Paving the translational ageing research pathway – training the next generation of researchers

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Abstract

Ageing is an archetypal translational research topic, spanning a breadth of academic disciplines. This poses challenges for researchers aiming to act upon laboratory findings to develop and implement interventions that directly benefit older people. Divisions between distinct academic research cultures present barriers to collaborative working. We present potential strategies to improve the translation of ageing research with examples of successful projects working across disciplines. Researchers and clinicians in ageing should be supported to develop a translational interest and receive specific training about translational research.

Key words: translational research, training, multidisciplinary, multimorbidity, older people.

Key points

- Translational research about ageing and multimorbidity has the potential to directly improve the lives of older people
- Barriers to translation include different cultures and normative languages across academic and clinical disciplines
- Researchers and clinicians from different professional backgrounds can successfully collaborate to accelerate translation
- Translational research training would help researchers and clinicians from different backgrounds develop mutual understanding

Ageing and multiple long-term conditions are core business for geriatricians and increasingly the focus of research across a range of disciplines. The holy grail is translation of discovery science such as lab-based research into first in man studies (experimental medicine), randomised controlled trials and applied research that can benefit patients directly. A recent Academy of Medical Sciences report explicitly focused on 'Bridging the pre-clinical boundary' [1]. However, this translational pathway is in its infancy with regard to research relevant to older people [2]. This commentary outlines the importance of translational research for older people and those living with multiple long-term conditions (also known as multimorbidity) and addresses potential strategies to enhance translational research within the academic community.

The science of ageing is an archetypal translational topic – to make a difference to older people (and more widely to those living with multimorbidity) we need to understand an intimidatingly large span of science. Translational medicine can be defined as *"an interdisciplinary branch of the biomedical field supported by three main pillars: benchside, bedside and community. The goal of translational medicine is to combine disciplines, resources, expertise, and techniques within these pillars to promote enhancements in prevention, diagnosis, and therapies."* [3]

Applying this to ageing we need a breadth of academic expertise, from the genetics of ageing, to cellular changes seen in ageing bone and muscle, and from the pharmacology of primary prevention to the impact of social isolation on mental and physical health. As health leaders have increasingly emphasized, tackling multimorbidity should be the direction of travel for the whole of the medical workforce [4] and this applies equally to the academic community.

There are significant challenges for this translational aspiration across the pathway from research inception to dissemination. These include cultural gaps between the "basic" science of the laboratory, the applied world of clinical medicine and the wider field of social sciences. Typical translational "gaps" were outlined in a review of UK Health Research in 1996 (Figure 1) [5]. Divisions are made plain by funding priorities, academic history and publishing norms. Until recently, older people and those living with multimorbidity have been relatively neglected as a research focus, despite the global impact on human quality of life. Fortunately, research funders are now beginning to collaborate to address the gaps in funding and prioritisation which currently limit capacity for this type of complex research [6].

In comparison to disciplines with a longstanding academic pedigree such as cardiology and neuroscience, geriatric medicine is at an earlier stage of integrating and supporting geriatricians with academic talent [7]. Design and delivery of successful clinical trials with older people and those with multimorbidity is complex, as is dissemination of the outcomes. The range of prestigious basic science studies on mechanisms of ageing in *Nature* or *Science* rarely progress beyond the laboratory, and translating this knowledge into interventions that benefit older people will require geriatricians able to span the first translational gap shown (Figure 1).

One of the ways to address cultural gaps between academic disciplines is for them to better understand each other. As in the UK, the US has a "pipeline challenge" leading to a paucity of clinical academics who have expertise in the translation of ageing biology to patient care [8] – in the US this is termed 'translational geroscience' (Figure 2). In response, US educators have suggested raising awareness of the translational pathway in undergraduate education and developing bespoke training programmes for junior healthcare professionals and laboratory scientists. An exemplar is the training programme developed by the *Geroscience Network,* open to candidates from a variety of professional backgrounds, which aims to upskill academics in the parts of the translational knowledge spectrum with which they are least familiar [9].

For a geriatrician this might be study and application of biological mechanisms, and for a laboratory scientist an introduction to the health and care of older people – both parties would move laterally and develop insight into the knowledge and skills of the other, whilst learning the normative language and culture of the other's academic realm. It is intended that this type of training infrastructure will facilitate both early-stage proof-of-concept and clinical trials in groups of older people with multimorbidity. Researchers from other fields such as neurology, cardiology or surgical specialties with an interest in older people could also join the training programme to collaborate with established "geroscientists".

In England the central rationale for the National Institute of Health Research (NIHR) Biomedical Research Centres (BRCs) is to similarly facilitate the links between the laboratory and clinical settings. There are 20 BRCs working on translational topics including cancer, mental health and surgery [10]. The [anon for review] is the only one explicitly focusing on ageing and long-term conditions and is building capacity in translational research by bringing together a cohort of PhD fellows from biomedical sciences and a wide range of clinical backgrounds. The focus of each

trainee's research varies, and yet they are united by their goal to improve the lives of older people and those with multimorbidity.

As an innovative example of translational ageing research, one of [anon for review] PhD trainees has developed a non-invasive method of electromyography employing MRI to map the loss of motor units in muscles associated with sarcopenia (MUMRI - Figure 3 [11]). He aims to apply this technique in a group of ageing individuals who already have a well characterised muscle phenotype, and by doing so explore how it could be used in the assessment of sarcopenia [12]. As a medical physicist he brings knowledge of physics, physiology and engineering and is supervised by an academic geriatrician with in-depth knowledge of the sarcopenia phenotype and the impact of sarcopenia on the lives of older individuals. Working in parallel with a multidisciplinary team of academics interested in ageing, expertise from diverse scientific fields has allowed them to refine their research design and increase the likely impact of their work.

A second example of translational research as applied to sarcopenia involves a trainee investigating the impact of cellular senescence in muscle to determine its functional consequences and identify possible interventions to improve health outcomes in ageing populations. Through the [anon for review], she has access to epidemiological and clinical studies of sarcopenia which enables her to develop and test 'senescence markers' by employing powerful cellular and molecular techniques in-vitro. Such markers build a unique signature of the muscle ageing phenotype allowing better identification of therapies with the potential to ameliorate sarcopenia [13]. Additionally, her laboratory work has involved working with novel models of ageing developed by the Mayo Clinic in the US in order to characterise the effects of cellular senescence in ageing muscle, adding to an explanatory framework for sarcopenia [14].

Addressing the challenges of ageing and multimorbidity requires a multi-faceted approach, but a key element of this is developing a network of researchers that are able to confidently span the translational spectrum. The recent co-operation amongst academic disciplines to rise to the challenge of COVID-19 is an example of what can be achieved when researchers innovate to work in new ways. In order to address COVID-19, the virology and immunology laboratory-based research on vaccines has had to be passed on to early translational researchers and will need clinical triallists, health services researchers as well as behavioural scientists for any effective vaccine to be successfully deployed and accepted by the public in due course.

Researchers and clinicians working in ageing should be supported to develop a translational interest, work with peers from different disciplines and receive specific training about translational research. Examples of successful translational research training programmes and translational collaborations should be disseminated across disciplines and thoroughly explored in order to identify and share good practice. We have an opportunity to unite talented researchers from distinct cultures in order to strengthen the impact of their work to improve the lives of older people.

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Figure 1. Pathway for translation of health research into health improvement [5]

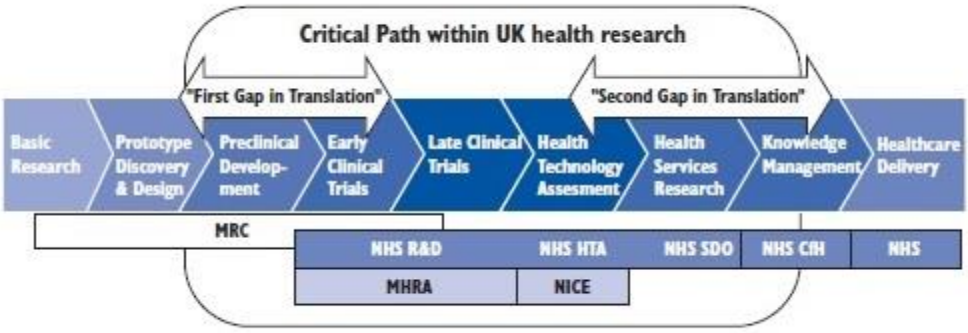

Figure 2. Scope of translational geroscience topics [9]

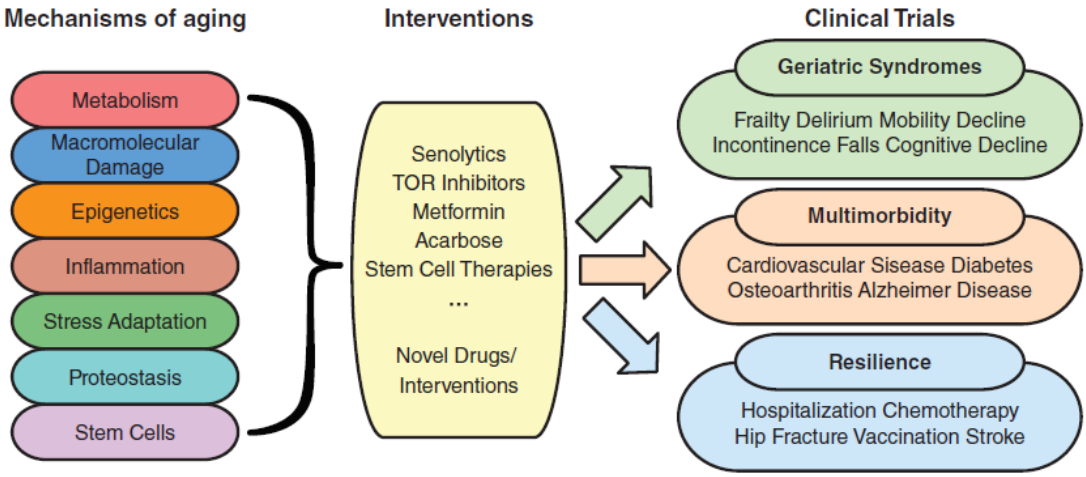

Figure 3. Motor Unit Magnetic Resonance Imaging (MUMRI) image of the lower leg in cross section, signal void in extensor digitorum longus (EDL) muscle indicated by red arrow is caused by motor unit firing and muscle fibres contracting.