Multimorbidity: Definition, Assessment, Measurement and Impact

Pauline Boeckxstaens and Mirko Petrovic, Ghent University, Ghent, Belgium

© 2020 Elsevier Inc. All rights reserved.

Defining Multimorbidity

Defining and categorizing the population with multiple chronic diseases is difficult and consensus on terminology to describe the co-existence of several diseases is missing (José Almirall, 2013; Van Weel and Schellevis, 2006a). The term most frequently used is multimorbidity but even then, a number of definitions of multimorbidity are found. Most authors do not even define the term, hereby mistakenly assuming that the meaning of the term is generally understood.

To start with, the diseases and medical conditions included in studies on multimorbidity vary. Some research uses a selection of specific diseases while other, open list studies put no limits on the type and number of medical conditions studied. Besides, there is a difference between studies assessing only somatic diseases opposed to studies which also include mental health problems, social problems and risk factors in their assessment of multimorbidity. As a matter of fact, defining multimorbidity is closely related to another conceptual debate namely how to define (chronic) disease. The term disease refers to a defined pathophysiological process with a characteristic set of signs and symptoms. Condition can be used as a broader term that includes not only disease but also other health issues which fall outside of the traditional disease model. Examples of such health issues include risk factors like arterial hypertension and hyperlipidaemia which do not cause any symptoms but still may have a substantial impact on clinical care as they require continuous follow-up and treatment. Other examples are geriatric conditions such as fall and incontinence which are often not included in studies on multimorbidity despite their considerable impact on patients’ functional status and quality of life. Mental health problems such as depressive symptoms, tobacco and alcohol abuse and social issues like financial or family problems are also often omitted from multimorbidity assessment but can all be very important in the way care givers deal with chronic diseases and how they provide care. The term illness refers to the patients’ personal experience of their health problems, which allows the inclusion of symptom diagnoses (that constitute 15% of all diagnostic labels in primary care (O’Halloran et al., 2004)) such as dizziness or low back pain provided these have considerable impact on the patient.

The European General Practice Research Network (EGPRN) has proposed a definition of multimorbidity based on a systematic review of the relevant literature and expert consensus (Le Reste et al., 2013). This definition shows the intrinsic complexity of the concept and stresses the controversy between providing a definition which is comprehensive enough to capture the clinical reality of multimorbidity and a definition which is specific enough to allow development of tools to measure the concept of multimorbidity in research. Furthermore, this definition clearly does not resolve the conceptual issue related to the definition of “disease.” As a result, although this definition is not generally accepted and runs the risk of categorizing almost every single patient as “multimorbid,” it describes very well the complexity of the concept.

From a conceptual point of view, it is essential to distinguish the concepts of comorbidity and multimorbidity (van den Akker et al., 1996). Comorbidity entails an index disease and other related diseases (e.g. “Chronic Obstructive Pulmonary Disease (COPD)” or “the comorbidity of Diabetes”) while multimorbidity is defined as any cooccurrence of medical conditions within a person. From the viewpoint of primary health care multimorbidity is the more relevant perspective since general practitioners deal with the broad spectrum of the morbidity of the patient without giving priority to specific disease categories. Besides, from the patients’ perspective, the difference between index diseases and comorbid diseases is seldom relevant as the impact of cooccurring diseases on patients’ individual situation goes beyond individual diseases. Also with increasing age the way diseases interact and intersect becomes more intertangled which leads to the use of nondisease specific concepts such as frailty and vulnerability that are used to describe these patients (Fried et al., 2004a).

Assessing the Prevalence of Multimorbidity

The prevalence of multimorbidity is high and constantly increasing but the absence of a consensus definition and subsequently the lack of comparability between studies prevents giving a unique estimate of the prevalence of multimorbidity. In any case, prevalence figures strongly depend on the operational definition of multimorbidity that is used (Fortin et al., 2010, 2012; Salive, 2013). Actually, the number of chronic conditions included to assess multimorbidity is most decisive for prevalence figures of multimorbidity:
a study assessing a selection of five chronic diseases showed a prevalence of multimorbidity of 3.5% while another comparable study using an open list of diagnoses reported a prevalence of 98.5% for the same age group (Fortin et al., 2012).

Studies including < 10 chronic conditions clearly illustrate lower prevalence rates (Salive, 2013). Consequently, to avoid underestimation of multimorbidity Fortin et al. have proposed to include a minimum number of 12 chronic diseases in multimorbidity assessments (Fortin et al., 2012). On the other hand, these recommendations do not comprise any specification or advice on which specific diseases or conditions to include.

The prevalence of multimorbidity is determined by the population studied as well. Since the prevalence of most chronic conditions increases with age, prevalence figures of multimorbidity will obviously be higher in older populations. In contrast, absolute numbers of patients with multimorbidity are shown to be higher under the age of 65 (Anderson, 2002; Barnett et al., 2012a; Fortin et al., 2005; Hoffman et al., 1996; Taylor et al., 2010).

Prevalence estimates are higher in primary care than in the general population (Fortin et al., 2012). Consequently, it is also important to consider whether a study has been performed at the level of population, family practice or population of patients hospitalized or diagnosed with a specific index disease (Fortin et al., 2010). Also, in order to assess multimorbidity, studies can include conditions diagnosed by a physician or can use patient-reported problems or conditions. The impact of all these differences on the prevalence of multimorbidity is not always easy to predict. However, as these figures may be used for health care planning it is important to take them into consideration (Schram et al., 2008). Some authors have therefore clearly recommended comparing data from different sources (van den Bussche et al., 2013).

Additional aspect which influences the prevalence of multimorbidity is the cut-off used to define multimorbidity. Defining multimorbidity just as the presence of two or more diseases is not generally accepted particularly when highly prevalent risk factors as hypertension, lipid disorders and osteoporosis are included. Very high prevalence of multimorbidity will be noted even in patients who feel little or no impact of disease on symptoms, functional status and quality of life. Some authors have therefore proposed a higher cut off to define multimorbidity or use more strict definitions of chronic disease.

**Measuring Multimorbidity**

An essential prerequisite for research is the disposal of validated instruments to quantify multimorbidity. Some measures of multimorbidity came from research on comorbidity so the terms of co- and multimorbidity are often used interchangeably to depict these measures in more detail.

Most studies use simple disease counts but there is a huge heterogeneity in the number and type of conditions included. Disease counts including up to 35 items have been described and some studies have used open lists (de Groot et al., 2003). The items included in these counts may be individual diseases or health problems or categories of conditions or diseases (Deyo et al., 1992). Many studies do not comprise psychiatric disorders or even use them as exclusion criteria. While long lists of chronic conditions improve the accuracy of measuring multimorbidity, they also contribute to the complexity of the study and may hinder comparisons to other studies (van den Akker et al., 1996).

A potential drawback of summing long lists of conditions, some of which are possibly not very relevant to the patients’ current health status, is that this can create a misleading measure of comorbidity as a patient with many mild conditions might turn out seeming worse than another patient with two very severe conditions (Guralnik, 1996). Furthermore, just counting diseases assigns the same weight to each disease, but in fact these different diseases may have very different impacts on health and survival. Moreover, within one specific disease, different levels of severity may also enfold very differing impacts. For example, in case of osteoarthritis, COPD or diabetes, patients with the same disease label may have very different functional status or prognosis.

In addition to simple disease counts, over 15 measures have been described to measure multimorbidity by means of weighted scores, which assign a different weight to the conditions included in the measure. These weights can be based on the relationship of individual conditions with mortality, resource utilization, severity, etc. (de Groot et al., 2003; Huntley et al., 2012).

We will mention a few often used measures, not as an exhaustive overview, since new measures are still being developed, but more as an illustration of the challenges related to measuring multimorbidity.

The Charlson comorbidity index (CCI) is the most extensively studied measure of multimorbidity (Charlson et al., 1987). As it was originally developed to predict 1-year mortality among hospitalized patients, the conditions included in the index have merely been selected and weighted based on their association with mortality. In addition to its close relationship with mortality, the CCI has also been validated against length of hospital stay, postoperative complications, institutionalization, disability, hospital readmissions and hospital charges (de Groot et al., 2003; Charlson et al., 2008). Since the CCI was initially developed for risk adjustment to predict mortality, age is also assigned a certain weight, given the fact that every decade above the age of 40 adds a score of +1 to the CCI. Different forms of the CCI have been developed, which can be administered by a health professional both paper based and electronically or self-completed as a questionnaire by patients. In addition, it has been adapted for use in ICD-9 (International Classification of Diseases) databases which allows automated extraction of data (Deyo et al., 1992; Romano et al., 1993).

The Cumulative Illness Rating Scale (CIRS) is a comprehensive measure of multimorbidity which does not imply a preselected list of chronic diseases (Linn et al., 1968). By itself the CIRS is the only measure where rare chronic diseases (e.g. amyotrophic lateral sclerosis), symptom diagnoses or less known conditions (e.g. irritable bowel syndrome or chronic fatigue) with high impact on the
patients’ quality of life or functional status can be included. Each item is assigned a severity score by means of an assessment of the impact on the patient, which is performed by the patient himself or a care giver: 1 (no problem), 2 (current mild problem or past significant problem), 3 (moderate disability or morbidity), 4 (severe problem), 5 (extremely severe or life threatening problem). The CIRS classifies all items into 14 body systems (Hudon et al., 2007). The CIRS-CI (CIRS Comorbidity Index) counts the number of body systems affected while other operationalizations of the CIRS sum the severity scores of all body systems (Hudon et al., 2007). When using sums of severity scores, patients with single but very severe disease can have higher CIRS scores than patients with several mild diseases. With the use of the CIRS-CI, a CIRS > 1 will always indicate at least two diagnoses within two different body systems. The CIRS can be applied directly in consultations by care giver of the patient or it can be validly reproduced out of chart review (Hudon et al., 2005).

Since CIRS requires appraisal about individual patients it is less suitable for use with data collected by automated extraction (e.g. administrative claims data, also called routine data).

Regarding older people in particular, the Cumulative Illness Rating Scale—Geriatrics (CIRS-G) represents the instrument of choice. This scoring system measures the chronic medical illness (“morbidity”) burden while taking into consideration the severity of chronic diseases in 14 items representing individual body systems. The general rules for severity rating are: from 0 (no impairment) to 4 (extremely severe impairment), based on clinical judgment. It has been validated in geriatric inpatients and outpatients, and in long-term patients. Criterion validity has been confirmed using autopsy as gold standard, and the instrument has good inter-rater and test-retest reliability. It predicts mortality, hospital readmission, prolonged hospital stay and nursing home admission. The availability of detailed guidelines for scoring (Salvi et al., 2008) and its validation in different settings and populations of older subjects suggest that CIRS-G, a scale based on medical record can be employed in clinical practice as well as in clinical research (Belooesksy et al., 2011). Geriatric Index of Comorbidity (GIC) may be a valid alternative.

The Adjusted Clinical Groups (ACG) is a case-mix adjustment system initially developed to predict morbidity burden and use of health care resources (Health HBIsOP, 2003; Starfield et al., 1991). ACG measures the morbidity burden of patient populations based on their disease patterns, age and gender and is mostly used for resource allocation. It depends on the diagnostic and/or pharmaceutical code information mentioned in insurance claims or computerized medical records. The fact that ACG can be calculated from electronic patient records or administrative data makes it appropriate for large volumes of data. Despite the strong evidence that ACG predicts mortality, future morbidity and use of health care resources, the scarcity of transparency and the substantial costs to end users hinder its use for research both at the level of feasibility as at the level of interpretation.

The Duke Severity of Illness (DUSOI) is an instrument for measuring a patient’s illness severity that consists of four elements for each condition, that is, symptoms, complications, prognosis without treatment and treatment potential (Parkerson Jr. et al., 1993). DUSOI quantifies the burden of illness assessed by the physician. Since DUSOI requires judgment of individual patients by their care giver it is less suitable for large volumes of data.

Besides, applying DUSOI requires training. Other measures of multimorbidity such as the Index of Co-existing diseases (ICED), Kaplan and others are less often used and therefore here not discussed in detail (de Groot et al., 2003; Huntley et al., 2012; Selim et al., 2004).

Measures of multimorbidity can be self-rated, clinician rated or excerpted from records. Each method has its specific strengths and limitations. Numerous multimorbidity studies are based on interviews with patients or self-administered questionnaires. Overall, the validity of self-reported disease counts is high (Selim et al., 2004). Nevertheless, they should be used carefully in multimorbidity research because the agreement between self-reports and medical records is limited for patients with multiple diseases and because older patients have in general less accurate self-reports of diseases status (Kriegsman et al., 1996; Simpson et al., 2004). Instead, self-reports have the main advantage to allow the assessment of the impact of diseases on individual patients. Additionally, self-reported measures within population studies are useful because they enable assessment of health independently of a health care encounter.

Studies based on clinicians’ chart reviews are both comprehensive and objective, particularly if data are collected within primary care since general practitioners have the most comprehensive view on the health status of their patients. In addition, practice based data can provide insight into the impact of multimorbidity on clinical care. However, medical records may be sensitive to biases due to low quality of data collection. Charts may be incomplete due to fragmentation of care or underregistration of health problems by providers. Likewise, medical records may be susceptible to underestimating multimorbidity because of un(der)diagnosis. On the other hand, the relationship between multimorbidity and consultation rate also has a risk of circularity, which means that patients who consult more frequently may also have more conditions diagnosed. A last limitation of these practice based analyses is that they will not identify people who do not consult. The latter might also include patients with limited access to healthcare- due to financial constraints- who are in fact more sensitive to multimorbidity due to their socio-economic deprivation (Orueta et al., 2013; Salisbury et al., 2011; Schafer et al., 2012).

Many of the major studies on multimorbidity are based on administrative data such as claims data (collected by health insurance companies) or automated extraction of data out of medical records (Elixhauser et al., 1998). Although these routine data have the advantage of large and representative study samples, they do not offer any understanding of the impact of the disease(s) at the level of the individual patient. For instance, every low back pain will be included, because the disease code will be the same for every patient, irrespective of whether the low back pain has a substantial impact on the patients’ functional status, social participation or quality of life. In addition, claims data and other administrative databases may be susceptible to over- or underreporting and inadequate coding. These risks will be closely related to the specific setting and purpose for which the data are to be made available.
In addition to self-rated, clinician-rated and administrative data, multimorbidity can also be assessed by the golden standard diagnostic inclusion and exclusion criteria for every disease included in the assessment of multimorbidity. By itself, each diagnose will be validated precisely at the time of inclusion (e.g. a new spirometry will be performed for COPD) (Hofman et al., 2007). But, this approach is very time consuming and not always feasible. In addition, it includes a risk of over-diagnosis and over-medicalization of otherwise healthy people (Kuehlein et al., 2010; Mcwhinnie, 1981; Rosenberg, 2002).

In a nutshell, regardless of an increasing quantity of research on multimorbidity, the “concept of multimorbidity” remains difficult to define and to measure. Therefore, clear choices have to be made. These choices should be directed by the objectives of the research in which they will be used (Holzhausen et al., 2011). For instance, if the aim of the study is to attain a clear perception of the impact of multimorbidity on individual patients then multimorbidity measures based on patient surveys will perhaps be most useful. If we want to provide useful evidence to providers currently dealing with multimorbidity in clinical practice, it is essential to attain deeper knowledge about the way multimorbidity presents at the level of clinical practice. This will necessitate practice based epidemiological research (Valderas et al., 2009), in which data are provided at the point of care. However, if the aim of a study is to define (causal) associations between different diseases, these diseases will have to be defined and diagnosed as precisely as possible (Hofman et al., 2007) or the analyses will have to be based on very large databases to create hypothesis on possible causes of associations beyond the pitfalls of ecological misconception (Aarts, 2012; Pearce, 2000). Overall, the measurement of multimorbidity for research asks for a pragmatic approach focused on finding a measurable proxy like medication counts or unweighted disease counts.

The Impact of Multimorbidity

The European General Practice Research Network (EGPRN) definition of multimorbidity regards disability (i.e. dependency in carrying out activities essential to independent living) and frailty (i.e. a state of high vulnerability for adverse health outcomes) as major outcomes of multimorbidity. Moreover, Marengoni et al. (2009) have found that a higher number of chronic diseases relates to increased disability and Fried et al. (Fried et al., 2004b) reported a statistically significant trend of increasing prevalence of frailty in patients with more diseases. However, not all studies confirm these relations (Boeckxstaens et al., 2014; Manton et al., 1997). Increasingly, multimorbidity, frailty and disability are considered as an integrated conceptual framework reflecting clinical complexity. Besides, in the most deprived patient groups multimorbidity is socially patterned with a 10–15 year gap in terms of onset which actually may ask for a complexity approach to patients with multimorbidity (Barnett et al., 2012b; Schaink et al., 2012). In any way, the clinical care for multimorbidity requires a multidimensional assessment focused on the physical, psychological, functional and social determinants of the health status of the person irrespective of and beyond disease specific biomedical goals (Manton et al., 1997). This will help patients and providers to come to decisions that cover different conditions instead of focusing on separate diseases (Fried et al., 2004b; Marengoni et al., 2009).

References

Further Reading

