

COMMENTARY

Multimorbidity and comorbidity revisited: refining the concepts for international health research

Kathryn Nicholson^{a,b,*}, Tatjana T. Makovski^{c,d,e}, Lauren E. Griffith^b, Parminder Raina^b, Saverio Stranges^{a,c,f}, Marjan van den Akker^{d,g}

^aDepartment of Epidemiology & Biostatistics, Western University, London, Ontario, Canada

^bDepartment of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada

^cEpidemiology and Public Health Research Unit, Department of Population Health, Luxembourg Institute of Health, Strassen, Luxembourg

^dDepartment of Family Medicine, Care and Public Health Research Institute, Maastricht University, Maastricht, the Netherlands

^eChairgroup of Complex Genetics and Epidemiology, Care and Public Health Research Institute, Maastricht University, Maastricht, the Netherlands

^fDepartment of Family Medicine, Western University, London, Ontario, Canada

^gAcademic Center for General Practice, Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium

Accepted 4 September 2018; Published online 22 September 2018

1. Introduction

In more than 20 years since advocating for the distinction between the terms “multimorbidity” and “comorbidity” [1], there continues to be exponential growth in the amount of quantitative and qualitative research published on the prevalence, characteristics, and outcomes of living with multiple health issues in populations across the world [2–4]. As indicated in an overview of 53 systematic reviews, much of this research has relevance to patients and caregivers, academic researchers, health policy-makers, and practicing health care professionals [2]. Most identified reviews in the literature examined the topics of definition and measurement, prevalence levels, disease clusters and patterns, risk factors, outcomes, medication, intervention, and management [2]. A recent study of 28 countries using the World Health Survey shows that the increasing prevalence of multiple chronic conditions is now a global phenomenon affecting both low- and middle-income countries, as well as high-income countries [4]. Indeed, the lifespan of populations around the world is increasing because of improvements in public health measures and the significant success of modern medicine and technology [5,6]. However, we have not achieved an equal increase in the health span of individuals or their quality of life, meaning that although populations are living longer, they are not necessarily living disease-free for a longer period.

Instead, aging populations have increasingly created a new health scenario in which there is a higher prevalence of

comorbidity, multimorbidity, polypharmacy, complexity, disability, and frailty [2,7,8]. This coexistence of interrelated health states (which may or may not be mutually exclusive categories depending on the definition and measurement of concepts by the research team), particularly in the broader context of aging, has created challenges in adequately capturing or conceptualizing the burden of living with multiple chronic conditions or multiple health issues. Additionally, as first noted in a commentary published in 2001 in this journal, there continue to be conceptual and practical issues in determining the appropriate occurrence rates of living with multiple health issues [9]. Therefore, the objective of this commentary is to highlight the current issues in defining the broad concept of multimorbidity within the context of international research and to re-establish the distinction between the concepts of “multimorbidity” and “comorbidity.” These terms continue to be used interchangeably despite the notable implications of ongoing misuse and misclassification. For the purposes of this commentary, our use of the terms will be focused on multiple chronic conditions (and not on co-occurring symptoms or risk factors). This re-emphasis on conceptual clarity is timely, given the ever-increasing number of studies examining the impact of multiple chronic conditions, in both developed and developing countries (often explored in aging populations), and with the recent assignment of a Medical Subject Headings (MeSH) for “multimorbidity” (now distinct from the MeSH term of “comorbidity”) in January 2018.

2. Refining the concept of multimorbidity

The term “multimorbidity” is often defined as the co-occurrence of multiple chronic conditions within the same

Conflicts of interest: The authors of this commentary have no conflicts of interest to declare.

* Corresponding author. Tel.: +1 519 661 2162; fax: +1 519 661 3766.

E-mail addresses: kathryn.nicholson@schulich.uwo.ca or nichok5@mcmaster.ca (K. Nicholson).

What is new?**Key findings**

- This commentary highlights a renewed distinction between the concepts of multimorbidity and comorbidity, within the broader contexts of clinical and academic settings.
- While both terms focus on the occurrence of multiple chronic conditions within the same individual, the term “comorbidity” refers to the combined effects of additional conditions in reference to an index chronic condition (such as comorbidity in diabetes mellitus, stroke, depression or cancer). In comparison, the term “multimorbidity” indicates that no single condition holds priority over any of the co-occurring conditions from the perspective of the patient and the health care professional.

What this adds to what was known?

- This commentary builds from existing literature and ongoing conversations among clinical and research teams regarding the challenges of properly framing the management and study of multiple chronic conditions, particularly for cross-national health research.
- This commentary aims to provide further guidance on when to select a comorbidity or multimorbidity framework in the clinical or academic setting.

What is the implication, what should change now?

- This distinction between multimorbidity, comorbidity and related terms is particularly timely with the ever-increasing number of studies examining the impact of multiple chronic conditions, in both developed and developing countries in international research (often explored in ageing populations), and with the recent assignment of a MeSH term for multimorbidity (now distinct from comorbidity) in January 2018.
- Researchers must continue to be diligent in their selection, definition, measurement and reporting of the concepts they are using in their study design and publication moving forward.

individual, in which a condition is classified as chronic if it is permanent, it is caused by nonreversible pathologic alterations or requires rehabilitation or a long period of care [1,8,10,11]. The term “comorbidity” refers to the combined effects of additional conditions in reference to an index disease (such as comorbidity in diabetes mellitus,

stroke, depression, or cancer). In comparison, the term “multimorbidity” indicates that no single condition holds priority over any of the co-occurring conditions from the perspective of the patient, health care professional, or academic research team [1,10]. These two terms have provided the necessary basis to begin to explore the prevalence, characteristics, and burden of multiple chronic conditions for patients, health care professionals, and the health care system. It remains challenging to achieve a balance between patient-centered and research-practical definition and measurement. This ongoing challenge was articulated in a recent Letter to the Editor in this journal from Boeckxstaens and et al. who summarized the disillusion with inadequate measures of multimorbidity and proposed an integrative biopsychosocial model for assessing the various dimensions of multimorbidity [12]. This model incorporates the potential causes and consequences of multiple health problems within an individual, including physiological, functional, social, environmental, and personal factors [12], which begins to align with complexity frameworks that have been presented by others [13,14]. Certainly, this proposed model can move toward a more multidimensional understanding of living with multimorbidity, compared with a focus merely on establishing a “gold standard” list of multiple chronic conditions.

Although multimorbidity is often attributed to the aging process, the occurrence of multimorbidity is more realistically conceptualized as the interaction among genetic predisposition, socioeconomic disparities, unhealthy lifestyle choices, cumulative deficits, multisystem failures, and, interestingly, regular or irregular contact with the health care system. Although an aging population is particularly burdened by the accumulation of multiple chronic conditions over time [15–17], this can be an incomplete depiction. In fact, the accumulation is increasingly occurring in younger age groups, indicating a timely opportunity for prevention and a need to focus on patient-relevant outcome measures (PROMs). To date, a large focus of academic research has been placed on chronic multimorbidity and the type and number of individual chronic diseases that should be included for an adequate or valid multimorbidity measure [2,18]. In comparison, the functional and social health issues (such as functional disability or low levels of social support) tend to be included as outcomes or effect modifiers for multimorbidity. Research has indicated that to assess patient-relevant outcomes, both social and medical components should be included to address the spectrum of factors that drive patient complexity with multimorbidity [4,19]. These have been more explicitly identified in the Core Outcome Set for Multimorbidity Research (COSmm) by Smith et al. [20].

Additional concepts related to this more holistic view of multimorbidity are disability, frailty, and complexity. These concepts may complement the understanding of multimorbidity or become the main focus of health professionals or research teams. The term disability refers to a need for

assistance with or an inability to perform basic or instrumental activities of daily living [21,22], whereas frailty refers to a dynamic and multidimensional clinical condition of increased vulnerability and cumulative decline that erodes homeostatic reserve when individuals encounter a stressor event [23–25]. The term complexity emerges when the persistence and progression of diseases and courses of treatments, as well as the many contextual factors in an individual's life and clinical care are considered [13,14,26]. As such, clinical and academic teams must be diligent in their selection, definition, measurement, and reporting of concepts that are adopted within research study designs and eventual reporting of findings. This would facilitate a more refined understanding of these related concepts, particularly in the context of international health research and cross-country comparisons moving forward.

3. Distinguishing between multimorbidity and comorbidity

The terms “comorbidity” and “multimorbidity” have been used somewhat interchangeably in published literature, creating a knowledge base that can easily conflate these two concepts. However, the creation of a MeSH for “multimorbidity” in January 2018 indicates the important distinction that should occur in publications and systematic searches for literature examining either the concept of multimorbidity or comorbidity (<https://meshb.nlm.nih.gov/record/ui?ui=D000076322>). Although this will facilitate more efficient indexing and searching of published articles on the subject of multimorbidity, it is important that researchers apply considerable care when interpreting a published study or creating their own study examining multiple health conditions. As such, we feel that it is both timely and relevant to re-emphasize the distinction for academic and clinical clarity between these terms moving forward. For example, some published literature has used the term “comorbidity” when “multimorbidity” would be more appropriate; “multimorbidity” when “comorbidity” would be more appropriate; and even the term “multiple comorbidities,” which can be a particularly vague and inappropriate combination of the two distinct terms. More appropriate uses of the term comorbidity exist in the literature and are framed as a focus on patients living with a specific chronic condition (such as diabetes, stroke, or dementia) and the implications of these conditions for complex management programs and clinical care delivery [27–29]. Because of the lack of clinical guidelines that actively account and respond to the challenges of multimorbidity in clinical management [15,30,31], the tools that are available to health care professionals often have a comorbidity orientation by assessing the impact of a co-occurring condition (or its management protocol) on another condition. As yet, those clinical interventions that have been specifically designed to focus on comorbidity can show more

significant effects than interventions that are designed for multimorbidity [32]. The recent recommendations from the National Institute for Health and Care Excellence (NICE) help to provide guidance on the optimum management that takes account of an individual's multimorbidity [33]. Further exploration of successful clinical and public health interventions and successful integration of guidelines (such as those provided by NICE and the Ariadne principles described in the following), with a careful distinction between comorbidity- and multimorbidity-specific contexts, is important.

The inappropriate use of terminology has implications in clinical and academic contexts when delivering care and when answering a research question. The fluctuation in health status has been extensively described in the Ariadne principles, which were created to provide an orientation in decision-making during clinical care encounters [31]. In a clinical environment, health care professionals encounter patients who are living with distinct or fluctuating health issues, and typically, the approach to clinical management can be driven by the presenting problem(s) from the patient. As described in these principles, the presenting problem(s) may be focused on a single chronic condition (creating a comorbidity framework) or may be complicated by the presence of the patient's existing chronic conditions or from treatment of those conditions (creating a multimorbidity framework) [31]. In an academic environment, the framework that is adapted should be informed by the a priori research question. For example, a research question may aim to understand the implications from a single index chronic condition and assess any future risk for subsequent health problems from this single condition (creating a comorbidity framework). In contrast, a research question may be broadened to understand the causes or consequences of multiple chronic conditions in which no single condition holds priority, and a more holistic approach is desired by the research team (creating a multimorbidity framework). An awareness of the distinction between these complementary frameworks will help to ensure that an appropriate approach is taken to understand and communicate the complexities of multiple chronic conditions.

4. Conclusion

This commentary highlights a renewed distinction between the concepts of comorbidity (multiple co-occurring chronic conditions, but with a focus on a singular condition) and multimorbidity (multiple co-occurring chronic conditions, but with a focus on multiple conditions), within the broader context of cross-national health research. This commentary builds from existing literature and ongoing conversations among international research teams regarding the challenges of properly defining, measuring, and applying the interrelated concepts of multimorbidity and comorbidity

in diverse populations. This commentary also has highlighted the important ongoing work that integrates biopsychosocial factors into the assessment of the impact of multiple chronic conditions (such as through the use of PROMs or the COSmm). Moreover, the authors acknowledge the complex interplay between comorbidity, multimorbidity, functional impairments, frailty, aging, patient-centeredness, and complexity. Each of these distinct and interrelated concepts has important implications in both academic contexts and clinical settings. These concepts are also experienced differently by individuals living with multiple chronic diseases and within different international contexts. The research community should (re)acknowledge the important distinction between comorbidity and multimorbidity. Of course, there are conceptual and practical challenges to operationalize these terms; however, we consider this to be a particularly important time to define these concepts and to differentiate between similar notions. Resources available to the research community like the International Research Community on Multimorbidity (<http://crmcspblog.recherche.usherbrooke.ca>), Methods Crystals for Multimorbidity [34], and now distinct MeSH terms for multimorbidity and comorbidity are particularly significant to facilitate ongoing distinction between the concepts and encourage discussion and collaboration among international research teams. Researchers must continue to be diligent in their selection, definition, measurement, and reporting of the concepts they are using in their study design and publication to ensure that multimorbidity and comorbidity research is clear and impactful moving forward.

References

- [1] van den Akker M, Buntinx F, Knottnerus AJ. Comorbidity or multimorbidity: what's in a name? A review of literature. *Eur J Gen Pract* 1996;2:65–70.
- [2] Xu X, Mishra GD, Jones M. Mapping the global research landscape and knowledge gaps on multimorbidity: a bibliometric study. *J Glob Health* 2017;7(1):010414.
- [3] McPhail SM. Multimorbidity in chronic disease: impact on health care resources and costs. *Risk Manag Healthc Policy* 2016;9:143–56.
- [4] Afshar S, Roderick PJ, Kowal P, Dimitrov BD, Hill AG. Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the World Health Surveys. *BMC Public Health* 2015;15:776–86.
- [5] World Health Organisation. World health statistics 2014. Geneva: WHO; 2014.
- [6] World Health Organisation. Strategy and action plan for healthy ageing in Europe, 2012–2020. Copenhagen, Denmark: WHO; 2012.
- [7] Fabbri E, Zoli M, Gonzalez-Freire M, Salive ME, Studenski SA, Ferrucci L. Aging and multimorbidity: new tasks, priorities and frontiers for integrated gerontological and clinical research. *J Am Med Dir Assoc* 2015;16:640–7.
- [8] Villacampa-Fernández P, Navarro-Pardo E, Tarín JJ, Cano A. Frailty and multimorbidity: two related yet different concepts. *Maturitas* 2017;95:31–5.
- [9] van den Akker M, Buntinx F, Roos S, Knottnerus JA. Problems in determining occurrence rates of multimorbidity. *J Clin Epidemiol* 2001;54:675–9.
- [10] Boyd CM, Fortin M. Future of multimorbidity research: how should understanding of multimorbidity inform health system design? *Public Health Rev* 2010;32(2):451–74.
- [11] Fortin M, Lapointe L, Hudon C, Vanasse A. Multimorbidity is common to family practice: is it commonly researched? *Can Fam Physician* 2005;51:245–51.
- [12] Boeckxstaens P, De Sutter A, Vaes B, Degryse JM. Should we keep on measuring multimorbidity? *J Clin Epidemiol* 2016;71:113–4.
- [13] Schaik AK, Kuluski K, Lyons RF, Fortin M, Jadad AR, Upshur R, et al. A scoping review and thematic classification of patient complexity: offering a unifying framework. *J Comorb* 2012;2:1–9.
- [14] Shippee ND, Shah ND, May CR, Mair FS, Montori VM. Cumulative complexity: a functional, patient-centered model of patient complexity can improve research and practice. *J Clin Epidemiol* 2012;65:1041–51.
- [15] Banerjee S. Multimorbidity - older adults need health care that can count past one. *Lancet* 2015;385:587–9.
- [16] Prince MJ, Wu F, Guo Y, Gutierrez Robledo LM, O'Donnell M, Sullivan R, et al. The burden of disease in older people and implications for health policy and practice. *Lancet* 2015;385:549–62.
- [17] Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Ageing with multimorbidity: a systematic review of the literature. *Ageing Res Rev* 2011;10(4):430–9.
- [18] Calderón-Larrañaga A, Vetrano DL, Onder G, Gimeno-Feliu LA, Coscollar-Santaliestra C, Carfi A, et al. Assessing and measuring chronic multimorbidity in the older population: a proposal for its operationalization. *J Gerontol A Biol Sci Med Sci* 2017;72(10):1417–23.
- [19] Zullig LL, Whitson HE, Hastings SN, Beadles C, Kravchenko J, Akushevich I, et al. A systematic review of conceptual frameworks of medical complexity and new model development. *J Gen Intern Med* 2016;31:329–37.
- [20] Smith SM, Wallace E, Salisbury C, Sasseville M, Bayliss E, Fortin M. A core outcome set for multimorbidity research (COSmm). *Ann Fam Med* 2018;16(2):132–8.
- [21] Chatterji S, Byles J, Cutler D, Seeman T, Verdes E. Health, functioning, and disability in older adults - present status and future implications. *Lancet* 2015;385:563–75.
- [22] Boeckxstaens P, Vaes B, Legrand D, Dalleur O, De Sutter A, Degryse J-M. The relationship of multimorbidity with disability and frailty in the oldest patients: across-sectional analysis of three measures of multimorbidity in the BELFRAIL cohort. *Eur J Gen Pract* 2015;21:39–44.
- [23] Clegg A, Young J, Iliffe S, Olde Rikkert MGM, Rockwood K. Frailty in elderly people. *Lancet* 2013;381:752–62.
- [24] Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146–56.
- [25] Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004;59:255–63.
- [26] Grembowski D, Schaefer J, Johnson KE, Fischer H, Moore SL, Tai-Seale M, et al. A conceptual model of the role of complexity in the care of patients with multiple chronic conditions. *Med Care* 2014;52: S7–14.
- [27] Markle-Reid M, Ploeg J, Fraser K, Fisher KA, Bartholomew A, Griffith L, et al. Community program improves quality of life and self-management in older adults with diabetes mellitus and comorbidity. *J Am Geriatr Soc* 2018;66(2):263–73.
- [28] Fisher K, Griffith L, Gruneir A, Panjwani D, Gandhi S, Sheng LL, et al. Comorbidity and its relationship with health service use and cost in community-living older adults with diabetes: a population-based study in Ontario, Canada. *Diabetes Res Clin Pract* 2016;122: 113–23.
- [29] Griffith LE, Gruneir A, Fisher K, Panjwani D, Gandhi S, Sheng L, et al. Patterns of health service use in community living older adults

- with dementia and comorbid conditions: a population-based retrospective cohort study in Ontario, Canada. *BMC Geriatr* 2016;16:177–87.
- [30] Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *JAMA* 2005;294:716–24.
- [31] Muth C, van den Akker M, Blom JW, Mallen CD, Rochon J, Schellevis FG, et al. The Ariadne principles: how to handle multimorbidity in primary care consultations. *BMC Med* 2014;12:223–34.
- [32] Smith SM, Soubhi H, Fortin M, Hudon C, O’Dowd T. Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. *BMJ* 2012;345:e5205–15.
- [33] Farmer C, Fenu E, O’Flynn N, Guthrie B. Clinical assessment and management of multimorbidity: summary of NICE guidance. *BMJ* 2016;354:i4843.
- [34] Stewart MA, Fortin M, Britt HC, Harrison CM, Maddocks HL. Comparisons of multi-morbidity in family practice—issues and biases. *Fam Pract* 2013;30:473–80.