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Is this input submitted as an organisational or individual response? Organisation

Are you happy for your response to be published by the Academy? Yes

Definitions

1. There is no standard definition of 'multimorbidity' – various different definitions are used. Which definitions (or aspects of definitions) do you think are most helpful to efforts to describe and understand multimorbidity?

Please provide references for any published research, and highlight any other initiatives related to multimorbidity that the Academy may be interested in.

Morbidity classically refers to a diseased state, disability or poor health due to any cause. Multimorbidity is the presence or co-existence of multiple morbidities and hence by definition is complex because it needs to consider not only pathological conditions but also all factors that will impact disease, disability and poor health, including social, environmental, political and economic factors (1). All these factors need to be built into new methodologies to study multimorbidity. It would be useful to adopt the definitions in the recent NICE guideline on Multimorbidity (2) and outlined in key papers on this topic (1) which suggest multimorbidity be defined as the existence of two or more long term conditions. The NICE guideline further defined this to ensure in this context long term conditions included: defined physical and mental health conditions such as angina or bipolar disorder; ongoing conditions such as learning disabilities; sensory impairments such as visual or hearing impairments; addictions such as alcohol or drug misuse; and symptom complexes such as frailty and chronic pain (2).

Current knowledge base

When answering these questions, please consider both national and international populations of high, middle, and low income countries. Please provide examples and case studies to illustrate your arguments where appropriate. Please provide references for any published research.

2. What are the key data, and what data sources exist, on the prevalence, burden (including costs and impact on health systems) and determinants of multimorbidity? Are there significant gaps in such data and, if so, what are they?

There is growing evidence on the prevalence of multimorbidity including determinants (3). Barnett et al. outlined the extent of multimorbidity in the UK and highlighted this is no longer just a problem of old age (1). Importantly it showed multimorbidity occurs a full decade earlier in those from more deprived areas (1) suggesting deprivation, as well as age (3) is an important determinant of multimorbidity. Studies from elsewhere in the world (3) show it is a growing international problem. While there is growing evidence of the adverse effects of multimorbidity on mortality (4), health care utilisation (4) and quality of life (6), we still do not fully understand which combinations of multimorbidity are associated with the worst outcomes or greatest economic cost. There are significant gaps in current understanding of multimorbidity so we have no effective means of risk stratification. We also know insufficient about the problem of multimorbidity in young people or vulnerable populations such as those with learning disabilities, serious mental health problems, addiction issues or migrants.

There is some information about the burden of treatment (7-12), that is the demands health and social care services make of patients and caregivers. New theoretical models have been proposed to help better understand treatment burden and how the capacity of individuals and their wider support network can influence an individual's ability to cope with a given level of treatment burden (13,14). We also need a greater understanding of the implications of polypharmacy (15,16) and of the costs to, and impact on, health systems of multimorbidity.

3. What are the key data, and what data sources exist, on the prevention of multimorbidity? Are there significant gaps in such data and, if so, what are they?

There are major deficiencies in our knowledge about how to prevent multimorbidity. We do know a lot about policy, public health, community based and primary care based interventions and efforts to promote healthy lifestyles through increased exercise, reduction of sedentary time, healthier diets, decreased alcohol intake, stopping smoking, etc. that have positive effects on development of cardiometabolic conditions, mental health problems and dementia but little, if anything, about prevention of multimorbidity. In particular, we do not know which prevention activities will be most important or their relative benefits in multimorbid individuals. Nor do we have much evidence about prevention of functional decline in those with multimorbidity.

4. What are the key data, and what data sources exist, on the management of multimorbidity? Are there significant gaps in such data; if so, what are they?

The term 'management' here could refer to clinical interventions designed to specifically treat patients with multimorbidity as well as strategies for the delivery of healthcare services patients with multimorbidity. The term also refers to a wide range of management approaches that may differ by the specific diseases that co-exist.

The management of multimorbidity is a greatly under researched topic. We know, for example, people with multimorbidity are troubled by a growing burden of treatment (7-12), that is the

workload of healthcare for individuals and caregivers, and this can negatively impact wellbeing. We also have emerging evidence that interventions aimed at increasing individual capacity may reduce 30 day readmission rates after hospitalisation for medical or surgical causes (17). However, we know little of the effects of multimorbidity interventions on longer term outcomes. In addition, there is a scarcity of intervention trials aimed to optimise the care of those with multimorbidity (18). There has been some published pilot (19) and trial work (18) and there are ongoing trials (20) but more investment in intervention research for multimorbidity is merited. Agreement is needed on the best outcome measures to be employed in such trials.

5. What are the key sources of funding for research into multimorbidity? Are there gaps in funding and, if so, where?

There is a distinct lack of funding for multimorbidity research compared with disease specific research. Most research councils and charities that fund research have a disease specific focus and most funding panels are dominated by individuals with disease specific interests.

In the UK, NIHR, and in Scotland, the CSO, are potential sources of funding. The EU has been a potential source of funding for this type of work but with Brexit may be lost to UK researchers. There remains a focus on funding for disease specific research proposals with funders often deterring multimorbidity bids as “too difficult to research” with no agreed “outcome measures”.

The current large scale NPRI funding initiative also demonstrates a preference for primary preventive research which militates against prevention of multimorbidity, which may need to focus on those with pre-existing chronic illness.

Looking forward

6. What should the definition of ‘multimorbidity’ be? How would this definition improve research and/or treatment?

The definition in the recent NICE guidance (2), described in Section 1, should be the preferred definition. Consistency in definition will be an important step in advancing research/treatment.

7. What are the priorities for research about the prevalence, burden and determinants of multimorbidity?

In the same way cancer researchers have embraced the concept of international benchmarking, it would be useful to adopt a similar approach to monitor the prevalence, burden (including treatment burden (7)), costs and benefits of interventions in multimorbidity internationally. New scales measuring treatment burden have been developed, the Patient Experience with Treatment and Self-management (PETS) measure and the Treatment Burden Questionnaire (TBO) (21,22) and these or any others should be considered for use in multimorbidity research.

As disease centred guidelines persist and remain important, it will be essential to take greater account of multimorbidity. This is a neglected and under-researched area. As the recent NICE clinical guideline (1) points out, much clinical trial work has focused on single diseases and does not address the problem of multimorbidity and, in fact, often actively excludes those with multimorbidity or other capacity issues (23,24) resulting in guidelines that neglect these important issues of growing importance to delivery of healthcare. We are not using “best evidence” to inform decision making for the vast majority of patients if we persist with “pure” single disease models of treatment and management (23,24). Much more research, both

epidemiological and interventional, is needed in this area if we are to be able to inform disease specific guidelines to ensure they are appropriate and fit for purpose for application with those with multimorbidity. We need to ensure more research is undertaken to examine the prevalence of multimorbidity in a range of common index conditions and to determine which combinations of chronic illness are associated with the worst outcomes and why.

8. What are the priorities for research about the prevention of multimorbidity?

To understand the risk factors and what can and cannot be explained by traditional risk factors. Research in multimorbidity is needed not only at the individual and population levels, but also at the fundamental level where mechanisms of disease and impact of risk factors and environment need to be better understood, so that detection, prevention and treatment could be more appropriate in the clinical and population settings. This will mean new experimental and pre-clinical models need to be developed to represent "real life". For example, to understand mechanisms of human hypertension in animal models, one would need to study a model that is obese, with dyslipidaemia and diabetes, exposed to environmental microparticles, pollution and cigarette smoking, have a genetic predisposition, consume a high salt diet and alcohol and that is treated with multiple drugs, besides antihypertensive agents, because this is what the "real" hypertensive patient with multimorbidities presents with at the clinic.

A way to address multimorbidity is to start with risk factors that are shared between common diseases and can be addressed on a global scale. Smoking contributes to cardiovascular diseases but also to cancer and COPD. The same is true for obesity which also contributes to poor mobility, osteoarthritis and inflammatory conditions and of course diabetes. Hypertension is a risk factor for a range of cardiovascular conditions including stroke, myocardial infarction and heart failure. Social deprivation and poor income contribute to virtually all major common conditions worldwide. The same is true for poor diet and other lifestyle issues. Therefore, addressing these risk factors would be a simple way to prevent common diseases worldwide. One could also take hypertension as a specific example as it is the immediate cause of many cardiovascular conditions but goes along with other risk factors and conditions such as obesity. The Lancet Commission paper (25) could serve as supporting document in this regard.

9. What are the priorities for research about the management (as defined above) of patients with multimorbidity?

We need to prioritise research that examines how changes in approaches to management of multimorbidity can influence clinical outcomes and to examine cost effectiveness. Interventions could be aimed at the primary care or wider community care level or target the primary and secondary care interface or look at integrated care models for this patient population.

Digital health has potential in the sphere of multimorbidity and consideration needs to be given as to how digital health may help to overcome problems of fragmented and poorly coordinated care and how it may enable patients, carers and professionals to better manage multimorbidity. Such interventions could range from integrated electronic medical record systems, computerised decision support, through to apps and internet resources or telecare services. Greater consideration needs to be given to developing an understanding of what types of digital health would have a role in multimorbidity. Clinical trials of digital health interventions to promote better management and increased wellbeing in multimorbidity are also needed.

10. What should be the strategic response of both national and international research funders and agencies be to multimorbidity?

Multimorbidity is common and likely to become the norm in modern society. However, research generally investigates each condition as a single entity. "Real life situations" would benefit from research where multiple conditions are considered together or as one entity. There is a research gap regarding such an approach. This would demand new research strategies, new analytical tools and new methods for multimorbidity research. Specific needs would need to be defined and new strategies developed. Appropriate funding schemes would need to be in place. There is an urgent need for funders to acknowledge multimorbidity as a key health challenge and to promote funding opportunities across basic science to applied health services research spectrum. Research at the genomic and precision medicine end of the spectrum as well as epidemiological and health services research studies merit investment with potential to provide new and important insights into the complex problems of multimorbidity and its management.

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