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Research paper

Multimorbidity and depression: A systematic review and meta-analysis

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ABSTRACT

Background: Multimorbidity, the presence of two or more chronic conditions, is increasingly common and complicates the assessment and management of depression. The aim was to investigate the relationship between multimorbidity and depression.

Method: A systematic literature search was conducted using the databases; PsychINFO, Medline, Embase, CINAHL and Cochrane Central. Results were meta-analysed to determine risk for a depressive disorder or depressive symptoms in people with multimorbidity.

Results: Forty articles were identified as eligible (n = 381527). The risk for depressive disorder was twice as great for people with multimorbidity compared to those without multimorbidity [RR: 2.13 (95% CI 1.62–2.80) $p < 0.001$] and three times greater for people with multimorbidity compared to those without any chronic physical condition [RR: 2.97 (95% CI 2.06–4.27) $p < 0.001$]. There was a 45% greater odds of having a depressive disorder with each additional chronic condition compared to the odds of having a depressive disorder with no chronic physical condition [OR: 1.45 (95% CI 1.28–1.64) $p < 0.001$]. A significant but weak association was found between the number of chronic conditions and depressive symptoms [$r = 0.26$ (95% CI 0.18–0.33) $p < 0.001$].

Limitations: Although valid measures of depression were used in these studies, the majority assessed the presence or absence of multimorbidity by self-report measures.

Conclusions: Depression is two to three times more likely in people with multimorbidity compared to people without multimorbidity or those who have no chronic physical condition. Greater knowledge of this risk supports identification and management of depression.

1. Introduction

Multimorbidity, a term which is now commonly used to describe the presence of two or more chronic physical conditions (van den Akker et al., 2001), is a growing presentation found in medical practice. The prevalence of multimorbidity is increasing, largely due to the global aging population trend (Lutz et al., 2008) with people living longer with clusters of illnesses. A study of the prevalence of multimorbidity conducted through general practice surgeries in Australia found that 75% of those aged 65–74 years had multimorbidity with the proportion rising to 80% of those aged 75 years or older (Britt et al., 2008). Multimorbidity, however, is not confined to older adults with a recent population based study in Ontario showing rates from 7% to 35% for adults aged 18–65 years (Koné Pefoyo et al., 2015). As multimorbidity becomes increasingly common, demanding further attention and new ways of managing healthcare (Boyd and Martin Fortin, 2010), support in terms of building a greater understanding of the impact of multimorbidity on overall patient health is required. In addition to the increased complexity in the management of medical needs of people living with multimorbidity, compared to those with a single illness, there are a range of impacts on social and emotional function which require consideration (Roland and Paddison, 2013). An important one of these is the risk for depression.

Depression is one of the leading diseases contributing to global disease burden (Lopez et al., 2006). Lifetime prevalence of depression is estimated to be between 10% and 15% based on large epidemiological surveys (Lepine and Briley, 2011) with over 350 million people currently affected (Marcus et al., 2012). Prevalence rates for depression in various settings include 3–10% in the general population (Lazarou et al., 2010), 4.9% of people in community samples (Blazer et al., 1994), 10% of primary care patients (Craven and Bland, 2013) and 10–14% of hospital patients (Katon and Schulberg, 1992). A study conducted with older adults in Australia (Anstey et al., 2007) identified rates of depression at 14.4% for community dwellers and 32.0% for

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those in residential care. Although depression prevalence is generally lower in population groups aged 60 years and over, compared to younger age groups, higher rates are found in sub-groups such as those with chronic physical conditions (ATHW, 2015). Particular risk factors for depression include stressful life events (Kendler et al., 1999), genetics (Sullivan et al., 2000), adverse childhood incidents (Cassano and Fava, 2002), disability, new illness, poor health status, prior depression, bereavement and sleep disturbance (Cole and Dendukuri, 2003).

Over past decades, interest in the relationship between chronic physical conditions and depression has grown. Higher prevalence of depression has been found for patients with a range of conditions including cardiovascular disease (17 – 27%) (Rudisch and Nemeroff, 2003), diabetes (11–31%) (Anderson et al., 2001a) and arthritis (10–24%) (Matcham et al., 2013b). The WHO World Health Survey found a greater prevalence of depression in people who had at least one chronic physical condition (9.3–23%) compared to those with none (3.2%).(Moussavi et al., 2007) Additionally, a meta-analysis by Chang-Quan et al. (2010) found that older adults with a chronic physical condition had a higher risk for depression.

There are numerous potential reasons why multimorbidity may be associated with depression, with the relationship between illness and depression suggested to be bidirectional (Katon, 2011). Multimorbidity may lead to depression through factors such as increasing symptom burden, disability, decreasing quality of life, (Katon, 2003) pain, (Bair et al., 2003) beliefs about disease and coping style (Ziarko et al., 2014). The presence of significant depressive symptoms, on the other hand, may increase the probability of engaging in health risk behaviours, which may contribute to the development of multimorbidity. In addition, poorer disease management may occur in people with depressive symptoms as they may be less likely to adhere to their medical regimens, (Alexopoulos et al., 2008) contributing to increasing risk for multimorbidity. An example of this bi-directional relationship is found with cardiovascular disease and depression, in that depression increases the risk for onset of cardio-vascular disease by 80–90% (Nicholson et al., 2006) and depression is three times more likely after a heart attack (Williams, 2011).

Theoretical explanations for the relationship between multimorbidity and depression can be found in Beck's Developmental Model of Depression (Beck, 2008b) which sees depressive symptoms manifesting from an individual's negative interpretation of their experience, which in this case is their experience of multimorbidity. These negative interpretations are rooted in dysfunctional attitudes and beliefs held about self, others and the world which have developed from early life experiences and may be activated during times of stress, such as when dealing with a number of chronic conditions. The Activity Restriction Model of Depressed Affect (Williamson and Shaffer, 2000) also provides a theoretical understanding of the relationship between multimorbidity and depression. This model attributes a substantial proportion of the depressive symptoms seen in patients with chronic illness to the psychological impact of having to give up valued activities in response to illness. The Psychological and Biological Pathways Model (Schulberg et al., 2000) also provides a representation of the relationship between illness and depression, proposing that physical illness can result in a decreased ability to implement strategies which help to maintain control of important aspect of life and that this, in conjunction with neurochemical and neuroanatomical changes associated with illness, may result in depressive symptoms.

There is growing evidence that neurobiological changes associated with some medical conditions, or related to the stress of having a medical illness, can contribute to the incidence of depression. Vascular lesions in the brain, commonly seen in patients with degenerative neurological diseases such as Alzheimer's disease and Parkinson's disease, appear to be associated with depressed mood (Camus et al., 2004). Additionally, vascular depression is frequently present in patients with a history of stroke or chronic ischemic injury (Alexopoulos, 2005) and those with higher rates of cerebrovascular risk factors (Mast et al., 2004). Increased stress related to having a number of chronic conditions and subsequent prolonged activation of the hypothalamic-pituitary-adrenal axis is also likely to increase the chances of depressive disorder (Pariante and Lightman, 2008); particularly in individuals with a genetic predisposition or early life factors which contribute to hyperactivity of this axis. Additionally, both metabolic and immune-inflammatory dysregulation, which are common in many chronic conditions, are also associated with depression (Penninx, 2017).

Regardless of the causes of depression, the presence of co-occurring depression and multimorbidity is concerning because of the overall negative impact of having both. There is evidence that patients with both depression and chronic physical conditions have considerably poorer quality of life than those with a chronic physical condition who are not depressed (Moussavi et al., 2007). There is also evidence that people with depression die between five and ten years earlier due to chronic physical conditions (Chang et al., 2010). An additional concern is health care costs, which are approximately 50% greater for patients with depression and a chronic physical condition than for those with a chronic physical condition alone (Luber et al., 2000). Given there is evidence that depression management can reduce mortality related to the combined impacts of having multimorbidity and depression (Gallo et al., 2016), greater understanding of the risk for depression in people with multimorbidity is warranted.

There are a large number of studies that have observed the relationship between particular chronic physical conditions and depression (Anderson et al., 2001b; Matcham et al., 2013a; Rudisch and Nemeroff, 2003). There is also evidence that illness severity is associated with depression (Ostergaard and Foldager, 2011). There is less research, however, that has investigated the relationship between multimorbidity and depression, and most of the studies have reported the relationship as a secondary focus. To our knowledge, there has been no meta-analysis of the literature specifically looking at multimorbidity and depression, nor examining the relationship between multiple physical illnesses and depression. As multimorbidity is a growing presentation found in medical settings, it is timely that this review be conducted to contribute to a greater understanding of the care needs of this patient group.

The aim of this meta-analysis is to assess the relationship between multimorbidity and depression in adults. It aims to do this by answering the following questions: 1) Is there a significant increased risk for depressive disorders in people with multimorbidity compared to those without multimorbidity, and compared to those with no chronic physical condition?; 2) Is there a significant increased risk of having a depressive disorder with increasing number of chronic physical conditions?; 3) Is there a significant positive relationship between the number of chronic physical conditions and level of depressive symptoms?; 4) If these risks and relationships are present, how strong are those relationships?; and 5) Do any of these risks or relationships differ significantly across age groups, settings or according to the way depression is measured?

2. Method

2.1. Defining terms

Three groups were used for making comparisons in these meta-analyses; people with multimorbidity, people without multimorbidity and people with no chronic condition. People with multimorbidity are those identified in studies as having two or more chronic physical conditions. People without multimorbidity are those identified as having either no chronic physical condition or only one condition, therefore not falling into the category of people with multimorbidity. People with no chronic condition are those without any chronic physical condition. Although the category of *people without multimorbidity* is not commonly seen in the literature, results for this group of patients are commonly reported. Naming and defining this category in the meta-