

The Multi-morbidity Working Group Impact

Summary

Multi-morbidity - the presence of two or more long-term health conditions and mental disorders – is already affecting a large number of people in high-, middle- and low-income countries (by some estimates, around one third of the population), with figures set to rise further. However, healthcare delivery tends to be organised around individual diseases rather than integrating management across multiple diseases. Patterns of co-occurring diseases as well as strategies that prevent or treat multi-morbidity differ between high-income countries and low- and middle-income countries (LMICs). Researchers need to capture the situation and conditions in LMICs to find ways to prevent and treat multi-morbidity - an important element in achieving UN Sustainable Development Goal 3 (SDG 3): *Ensuring healthy lives and promoting well-being for all at all ages*.

GACD Network meetings are unique in bringing together researchers and health-care professionals who specialise in different non-communicable diseases (NCDs). The forum enables sharing of experiences and provides a 'safe space' to discuss challenges. At the 2017 GACD Network meeting, researchers with different specialisms identified their common interest in going beyond 'their' NCD and address multi-morbidity. This sparked the formation of the GACD Multi-morbidity Working Group, which has grown to **74 members** from across disease areas, with around half of its members located in middle-income countries. Since its establishment, the group has tackled a series of tasks:

- A **joint statement and a policy brief** to draw the attention of research funders and policy makers to the importance of multi-morbidity research
- Development of a set of **core outcomes measures for multi-morbidity trials in LMICs**, in consultation with LMIC stakeholders. This will enable research results from across studies to be combined, increasing the strength of the evidence and its potential for impact
- A research prioritisation exercise, consulting with GACD Network members to assemble a '**top ten**' list of **urgent questions** linked to international health targets such as the 2030 SDGs

The working group's efforts are galvanising the research community and preparing the ground for future multi-morbidity research. They have already addressed one of the GACD funders' main concerns – a lack of robust multi-morbidity outcome measures. As a result of such progress in the field, the funders have agreed that the 2023 GACD call for proposals will fund 'implementation science research focused on integrating interventions for optimising management and care for patients with multimorbidity in LMICs as well as vulnerable populations in HICs'.

1.1 Introduction

It is common for individuals to suffer from more than one non-communicable disease (NCD), e.g. diabetes and cardiovascular disease or depression. This presence of two or more long-term health conditions and mental disorders is termed 'multi-morbidity'. Patients with multi-morbidity tend to require more frequent health care consultations and longer hospital stays, and have a reduced quality of life and higher mortality. Multi-morbidity leads to considerable health care costs; for example, the treatment and care for people with long-term conditions was estimated to take up around 70% of total health and social care expenditure in England.¹ A recent review found that around 38% of the population in high-income countries (HICs) and 30% in low- and middle-income countries (LMICs) may be affected by multi-morbidity (with estimates varying widely due to a lack of robust data).² This figure is expected to rise further driven by wider trends such as changes in life expectancy and lifestyle. Chronic co-morbidities such as hypertension, diabetes and respiratory disease may also worsen outcomes for other diseases, a particular concern during the COVID-

¹ Department of Health Report 2012. Long-term conditions compendium of Information: 3rd edition. Available via <https://www.gov.uk/government/publications/long-term-conditions-compendium-of-information-third-edition>. Accessed on 19 May 2021

² Nguyen H, Manolova G, Daskalopoulou C, et al. Prevalence of multimorbidity in community settings: A systematic review and meta-analysis of observational studies. Journal of Comorbidity 2019. doi:10.1177/2235042X19870934

19 pandemic.³ Prevention and/or successful treatment of multi-morbidity are hence important elements in achieving UN Sustainable Development Goal 3 (SDG 3) of ensuring healthy lives and promoting well-being for all at all ages, and SDG target 3.4 of reducing premature mortality from NCDs by one-third between 2015 and 2030.⁴

Healthcare delivery tends to be organised around single diseases, requiring patients with more than one condition to make multiple appointments, develop relationships with multiple healthcare professionals and keep track of multiple treatments.⁵ In addition to the increased effort - and often higher cost - of accessing care, prescription of several medications ('polypharmacy') can also lead to adverse drug reactions and lower adherence. Research has shown that patients receiving integrated care for chronic diseases experience an improvement in their quality of life.⁶ Successful management of multi-morbidity thus requires a shift in the way healthcare is delivered, away from siloed specialisms and towards integrated disease management which connects inputs from across clinical disciplines and across household members.

HICs and LMICs are likely to differ in the pattern in which diseases co-occur, and the population groups they affect. For example, patients in LMICs are more likely to suffer from long-term infectious conditions (such as Tuberculosis and HIV/AIDS) and NCDs that often start at a younger age than in HICs.⁷ In addition, strategies for prevention and treatments need to be suitable and affordable in an LMIC context, as many settings face the challenges of poorly resourced healthcare systems, as well as limited health infrastructure and human health resources.⁸

1.2 Origin of the GACD Multi-morbidity Working Group

GACD working groups are bottom-up initiatives in which GACD Network members collaborate on shared interests. Members volunteer to contribute to activities of the working groups; the GACD secretariat provides logistical support and covers the cost of open-access publications resulting from this work.

The idea for the Multi-morbidity Working Group was conceived during the 2017 GACD Scientific Meeting when GACD network members working on different NCDs discovered their shared experiences and research interests: "We realised that we actually have more in common than we have differences. The challenges of delivering an implementation science project in cardiovascular disease, in diabetes, or in respiratory diseases – they are not really different [from each other]". At the same time, the researchers recognised the importance of multi-morbidity for global health, and the specific need for multi-morbidity research in LMICs and vulnerable populations in HICs. This provided the nucleus around which the multidisciplinary GACD Multi-morbidity Working Group formed. As one researcher explained: "We were talking to researchers looking at other NCDs and we realised we were interested in the same issues and that we wanted to work together."

1.3 A key enabler: the GACD network

The GACD network meetings provide a unique opportunity for the evolution of researcher-led initiatives that cut across research specialism 'silos': While most scientific conferences focus on a single disease, the GACD meeting enabled researchers from across disease areas to share experiences and build relationships. In addition, GACD meetings are perceived to be 'safe spaces' which foster open dialogue on research challenges participants encounter. As one meeting participant commented: "I would never dream of talking to researchers working on other diseases, because that would

³ Zhou y, Yang Q, Chi J et al. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis. *Int J of Infect Dis* 2020; 99: 47-56

⁴ United Nations. Transforming our world: the 2030 agenda for sustainable development. Sustainable Development Knowledge Platform. 2015. Available via <https://sdgs.un.org/2030agenda>. Accessed 1 June 2021

⁵ Prathapan S, Fernando GVMC, Matthias AT, et al. The rising complexity and burden of multimorbidity in a middle-income country. *PLoS ONE* 2020 15(12): e0243614

⁶ Flanagan S, Damery S, Combes G. The effectiveness of integrated care interventions in improving patient quality of life (QoL) for patients with chronic conditions. An overview of the systematic review evidence. *Health Qual Life Outcomes*. 2017;15(1):188. doi: 10.1186/s12955-017-0765-y

⁷ Afshar S, Roderick P, Kowal P et al Global Patterns of Multimorbidity: A Comparison of 28 Countries Using the World Health Surveys. In: *Applied Demography and Public Health in the 21st Century* [Internet]. 2017, p 381-402. Available via <https://www.researchgate.net/publication/308967883>. Accessed 28 May 2021

⁸ Hurst JR, Dickhaus J, Maulik PL, et al. Global Alliance for Chronic Disease researchers' statement on multimorbidity. *Lancet Glob Health* 2018; 6: e1270–71

mean leaving my comfortable silo. But of course, I was forced to do that at the GACD meeting. [...] And that's what the GACD is about.”

From a handful of researchers in 2017, the multi-morbidity working group grew to 23 participants in 2018⁹, and 74 members in 2021¹⁰. The group's current make-up clearly demonstrates the GACD's value in bringing together networks across disciplines and geographic locations: Around one third of members each are involved in GACD research on diabetes (35%) or lung diseases (31%), while 22% conduct research on hypertension and 12% on mental health. Working group members hail from 28 countries, with nearly 50% from MICs, especially in Asia (19%) and Africa (16%).

1.4 Working group activities

After its establishment in 2017, members of the Multi-morbidity Working Group continued to collaborate and agreed on an agenda and prioritised list of tasks to tackle. Each task is led by a working group co-chair, with group members volunteering their support. These activities and progress made are presented to the entire network at the annual GACD Scientific Meetings, keeping other GACD members informed and enabling those who are interested to join.

The work group started by authoring a statement to draw the attention of research funders and policy makers to the issue. The 'GACD Researchers' Statement on Multi-Morbidity' was published in late 2018 in *The Lancet Global Health*¹¹ and on the GACD website¹², ahead of the United Nations General Assembly high-level meeting on NCDs: *“The GACD Research Network believes that a greater focus on multimorbidity is overdue and necessary to successfully improve global health outcomes.”* The working group has also developed a policy brief, which sets out the evidence and actions needed to tackle the burden of multimorbidity in LMICs, to spark discussions with funders and policymakers.¹³

Discussions with funders enabled by the GACD network revealed that they were in principle open to considering a call for multi-morbidity research proposals – but that they had a major concern which blocked funding: Their perception was that the research community did not have robust agreed outcome measures to carry out this type of research in LMICs¹⁴. To overcome this barrier, the working group decided to address this gap. First, the group conducted a review of outcome measures that had been used in multi-morbidity research. From this, the group selected measures for different aspects of impact, ranging from individual-level outcomes to health service and health system effects, by applying selection criteria tailored to LMIC contexts.¹⁵ These included ease of measurement (e.g. availability of data and ease of data collection) and generalisability (i.e. the outcome applies across diverse populations within and between LMIC settings). The review, published in *BMJ Open*, provides a summary for researchers can draw on when designing projects and encourages the use of outcomes measures tailored to multi-morbidity questions.

Next, the GACD multimorbidity working group agreed to develop an international consensus on a core outcome set for multimorbidity trials specifically for studies in LMIC settings, using best practice methods.¹⁶ The ability to synthesise

⁹ John Hurst: GACD Mitigating Multi-morbidity. Available via <https://www.gacd.org/perch/resources/multimorbidity-working-group.pdf>. Accessed 28 May 2021

¹⁰ Personal communication, GACD Secretariat. Data from 4 June 2021.

¹¹ Hurst JR, Dickhaus J, Maulik PL, et al. Global Alliance for Chronic Disease researchers' statement on multimorbidity. *Lancet Glob Health* 2018; 6: e1270–71

¹² GACD Researchers' statement on multimorbidity. Available via <https://www.gacd.org/research/publications-and-references/gacd-researchers-statement-on-multimorbidity>. Accessed on 19 May 2021

¹³ Global Alliance for Chronic Diseases Multimorbidity Working Group (2021) Policy Brief for Research and Action on Multimorbidity in Low and Middle Income Countries. Available via <https://www.gacd.org/perch/resources/content/mm-policy-briefvfinal-gacd.pdf>. Accessed 28 March 2021

¹⁴ Outcomes measures are measurements researchers collect to assess the effect of interventions they are testing. These must fulfil several criteria. For example, they have to reliably measure effects linked to the interventions tested and to the issues the interventions were designed to address. Their collection also has to be feasible and acceptable for health professionals and patients, including across diverse LMIC and HIC settings.

¹⁵ Hurst, JR; Agarwal, G; van Boven, JFM et al. Critical review of multimorbidity outcome measures suitable for low-income and middle-income country settings: perspectives from the Global Alliance for Chronic Diseases (GACD) researchers. *BMJ Open* 2020;10:e037079

¹⁶ Boehnke, JR; Rana, RZ; Kirkham, JJ et al. Development of a core outcome set for multimorbidity trials in low- and middle-income countries (COSMOS): Study Protocol. *medRxiv* 2021; <https://doi.org/10.1101/2021.03.23.21253685> (preprint)

research results from across different research projects increases the strength of the evidence base, which in turn enhances the potential for impact. However, data can only be combined if studies measured the same outcomes in the same way. This requires researchers to agree on a number of prioritised outcomes - a 'core outcome set'.¹⁷ A core outcome set for multimorbidity trials had already been developed but was largely based on evidence and expert opinions from HICs.^{18,19} As LMIC stakeholders had not been involved in reaching consensus, the set did not consider their priorities nor did it take account of differences in what is feasible to measure between HICs and LMICs.²⁰ To address this gap, the GACD multimorbidity working group is following a four-stage process to develop the core outcome set for multimorbidity trials in LMICs. This includes a literature review of multimorbidity trial outcomes in LMICs, consultation with patients and caregivers in 10 LMICs to gather views on outcomes, and multiple rounds of consultation – using Delphi survey methods - with stakeholders living or working in LMICs, including people living with multimorbidity and their family caregivers, healthcare professionals, policy makers, and researchers interested in multimorbidity with experience in LMIC contexts. The final stage will be a series of consensus workshops.²¹ This work has benefitted from access to the GACD network of researchers, which has allowed the group to identify a diverse range of countries to participate in the process.

In addition, the working group has initiated a research priority setting exercise, which will build consensus around a list of top ten research priorities linked to international health targets such as the 2030 SDGs in consultation with GACD network members.

1.5 Next steps for GACD multi-morbidity research

The working group's efforts have already paid off: Persuaded by progress in the field including the critical contributions by the working group, the funders of the GACD agreed that the 2023 call for proposals will fund implementation science research focused on integrating interventions for optimising management and care for patients with multimorbidity in LMICs as well as vulnerable populations in HICs.²² The working group's consultations and outputs are laying the groundwork for the success – and impact – of this research call, galvanising the research community around research priorities and common outcome measures. Regular interactions as part of the working group are also strengthening relationships between group members, facilitating information exchange across research specialisms, which may benefit future research proposals and projects. As one researcher commented: "We are positioning the group and the research community more widely to be able to do studies in multi-morbidity, which are really, really, really, really needed. I would see that as the successes of that group."

¹⁷ COMET Initiative Core Outcome Measures in Effectiveness Trials. Available via <https://www.comet-initiative.org/>. Accessed on 10 June 2021

¹⁸ Smith SM, Wallace E, Salisbury C, et al. Core Outcome Set for Multimorbidity Research (COSmm). *Ann Fam Med*. 2018 Mar 1;16(2):132–8

¹⁹ Lee A, Davies A, Young AE. Systematic review of international Delphi surveys for core outcome set development: representation of international patients. *BMJ Open*. 2020 Nov 1;10(11):e040223

²⁰ Development of a core outcome set for multimorbidity studies in low and middle income countries (COSMOS). Available via <https://www.comet-initiative.org/Studies/Details/1580>. Accessed 28 May 2021

²¹ Boehnke, JR; Rana, RZ; Kirkham, JJ et al. Development of a core outcome set for multimorbidity trials in low- and middle-income countries (COSMOS): Study Protocol. medRxiv 2021; <https://doi.org/10.1101/2021.03.23.21253685> (preprint)

²² GACD announces topics for 2021-2023 funding calls. Available via <https://www.gacd.org/news/2020-12-08-gacd-announces-topics-for-2021-2023-funding-calls>. Accessed on 19 May 2021