The Academy of Medical Sciences

Multiple morbidities as a global health challenge

Summary of a roundtable meeting held on 7 October 2015 hosted by the Academy of Medical Sciences

The Academy of Medical Sciences

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Summary

This report reflects discussions held during a meeting on 'Multiple morbidities as a global health concern', hosted at the Academy of Medical Sciences on 7 October 2015. A list of attendees and contributors can be found at the end of this document.

The summarised points from the meeting are:
- Multiple-morbidities are a growing health concern across the world, driven by wider trends including ageing populations and improving public health measures.
- There are major challenges to fully understanding the extent of this fast-developing issue, compounded by fragmented research frameworks and data gaps.
- There is a particularly pressing need to understanding how multiple morbidity relates to driving forces in disease landscape, including ageing, poverty and geography.
- New models for delivering health care will need to accommodate the wider context of an individuals' conditions, for example, working to connect input from across clinical disciplines, and across household members.
- Tackling multiple morbidities requires a greater understanding of the underlying biology, to map clusters of conditions and explore sequential and spatial relationships in order to identify key targets for interventions.
- At each level – the individual, household and community - it is important to clarify whether multiple morbidity represents a known problem, which now requires a solution, or whether the true extent of the challenge has yet to be fully defined.
- A unifying definition and model are needed at a fundamental level to drive research into these questions, and shape the future delivery of health care.

Background

Throughout the world, populations are ageing and non-communicable diseases (NCDs) are on the rise. The UN's 2013 World Population Ageing report notes that population ageing is taking place in nearly all countries as a result of decreasing mortality and fertility.[1] The global share of older people (i.e. those over 60) rose from 9.2% in 1990 to 11.7% in 2013 and will keep growing, reaching 21.1% by 2050. The World Health Organization (WHO) reports that NCDs were responsible for 68% of all deaths globally in 2012, which rose from 60% in 2000, and that about 75% of global NCD deaths in 2012 occurred in Low-to-Middle Income Countries (28 million out of 38 million).[2] At the same time, infectious diseases (IDs) continue to affect millions of people every year – the HIV pandemic being a key driver of morbidity in the realm of IDs. Given this context, multiple morbidity is likely to become a significant global health issue over the next decade, in every country in the world.

The statistics noted above are the result of significant efforts to understand the global burden of diseases, which have been invaluable to work to improve global health. However, such data reveal only the relative burden of single diseases across the world, there is very little data on the burden of multiple morbidity. A small number of studies have started to explore prevalence, but while these are helpful, they are usually limited in scope, e.g. to a small number of countries. Nevertheless, research to date suggests that more than a fifth of the world's population suffer from multiple morbidity. For example, one study in Scotland found that 23.2% of patients had multiple morbidities, although the researchers noted that estimates of prevalence vary widely.[3] In August 2015, data from six LMICs revealed that the prevalence multiple chronic diseases was 21.9%, but it varied from 20.3% to 34.7% for the six countries studies.[4]

At a fundamental level, multiple morbidity has no single definition (and, in fact, multiple terms – such as multimorbidity and co-morbidity). A very general definition, such as 'individuals who have two or more chronic/long-term conditions occurring simultaneously', does not easily allow identification or diagnosis of multiple morbidity. For example, it does not define 'long-term' and does not specify whether the conditions in question must be separate or if they can be causally linked. In addition, multiple morbidity might also be thought of at a household or community level. To address the future global challenge of multiple morbidity, we must understand the problem better.

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[1] United Nations (2013). World Population Ageing 2013.

[2] World Health Organisation data: http://www.who.int/mediacentre/factsheets/fs310/en/index2.html

[3] Barnett K, et al. (2012). Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. The Lancet 380(9836), 37-43.

[4] Arokiasamy P, et al. (2015). The impact of multimorbidity on adult physical and mental health in low- and middle-income countries: what does the study on global ageing and adult health (SAGE) reveal? BMC Medicine.

Multiple morbidities as a global health challenge

Participants at the roundtable focussed on establishing and understanding the challenges of multiple morbidity, including the scope of existing epidemiological data across all settings. A small number of speakers stimulated discussion by sharing insight into potential sources of data on the problem, and what these sources might indicate in terms prevalence and profile of disease. Multiple morbidity was also considered in the context of ageing, including its relationship to frailty. Recent analysis of UK research funding across infectious disease was presented, and participants considered how this might inform the direction of research.

Multiple morbidities in LMICs

Mortality is falling across the majority of nations, a trend driven in part by a combination of more effective prevention, and improved healthcare provision.[5] The recent Sustainable Development Goals will mean that the post-2015 agenda will be substantially influenced by a focus on 'health in all ages', including Target 3.8 which aims to achieve universal health coverage. The realisation of these goals, and other wider development targets, will require multiple morbidity to be addressed.

The observed decline in mortality is a global phenomenon, and is affecting all age groups. One downstream consequence of this trend may be an increase in morbidities, with multiple morbidity becoming increasingly common. Participants discussed the evidence for such a link between declining mortality and rising morbidity, suggesting that the impact may be unequally distributed across different age groups. An example included the cross-sectional study, discussed above, of routine electronic data from 1.7m patients in Scotland, which reported increased prevalence of multiple morbidity with age, but with absolute number of cases highest among those under 65 years of age, rather than above.[3] Although the sub-65 demographic was a larger group overall, this still represents a concerning trend in the distribution of multiple morbidity. This study also noted that the onset of multiple morbidity occurred 10-15 years earlier in those living in deprived conditions, when compared to more affluent areas – evidence of further social stratification. Participants felt that more data is needed to resolve questions around whether the onset of multiple morbidity is shifting in the life course, and they felt consideration should be given to the experience of each age-group individually.

Participants acknowledged that data remains a major challenge for this area of research. Attention was directed towards a 2012 publication which quantified Years Lived with Disability (YLDs) based on data from the Global Burden of Disease study, but which "could not identify sufficiently large datasets" to measure whether co-occurrence of conditions was dependent or independent of one another.[6] This weakness in the data severely limits the research and health community's ongoing appraisal of the problem, and participants

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[5] Norheim, *et al.* (2015). *Avoiding 40% of the premature deaths in each country, 2010–30: review of national mortality trends to help quantify the UN Sustainable Development Goal for health.* Lancet.

[6] Vos et al (2012) Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet.

felt there was a pressing need to draw-together existing primary and secondary sources to evaluate the contribution they could make to understanding multiple morbidity.

Participants considered sources of data on this issue, and noted that a comprehensive evaluation would be valuable. Such analysis should account for existing sources and those with potential for the future, and participants highlighted several examples:

- *Cohort studies* – these sources benefit from largely consistent definitions and the collection of detailed information, but are frequently small and non-representative, and follow-up studies are likely to focus on incidence (i.e. the number of new infections) rather than prevalence (i.e. the total number of infections). There is also a challenge in the exclusion criteria for participants, which often removed patients with multiple morbidities as complicating factors.
- *Routine administration data* – these sources are often national (or semi-national) and continuously collected. However, there is a significant challenge to linking data across often complex and hard-to-access silos. This is amplified in private provider and multi-payer systems, and any approach needs to accommodate the wider cultural mood around access to patient data which varies across nations.
- *Population-based health surveys* – these sources are more representative of populations, capturing both diagnosed and undiagnosed people. Their broad scope often includes other variables of interest, including education and health behaviours. However, fewer clinical end points are typically measured and follow-ups are not routine.
- *Advances in classification methods* – further clarity on the classification of patients could generate useful data from clinical judgements. Questions remained around how to best record such data, and how data science could draw clinical data closer to the quantitative community.

A major obstacle to improved data coherence is the establishment of a shared definition across the field. In particular, clarity is needed on how acute conditions are included, or excluded, when these occur in the context of a chronic background condition. Particular examples, such as sepsis after surgery, were raised as sources of contention. Participants also felt that any unifying framework would need to capture the severity and impact of individual conditions affecting a patient, recognising that some combinations of diseases have significantly more impact on health than others.

Multiple morbidities in ageing populations

Research on the burden of multiple morbidity in older people is growing, but is doing so from a low baseline. A range of contributing conditions are encountered disproportionately within this group, particularly degenerative disorders, including those affecting the mind. However, these occur against a broad background of other contributors including wider sensory conditions, digestive issues, respiratory complications and diseases such as diabetes.[7] It was noted that, for this age group, multiple morbidity became the rule rather than the exception. With the majority of conditions being chronic in nature, the disease

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[7] Prince et al (2015). A premature mortality target for the SDG for health is ageist. The Lancet.

landscape generates unique implications for health policy and practice.[8] Participants discussed whether the elderly remain underserved by research on this topic, despite the burden of multiple morbidity within this group being highest for both the patient and the healthcare system.[9]

Concerns were raised that clinical guidelines are creating a siloed approach to the treatment of disease, frequently leading to polypharmacy which is associated with adverse drug interactions and higher costs. Approaches to treatment are typically 'monomorbid', a structure often mirrored within the research landscape which leaves little space for multiple morbidities. Discussion centred on whether greater coordination is needed around treatment, drawing on the contribution of both specialists and generalists to ensure a coherent and simplified patient experience, which identifies and treats conditions in parallel. It was noted that this approach had successfully demonstrated an ability to reduce unnecessary hospitalisation associated with multiple morbidity, through case management techniques such as the PRISMA coordinated care model.[10] Although disease-specific approaches remain valuable, there is a need to create treatment narratives for individuals, tailored to their cultural and environment context. To adapt, clinical guidelines need to reflect that although the diseases being encountered are not new, the combinations frequently are and this greatly influences outcomes.

Participants discussed the overlap between multiple morbidities and frailty, noting the debate on definitions for both terms. They felt that frailty offers a useful risk stratification marker and studies, such as the 10/66 population-based cohort study, demonstrate its use in identifying vulnerable individuals likely to develop a need for care.[11] Participants discussed how to best identify such groups, and the challenge of self-reporting bias for frailty. However, there was a general consensus that screening methods concerning frailty offer value when seeking to identify vulnerable people. Participants discussed different approaches to trial design in this area, noting that trials could be centred on individuals, diseases or symptoms. Trial design is likely to become substantially more complex, particularly in elderly patients where ethnic and cultural expectations had a major influence on the process of ageing.

Questions remained on whether there were patterns or clusters in the development of multiple conditions. The constructs through which such conditions are measured remains critical to clearly identifying such trends within the data, with many clinical definitions relying on the absolute number of accumulated conditions or symptoms, rather than the type and impact of the conditions present. Only through efficient capture of this data can research questions on the interactions between such conditions be explored, and the underlying biology understood. Through this process, the community might be able to define a link between simple indicators and complex outcomes, allowing the predictive capacity of these indicators to be harnessed to improve health outcomes.

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[8] Prince et al (2014). The burden of disease in older people and implications for health policy and practice, Ageing 2.

[9] Lancet Ageing Series (2015). The Lancet

[10] PRISMA trial: https://www.clinicaltrials.gov/ct2/show/NCT00643474

[11] Jotheeswaran et al (2015). Frailty and the prediction of dependence and mortality in low- and middle-income countries: a 10/66 population-based cohort study. BMC Medicine.

Challenges currently facing the health sector include limited help-seeking and poor integration.[12] Participants felt that vertical solutions, such as the World Health Organisation Mental Health Gap Action Programme (mhGAP), could contribute to the integrated care pathway, but they noted some caution.[13] For example, such programmes can offer value in low-resource settings but can also exacerbate fragmentation within healthcare. Vertical solutions can only ever be part of an effective primary care model, in which coordinated care is provided at the community level, with the support of specialist services, as necessary. Vertical solutions must be integrated with the activities of Non-Governmental Organisations, local communities and families, as well as efforts to improve self-management. Viable solutions will need to address how best to identify vulnerable people, how to effectively monitor elderly patients and which underlying mechanisms are contributing the wider disease landscape. Particularly for the elderly, the importance of brain conditions needs to be considered alongside physical morbidities.[14]

Research funding patterns - infectious disease as a case study

Participants considered data describing the allocation of research investments for infectious disease research to UK institutions. It was discussed whether such data provides insight into the funding for multiple morbidity research, whether it identified knowledge gaps which had yet to be addressed and whether similar methodologies could be applied to identify co-morbidity research portfolios.

The data shared suggests that research projects involving two infectious disease areas (for example, co-infection of HIV and tuberculosis) attract greater funding than those concerning the interface between infectious and non-communicable diseases (e.g. there has been little investment for tuberculosis and diabetes research), with the notable exception of cancer and Human Papilloma Virus. Participants considered the variation of funding over time, and how several key diseases ranked according to their disease burden.[15]

Several key questions were raised and discussed. These included whether the indicated increase in the number of research team consortia is supporting greater inter-disciplinary research across disease silos, or whether it is largely fostering connections within silos. Antimicrobial resistance research was noted as an example of the importance of quantifying economic and disease burden in order to attract an appropriate level of attention from policy-makers. Participants felt that this situation in particular holds many lessons for multiple morbidity research, the challenge of which needs to be fully considered at the level of decision-makers.

Participants discussed the challenge of assessing funding levels across short timescales, noting that feasibility and capacity could influence investment– syphilis was raised as an

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[12] Prince et al, World Psychiatry, 2007
[13] http://www.who.int/mental_health/evidence/mhGAP/en/
[14] Sousa et al, Lancet, 2009; BMC Geriatrics 2010
[15] Head et al, *UK investments in global infectious disease research 1997-2010: a case study*. Lancet Infectious Diseases (2013).

example where promising research targets for treatment are increasingly challenging to identify, and funding has fallen. Participants felt that the supply-side of interdisciplinary work needs to be examined, suggesting that many funding calls were experiencing poor uptake, possibly due to insufficient capacity within the skills base. This needs to be addressed to ensure a strong and sustainable research community is fostered.

Mechanisms underlying multiple morbidities

Participants focussed on how we might conceptualise multiple morbidities, by identifying some of the mechanisms that generate them and thinking about the levels at which they operate and should be targeted.

Models for understanding multiple morbidity

Understanding the problem, for both infectious and non-communicable diseases, will require a wider consideration of the factors influencing an individual's health. Participants considered a three-level model, in which mechanisms could differ between each layer:

Level 1: Individuals
Participants considered how research could uncover relationships between multiple conditions within a single patient, such as cardiac complications and depression, and whether certain conditions generate others, or if there are shared determinants and common aetiologies. Participants explored current understanding of whether treatment for one condition could raise the risk of a second (e.g. via polypharmacy), whether one chronic condition could induce another (e.g. depression stemming from coping with another chronic condition) or whether there were common determinants.

Level 2: Households
Discussion focussed on how conditions cluster within households and how cohabitation between genetically unrelated patients alters risk profiles for the development of multiple morbidities. Participants felt that research should better capture the common and modifiable risk factors which can lead to morbidities in multiple household members at different stages in the life course. A broader understanding of the mechanisms of interaction within this setting could have major implications for treatment regimes, and influence the broader trend of health within households through pre-emptive action against risk factors beyond the primary patient.

Level 3: Neighbourhoods
There were many factors which might influence the pathway of disease at a local area level, including the provision of green spaces and access to healthy foods. Observations and understanding at a community level could play a major role in prevention efforts, and it was noted that Public Health England is undertaking a surveillance project on syndromic infectious diseases which could provide insights at a community level.[16]

Understanding clustering within multiple morbidity

Participants discussed the clustering of diseases, with some relationships being readily apparent and others requiring a greater level of data and understanding. It was vital to understand the gradient of clustering, with some conditions clustering so tightly they effectively represent a single disease, to conditions with a far weaker level of association.

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[16] https://www.gov.uk/government/collections/syndromic-surveillance-systems-and-analyses

It is important to differentiate random clustering from sequenced relationships – where declining health follows a repeatable pathway of disease progression and accumulation. Lessons may be learned from similar classification drives which have occurred in other fields, with Congenital Heart Disease raised as an example.[17]

Participants felt that if the research community was able to make progress in understanding the underlying mechanisms of multiple morbidity, and coupled this with desired outcomes of treatment for patients, then interventions could shift towards a prevention paradigm in which the pathway of one disease to another could be altered, or a specific risk factor addressed before a condition occurred. Early intervention within a set of sequenced conditions could generate a magnifying effect on downstream outcomes, blurring the line between treatment and prevention.

Participants felt that an effective area to target first would be non-randomly clustered conditions, which indicated a smaller set of underlying risk factors. Participants discussed the need to realign clinician mind-sets, which are currently focussed on identifying a disease, administering pharmacological treatment, and ensuring adherence – to instead considering the preventative value of treating one condition to halt another, avoiding the pathway to polypharmacy. Several features of sequential clusters would need to be considered, including:

- Cycling – where groups of risk factors create inescapable cycles of disease, the cyclical nature of poverty and malaria was raised as an example.
- Compounding – whether a highly targeted intervention could de-escalate an accelerating deterioration of an individual's health, by knocking out key trigger points and restoring a level of functionality that maintained quality of life. Such an approach has significant implications for the elderly, where deterioration can occur rapidly.
- Small, long-term improvements – it is vital that the value of small changes, magnified over long durations, is fully recognised in intervention planning. The chronic nature of many multiple morbidities means this is a powerful mechanism.

Participants discussed whether multiple morbidity represents a known problem, which now requires a solution, or whether the true extent of the challenge has yet to be fully defined. Clustered conditions might offer a foothold to a wider understanding of the issue, and a route to generating meaningful impact in the near-term.

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[17] Valderas et al (2009) Defining Comorbidity: Implications for Understanding Health and Health Services, Annals of Family Medicine.

Issues to be addressed

Advances in public health have led to an aging demographic in all nations, with HICs already well-advanced in this shift. This change means that the observed trend of rising multiple morbidity is likely to continue, representing one of the most substantial health burdens for the future and a cost which will be challenging to meet for both HICs and LMICs. Based on the universal nature of this threat, participants questioned whether it is helpful to consider HICs and LMICs separately, and concluded that there were many common lessons to be shared across all global settings.

Research in this area has met with many of the challenges associated with a fast-developing field, including fragmentation of definitions and disunity within research methodologies. With this topic growing rapidly in prominence, it is important to tackle these fundamental research issues early and provide a firm foundation for future work. An improved understanding of the impact and scale of multiple morbidity within the disease landscape, and a clear and pragmatic framework within which to study the topic, would both support greater engagement with, and awareness among, policy makers.

Participants sought greater clarity on the determinants of multiple morbidity and how best to separate morbidities from the risk factors which cause them. Through this, it would be possible to begin exploring the underlying biology behind these conditions and delineate the relationships which link them together. This should be combined with emerging insights from epigenetic research on the cause and amelioration of disease burden. Such an understanding needs to account for the wider sources of influence on chronic disease, including environmental determinants such as air pollution and physical inactivity. Evidence is emerging, but further research is needed to explore how such risk factors can influence the risk profile of several conditions, and the tendency for socio-economic and environmental risk factors to cluster in certain social groups.[18] Through a combined approach to collate new understandings from life course epidemiology, sociology and biology, researchers could develop a model to inform policy.

Data remains a key issue throughout all the areas discussed above, and participants felt there is clear demand for 'taking stock' of the current patchwork of research, identifying knowledge gaps, and creating a unified strategy for further progress. Data is needed across all contexts and demographics, to ensure that the field can improve its predictive capacity and target interventions in a manner which maximises impact and minimises the use of limited resources.

Solutions to this challenge need to be context-specific – across LMICs, wage growth is forecast to be significant in coming years, making the cost of labour an increasing limitation in any health care solution. As part of the wider patient-centred care movement, it is vital that models for studying and tackling multiple morbidity are considered to ensure the potential to improve health outcomes is captured.

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[18] Wang et al (2014) Relationships of Multimorbidity and Income With Hospital Admissions in 3 Health Care Systems, Annals of Family Medicine.

Roundtable delegates

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