

GCRF Global Multimorbidity – Seed-funding 2019

The GCRF global multimorbidity seed-funding call was an MRC initiative that had been developed in collaboration with Wellcome, the National Institute for Health Research, and the Academy of Medical Sciences. The Panel awarded funding to 13 projects that would lay the foundations for addressing multimorbidity in low- and middle-income countries (LMICs), including the formation of new equitable partnerships, the collection of preliminary data, the analysis of existing data, and the development of novel tools and methodologies. The research funded through this GCRF call contributed to the UK's commitment to [Official Development Assistance \(ODA\) to LMICs](#).

Funded Proposals

Levitt, Naomi Dinky (MR/T03775X/1, 18 months)

Exploring treatment burden and capacity for self-care among patients with HIV/NCD multimorbidity in South Africa to inform interventions (EXTRA)

Principal Investigator Naomi Dinky Levitt, University of Cape Town

Co-Principal Investigator Frances Mair, University of Glasgow

Co-Investigator Carl May, London School of Hygiene and Tropical Medicine

Co-Investigator Katherine Murphy, University of Cape Town

Summary:

South Africa (SA) and other sub-Saharan African countries are experiencing a double burden of chronic disease epidemics: one of infectious disease, most notably HIV, and the other, a rapidly evolving epidemic of non-communicable diseases (NCDs) such as diabetes and cardiovascular disease. This is resulting in different patterns of multi-morbidities (two or more simultaneously occurring long term diseases or conditions) to those commonly seen in high income countries.

Concerningly, these chronic diseases are being increasingly seen in younger people, which has implications for their families, economic productivity and healthcare costs.

Currently, chronic healthcare for patients with multimorbidity in SA is fragmented and uncoordinated and does not take into account the increased challenges the patient faces in trying to manage their conditions. The primary aim of this Seed Funding Application is to identify and understand the illness 'workload' experienced by patients with HIV/NCD multimorbidity, as well as their caregivers. This information will be used to ensure that the patient perspective is fully considered in the healthcare reform initiatives that are currently underway in SA, which aim to improve chronic care services. A further aim is to explore the relevance and applicability of existing models that explain the workload involved in NCD treatment and patients' capacity to deal with it. Existing models have been developed in high income countries and we are interested to adapt them to our setting so that they can inform future research and interventions in South Africa and potentially in other low-and middle-income countries.

We will use interviews and discussion groups for this study. We will interview a range of patients and their care givers to explore how they experience self-management workload and their capacity to deal with it. This will be in both an urban and rural setting in the Western Cape province as for example, peoples' access to services may differ. We will then recruit healthcare managers, doctors, nurses and community health workers from the same settings into 'task groups' to discuss these findings and consider what they mean for the redesign of local services and interventions that might reduce patient burden and increase their capacity. We will also hold further meetings to present our findings to policy and health managers at a provincial and national level to influence reforms in the health system.

This project will help us develop a culturally and contextually appropriate model of HIV/NCD workload and capacity for a low -to- middle income setting such as SA. This work will contribute to development of interventions that can then be tested across different settings.

Harding, Richard (MR/T037660/1, 18 months)

MAP-care: Multimorbid Ageing Primary Palliative Care in Ghana, Malawi and Zimbabwe.

Principal Investigator Richard Harding, King's College London
Co-Investigator Catherine Evans, King's College London
Co-Investigator Dickson Chifamba, Island Hospice and Healthcare
Co-Investigator Edwina Beryl Opore-Lokko, Ghana College of Physicians and Surgeons
Co-Investigator Kennedy Bashan Nkhoma, King's College London
Co-Investigator Maya Bates, Malawi College of Medicine
Co-Investigator Mike Chirenje, University of Zimbabwe

Summary:

What is the problem?

People around the world are ageing, especially low and middle income countries. This presents a new challenge- how can we provide care that is focused on the person rather than the multiple illnesses that they are likely to live with? Long term illnesses are becoming more common as people age, and living with these multiple illnesses can present many symptoms, psychosocial and spiritual concerns. Survival can be unpredictable, and cure cannot be achieved for many conditions associated with ageing.

What might be a solution?

We are a group of researchers, doctors and nurses working in palliative care. Palliative care helps to reduce the burden of symptoms and concerns faced by people whose disease cannot be cured, and which will worsen leading to death. Palliative care focuses on the patient, their family rather than their disease. Because of this, palliative care has been recommended for people who are living within multiple illnesses. Most contact with health staff, especially in rural areas, is with primary care. Primary care offers a strong potential to improve the care of older patients and families who are facing serious multiple illnesses by delivering palliative care.

What do we plan to do?

We will work with patients, families, health staff and Ministry of Health to design a new way to deliver palliative care from within primary care for older patients with multiple serious illnesses. We will then try delivering this new way to deliver care within primary care, and find out if it is delivered in the way we expected and what patients, families and staff think of the new way of working. This will happen in Ghana, Malawi and Zimbabwe.

We will do this in a number of steps. First, we will work with patients and families to find the best way for them to be able to give their thoughts and views on this study. Then we will talk to a range of patients, families and staff to get their views on how the new way of delivering care might look and how it could work. We then hold a meeting for all those people who are relevant to this goal (patients, families, clinical staff, clinical managers, Ministry of Health) to work together to build the new way of caring for patients. The research team will also use the information from patients, families and staff to work on a measure of care costs to ensure it is relevant for older people with multiple serious illness.

Once these steps are complete we can then try delivering this model of care at a rural district hospital primary care service. Using questionnaires we will ask patients about their health and wellbeing and the quality of care they receive both before delivery. We will also have in-depth discussions with patients, families and staff to ask their views and experiences of the care, and to try and discover whether it worked in the way we planned.

What do we hope will be achieved?

We know that palliative care improves patient and family wellbeing and can also be cheaper than care usually received. In Africa, palliative care has not focused on the common diseases of older people. In our three partner countries we will move forward our understanding of how to expand the benefits of palliative care into primary care for older

people with multiple serious illnesses. We will deliver a series of new advances: how to work with patients and families to inform work in this field; report the palliative care needs of older patients with multiple serious illnesses and staff views on how to meet them within existing settings; clear understanding and detailed description of how to achieve the care delivery from the views of all needed to engage for success; adapted questionnaire that will allow us to measure the costs of care for patients, families and the health system; views from those delivering and receive the care on what helps it to improve wellbeing

Kabudula, Chodziwadziwa Whiteson (MR/T038241/1, 18 months)

Self-management approaches for individuals with multiple chronic health conditions in rural South Africa

Principal Investigator Chodziwadziwa Whiteson Kabudula, University of the Witwatersrand, South Africa

Co-Principal Investigator Dr. Rochelle Burgess Institute for Global Health, University College London

Co-Investigator Edward Fottrell, University College London, UK

Co-Investigator Francesc Xavier Gómez-Olivé, University of the Witwatersrand, South Africa

Co-Investigator Alisha Wade, University of the Witwatersrand, South Africa

Co-Investigator Nicola Christofides, University of the Witwatersrand, South Africa

Co-Investigator Stephen Tollman, University of the Witwatersrand, South Africa

Summary:

Chronic health conditions, including non-communicable diseases (NCDs), mental disorders, and certain long-term infectious diseases such as HIV/AIDS have emerged as leading causes of morbidity and mortality in low and middle-income countries including South Africa (SA). This growing burden demands an innovative response. As most of the management of chronic diseases, which includes taking medication, making lifestyle changes, or undertaking preventive action occurs in homes, communities and outpatient settings, it involves patients, their carers or both making the day-to-day decisions about what actions to take. Involvement of patients in the management of their care for chronic diseases is referred to as self-management. A prerequisite for self-management to be effective is self-monitoring which is the "ability to monitor one's condition to effect the cognitive, behavioural and emotional responses necessary to maintain a satisfactory quality of life".

Self-monitoring broadly includes the monitoring of clinical parameters (such as weight, blood pressure, blood glucose and lung function), symptom measures (such as fatigue, stress and pain) and features of daily life (such as physical activities, dietary intake, and sleep patterns). Key attributes of self-monitoring are: (i) awareness of bodily symptoms, sensations, daily activities, and cognitive processes and, (ii) measurements, recordings, or observations that inform cognition and provide information for independent action or consultation with care providers. As health-related behaviours and practices are known to be distinctly different between geographical settings and between individuals within a particular setting, similarly is the case of self-monitoring of personal health. Evidence from high income settings has demonstrated that self-monitoring of personal health can improve self-management, symptom management and disease regulation, and can lead to reductions in complications, improvement in patients' coping and attitudes toward their disease, realistic goal setting and an enhanced quality of life. However, it is unknown whether, how and the extent to which the benefits of self-monitoring observed in high income settings can be realised in low and middle-income countries especially in rural settings. This project aims to assess the extent to which individuals with multiple chronic health conditions living in rural South Africa self-monitor their health, what methods they use, and the effect of different self-monitoring approaches on behaviours and health outcomes - as a basis for improving self-management among individuals with multiple chronic health conditions. The research for the project will be conducted in the Agincourt health and socio-demographic surveillance system study area in Agincourt sub-district in Mpumalanga province, in northeast South Africa. Data will be collected using questionnaires administered to patients aged 40 years and older with chronic health conditions, interviews with patients and health care professionals, and discussions

with patients, care givers and community members. Our research activities are expected to contribute to efforts to effectively tackle the rising burden of multimorbidity of chronic health conditions and subsequent mortality among rural populations in South Africa and other rural settings in East and Southern Africa.

Prina, Matthew Matthew (MR/T037423/1, 18 months)

Investigating MULTImorbidity ThroUgh cApacity building (MUTUAL)

Principal Investigator Matthew Matthew Prina, King's College London

Co-Principal Investigator Charlotte Hanlon, King's College London, UK /Addis Ababa University, Ethiopia

Co-Principal Investigator Graciela Muniz Terrera, University of Edinburgh, UK

Co-Principal Investigator Barbara Barrett, King's College London, UK

Co-Investigator Cleusa P. Ferri, Universidade Federal de São Paulo, Brazil

Co-Investigator Erico de Castro e Costa, Rene Rachou Institute, Brazil

Co-Investigator Girmay Medhin, Addis Ababa University, Ethiopia

Co-Investigator Abe Fekadu Wassie, Addis Ababa University, Ethiopia

Co-Investigator Tin Tin Su, Monash University Malaysia, Malaysia

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Summary:

More than a third of adults around the world live with more than one chronic condition. This accumulation of diseases is otherwise known as multimorbidity. Existing studies of multimorbidity have identified that the number of people living with multimorbidity in communities is similar between High (HIC) and Low- and Middle-Income Countries (LMICs). However, very fewer studies have been carried out in LMICs. Not everyone who has multimorbidity share the same diseases, and several different possible patterns are thought to exist. These patterns are normally referred to as clusters, as they represent the clusters formed by different diseases. Most of the research on clusters has been carried out in HIC, with very few studies being conducted in LMICs. Some existing studies carried out in HIC have showed that when a person has both physical and mental disorders, their quality of life is lower, their risk of dying is increased, and their economic burden is higher, compared to a person who only has physical illnesses. This area of work has however been largely under-researched in LMICs, partly for the following reasons: a) analysing multimorbidity clusters is challenging and requires advanced training in data analysis; b) lack of suitable and up-to date data; c) neglect of LMICs mental health research more generally, and d) lack of interdisciplinary researchers trained with appropriate skills to address this complexity, especially in LMICs. With MUTUAL we will develop a platform for high-quality, LMIC-led research to investigate knowledge gaps in our understanding of multimorbidity associated with both mental and physical illnesses (MPM) in LMICs. This will be done by creating a capacity building programme taking place across three countries, in three continents, and with different levels of economic development: Brazil, Ethiopia and Malaysia. Training will be delivered by tutors and mentors in 3 areas of need: a) advanced statistical methods and epidemiology; b) health economics; and c) evidence synthesis. This will be further enhanced by training in transferable skills (e.g. research dissemination, public speaking, leadership, impact, data security). Training resources will be made available outside of the network so that other researchers interested in the training will be able to access it. Early career researchers across the three countries, with support of both UK and in-country tutors, will then work mutually to advance our understanding of multimorbidity using existing datasets of people living in the three countries, with detailed information of health status. This will be carried out using advanced statistical analysis. Health economics techniques will also be used to understand the economic impact associated with specific clusters, to assess which are the most burdensome. Our final objective is to create a network and platform for future training and for further research activities around the topic of multimorbidity. We hope that this project will have a direct impact on people's lives, both individuals living with multimorbidity, but also on early career researchers.

Abas, Melanie Amna (MR/T038179/1, 18 months)

Pilot of an Intervention for Malawian Pregnant Women with HIV to Improve Depression, Viral Suppression and Engagement of Partners in HIV Self-Testing

Principal Investigator Melanie Abas, King's College London
Co-Investigator Kazione Kulisewa, University of Malawi
Co-Investigator Liz Corbett, London Sch of Hygiene and Trop Medicine
Co-Investigator Michael Udedi, Ministry of Health Malawi
Co-Investigator Moses Kumwenda, Malawi Liverpool Wellcome Trust
Co-Investigator Mwawi Ng'oma, Malawi College of Medicine
Co-Investigator Rebecca Jopling, King's College London

Summary:

HIV infection remains one of the biggest killers globally. Malawi has a successful programme for prevention of mother to child transmission of HIV based on routine antenatal testing. However, 23% of women attending HIV antenatal care are lost to care at one year. Depression is an important cause of poor adherence to medication for the treatment of HIV and disengagement from HIV care. Depression is two to three times higher in people living with HIV than in the general population, and common in pregnant and post-natal women in Southern Africa. Symptoms of depression such as reduced concentration, memory, problem-solving ability and motivation, adversely affect engagement with health care and adherence to medication.

Malawi's successful programme of antenatal testing presents an opportunity to engage their male partners in HIV testing. Men are less likely than women to test for HIV and know their status. In Malawi over 45% of HIV-positive women in stable relationships have an HIV-negative partner. Without intervention, HIV-negative partners acquire HIV at up to 12% per year. Supporting women to adhere optimally to their HIV medication to ensure their virus is well controlled reduces the risk of transmission to zero. HIV self-testing, whereby an individual collects their own sample, conducts the test and interprets their result increases coverage and frequency of testing. Partner-delivered self-test kits, where woman distribute a test to their male partner, is becoming routine antenatal policy and practice in high HIV prevalence settings including Malawi.

The aim of the proposed research is to finalise and test the feasibility and acceptability of an intervention for pregnant women living with HIV and depression, to reduce depression and optimise engagement in HIV care, and to increase uptake of HIV testing, prevention and care for their male partners. This will be achieved through conducting formative work using qualitative methods to adapt an intervention to treat depression and optimise adherence to HIV medication for the Malawian antenatal context. For the male partners of HIV positive pregnant women, we will develop a mobile phone based SMS platform where the male partner will be able to receive instructions on how to use an HIV self-test kit via SMS. We will develop messages providing key information on living with HIV, or HIV prevention strategies

The study will take place in an antenatal clinic in Blantyre, Malawi. We will recruit 40 HIV positive women in the 2nd trimester of their pregnancy and randomise them to receive the intervention or enhanced usual care. The 'TENDAI Together' intervention will consist of six sessions of therapy for depression and engagement in HIV care delivered by a trained and supervised HIV Diagnostic Assistant, an assessment for an antidepressant. The women recruited to the trial will also be given a self-test kit to distribute to their male partners. Instructions on how to use the self-test kit and key information on living with HIV or with an HIV positive partner to address post-test worries will be sent via SMS.

We will collect assessment measures at baseline and at 6 month follow up. This will include outcomes to determine the feasibility of a larger trial, such as the proportion of eligible participants recruited and then retained in the study. We will assess the acceptability of the intervention by the number of sessions attended and exit interviews with the women who received the intervention. We will also determine feasibility of collecting clinical outcome measures such as HIV and depression outcomes for the women and her male partner, and

clinical outcomes for the infant 2 months post-delivery. Locally validated, evidence-based measures will be used for the psychological entry criteria and outcome data.

Mair, Frances (MR/T037849/1, 18 months)

Multimorbidity in Africa - Increasing Understanding of the Patient Experience and Epidemiology (MAfricaEE)

Principal Investigator Frances Mair, University of Glasgow

Co-Investigator Chris Bunn MA, University of Glasgow

Co-Investigator Dr Bhautesh Jani, University of Glasgow

Co-Investigator Janet Seeley, London Sch of Hygiene and Trop Medicine

Co-Investigator Alison Price, London Sch of Hygiene and Trop Medicine

Co-Investigator Amelia Crampin, University of Glasgow

Co-Investigator Andrew Prentice, London Sch of Hygiene and Trop Medicine

Co-Investigator Gertrude Chapotera, University of Malawi

Co-Investigator Modou Jobe, London Sch of Hygiene and Trop Medicine

Summary:

Multimorbidity, the presence of 2 or more long-term conditions (LTCs), is an increasing global health challenge. Multimorbidity is increasingly common among younger and middle-aged as well as older people and is associated with adverse effects on health outcomes. Although multimorbidity is increasingly common in low and middle-income countries (LMICs), we have insufficient information on patterns, trends or determinants of multimorbidity in LMICs. Such information is crucial to inform health and social service planning across different LMIC health care systems.

Equally important is the call by the Academy of Medical Sciences to undertake research that includes "studies of the experiences and preferences of patients with different types of multimorbidity" in LMICs. Living with multiple LTCs is hard work and requires people to assume an increasing workload of self-management, something referred to as 'Treatment Burden.' Treatment burden refers to the work that people and their wider support network have to undertake. It covers a variety of activities ranging from: a) the work done to gain an understanding of conditions; b) the effort needed to navigate health and social care systems; c) the work of operationalising self-management such as attending appointments and taking medicines; and d) undertaking self-monitoring activities, such as checking blood sugars. The concept of treatment burden in those with multimorbidity is yet to be investigated in Sub Saharan Africa (SSA).

People can vary in their capacity to cope with any given level of treatment burden depending on a range of factors such as socioeconomic status, health literacy, language, level of educational attainment, location, personal beliefs and physical and mental abilities. As well as personal or individual resources, it is important to consider the role of the persons' wider social support network as well as healthcare organisations and health policy. Gaining an understanding of these concepts in a SSA context and enhancing understanding of the challenges faced by patients and practitioners would inform development of interventions to improve management of multimorbidity. Treatment burden and capacity issues are important as overwhelmed patients are less likely to adhere to therapies, resulting in wasted resources and poor outcomes. This proposal addresses important evidence gaps in multimorbidity research in SSA. Our project will involve 3 work-packages (WPs) and use data sources from 3 African nations (Malawi, Gambia and Uganda). The work represents a collaboration led by the University of Glasgow, which has particular expertise in multimorbidity research, using both data science and qualitative methods, along with partners in Malawi, the MRC Units in Gambia and Uganda and the London School of Hygiene and Tropical Medicine

Our project will address the following questions:

1. What is the prevalence and pattern of multimorbidity across different datasets in Malawi, Uganda and Gambia?
2. What is the cross-sectional relationship between demographic and lifestyle factors with prevalence and pattern of multimorbidity in Malawi, Uganda and Gambia?

3. What are the key similarities and differences in the observed findings across the 3 countries?
4. What are patients' experiences of the effects of multimorbidity on the work of self-management and their capacity to cope with self-management demands?
5. What are healthcare professionals' experiences of treating and managing patients with multimorbidity in each country and what do they see as the main barriers to optimal care provision?
6. What are the key targets for future research?

While this work is primarily exploratory, it will promote development of a new collaboration looking at multimorbidity in SSA and serve to highlight data gaps and opportunities that the team plans to address in future funding application.

Barreto, Mauricio Lima (MR/T03355X/1, 18 months)

The risk of a chronic clinical condition following a previous hospitalisation by a psychiatric disorder: a linkage nationwide study in Brazil

Principal Investigator Mauricio Barreto, Federal University of Bahia (UFBA)
Co-Investigator Daiane Borges Machado, Fiocruz (Oswaldo Cruz Foundation)
Co-Investigator Glyn Lewis, University College London
Co-Investigator Liam Smeeth, London Sch of Hygiene and Trop Medicine
Co-Investigator Luis Fernando de Araujo, Fiocruz (Oswaldo Cruz Foundation)
Co-Investigator Marcos Ennes Barreto, Federal University of Bahia (UFBA)
Co-Investigator Spiros Denaxas, University College London

Summary:

Multimorbidity is the occurrence of more than one chronic condition at a time. This can include conditions like cardiovascular disease, a mental health condition of long duration, such as a mood disorder or dementia or an infectious disease of long duration, such as Tuberculosis.

Multimorbidity increases with age and also presents certain distinct patterns related to sex. On the other hand, mental disorders are commonly found together and usually have consequences on other chronic physical condition that the patient may have. Mental health disorders, in particular depression, represent an important risk factor for premature mortality. Multimorbidity can also increase the treatment costs, as subjects with depression will cost 50% more to health systems than those with one chronic condition alone. Cardiovascular diseases are also found to co-occur with depression, this might happen because these patients show difficulties in following their GP 's recommendations. It is of note that women seem to be at higher risk of morbidity from cardiovascular disease, while they are also at a higher risk of depression suggesting gender-specific mechanisms. Analysis of a recent health survey in adult Brazilians observed that the prevalence rate of multimorbidity are higher among women compared to men, among older people and those with lower educational level.

We at the Center for Data Integration and Knowledge for Health (CIDACS) have access to very large datasets, which would commonly be known as Big Data. This data comprises information from Brazilian subjects that were listed or benefited by one of the several social programmes or were seen in any of the numerous public hospital of the country's universal health system.

This project aims at increasing knowledge over the relationship of mental disorders and other chronic conditions to ameliorate the lives of those affected. More specifically we want to (A) estimate the the risk of hospitalisations or death by diabetes mellitus, cardiovascular diseases or stroke following a hospitalisation due to depressive disorders, alcohol and substance use-related disorders, and schizophrenia; (B) To estimate the risk of the occurrence or death by tuberculosis following a hospitalisation due to depressive disorders, alcohol and substance use-related disorders, and schizophrenia; (C) To investigate how these chronic conditions goes together in clusters and how these patterns evolve over time and ageing.

Kinra, Sanjay (MR/T038292/1, 18 months)

Extending an inter-generational cohort to develop a multimorbidity research platform in rural and urbanising India

Principal Investigator Sanjay Kinra, London Sch of Hygiene and Trop Medicine

Co-Investigator Bharati Kulkarni, National Institute of Nutrition - NIN

Co-Investigator Hemant Mahajan, Public Health Foundation of India (PHFI)

Co-Investigator Om Kurmi, McMaster University

Co-Investigator Rajan SHUKLA, Public Health Foundation of India (PHFI)

Co-Investigator Shilpa Sadanand, Public Health Foundation of India (PHFI)

Summary:

In India, people that have more than one long-term health condition ("multimorbidity") are more likely to have high healthcare costs, which they usually pay out-of-pocket, and to be disabled which can affect their ability to work. As a result, multimorbidity can impact the economic well-being of people's families, potentially pushing them below the poverty line. Rural and urbanising communities are particularly vulnerable to rapid rises in multimorbidity because social changes are affecting behaviours (e.g. people are eating more processed foods) and environmental exposures (e.g. rising air pollution from traffic), while old, poverty-related health issues (e.g. malnutrition) remain common. Healthcare is also lacking in these areas, so people can struggle to manage their conditions. As a result of these factors, rising multimorbidity could inhibit future development in rural and urbanising areas. As such, it is important to understand what causes multimorbidity, so that we can develop ways to prevent it. This study will build on work done over the past 30 years in 29 villages on the outskirts of Hyderabad city, Telangana. The study team has previously collected detailed health data on families within these villages (the Andhra Pradesh Children and Parents Study) (~5% of the village population, N=6,972, aged ~22-50 in 2010-12) who were involved in a trial of nutritional supplements for pregnant women and young children in the 1980s. Our ultimate aim is to follow this cohort up over the long-term to see how conditions develop and cluster together at different life-stages, to examine what causes these clusters, and to develop ways to target these causes to prevent multimorbidity developing. We will particularly investigate how factors at early-life (e.g. malnutrition) and related to the rapidly changing environment (e.g. air pollution) are linked to multimorbidity, as their impact on multimorbidity has not been assessed. Nevertheless, we need to do considerable groundwork to be able to do this accurately. This current study will analyse previously collected data to understand which clusters of conditions and potential causes are important in the local community. We will also collect data on the presence of chronic conditions in the older sub-group of the cohort (N=~2,000, aged ~60 in 2020), who are more likely to experience multiple conditions. This will be analysed in combination with previously collected data (2010) and used to calculate how many community members we need to study to accurately quantify the impact of potential causes on the risk of multimorbidity. We will also interview people with varying severities of multimorbidity (and their family members) and conduct focus-group discussions with wider community members, to understand how multimorbidity affects people's lives and what they wish APCAPs to prioritise and research in the future. A final goal is to investigate how feasible it would be to develop a system that automatically collects data on community members' healthcare records, as this would allow us to collect data over the long-term and at low cost. We will do this by randomly selecting 200 of the surveyed cohort who have used healthcare in the past year, tracking down their records in local facilities, and comparing the diagnosis with results from our own clinical examinations. Working closely with community members and key parties (e.g. local health workers, village leaders), we will use the above findings to develop a research proposal for a multimorbidity research platform, to establish the causes of multimorbidity, assess its impact, and develop and test ways of preventing multimorbidity. We expect our findings will also be applicable to other communities experiencing similar social changes.

Panniyammakal, Jeemon (MR/T037822/1, 18 months)

Systems thinking approach to developing an integrated and patient-centred

intervention model for multimorbidity care in primary care settings in India

Principal Investigator Jeemon Panniyammakal, Sree Chitra Tirunal Institute for Medical Sciences and Technology, India

Co-Principal Investigator Semira Manaseki-Holland, University of Birmingham

Co-Investigator Harikrishnan Sivadasanpillai, Sree Chitra Tirunal Institute for Medical Sciences and Technology, India

Co-Investigator Jissa Thulaseedharan, Sree Chitra Tirunal Institute for Medical Sciences and Technology, India

Co-Investigator Justine Davies, University of Birmingham

Co-Investigator Paramjit Gill, University of Warwick

Co-Investigator Pratap Kumar, Strathmore University, Kenya

Co-Investigator Linju Mariam Joseph, Centre for Chronic Disease Control, New Delhi.

Researcher Co Investigator Mathew J Valampampil, Sree Chitra Tirunal Institute for Medical Sciences and Technology, India

Summary:

Multimorbidity is the existence of multiple long-term mental, physical, and cognitive disorders in one patient. These could include diabetes, hypertension, lung diseases, heart attacks, stroke, kidney failure, and liver problems or other conditions. Multimorbid conditions can share common disease causes and consequences. The rate of multimorbidity is rapidly increasing in low resource countries (low and middle-income countries - LMIC) such as India. Importantly, multimorbidity leads to reduction in quality of life, increase in use of health services and reduction in life expectancy. However, in management of multimorbidity, it is often considered as an assortment of disconnected diseases. Hence patients with multimorbidity receive less than optimal care. A concerted effort from the health system for re-orienting the delivery of primary care is important in improving the quality of life of people with multiple chronic conditions. Our proposed study in primary care settings of Kerala, India will try to better understand the complexity of workforce strengths, system capabilities, human behaviours, link to social resources and their interactions most aptly framed from a health system perspective in developing an innovative and patient centred model for management of multimorbidity. We will adopt the following steps:

1. We will use different qualitative (discussions and observations) methods to investigate what is currently happening in our health facilities with services that multimorbidity patients receive. In this way we will understand the perceptions of health system managers, health care providers and patients in terms of the barriers and facilitators of provision of care for patients with multiple long-term (chronic) conditions.
2. We will identify successful models of interventions for managing multimorbidity in other settings by conducting a comprehensive review of available literature.
3. We will use this literature review and data from our research to develop context specific interventions for managing multimorbidity in primary care settings. Additionally, we will explore ways in which the care for people with multiple chronic conditions can be organised and integrated within the community through community health workers.
4. We will then use methods to visualise how different variables in a system are interrelated (causal loop model) and identify how changes in one variable affects others in the loop.
5. We will identify options for improving access to social resources (eg: accessibility for physical activity for females, rehabilitation services etc.) for managing multimorbidity, which can then be incorporated into the intervention models developed in step 3 and 4.
6. Further, we will identify interventions that potentially have a more direct impact on patients, prioritise them and finalise them after incorporating comments from all stakeholders as in step 1.
7. Finally, materials and protocols will be developed for prioritised intervention items.

Optimal involvement of clinical and health system leadership, engagement of all potential

stakeholders including patients in the intervention development are unique to this project. Finally, a detailed plan will be developed for formal evaluation of the developed intervention in a confirmatory study in future. The key lessons from this project may help to transform the current health-care delivery system into a patient-centered and coordinated system for managing multimorbidity in primary care.

Tiffin, Nicki (MR/T037733/1, 18 months)

The Khayelitsha Comorbidity Cohort: Establishing a multimorbidity cohort with integrated clinical, genomic and epidemiological data in South Africa.

Principal Investigator Nicki Tiffin, University of Cape Town
Co-Investigator Andrew Boulle, University of Cape Town
Co-Investigator Kirsten Bobrow, University of Cape Town
Co-Investigator Nicola Mulder, University of Cape Town

Summary:

In the Western Cape Province of South Africa, there is a large burden of diseases including infectious diseases HIV and TB as well as chronic diseases like hypertension, diabetes and kidney disease. Often patients have more than one condition at the same time. The Provincial Health Data Centre (PHDC) at the Department of Health collects ongoing patient information about their visits to health facilities, medicines received and laboratory tests done, in order to provide health care. Where patients consent, these health data can be used for research to better understand health conditions.

Genes and DNA are unique to each individual and can affect whether they will get some diseases, how ill they will get with those illnesses, and how they respond to treatment. By understanding this relationship between DNA and diseases, individual patients will be able to receive better health care tailored to their own DNA sequence. Most of the research done on DNA and diseases until now has been done on Caucasian populations, and African patients have been poorly represented in research. This means that most health care is not optimised for Africans, even though African populations have rich genetic diversity which can provide many insights into the mechanisms of disease through biomedical research. In addition, research about genetic effects on disease have generally been conducted from the perspective of looking at a single disease and doing the analysis on who has the disease or not without taking into consideration other health conditions that the participant might also be experiencing.

Recently, the H3Africa Bioinformatics Network (H3ABioNet) developed the H3Africa Illumina genotyping chip, a tool that is specifically optimised for measuring DNA variation in Africans, across the whole human genome. With the consent of research participants, health data from the PHDC can be combined with genetic data generated using the H3Africa genotyping chip, making it possible to research the relationship between DNA and different diseases in African individuals. In the first instance, this project aims to collect 700 DNA samples from consenting participants and link their DNA data to their health data from the PHDC. In this first stage it will be possible to research the more common diseases - hypertension, diabetes and kidney disease; but as the number of research participants increases in the future it will also become possible to research the less common illnesses. Updated health information will be received from the PHDC twice a year, to document all health outcomes as they occur in participants going forward. An additional benefit to this research is that it will use a participant-based approach rather than a disease-based view, researching the whole health profile of the participant instead of only looking at whether they have a single disease or not. By working in collaboration with the Department of Health, a system will be set up to return useful findings from the research so that they can be used to provide better tailored health care by the Department of Health for individuals as well as the whole population. The information will also help to inform health care in other African countries, and well as providing research insights that can help improve our understanding of disease processes across the world.

Pati, Sanghamitra (MR/T03839X/1, 18 months)

Catalysing multimorbidity research in Low and Middle Income Countries through a "community of practice" approach: An India-Brazil-UK Initiative

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Summary:

This international network between India Brazil and UK aims to foster global south-south collaboration to research on multimorbidity across Low and Middle Income Countries by creating "community of practice" as an enabling platform to address the challenges of multimorbidity in respective countries through shared learning, capacity building and collaborative research. We envisage that this mutually enriching coalition between India and Brazil, with the overarching support of UK, a leader in primary care multimorbidity, will not only catalyse multimorbidity research in individual countries, but further lead to a larger trans-continental (South Asia- South America-UK) collaboration and pave path for the LMIC Network on multimorbidity.

Principal objectives of this project are to:

1. Set up systems and bring synergy within public health care environment to develop a "community of practice" on multimorbidity using the existing networks and institutions through a mix of strategies comprising coalition building, advocacy and multidisciplinary capacity building. This community of practice will be a self-driven cohesive platform and would sustain the research momentum in the region and design locally relevant for mitigating the care challenges of patients living with multimorbidity.
2. To come up with a simple yet useful capacity building framework/ training program for general practitioners, public health researchers, academicians, and health service managers to appreciate the multiple challenges of multimorbidity on health care and patients and identify the immediate research priorities to respond to this challenge as a team.
3. We believe that this in turn would improve better assessment and management of multimorbidity in primary care leading to improved patient outcomes through provision of continuous, coordinated and tailor-made care based on evidence and consultatively develop, design or contribute to contextualized care protocols.
4. To provide an adaptable template for building multimorbidity research capacity in low and middle income country settings by sharing with both policy and scientific community.
5. To collaboratively work with our "community of practice" and apply for large grant to develop, implement and evaluate a patient focused integrated system of care based in primary care practice for people with multimorbidity.

The International and national network created would spearhead advocacy and engage with policy makers, health planners and health care managers in respective countries and across LMIC for considering multimorbidity while reorienting the health services to strengthen primary care under the ambit of universal health coverage. With the help of the project findings, we would also continue dialogues with the National research agencies to include multimorbidity as a new research priority and provide grant opportunities for further research.

We additionally plan to disseminate our findings with diverse audience through national workshops, publications in international journals, stakeholder reports and bulletins, guidelines and linkages with government and non-government stakeholders. Through these

channels we will deepen the evidence base, further the research agenda of multimorbidity and ultimately influence health and social policy and practice. Our work will have applicability nationally and internationally especially in the low and middle income countries strengthened by our collaboration with researchers from and thus contribute significantly to the social and economic development.

Ajay, Vamadevan S (MR/T038004/1, 18 months)

Developing a Digital Health-enabled Intervention to tackle Multimorbidity in Primary care in India

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Summary:

One in four people seeking primary healthcare facilities in India is estimated to have multimorbidity, which is characterised by the co-occurrence of two or more medical conditions. People with multimorbidity are less likely to receive appropriate care for the individual diseases they have, primarily because clinical care systems are designed around single conditions or body systems. The overarching aim of this research proposal is to develop a digital health-enabled intervention for multimorbidity management in the primary care setting, test its feasibility, and pilot it for deriving inputs for planning a larger evaluation in future. The proposed research work will be carried out in the north-Indian state of Tripura in India. As part of India's National Programme on Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS), Tripura has established 40 Non-communicable Disease (NCD) clinics in the state. Over the past 29 months, the healthcare team in these NCD clinics has been using a digital health system namely the mPower Heart Digital Health System to compute the clinical management plan and maintain patient health record electronically. This digital health system is unique because the healthcare team used to capture information on presence/absence of 14 medical conditions that are frequently seen among people with chronic conditions such as hypertension, diabetes, dyslipidemia, chronic obstructive pulmonary diseases, alcoholism and tobacco use.

In the proposed research work, we will attempt discovering the most frequent multimorbidity patterns seen among patients who sought care for the past 29 months from 40 NCD clinics in Tripura. Using these inputs, along with advice from experts, we will develop a package of intervention, that involves modifying the mPower Heart digital health system for addressing most frequent and severe multimorbidity patterns. The development of the intervention package will be carried out involving experts, health administrators, members of the healthcare team and patients. The intervention development will consider the key components of the health system - such as service delivery, workforce, supply of essential medicines/diagnostics, health information system, financing, and governance/leadership - and other contextual factors that have a role in the successful implementation of the package in the health facilities. The intervention package will be piloted in two health facilities to assess its feasibility and acceptability in the real world helps design an evaluation that will work and be implemented in real-world health systems, rather than just an intervention that it is possible to evaluate in a research setting. We will be then developing a research proposal to evaluate the intervention in a large scale to know the impact of such an

intervention in improving quality of care and patient outcomes. This work will have high scalability and national significance in reorienting the NPCDCS from a vertical, disease-oriented model into a holistic, patient-oriented care delivery model. The NPCDCS is providing access to millions of people with chronic diseases in India in primary care. Thus this proposal aligns with the UN sustainable development Goals (No -2: Good Health and Wellbeing) explicitly addressing the UNSDG Target 3.3 (fight communicable diseases) and Target 3.4 (Reduce mortality from non-communicable diseases and promote mental health).

Siddiqi, Najma Najma (MR/T037806/1, 18 months)

Addressing TBMM

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Co-Investigator Helen Elsey, University of York
Co-Investigator Kamran Siddiqi, University of York
Co-Investigator Nyanda Elias Ntinginya, National Institute for Medical Research
Co-Investigator Rachel Tolhurst, Liverpool School of Tropical Medicine
Co-Investigator Razia Fatima, National Tuberculosis Center (NTC)
Co-Investigator Sameen Siddiqi, The Aga Khan University, Pakistan
Co-Investigator Uzochukwu Egere, Liverpool School of Tropical Medicine
Co-Investigator Zia Ul Haq, Khyber Medical University (KMU)

Summary:

Tuberculosis (TB) is a chronic infectious disease. Every year, approximately 10 million people fall ill with TB and 1.6 million die from it. TB often coexists with other chronic diseases including chronic non-infectious conditions (e.g. lung disease and diabetes), mental health conditions (e.g. depression), and chronic infectious diseases (e.g. HIV/AIDS). This coexistence (or 'multimorbidity') is common because these illnesses share similar risk factors. For example, smoking can lead to both chronic lung disease and TB. Having one condition also increases the risk of another; for example, people with diabetes have poor defences against infections making them vulnerable to developing TB. Coexisting conditions also interact adversely with each other, worsening health, quality of life and survival for each, compared with having just one condition alone.

Healthcare services for people with TB should, therefore, offer prevention, detection and treatment of other coexisting chronic illnesses. Traditionally, however, services, including TB programmes, typically focus only on a single condition. Our overall goal is to support TB programmes in low- and middle-income countries to improve the prevention, screening, and management of the most common and most devastating chronic illnesses that coexist in people with TB. This approach may improve quality of life and survival for individuals and also help control the rapidly increasing epidemics of chronic conditions.

We focus on conditions coexisting with TB due to their common occurrence and their significant negative health consequences. We think that there may be opportunities to integrate care for multimorbidity within relatively well-resourced and functioning TB programmes (compared with other parts of the health system). Knowledge gained about managing multimorbidity could also be transferable to other services.

Multimorbidity can manifest in many patterns or combinations of conditions (clusters). In this 'seed-funding' project, we will first estimate how common are the various co-existing illnesses, and identify the clusters that contribute the greatest burden in terms of shortening life expectancy, causing ill health and incurring healthcare costs for people with TB. We will then explore potential interventions for these conditions.

To do this, we will review published academic literature on coexisting chronic conditions in people with TB and analyse data from a large world health survey. This will allow us to estimate how common is multimorbidity and how it affects the health, quality of life and life

expectancy of people with TB. It will also help to identify the clusters of conditions that cause the most burden for patients, and to understand the sorts of interventions that are effective for these target conditions, which may be feasible to deliver integrated within TB programmes. We will also look for other sources of information on multimorbidity in people with TB, collected in study countries.

We will establish a global TB Multimorbidity Network of people and organisations that can contribute expertise in the topic, support efforts to spread our findings to a wide audience, help identify additional countries to improve generalisability of, and support the next stage of research. We will also grow capacity in research methods, leadership and management of research funding, required for a low- and middle income partner organisation to take a lead role in a future programme.

We build this proposal on previous work in TB, mental health, chronic diseases and HIV, and expertise in health systems and policy. Our team has established collaborations in global mental and physical health and TB and lung health in South Asia and Africa.

This preliminary work will inform plans for a future research programme, in which we will develop and test a package of interventions to prevent multimorbidity.