**22.507*****	6.719-75.392	**22.507*****	6.719-75.392
Wave 5	**59.579*****	7.359-482.356	**59.579*****	7.359-482.356
Multimorbidity[a]				
Wave 2	**10.850*****	3.609-32.624	**10.986*****	3.659-32.988
Wave 3	**17.802*****	5.812-54.529	**18.395*****	6.021-56.196
Wave 4	**29.085*****	9.517-88.887	**29.085*****	9.517-88.887
Wave 5	**22.897****	2.869-182.730	**22.897****	2.869-182.730

[1] Adjusted for sociodemographic characteristics: sex, age, living conditions, employment status, any standard/high educational qualification, social class

[a] One or more mental and one or more physical illness in the same person

* The significance of bold value is $p < 0.05$

** The significance of bold value is $p < 0.01$

*** The significance of bold value is $p < 0.001$

Table 5. Unadjusted logistic regression investigating the relationship of past year suicidal thoughts, suicide attempts and suicidality with health groupings among twenty-07 participants (version 3).

	Suicidal thoughts			**Suicide attempts**			**Suicidality**		
Neither physical nor mental	n	OR	95% CI	n	OR	95% CI	n	OR	95% CI
Wave 2	4	1 (ref)	-	0	1 (ref)	-	4	1 (ref)	-
Wave 3	6	1 (ref)	-	3	1 (ref)	-	6	1 (ref)	-
Wave 4	3	1 (ref)	-	1	1 (ref)	-	3	1 (ref)	-
Wave 5	1	1 (ref)	-	0	1 (ref)	-	1	1 (ref)	-
One or more physical health condition									
Wave 2	9	1.395	0.428-4.544	-	-	-	9	1.395	0.428-4.544
Wave 3	2	0.254	0.051-1.262	1	0.255	0.026-2.452	3	0.382	0.095-1.530
Wave 4	7	1.425	0.367-5.526	0	-	-	7	1.425	0.367-5.526
Wave 5	6	2.760	0.332-22.974	0	-	-	6	2.760	0.332-22.974
One or more mental health condition									
Wave 2	6	**14.386**	3.979-52.009	-	-	-	7	**16.988**	4.870-59.253
Wave 3	6	**9.543**	3.008-30.275	2	**6.086**	1.003-36.936	6	**9.543**	3.008-30.275
Wave 4	8	**22.900**	5.976-87.760	2	**16.214**	1.457-180.371	8	**22.900**	5.976-87.760
Wave 5	12	**78.442**	10.084-610.178	3	-	-	12	**78.442**	10.084-610.178
Multimorbidity[a]									
Wave 2	22	**16.336**	5.579-47.831	-	-	-	22	**16.336**	5.579-47.831
Wave 3	23	**12.295**	4.949-30.547	3	2.973	0.596-14.821	23	**12.295**	4.949-30.547
Wave 4	31	**27.677**	8.401-91.179	4	**9.882**	1.100-88.733	31	**27.677**	8.401-91.179
Wave 5	37	**52.220**	7.138-382.030	6	-	-	37	**52.220**	7.138-382.030

[a]One or more mental and one or more physical condition in the same person

The significance of bold value is p< 0.001

Table 6. Adjusted logistic regression analyses for sociodemographic characteristics, investigating the relationship of past year suicidal thoughts and suicidality with physical and mental health disorders among twenty-07 participants (version 3).

	Suicidal thoughts		Suicidality	
Neither physical nor mental	OR	95% CI	OR	95% CI
Wave 2	1 (ref)	-	1 (ref)	-
Wave 3	1 (ref)	-	1 (ref)	-
Wave 4	1 (ref)	-	1 (ref)	-
Wave 5	1 (ref)	-	1 (ref)	-
One or more physical health condition				
Wave 2	1.231	0.337-4.490	1.244	0.342-4.531
Wave 3	0.275	0.032-2.393	0.563	0.107-2.955
Wave 4	1.924	0.424-8.720	1.924	0.424-8.720
Wave 5	2.237	0.229-21.814	2.237	0.229-21.814
One or more mental health condition				
Wave 2	**7.449***	1.593-34.829	**10.263****	2.444-43.089
Wave 3	**7.825***	1.775-34.498	**7.912***	1.792-34.927
Wave 4	**18.621*****	4.577-75.761	**18.621*****	4.577-75.761
Wave 5	**53.497*****	6.523-438.752	**53.497*****	6.523-438.752
Multimorbidity[a]				
Wave 2	**13.004*****	3.948-42.830	**13.230*****	4.022-43.520
Wave 3	**17.802*****	5.812-54.529	**18.395*****	6.021-56.196
Wave 4	**33.022*****	9.282-117.487	**33.022*****	9.282-117.487
Wave 5	**18.983****	2.330-154.641	**18.983****	2.330-154.641

[1] Adjusted for sociodemographic characteristics: sex, age, living conditions, employment status, any standard/high educational qualification, social class[a]One or more mental and one or more physical illness in the same person

* The significance of bold value is $p < 0.05$

** The significance of bold value is $p < 0.01$

*** The significance of bold value is $p < 0.001$

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