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How can we fund research for people, not conditions?

Research funders need to respond to the significant challenges of multimorbidity, say Tara Lamont and colleagues

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It is more than 10 years since landmark UK studies underlined the “new normal” of multiple morbidity.^{1,2} More people now live with several health problems at an earlier age and health inequalities have increased, but most clinical services remain geared towards management of single diseases.^{3,4} Research systems have reinforced these distortions, with a focus often on single condition research, typically excluding people with comorbidities as trial participants.⁵

In 2018, the Academy of Medical Sciences set out some important correctives.⁶ As a leading UK funder, the National Institute for Health and Care Research (NIHR) has identified multiple long term conditions (multimorbidity) as a major strategic priority. NIHR has funded landmark studies advancing knowledge, including research with the National Institute for Health and Care Excellence (NICE), to develop the first multiple condition clinical guidelines and evaluations of complex service solutions to meet these needs, from integrated care hubs for older people and models of clinical generalists to holistic case management approaches in general practice.^{7–10} A review of the portfolio identified more than 190 awards totalling more than £135m of directly relevant research. Recent investments include more than £20m for large scale research collaboratives using artificial intelligence to strengthen understanding of disease clusters and determinants.

Progress has been made in agreeing common definitions, identifying research priorities, and establishing basic principles such as inclusive trial recruitment. But there is still a long way to go in advancing knowledge. A recent Cochrane review showed little impact on quality of life outcomes in the limited evidence base to date.¹¹ Loose definitions, diversity of outcomes, and multiple components of complex interventions make comparison and consolidation of findings difficult.

These are the challenges facing funding bodies the world over that want to support new multimorbidity research. NIHR has issued several calls over the past five years with poor levels of response and fundable studies. A workshop in March 2022 brought together public participants with more than forty leading NIHR investigators, programme directors, practitioners, and others to identify ways of getting more high quality multimorbidity research funded. What did we learn?

Embracing complexity, innovation, and risk

The research funding system, from expert reviewers to panels, may be conservative when faced with new and complex study designs. Interventions to redesign

care for the people who use it will be multifaceted and may not be well defined at the outset.¹² Updated guidance on evaluating complex interventions is helpful but is not intended simply to provide a blueprint for optimal study design.¹³ Healthy debate will continue on how to incorporate innovative methods which embrace complexity, but which are also robust and deliver transferable learning. At times this may mean accepting higher levels of uncertainty at the point of funding. It might include use of bridging development grants and flexible approaches with mid-project review against less specified starting plans. A watching brief is needed for more radical experiments in funding, for example, modified lotteries for grants reaching certain quality standards, which are being tested in New Zealand and elsewhere.¹⁴

Engaging the right people in the right way

Research teams may need more time and money to do this well—a multiple long term conditions “premium.” Larger sample sizes may be needed to allow for diversity and stratified analysis of subgroups where appropriate. Thought is needed on groupings that make sense to people taking part in research. Studies often focus on common clusters of physical and mental health conditions,¹⁵ but people may identify more with symptoms or problems, such as living with pain or low mobility. There are no short cuts to embedded and meaningful patient, carer, and public involvement; given the intersectional nature of multimorbidity and its association with disadvantage and risk, researchers need time to work out how to recruit and engage marginalised groups. Enhancement awards to existing programmes, exemplar studies, and other steps to reward inclusive research practices are welcomed.

Which outcomes matter?

Much debate focuses on identifying appropriate outcomes to measure impact.¹⁶ At a service level, outcomes might include greater continuity of care or appropriate service use. At an individual level, they will include functional outcomes such as ability to carry out everyday activities, as well as quality of life, treatment burden, and self-efficacy or patient activation (confidence of people in managing their own health). Funding panels may judge some of these as process, mediator, or proximal outcomes rather than endpoints in themselves. In addition, generic outcomes of any kind may not be sensitive to small changes or capture what matters most to individuals when changing services. Debate about what constitutes a “proper” outcome is needed throughout the research system. It may not be appropriate to fix

on a single primary outcome, as noted in recently updated Medical Research Council guidance.¹³ More work is needed on the best ways of using multiple outcomes to capture important elements while avoiding selective reporting.

Workshop participants articulated the challenges of funding research in this area, but also the opportunities afforded by integrated research systems like NIHR. Positive steps included targeted fellowships and exchange schemes building skills across disciplines and settings, as well as longer call windows and phased grants for researchers to build partnerships and test ambitious designs. The pandemic showed how NIHR and other research funders worldwide responded flexibly to new and urgent needs. Legacy challenges in managing and understanding long covid may prove decisive in breaking down single condition silos of clinical and research expertise. Participants confirmed the need for radical solutions to fund high quality multimorbidity research that stays close to the reality of peoples' lives.

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- 1 Salisbury C, Johnson L, Purdy S, Valderas JM, Montgomery AA. Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. *Br J Gen Pract* 2011;61:21. doi: 10.3399/bjgp11X548929 pmid: 21401985
- 2 Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380:43. doi: 10.1016/S0140-6736(12)60240-2 pmid: 22579043
- 3 Head A, Fleming K, Kypridemos C, Schofield P, Pearson-Stuttard J, O'Flaherty M. Inequalities in incident and prevalent multimorbidity in England, 2004-19: a population-based, descriptive study. *Lancet Healthy Longev* 2021;2:97. doi: 10.1016/S2666-7568(21)00146-X pmid: 36097998
- 4 Whitty CJM, Watt FM. Map clusters of diseases to tackle multimorbidity. *Nature* 2020;579:6. doi: 10.1038/d41586-020-00837-4 pmid: 32210388
- 5 Buffel du Vaure C, Dechartres A, Battin C, Ravaud P, Boutron I. Exclusion of patients with concomitant chronic conditions in ongoing randomised controlled trials targeting 10 common chronic conditions and registered at ClinicalTrials.gov: a systematic review of registration details. *BMJ Open* 2016;6:e012265. doi: 10.1136/bmjopen-2016-012265 pmid: 27678540
- 6 Academy of Medical Sciences. Multimorbidity: a priority for global health research. 2018. <https://acmedsci.ac.uk/file-download/82222577>
- 7 Guthrie B, Thompson A, Dumbreck S, et al. Better guidelines for better care: accounting for multimorbidity in clinical guidelines—structured examination of exemplar guidelines and health economic modelling. *HSDR* 2017;5:doi: 10.3310/hsdr05160.
- 8 Bower P, Reeves D, Sutton M, et al. Improving care for older people with long-term conditions and social care needs in Salford: the CLASSIC mixed-methods study, including RCT. *Health Services and Delivery Research* 2018;6:.. doi: 10.3310/hsdr06310 pmid: 30183219
- 9 Vaughan L, Bardsley M, Bell D, et al. Models of generalist and specialist care in smaller hospitals in England: a mixed-methods study. *Health Services and Delivery Research* 2021;9:.. doi: 10.3310/hsdr09040 pmid: 33651526
- 10 Salisbury C, Man M-S, Bower P, et al. Management of multimorbidity using a patient-centred care model: a pragmatic cluster-randomised trial of the 3D approach. *Lancet* 2018;392:50. doi: 10.1016/S0140-6736(18)31308-4 pmid: 29961638
- 11 Smith SM, Wallace E, O'Dowd T, Fortin M. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. *Cochrane Database Syst Rev* 2021;1:CD006560.pmid: 33448337
- 12 Salisbury C. Multimorbidity: redesigning health care for people who use it. *Lancet* 2012;380:9. doi: 10.1016/S0140-6736(12)60482-6 pmid: 22579042
- 13 Skivington K, Matthews L, Simpson SA, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *BMJ* 2021;374:.. doi: 10.1136/bmj.n2061 pmid: 34593508
- 14 Liu M, Choy V, Clarke P, Barnett A, Blakely T, Pomeroy L. The acceptability of using a lottery to allocate research funding: a survey of applicants. *Res Integr Peer Rev* 2020;5:.. doi: 10.1186/s41073-019-0089-z pmid: 32025338
- 15 Cassell A, Edwards D, Harshfield A, et al. The epidemiology of multimorbidity in primary care: a retrospective cohort study. *Br J Gen Pract* 2018;68:51. doi: 10.3399/bjgp18X695465 pmid: 29530918
- 16 Smith SM, Wallace E, Salisbury C, Sasseville M, Bayliss E, Fortin M. A core outcome set for multimorbidity research (COSmm). *Ann Fam Med* 2018;16:8. doi: 10.1370/afm.2178 pmid: 29531104