



Workshop Proceedings

**Addressing the global challenges of multimorbidity
– lessons from South Africa**

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The Academy of Medical Sciences

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Addressing the global challenges of multimorbidity: lessons from South Africa

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Introduction

Throughout the world, as life expectancy increases, the population incidence of non-communicable diseases (NCDs) is also increasing. In addition, communicable diseases continue to affect millions of people every year. All of these factors together mean that multimorbidity has become, and will increasingly be, an international health challenge.

However, currently there is no commonly used framework for defining or more widely understanding multimorbidity. Furthermore, most health related research is currently focused on the prevention and management of disorders in isolation. Consequently, it is difficult to compile a coherent body of research in this area or develop evidence-based strategies for use in healthcare systems.

In order to address the international challenge of multimorbidity, we must understand the problem better. Most of the evidence on multimorbidity, its prevalence and effects, comes from high-income countries (HICs). Less is known about multimorbidity in low- or middle-income countries (LMICs), particularly in Sub-Saharan Africa.

South Africa is a dynamic and complex country. It is a middle-income nation that has dedicated substantial resources to health and human capital investments. In addition, it has a progressive Constitution that guarantees the right to health care. National Health Insurance is the central means by which the Government aims to achieve universal coverage, under the principles of social solidarity and equity set out in the National Development Plan. However, despite improvements in life expectancy and progress being made against HIV/AIDS and tuberculosis, South Africa has an ageing population and approximately two in five deaths are now attributable to NCDs.¹ Multimorbidity therefore represents a growing concern in South Africa.

The main objective of this workshop was to consider the burden of multimorbidity in South Africa and the UK, and ask how we can achieve a more coherent and consistent approach to defining, researching, and addressing multimorbidity. The workshop brought together experts and evidence from South Africa, the UK and other countries on the prevalence, burden, and determinants of multimorbidity.

The aims of the workshop were as follows:

- Identify gaps in our knowledge on the basis of the available evidence and identify the associated research priorities required to address them.
- Consider how health systems in both the UK and South Africa are currently dealing with multimorbidity, and in particular discuss the key challenges and the costs and financing issues associated with multimorbidity – particularly in light of efforts to achieve universal health care.
- Consider lessons that can be learned by each country from the other.
- Ask how we can achieve a more coherent and consistent approach to defining, researching, and addressing multimorbidity.

¹ World Health Organization (2014). *Non-Communicable Diseases (NCD) Country Profiles, 2014*. http://www.who.int/nmh/countries/zaf_en.pdf?ua=1

This workshop was funded by the UK Government's Global Challenges Research Fund² and was the first of six 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 at www.acmedsci.ac.uk/GCRF

² The Global Challenges Research Fund (GCRF) is a £1.5bn fund announced by the UK Government to support cutting-edge research that addresses the challenges faced by developing countries through:

- Challenge-led disciplinary and interdisciplinary research.
- Strengthening capacity for research and innovation within both the UK and developing countries.
- Providing an agile response to emergencies where there is an urgent research need.

The GCRF is administered through delivery partners including the Research Councils and National Academies.

Day 1: Prevalence, burden, determinants and risk factors (Chair: Professor Karen Hofman)

Session 1: What is multimorbidity and why is it important?

There are a number of different definitions for what multimorbidity is and there is no commonly used framework for defining or more widely understanding the issue. This session set the context for the meeting. It touched on the prevalence and burden of multimorbidity, key diseases, and any headline clusters or risk factors that indicate particular populations affected, including the poorest communities and particular demographic challenges. It also helped to highlight the importance of this issue in South Africa, the UK and more broadly across the world.

Key points from the session's presentations were:

- Multimorbidity is a global phenomenon that increases mortality, healthcare utilisation, hospital admissions and duration of stay, and the burden on patients, and decreases quality of life. In the UK multimorbidity is the norm in the ageing population but it also occurs at a younger age in people of lower socioeconomic status.
- Policymakers worldwide need to address health inequalities and support the complex service needs of a growing multimorbid population.
- Chronic disease management, including in mental health, has a strong single disease focus based on guidelines that exclude multimorbid patients.
- Much more is required in terms of developing the evidence base, the effective integration of health and social care services through adopting a holistic approach, and research to assess the gaps in community resources for providing services to multimorbid patients.
- It is necessary to increase activities and expand measures to reduce the modifiable risk factors that drive multimorbidity prevalence.
- The number of adults in South Africa with high levels of key risk factors has escalated over time, surpassing any adjustments that are made to the healthcare system (from a case study).
- There is a gap between the knowledge and the ability to address the high mortality from chronic conditions in South Africa, and there are difficulties in the implementation of integrated chronic care.

World Health Organization (WHO) perspective (Dr Taskeen Khan, WHO South Africa)

In terms of the epidemiological transition, there has been a shift from communicable diseases to NCDs. Many HICs have experienced the transition and are seeing the after-effects, which have made NCDs the leading cause of global mortality. The double burden of communicable diseases and NCDs evident in Africa has been difficult for policymakers to respond to. The importance of research in producing the evidence to draw attention to the rising burden of disease cannot be underestimated. The demographic transition reflects a shift to an ageing population and increases in multimorbidity globally are expected.

Most global studies of multimorbidity prevalence and determinants have been single disease focused and in HICs. Studies from HICs have shown that multimorbidity is progressively more common among older adults, but recent evidence shows that younger adults are also affected. There is little research to date in terms of NCD research and data in Africa. The large and growing burden of NCDs in LMICs, particularly when coupled with limitations in resources and competing public health priorities, points to the need to understand the burden of multimorbidity.

WHO has contributed to two recent studies in order to gain insight and evidence concerning multimorbidity:

- Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the World Health Surveys and focusing on LMICs.³
- Study on Global Ageing and Adult Health (SAGE), a longitudinal ageing and health study with nationally representative samples of adults from six countries: China, Ghana, India, Mexico, Russia and South Africa.⁴

Conclusions drawn from both studies are that multimorbidity is a global phenomenon, that it does not just affect older adults in HICs, and that policymakers worldwide need to address health inequalities and support the complex service needs of a growing multimorbid population.

Better coordination and support through informed planning of healthcare systems are required, and it is also necessary to increase activities and expand measures to reduce the modifiable risk factors that are driving multimorbidity prevalence. In addition, more research is required to assess the gaps in community resources for providing services that maintain quality of life in the face of declining health.

Perspective from the UK (Professor Stewart Mercer, University of Glasgow)

In the UK, most studies, as well as the National Institute for Health and Care Excellence (NICE) Guidelines,⁵ define multimorbidity as two or more long-term health conditions within an individual. Different studies would require more appropriate definitions depending on the specific research question.

A landmark study of 1.8 million patients across Scotland showed the importance of routinely recorded electronic data in primary care and found that multimorbidity is common, complex, increases with age and is socially patterned, being more common and occurring at a younger age in areas of high socioeconomic deprivation. It also found that mental-physical multimorbidity increases with the number of physical conditions and is particularly strongly socially patterned.⁶

UK and international studies and systematic reviews have shown that multimorbidity increases mortality, healthcare utilisation, hospital admissions and duration of stay, and the burden on patients, and decreases quality

³ Afshar S, et al. (2015). *Multimorbidity and the Inequalities of Global Ageing: A Cross-Sectional Study of 28 Countries Using the World Health Surveys*. BioMed Central (BMC) Public Health **15**, 776.

⁴ World Health Organization. *Study on Global Ageing and Adult Health (SAGE)*. <http://www.who.int/healthinfo/sage/en/>

⁵ National Institute for Health and Care Excellence (NICE) (2016). *Multimorbidity: Clinical Assessment and Management*. <https://www.nice.org.uk/guidance/ng56/resources/multimorbidity-clinical-assessment-and-management-1837516654789>

⁶ 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.

of life.⁷ The cost of multimorbidity on the healthcare system depends to some extent on the nature of the healthcare system but it is now the key driver of healthcare costs worldwide.

The UK National Health Service (NHS) ensures universal coverage of the whole population. It is free at the point of care to the entire population and it is based on a strong general practice and primary care system as a gatekeeper to secondary care. In terms of multimorbidity, general practice carries out most chronic disease management, including mental health. However, there is a strong single disease focus based on guidelines that exclude multimorbid patients, and health and social care needs are often poorly integrated.

In summary, multimorbidity in the UK is the norm and not the exception in the ageing population. It reduces the length and quality of life and is socially patterned, in that it is more common and occurs at a younger age in people of lower socioeconomic status.⁸ The NHS, strong general practice and primary care remain central to the effective and equitable management of patients with multimorbidity. However, much more is required in terms of the evidence base and the effective integration of health and social care services, and it is necessary to move from a silo approach to a much more integrated and holistic approach.

Perspective from South Africa and beyond (Professor Steve Tollman, University of the Witwatersrand)

The presentation focused on an in-depth case study from rural south and southern Africa. The study is based in Agincourt, a sub-district of Bushbuckridge in the rural north-east of the country with a population of about 120,000 people.⁹ The study capitalises on a health and socio-demographic surveillance system (HDSS), which covers the sub-district and provides robust longitudinal information to whole communities especially those that are under resourced. Although HDSSs tend to be used for vaccine trials and child and women oriented interventions, they also have applicability to issues in relation to multimorbidity. These systems are versatile (they can support multiple designs that are cross-sectional or longitudinal) and attempt to capture elements of both the demographic transition and the epidemiological transition, as well as some of the social and biological drivers.

The study findings relate to increasing mortality from NCDs (despite highly prevalent HIV/AIDS), the ageing population, patterns in respect of key determinants (such as migration, stunting, obesity and malnutrition), the impact of multimorbidity on physical and mental function, the continuum of care and the way health services are structured. The number of adults with high levels of key risk factors has escalated over time and this dynamic change is a reality that surpasses any adjustments that are made to the healthcare system.

There is a gap between the knowledge of the disease burden and how best to address the high mortality and risks from chronic conditions (infectious and non-communicable). While in principle the approach may be appropriate, the implementation of integrated chronic care is proving difficult.

The recent introduction of regulations to reduce the salt content in food is an example of efforts in South Africa to work outside the healthcare system through regulatory and fiscal interventions that affect health.

Panel discussion (Panellists: Professor Stewart Mercer, Professor Steve Tollman, Dr Taskeen Khan)

Clustering of chronic conditions, based on the most prevalent conditions, in order to undertake comparisons and coordinate research will depend on the purpose of the specific investigation. The same conditions have to be

⁷ Payne RA, et al. (2013). *The Effect of Physical Multimorbidity, Mental Health Conditions and Socioeconomic Deprivation on Unplanned Admissions to Hospital: A Retrospective Cohort Study*. Canadian Medical Association Journal **185**(5), e221–e228.

⁸ Lawson KD, et al. (2013). *Double Trouble: The Impact of Multimorbidity and Deprivation on Preference-Weighted Health Related Quality of Life a Cross Sectional Analysis of the Scottish Health Survey*. International Journal for Equity in Health **12**, 67.

⁹ Kahn K, et al. (2012). *Profile: Agincourt Health and Socio-demographic Surveillance System*. International Journal of Epidemiology **41**(4), 988–1001.

compared and it is difficult to generalise in terms of research on multimorbidities.

The NCD and disease-specific work is important, but there is an absence of pragmatic, complex interventions that have been tested in adequately powered cluster randomised controlled trials (RCTs), then implemented and evaluated. There is ample opportunity to do such work in South Africa and elsewhere. Although everyone is striving towards the patient-centric approach, each specific approach depends entirely on what the evidence shows, and variation across settings is inevitable. Integration needs to be defined and harmonisation of data is key. There are many opportunities to address these issues. The South African Department of Health is serious about primary care and community oriented care, and a patient-centric approach. Since nurses provide frontline primary care, they may have to 'unlearn' some of what they have been schooled to do and how they have been instructed to be accountable 'upwards'.

It is probably tractable to address the question of whether younger people are less affected by multimorbidity in terms of the differential impacts and whether the progression of conditions can be interrupted at certain stages. It would be interesting to evaluate the relationship between resilience and age, and whether or not increasing age affects the ability to cope. Resilience is complex (hard to define and hard to measure) but an important concept that could be addressed both from a life-course approach, and in terms of the interplay between a condition or conditions and physical and mental function.

In general, guidelines for chronic conditions focus solely on the one condition they cover, with no overlap to other conditions. Work could be done around a 'golden timeframe' for controlling an index condition once it has been diagnosed and before progression to multimorbidity and comorbid conditions. This is an area where there is potential for initial impact. The NICE guidelines on multimorbidity flag big issues such as polypharmacy; inevitably the combination of multimorbidity with single disease guidelines leads to this problem.¹⁰ The implications in terms of cost, drug interactions and adverse effects are huge. The way forward would be to look at the substantial contraindications and prevailing confusions in relation to the guidelines for heart disease, diabetes and depression, and to electronically link guidelines to enable a practitioner to give an immediate response. The South African hypertension guidelines make minor reference to HIV and no reference to mental health. Some of the large issues could be addressed if multimorbidity were used as a lens.

An evidence-based guideline called Primary Care 101 (PC101) and now known as the Practical Approach to Care Kit (PACK) is being put in place to support the management of chronic conditions in adults throughout the primary health care setting in South Africa.¹¹ The key outcome of a recent pragmatic trial to evaluate the implementation of PC101 was the intensification of treatment. Although there are many gaps, South Africa is at the cutting edge of implementation research in relation to chronic disease and integration of care. There is nevertheless still a lack of research and frameworks, and ways of thinking are limited. While potentially ground-breaking, these efforts have not had the breadth or the speed of uptake that allow for lessons to be taken forward.

The stigma around mental health exists not only in India, as pointed out by Indian participants, but also in the UK. Sometimes the label 'depression' is not helpful to a patient with multiple conditions. The role of primary care and continuous care is very important, with wellbeing as the focus. The physical conditions experienced by people with severe mental health problems should not be neglected and services should be better integrated. Cognitive assessment in multicultural environments is challenging, but is helpful in understanding the pathways involved and the bi-directional interplay between the physical, mental and emotional.

The sustainable approach to providing care is, as far as possible, to prevent or effectively manage the diseases in the first place. This also means addressing or tackling the social determinants of health (SDH). In working towards affordable solutions, South Africa should not make the same errors as the UK and should take a multipronged approach from the start, with better and more cost effective interventions for people who are already multimorbid.

¹⁰ National Institute for Health and Care Excellence (2016). *Multimorbidity: Clinical Assessment and Management*. <https://www.nice.org.uk/guidance/ng56/resources/multimorbidity-clinical-assessment-and-management-1837516654789>

¹¹ Knowledge Translation Unit. *Primary Care 101*. <http://knowledgetranslation.co.za/programmes/pc-101/>

Session 2: Showcasing research into multimorbidity

Despite there being gaps in research on multimorbidity, there are a number of pieces of research that have looked into this issue in both South Africa and the UK. This session therefore featured research studies into multimorbidity in the UK, South and Sub-Saharan Africa in more depth. The talks noted findings that relate to prevalence and burden, in particular, but also determinants and risk factors where they exist.

Key points from the session's presentations were:

- Mental health should be integrated in primary health care (through task sharing).
- A collaborative chronic care model should be adopted. Nurses need to be oriented to take a patient-centred approach and provided with clinical communication and emotional coping skills training.
- Health information systems in South Africa need to be strengthened.
- It is essential to focus on the data when addressing the question of whether care should be managed differently in the presence of multimorbidity.
- It is necessary to identify the burden from comorbidity, the evidence gap, and the routes to intervene, and to consider how best to apply existing knowledge to improve healthcare outcomes; whether comorbidity affects the response to interventions; the impact of a life-course approach, and how to design a healthcare delivery system that focuses on quality of life.
- Tuberculosis (TB) and HIV are the main causes of death in South Africa. The presence of multimorbidity is generally not picked up as part of the surveillance programmes, which also do not provide a sense of the extent to which NCDs are emerging in the HIV setting.
- More work needs to be done in relation to the adequacy of the current hospital-based model of prevention and care, and the delivery of patient-centric prevention and control services for cardiometabolic diseases.

Mental health disorders and other conditions (Professor Inge Petersen, University of KwaZulu-Natal)

The presentation focused on common mental disorders (CMDs) and the rising burden of chronic conditions in South Africa. CMDs, particularly depression and alcohol use disorders, play a significant role in exacerbating these epidemics. Depression is the third leading cause of disability-adjusted life years (DALYs). Mental, neurological and substance use disorders (MNS) are the leading cause of DALYs globally^{12,13} with alcohol being the leading substance abuse disorder and one that is strongly associated with numerous physical illnesses.¹⁴

International and local studies on comorbidity of CMDs with other chronic conditions (NCDs and HIV) showed the prevalence of and risk factors associated with coexisting mental and physical chronic conditions.^{15,16,17,18,19,20,21} Key conclusions from the studies indicate that different study designs, sampling and measurements may result in variations in the findings; that there are high rates of coexisting CMDs in people with other chronic conditions, and

¹² Mayosi BM, et al. (2012). *Health in South Africa: Changes and Challenges Since 2009*. The Lancet **380(9858)**, 2029-2043.

¹³ Whiteford HA, et al. (2015). *The Global Burden of Mental, Neurological and Substance Use Disorders: An Analysis from the Global Burden of Disease Study 2010*. PLoS One **10(2)**, e0116820.

¹⁴ *Ibid.*

¹⁵ Moussavi S, et al. (2007). *Depression, Chronic Diseases, and Decrements in Health: Results from the World Health Surveys*. The Lancet **370(9590)**, 851-858.

¹⁶ Ciesla JA & Roberts JE (2001). *Meta-Analysis of the Relationship Between HIV Infection and Risk for Depressive Disorders*. American Journal of Psychiatry **158(5)**, 725-30.

¹⁷ Neuman MG, et al. (2012). *Alcohol Consumption, Progression of Disease and Other Comorbidities, and Responses to Antiretroviral Medication in People Living with HIV*. AIDS Research And Treatment **2012**, 751827.

¹⁸ Lönnroth K, et al. (2008). *Alcohol Use as a Risk Factor for Tuberculosis – A Systematic Review*. BMC Public Health **8**, 1-12.

¹⁹ Grimsrud A, et al. (2009). *The Association Between Hypertension and Depression and Anxiety Disorders: Results from a Nationally-Representative Sample of South African Adults*. PLoS One **4(5)**, e5552.

²⁰ Sorsdahl K, et al. (2016). *The Association Between Psychological Distress, Alcohol Use and Physical Non-Communicable Diseases in a Nationally Representative Sample of South Africans*. Journal of Health Psychology, pii: 1359105316642832.

²¹ Freeman M, et al. (2007). *Factors Associated with Prevalence of Mental Disorder in People Living with HIV/AIDS in South Africa*. AIDS Care **19(10)**, 1201-1209.

that the identification and treatment rates for CMDs in South Africa are very low.

Coexisting depression and alcohol use disorders (AUD) compromises the prevention of NCDs and infectious diseases through exacerbating modifiable risk factors and self-care.^{22,23} Coexisting depression results in greater health decrements than when only one or more physical conditions are present, and coexisting CMDs compromise adherence to treatment regimes.^{24,25,26,27} In addition, comorbid mental disorders are associated with greater healthcare utilisation.²⁸

Rheumatological and musculoskeletal disorders (Professor Alan Silman FMedSci, University of Oxford)

It is essential to focus on the data when addressing the question of whether care should be managed differently in the presence of multimorbidity. Multimorbidity should be interpreted separately in the context of each of the three broad groups of rheumatological and musculoskeletal disorders: the osteoarthritis and osteoporotic fractures groups are associated with increasing age and frailty, whereas the rheumatoid arthritis (RA) and related disorder group is often concentrated in younger people and, as it involves other systems, the multimorbidity is frequently related.

There is also multimorbidity that is caused by medical treatments. Managing frail patients with musculoskeletal disorders (which should include mental health as much as physical health) raises different issues compared to managing just single morbidities. There are several overlapping pathways of causation of multimorbidity including: random co-occurrence, shared risk factors, shared pathogenesis (inflammation being a key pathological process in many different disorders) and the impact of therapy. Indirect consequences of musculoskeletal disease result in an adverse lifestyle, for example the reduction in levels of physical activity that are required to maintain good general health.

In terms of the priorities for research and advocacy with government healthcare providers, it is necessary to know where the burden from comorbidity is and what the evidence gap is that needs to be filled. It is also important to know about the routes to intervene, how best to apply existing knowledge to improve healthcare outcomes and whether comorbidity affects the response to interventions. Further there is a need to consider a life-course approach for musculoskeletal disorders, many of which can affect individuals for several decades, and the requirements of the healthcare delivery system, which in turn should focus on quality of life.

When considering disease states, it is important to consider adverse health states that are not specific pathological disorders such as obesity, physical inactivity, cognitive decline, psycho-social wellbeing and quantitative contribution from age per se.

To prioritise research targets, the comorbidity should be common in target disorders, contribute to the decrement of quality of life and be related to nuance of disorder.

HIV and related infectious diseases (Dr Halima Dawood, University of KwaZulu-Natal)

²² Lönnroth K, et al. (2008). *Alcohol Use as a Risk Factor for Tuberculosis – A Systematic Review*. BMC Public Health **8**, 1-12.

²³ Hahn JA, et al. (2011). *Adding Fuel to the Fire: Alcohol's Effect on the HIV Epidemic in Sub-Saharan Africa*. Current HIV/AIDS Reports **8**, 172-180.

²⁴ Moussavi S, et al. (2007). *Depression, Chronic Diseases, and Decrements in Health: Results from the World Health Surveys*. The Lancet **370(9590)**, 851-858.

²⁵ Gonzalez JS, et al. (2011). *Depression and HIV/AIDS Treatment Nonadherence: A Review and Meta-Analysis*. Journal of Acquired Immune Deficiency Syndromes **58(2)**, 181-7.

²⁶ Nakimuli-Mpungu E, et al. (2011). *Depression, Alcohol Use and Adherence to Antiretroviral Therapy in Sub-Saharan Africa: A Systematic Review*. AIDS and Behavior **16(8)**, 2101-18.

²⁷ Samet JH, et al. (2007). *Alcohol Consumption and HIV Disease Progression*. Journal of Acquired Immune Deficiency Syndromes **46(2)**, 194-9.

²⁸ Gijsen R, et al. (2001). *Causes and Consequences of Comorbidity: A Review*. Journal of Clinical Epidemiology **54(7)**, 661-674.

In 2012, the top three causes of mortality in South Africa were HIV/AIDS, stroke and diabetes. In 2013 it became clear that HIV, TB and lower respiratory infections contributed to years of life lost (YLLs).²⁹ South Africa has 18% of the total number of HIV infections across the world, with 30.5% of all deaths in South Africa being HIV related.³⁰ Over 2.5 million people are on antiretroviral therapy (ART) but HIV has yet to be controlled. Key obstacles to an AIDS-free generation include dysfunctional health systems, the continuous growth of HIV in key populations, and stigma and discrimination associated with testing and accessing prevention and care services.

The Centre for the AIDS Programme of Research in South Africa (CAPRISA) has been looking at HIV prevalence and incidence in the Vulindlela district of the country for some years.³¹ There is evidence that the prevalence and incidence of HIV is higher in young women between 15 and 24 years, but that there has been poor uptake of the attempts to link this monitoring to comorbidities and NCDs in young women.³²

The other important factor from the infectious diseases perspective is the high mortality and morbidity rates in relation to HIV and TB coinfection.³³ Improvements have only just begun to be made to the incidence and prevalence data in terms of these two conditions.

The Group for Enteric, Respiratory and Meningeal Disease Surveillance (GERMS) system started in 1999 by looking at vaccine preventable diseases, and surveillance of various other infectious diseases has been added to the platform since then.³⁴ A second surveillance system linked to GERMS is the prospective hospital-based sentinel surveillance programme that could be used to determine the relative contribution of influenza and other respiratory viruses to this disease presentation in a setting with a high prevalence of HIV; inform public health policy regarding severe acute respiratory infection (SARI) management, prevention and control in South Africa, and assist in planning for future influenza pandemics.

TB surveillance was added to the platform in 2010, making it possible to illustrate that influenza and TB coinfection has a higher mortality rate.³⁵ Attempts to link this surveillance to comorbidities and NCDs have not been successful and the presence of multimorbidity is generally not picked up as part of the surveillance programmes. There has been a decline in incidence rates and case fatality ratios in relation to opportunistic infections, primarily due to the effect of ART and TB control. In vaccine preventable diseases, there has been a marked decline in incidence rates and antimicrobial non-susceptibility. Work relating to addressing the concerning increase in antimicrobial resistance to first-line drugs in hospital associated infections began recently.

Major cardiometabolic diseases and risk factors (Professor Andre Pascal Kengne, South African MRC)

Cardiovascular disease (CVD) is among the top causes of death in the world and accounts for approximately 17 million deaths a year globally.³⁶ Hypertension is shown to be prevalent in about one-third of the adult population in Sub-Saharan Africa.³⁷ Most people with hypertension across the continent are currently undiagnosed, and less than 20% of those who have been diagnosed are currently receiving treatment.³⁸ Diabetes is on the increase in

²⁹ Health Systems Trust. *District Health Barometer 2014/2015*. http://www.hst.org.za/sites/default/files/Complete_DHB_2014_15_linked.pdf

³⁰ UNAIDS (2014). *Global AIDS Response Progress Reporting*. http://www.unaids.org/sites/default/files/media_asset/GARPR_2014_guidelines_en_0.pdf

³¹ <http://www.caprisa.org/Pages/Research-Activities>

³² Abdool Karim SS, et al. (2009). *HIV Infection and Tuberculosis in South Africa: An Urgent Need to Escalate the Public Health Response*. *The Lancet* **374(9693)**, 921-33.

³³ World Health Organization (2015). *Global Tuberculosis Report*. http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf

³⁴ GERMS South Africa. <http://www.nicd.ac.za/?page=germs-sa&id=97>

³⁵ Walaza S, et al. (2015). *Influenza Virus Infection is Associated with Increased Risk of Death Amongst Patients Hospitalized with Confirmed Pulmonary Tuberculosis in South Africa, 2010-2011*. *BMC Infectious Diseases* **15**, 26.

³⁶ WHO Cardiovascular Disease Factsheet, <http://www.who.int/mediacentre/factsheets/fs317/en/>

³⁷ Mills KT, et al. (2016). *Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries*. *Circulation* **134(6)**, 441-50.

³⁸ Ataklte F, et al. (2015). *Burden of Undiagnosed Hypertension in Sub-Saharan Africa: A Systematic Review and Meta-Analysis*. *Hypertension* **65(2)**, 291-8.

Sub-Saharan Africa, with the highest rates of diabetes being in South Africa, particularly among people living in urban areas.^{39,40,41,42}

It has been conceptualised that the drivers of the hypertension burden are the combined effect of environmental factors and genetic disposition. The rapid growth of CVD in Africa is connected to the environment and cannot be attributed to genetic disposition alone. Further drivers in Sub-Saharan Africa are obesity and urbanisation.

Questions that should be asked going forward are about the adequacy of the current hospital-based model of prevention and care, the sufficiency of the current passive/opportunistic approach to prevention and care, and how best to deliver prevention and control services for cardiometabolic diseases while integrating the needs and circumstances of individuals.

The way forward is to adopt an integrated life-course perspective to health promotion and prevention.

Panel discussion (Panellists: Professor Inge Petersen, Professor Alan Silman FMedSci, Dr Halima Dawood and Professor Andre Pascal Kengne)

One of the major problems in treating people with musculoskeletal disorders who also have hypertension, for example, is the incompatibility of one of the pillars of treatments – nonsteroidal anti-inflammatory drugs. This raises several points about drug interactions, polypharmacy, decision-making, and following guidelines. There is a need for simple, common guidelines for the most frequent comorbidities that could be transferred down to primary care physicians. Drug regulatory agencies tend to consider problems with drugs in silos in relation to specific indications and there are concerns about the medico-legal consequences, risk reduction and so forth. This also applies to antiretroviral (ARV) treatment. The specifics of assessing drug safety should not be considered by individual comorbidities.

From a primary care perspective, putting everything together into a super algorithm will bring about an intolerable burden of disease, interactions between drugs, lack of compliance and complications of treatments. The expert generalist should also include the patients' preferences for treatment and lifestyle. From a secondary care point of view, elderly patients screened positively for frailty should be managed by a multidisciplinary geriatric team. However, primary healthcare providers are being trained to take a vertical approach and the Government's integrated chronic care approach does not look sufficiently at workforce preparedness for patient-centred care to support the changing health system. Primary healthcare providers need orientation to patient-centred care and training in clinical communication skills to be able to take both the biomedical and patient perspectives into consideration.

The rapidly transitioning, high burden, complex interaction environments that we find in South and Sub-Saharan Africa, together with social determinants, clinical pathways and outcomes, may contribute to the creation of a portfolio of interventions. It is important to connect the clinical pathways with the social and cultural determinants in health care and healthcare acceptance. Clarity in this regard would help develop a framework to address some of the interacting disorders, which are currently overburdening. It is important to look at the issues that impact on quality of life and understand the pathways of care, and deliver these rather than attempting to have multiple guidelines from multiple disorders.

A framework for researching multimorbidity as well as a framework for addressing it would help manage the multimorbidity challenge. This is beyond what individual researchers can achieve in isolation and calls for a multisectoral approach. From an HIV and infectious diseases point of view, help is needed in managing NCDs

³⁹ Peer N, et al. (2014). *Diabetes in the Africa Region: An Update*. *Diabetes Research and Clinical Practice* **103(2)**, 197-205.

⁴⁰ International Diabetes Federation (2015). *Diabetes Atlas*. <http://www.diabetesatlas.org/resources/2015-atlas.html>

⁴¹ Peer N, et al. (2012). *Rising Diabetes Prevalence Among Urban-Dwelling Black South Africans*. *PLoS One* **7(9)**, e43336.

⁴² Erasmus RT, et al. (2012). *High Prevalence of Diabetes Mellitus and Metabolic Syndrome in a South African Coloured Population: Baseline Data of a Study in Bellville, Cape Town*. *South African Medical Journal* **102(11)**, 841-4.

where there are known interactions (not only with HIV).

Whereas in the UK, there may be an advantage in considering multimorbidity in people over 75 as the single entity of frailty, it is more complex in South Africa. There, the data on the proportionate impact from HIV is staggering and there are real issues in managing HIV, taking into account comorbid depression. It requires consideration of appropriate therapies, as well as prevention and lifestyle. The next stage of studies should look at whether depression is a risk for hypertension and how to prevent the consequent complications of hypertension or diabetes. It is also important to look at social factors in addition to biomedical factors.

Session 3: Determinants and risk factors of multimorbidity

In order to establish how to tackle the challenges of multimorbidity, it is crucial to first understand the determinants and risk factors. This session therefore identified key determinants and risk factors of multimorbidity and looked at how they might help us better understand and predict the burden of multimorbidity.

Key points from the session's presentations were:

- Deprivation, obesity and living in an urban area are significantly associated with multimorbidity in terms of the spatial patterns of multimorbidity and socioeconomic disadvantage in South Africa.
- Deprivation and social determinants are key contributors to the burden that patients with multimorbidity (particularly HIV and diabetes) experience.
- Sodium consumption may link high blood pressure, obesity and diabetes and there is a variation by ethnic origin in the sensitivity to the effects of salt. This can be explored in order to reduce blood pressure in patients with comorbidities involving hypertension and metabolic syndrome.
- Non-adherence in polypharmacy patients and the concept of the polypill to reduce the number of medications and increase adherence, and the need to improve applied research, particularly in South Africa, are among the most crucial challenges facing CVD control.
- There is a connection between inflammation, insulin resistance and diabetes as a result of an infection. In addition, ART is thought to modify the genetic effect of diabetes-associated risk variants.

Determinants of multimorbidity (Dr Tolu Oni, University of Cape Town)

In addition to age, sex, hereditary and individual lifestyle factors, living and working conditions and socioeconomic, cultural and environmental conditions are drivers of patterns of disease. Common risk factors that are attributed to DALYs also contribute to a wide range of morbidities. Shared risk factors are common to chronic infectious diseases as well as NCDs. This is important in terms of management and control, as well as prevention.⁴³

A recent study investigated spatial patterns of multimorbidity and socioeconomic disadvantage in South Africa using the Multidimensional Poverty Index (MPI) to provide a proxy indicator for socioeconomic disadvantage. Participants were grouped into different categories of deprivation. Two framing concepts, equity and life course, were applied.⁴⁴

The study found that deprivation, obesity and living in an urban area were significantly associated with multimorbidity; that deprivation and multimorbidity clustering corresponds with the socioeconomic disadvantage spatial pattern (with implications for government, urban planners and policymakers); and that deprivation and social determinants were key contributors to the burden that patients with multimorbidity experienced.

⁴³ Oni T, et al. (2015). *Why the Communicable/Non-Communicable Disease Dichotomy is Problematic for Public Health Control Strategies: Implications of Multimorbidity for Health Systems in an Era of Health Transition*. *International Health* **7**(6), 390-9.

⁴⁴ Weimann A, et al. (2016). *A Cross-Sectional and Spatial Analysis of the Prevalence of Multimorbidity and its Association with Socioeconomic Disadvantage in South Africa: A Comparison between 2008 and 2012*. *Social Science & Medicine* **163**, 144-56.

Knowledge gaps were identified in the following areas: disaggregated population data in both rural and urban settings; models of chronic HIV/NCD integrated care, especially in the context of generalised HIV epidemics; the integrated prevention of multimorbidity in patients with an existing chronic condition especially in HIV-infected adolescents; shared risk factor approaches to addressing multimorbidity; and inter-sectoral collaboration for integrated prevention strategies. The key exposures to be targeted in the context of inter-sectorality can be summarised as the 'seven Ss of urban exposure': sugar and salt, smoke and smoking, sleep and stress, sports and recreation, sanitation and water, safe housing and social cohesion, and sex.

Cardiovascular disease: aetiology and multiple related conditions (Professor Francesco Cappuccio, University of Warwick)

CVD as a leading cause of death globally needs to be addressed. In southern Sub-Saharan Africa about 60% of the attributable DALYs are due to the risk factors of cardiometabolic disease.⁴⁵ Globally, 11 million fatal events a year are attributable to the combined effects of high body mass index (BMI), blood pressure, serum cholesterol and blood glucose (cardiometabolic comorbidities). 70% of the deaths occurred in LMICs and were preventable.⁴⁶ From the global burden of disease perspective, this introduces the clinical concept of metabolic syndrome.

Approximately one in three patients over the age of 50 presenting for primary care in the UK have two or more cardiometabolic diseases, the majority of which are modifiable. Children between the ages of 12 and 16 have started to be seen with hypertension, in most cases driven by obesity. Coronary heart disease is the most common cause of death in the UK. There has been a significant decrease in the rate of CVD and premature death due to improvements in treatment and management, however, the prevalence of other conditions, particularly stroke, has increased.⁴⁷ Although people are living better for longer, more expensive treatment is being provided and the burden of disease is not being reduced. The already significant proportion of the NHS budget spent on CVD is expected to increase.

One of the most cost-effective non-pharmacological ways of lowering blood pressure, a driving risk factor for stroke, is the reduction of salt intake. The UK national programme for population salt reduction managed to reduce the average salt intake of the population by 1.4 grams over eight years. During the same period, and with parallel interventions, a significant fall in hypertension and a significant reduction in strokes and ischemic heart disease mortality were recorded.⁴⁸

Abnormalities in the way the kidneys handle sodium may link high blood pressure, obesity and diabetes. People with metabolic syndrome are in the sodium retentive state and clinically, both diabetics and people who are obese are salt sensitive. There is a variation by ethnic origin in the sensitivity to the effects of salt. This can be explored in order to reduce blood pressure and CVD outcomes, mainly stroke and kidney disease, in comorbidities with hypertension and metabolic syndrome, for example.

Non-adherence in polypharmacy patients and the concept of the polypill to reduce the number of medications and increase adherence, and the need to improve applied research, particularly in South Africa, are among the most crucial challenges facing CVD control.

⁴⁵ GBD 2015 Risk Factors Collaborators (2016). *Global, Regional, and National Comparative Risk Assessment of 79 Behavioural, Environmental and Occupational, and Metabolic Risks or Clusters of Risks, 1990-2015: A Systematic Analysis for the Global Burden of Disease Study 2015*. The Lancet **388**(10053), 1659-1724.

⁴⁶ The Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (2014). *Cardiovascular Disease, Chronic Kidney Disease, and Diabetes Mortality Burden of Cardiometabolic Risk Factors from 1980 to 2010: A Comparative Risk Assessment*. The Lancet Diabetes & Endocrinology **2**(8), 634-47.

⁴⁷ British Heart Foundation (2015). *Cardiovascular Disease Statistics*. <https://www.bhf.org.uk/publications/statistics/cvd-stats-2015>

⁴⁸ He FJ, et al. (2014). *Salt Reduction in England from 2003 to 2011: Its Relationship to Blood Pressure, Stroke and Ischaemic Heart Disease Mortality*. BMJ Open **4**(4), e004549.

Aetiology and multiple unrelated conditions (HIV, obesity and diabetes) (Professor Naomi (Dinky) Levitt, University of Cape Town)

In the midst of the HIV epidemic in the early 2000s, the impact of HIV/AIDS on the number of people with diabetes in South Africa between 1995 and 2010 was assessed. There was about a 50% increase in diabetes prevalence over this period.⁴⁹

In Sub-Saharan Africa there are about 11.7 million people (about 3.4 million in South Africa) on ART and about 25 million people with diabetes. There has been a phenomenal reduction in AIDS related deaths as a result of ART, with an increase in life expectancy from 54 to 62 within a 10-year period.⁵⁰

The two large mechanisms that can result in an increased association between HIV and diabetes are ART, mitochondrial toxicity and thus insulin resistance, and inflammatory reaction.

A study that prospectively looked at a range of cytokines and inflammatory markers found that in people that are HIV positive, but not on ART, there are a range of biomarkers that are remarkably elevated, confirming the fact that HIV is associated with inflammation.⁵¹ However, when people are on ART and are HIV suppressed, there is an improvement in many of the biomarkers, although some are still elevated suggesting ongoing inflammation. Therefore, there is a connection between inflammation, insulin resistance and diabetes on the basis of the infection. In addition, ART is thought to modify the genetic effect of diabetes-associated risk variants.⁵² Global data on the incidence rates of diabetes among people living with HIV shows enormous variation in incidence due to heterogeneity of the participants.⁵³ There is an association between diabetes and ARVs, in particular efavirenz, which is the cornerstone of ART in Sub-Saharan Africa.

A systematic review of many studies in Sub-Saharan Africa shows that the BMI of people who are HIV positive is lower than those who are HIV negative.⁵⁴ HIV is associated with weight loss. It has been found that the longer people are on ART the more they gain weight and their BMI rises.⁵⁵ It is also associated with fat redistribution where there is peripheral fat loss and central fat accumulation.

The knowledge gaps that were identified were in relation to the true prevalence and incidence of multimorbidity, diabetes and HIV using standardised methods in Sub-Saharan Africa; the impact of the coexistence of diabetes and HIV on diabetes complications; and the prevention of progression to diabetes through lifestyle modification in people with HIV.

Panel discussion (Panellists: Dr Tolu Oni, Professor Francesco Cappuccio, Professor Naomi (Dinky) Levitt)

There is a lot of marketing in South Africa around poor food choices, often targeting people from economically disadvantaged backgrounds and children, and there is a lack of transparency about food, food containers and labelling. People are not empowered to make healthy choices. Inequality is not just about inequitable negative exposure, but also about increased exposure and the lack of positive interventions, thus widening the inequality. In

⁴⁹ Levitt NS & Bradshaw D (2006). *The Impact of HIV/AIDS on Type 2 Diabetes Prevalence and Diabetes Healthcare Needs in South Africa: Projections for 2010*. *Diabetic Medicine* **23**, 103–104.

⁵⁰ Global AIDS Response Progress Reporting (2016). https://aidsreportingtool.unaids.org/static/docs/GARPR_Guidelines_2016_EN.pdf

⁵¹ Wada NI, et al. (2015). *The Effect of HAART-Induced HIV Suppression on Circulating Markers of Inflammation and Immune Activation*. *AIDS* **29(4)**, 463–71.

⁵² Frasco MA, et al. (2015). *Antiretroviral Therapy Modifies the Genetic Effect of Known Type 2 Diabetes-Associated Risk Variants in the Women's Interagency HIV Study*. *AIDS* **28(12)**: 1815–1823.

⁵³ Nigatu T, et al. (2012). *Magnitude of Diabetes Comorbidity among People Living with HIV: A Systematic Review*, *International Journal of Diabetes Research* **1(5)**, 81–86.

⁵⁴ Dillon DG, et al. (2013). *Association of HIV and ART with Cardiometabolic Traits in Sub-Saharan Africa: A Systematic Review and Meta-Analysis*. *International Journal of Epidemiology* **42(6)**, 1754–71.

⁵⁵ Feigl AB, et al. (2016). *The Effect of HIV and the Modifying Effect of Anti-Retroviral Therapy (ART) on Body Mass Index (BMI) and Blood Pressure Levels in Rural South Africa*. *PLoS One* **11(8)**, e0158264.

the context of limited resources and shared risk factors, it is more efficient to have an approach that targets the risk factors in a way that impacts on exposure. The prevention message within the healthcare system must be packaged on a population level as well as on an individual level.

From a practical perspective of how to manage the conditions, particularly in a resource-poor setting, it is necessary to be restrictive about the components included in the definition of multimorbidity. Decisions should be based on the health economic agenda, maximising the return and minimising the cost. The real issue is that the evidence and resulting desired outcomes go beyond what is affordable and diagnosis is very costly. Evidence suggests that people with high cardiovascular risk should be targeted. This is extremely cost effective and the best use of resources.

In terms of the social determinants framework and the idea of modifiable risk factors, one of the studies showed that an urban setting seemed to have higher risks of multimorbidities. This could indicate how risks are distributed and the relationship with socioeconomic related risks, and whether poverty is especially a risk factor of multimorbidity. There is an urbanising exposure that is not limited to urban settings. It is important to think beyond urban versus rural to quantify the components of the exposure and to not then think about these components in relation to any one disease, knowing that some of the exposures overlap across different diseases.

Vulnerabilities lie in the combination of inequality and the exposure to some of the factors that drive chronic diseases. Together they can result in poorer health outcomes. This discussion could be framed in Sustainable Development Goals (SDGs) because multimorbidity is about equity and poverty.

A practical approach is necessary when considering what drugs should make up the polypill, particularly in order to address the double burden of disease in Africa. Results of current trials should be awaited before any decision about the polypill can be taken. There are major advocates of the polypill and there are those who disagree with it. It is to do with simplifying therapies in multimorbid type environments in order to bring about proportion. From a regulatory point of view it would be necessary to know whether specific clinical trials need to be done in populations to examine the effectiveness of new drugs because responses to medications can vary as a result of genetic differences. Many studies have shown that based on life-time experience the risk and outcome do not match in different populations. Local data needs to be produced. Some of the evidence may have to be reworked in a specific country context and simple practical outcome and implementation trials done, or else errors could be made and resources wasted. There are limited resources in Africa and having to work through all the evidence causes delays. It is difficult to reconcile the debates around different responses in different populations to certain drugs and the implementation science agenda.

With respect to the issue of HIV, ART and the relationship to diabetes it is unknown whether there could be changes that would offset the dramatic rise in diabetes in Africa because there are no longitudinal studies, the data is not good enough and ART is changing. It can be expected that the whole profile of metabolic complications could change.

Session 4: Analysing the evidence and identifying research gaps in South Africa and beyond

In order to define and understand the burden, risk factors and determinants of multimorbidity in South Africa and beyond, it is critical to bring together and analyse the evidence available and identify further research gaps. This breakout session therefore aimed to give all participants the opportunity to discuss the evidence base in more detail and what lessons might be learned between countries. Each of the four groups focused on a key issue, including the most pressing gaps in the evidence, and where possible provided solutions.

Key points raised in the discussions were:

- There was clarity that the definition of multimorbidity should go beyond the standard international definition, although there was no conclusion about a final definition.
- In order to better understand the burden of multimorbidity, it is necessary to improve the quality and adequacy of the data, and biomarker measurements versus self-report, ensure adequate disaggregation of the data (in many dimensions), identify the extent of diseases covered and address the complexity of the data.
- Lessons should be learnt from the HIV model and that much can be done to build on the model and ensure cost effectiveness.
- The opportunity to have a broad package of screening of younger age groups and to prevent risk in the adolescent age groups should be taken up.
- Patient identifiers and efficient information systems would allow for a patient-centred focus through which a better understanding of the burden on quality of care could be gained.
- Pharmacovigilance data should be kept more rigorously and separately, and an integrated strength in pharmacovigilance including side effects and efficacy should be considered.
- Private sector data could be helpful to evaluate interventions with a view to addressing inequity.
- Although HIV is a major dimension in South Africa, gender and social roles play a very important part in causing multimorbidity.
- It is necessary to address the interventions at multiple levels and make provision for patient engagement, empowerment and support in managing self-prevention and treatment.
- A health systems approach should be used for understanding prevention and treatment.
- Research questions should address the need to strengthen implementation research and pragmatic trials to understand the effectiveness of interventions, and how to allocate resources in relation to risk stratification for severity in the local context.

Group 1: Defining multimorbidity

The group addressed the following questions:

- What are current definitions of multimorbidity in the South African context?
- How do definitions differ between countries and what research challenges do these pose?
- Can we reach a universal definition for multimorbidity?

The group did not come to a conclusion about a final definition of multimorbidity, but there was a clear view that it should go beyond the standard international definition (two or more chronic conditions) and that it should be informative and pragmatic for South Africa and other LMICs. It was also agreed that it should include pathways as well as consequences of multimorbidity; incorporate the social factors and vulnerabilities; be context relevant in terms of geographies and purpose for individuals and populations, address the specific audience, and make sense to policymakers and clinicians as well as the public and communities.

The key dilemma was whether the definition should be kept strictly medical and therefore accountable (this would depend on systems being in place to accurately make and record diagnoses), or whether to make a broad

definition that encompasses the bio-psycho-social framework.

The strength of the minimalist definition (the lowest common denominator of two or more chronic conditions) is that there cannot be disagreement about it and that it is amendable to a certain dimension of measurement, but it is not very informative as it does not give an idea of cause or consequence and therefore evades multimorbidity. It also excludes the key issues, which are around need (burden of disease, burden of treatment and resilience/social vulnerabilities). It was agreed that the way multimorbidity is defined will depend on the specific research question being asked. A simplistic definition will not work and any definition still needs flexibility. It remained unclear whether the addition of the many social and risk factors could help define multimorbidity in any way.

Group 2: Understanding the burden of multimorbidity

The group addressed the following questions:

- Is the burden of multimorbidity known in South Africa? If so, can this be improved?
- How is the burden of multimorbidity measured in other countries and can this be replicated in other contexts?
- What are the research barriers to knowing the burden of multimorbidity in South Africa and the UK?

Although much is known about the burden of multimorbidity in South Africa, a lot more needs to be known in order to define it better. It was agreed that more work is required in order to identify what needs to be known and what the purpose of building this knowledge is. Some of the areas that could be worked on in order to improve the understanding of the burden of multimorbidity are the quality and adequacy of the data, the extent of diseases covered, biomarker measurements versus self-report, adequate disaggregation of the data (in many dimensions), and addressing the complexity of the data. The data and systems in South Africa are undeveloped and it is often unclear as to what it is that is needed and then that what is produced is what was required.

There was discussion around the belief that HIV should not be treated separately to NCDs particularly in view of HIV becoming more chronic and the shared issues around health systems improvements that are needed in order to manage the burden of multimorbidity. Lessons should be learnt from the HIV model and much can be done to build on that model and ensure cost effectiveness.

It was agreed that the opportunity to have a broad package of screening of younger age groups should be taken up. Sufficient local data would be required in order to determine the ages for screening, the kind of screening that should be targeted and the frequencies at which screening should be done.

In terms of overcoming the barriers to accessing data to describe the burden, the option of tapping into transactional or self-collected data (such as pharmaceutical prescription data and pharmacovigilance) could be useful and would be possible in the context of National Health Insurance (NHI).

Current routine information systems in South Africa lack a patient-centred approach and tend to be disaggregated and anonymised. The move towards patient identifiers and information systems that would allow for a patient-centred focus to gain a better understanding of the burden on quality of care was supported. It was agreed that innovative sources should be used and that new ways need to be found to understand the burden.

Work has been done in South Africa with an actuarial group who manages multiple medical schemes to look at private sector data, which needs to be taken advantage of. It was noted, however, that this information is representative of only a small percentage of the total population and is therefore biased. Data from medical schemes could be used in some contexts to gain understanding of the burden across the population and the social gradient, from the policy perspective for example. Private sector data could be used to evaluate interventions with a view to addressing inequity. In the US there are numerous databases that are capturing prescribing linked to the indications. Although the databases are not representative of the entire population, they could still be helpful.

Universal health coverage is intrinsic to the SDGs, which could form the framework for addressing multimorbidities in South Africa as the discussion on multimorbidity is relevant to coverage. It was agreed that it is

necessary to strengthen data systems to get a balance between the registers and other data sources and the population because some of the exclusions could be greater than expected.

Group 3: Understanding the causes of multimorbidity

The group addressed the following questions:

- What are the known and unknown causes and common risk factors of multimorbidity in South Africa?
- How do the causes of multimorbidity differ between countries and can lessons be learned from one another?
- How can the understanding of the causes of multimorbidity be improved through research in South Africa and the UK?

Although HIV is a major dimension in South Africa, gender also plays a very important part. This is not only in relation to vulnerabilities but also opportunities, for example, in reproductive health for women attending clinics for antenatal care. Such clinics enable secondary prevention by picking up issues in advance. Social roles also play a major part in exposures and pressures and stress on people.

It was agreed there should be a focus on the younger population rather than on an average set of conceptions around multimorbidities, particularly in relation to prevention. There are even opportunities in the adolescent age groups for preventing risk, which if not taken, would create problems for the population going forward. The life-course approach should be taken.

Diet is a risk factor in terms of common pathways in comorbidities. In the South African context, this is not only to do with poor diets. While there is a high prevalence of obesity and high consumption of salt, there is coexistence of food insecurity and limited food options that relate to socio-structural diversity.

It was thought that a possible research question could be around whether enough is understood about obesity and genetic types of risks, and how fat is laid down differently through the life stages in ways that affect the risk as a precursor to comorbidities.

Much is known about the underlying causes of multimorbidity, but population differences cannot all be explained. The challenge is whether there is something to be discovered about the underlying causes that will make a difference to how multimorbidity is managed.

Only a handful of studies have been published on risk factors for multimorbidity in general and there are very few longitudinal studies. Socioeconomic status has been shown to have an impact over and above the traditional risk factors.

It was agreed there is a need for disaggregated data from more local settings. The balance between national surveys (that are often underpowered and difficult to use when there is a high degree of heterogeneity across the country) and local surveys was a recurring theme of the discussions.

There are no cohort studies that have produced African data on the risk factors, but there are association studies. When looking at the variants it is clear that the right risk factors and the psycho-social risk factors have not been measured. It was agreed that clarity was needed about whether a better understanding of the social determinants was required or whether identifying, preventing and managing multimorbidity should be the focus.

Group 4: Preventing and treating multimorbidities

The group addressed the following questions:

- What are the current methods of preventing and treating multimorbidity in South Africa and are these optimal?
- How do the methods differ between countries and can lessons be learned from one another?
- What are the main needs in research to improve the prevention and treatment of multimorbidity in South Africa and the UK?

Interventions for preventing and for treating multimorbidities should be thought of as separate areas although they do intercept. It was agreed it is necessary to address the interventions at multiple levels (regulatory/population level, health system level, facility level and patient level), and make provision for patient engagement, empowerment and support in managing self-prevention and treatment. Tobacco control and sugar tax are two of the measures that are already in place to address the prevention and treatment of multimorbidities, as well as processes to assist with integration.

A health systems approach should be used for understanding prevention and treatment, taking into account the six building blocks of health systems.

It was agreed that research questions should address the need to strengthen implementation research and pragmatic trials to understand the effectiveness of interventions, and to understand how to allocate resources in relation to risk stratification for severity in the local context.

Enough is already known about multimorbidity risk factors to be thinking about putting interventions in place. Targeted complex interventions for multimorbidity should be considered.

Whether clinicians require guidelines to treat comorbidities should also be clarified.

Day 2: Research and health systems (Chair: Professor Stephen MacMahon FMedSci)

Session 5: Challenges and opportunities for clinical care and research

To better understand what is needed within the health system to address multimorbidity, it is crucial to analyse the current methods for multimorbidity guideline development as well as the challenges of clinical care in South Africa. Therefore, this session looked at particular aspects of clinical care where multimorbidity is seen – what is known about them from research and experience, and how they could be treated or prevented.

Key points from the session's presentations were:

- Systems are needed to support transparent, collaborative and quality guideline development that explicitly considers patients with multimorbidities, and that work to inform guideline development with the best available evidence should be coordinated nationally.
- Knowledge translation is essential in order to close the gap between knowledge and its implementation in practice.
- The results of four South African pragmatic RCTs have shown that the implementation of PACK has brought about consistent improvements (and reproducible improvements) across a range of outcomes and behaviours, particularly in respect of healthcare workers.
- Data shows that patients' experience of care is that it is not patient-focused and that it is fragmented, providing an opportunity for integration and consolidation of all the guidelines and information into one tool, and for this to be prioritised.

Methods for multimorbidity guideline development and the local guideline landscape for South African primary care (Dr Tamara Kreda, South African MRC)

According to WHO, guidelines are recommendations intended to assist providers and recipients of health care and other stakeholders to make informed decisions.⁵⁶ The question is whether guidelines, which generally focus on single conditions, assist informed decision-making in managing comorbidity or multimorbidity.

The problem in the context of clinical practice guidelines is the evidence base that is used to inform guideline groups. Currently, multimorbidity is managed at clinicians' discretion. There is evidence to suggest that even when there is a reasonable body of evidence to guide complex decisions, clinicians are not prioritising correctly. Patients and their wishes should play a critical part in how multimorbidity is managed.

A typical guideline development process involves convening a guideline group who appraise and synthesise best available evidence to inform recommendations. Multimorbidity should be considered throughout the process of guideline development in aspects such as defining the scope of the guidelines, convening the guideline development group (ensuring input from patient groups/consumer representatives) and formulating the questions. The methods are not unanimously agreed and there is a need to share models from various settings. The evidence base for multimorbidity is not as robust as it could be, and sub-groups and indirect evidence with lower certainty are more likely. Therefore patient preferences and values play key roles and should be supported by better shared decision-making tools.

When developing guidelines, WHO does surveys in advance to inform recommendations that are made from a global perspective. This approach could be considered from a localised perspective.

Guideline development in South Africa is driven by the National Department of Health (DoH) where there is a long history of contributions from groups, including the Essential Drug List group that developed Standard Treatment Guidelines to inform decisions linked to essential medicines in order to address equity issues. There are no agreed standardised methods nationally for guideline development and there is no centralised coordination of activities. In the move towards NHI there is a commitment to clinical guidelines and a desire to have a health technology assessment unit. Interviews done with national guideline developers across all disciplines raised issues of concern such as fragmentation, human resource capacity shortages and poorly standardised systems. Implications are that guideline reporting is poor by Appraisal of Guidelines Research and Evaluation (AGREE II) standards, although they fare well in terms of content.⁵⁷ Clinicians in rural primary care and other settings are of the view that guidelines are helpful, but patients' views on the matter are unknown.

Few guidelines in South Africa have explicitly considered the management of multimorbidities and systems are needed to support transparent and collaborative guideline development in general. National coordination of activities to inform guideline development with the best available evidence would be helpful, and the quality of methods generally, including public engagement in guidelines, needs to be improved. Decision aids and transparency are important to address the uncertainty between clinicians and patients, particularly in the South African context. Gaps exist in research in terms of the effectiveness of shared decision-making strategies locally and in pragmatic complex intervention clinical trials to inform knowledge of what works and what may be safe.

Challenges of clinical care for co-occurring infectious and non-communicable diseases (Professor Lara Fairall, University of Cape Town)

Knowledge translation is essentially about closing the gap between what we know and what we do. The work of the Knowledge Translation Unit (KTU) at the University of Cape Town Lung Institute over the past 17 years has

⁵⁶ World Health Organization *Handbook for Guideline Development*. http://apps.who.int/iris/bitstream/10665/75146/1/9789241548441_eng.pdf?ua=1

⁵⁷ Machingaidze S, et al. (2016). *Quality and Reporting Standards of South African Primary Care Clinical Practice Guidelines*. *Journal of Clinical Epidemiology* **50895-4356(16)**, 30617-5.

focused towards the development of a product called the Practical Approach to Care Kit (PACK). PACK has four key components: an integrated guide; implementation through a programme of educational outreach; health systems change setting the scene for multidisciplinary teams to work easily and without conflict; and a scalable training model, which has reached more than 20,000 health workers in 2,000 clinics within four years.⁵⁸

The development of PACK has followed a life-course approach starting in the early 2000s with WHO's Practical Approach to Lung Health and expanding the product to PACK Child and PACK Adolescent.^{59,60} The knowledge to action cycle shows how knowledge translation is positioned in the generation of knowledge and its implementation into practice. The KTU looks at how to take information in guidelines and put it into practice. This requires substantial harmonisation and resolution of conflicting recommendations between guidelines.

Eight trials connected to PACK (pragmatic RCTs in real-world circumstances) have been undertaken over the last 16 years, four of which are complete. A trial that has just started in Brazil is looking at a setting where there is a much greater mix of doctors and nurses. This presents an opportunity to do research in a LMIC where there are more doctors than in Sub-Saharan Africa. The results of the four completed South African pragmatic RCT's have shown modest but consistent improvements (and reproducible improvements) across a range of outcomes and behaviours. The real effect of the work is on the healthcare workers themselves who describe PACK as a tool to use every day with every patient, for instance.

Baseline data from two of the trials show that multimorbidity is exceptionally common and that patients' experience of care is that it is not patient-focused and fragmented. This provides an opportunity for integration, by consolidating all the guidelines and information into one tool, and for this to be prioritised. Updating PACK's content is done through partnerships with knowledge producers. PACK Adult's 2,372 recommendations are linked to Best Practice (the tool produced by the Evidence Centre of the British Medical Journal (BMJ)) that is used as a mechanism for streamlining the content updating process. The KTU is also working with the BMJ Group to leverage their global footprint to support the spread of the unit's programmes in underserved areas through tools, partnerships and mentorship. These are currently active in Brazil, Nigeria, Uganda, India, China and Ghana. NCD care is highly ritualised and difficult to change. This challenge can be addressed by repositioning and valuing this approach, working with it rather than against it in order to bring about improvements.

Panel discussion (Panellists: Dr Tamara Kreda, Professor Lara Fairall)

From experiences in both India and China it has not been difficult to get community care workers to change the way that they think about managing cardiovascular care. The biggest challenge is to get primary care doctors to change. The concern about trying to make incremental changes to the way care is managed is that many more people will die while waiting for clinical care at the level of the primary care centre to change. This is an enormous task, particularly for LMICs. It is necessary to intervene in the way doctors are trained before they graduate so that they move from an all-knowing paradigm to an all-learning paradigm. One way to do this is in the area of HIV and TB because it is difficult to deal with these complex conditions without referring to some sort of guidance. The challenge is how to expand this to NCD care. The regulatory system does not support community extension beyond the primary care system. The KTU has been asked to work with Building Resources Across Communities (BRAC) in Bangladesh where there are 100,000 community health workers who are restricted to primary care service. The polypill has enormous potential in this area.

PACK takes a multipronged approach with a focus on CVD risk as opposed to hypertension as a single risk factor for initiating treatment and treatment advice for CVD. Screening is done (blood pressure is taken only for targeted groups of people) and results are forwarded to the nurse. Symptoms are used to prompt the diagnosis of conditions in the second half of the guidelines.

⁵⁸ *Practical Approach to Care Kit (PACK)*. <http://pack.bmj.com/>

⁵⁹ *WHO Practical Approach to Lung Health (PAL)*. http://www.who.int/tb/health_systems/pal/en/

⁶⁰ *PACK Child – Western Cape, South Africa*. <http://knowledgetranslation.co.za/pack-child-wc-sa/>

The guidelines are not suitable for hypertension because most of hypertension is asymptomatic, while established CVD is symptomatic. A comorbidity approach is used in the chronic disease section where common comorbidities are identified and screening is done. The guidelines are a small component of the overall approach supported by professional education, audit and feedback. Unlike the UK and other countries, clinicians in South Africa are not appraised in relation to guidelines.

The extent to which PACK has given advice on multimorbidity and comorbidities is a major shortcoming. The KTU is working on digitisation of the tool to see whether comorbidities can be catered for and to outline an approach that could be used when a patient presents at a clinic with the five comorbidity clusters. However, this is proving to be difficult because identifying everything that has to be done for each patient and for every disease is an ambitious plan. Prioritisation of the most cost-effective methods is essential.

Another point is to look at the process of care that is followed and see whether there are generic levers that could be used to prompt a more consolidated approach. For example, the ideas of frailty and ritual could be used as a means to see whether some of the content around the process of care can be restructured.

The underlying issue remains identifying the most effective, including cost-effective, ways to manage clinical care. Multimorbidity is an opportunity, with regard to using the South African and African experience, to take another step towards building excellence. Much has been done in terms of assessing the landscape. The next step is to bring groups together because although there is goodwill and commitment to do better, there is a need for coordination. It is about learning from the models and from mistakes, and ensuring that the system is improved by building on what is already in place. South Africa leads the way in the region. The NHI is a potential platform for this.

In terms of management of multimorbidity being initiated outside of the clinic, there is some evidence around task shifting and decentralisation in the HIV arena, including recommendations from WHO. There is a need for the pragmatic RCTs to incorporate multimorbidity and there is space to extrapolate. In key areas of need, programmes are starting up regardless of trial data. It is necessary to look at programmatic data on managing multimorbidity. Greater cadres of people should be encouraged to be involved in care and empowered to do so, but caution must be taken in terms of giving the responsibility, not only of starting treatment but also of terminating it.

CVD mortality has dropped dramatically and life expectancy in the UK has increased by three months every year over the last 20 years. Possibly, half of this is due to medical care and the other half to other factors. The care situation has changed as a result of a large, sophisticated and expensive process over a ten- to 15- year period. There is no simple or straightforward solution for improving care. The question is whether there is an alternative way for LMICs to develop a process that will bring the same results more rapidly.

There is a tremendous opportunity to use community-based workers to treat common mental disorders with psychological therapies and psycho-social interventions that do not necessarily need to occur in clinics. An example of this comes from Zimbabwe where trained counsellors (community health worker level) screen and independently link patients into counselling groups. There is substantial evidence that psychological treatments are as effective as drug treatments. The role that common mental disorders play in the course of many chronic diseases and in adherence, as well as the role of the patient in driving change in clinical care and consumer led initiatives should be considered.

Session 6: Delivering health services for patients with multimorbidity

At the centre of the issue of multimorbidity is the patient and how to deliver the best health service for these patients. This session therefore identified key challenges to health systems and how they can be addressed across South Africa, the UK and India. A particular focus was on structuring and financing services and the key policy challenges, especially cross-departmental working in government.

Key points from the session's presentations were:

- In South Africa, consumers' choice of a medical scheme is made on the basis of the scheme's ability to purchase high value care at affordable premiums. It is possible to make a commercial purchaser/provider split work in health care that is neither profiteering nor disinterested in patient care and good outcomes.
- The South African state needs to manage the structural capacity of the system and regulate the funders and the supply side performance.
- The goal of delivering health services to people with multimorbidities in the UK and elsewhere (complex needs) is to achieve improved care, improved outcomes and cost containment.
- Recommendations from a Commonwealth Fund study to policymakers in respect of designing a high performing healthcare system for patients with complex needs are relevant to South Africa, and if adopted would contribute towards strengthening the DoH's initiatives for universal health access.
- Collaborative care models for multimorbidity, such as those in India, need to target patients, health professionals, health workers, medical students and policymakers.

Delivering health services in South Africa (Dr Brian Ruff, PPO Serve)

Data available in the private sector via the Council for Medical Schemes in relation to chronic illness prevalence in medical schemes shows the extent of multimorbidity and the related spend. This is vast in later life and relates to multimorbidity and extensive over-servicing. The latter is due to imbalances in the South African private sector which result in suboptimal services. The current economic arrangement is purchaser/provider (medical schemes) involving dominant players and competition between the schemes. They offer extremely unbalanced hospicentric benefits and pay clinicians on a fee for service basis, with fees paid to individuals and not to teams. The result is unaffordable premiums and a shrinking industry. Powerful hospital groups (national networks) have nearly 40,000 beds resulting in a very high admission rate, high numbers of bed days and weak community services. There are about 14,000 independent clinicians in the private sector. General practitioners are marginalised and their role in complex patient care is practically non-existent. They have no autonomy or accountability and huge scheme administrative costs. The patient is lost in the system.

In South Africa, the problem is weakness in public sector management. PPO Serve believes that it is possible to make a commercial purchaser/provider split work in health care that is neither profiteering nor disinterested in patient care and good outcomes. On the supply side there should be competition on value and on the other side of the equation there should be funders who purchase effectively for the demand (member population). The consumer's choice of a medical scheme should be made on the basis of a scheme's ability to purchase high value care at affordable premiums. The state needs to manage the structural capacity of the system and regulate the funders and the supply side performance.

This would require a team based in a particular location that competes on value and argues for branded local systems of organised multidisciplinary clinical teams that are sensitive to local problems and strive for continual improvement. Families and businesses would choose between local systems via a local fund.

Delivering health services: International experience (Professor Martin Roland FMedSci, University of Cambridge)

The goal of delivering health services to people with multimorbidities is to achieve the ‘triple aim’ of health care for patients with complex needs: improved care, improved outcomes and cost containment.

The presentation focused on the Commonwealth Fund’s study on designing a high performance healthcare system for patients with complex needs. The purpose of the project was to produce recommendations for policymakers for presentation to the Organisation of Economic Cooperation and Development (OECD) health ministers in Paris in January 2017. The recommendations to policymakers of how to construct a high performing health care system for patients with complex needs are:

- 1. Make care coordination a high priority for patients with multimorbidity.** Patients with complex needs receive care from a wide range of providers, care often becomes fragmented and these patients need an identified person with responsibility for coordinating care.
- 2. Identify patients at greatest need of proactive, coordinated care.** Several methods have been developed to identify patients with complex needs though countries will have different types of data available, and so the models may need adaptation and validation in individual countries.
- 3. Train more primary care physicians and geriatricians.** In most countries, the number of sub-specialists has increased at a much higher rate than generalists, a trend which leads to fragmented care and needs to be reversed to meet the needs of ageing populations.
- 4. Facilitate communication between providers, e.g. by integrating clinical records.** Providers need to share information about patients with multimorbidity so that each has the information they need at the time they need it, ideally, accomplished by a single electronic record for all of a patient’s medical care.
- 5. Engage patients in decisions about their care.** Patients with multimorbidity need an open discussion of the benefits and risks of individual treatments, allowing patients to bring their own needs, preferences and hopes into the conversation.
- 6. Provide better support for carers.** Health services need to take active steps to identify and support family and friends who are carers, including respite care for the patient to give the carer a break.
- 7. Redesign funding mechanisms to meet the needs of patients with complex needs.** Payment systems for complex patients need to be redesigned so that they reduce barriers to collaboration, adequately compensate for the complexity of cases treated, and provide incentives for hospitals to work with community providers.
- 8. Integrate health and social care, and physical and mental healthcare.** Care for patients with complex needs therefore requires close cooperation between health and social care and between physical and mental healthcare providers.
- 9. Engage clinicians in change, train and support clinical leaders.** Clinical leadership is key to delivering successful change to meet the needs of patients with complex conditions.
- 10. Learn from experience and scale-up successful projects.** Different solutions will suit different places and policymakers and healthcare managers need to provide an environment with opportunities to share experiences and learn from both successes and failures of others.

Conclusions

These recommendations are challenging, requiring profound paradigm shifts away from disease-specific towards patient-centered approaches to care and away from single physician- or single provider-models towards cooperation and teamwork. However, implementation of these recommendations has the potential to transform care for this complex and costly group of patients.

Indian collaborative care models (Dr Rajesh Sagar, AIIMS)

A secondary analysis of SAGE Indian data showed that 28.5% of the respondents have one NCD and 8.9% have

more than one NCD, as well as there being an increase in multimorbidity with age.⁶¹ The higher prevalence of multimorbidity in higher socioeconomic status is due to the fact that people of a higher socioeconomic status tend to seek medical help and present for chronic conditions, whereas those of a lower socioeconomic status do not seek help.⁶² This aspect is important, particularly in the context of LMICs.

There is a very strong link and a bi-directional relationship between mental disorders and NCDs. Collaborative care models for mental health have to take into account the burden, the stigma attached to mental disorders, poor resources, the lack of manpower, training, awareness and will, the treatment gap and poor funding. WHO has recommended the application of the collaborative care model to manage mental disorders and comorbid chronic diseases in primary care settings. Patients, health professionals, health workers, medical students and policymakers are targeted in addressing collaborative care models in respect of multimorbidity.

The Indian Government implemented the National Mental Health Programme in 1982 to address the huge burden of mental health disorders and the shortage of qualified professionals in this field. The programme aims to ensure the availability and accessibility of minimum mental healthcare for all; encourage the application of mental health knowledge in general healthcare and in social development; enhance human resources in mental health sub-specialties, and promote community participation in mental health service development.

Two of several collaborative care research studies that AIIMS is involved in are:

- Integrating DEPrEssion and Diabetes TreatmENT Study (known as 'INDEPENDENT') to test a translatable way of delivering care for comorbid chronic conditions and depression.⁶³
- Depressive and Anxiety Disorders in the Postpartum Period: Prevalence, Psycho-Social Correlates, and Effect on Mother to Infant Bonding.

Session 7: Addressing the research gaps and challenges for multimorbidity in South Africa (Chair: Professor Stephen MacMahon FMedSci)

This session aimed to consider all the evidence and information shared over the course of the workshop and give all participants the opportunity to discuss and suggest solutions to some of the research gaps and challenges of multimorbidity in South Africa. The overall question about the key priority research areas for multimorbidity in South Africa and how these can be addressed in the short and long term was discussed by considering the following questions:

1. Based on what has been presented at this workshop, what are the research priorities in South Africa?
2. What lessons can be learned between different country contexts on multimorbidity?
3. Are current research methods good enough in South Africa? What are the strengths and weaknesses?
4. What are the biggest barriers to conducting research/making use of the outcomes of research in South Africa?
5. What improvements can be made to researching multimorbidities in South Africa?

The key focus of the potential research questions was clarified and summarised as follows:

⁶¹ Pati S, et al. (2014). *Non Communicable Disease Multimorbidity and Associated Health Care Utilization and Expenditures in India: Cross-Sectional Study*. BMC Health Services Research **14**, 451.

⁶² Pati S, et al. (2015). *Prevalence, Correlates, and Outcomes of Multimorbidity Among Patients Attending Primary Care in Odisha, India*. Annals of Family Medicine **13(5)**, 446-50.

⁶³ Integrating DEPrEssion and Diabetes treatment (INDEPENDENT) Study. <https://clinicaltrials.gov/ct2/show/NCT02022111>

Proposed research topic one: Sugar tax legislation

South Africa is one of several countries across the world that is introducing a tax on sugary soft drinks. The Government has proposed a 20% tax on sugary drinks that will be levied with effect from 1 April 2017 with the aim of addressing obesity and the increased risk for lifestyle-related diseases such as type 2 diabetes, heart disease, and stroke.

Workshop delegates recognised that the introduction of the sugar tax in South Africa creates a timely opportunity to collect baseline data before its introduction and would allow for an analysis of the impact of this legislation on targeting the pre-morbidity population. They considered that as part of this wider analysis, it would also be important to monitor the impact of the tax on, for example, different socioeconomic groups, and look to investigate whether the tax would differentially reduce multimorbidity across these cohorts. The health data would need to be collected pre and post, in cohorts, aiming towards long-term data.

Proposed research topic two: Psycho-social factors as determinants of multimorbidity

There are a number of disadvantaged and vulnerable populations that are considered particularly at risk of multimorbidity in South Africa and where there is an increased burden, particularly in internal migrant populations. Exposure of recent migrant returnees to the set of determinants that heightens risk is reflected in their NCD or HIV mortality. This helps to understand the amplification of burden that occurs in migration.

However, there is specifically a lack of evidence-based medicine and guidelines for managing multimorbidity in these populations. This means it is an area that represents a distinct opportunity for further research to focus on preventive interventions and access to appropriate care.

With this in mind, migrant populations present an opportunity to look at which factors affect their health and what the determinants, prevalence, and outcomes of multimorbidity might be for them. This could focus on the adverse effect on migrants' health due to multimorbidity in relation to HIV (because of the extent of migration within South Africa) and the possibility of identifying reversible risk factors that could reduce the adverse consequences of migration in the HIV infected population. It is known that people with HIV have increased multimorbidity that affects their health and as this is heightened in migrant populations, this research could therefore quantify this detriment to migrants and identify reversible risk factors.

Proposed research topic three: Combined care for people who have multimorbidities

There is a specific need and a unique opportunity for further research on combined care for patients who have infectious and chronic non-infectious conditions, and for such research to produce a more integrated programme that would improve the care of each individual condition. In addition, there is a case for treating multimorbidities together and not individually, particularly in terms of the pharmacology associated with treating each disease, the interactions of the drugs and the compounding effects.

With this in mind, participants agreed that it is important to consider clinical pathways through the life course and that how best to utilise the life-course approach is a fundamentally important question to explore further. Taking advantage of initial presentation to sexual reproductive health services as a means to beginning longer-term life-course care for women was a specific area that could be considered. Therefore future research could be formulated around high-risk pregnancies in women with a history of gestational diabetes, and those who have had severe stressors during pregnancy (as hypertension was a coexistent factor in almost all cases). The integration of care afterwards could also be looked at from the point of view of multimorbidity with the combination of infectious and non-infectious factors.

Proposed research topic four: Role of the patient (how the patient can be better involved in the management process)

There is an opportunity for further research into health seeking behaviour including into the perceptions and desire for shared decision-making and self-management. It is important to better understand the wishes of patients, before identifying the barriers which might limit the introduction and utility of strategies to improve patient engagement in care.

Although this is already being done in the Co-morbidity of AIDS/HIV Affective Disorder and Long Term Conditions and the Improving Mental Health Care (COBALT/PRIME) trials, there is scope to look further at patients as 'users of health care' so they are better empowered. This could be an observational (rather than interventional) study that considers the preferences of patients with multimorbidity. Interventions should not be developed without taking into account the views of the multimorbid population.

Appendix A: Attendees List

Dr Yasmin Adam

University of the Witwatersrand, SA

Dr Soter Ameh

University of Calabar, Nigeria

Dr Rachel Brown

Academy of Medical Sciences, UK

Prof Francesco Cappuccio

University of Warwick, UK

Prof Mark Collinson

University of the Witwatersrand, SA

Dr Halima Dawood

University of KwaZulu-Natal, SA

Dr Candy Day

Health Systems Trust, SA

Prof Roseanne Diab

Academy of Science of South Africa

Prof Lara Fairall

University of Cape Town, SA

Prof Melvyn Freeman

Department of Health, SA

Dr Santoshni Govindasamy

GlaxoSmithKline, SA

Prof Karen Hofman

University of the Witwatersrand, SA

Mr Alex Hulme

Academy of Medical Sciences, UK

Prof Andre Pascal Kengne

Medical Research Council, SA

Dr Taskeen Kahn

World Health Organization, SA

Dr Tamara Kredo

Medical Research Council, SA

Prof Naomi (Dinky) Levitt
University of Cape Town, SA

Ms Catherine Luckin
Academy of Medical Sciences, UK

Prof Stephen MacMahon FMedSci
George Institute for Global Health, UK

Prof Stewart Mercer
University of Glasgow, UK

Dr Lisa Micklesfield
University of the Witwatersrand, SA

Dr Keren Middelkoop
Desmond Tutu HIV Foundation, SA

Ms Phakamile Mngadi
Academy of Science of South Africa

Prof Tolu Oni
University of Cape Town, SA

Prof Inge Peterson
University of KwaZulu-Natal, SA

Prof Nancy Refilwe Phaswana-Mafuya
Human Sciences Research Council, SA

Prof Helen Rees
Wits Reproductive Health and HIV Institute, SA

Prof Martin Roland FMedSci
University of Cambridge, UK

Dr Brian Ruff
PPO Serve, SA

Dr Rajesh Sagar
All India Institute Of Medical Sciences, India

Prof Alan Silman FMedSci
University of Oxford, UK

Ms Sandhya Singh
Department of Health, SA

Prof Stephen Tollman
University of the Witwatersrand, SA

Dr Jenny Tran
University of Oxford, UK

Appendix B: List of acronyms

AGREE	Appraisal of Guidelines for Research and Evaluation
AIDS	Acquired Immune Deficiency Syndrome
AIIMS	All India Institute Of Medical Sciences
ART	Antiretroviral therapy
ARV	Antiretroviral
ASSAf	Academy of Science of South Africa
AUD	Alcohol use disorders
BMI	Body mass index
BMJ	British Medical Journal
BRAC	Building Resources Across Communities
CAPRISA	Centre for the AIDS Programme of Research in South Africa
CMD	Common mental disorders
CVD	Cardiovascular disease
DALYs	Disability adjusted life years
DoH	Department of Health
GERMS	Group for Enteric, Respiratory and Meningeal Disease Surveillance
HDSS	Health and socio-demographic surveillance system
HICs	High-income country
HIV	Human Immunodeficiency Virus
KTU	Knowledge Translation Unit
LMIC	Low- and middle-income country
MNS	Mental, neurological and substance use disorders
MPI	Multidimensional Poverty Index
MRC	Medical Research Council
NCD	Non-communicable diseases
NHI	National Health Insurance
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OECD	Organisation for Economic Co-operation and Development
PACK	Practical Approach to Care Kit
PPO Serve	Professional Provider Organisation Services
RCT	Randomised controlled trials
SAGE	Study on Global Ageing and Adult Health
SARI	Severe acute respiratory infection
SDGs	Sustainable Development Goals
SDH	Social determinants of health
TB	Tuberculosis
WHO	World Health Organization
WHS	World Health Surveys
YLLs	Years of life lost

Appendix C: Workshop programme

Addressing the global challenge of multimorbidity: Lessons from South Africa, 2–3 November 2016, Johannesburg

Day 1: Prevalence, burden, determinants and risk factors

09:00-09:30	Registration
09:30-09:40	Chairs' welcome and introductions Meeting co-chairs: Professor Stephen MacMahon FMedSci and Professor Karen Hofman
09:40-11:10	Session 1: What is multimorbidity and why is it important? Speakers: The World Health Organization (WHO) perspective Dr Taskeen Khan, WHO South Africa Perspective from the UK Professor Stewart Mercer, University of Glasgow Perspective from South Africa and beyond Professor Steve Tollman, University of the Witwatersrand Panel discussion (30 mins)
11:10-11:30	Break
11:30-13:00	Session 2: Showcasing research into multimorbidity Speakers: Mental health disorders and other conditions Professor Inge Petersen, University of KwaZulu-Natal Rheumatological and musculoskeletal disorders Professor Alan Silman FMedSci, University of Oxford HIV and related infectious diseases Dr Halima Dawood, University of KwaZulu-Natal Major cardiometabolic diseases and risk factors Professor Andre Pascal Kengne, South African Medical Research Council Panel discussion (30 mins)
13:00-14:00	LUNCH
14:00-15:15	Session 3: Determinants and risk factors of multimorbidity Speakers: Determinants of multimorbidity Dr Tolu Oni, University of Cape Town Cardiovascular disease: Aetiology and multiple related conditions Professor Francesco Cappuccio, University of Warwick Aetiology and multiple unrelated conditions (HIV, obesity, and diabetes) Professor Dinky Levitt, University of Cape Town Panel discussion (30 mins)
15:15-15:30	Break
15:30-16:30	Session 4: Analysing the evidence and identifying research gaps in South Africa and beyond This session will aim to give all participants the opportunity to discuss the evidence base in more detail and what lessons might be learned between countries. Participants will be assigned to a specific breakout group.

	<p>Groups will focus on the main issues, including the most pressing gaps in the evidence, in the following areas:</p> <p>Group 1: Defining multimorbidity What are current definitions of multimorbidity in the South African context? How do definitions differ between countries and what research challenges do these pose? Can we reach a universal definition for multimorbidity?</p> <p>Group 2: Understanding the burden of multimorbidity Is the burden of multimorbidity known in South Africa? If so, can this be improved? How is the burden of multimorbidity measured in other countries and can this be replicated in other contexts? What are the research barriers to knowing the burden of multimorbidity in South Africa and the UK?</p> <p>Group 3: Understanding the causes of multimorbidity What are the known and unknown causes and common risk factors of multimorbidity in South Africa? How do the causes of multimorbidity differ between countries and can lessons be learned from one another? How can the understanding of the causes of multimorbidity be improved through research in South Africa and the UK?</p> <p>Group 4: Preventing and treating multimorbidities What are the current methods of preventing and treating multimorbidity in South Africa and are these optimal? How do the methods differ between countries and can lessons be learned from one another? What are the main needs in research to improve the prevention and treatment of multimorbidity in South Africa and the UK?</p>
16:30-17:15	Feedback from breakout groups
17:15-17:30	Daily wrap up Meeting co-chair: Professor Karen Hofman

Day 2: Research and health systems

09:00-09:05	Welcome Meeting co-chair: Professor Stephen MacMahon FMedSci
09:05-10:20	<p>Session 5: Challenges and opportunities for clinical care and research</p> <p>Speakers: Methods for multimorbidity guideline development and the local guideline landscape for South African primary care Dr Tamara Kredon, South African Medical Research Council Challenges of clinical care for co-occurring infectious and non-communicable diseases Dr Lara Fairall, University of Cape Town Lung Institute Panel discussion (30 mins)</p>
10:20-10:50	Break
10:50-12:20	<p>Session 6: Delivering health services for patients with multimorbidity</p> <p>Speakers: Delivering health services in South Africa Dr Brian Ruff, PPO Serve</p>

	<p>Delivering health services: International experience Professor Martin Roland FMedSci, University of Cambridge Indian collaborative care models Dr Rajesh Sagar, All India Institute Of Medical Sciences Panel discussion (30 mins)</p>
12:20-13:20	LUNCH
13:20-15:00	<p>Session 7: Addressing the research gaps and challenges for multimorbidity in South Africa Session Chair: Professor Stephen MacMahon FMedSci</p> <p>This session will aim to consider all the evidence and information shared over the course of the workshop. It will give all participants the opportunity to come together as one to discuss and suggest solutions to some of the research gaps and challenges of multimorbidity in South Africa.</p> <p>The overall question that we will aim to answer in this session is:</p> <p>What are the key priority research questions for multimorbidity in South Africa and how can these be addressed in the short and long term?</p> <p>This session will take place in plenary and participants will contribute to the discussions by considering some of the following questions:</p> <p>Based on what has been presented at this workshop, what are the research priorities in South Africa? What lessons can be learned between different country contexts on multimorbidity? Are current research methods good enough in South Africa? What are the strengths and weaknesses? What are the biggest barriers to conducting research/making use of the outcomes of research in South Africa? What improvements can be made to researching multimorbidities in South Africa?</p>
15:00-15:45	<p>Conclusions from across the two days Meeting co-chairs: Professor Stephen MacMahon FMedSci and Professor Karen Hofman</p>
15:45	END

Appendix D: Workshop steering committee

The organisation of the workshop was overseen by a steering committee based in both the UK and South Africa. The steering committee members are:

Meeting co-chair: Professor Karen Hofman, Associate Professor, University of the Witwatersrand

Meeting co-chair: Professor Stephen MacMahon FMedSci, Principal Director, George Institute for Global Health
Professor Kara Hanson, Professor of Health System Economics and Associate Dean for Research, London School of Hygiene and Tropical Medicine

Dr Tolu Oni, Senior Lecturer, University of Cape Town

Dr Nesri Padayatchi, Deputy Director of CAPRISA, University of KwaZulu-Natal



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