Linking Geroscience and Integrated Care to Reinforce Prevention

J.R. Beard

Correspondance author: ARC Centre of Excellence in Population Ageing Research, University of New South Wales, Sydney, Australia, DrJohnBeard@outlook.com

J Prev Alz Dis 2020;2(7):68-69
Published online March 23, 2020, <http://dx.doi.org/10.14283/jpad.2020.13>

Recent advances in the field of geroscience are causing us to rethink traditional models of health and health care. Conventional approaches generally start with the diagnosis of a health condition, identify a proximal cause (and if possible, abolish it), and manage any adverse consequences. Prevention often focuses on proximal risk factors. These disease-based models worked well for infectious disease and other acute conditions but have been less successful with the chronic conditions which are now the dominant disease burden in the second half of life.

These chronic disorders require ongoing management, rather than cure. And since they commonly manifest as multiple morbidities, they often require coordinated clinical care from a diverse range of providers. Systems developed to respond to acute conditions independently are rarely structured in a way that facilitates delivery of these multidisciplinary services. Moreover, disease-based approaches may also limit the evolution of innovative research into causation and prevention since they are typically linear and siloed in nature.

Because the risk of most chronic disease increases with increasing age, the emerging field of geroscience makes the assumption that age itself is a key driver in the development of these conditions. It explores the underlying physiologic changes that occur with increasing age and looks at whether these can be prevented or delayed through lifestyle or therapeutic intervention (1). This is consistent with the observation that comorbidities are not random – certain, apparently unrelated, conditions tend to occur together. For geroscience, this is a logical result of shared biologic determinants that are themselves interrelated. Until recently, analytical models have struggled to adequately consider these complex inter-related and dynamic processes, but advances in fields such as machine learning may enable more integrated analysis of these underlying age-related changes.

While it is early days, this approach is already starting to bear fruit. For example, age-associated changes such as genomic instability and proteostatic stress are now known to trigger the development of senescent cells that are resistant to apoptosis, linger in the body and stimulate inflammation in neighbouring tissue through “a senescence-associated secretory phenotype”. By targeting these cells and their drivers, new treatments are emerging

for common conditions of older age such as osteoarthritis (2).

However, if this field is to progress, new ways are needed to measure and monitor these complex changes. Guerville et al summarise current and emerging biomarkers that might meet this need, and it is encouraging that this paper appears in a journal focused on the prevention of dementias, which are classic age-related conditions.

As Guerville et al (3) report, multiple geroscience processes have been linked to cognitive decline and/or the development of dementia. These include genomic and epigenetic changes, loss of proteostasis, deregulation of nutrient sensing, mitochondrial dysfunction, and inflammation. By highlighting these very distal influences on cognitive functioning, new aetiological models might be identified that create opportunities for prevention.

Because these very early influences are highly interrelated, it is likely that these pathways and their impacts will relate to more than just cognitive capacity. This is consistent with the close relationships observed clinically between cognitive capacity and cardiovascular functioning (for example the impact vascular disease can have on the progress of Alzheimer's Disease) and between cognitive and physical capacities (for example the association between high cardiorespiratory fitness and maintenance of cognitive functioning) (4).

Notably, the association between cognitive impairment and reduced cardiorespiratory fitness and motor fitness is also detectable in younger non demented subjects without marked physical morbidity (5). This highlights the importance of researching these possible determinants of dementias as early as possible in life.

Improved geroscience biomarker monitoring will help, but this will also require subtle monitoring of both physical and cognitive capacities, as well as of biomarkers linked to the development of conditions such as Alzheimer's Disease, across the life course. This functioning based monitoring has been proposed by WHO as the basis for an integrated approach to care delivery (6). This is a key focus of the INSPIRE project that is described by Takeda (7). This clinical cohort of over 1000 participants will objectively monitor key domains of intrinsic capacity every 4 months. When decline is detected, biological specimens will be collected

to explore possible causes. This ambitious project will thus both test the clinical applicability of the WHO Integrated Care for Older People approach and link this to recent advances in the field of geroscience. Together this research offers intriguing new possibilities for prevention, not just of dementias but of broader age-related declines.

References

1. Ferrucci L, Gonzalez-Freire M, Fabbri E, Simonsick E, Tanaka T, Moore Z, et al. Measuring biological aging in humans: A quest. *Aging Cell*.n/a(n/a):e13080.
2. Childs BG, Gluscevic M, Baker DJ, Laberge R-M, Marquess D, Dananberg J, et al. Senescent cells: an emerging target for diseases of ageing. *Nature Reviews Drug Discovery*. 2017;16(10):718-35.
3. Guerville F., De Souto Barreto P., Ader I. et al. Revisiting the Hallmarks of Aging to Identify Markers of Biological Age. *J Prev Alz Dis* 2020;1(7):56-64
4. Kurl S, Laukkanen JA, Lonnroos E, Remes AM, Soininen H. Cardiorespiratory fitness and risk of dementia: a prospective population-based cohort study. *Age and Ageing*. 2018;47(4):611-4.
5. Gnosa K, Marczak A, Binder J, Adler G. Impact of Physical Fitness on Cognitive Performance in Patients at a Memory Clinic. *Dementia and Geriatric Cognitive Disorders Extra*. 2019;9(1):129-35.
6. Thiyagarajan JA, Araujo de Carvalho I, Peña-Rosas JP, Chadha S, Mariotti SP, Dua T, et al. Redesigning care for older people to preserve physical and mental capacity: WHO guidelines on community-level interventions in integrated care. *PLoS Med*. 2019;16(10):e1002948-e.
7. Takeda C., Guyonnet S., Sumi Y. et al.. Integrated Care for Older People and the Implementation in the INSPIRE Study. *J Prev Alz Dis* 2020;2(7):70-74