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Multiple Chronic Conditions and Healthcare Costs among Adults

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Abstract

The prevalence of multiple chronic conditions (MCC) is increasing among individuals of all ages. MCC are associated with poor health outcomes. The presence of MCC has profound healthcare utilization and cost implications for public and private insurance payers, individuals, and families. Investigators have used a variety of definitions for MCC to evaluate costs associated with MCC. The objective of this article is to examine the current literature in estimating excess costs associated with MCC among adults. The discussion highlights some of the theoretical and technical merits of various MCC definitions and models used to estimate the excess costs associated with MCC.

Keywords

multiple chronic conditions; multimorbidity; expenditures; cost burden; out-of-pocket costs; comorbidity

Introduction

Research on multiple chronic conditions (MCC) has proliferated in recent years. Epidemiological studies across the world indicate the rising prevalence of MCC in the population. In the United States (US), almost half of the adults (117 million) suffered from a chronic condition, and one out of four adults had MCC [1]; 68.4% elderly individuals had 2 or more chronic conditions, and 36.4% had 4 or more chronic conditions [2]. The reported prevalence of MCC (i.e. presence of two of more conditions in the same individual) was 56.3% (35 to 75 years) in Sweden [3]. Besides, there is an increase in the prevalence of MCC over the last decade. In the US, the presence of MCC has steadily risen from 21.8% in 2001 to 26.0% in 2010 [4]. This high prevalence in MCC can be attributable to several reasons: an aging population [5], improved diagnosis and detection of diseases [6], lifestyle changes (e.g., high-calorie diet and sedentary lifestyle associated with increased risk of diabetes), environmental issues [7], drug-disease interactions (e.g., antidepressants and statins have been linked to elevated risks of new-onset diabetes [8]), and disease-disease interactions (e.g., a cancer diagnosis may lead to higher risks of depression and anxiety [9]).

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The presence of MCC in the same individual has profound implications for healthcare costs and utilization. A systematic review of healthcare utilization and costs of elderly individuals with MCC concluded that among 35 studies, only three studies did not find a positive association between healthcare expenditures and MCC [10]. The review also found that individuals with MCC have higher healthcare expenditures compared to those with a single chronic condition [10].

There are significant challenges to estimating the excess cost burden associated with MCC. The published studies on the association between MCC and costs differ in definitions of MCC, sources of data, measurement of costs, and statistical methods. Therefore, in this paper we have summarized, critically analyzed the results of recent studies, and discuss the challenges in examining the direct medical expenditures from both insurance payers and out-of-pocket spending by the patients and their families. Due to the differences in time periods and monetary units, we have mainly reported the excess cost burden of MCC in terms of percent differences rather than absolute differences in costs. In addition, the current paper highlights the knowledge gaps about the association between MCC and costs and provides recommendations for future research. It has to be noted that this review is not meant to be an exhaustive and systematic review of all the studies that have ever been conducted in the areas of MCC and healthcare costs.

Definitions of MCC

There has not been a universally accepted standard for defining MCC. Investigators have interchangeably used the terms “multiple chronic conditions”, “multimorbidity”, and “comorbidity” [11]. Therefore, a substantial heterogeneity in defining and measuring MCC has been documented [12]. Some studies have measured MCC as the presence of comorbid conditions in the context of a single disease. These studies have used pre-existing [13], co-existing [14], and newly developed conditions in the context of an index chronic condition [15]. Within the framework of an index disease, these combinations have been grouped using a conceptual framework based on clinical management of the index disease. For example, Piette and Kerr used a conceptual framework to classify conditions that coexist with diabetes into concordant, discordant and dominant conditions [16]. Uhlig et al (2014) also proposed a framework to help develop clinical practice guidelines for the care and management of people with MCC [17]. Valderas et al (2009) also defined and explained the interactions among comorbidity of an index disease, multimorbidity, morbidity burden, and patient complexity [18]. There are also heterogeneity in defining and grouping chronic conditions in the literature, which may further cause inconsistencies in definitions of MCC. The Robert Wood Johnson Foundation defined chronic conditions as “last a year or longer, limit what one can do, and/or may require ongoing medical care.” [19], while the World Health Organization (WHO) considers chronic conditions as noncommunicable diseases that are of long duration [20]. Many studies used a count of selected chronic conditions based on certain criteria to define MCC [21–26]. Other studies have defined MCC as combination of conditions from a selected list of conditions [27–29]. Cluster analysis has been used to define MCC [30].

Studies have also defined MCC using weighted indices. According to a systematic review of 39 studies on the measurement of MCC [12], Charlson Comorbidity Index (CCI) is the commonly used multimorbidity index. CCI was constructed to predict excess mortality due to chronic conditions. Other indices used to define MCC were: the cumulative multimorbidity score [31], the Adjusted Clinical Groups [ACG] [32], Rx-defined morbidity groups [Rx-MG] (a component of the Johns Hopkins ACG case mix system) [33], and the pharmacy-based cost group [34]. Only one index – Shwartz Index – is designed exclusively to assess patient costs [35]. Although the investigators did not report the magnitude of costs associated with MCC, the Schwartz index increased the R^2 value of a model to predict costs based on diagnosis-related groups from 0.42 to 0.50, suggesting that costs vary by the presence of MCC.

Cost Burden Associated with MCC

1) Costs of MCC Evaluated with the Number of Chronic Conditions—Using some of the definitions mentioned above, investigators have examined the relationship between MCC and healthcare costs. When MCC were defined as the number of chronic conditions, the average per-capita Medicare costs in 1999 associated with 2, 3, and ≥4 chronic conditions increased 107.4%, 307.4%, and 1110.8%, respectively, as compared to the costs associated with one chronic conditions [32]. In 2005, when compared to one chronic condition, the increases in average Medicare costs per beneficiary associated with 2 and ≥3 chronic conditions were 108.2% and 117.6%, respectively [21]. Similarly, In Ireland, the adjusted per-capita total healthcare costs associated with 2, 3, 4 and >4 chronic conditions increased 48.6%, 83.7%, 163.3%, and 241.0%, respectively, when compared to those associated with one chronic conditions [36].

2) Costs of MCC Evaluated by Using Weighted Scores—When healthcare costs were evaluated using weighted scores, the average costs between lower and higher scores are compared to discern the association between MCC and costs. For example, using hip fracture as an index condition, it was found that those who had CCI scores of 3 or more had 134% greater inpatient expenditures as compared to those who had a CCI score of zero [37]. In a cohort of primary care patients, those with CCI scores of 6 had 598% greater costs as compared to those with a CCI score of zero [38]. It has to be noted that a CCI score of 6 can represent a single condition rather than the presence of MCC. For example, a patient with only AIDS will have a CCI score of 6 and a patient with 4 conditions (e.g., diabetes, depression, congestive heart failure and COPD) will have a score of 4 [39]. Thus, CCI can represent the complexity of care rather than the mere presence of MCC. Furthermore, many modifications of the CCI have been used. One study identified at least eight modifications of the CCI [40]. Furthermore, weighted scores cannot distinguish between the high-cost and the low-cost chronic conditions. In the US, among elderly and non-elderly Veterans Affairs patients, it was found that non-elderly patients with chronic heart failure, chronic renal failure, and COPD represented the most costly triad of chronic conditions; while diabetes, hypertension and spinal cord injury represented the most costly triad for elderly patients [25].

3) Costs of MCC Evaluated by Defining an Index Condition—Some studies have evaluated the economic burden of MCCs by defining an index condition and calculating the excess costs of the index condition when other conditions co-occur. For example, among patients with diabetes, those with depression had 4.5 times greater expenditures than patients with diabetes and without depression [14]. Similarly, among patients with COPD, those with gastroesophageal reflux disease (GERD) had 1.5 times greater expenditure compared to those with COPD and without GERD [41].

4) Costs of MCC Evaluated by Selecting a Small Number of Chronic Conditions—Other studies have used a small number of chronic conditions to study the effects of MCC on costs. Among primary care patients with either arthritis or hypertension, those with osteoarthritis and hypertension had lower total costs as compared to those with osteoarthritis [38]. Among adults with arthritis, diabetes mellitus, heart disease, and hypertension, it was reported that adults with diabetes and heart disease had similar expenditures as compared to those with all the four conditions [27]. Findings from the studies mentioned above suggest that the mere presence of an additional condition may not be associated with increased costs.

5) Causes of Excess Cost Burden associated With MCC—Attention to MCC patients is very costly due to many reasons. First, the presence of MCC is also associated with increased healthcare utilization. Nearly 70% of the elderly population with 6 or more chronic conditions (out of a selected list 15 common chronic conditions) had an emergency room visit as compared to only 14% among those with no or one chronic condition [42]. Of the 28 million hospital discharges in 2009 in the US, nearly three-quarters of the discharges were among individuals with MCC [43]. Secondly, MCC can place an enormous financial burden on the patients and their families and caregivers through increased out-of-pocket healthcare expenditures. The burden of out-of-pocket healthcare expenditures defined as the percent of income spent out-of-pocket on healthcare was higher among those with MCC as compared to those without MCC [22]. In addition, individuals with MCC have complex disease trajectories due to interactions among the co-existing conditions as well as the interactions of the concomitant medications [44]. These interactions can increase the risk of polypharmacy leading to the soaring healthcare costs [45]. Also, adults with MCC were more likely to have polypharmacy as compared to those without MCC [46], increasing the risk of adverse drug events [47]. Adverse drug events contributed $3.5 billion (2006 US dollar) to total healthcare costs [48]. Individuals with MCC tend to seek more specialty services as compared to those without MCC [49], which may also lead to higher costs.

However, under healthcare systems designed to provide care on a fee-for-service and disease-by-disease basis, the presence of MCC often leads to inadequate care coordination [50, 51]. Such fragmentation in care for patients with MCC is often associated with negative consequences. Using the Herfindahl-Hirschman concentration index (HHI), researchers have found that nearly 30% of individuals with MCC had the most fragmented care; such fragmented care among individuals with chronic conditions can lead to increasing costs [52]. Also individuals with MCC were more likely to have preventable hospitalizations as compared to those without MCC [53].

Furthermore, many randomized clinical trials (RCTs) exclude individuals with MCC. However, almost all patients eligible for RCTs had MCC [54]. Consequently, there is a lack of clinical practice guidelines for the management of MCC [55]. Even when clinical practice guidelines attempt to incorporate the presence of MCC, the guidelines are often drafted in the context of a single disease [56]. Therefore, many individuals with MCC receive treatments that conflict with other treatments or receive potentially inappropriate treatment [57], which can lead to increased costs.

Study Designs for Examining the Association between MCC and Costs

An overwhelming majority of the studies adopted the retrospective cross-sectional design [10]. Two German studies utilized prospective cohort data from clinical trials [26, 31]. In terms of time horizon, the common time unit used to adjust cost related to MCC was one year or less, but there are studies particularly interested in lifetime cost evaluation [58].

Data Sources for Examining the Association between MCC and Costs

Costs are estimated using a variety of data sources. In the US alone, 88 data sources were available for measuring healthcare costs [59]. Fee-for-service claims, electronic health records, and self-reports have been the common sources of data to examine the relationship between MCC and costs. Many studies used claims data [21, 23, 32–34, 43, 60–61]. Other studies have used self-report data for chronic conditions and a hybrid of billing data and self-reported data for costs [22, 24, 27, 29, 31, 62, 63]. Some also utilized clinical data mainly from medical records [25, 28, 36, 58].

When using claims data, MCC are often identified using the International Classification of Diseases (ICD) codes [40] or prescription drug codes such as the National Drug Code (NDC) in the Rx-MG [33]. Costs are ascertained using fee-for-service payments to the providers [59] or activity-based payments [64]. There are various strengths and limitations associated with the use of each dataset related to the evaluation of MCC and costs. For example, cost estimates obtained from claims data only represents the actual reimbursable amount and do not capture the non-reimbursable health services, out-of-pocket costs. Furthermore, costs due to lost productivity and decrement in quality of life are not included in assessment, resulting in an underestimation of the total economic burden on individuals and families [32–34]. Also, claims data oftentimes do not capture the severity of clinical conditions. Furthermore, in countries such as the US, where an individual may be covered by multiple types of health insurance (e.g., Medicare/VHA, Medicare/Medicaid, private/public), using data from only one of the payers can underestimate costs and group differences in costs [32–34]. Medical record data [36] could be time-consuming and labor intensive and may not be easy for population-based research. On the other hand, self-report data may be associated with recall and response bias [27].

Types of Costs Used in Examining the Association between MCC and Costs

Direct Versus Indirect Costs—In assessing the economic burden of MCC, a distinction between direct and indirect costs associated with healthcare need to be made. Direct costs can consist of costs incurred by healthcare systems, individuals, families, and communities to manage diseases and illnesses. Direct costs include direct medical costs that are paid

specifically for healthcare services and direct non-medical costs that can enable patients to receive healthcare services such as transportation and special diet [65]. Indirect costs are not directly accountable by illnesses or diseases such as costs of lost productivity due to the illness. Studies evaluating healthcare costs have typically included direct medical costs. These costs can include direct medical costs associated with MCC and paid by insurance providers [27, 31, 32, 34, 36] or the out-of-pocket spending on healthcare by patients or their families [27, 63]. The direct medical costs by the payers have been further divided by the type of service such as inpatient visit, outpatient visit, physician office visit, pharmacy, emergency department, diagnostic and laboratory tests, nursing home care and hospice care [34, 36]. For example, a Swiss study estimated that the average total healthcare costs were 5.5 times higher in elderly patients with MCC as compared to elderly patients without MCC; 50.8% of the total cost comprised of outpatient visits, 24.1% were for inpatient visits and 25.1% were for prescription drugs [34]. Another study carried out in Germany among 1,937 elderly (>=72 years) individuals with MCC also provided percentage of costs spent on each component: 25% on inpatient care, 20% on outpatient care, 20% on prescription drugs, 12% on assisted living and transportation, 8% on healthcare products and dentures, 7% on rehabilitation, 5% on outpatient non-physician providers and 3% on mandatory long-term care insurance [31]. Studies generally specify the components of costs used to calculate the total costs. For example, in one study among the Veterans in the US, the total costs were derived by adding the inpatient, outpatient, pharmacy, and contract care costs [25].

The out-of-pocket costs are represented by out-of-pocket spending burden, defined as the ratio of out-of-pocket spending to personal income [62, 66]. High out-of-pocket spending burden is sometimes represented as spending 10% or more of personal income on healthcare. According to Hwang et al., 2001, 21.2% of families with members having two or more chronic conditions spent 10% or more of their income on healthcare as compared to only 4.3% of families spending 10% or more of their income on healthcare [62]. Among adults with arthritis, diabetes mellitus, heart disease, and hypertension, no statistically significant differences in out-of-pocket expenditures were found [27]. Another study done in Australia [22] estimated out of pocket spending burden in terms of moderate (if out of pocket spending <= 10% annual income) versus severe financial stress (if out of pocket spending >=20% of annual income).

Indirect Costs—Indirect costs are defined as costs incurred due to cessation or reduction in worker productivity as a result of morbidity and mortality of illnesses. These are typically measured in terms of lost wages or income, work disability, lost leisure time, productivity loss to employers, and others. Very few studies have assessed the indirect costs of MCC, perhaps due to the difficulties in capturing non-monetary costs. Studies have typically estimated indirect costs due to lost productivity rather than other intangible costs such as decrements in the quality of life. A study done in Canada, estimating both direct and indirect cost among patients with three chronic conditions: osteoarthritis, rheumatoid arthritis and hypertension. This study estimated the total indirect costs of the chronic conditions by assessing the time costs incurred by patients and caregivers due to absence from work as well as by estimating the time costs due to the patient's inability to perform household chores [38].

Charges, Payments, and Activity-based costs—While the measurement of out-of-pocket costs is clear, the measurement of costs other than out-of-pocket costs varied across studies. For instance, studies using the US Healthcare Cost and Utilization Project (HCUP) data, hospital charges are often adjusted with the charges to costs ratio to represent inpatient costs [67]. However, such ratio is a poor proxy for costs [68]. Indeed, one study estimated an error rate of 10% in charges to costs conversions [68]. Furthermore, hospital charges do not necessarily represent the actual cost as most insurance payers negotiate reimbursement rates and receive discounts that might lead to substantial overestimation of the hospital cost [43].

Some studies have examined the cost burden of MCC using costs using an activity-based cost allocation system [69], in which costs are assigned to patients and encounters based on the workload. In the US, Veterans Health Administration uses an activity-based cost allocation system to calculate medical care costs of services delivered to veterans [70]. As pointed out by Lipscomb and colleagues, such costing may be specific to a particular site and may not be generalizable across various sites [71]. Furthermore, activity-based cost allocations are not widely practiced.

Multivariable Methods of Determining the Association between MCC and Costs

A variety of clinical and non-clinical factors influences healthcare costs. Therefore, many studies have used regressions models examine the association between MCCs and costs. In these studies, the presence of MCC was included as one of the independent variables. These studies have considered the influence of the number of chronic conditions [22, 36], combinations of chronic conditions [27], complexities of chronic conditions [60], rate of increase in MCC [31] on costs. In an Australian study, McRae and colleagues found that financial burden due to healthcare costs significantly increased with increase in number of chronic conditions after adjusting for socioeconomic conditions and general health among elderly population [22]. In another study carried out in Ireland, Glynn and colleagues found that after controlling for age, gender and free medical care eligibility, total healthcare costs increased significantly with the increase in number of chronic conditions [36]. In a study conducted in the US, Meraya and colleagues examined how healthcare costs was affected by the combinations of four chronic conditions and found that adults with co-existing diabetes and hypertension and adults with coexisting hypertension and arthritis incurred significantly lower healthcare costs as compared to adults with diabetes and heart disease after adjusting for socio-demographic factors, health status and comorbidities [27]. Investigators have also used number of different chronic conditions as a proxy for a measure of complexity, and concluded that number of chronic conditions was an independent predictor of per patient hospital costs after controlling for hospital-level factors such as ownership, large size, urban/rural location, and teaching status [60]. Investigators found that at the population level, certain pairs of chronic conditions are more “severe” based on the total healthcare cost with diabetes, and hypertension identified as “low severity” to heart failure and chronic kidney disease identified as “high severity”. After adjusting for age, gender and deprivation, investigators found that all pairs of chronic conditions incurred significantly higher costs than the respective single conditions [28]. In a study conducted in Germany, investigators examined the impact of the rise in the rate of MCC on mean total healthcare costs and

concluded that rate of multimorbidity could explain 11.5% of the variation in total healthcare costs [31].

Ordinary Least Squares (OLS) Regression on Log-transformed Costs—The use of OLS regressions in estimating costs is not straightforward. Because of the characteristics of costs (e.g., the zero mass, skewness, nonlinearity), many investigators have used log-transformed costs. For example, using log-transformed costs, Kuo and Lai (2013) found that estimated total annual costs associated with 1–4, 5–8 and >8 Rx-MG classified chronic conditions increased by 11.6 times, 12.7 times, and 13.8 times, respectively, as compared to those who with no chronic conditions [33].

Generalized Linear Models of Costs—The exponentiation of parameter estimates from the OLS regression on log-transformed expenditures provide an estimate of the geometric mean rather than the arithmetic mean. Because mean and geometric mean expenditures are usually different, a factor is needed to correct for the retransformation bias. A nonparametric approach called the Duan Smear, is used to correct this retransformation bias [72]. The retransformation may require subgroup-specific smearing factors, in which case it gets complicated. The generalized linear model (GLM) is an especially attractive alternative [73] because it has the advantages of the log models and does not require smearing correction and can be easily converted to original dollars. Some studies have used the GLM to examine the association between MCC and healthcare expenditures [36, 74]. Using the GLM with a log-link function and gamma error distribution, a study from Ireland found that patients with 4 or more conditions had 539% higher costs as compared to those with no chronic condition [36], Using the GLM model with a log-link, Banerjea and colleagues found that individuals with MCC had 320% greater expenditures as compared to those without MCC [74]. It has to be noted that the presence of MCC was defined within a selected list of mental health conditions and substance use disorders.

Accounting for Zero Costs—Some types of healthcare costs such as inpatient costs have zero masses (numerous non-users). In such cases, one of the solutions can be a two-part model. Under this approach, the first stage models the probability of use and the second stage GLM models are used to examine expenditures. One study from Germany used Tobit regressions, which combined the users and non-users to predict costs [75]. Using a modified cumulative illness rating scale, this study found that for each unit increase in the scale, total costs for the 3-month period increased by 42 Euros.

Quantile Regression—The association between MCC and costs can also be examined at 25^{th}, 50^{th}, 75^{th}, and 90^{th} percentile of the expenditure distribution to consider whether the effects are weaker or stronger at some points of the distribution. Median regression is a special case of quantile regression. Median regression estimates a line through the data that minimizes the sum of absolute residuals (rather than the sum of the squared residuals, as in ordinary least squares estimator). Different quantiles are estimated by weighting the residuals differently. For the median regression, all residuals receive equal weight. However, when estimating the 75^{th} percentile, negative residuals are weighted by 0.25 and positive residuals by 0.75. The criterion is minimized, when 75% of the residuals are negative. Thus,

even for the extreme quantiles all the sample observations are used to fit the model. An advantage of these quantile regression estimators is that they give less weight to outlier data points on the dependent variable that may affect the influence of such data points on the findings [76].

Survival Models of Costs—As individuals with MCC are at higher risk for mortality [77], studies tend to exclude individuals who died during the study period from the estimation of costs. These individuals might have either very high healthcare expenditures if most of their end of life was captured or very low expenditures if they contributed only very few months of observations [78]. Survival analysis techniques have been proposed to analyze costs [79]. A few studies have analyzed costs with survival models [80, 81], yet the application of survival models to cost data may be questionable because of high tendency to violate the assumptions of the models [81].

Other Statistical Approaches—König et al. (2013) used a conditional inference tree (CTREE) algorithm to facilitate the visualization of data hierarchy and identify the underlying structure and influential variables [26]. The study found that Parkinson's and cardiac diseases had the highest impacts on total costs, increasing the total mean health costs by 3.5 times and twice, respectively, compared to those without these two kinds of diseases.

Understanding the Factors that Contribute to the Excess Cost Associated with MCC

As medical decisions and costs are often influenced by non-clinical factors [82], some studies have attempted to understand the extent to which excess cost burden associated with MCC can be explained by differences in characteristics between those with MCC and without MCC. These studies have typically applied the post-regression linear decomposition techniques developed by Blinder-Oaxaca [83, 84]. The linear decomposition technique enables investigators to assess how much of the differences in expenditures of the two groups (MCC and no MCC) may be due to observed factors and unobserved factors [41, 85]. Using the decomposition techniques, these studies find that most of the cost differences between those with and without MCC remain unexplained.

Expert Commentary

There are many challenges in estimating excess costs associated with MCC. It is not possible to summarize the excess cost burden associated with MCC in one simple measure. First, there is neither a universal operational definition of MCC available in the literature nor a standard way to estimate MCC, which in turn complicates cost evaluation of MCC. It is suggested that there is no gold standard definition or method that could serve all purposes [86]. For the cost evaluation of MCC in the US healthcare system, the clinical classification system developed by the US Agency for Healthcare Research and Quality (AHRQ) and the Multiple Chronic Conditions Measurement Framework developed by the US National Quality Forum may be a good starting point. The clinical classification system has been validated in several studies [62, 60, 61, 63] and Hwang et al. (2001) have provided good examples of how to use it as a tool to group chronic conditions into mutually exclusive, clinical heterogeneous condition categories and then estimate associated medical costs [62]. On the other hand, there are researchers working on establishing a standard methodology to

study MCC. Fortin and colleagues (2012) have recommended that at least 12 chronic conditions should be included when studying MCC and they suggested using “three or more co-existing chronic conditions” as the definition of MCC. As per the investigators, such a definition can identify the true high-risk target population with complex medical care needs [87].

Second, most studies have used additive models to estimate costs. Some studies have used categories of MCC to account for the non-linear relationships in costs. Such adjustments may not be adequate because chronic conditions may have complex interactions and the relationships among groups of chronic conditions could be concordant or discordant. For example, diabetes and hypertension require similar treatment regimen and share some of the same quality indicators, which in turn can lead to lower health utilization [28] and lower total medical costs even after controlling other variables than other types of combination [27]. On the other hand, diabetes and depression may be considered as discordant because tricyclic antidepressants might result in a decrease in glucose tolerance and deteriorate diabetic control [88]. Additionally, the negative impact of depression itself on adherence to medications treating chronic conditions has been well-studied [89], which could further result in worse treatment outcomes and increased healthcare costs. Therefore, given that costs could vary by different types of combination of chronic conditions [27], cost estimation of MCC should also take into account these interactions and their effects on costs [10]. Examining common combinations of different chronic condition in the target population, as demonstrated in Schoenberg et al. (2007) [29], is an important way of accounting for the interactions between chronic condition. Such definitions could be more relevant to clinical practice and policy interventions.

Third, there exist significant knowledge gaps in this field. There is limited literature on the indirect costs associated with MCC. A good estimation of monetary evaluations of productivity losses is needed. In this context, the published study by Grosse and colleagues is a step in the right direction [90]. This study has estimated the average hourly, annual, and life productivity of both market and household. These calculations are available for 5-year age groups, for men, women, and both sexes in the United States.

As pharmacotherapy is an important modality of treatment for many chronic conditions, future research need to focus on polypharmacy (the use of multiple medications) in MCC and their impact on healthcare expenditures [10]. Elderly with multiple chronic conditions account for 57% of total drug expenditures [91]. If a patient were prescribed as per the clinical practice guidelines, an elderly individual with hypertension, diabetes, osteoporosis, osteoarthritis, and COPD would use 12 separate medications with 19 doses per day [92]. In the light of new evidence on the use of commonly prescribed medications leading to chronic conditions [8] or having protective effect for certain chronic conditions [93], it is important to focus on the specific classes of medications and their impact on total healthcare costs.

Most of the studies have used cross-sectional designs. In cross-sectional studies, a prevalence-based approach is used to assess costs. Under this approach, costs for those with a new diagnosis of a chronic condition and costs for those with the prevalent condition are combined; disease severity and duration of MCC are generally ignored. Furthermore, studies

using cross-sectional designs do not address the causal association between MCC and costs. Approaches (marginal structural models) may be needed to confirm that it is the MCC that lead to excess financial burden rather than some other shared risk factors.

Five-year view

Research on MCC and associated costs is still an emerging field. In reviewing current available evidence on the cost burden associated with MCC, we propose some suggestions here for future research: there is a need for studies that focus on how MCC affect total healthcare costs that include direct non-medical costs and indirect costs as well. Studies that track costs over a period of time are needed so that programs and interventions can be executed at specific time periods when costs peak. The extent to which non-clinical factors (both modifiable and structural) contribute to the excess cost burden associated with MCC need to be examined, which may be achieved through econometric methods such as the post-linear regression decomposition techniques.

To meet complex needs of the patients with MCC, in the US, healthcare delivery models such as the Accountable Care Organizations (ACO) and patient-centered medical homes (PCMH) are being considered as alternatives to the traditional practice models. To make these models sustainable, we need to evaluate costs by following individuals with MCC over a period of time rather than comparing costs between individuals with and without MCC. Furthermore, in the US, one of the payment reforms includes bundled payments for services. It is assumed that such payment models will encourage the care to be patient-centered rather than disease-centered. The bundled payments are based on an episode of care approach as opposed to a capitation model in which lump sum payments to providers are made to take care of a patient. Currently, 48 episodes are eligible for bundled payments [94]. Currently, the bundled payments are targeted towards acute and post-acute care. The numerous challenges to implementing such policies in cardiovascular conditions and the mixed evidence for patient care have been highlighted [95]. However, policy makers and insurance providers could adopt a similar approach to provide ongoing care for those with MCC, especially for patients with naturally clustering chronic conditions.

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Key issues

- Multimorbidity is highly prevalent throughout the world.
- The presence of multiple chronic conditions (MCC) in the same individual has profound implications for healthcare costs and utilization.
- There is neither a universal operational definition of MCC available in the literature nor a standard way to estimate MCC, which in turn complicates cost evaluation of MCC.
- Most current studies used additive models to assess costs, but given that costs could vary by different types of combination of chronic conditions, cost estimation of MCC should also take into account these interactions and their effects on costs.
- There is limited literature on indirect costs associated with MCC. A good estimation of monetary evaluations of productivity losses is needed.