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Multimorbidity and quality of life at mid-life: A systematic review of general population studies

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ABSTRACT

There is substantial multimorbidity at mid-life but little is known about the strength of evidence on multimorbidity and health-related quality of life (HrQoL) at mid-life. This review addresses this gap, focusing on studies of the general population. PubMed, Web of Science, Embase and APA PsycNET databases were screened on 6 March 2017 for original research on multimorbidity and HrQoL in adults aged 40–65 years from the general population. Studies focused on index conditions, using single-item HrQoL measures, unlikely to represent the general population (e.g. primary care), and papers that were not in the English language were excluded. A narrative synthesis was presented due to heterogeneity in the measurement of multimorbidity. Of the 2557 articles, 83 underwent full text screening and 8 were included in the review. Included studies were of moderate to high quality and no exclusions were made on the basis of quality or bias. Multimorbidity was associated with poorer HrQoL at mid-life. Two cross-sectional studies found that adults with multimorbidity at early mid-life reported poorer HrQoL than adults with multimorbidity at late mid-life, while another found the reverse. Two distinct disease clusters were identified: mental health conditions and cardiovascular disease (CVD). Those in the mental health cluster reported poorer HrQoL than those in the CVD cluster, women more so than men. Limitations of the selected studies include lack of longitudinal evidence, use of self-reported conditions and no assessment of disease severity. Multimorbidity is associated with poor HrQoL at mid-life at the population level, with some evidence of differences in association with age and disease cluster and sparse evidence on sex differences. Longitudinal research using a weighted disease severity index and multimorbidity trajectories is needed to strengthen the evidence base.

1. Introduction

Multimorbidity, the co-occurrence of at least two health conditions in an individual [1–6], is an increasing health problem. It is brought about by population aging, unhealthy lifestyle habits, emerging chronic conditions, reduced mortality from improved medical care and technologies, and earlier detection and treatment of conditions [7]. Globally, multimorbidity prevalence is estimated to be between 3.5% and 100% [8]. The large variation is estimates observed is driven by differences definition and measurement of multimorbidity, population setting, participant age range, and country income levels [9]. Despite this, there is consensus that multimorbidity represents significant and growing burden to society [7]. Increased multimorbidity burden can lead to greater complexity in patient health management, reduced health related quality of life (HrQoL), and increased health care use and costs [10–12].

While multimorbidity is common in older adults, studies have shown that those under 65 years old also experience a substantial multimorbidity burden [1,13–15]. A recent systematic review highlighted a 'S' shape curve of multimorbidity prevalence with age [2], where prevalence increased steeply at mid-life, and plateaued in those age 75 years and above. The onset of conditions at mid-life may affect HrQoL. Previous systematic reviews on multimorbidity and HrQoL have focused on primary care populations[12,16] or older adults (age 65+) [17] and have shown that multimorbidity is negatively associated with HrQoL in these populations. However little is known on the strength of evidence on multimorbidity and HrQoL at mid-life or at the general population level. Given the substantially higher prevalence and disease burden of multimorbidity in primary care compared to the general populations [18], there need for synthesis of evidence at a population level to assist in health service planning.

It is unclear whether multimorbidity rates differ between males and

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females. The prevalence of multimorbidity is slightly higher in females compared to males, however findings are inconsistent [7,14,19]. Some patterns of multimorbidity differ between males and females [19]. For example, depressive symptoms is more common in females while psychiatric and substance abuse is more common in young males [19]. These sex differences in prevalence and patterns of multimorbidity coupled with the onset of conditions at midlife may modify the association between multimorbidity and HrQoL.

This review aims to quantify the relationship between multimorbidity and HrQoL at mid-life, at the population level. It will clarify whether the relationship is consistent between sexes, for different methods to measure multimorbidity, and between preference weighted and non-preference weighted HrQoL instruments.

2. Methods

2.1. Protocol and registration

The corresponding review protocol is registered at PROSPERO (CRD42017056911).

2.2. Study selection

This review focused on original quantitative epidemiological research that evaluated the association between multimorbidity and HrQoL in mid-age adults (aged 40–65 years) in the general population. We also included cohort or cross-sectional studies on adults where separate estimates of multimorbidity and HrQoL were available for adults aged 40–65 years. For the purpose of this review, multimorbidity is defined as "multiple acute or chronic medical and/or psychiatric conditions which may or may not be related" [1–4]. Studies using validated measures of HrQoL which encapsulate multiple dimensions (e.g. physical function and psychological health) with multimorbidity definitions consistent with this review were considered eligible for inclusion.

2.3. Search strategy

Primary searches were conducted using PubMed, Web of Science, Embase and APA PsycNET databases, illustrated in Fig. 1. Relevant studies available on 6 March 2017 were extracted from each database. Initial searches for each topic (multimorbidity, quality of life, adult, middle age, general population) were conducted separately, using a combination of keywords and subject headings (MeSH/Emtree/Thesaurus) terms (Supplementary data, Table A). Existing literature were used to identify common and popular keywords [1,20]. Variants of terms including mis-spellings were also used as search terms (Supplementary Table A). As some studies use comorbidity to mean multimorbidity; keywords on "Co-morbidity" were also included in the search to capture all relevant literature. Parallel strategies were used to identify studies on quality of life; adults; at mid-life and from community settings. Search results were then combined using Boolean terms (Supplementary data; Supplement 1).

2.4. Selection criteria

One reviewer performed the 'Title-Abstract' screening process (JK), where literature was refined based on inclusion and exclusion criteria. Only peer reviewed articles published or were in-press were considered. No language or document type distinction was applied during the search. However, only original articles written completely in English were considered for full text screening, to ensure uniform level of comprehension of the articles. Full text were screened based on the inclusion and exclusion criteria to further refine the literature.

Inclusion criteria:

1) Original peer reviewed published or in-press research written in English
2) Studies conducted in the general population that estimated the association between multimorbidity and HrQoL in mid-age adults (aged 40–65 years).
3) Studies consistent with the definition of HrQoL and multimorbidity described

Exclusion criteria:

1) Studies on single health conditions or focused on an index condition
2) Studies unlikely to represent the general population (e.g. primary care, clinical setting, or specific patient or user populations)
3) Studies which used single item self-rated health instrument to measure HrQoL

2.5. Critical appraisal

The critical appraisal of original papers was conducted independently by two reviewers (JK and MW) based on evaluation criteria adapted from Fortin et al. [12], used to assess for methodological quality (Supplementary data, Supplement 2). Each article was scored out of 30, based on criterions on originality, population studied, definition and measurement of multimorbidity and HrQoL, and limitations of the study. Risk of bias was assessed using an adapted version of the Newcastle-Ottawa Scale(NOS) [21] (Supplementary data, Supplement 3) suitable for observational studies, with good reliability and face validity [22]. Studies with scores of at least 15 out of 30 using the Fortin checklist, and 4 out of 9 stars using the NOS were eligible for data extraction and synthesis. There were no disagreements between the two reviewers eligibility of the included studies.

2.6. Data extraction

Data eligible for synthesis were extracted using a pre-defined questionnaire (see Supplementary Data, Supplementary Methods). The prevalence of multimorbidity defined as the presence of two or more conditions (MM2+) or three or more conditions (MM3+) were reported. Multimorbidity prevalence is associated with aging [8]. Hence to ensure fair comparisons between studies when reporting prevalence of multimorbidity and its association with HrQoL, studies were grouped based on whether they were from adult populations spanning young to late adult life (Adult studies, age 16+, n = 5) [23–27] or studies focused at mid-life (Mid-life studies, age 40+, n = 3) [28–30]. Prevalence specific to mid-life (age 40–65 years), and gender were reported where possible. However, as few studies report prevalence of multimorbidity specific to mid-life, overall prevalence in the study was presented to give an indication of the heterogeneity of multimorbidity across studies. Estimates on the association between multimorbidity and HrQoL (mean or mean difference), overall, and by life-stage and gender were extracted where available. Due to substantial heterogeneity in the measurement of multimorbidity and in association with HrQoL, and 'mid-life' age groups across studies, *meta*-analysis was not performed, instead a narrative synthesis is presented. Additional details on data extracted for synthesis are available at Supplementary data, Supplement Methods.

3. Results

3.1. Study selection: overall description of screening/assessment process

A total of 3698 articles were identified from the four databases, and 2557 were screened based on title and abstract (Fig. 1). After full text screening and quality and risk of bias assessment, 8 articles were included in the review, of which one article was identified from the reference list of an included article. All articles included in synthesis were moderate to high quality based on the Fortin and NOS assessments