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COMMENTARY

Translational research on aging: clinical epidemiology as a bridge between the sciences

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Using the principles of clinical epidemiology, public health officials were able to organize society to prevent the transmission of disease and premature death well before the basic science mechanisms of such interventions were understood.[1] Using the same principles, the association between aging, disease, disability, and social structures has been recognized for at least a century.[2] Community-based surveys in the 1950s identified a litany of medical, psychological, and social ailments common among older adults. Since that time, dozens of longitudinal cohort studies in multiple countries have reported similar findings: (1) most older adults live independently at home and most of their needs are provided through informal care systems; (2) these older adults suffer from unmet social and medical needs; and (3) the lack of social, economic, recreational, and educational opportunities contribute to disability.[2] These studies also revealed that conditions once thought to be inevitable concomitants of normal aging were, in fact, preventable or could be properly managed so as to prevent excess disability. A cohort study of older adults in 2013 would reach similar conclusions. What continues to change, however, is this boundary between normal aging and disease and, thus, the range of potential targets for medical or social intervention.

In the 21st century, the pathophysiology and cellular mechanisms of certain diseases were found to overlap with the basic mechanisms responsible for cellular homeostasis as well as cellular senescence. Furthermore, scientists reported that changes in the micro and macro environment could modulate these basic cellular mechanisms, and some of these mechanisms may be in a competitive balance. Thus, the mechanisms that protect against cancer might also program cell death, and changes associated with an aging organism might also increase susceptibility to cancer.[3] With a growing understanding of cellular mechanisms, are we now poised to influence both the prevalence of age-related disease and slow the rate of aging? Given such tools, could society organize itself in such a way to apply these principles?

This special issue of *Translational Research* provides an update on our progress in translational research on aging. Viewed from a scientist's perspective, our progress over the past century has been astonishing. Viewed

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from the perspective of public health, our progress has been meandering, poorly integrated, imbalanced, with low impact, and high cost. We can cure some cancers and prevent heart disease, but millions of humans still have no safe drinking water. Our stakeholders are understandably inpatient about the slow rate of translation between basic science discoveries and improvements in the effectiveness and efficiency of public health. While the chorus may have grown louder regarding the importance of translational research, the concept is hardly new. Fifty years ago, President Johnson empanelled a Presidential Commission because cancer, heart disease, and stroke were identified as the new leading causes of death.[4] The President suggested that the excess mortality was due both to insufficient biomedical knowledge and a failure of the benefits of what was already known to reach the public. While tremendous advances have been made in our understanding of basic biological mechanisms, the progression and implementation of these new ideas into practice is too slow—variously described as a gap or a chasm—between what we know and what we do.[5]

To overcome this "translational" gap, much of the current national efforts have focused on developing new research methodologies, new mechanisms of funding research, and the need to create multidisciplinary research teams with expertise in translational sciences. One such 'roadmap' initiative from the US National Institutes of Health (NIH) resulted in the establishment of Clinical and Translational Science Awards in 2006.[6] This new research infrastructure funding mechanism sought to establish "integrated homes" across academic medical centers for supporting clinical and translational research. A key feature of these awards was the mandate to develop research infrastructure through partnerships with academic centers, clinical service providers in the community, and commercial organizations developing novel therapies.[7] Following the funding of about 60 Clinical and Translational Science Awards across the US, the NIH established a new center in 2012, the National Center for Advancing Translational Sciences to manage the network of Clinical and Translational Science Awards as well as promote novel approaches to translating research evidence into effective therapies and clinical interventions.[8] At the request of Congress and the NIH, the Institute of Medicine recently completed an evaluation of the Clinical and Translational Science Awards. The conclusions of this report recognized the need and importance of this infrastructure as well as its future importance in helping move discoveries toward impactful interventions at the level of communities.[9]

As programs such as the Clinical and Translational Science Awards have developed, translational scientists have increasingly recognized the importance of the bidirectional or multidirectional exchange between basic science, clinical medicine, and public health.[10] Before commenting on the articles in this special issue, we turn first to a brief review of the history of aging research as evidence of the fundamental role of clinical epidemiology in facilitating the bidirectional exchange of knowledge between basic science, clinical medicine, and public health. We also suggest a continuing role for clinical epidemiology as the bridge between the sciences.

One of the first textbooks devoted to aging was published in 1939 under the editorship of Vincent Cowdry, a cytologist at Washington University in St. Louis.[11] Cowdry's textbook might rate as one of the broadest interdisciplinary treatise on aging ever published. The text included chapters ranging from the aging of plants, to age-related diseases in humans, to mental health in older adults, to the sociology of aging. Writing in the foreword to Cowdry's textbook, Lawrence K. Frank, from the Macy Foundation summarized the state-of-the-art:

> *"Two conflicting views are held today by students of aging in man. One considers aging as an involutionary process which operates cumulatively with the passage of time and which is revealed in different organ systems as inevitable modifications of cells, tissues and fluids; the other view interprets the changes found in aged organs as due to infections, toxins, traumas, and nutritional disturbances or inadequacies which have forced cells, tissues and fluids to respond with degenerative changes and impairments. It appears, however, that at least some of these changes serve to maintain functioning and are therefore protective. The issue becomes sharply focused upon the possibility of distinguishing between the cumulative but physiological involutions that inevitably take place in all individuals as they grow older, and pathological changes that occur in aging individuals as the results of adverse environmental conditions."*

At the time the quotation above was written, there were no systematic epidemiologic data regarding the scope and magnitude of problems in old age, no antibiotics, and no gene sequencers, among many other post 1940 developments. There was also little understanding of the difference between normal and pathologic aging and, therefore, an ambiguous role for medical care in the problems of old age. An early admonition about the poor care of the aged was published in *Lancet* in 1946.[12] Dr Warren provided a graphic and disturbing first-hand account of institutionalized older adults: