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What do we mean by multimorbidity? An analysis of the literature on multimorbidity measures, associated factors, and impact on health services organization

Qu'entendons-nous par : « polypathologie chronique » ? Une analyse de la littérature des mesures, des facteurs associés et de l'impact sur l'organisation des soins de la polypathologie chronique

T. Lefèvre^{a,b}, J.-F. d'Ivernois^b, V. De Andrade^b, C. Crozet^b, P. Lombrail^b, R. Gagnayre^{b,*}

^a Department of forensic medicine, hôpital Jean-Verdier, AP-HP, 93140 Bondy, France

^b Laboratoire « Éducatives et pratiques de santé » EA3412, université Paris-13 Sorbonne - Paris Cité, 93017 Bobigny, France

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Abstract

Background. – Multimorbidity is a consequence of both epidemiological and demographic transition. Unlike comorbidity, it currently has no consensus definition, making it difficult to assess its epidemiological and socioeconomic burden, to organize healthcare services rationally, and to determine the skills needed for patient self-reliance. The aim of this study is to define the spectrum of multimorbidity and to discuss current implications for the organization of care.

Methods. – Two independent readers analyzed the literature indexed in PubMed, Embase, CINAHL, and Scopus.

Results. – The bibliographic search conducted on July 16, 2013, retrieved 2287 articles (670 in PubMed, 666 in Embase, 582 in Scopus, and 369 in CINAHL). Of these, 108 articles were retained. Multimorbidity is designated by a variety of terms, none of them being MeSH terms. There is no single measure of multimorbidity, as this entity is usually studied for its functional or economic impact, rather than its causes. The prevalence varies considerably, depending on the measure used and the population studied. Factors associated with multimorbidity are age, gender, and socioeconomic characteristics of the populations studied. Studies evaluating the organization-of-care are inconclusive or insufficient.

Conclusions. – Multimorbidity serves as an avatar for the fundamental, recurrent problems of modern medicine and the organization-of-care. It may be defined by its causes or its consequences and reflects our concept of both individual health and its collective management. Tools that would allow a more appropriate measurement of this entity are available; we should use them to match medical reality to the needs of patients.

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Keywords: Multimorbidity; Multiple chronic conditions; Comorbidity

Résumé

Position du problème. – La polypathologie chronique est une conséquence de la double transition épidémiologique et démographique. Distincte de la comorbidité, il n'en existe aujourd'hui aucune définition consensuelle, ce qui rend délicates l'évaluation de son poids épidémiologique et socio-économique, l'organisation raisonnée et adaptée des services de santé ou encore la détermination des compétences nécessaires à l'autonomie des patients. Le but de ce travail est de délimiter un spectre de la polypathologie chronique et d'en discuter les implications actuelles quant à l'organisation des soins.

Méthodes. – Analyse de la littérature référencée par PubMed, Embase, CINAHL et Scopus par deux relecteurs indépendants.

Résultats. – La recherche bibliographique a permis d'identifier 2287 articles au 16/07/2013 (PubMed : 670, Embase : 666, Scopus : 582, CINAHL : 369). Au total 108 articles ont été retenus. La polypathologie chronique est désignée sous différents termes, dont aucun n'est un terme MeSH. Il n'existe pas de mesure unique de la polypathologie chronique, cette entité étant plus souvent étudiée pour ses conséquences fonctionnelles ou économiques, non pour ses causes. Selon les mesures et les populations étudiées, la prévalence varie considérablement. Les

* Corresponding author.

E-mail address: remi.gagnayre@univ-paris13.fr (R. Gagnayre).

facteurs récurrents associés à la polypathologie chronique sont l'âge, le sexe et les caractéristiques socio-économiques des populations. Les résultats des évaluations visant l'organisation des soins sont peu concluants ou les études présentent des insuffisances.

Conclusion. – La polypathologie chronique se pose comme un avatar des problèmes fondamentaux récurrents de la médecine moderne et de l'organisation des soins. Elle pose la question de sa définition, à partir de ses causes ou de ses conséquences, et renvoie à notre conception à la fois de la santé individuelle et de sa gestion collective. Il existe des outils permettant une mesure plus adaptée de cette entité, qu'il serait intéressant de mobiliser afin de marier réalité médicale et besoins des patients.

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Mots clés : Polypathologie chronique ; Comorbidité

1. Introduction

Most countries that have started or completed their demographic transition are experiencing an epidemiological transition as well. The growing burden of chronic illness [1,2] on a country's healthcare system, social services, and economy can no longer be ignored [3,4].

The effort to rationalize care and healthcare costs has produced a plethora of best practice guidelines on specialized care for the main chronic diseases, established independently from one another [5], with which specialists to consult and which tests and investigations to arrange for. This is, however, an idealized version of reality; chronic diseases rarely occur in isolation, especially as life expectancy increases and people acquire a growing number of illnesses [6]. Treating each of a person's chronic diseases separately basically sums the individual costs, which is suboptimal at best. It is therefore no longer a matter of chronic versus acute disease, but more likely of multiple chronic diseases, or multimorbidity. At a minimum, multimorbidity is defined as the co-occurrence of at least two chronic conditions in the same person.

In a context in which we wish to foster patients' self-reliance with respect to their diseases and the healthcare system, multimorbidity is a challenge. While some recent studies have attempted to formalize complex interventions, including self-management support programs [7], the majority of therapeutic patient education (TPE) programs are designed for a single disease. As pointed out by d'Ivernois and Gagnayre (2013) [8], there are currently no operative therapeutic education models for people with several chronic diseases, given that education cannot be obtained by adding together different existing "single-disease" programs. We know, for example, how to educate a diabetic patient, a chronic bronchitis patient, and a hypertensive patient, but we do not know, in practical terms, how to educate a patient with all three diseases. The difficulty is in identifying, out of all of the skills the patient has to master, which of his various diseases should take priority, and assembling the educational sequences accordingly.

Numerous studies over the past 20 years have shown that multimorbidity represents a significant problem, reporting high prevalence and incidence, high costs and inadequate healthcare services. Evaluating its importance in terms of public health, however, remains difficult. The problem, as much for researchers as for clinicians and patients, is further complicated by the fact that the concept of multimorbidity probably differs from the concept of comorbidity. Following Feinstein [9], van

den Akker et al. [10] suggest keeping the term "comorbidity" when talking about a disease of interest – or "index disease" – for which there are coexisting conditions that are not necessarily complications of the index disease, called comorbidities. Multimorbidity then designates all situations in which several conditions coexist, but none of them takes precedence over the others – that is, situations in which there is no index disease. Researchers are still divided as to the conceptual differences between multimorbidity and comorbidity, and it is not at all rare – especially in the United States – to see comorbidity used when talking about multimorbidity.

Given the variety of approaches and results dealing with comorbidity and multimorbidity, as reported in the literature, we sought to answer the following question: what do we currently mean by "multimorbidity"? Defining the boundaries of a nosological entity that has no unambiguous definition involves documenting not just the measures (i.e. the practical and operational definitions) used to approach it, but also the related available epidemiological data and the factors frequently identified as being associated with it. We decided to look at the literature indexed in various medical databases in order to try to answer this question. Based on the information obtained, we also propose to discuss the current organization-of-care issues relating to multimorbidity.

2. Methods

Our methodology is based on a study by Vogeli et al. (2007 [11]), presented as a semi-structured literature review consisting in a two-step bibliographic search: an initial search targeting the heart of the subject (for Vogeli, articles identified in PubMed with the MeSH terms "chronic diseases" and "comorbidity"), and then a second search based on the articles identified in the first step, this time targeting more specific characteristics (for Vogeli, for example: prevalence, access to care, mortality rate, and healthcare expenditures).

In order to collect material for analysis, we did a primary search on the PubMed database on July 16, 2013, using the following search string: "multipathology" [Title/Abstract] or "pluripathology" [Title/Abstract] or "multiple chronic conditions" [Title/Abstract] or "multimorbidity" [Title/Abstract] or "polymorbidity" [Title/Abstract]. From this first set we kept articles written completely in English, but not those in which only the abstract was in English, to ensure a uniform level of comprehension of the articles.

That primary search was supplemented by a second literature search in three other databases – Embase, CINAHL, and Scopus – using the same search criteria. The aim of the second search was basically to verify whether the results found in PubMed were representative of the problem, and if not, to fill in any references missing from the first selection. Note that, to the best of our knowledge, there are currently no MeSH terms dedicated to multiple chronic conditions. In addition, we tested the same search string with the prefix “comorbid*” added.

We applied secondary criteria to choose articles for a full reading, to cover the following four areas: the definitions of, or if lacking, the measures used to identify people with, multimorbidity; the epidemiological data regarding multimorbidity (prevalence and determinants); the factors associated with it (mortality, functional capacity, and quality of life); and the organization-of-care targeting multimorbidity. Articles that did not explicitly mention those aspects were rejected. Lastly, we gave priority to systematic reviews involving one of the areas above. The method is summarized in Fig. 1.

Two readers read the abstracts from the first selection and independently performed a second selection using the secondary criteria. In case of disagreement, a third reader

was designated to intervene to decide whether or not to include the article.

3. Results and discussion

3.1. Articles identified

The search string retrieved 2287 articles from PubMed (670), Embase (666), CINAHL (369), and Scopus (582) on July 16, 2013. There were 1011 remaining articles after duplicates were removed (46.6% recovery rate). Adding (OR “comorbid”) that same date retrieved 22,465 results from PubMed alone.

The initial selection ultimately yielded 200 eligible articles from PubMed, 20 from Embase, 17 from CINAHL, and 13 from Scopus, for a total of 250 articles (Fig. 1). The articles rejected at that stage did not actually mention multimorbidity explicitly, or referred only to comorbidity, despite the form of the search string.

Of those 250 articles, 108 were read in their entirety, including eight systematic reviews, all of them indexed in PubMed. There were no significant disagreements between the readers necessitating the third reader’s intervention.

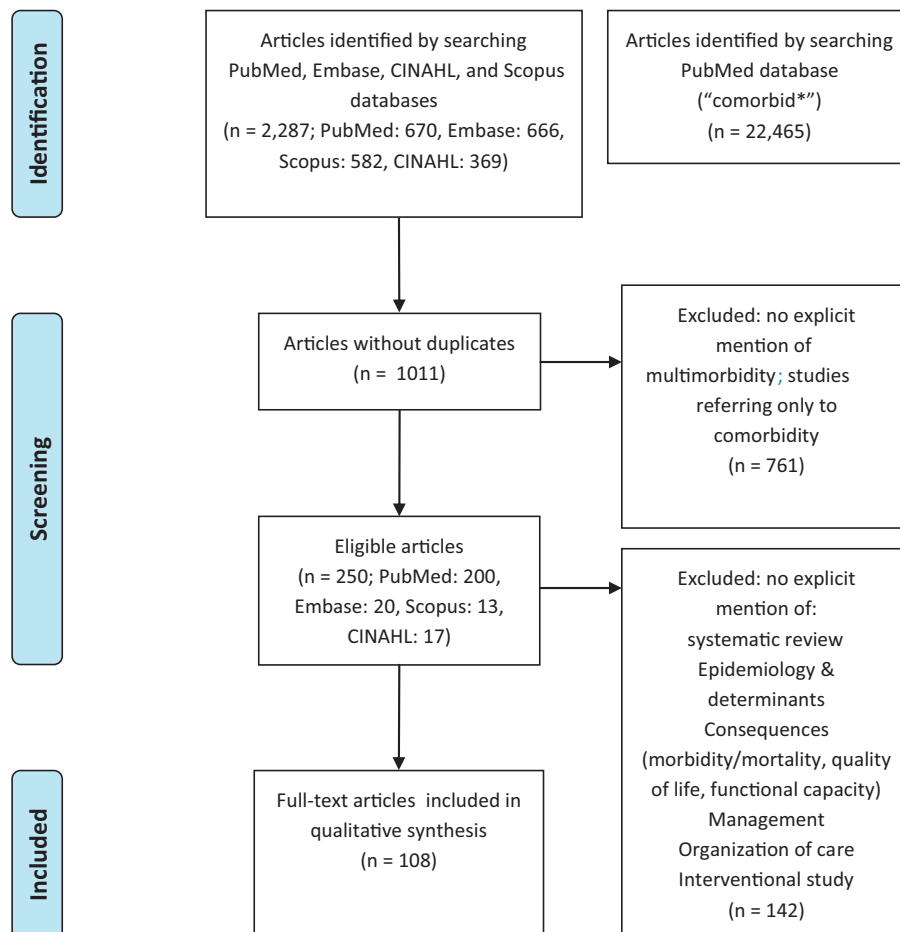


Fig. 1. Selection procedure for articles used in the literature analysis.

3.2. Limitations of the study

There have been numerous studies on multimorbidity in the past 20 or so years, and a comprehensive review of the issue via a literature analysis seemed necessary. While our study attempted to do this, it has certain limitations.

Our decision not to consider studies on comorbidity may have cost us some original results. However, we believe that the concept of comorbidity is either included in the broader concept of multimorbidity (and most of the comorbidity studies would only have contributed to more specific and detailed results than those we cite) or is a totally different concept than that of multimorbidity, in which case the comorbidity studies did not belong in this analysis.

In addition, there is gray literature regarding choices in health policy orientation and the organization-of-care in various countries that is difficult to use, due to the general nature of the proposals and their lack of practical evaluation or implementation. Moreover, most of the references cited in that type of document were found in our own search. We may also have misread articles that were not written in English. That risk, however, is negligible, given the very small percentage of articles found on the subject that were written in a language other than English.

While very similar to the 2007 study by Vogeli et al. [11], our study is not equivalent to theirs. Vogeli et al. attempted to define the boundaries of multimorbidity, but considered only some of the terms used to designate it or primarily studies of comorbidity, thus making no distinction between the two concepts. In addition, the number of articles found by the authors seems low to us (623, including the comorbidity articles). While the decision to consider “core journals” is acceptable, we find it limiting. Lastly, several systematic reviews have been published in the seven years since that study, justifying a new analysis.

3.3. The different measures of multimorbidity

Among the studies included (comorbidities excluded), the instances of different terms varied; “multimorbidity” or “multimorbid*” and “multiple chronic illnesses” or “multiple chronic conditions” were the terms used most frequently in our selection.

We listed four major measures of multimorbidity:

- simply counting the number of chronic conditions from a list of individual conditions, with the list sometimes varying from one study to another (rheumatologic conditions such as osteoarthritis or arthritis might not, for example, be on the list);
- grouping chronic diseases, which are also chosen from a list that varies between studies, by dyads or triads;
- using an index of variable complexity based, for example, on risk or on past healthcare utilization identified as associated with substantial future care;
- identifying homogeneous groups of people with common diseases and characteristics.

Some of these approaches may use the same classification techniques but have different objectives; for example, an index may be constructed based on the same techniques as those used to identify homogeneous groups. An index of this type, however, is generally constructed in connection with a particular patient characteristic, such as healthcare utilization or premature death. The aim or intention governing the use of one type of measure rather than another thus determines the type of measure chosen more than the technique used to construct it. Two studies, by Huntley et al. (2012) and Diederichs et al. (2011) [12,13], examined the different measures used for research. A third study by Le Reste et al. (2013) [14] recently attempted to propose a definition of multimorbidity at the primary care level, based on a systematic review. Rather than finding a single consensus measure, the authors listed the constitutive dimensions of multimorbidity (i.e., having at least one other disease in addition to an index chronic disease, or a so-called biopsychosocial factor, or a somatic risk factor) and the factors modulating the effects of the multimorbidity on health (e.g., coping strategies, social network, or other somatic risk factors). Hence, rather than a synthesis, it is an analysis of the candidate dimensions for measuring multimorbidity, or an attempt to characterize the different possible care situations.

The study by Huntley et al. [12] counted 17 different measures in 194 primary care studies, including a simple count of conditions but excluding analyses of homogeneous groups [12]. More than half of the studies (98/194) used simple counting. The performance of these measures varied depending on the assumed consequence of multimorbidity to which they were assumed to be related: quality of life, mortality, or functional capacity.

A strong trend seems to exist that measures chronic multiple diseases in a patient by simply adding up chronic diseases, selected in lists of diseases that differ from one author to another. Other more or less complex means of measuring this phenomenon have been proposed, but none has met with consensus. While counting is a simple, naïve, and possibly pertinent way to qualify multimorbidity, it automatically deprives it of any possible nosological independence [6]. Identification by common dyads or triads is a pragmatic compromise, recognizing the epidemiological particularities of certain multimorbidities, while remaining simple, but it leaves out others that, while fewer in number, are not necessarily less important [15]. Indices, which are generally constructed with the idea of predicting one type of impact, thus define multimorbidity in a way that prioritizes a single type of presumed impact [16,17]. Lastly, the homogeneous groups approach prioritizes adherence to specific epidemiological features, extends the identification spectrum to non-biomedical characteristics, and permits preliminary exploration to find a common pathophysiological basis for multimorbidity and a common set of skills required by such patients [18]. Disease counting seems to be the default identification method of choice, due to its ease of use.

The question of whether multimorbidity should be defined by its consequences or its causes was posed some 15 years ago, but does not yet appear to have been satisfactorily answered [19,20]. Van den Akker et al. (1996) [10] questioned whether using the concept of multimorbidity – as distinct from comorbidity – was necessary. They suggested reserving the term “comorbidity” to designate so-called index diseases, coexisting with other conditions such as complications of the index disease or conditions whose treatment has led to complications (iatrogenic conditions). They suggest using “multimorbidity” when a person suffers from several conditions. However, that suggestion conflicts with the fact that simply counting diseases does not appear to be sufficient, and that incorporating non-biomedical dimensions such as self-efficacy, financial constraints, and related or concomitant functional limitations [21] might be useful. Clearly, the choice of which measure to use matters, because it influences our representation of the condition and its epidemiology [17].

In fact, the problem of measuring multimorbidity and of its definition may be inherited from more primitive causes. On one hand, if multimorbidity deals with the co-existence of multiple chronic conditions in one person, one should ask if the concept of chronic condition is as clear as it seems. A chronic condition or disease asks the question of the duration of this condition, which was very likely to be defined in contrast to acute conditions. For a long time, acute conditions were the rule for many people, since many non-acute conditions are associated with aging. Beyond the issue of duration, there is still the problem of the exhaustive and consensual list of conditions that everyone recognizes as being chronic conditions.

We could also add to these issues the fact that chronicity can sometimes be confounded with severity, or even other concepts such as handicap, deficiency, or quality of life. Finally, when it comes to the concept of multimorbidity, one could also wonder if only chronic conditions should be considered or if acute or transient conditions should be incorporated.

3.4. Epidemiological data concerning the concept of multimorbidity

One of the first things we might be tempted to ask about the importance of multimorbidity would be how many people have it – that is, its prevalence. The use of different measures of

multimorbidity leads to quantitative differences among prevalence studies, independent of the subpopulation being considered. A systematic review on prevalence revealed even larger differences, depending on the population in question: from 3.5% to 98.5% in people over 75 years of age, and from 13.1% to 71.8% in the general population [22]. The prevalence varies not only with the type of measure, but also with the category of multimorbidity; in the case of disease counts, prevalence varies depending on whether the criterion used is two, three, or more conditions. It has been suggested that the prevalence increases with the number of candidate diseases [20]. A large number of studies also concern the elderly [23–26], under the assumption that there is a strong link between multimorbidity and aging. A sample of the different prevalence found is shown in Table 1.

The main entities found, by the measure used, are shown in Table 2. The particular position of mental health should be noted; if the problem appears to be recognized by the psychiatric profession [27], the approach is significantly different. It is usually a question of improving psychiatric patients' physical care, or measuring the impact of their mental illness on their physical ailment [28–30]. One study, however, pointed out that the likelihood of a mental disorder being among the multiple morbidities increased with the number of physical disorders in a given person, and that the prevalence of a psychiatric component increased significantly with the degree of deprivation [6].

Whatever the measure used, there are basically three factors repeatedly associated with multimorbidity: age, gender, and socioeconomic status. While age might be expected, multimorbidity should not be understood solely as the effect of aging; it does occur in specific young or middle-aged groups, in people with endocrine disorders (for example, see [18]). In fact, in absolute terms, more young than elderly (i.e. over age 65) people were found to have multimorbidity [6]. All of the studies that looked at the impact of socioeconomic status concluded that there was a higher prevalence of multimorbidity among the poor, with possible qualitative differences (for example, a higher prevalence of mental illness appearing as one of the first pillars of multimorbidity in that population) [6,16]. Ethnicity also plays a role, with distinct temporal trajectories [31].

Due to the chronic nature of multimorbidity, its estimated prevalence, and the burden it represents in terms of diminished

Table 1
Examples of multimorbidity prevalence, by measurement method and study population.

Prevalence (%)	Measure	Population	Reference
14	Disease count ^a	99,997 British adults seen by general practitioners	Salisbury, 2011 [16]
56	Index (ACG)		
23.2	Disease count ^a	1,751,841 Scottish patients seen by general practitioners	Barnett, 2012 [6]
71.2	Disease count	28 million American adults admitted to the hospital over 1 year (NIS)	Steiner, 2013 [15]
24.5	Disease count	198,670 Spanish patients (age > 14 years) seen by general practitioners	Garcia-Olmos, 2012 [18]
29.7	Disease count	60,857 Dutch patients seen by general practitioners	van den Akker, 1998 [60]
37.1	Index (CIRS)	3398 Australian adults seen by general practitioners	Britt, 2008 [61]
19.3	Disease count	13,806 Dutch patients (age > 16 years) seen by general practitioners	Westert, 2001 [62]

^a Rheumatologic conditions excluded. ACG: Johns Hopkins University adjusted clinical groups; CIRS: Cumulative Illness Rating Scale; NIS: nationwide inpatient sample.

Table 2
Examples of large multimorbidity groups by measurement method, comorbidity studies excluded.

Groups	Measure	Description	Reference
4 groups	PCA	Group A: cardiac arrhythmias, hyperlipidemia, hypertension, diabetes, age > 70 Group B: ischemic heart disease, cerebrovascular disease, chronic kidney failure, congestive heart failure, age > 80 Group C: asthma, thyroid disease, anxiety or depressive disorder, schizophrenia, age < 30 Group D: other conditions (obesity, osteoporosis, deafness, cancer, etc)	Garcia-Olmos, 2012 [18]
12 dyads	Disease count	Four most common dyads: Arthritis + vascular disorder Psychiatric + vascular disorders Arthritis + psychiatric disorder Cardiac + vascular disorders	Britt, 2008 [61]
5 groups	FA + index (ACG)	Cardiometabolic disorder group (cross-sectional) Psychiatric disorder/substance abuse group (young men) Mechanical disorder/obesity/thyroid disease group (men < 45 years) Psychogeriatric disorder group (women > 65 years) Depression/behavior disorder group (women > 45 years)	Prados-Torres, 2012 [63]
5 most common dyads	Disease count	Hypertension/hyperlipidemia Hypertension/diabetes Hypertension/arthritis Hyperlipidemia/diabetes Hypertension/depression	Ashman, 2013 [64]

PCA: principal component analysis; FA: factor analysis; ACG: Johns Hopkins University adjusted clinical groups.

functional capacity and social costs, several characteristics have been the subject of specific studies.

However, most of the results fail to provide a precise set of data.

Most studies agree that there is excess mortality due to multimorbidity [15]. Some studies, however, suggest that the higher mortality is associated with disability, rather than multimorbidity; this was shown in one longitudinal study following elderly patients [32]. In this study, the degree of disability was better correlated with excess mortality than was multimorbidity itself.

The impact of multimorbidity on quality of life is not clear. Some studies show a worse quality of life overall [33], though not all aspects of quality of life are inversely related to multimorbidity (that is, the reduction in quality of life does not seem to be systematically proportional to the number of conditions). Social and psychological aspects appear to be increasingly degraded as the number of conditions rises above three.

Regarding the quality of care and prevention given multimorbid patients by caregivers, while not all of the results agree, there seems to be a trend toward better quality care [34] and prevention [35] among people with multimorbidity. The authors attribute better-quality care to more frequent or redundant contact with the healthcare system, as people are seen for each condition separately. This is the case, for example, for people followed for both cardiovascular disease and diabetes, who may be prescribed testing, advice, and consultations by each of the specialists (the cardiologist, the diabetologist and, possibly, the primary care physician). The quality would therefore not be attributable to synergistic

care or to potentiation of more effectively delivered messages, but rather to the patient's higher probability of being seen by a healthcare professional. But as Langan et al. (2013) [27] point out, this observation mainly reflects somatic multimorbidity, without sufficient consideration for, or focus on, the psychiatric component. Moreover, it should be noted that the opportunities for catch-up increase, mainly because the care model is still focused on the concepts of comorbidity and biomedical measurements. Also worth noting is that this better quality does not apply to all types of care; despite their high prevalence, the literature has little or no discussion of dental and ophthalmological care.

Similarly, more frequent contact with the healthcare system, for each separate condition and repeated over time, automatically means higher healthcare utilization – such as more hospital admissions and outpatient visits – and hence higher costs [15]. We can also note that one definition of multimorbidity is based on the risk of high future healthcare utilization [16]. Conversely, the 2012 Brilleman and Salisbury study [36] compared the usefulness of different measures of multimorbidity in terms of the primary outcome to be measured. It turns out that the number of drugs prescribed was the best predictor of future outpatient visits, and the second-best predictor of mortality. However, most of the indices were good predictors of 3-year mortality.

Another important aspect of the epidemiological approach of multimorbidity relies on novel and expanding ways to harvest and analyze personal and population data. The information and healthcare systems are increasingly developing in hospitals and many healthcare or health-related databases are already available (e.g., claims databases).

In France, the *Programme de médicalisation du système d'information* (PMSI) is both a medical and administrative database. The main medical data available in the PMSI are the primary diagnosis (the primary motive for being in the hospital at this time) and the secondary or associated diagnoses (co-occurring diseases or complications of the primary motive, for example). From this point of view, approaches and measures of multimorbidity are obviously limited or biased. The structure and composition of medical databases can thus be an important obstacle to the development of appropriate or novel approaches [37,38]. Nonetheless, the integration of data of diverse types (e.g. social habits or lifestyle) may address these issues. This is the purpose of so-called big data [39].

Furthermore, considering a particular database, one will have to address a second type of problem. Novel and appropriate analysis tools should be used to overcome current limitations due to classical and reductionist methods [40].

3.5. Multimorbidity-specific treatments and healthcare system organization

From an organizational point of view, Tinetti et al. (2012) and Boyd (2005) [41,42] noted the mismatch between the reality in the field (that chronic disease rarely occurs in isolation), the narrowly disease-specific nature of treatment and reimbursement, and best practice guidelines targeting only single diseases. Compartmentalization by medical and paramedical specialty leads to the fragmentation of patient care, resulting in a loss of meaning that is felt by patients; they report that they do not understand the logic of the system or how it relates to their own experience. Their care becomes a string of appointments that fails to offer any clear understanding of the conditions from which they suffer [26].

Depending on the number of chronic conditions, following guidelines was considered unworkable, too burdensome, or even contradictory [5]. An examination of those same recommendations shows that comorbidities and their specific features are only rarely mentioned. Moreover, while those guidelines are recognized as being highly evidence-based (since they generally came from randomized controlled trials), there were doubts about the external validity of those trials when it came to extrapolating their results to multimorbidity, and due to their artificial nature, since diseases rarely occur singly [43,44]. For example, the vast majority (from 89% to 100%) of people selected for five clinical trials on hypertension actually had multiple chronic conditions [44].

Most of the interventions to improve care for people with multiple conditions for which randomized controlled trials were conducted were based on modifying the primary care system to various degrees. Some of the studies looked primarily at alternative ways of organizing care: having a third party coordinator (“integrated care manager”) work with general practitioners and patients to improve management of comorbid hypertension and depression [45]; having a pharmacist suggest more appropriate, synergistic prescriptions in cases of multiple drug therapy [46]; and having a general practitioner, dedicated nurse, and social worker work together to reach a better overall

understanding of the patient’s situation [47]. The other studies looked more at so-called patient-centered approaches: having therapeutic patient education by occupational therapists and physical therapists for better management of the patient’s cognitive, physical, and environmental resources [48], or offering workshops to help patients get the most out of their visits [49].

These interventions were the subject of a Cochrane Library systematic review, which looked at ten of them [50]. The studies were heterogeneous in terms of objectives and intervention methods, had a very moderate impact, and were difficult to compare. In particular, the Cochrane review stressed the need to evaluate interventions that work with, or are integrated into, the healthcare system, to ensure their sustainability should show positive results. It has also been suggested that minor adjustments to the existing system – via a process or pathway set up alongside the usual care for chronic conditions, for example – would not suffice [51]. The Cochrane review also pointed out that offering appropriate services completely divorced from the current systems and infrastructure without incurring significant costs would be difficult.

We identified six major coordinated management programs primarily targeting the elderly, and thus their multiple conditions. Boulton and Wieland (2010) [52] compared three initiatives launched in the United States: Program of All-inclusive Care for the Elderly (PACE), Geriatric Resources for Assessment and Care of Elders (GRACE), and Guided Care. Three other countries have implemented this type of program: the United Kingdom (Evercare), Canada (SIPA), and the Netherlands (EASYcare) [51,53,54]. While the studies do not explicitly or directly target multimorbidity as such (which is why they were not included in the Cochrane review), they do offer a controlled evaluation of the organization-of-care for fragile or at-risk elderly – practically speaking, those with multimorbidity. Regarding the three U.S. programs, each has specific limitations, according to Boulton and Wieland [52]: restrictive program eligibility criteria and regional disparities between dedicated facilities, together with a relatively small total number of such facilities, which are rapidly approaching capacity.

The other three initiatives generally show increased patient satisfaction or well-being of subject groups, with fewer hospital admissions at costs that are similar and constant overall [53] in some cases, or no gain in terms of healthcare utilization (emergency room visits, for example) [51]. Though there may be a positive short-term impact on functional capacity, it is moderate and tends to disappear fairly quickly [54].

In addition to the Cochrane review, which looks only at randomized controlled trials in primary care, the systematic review by De Bruin et al. (2013) [55] more broadly examines evaluations of so-called comprehensive care programs aimed specifically at multimorbidity. This review surveyed 28 programs evaluated by 33 studies. Its conclusions are similar to those of the above-cited studies; such programs show a moderate impact on hospital admissions and healthcare costs, as well as on health behaviors, the perceived quality of care, and both patient and caregiver satisfaction. This systematic review

did not, however, find sufficient – or any – evidence regarding the impact of the programs on the quality of life, medication use, or utilization of outpatient care, mortality, or physical and cognitive functional capacity.

This picture of how the current healthcare systems try to cope with multimorbidity can be completed with the results of several qualitative studies. While studies asked patients to express their feelings about self-care and how they live with multimorbidity, others asked healthcare professionals how they manage or cannot manage patients with multimorbidity.

Asking patients for their opinion and feelings toward their conditions revealed several barriers to self-care in the case of multimorbidity. Among these barriers were physical limitations, lack of knowledge on their conditions, financial issues, and access to care. They also expressed the need for social and emotional support and reported issues attributed to multiple medications (e.g., managing and prioritizing medications or adverse events of one medication impacting another condition that is not the target of this medication) [56].

Primary care professionals (general practitioners and nurses) acknowledged that there were tensions between proposing quality care and accommodating patients' agendas. Conditions are managed in terms of priority in a system that works based on the management of individual conditions. Dealing with co-occurring somatic and psychic conditions was also considered as problematic [57].

3.6. Immediate prospects for multimorbidity

Reductive approaches and measures based on the consequences, rather than the causes, of multimorbidity have led to an incorrect statement of the problem. First, the measures used, though functional, do not lend themselves to either reproducible results or universal application. Indeed, the validity of the definitions seems to depend on the outcome one wishes to measure; a measure associated with the functional capacity outcome will not be easy to use to study quality of life outcomes [17]. Second, it has been shown that the definitions chosen would not prove sufficient to characterize the experience of patients, who beyond having multiple conditions, cite individual social, financial, and organizational impacts [14,21,26]. Moreover, from the perspective of improving the quality of care – particularly primary care by general practitioners – pay-for-performance (P4P) systems also create problems when it comes to patients with multimorbidity. As it now exists, P4P is based primarily on biomedical results, which may have little meaning to the people receiving the care; a more equitable payment system might adjust the payment based on the severity of a patient's health issues and thus on the degree of multimorbidity.

The degree of multimorbidity is closely linked with the individual's level of deprivation. The fact that multimorbidity, already quite prevalent, becomes even more so in poorer populations is a major challenge. Improving the health status of the general population would require tackling these social inequalities, given the burden of chronic disease, since the health of the most deprived contributes significantly to the total

burden of chronic conditions. The first step would require reducing the burden caused by chronic disease and the burden caused by social inequality simultaneously.

Beyond the difficulty of defining multimorbidity at the individual patient level, the subject of multimorbidity seems to be the symptom of a systemic, structural crisis in how we think about health and disease on a number of levels. Multimorbidity may be the prototype for a new way of defining disease, one already begun by the complex integration of the following realities: diseases as compared to syndromes, such as AIDS or metabolic syndrome; the growing number of indirect measures of a disease via diagnostic or prognostic markers; the reorganization of healthcare systems in accordance with efficiency or cost containment policies; and the desire for personalized, patient-centered medicine. Hence we might assume that the models already proposed for the individual and collective management, at various levels, of a single chronic condition – such as the Chronic Care Model – would not be sufficient or totally suitable for addressing the reality of multimorbidity. Moreover, it seems that patients are more and more willing to be active partners in the whole care chain.

Building upon a consensus operational definition of multimorbidity, we need more interventional research to determine not only the most effective, but also the most efficient and equitable forms of care and healthcare system organization. As the Cochrane review pointed out, it will be necessary to find a happy medium between creating new forms of care and integrating care into the existing system so that its development is sustainable. Beyond the biomedical aspect of multimorbidity, efficient organization will no doubt require recognition of patient expectations, including their need for overall meaning in their particular situation. This could be done by integrating different forms of therapeutic education into healthcare systems. In addition, rather than increasing the number of biomedical objectives in proportion to how many comorbidities a person has, it might be more relevant to try to build a common skills base aimed at the acquisition of individual behaviors enabling the patient to adapt and manage the different components of his condition and the constraints engendered by his illness(es) [58,59].

4. Conclusion

Multimorbidity is a reality that, while distinct from, or broader than, the concept of comorbidity, is difficult to define. The different measures used to identify it are ambiguous, if not contradictory. This leads to inappropriate responses at a number of levels. Current healthcare systems do not seem well-suited to the new medical and social reality that multimorbidity represents. Our review of the literature underscores this diversity and these contradictions.

Yet finding a single measure based on a consensus definition of multimorbidity is no simple matter, because multimorbidity is a complex combination of causes and effects, with many related factors. The search for such a measure also reflects different agendas, with some authors choosing some of the elements of this combination over others, to reduce its

complexity – and depending on what they are trying to show, not all actors seem to want a single measure. In any case, this undertaking surely strips multimorbidity of its specific irreducible features.

Converging toward consensus may require encompassing diverse strategies, including an appropriate use of big data, a collective reflection on the potential dimensions of multimorbidity to consider or the correct use of non-classical analysis methods such as clustering methods. The biomedical model may still provide valuable elements to start with while not being sufficient to deal satisfyingly with the complexity of multimorbidity.

Multidisciplinary research involving the patient, his family, his disease, and the healthcare system is therefore needed. In particular, it would be useful to determine whether there really are specific multimorbid patient profiles, and if so, how many. This research would be an opportunity to bring the focus back to the patient and encourage the design of new therapeutic education approaches with the patient. The operational definition of multimorbidity could thus come from a comparison of the common pathophysiological realities and from the skills needed for multimorbid patient self-reliance.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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