

Clinical Research: An Imperative for Global Ageing

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Background

Medical research underpins much of our ability to prevent and treat disease. Driving improvements in scientific knowledge and technology can help to improve health outcomes at scale. Good research is essential where it is needed most, and researchers, academia, funders, and national governments have the responsibility to recognise and address this.

It is well known that populations are ageing the world over. Life expectancies have been increasing across the life spectrum in virtually all parts of the globe, both developed and developing. Population projections for the two most populous countries, China and India, demonstrate the magnitude and speed of population ageing. China's 65 and over population is predicted to increase from 110 million in 2010 to 330 million by 2050; India's 65 and over population is estimated to increase from 60 million to 227 million over the same period.¹ This fundamental change to the age structure of societies will have enormous repercussions socially and economically. For example, how can we ensure that, despite the relative expansion of the older population, people can remain healthy and independent for as late into old age as possible?

Healthy life expectancy (HALE) figures suggest a more modest rise when morbidity data is factored in (9 months for every year gained in life expectancy between 1990 and 2010 at age 50 years), lending weight to the argument that much of the extra years gained at the end of life are spent in reduced health and functional ability.² This is attributed to the increased impact of non-communicable diseases such as diabetes, musculoskeletal

disorders, and certain neurological disorders such as Alzheimer's and Parkinson's disease. These, and other conditions such as ischaemic heart disease and stroke, are already a major source of ill-health and disability in older people in every world region, and this is only set to increase further in comparison to communicable diseases by 2030.^{1,3}

Research evidence of limited relevance to older people

Clinical research can aid the global challenge of reducing the impact of disease on older people in a number of ways. For example, it can test novel interventions in a careful, regulated way to determine if they can improve on standard care. The end product is scientific evidence of what works in the clinical population under study, which doctors can extrapolate to patients with similar characteristics in the real world. This continuous cycle of evidence generation ensures that day to day clinical decision making is supported by the latest and best research. Ideally, evidence based practice can help achieve better outcomes across different clinicians and institutions. However, the translation of research findings into clinical care falls short of this ideal for a number of reasons. Firstly, applicable research evidence, where it exists, is not always accessible to practicing clinicians. In fact, it can be argued that research evidence is least accessible to those who stand to benefit most from its availability (the most under-resourced and least integrated clinicians). Despite the drive towards Open Access⁴ publication of research findings, many scientific journals still require costly subscription fees. National healthcare guidelines based on systematic review of the best evidence are also normally the privilege of more affluent countries. Even setting aside the issue of accessibility, systematic reviews of the research evidence are heavily skewed towards the developed world since most clinical research is conducted in developed

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countries or studies from developing countries are crucially overlooked.⁵ This can greatly affect the translatability of research evidence to clinical practice within developing countries and patients, who despite having matching pathologies may experience very different extrinsic factors, such as how healthcare is delivered.

The translatability of research evidence may also be undermined where the study population is not representative of the clinical population it is drawn from. The prevalence of many long-term conditions such as heart disease, diabetes, and most cancers is strongly associated with age, yet older people are often excluded from clinical trials in these areas. This may be because a study employs an arbitrary upper age limit or because of other common exclusion criteria such as multimorbidity, multiple medication use, and functional limitations. Reasons for favouring this practice include a desire to demonstrate scientific rigour through maximising the internal validity of a study, and for fear of high study dropout rates. Regardless of motive, excluding older people from relevant research results in homogenised samples; disproportionately young with few or no co-morbidities and concomitant medications. Research findings based on younger, healthier population samples cannot be sensibly extrapolated to older people. This is because of important physiological differences with age affecting treatment response, an increase in risk of adverse events, and the potential for harmful interactions with co-morbidities and concomitant medications.⁶ Multimorbidity is now the norm in people with at least one chronic illness,⁷⁻⁹ and represents unique challenges in managing a person's overall health and assessing the benefits and risks associated with therapies. In addition, the priorities and preferences amongst older, multimorbid patients may be very different from that of their younger counterparts.¹⁰

Improving both research participation and access to findings

Tackling the under-representation of older people in research by, for example, ethics committees routinely rejecting applications for studies employing upper age limits would help to improve the generalizability of research findings. Older people are willing to volunteer for research if approached; research therefore, needs to make it easier for older people to take part.¹¹ Paternalistic judgments about older people being too frail and vulnerable to take part in research are often misplaced. Older people report being motivated by curiosity, altruism, the potential for personal

benefit, as well as the social contact inherent in much research.^{12,13} Common barriers restricting older people's access to research such as poor mobility, cognitive impairment, and transport problems, can often be anticipated and circumvented by good planning.¹⁴ As well as improve older people's access to clinical research, researchers need to deliver findings designed to be most useful to prospective users, chiefly clinicians and patients. The translational value of research evidence hinges on this. For example, researchers need to address interventions in multimorbid patients, and employ study outcomes which help this. In contrast to disease-specific outcomes, cross-disease, universal outcomes such as functional ability, symptom burden, and health-related quality of life yield considerably more on the impact of disease, and interventions for disease, on peoples' daily lives.¹⁵ They are also more aligned with older peoples' priorities and preferences.¹⁰

Internationally adopted person-reported outcomes help to tease out cross-region differences in the impact of disease on older people's lives. Examples include the SF-36 questionnaire or the Quality of Well-being Scale, which assess ability in Instrumental Activities of Daily Living (IADLs) (e.g. shopping, housekeeping, and transport use). However, it is crucial that any person-reported instrument is fully adapted for use in the local culture to preserve internal validity.¹⁶ Studies such as the Longitudinal Aging Study in India (LASI) are an exemplar, as the survey instrument it uses is carefully designed to be both sensitive to measuring health and functional status of Indian people and making comparisons with findings from sister health and retirement surveys in Asia such as the Chinese Health and Retirement Longitudinal Study (CHARLS) and the Korean Longitudinal Study of Aging (KLOSA).¹⁷

But even the best research is of little value if healthcare professionals are unaware of its findings. Initiatives including the World Health Organization (WHO) HINARI Access to Research in Health Programme¹⁸ provides access to major medical journals for free or at low cost to universities, hospitals and other not-for-profit institutions in many developing countries. Clinicians in countries with no clinical guidelines infrastructure may wish to view international guidelines, and frameworks exist to help adapt these locally, so preserving the quality and validity of the evidence.¹⁹

Better health outcomes for older people worldwide are possible through improved knowledge of what works and in which settings. High quality relevant research can transform the lives of older people across the globe.

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