Addressing the global challenge of multimorbidity:

Lessons from BRICS countries

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Contents

Executive summary

Key Context

With people living longer and surviving health challenges, increasing numbers of patients are living with a combination of chronic conditions. However, health systems, research and medical education are still primarily geared to the management of single conditions. Although it is an issue that primarily effects older generations, factors such as changing lifestyles and environmental degradation are leading to multimorbidity in the relatively young as well.

Multimorbidity is an international issue. In BRICS countries (Brazil, Russia, India, China and South Africa, five major emerging national economies that have established a range of mechanisms to support international cooperation), the rapid growth in non-communicable diseases and the persistence of infectious diseases are combining to make multimorbidity a major public health challenge. In addition, the majority of the limited evidence that is available on multimorbidity is from high-income countries.[1]

In the discussions and breakout sessions, workshop participants discussed the nature of the multimorbidity threats facing BRICS countries, the challenges they present to healthcare systems, the steps being taken to address them, and possible ways in which research could contribute to more effective responses. Participants identified a number of important knowledge gaps that could form the basis of a global multimorbidity research agenda, as well as several key themes that could facilitate the development of this agenda.

Key knowledge gaps

1. **The epidemiology of multimorbidity:** There are limited data on the extent, nature and impact of multimorbidity in BRICS countries and globally.
2. **Mechanistic understanding of multimorbidity:** Little is known about the relationship between comorbidities, such as shared risk factors or underlying pathways of disease, and how health conditions interact with one another physiologically. A better understanding of these mechanisms could have important implications for both prevention and treatment.
3. **Prevention of multimorbidity:** The prevention of multimorbidity is likely to draw on the same approaches as for the prevention of single conditions. However, sparse evidence is available on the effectiveness of clinical, behavioural, public health and wider public policy measures to prevent chronic conditions.
4. **Effective management of multimorbidity:** Little is currently known about (a) optimal clinical treatments for patients with multiple conditions and (b) how health systems should be organised to manage large numbers of patients with multimorbidity. A variety of approaches could be taken to fill these knowledge gaps, including randomised controlled trials, implementation research and other forms of health services research, while methodological innovations may also be needed.
5. **The economic impact of multimorbidity:** Estimates of the economic cost of multimorbidity can provide vital input to support evidence-based policymaking. However, insufficient health economic research has been carried out on the impact of multimorbidity (on individuals/households, health systems and wider economies). As well as additional data, there may also be a need for methodological advances to capture the full impact of multimorbidity on national economies.
6. **Implications for medical education:** Increasing levels of multimorbidity raise questions about the current emphasis on medical specialisation, the desired balance between 'generalists' and 'specialists', and the required skill sets of these two groups. Medical education research could play a role in exploring these issues and their implications for medical education and training of the next generation of healthcare professionals.

1.   Violan C, et al. (2014). Prevalence, Determinants and Patterns of Multimorbidity in Primary Care: A Systematic Review of Observational Studies. PLoS ONE 9(7): e102149.

Cross-cutting issues informing the research agenda

Participants identified a range of principles that could inform the development of this outline research agenda:

1. **The patient perspective:** It was suggested that all areas of research, from the assessment of the impact of health conditions to the redesign of health systems, should place particular emphasis on the needs of patients and the patient experience.
2. **The life-course perspective:** Although multimorbidity is common in older age, it is increasingly a concern across all ages and its roots often lie in much earlier stages of life. Adopting a life-course perspective could therefore inform the development of more effective preventive strategies.
3. **The need for equitable solutions:** Multimorbidity often shows a strong association with socioeconomic disadvantage. Solutions are therefore required that do not exacerbate existing social divides and address the needs of the poorest.
4. **Learning from experience:** Some medical disciplines – such as geriatric medicine, critical care and palliative care – already adopt more integrated patient-centred approaches based on the management of multiple conditions. These disciplines could hold important lessons for the improved management of multimorbidity.

Multimorbidity in BRICS countries

Participants identified a range of issues specific to multimorbidity in BRICS countries:

1. **Commonalities and differences:** BRICS countries share many health challenges, including a rising tide of non-communicable diseases, but also have their own individual, context-specific problems. There is sufficient overlap to warrant the development of joint approaches, but these are likely to require tailoring to local circumstances.
2. **Potential for cross-BRICS collaboration:** Building on existing international cooperation, there is potential for BRICS countries to learn from one another and to establish coordinated or collaborative approaches to understand the nature of multimorbidity challenges, and to develop and test new approaches to address them. As well as international collaborations, this work could be facilitated by harmonised data gathering and enhanced data sharing across countries, and more generally by the adoption of a shared research agenda.
3. **Health systems development:** BRICS countries typically have less well-established healthcare systems and these are often undergoing considerable redevelopment. Such redevelopment could provide opportunities for the re-engineering of health systems so that they focus more on multimorbidity. Deeply embedded systems typical of high-income countries may not necessarily be the best models to emulate – BRICS countries could 'leapfrog' them to establish integrated models more suitable for their populations experiencing high levels of multimorbidity.

Advancing the research agenda

Participants identified two overarching issues that could accelerate research on multimorbidity in BRICS countries and internationally:

1. **The need for agreed definitions:** There is no formally agreed definition of multimorbidity, hindering attempts to develop a shared understanding of the issue and coordinated responses. It may be helpful to consider a simple high-level definition or 'vision' of multimorbidity, capturing key concepts in a general way, which could act as an umbrella covering more specific and tightly defined categories of multimorbidity (a 'typology' of multimorbidity) to facilitate research, consistent data collection and coordinated policy responses.
2. **Need for advocacy:** The extent and implications of multimorbidity may not yet be fully appreciated. There may be a need to communicate more widely the importance of multimorbidity and its implications for health systems, research and medical education, particularly to mobilise political support and to influence policy and high-level strategy development.

Introduction

As longevity increases, more people are living with multiple health conditions. In many low- and middle-income countries, rising levels of non-communicable diseases are adding to an already high burden of infectious disease. Hence, rather than being the exception, multimorbidity is now generally the norm across the globe.[2]

Medicine has traditionally been based on the diagnosis and treatment of individual conditions. However, this model is increasingly being challenged: as people live longer and medical treatments enable patients to survive previously fatal conditions, more people are living with a combination of health conditions –multimorbidity.

Broadly speaking, multimorbidity can be defined as the presence of two or more long-term health conditions. In high-income countries, the decline in infectious disease over the past century and other factors have led to an increasing prevalence of non-communicable diseases, which often dominate discussions of multimorbidity. However, chronic infectious diseases can also contribute to multimorbidity. The importance of psychiatric disorders should also not be underestimated, while populations that are living longer are also leading to an alarming rise in dementia and neurodegenerative disease.[3]

Multimorbidity shows a strong association with age: it is more common in older age groups, and the number of conditions that patients have also increases with age. However, some studies suggest that around half of patients with multimorbidity are relatively young (under 65 years of age).[4] Multimorbidity is also strongly influenced by factors such as social disadvantage – which can bring forward the onset of multimorbidity and increase its impact.

Multimorbidity is therefore becoming the norm rather than the exception, particularly for patients in middle age and older, when the burden of non-communicable diseases typically begins to grow, and particularly under situations of socioeconomic stress. As well as its increasing prevalence, there are other reasons why multimorbidity warrants greater attention. For example, it is typically associated with higher mortality, lower quality of life for patients, increased health service usage and costs, and an increased risk of safety issues during treatment as patients with multiple conditions often require multiple medications.

Multimorbidity also presents a range of major challenges beyond those experienced by patients. Health systems and healthcare delivery are primarily organised around specialised disciplines and the identification and management of individual conditions. Similarly, medical training has a strong emphasis on specialisation. In addition, specific challenges related to multimorbidity are often neglected in unusual situations, particularly when dealing with younger patients. Medical research has also traditionally focused on understanding and developing treatments for individual conditions. Thus multimorbidity presents a profound challenge to the way medicine is delivered, taught and researched.

2. Violan C, et al. (2014). Prevalence, Determinants and Patterns of Multimorbidity in Primary Care: A Systematic Review of Observational Studies. PLoS ONE 9(7): e102149.

3. Valderas JM, et al. (2009). Defining Comorbidity: Implications for Understanding Health and Health Services. Annals of Family Medicine 7:357-63.

4. 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.

From the patient's point of view, there is not only the challenge of managing multiple health conditions but also of navigating health systems that, in general, have been set up to provide discipline-specific care rather than integrated patient-centric care.

In recognition of the growing challenge posed by multimorbidity, in 2015 the Academy of Medical Sciences established a working group to examine multimorbidity in an international context.[5] As well as soliciting written evidence, the working group also held a workshop in South Africa in November 2016, in partnership with the Academy of Science of South Africa, to examine the impact and management of multimorbidity in a middle-income country (South Africa).[6]

At the workshop, it became clear that many of the challenges facing South Africa also apply to other members of the so-called BRICS countries, and that there could be important opportunities for each to learn from the others. A follow-up workshop was therefore organised, held at the Academy of Medical Sciences in London, with a focus on multimorbidity in BRICS countries. The organisation of the workshop was overseen by a steering committee (Appendix 1).

This report is intended to provide a summary of the themes that emerged during workshop discussions, including key knowledge gaps identified by the participants that could provide an outline agenda for future research. It should be noted that this document reflects the views expressed by participants at the meeting and does not represent the views of all participants or of the Academy of Medical Sciences.

The workshop was funded by the UK Government's Global Challenges Research Fund and was one of a series of policy workshops co-organised by the Academy of Medical Sciences that aim to:
- Enable partners (primarily National Academies) in Official Development Assistance (ODA) eligible countries to consider how scientific evidence can help address key global health challenges.
- Build capacity in ODA countries for the provision of scientific advice.

Further information and reports from the programme of workshops can be found on the Academy of Medical Sciences' website.[7]

Multimorbidity in BRICS countries

While multimorbidity is posing a significant challenge to healthcare systems in high-income countries, non-communicable diseases are also a growing problem in emerging economies, ensuring that multimorbidity is a truly global issue. BRICS countries have a total population of 2.8 billion people, some 40 per cent of the world's population. With economic growth, greater adoption of westernised lifestyles and increasing longevity, they face a huge and growing challenge from non-communicable diseases and multimorbidity. However, the issue to date has received relatively little attention.

Ongoing dialogue and political cooperation between BRICS countries is presenting new opportunities for international collaboration, sharing of knowledge and experience, and the development of strategies that are tailored to the particular circumstances of BRICS countries, which may not be the same as those envisaged for high-income countries with more well-established healthcare systems. As multimorbidity becomes an ever-greater health issue in each country, it may be possible to establish collaborations or other mechanisms to accelerate the joint development and implementation of solutions, including a shared research agenda.

These ideas formed the starting point for the workshop at the Academy of Medical Sciences. In discussion sessions and breakout groups, several key knowledge gaps were identified and a range of important themes emerged.

5.   https://acmedsci.ac.uk/policy/policy-projects/multimorbidity

6.   https://acmedsci.ac.uk/policy/policy-projects/addressing-the-global-challenge-of-multimorbidity-lessons-from-south-africa

7.   www.acmedsci.ac.uk/GCRF

Key knowledge gaps

1. The epidemiology of multimorbidity: It was widely felt by workshop participants that too little is known about the extent, nature and impact of multimorbidity. This applies globally, but is particularly the case in BRICS countries.

A lack of data is an obstacle to the mobilisation of political support to tackle multimorbidity. Data on multimorbidity and associated risk factors are also needed to support the development of strategies to address multimorbidity and to assess the impact of preventive strategies and programmes.

While non-communicable diseases are widely recognised to be a major challenge to public health in BRICS countries, and strategies exist to address them, there is a risk that such strategies will not adequately reflect the importance of multimorbidity, particularly its implications for healthcare delivery.

In some countries, data are being collected that could shed light on the extent of multimorbidity, but may not be being made more widely available for analysis. It may be necessary to establish national strategies for data collection and multimorbidity surveillance. While such activities would be driven at a national level, harmonisation of data collection could avoid duplication of efforts and facilitate international comparisons. Growing use of technology and electronic health record systems could provide a platform for the efficient collection, integration and analysis of data.

2. Mechanistic understanding of multimorbidity: BRICS participants highlighted that there are a number of pathways by which multimorbidity can arise, which may be difficult to disentangle. A patient may develop two conditions by chance, but there may also be connections between the two, such as shared risk factors.[8] Obesity, for instance, increases the risk of a host of conditions, and any factors that affect the risk of obesity – such as poor diet or lack of physical activity – will therefore influence the risk of multiple conditions. Diseases may also share underlying pathology – chronic inflammation, for example, increases the risk of multiple conditions. Developing one condition may also predispose to another, through physiological or behavioural mechanisms (or both). An example is the increased risk of cardiovascular disease in patients with chronic kidney disease. In some cases, treatment of one condition can increase the risk of another morbidity.

Depression illustrates some of these complexities. It is very commonly associated with other chronic conditions, often showing a striking reciprocal relationship: the presence of depression can exacerbate physical symptoms, while a physical condition can worsen depression. These relationships can potentially be mediated by both physiological mechanisms, such as changes in cytokine levels, and behavioural pathways, such as reduced physical exercise or impacts on other aspects of personal care or health-seeking behaviour.

In some cases, conditions are likely to share underlying causes. Prevention and treatment addressing these shared factors may therefore deliver benefits across conditions. However, some common comorbidities may be quite dissimilar. For example, people with psychiatric disorders also experience extremely high rates of cardiovascular and other metabolic diseases, while tuberculosis (TB) appears to be associated with an increased risk of diabetes.

8.   Valderas JM, et al. (2009). Defining Comorbidity: Implications for Understanding Health and Health Services. Annals of Family Medicine 7:357-63.

Further complexity can arise when markedly different conditions generate very similar symptoms. Clinicians may, for example, find it difficult to distinguish heart failure from chronic lung disease on the basis of symptoms.

While infectious diseases have not always been considered relevant to multimorbidity, chronic infections – particularly HIV and TB – can require long treatment regimes. Furthermore, the distinction between infectious and non-infectious disease may not be clear-cut. Viral infections can be drivers of cancer and bacterial infections can increase the risk of non-communicable diseases – periodontal infections, for example, increase the risk of heart disease, while some infections can trigger longer-term autoimmune reactions (such as Guillain-Barré syndrome, a potentially serious muscle-wasting condition).

Such interactions argue for more integrated management of patients. However, in the absence of a deep understanding of how conditions interact, the best way to manage such patients or prevent the development of additional morbidities may not be clear. Hence there is a need to develop a much better understanding not only of the development of individual conditions but also of the physiological abnormalities underlying multiple conditions and the pathways by which one condition can accelerate the development of additional morbidities.

3. Prevention of multimorbidity: Participants noted that multimorbidity can be seen as the accumulation of individual conditions. Many of the behavioural, environmental and physiological risk factors for chronic conditions are well established, and the prevention of individual morbidities would by extension contribute to a reduction in multimorbidity by addressing shared risk factors or etiologically related conditions.

Some pharmacological interventions have been shown to be effective at lowering physiological parameters associated with increased risk of non-communicable diseases, such as blood pressure-lowering and cholesterol-lowering drugs. However, the widespread application of pharmacological approaches at a population level would present enormous financial challenges to middle-income countries. Hence, it may make more sense to focus on behavioural and environmental interventions that address key cardiometabolic risk factors, with the aim of reducing obesity and smoking, enhancing physical activity levels, and promoting healthy diets and healthier environments. It is tempting to speculate that targeting such factors in the wider context of public health measures – for example through tobacco control and sugar taxes etc. – might help reduce the incidence of multimorbidity through having wide-ranging consequences on multiple conditions.

However, a major drawback of such a strategy is that specific links between risk factors and disease may not be clear, making the design of such interventions difficult. For example, while salt intake has been linked to hypertension, 'ideal' levels of salt consumption are still disputed.[9] Furthermore, there is relatively little evidence on the effectiveness of clinical, behavioural, public health and wider public policy measures to influence health outcomes.

The development of a health condition can itself be a risk factor for further morbidities. More integrated approaches at 'first contact' with healthcare systems could therefore provide opportunities to reduce the risk of future comorbidities. A step in this direction can be seen in the greater focus being given to mental health in the treatment of cancer, and lifestyle interventions to reduce the risk of cardiometabolic disease in patients with schizophrenia.

9. Mente A, et al. (2016). Associations of Urinary Sodium Excretion with Cardiovascular Events in Individuals with and without Hypertension: A Pooled Analysis of Data from Four Studies. The Lancet 388(10043):465–75.

4. Effective management of multimorbidity: Workshop participants agreed that perhaps the most significant gaps in knowledge relate to the effective management of multimorbidity. This issue covers two related matters: the clinical approaches that should be adopted for individual patients with more than one health condition; and the organisation of health systems to manage large numbers of patients with multimorbidity.

The treatment of individual patients is very strongly rooted in the single-condition model. Interventions typically target one condition, and their efficacy is determined in randomised controlled trials that normally focus on an individual condition; patients with additional morbidities are routinely excluded from such trials. Similarly, regulatory frameworks and licensing decisions are generally based on the demonstration of efficacy in such rigorously controlled trials.

A major drawback of such an approach is that, in routine clinical practice, interventions are often used on patients with multiple comorbidities, who may be very unlike those participating in clinical trials. Patients may be taking multiple medications, and there may be very little evidence from clinical trials on how those treatments interact with one another or how the presence of a comorbidity might affect treatment responses (or the risk of adverse events).

Furthermore, clinical guidelines, designed to be the authoritative guidance on clinical decision-making, also typically focus on the management of single conditions. Faced with a patient with multiple comorbidities, a clinician may have to assess and integrate multiple clinical guidelines with potentially contradictory recommendations.

Possible ways forward include greater use of pragmatic trials to assess interventions in patients with multiple health conditions and more analysis of data from such patients collected in routine clinical practice. There may also be a need to engage with regulatory authorities to ensure their activities reflect the changing practice of medicine and the challenges of dealing with increasing levels of multimorbidity and polypharmacy.

In terms of clinical guidelines, the 'high dimensionality' of multimorbidity presents a major challenge – there are a potentially vast number of different combinations of morbidities. The UK National Institute for Health and Care Excellence (NICE) has developed guidelines for managing multimorbidity,[10] but these are more general principles of good practice rather than explicit treatment recommendations for particular combinations of conditions.

In terms of health systems organisation, multimorbidity argues for more patient-centric and integrated models of care. This model is poorly compatible with conventional health system models, which are generally structured around individual specialist disciplines. It has also been argued that actually the focus on multimorbidity as a problem of a subgroup of the population tends to place the emphasis on the development of bespoke interventions when actually system redesign is needed.[11] From a research perspective, there is also the question of how innovative models of healthcare delivery should be evaluated.

There is relatively abundant theoretical literature on approaches that could be adopted to improve the management of patients with multimorbidity. There is less information on the mechanisms of multimorbidity, including the identification of patients at risk of poor outcomes and how such poor outcomes come about. There is even less published evidence on practical evaluations of how care can be reorganised effectively to accommodate patients with multimorbidity.

10. NICE (2016). Multimorbidity: Clinical Assessment and Management (NICE Guideline NG56). Available at: https://www.nice.org.uk/guidance/ng56
11. Valderas JM (2015). Multimorbidity, Not a Health Condition or Complexity by Another Name. The European Journal of General Practice 21: 213–214.

However, it has been possible to run cluster randomised controlled trials in primary care in the UK. Examples include the CAPITOL,[12] CARE Plus[13] and 3D[14] studies. A recent Cochrane Review identified 18 trials evaluating complex interventions in primary care and community settings for people with multimorbidity, 12 of which focused on changes in health system organisation.[15] These studies have used methods such as the Patient Assessment of Chronic Illness Care (PACIC) tool to evaluate patient satisfaction with service provision.

Clinical trials to assess delivery mechanisms are also being organised in BRICS countries. These include the COBALT study in South Africa,[16] which is examining integrated care for HIV and depression, and the PRIME study,[17] which is looking at the impact of integrated care on mental health and hypertension in patients attending public sector primary care settings in South Africa, India and three other low- or middle-income countries (LMICs). Importantly, such studies are generating evidence that could inform the development of services in other resource-constrained environments.

These examples suggest that it is feasible to organise randomised controlled trials to evaluate new models of healthcare delivery in primary care. Alternatively, in the interest of producing generalisable knowledge, it could be more relevant to conduct a realist synthesis of the literature on models of care for multimorbidity in LMICs, focusing on how interventions are expected to work and in what circumstances they do so. In addition, there may be scope to apply other research methodologies, such as implementation research or other forms of health services research.

Practical Approach to Care Kit in South Africa

One approach developed in South Africa has been validated in multiple clinical trials[18] and widely implemented. The Practical Approach to Care Kit (PACK)[19] provides a practical toolkit for assessing 20 of the most commonly encountered health problems in primary care. Given the severe shortage of trained health professionals in South Africa, PACK was designed to support task shifting, enabling nurses to play a more active role in the delivery of care.

As well as a PACK Decision Aid to support diagnosis and clinical decision-making, the PACK programme also includes training, a guide to implementation, and tools to support the monitoring and evaluation of implementation. Used in more than 2,000 clinics by over 20,000 clinical staff, the PACK programme is also being adapted for use in other LMICs, including Botswana, Nigeria and Brazil.

12. http://hrep.lshtm.ac.uk/publications/Care%20planning_final_Bower%20et%20al_7%20Mar%2013.pdf

13. Mercer SW, et al. (2016). The CARE Plus Study – A Whole-system Intervention to Improve Quality of Life of Primary Care Patients with Multimorbidity in Areas of High Socioeconomic Deprivation: Exploratory Cluster Randomised Controlled Trial and Cost-utility Analysis. BMC Medicine 14(1):88.

14. Man MS, et al. (2016) Improving the Management of Multimorbidity in General Practice: Protocol of a Cluster Randomised Controlled Trial (The 3D Study). BMJ Open 6(4):e011261.

15. Smith SM, et al. (2016). Interventions for Improving Outcomes in Patients with Multimorbidity in Primary Care and Community Settings. The Cochrane Database of Systematic Reviews 3:CD006560.

16. https://clinicaltrials.gov/ct2/show/NCT02407691

17. Lund C, et al. (2012). PRIME: A Programme to Reduce the Treatment Gap for Mental Disorders in Five Low- and Middle-income Countries. PLoS Medicine 9(12):e1001359.

18. Fairall LR, et al. (2005). Effect of Educational Outreach to Nurses on Tuberculosis Case Detection and Primary Care of Respiratory Illness: Pragmatic Cluster Randomised Controlled Trial. BMJ 331:750–4; Zwarenstein M, et al. (2011). Outreach Education for Integration of HIV/AIDS Care, Antiretroviral Treatment, and Tuberculosis Care in Primary Care Clinics in South Africa: PALSA PLUS Pragmatic Cluster Randomised Trial. BMJ 342:d2022; Bachmann MO, et al. (2010). Effect on Tuberculosis Outcomes of Educational Outreach to South African Clinics During Two Randomised Trials. The International Journal of Tuberculosis and Lung Disease 14:311–7; Fairall LR, et al. (2012). Task Shifting of Antiretroviral Treatment from Doctors to Primary-care Nurses in South Africa (STRETCH): A Pragmatic, Parallel, Cluster-randomised Trial. The Lancet 380:889–98.

19. http://pack.bmj.com

5. The economic impact of multimorbidity: Workshop participants highlighted that multimorbidity is likely to have a range of economic implications but relatively little work has been carried out on its impacts. The direct costs of the management of conditions are borne by healthcare systems and/or households, depending on the type of healthcare systems in place. Out-of-pocket expenses for healthcare, including management of chronic conditions, can have a calamitous impact on households in many LMICs. Multimorbidity also has an indirect economic impact via lost productivity, of both patients and carers, which is again felt at both the household and national level.

One of the few studies to evaluate the economic impact of multimorbidity in middle-income countries found that multimorbidity is associated with greater healthcare utilisation and higher out-of-pocket expenses.[20] The burden of multimorbidity was greatest in Russia but the financial burden on individuals was highest in China and India, where individuals make a greater contribution to healthcare expenses. The study also identified a substantial burden among relatively young age groups, 40–49 years and 50–59 years, and in India and Russia multimorbidity was more common in those of higher socioeconomic status. The latter finding, the opposite of that typically seen in high-income countries, hints at significant complexity in how multimorbidity affects populations, which is likely to be highly context specific and influenced by factors such as income levels and mix of rural and urban populations, as well as access to care.

Some economic information is available on individual chronic conditions. However, extrapolating from single to multiple conditions is not straightforward, as it cannot be assumed that the impact of conditions is additive. Combined costs could be reduced if care of one condition contributes to the management of another, but it is also possible that a second condition will exacerbate and complicate management, adding to overall costs. A UK study suggested that conditions could be either cost-increasing or cost-limiting depending on other comorbidities, but depression was strongly associated with increased costs.[21] Although dementia was found to be cost-limiting for healthcare, it was found to be very cost-increasing when social care expenditure was included,[22] emphasising the importance of considering 'whole-system' costs.

Furthermore, there may be dangers in extrapolating findings from high-income to middle-income countries. Health systems are likely to differ significantly, and many modelling assumptions may not be appropriate for middle-income countries.

Therefore, as well as additional work on the prevalence and nature of multimorbidity, analyses of the economic impact of multimorbidity would be helpful to support policymaking. Methodological advances in the way that economic impacts are measured may also be required. Current health economic approaches are typically based on the 'cost of illness approach', which aggregates treatment costs and losses affecting patients and carers. This approach has drawbacks, however, potentially overvaluing carers' time in LMICs and neglecting wider economic impacts on a country. Some studies have adopted a wider macroeconomic viewpoint, for example to estimate the potential impact of Alzheimer's disease on the Chinese economy (the annual GDP impact was predicted to hit US$1trillion by 2050) with a significant share due to costs of lost productivity by carers.[23]

20. Lee JT, et al. (2015). Impact of Noncommunicable Disease Multimorbidity on Healthcare Utilisation and Out-of-pocket Expenditures in Middle-income Countries: Cross Sectional Analysis. PLoS One 10(7):e0127199.

21. Brilleman SL, et al. (2013). Implications of Comorbidity for Primary Care Costs in the UK: A Retrospective Observational Study. British Journal of General Practice 63(609):e274–82.

22. Kasteridis P, et al. (2014). The Importance of Multimorbidity in Explaining Utilisation and Costs Across Health and Social Care Settings: Evidence from South Somerset's Symphony Project. Centre for Health Economics, University of York. Available at: https://pure.york.ac.uk/portal/en/publications/the-importance-of-multimorbidity-in-explaining-utilisation-and-costs-across-health-and-social-care-settings(cc257267-2e28-465c-96f5-749c8bda4fa6).html

23. Keogh-Brown MR, et al. (2015). The Impact of Alzheimer's Disease on the Chinese Economy. EBioMedicine 4:184–90.

Health economic analyses may also need to consider the impact of multimorbidity on quality of life, as well as mortality. Various standardised tools are available to assess quality of life, providing opportunities to compare and integrate different data sets. Additional comorbidities typically lower quality of life, although not to an equivalent degree.[24] Notably, depression often has a markedly large impact on quality of life as a comorbidity.

In the UK, short- to medium-term modelling of the impact of multimorbidity is used to predict likely future primary health costs[25] and to guide the allocation of funds to clinical commissioning groups.[26] In general, although healthcare utilisation increases with age, multimorbidity is a better predictor of costs than age. Furthermore, participants suggested relatively simple count measures appear to be at least as effective as more complex measures of multimorbidity at predicting future costs.

6. Implications for medical education: There was wide agreement amongst participants that medical education currently places great store on the development of specialists with deep levels of expertise in relatively circumscribed areas of medicine. When fully trained, specialists may have limited contact with disciplines outside their speciality area. Generalists are more usually found in primary care and typically undergo less extensive training.

Increasing levels of multimorbidity raise questions about the suitability of this model. Patients are likely to have a combination of conditions, some potentially well outside an individual specialist's area of expertise. Hence there was much debate at the meeting on the desired balance between 'generalists' and 'specialists' and the appropriate skill sets of the two groups.

For example, it could be argued that specialists should develop the skills and expertise to manage common comorbidities. Alternatively, as management of chronic conditions generally centres on primary care, it could be more appropriate to address the education and training of healthcare professionals in primary care. An additional factor in middle-income countries is a severe shortage of trained healthcare professionals. This has been one factor driving task shifting and the development of innovative models of delivery in South Africa. In terms of a research agenda, medical education research could play a role in exploring these issues and their implications for medical education.

24. Fortin M, et al. (2004). Multimorbidity and Quality of Life in Primary Care: A Systematic Review. Health and Quality of Life Outcomes 2:51.

25. Brilleman SL, et al. (2014). Keep it Simple? Predicting Primary Health Care Costs with Clinical Morbidity Measures. Journal of Health Economics 35:109–22.

26. Chaplin M, et al. (2016). Refreshing the Formulae for CCG Allocations: For Allocations to Clinical Commissioning Groups from 2016-17 – Report on the Methods and Modelling. NHS England Analytical Services (Finance), NHS England. Available at: https://www.england.nhs.uk/wp-content/uploads/2016/04/3-rep-elland-all-sections.pdf

Cross-cutting issues informing the research agenda

As well as these specific knowledge gaps, participants from BRICS countries and the UK also identified a number of key principles that could guide future research.

1. The patient perspective: Multimorbidity has a major impact on patients, and a failure to take account of multimorbidity in service delivery can severely inconvenience patients and lower quality of care. There are opportunities to integrate the patient perspective at all stages of research, from the development of methods to assess the impact of multimorbidity to the design and evaluation of new models of integrated healthcare delivery. Details about how to integrate the patient perspective would also be needed with routine use of individualised patient reported outcome measures (PROMs) for goal elicitations and standardised PROMs for monitoring being a prime example of the potential approach.[27,28]

Although self-care is likely to be an important aspect of chronic disease management, it may be helpful to adopt the principles of 'minimally disruptive medicine',[29] which aims to minimise the burden of disease management by designing treatment and care programmes that fit better around the daily lives of patients.

2. The life-course perspective: Prevention is likely to be a key aspect of multimorbidity management. Although most chronic conditions typically arise in older age, their origins may lie in behaviours and exposures much earlier in life (even as far back as prenatal exposures). To be most effective, policies and strategies to address multimorbidity may need to consider this life-course perspective rather than focusing entirely on the ages at which chronic morbidities begin to arise.

3. The need for equitable solutions: Although the link between socioeconomic status and multimorbidity is likely to be complex, there is strong evidence that economic disadvantage is an important risk factor for multimorbidity and exacerbates its impact. In countries with poorly developed healthcare systems, out-of-pocket expenses associated with chronic diseases can have catastrophic financial impacts on households. In line with the principles of universal health coverage,[30] the design of new approaches for prevention or healthcare delivery for multimorbidity should consider the needs of disadvantaged groups in order not to exacerbate existing inequalities.

4. Learning from experience: Integrated models of care are likely to lie at the heart of new models of healthcare delivery for multimorbidity. Some areas of medicine – including geriatric medicine and palliative care – are often already practising such models. It may be possible to learn lessons from such disciplines that could be applied in the management of multimorbidity.

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Multimorbidity in BRICS countries

Delegates identified a range of issues related to multimorbidity and its management across BRICS countries.

1. Commonalities and differences: BRICS countries share a number of similarities, including a significant and growing chronic disease burden fuelled by common risk factors (particularly tobacco use, declining levels of physical exercise, and unhealthy diets). Although these risk factors are affecting all BRICS countries, their relative importance varies between countries.

On the other hand, BRICS countries each have their own unique features and health challenges, such as the high prevalence of HIV and TB in South Africa, multidrug-resistant TB in Russia and mosquito-transmitted infectious diseases in Brazil. In addition, the cultures of BRICS countries also show significant differences, influencing the risk factors for chronic diseases. Furthermore, this heterogeneity is also a feature of individual countries, which may encompass many different cultural groups. An acknowledgement of these differences will be important in the design of interventions.

BRICS countries also have markedly different healthcare systems, with significant differences in the balance between public and private healthcare provision. All are increasing their investments in health systems and making concerted efforts to improve primary healthcare coverage across their populations.

2. Potential for cross-BRICS collaboration: Despite these differences, there are significant opportunities for collaboration across BRICS countries. The countries face many similar issues, and solutions developed for one could be adapted for another, avoiding the inevitable duplication of effort if each country acts independently. Furthermore, joint strategies and policies could be developed that are shaped by the needs and circumstances of BRICS countries, which are not necessarily the same as those of high-income countries.

Approaches such as harmonised data collection and analysis would support international comparisons, and the joint development of tools would reduce the investment required by individual countries. The implementation of electronic health records could offer new opportunities for data capture, integration and analysis. Given these advantages, proposals that span BRICS countries could potentially be attractive to major international research funders.

3. Health systems development: BRICS countries have been engaged in national initiatives to develop their primary healthcare systems and improve health coverage, and re-engineering of healthcare systems is likely to be a continuing feature of BRICS countries for the foreseeable future. Nevertheless, healthcare expenditure is relatively low in some BRICS countries, and several are experiencing severe shortages of trained healthcare professionals.

Although high-quality care may be difficult to deliver through less well-developed healthcare systems, there may be more scope to re-engineer less deeply embedded health systems. Rather than mimicking systems based on individual specialisms which predominate in high-income countries, developments could facilitate the introduction of innovative new approaches more appropriate to the treatment of patients with multimorbidity, with more flexible use of healthcare workers.

Advancing the research agenda

Participants from the BRICS countries and the UK identified two key issues that could facilitate coordinated international research on multimorbidity.

1. The need for agreed definitions: A significant issue in the field is the lack of an agreed definition of multimorbidity. In many situations, a simple definition – the presence of two or more morbidities – can suffice, but this fails to address a number of detailed questions. Which morbidities should be included? Should just chronic conditions be included? When does a condition qualify as being 'chronic'? Should infectious diseases be included, and if so, which ones? Some conditions are closely related and have similar underlying risk factors or disease mechanisms ('concordant', such as hypertension and coronary heart disease) while others are highly distinct ('discordant', such as cancer and depression): should definitions take account of these differences? Should physiological risk factors, such as hypertension and dyslipidaemia, be counted as morbidities? Should conditions such as obesity also be included? What is the relationship between multimorbidity and other related concepts such as frailty and disability?

Continual redefinition of individual conditions presents an additional challenge. As thresholds are lowered, increasing numbers of patients are being diagnosed with hypertension, diabetes and dyslipidaemia. Furthermore, new categories have been established, such as pre-hypertension and pre-diabetes, which could conceivably also be included in definitions of multimorbidity.

It may be helpful to consider a two-tiered approach for defining multimorbidity. A simple high-level definition could support communication activities, to raise awareness of the importance of multimorbidity and the urgent need to address it. More detailed definitions could then be developed for research purposes to facilitate coordination of research, international comparisons and data sharing. Given the diversity of different forms of multimorbidity, potentially a range of definitions could be developed, creating an internationally agreed 'typology' of multimorbidity.

2. Need for advocacy: Multimorbidity is common, likely to grow and has major implications for healthcare systems, research and medical training. Arguably, however, it is yet to receive the attention it deserves. There may therefore be a need to communicate its importance to politicians and health policymakers and to other key stakeholders, such as regulatory bodies and funding agencies. An agreed simple definition of multimorbidity could support such advocacy activities. An important goal of such activities would be to promote investment in the research studies needed to address multimorbidity.

Conclusions

Multimorbidity is a huge global issue presenting major challenges to all nations, including BRICS countries and other emerging economies. Current trends suggest that chronic conditions, including long-term infections, will affect growing numbers of people in emerging economies, accounting for a huge burden of disease and having a major impact on economic development. While multimorbidity is most common in older age, there is also evidence that the total burden of multimorbidity is greatest in younger age groups, suggesting that multimorbidity is not simply an issue relevant to later-life care.

While the threat of non-communicable diseases is widely recognised, multimorbidity adds considerably to their management. The presence of additional morbidities typically increases use of healthcare resources and further decreases patients' quality of life. Crucially, multimorbidity adds to the complexity of patient management, and a fundamental rethink in how services are organised and offered to patients, and how healthcare professionals are educated and trained is required.

Despite a growing awareness of multimorbidity, political action and healthcare policymaking are held back by a lack of data, on both the nature and extent of multimorbidity and its economic implications, and on the most effective ways to prevent and manage multimorbidity. Research has a potentially critical role to play in filling these gaps, and there are encouraging signs that funding agencies have begun to recognise the importance of multimorbidity in global health. Within the general research agenda identified above, there is a need to scope out specific and detailed research priorities and potential programmes of work.

BRICS countries are likely to face a particularly high and growing burden of multimorbidity. Although each faces a unique combination of issues, they also share many features in common. Building on existing dialogue and cooperation, there is the potential to develop a shared research agenda that reflects their circumstances and needs, rather than those of high-income countries. As well as delivering more tailored solutions, international collaboration between BRICS countries could maximise their investments in research. Building the global research base in multimorbidity could be the cornerstone of evidence-based efforts to reconfigure models of delivery and healthcare systems, and medical education, to reflect the new reality where multimorbidity is the norm rather than the exception.

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