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Infrastructure and Resources for an Aging Population: embracing complexity in translational research

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Introduction

Why focus on aging research?

In the last two centuries, median life-expectancy in humans has increased markedly, from about age 45 to nearly age 80. It is generally agreed that most of this gain has come from improved sanitation, public health measures (e.g. work place safety) and advances in treating/preventing infections, but in the last fifty years remarkable medical advances for prevalent causes of middle-aged mortality such as cardiovascular disease and many types of cancer have also played a role. These developments have resulted in rapidly rising populations of older adults in all industrialized nations. For example, by 2030, approximately one in five Americans will be 65 years of age or older (Figure 1). This trend is occurring in developing countries as well, and at a much faster rate than occurred in Europe and the U.S. UN Aging statistics suggest more people age 80+ years will live in developing than developed countries by 2025 (<http://www.un.org/esa/population/publications/worldageing19502050/pdf/90chapteriv.pdf>).

As medical interventions have reduced death rates from acute illness there has been an increasing population living, and aging, with accumulated chronic illnesses. Many older adults experience multiple, chronic conditions which increases the risk of functional limitation and dependency^{1, 2}(Figure 2). It is, of course, much more expensive to care for those with multiple chronic conditions, and older adults account for the vast majority of health care expenditures due to their higher burden of illness and disability.

Lifespan vs. Healthspan—Despite marked increases in median lifespan, *maximum* human lifespan has remained essentially constant at just over 100 years. This realization has

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led to the concept of “healthspan” (reviewed in ³ – i.e. the period of time one spends in healthy, active life before the occurrence of chronic conditions, functional limitation, dependency or death.

Extending healthspan rather than focusing just on lifespan has become a major goal of gerontology and geriatric research. Focusing on healthspan may have a greater impact on healthcare cost than only addressing lifespan extension. Surviving one illness essentially means we live to experience another illness and another and another, increasing the lifetime cost of health care for an individual. However, improving healthspan has the potential to be markedly cost-saving if one can push severe, debilitating illnesses to the very end of life reducing the time one requires high cost, labor-intensive care and support.

“Return on Investment” of aging research

Of course, the goal of most biomedical research is to expand both healthspan AND lifespan. From this dual viewpoint, aging research dwarfs the potential payback of research focused on any single disease. For example, the average lifespan of a 50 year old human in the developed world is about 31 additional years. Because age is such a strong risk factor for multiple illnesses across many organ systems, addressing aging itself has a much greater benefit for extending lifespan, and certainly healthspan, than curing cancer, heart disease, diabetes, stroke, or any one illness ³. Thus, investing in aging research is likely to pay dividends in both lifespan and healthspan – and at least rivals, if not exceeds, the impact of research aimed at cure or prevention of specific diseases. Despite these strong arguments, aging research is often a difficult “sell” to the public, public/elected officials, or even the scientific community for support.

This paper describes the state of current workforce and infrastructure available for translational research in aging, and suggests important changes that are required to further translational research in aging and the care of older adults. It is imperative that isolated illness be studied in the most appropriate models, that multi-morbidity be explicitly included rather than excluded, and that outcomes of value to older adults (e.g. functional independence, quality of life), not just survival, be *primary* endpoints for translational aging research. While convincing the public of this need is an essential long-term goal, it is more important in the short-term to engage the scientific community and advance a change in the culture to one that embraces complexity – the key element, in the opinion of the author, needed to advance aging research across the translational continuum.

Finally, two key aspects of research infrastructure are NOT part of this review. Research funding is, of course, required to address the issues outlined, but the economics of research funding and priority-setting go beyond the scope of this review. Similarly, critical end-of-life issues are also integrally entwined in aging research, but palliative care and end-of-life research is a separate, though related, standing area of research that would require more space than is available within this review. Both issues, frankly, are also outside the expertise of the author, and thus, this review focuses on the common issues outlined in the prior paragraph.

Infrastructure Elements

I. Work Force

Declining numbers of physicians entering Geriatrics—Despite the tremendous need for geriatricians, there has been a precipitous decline in physicians becoming certified in geriatric medicine (Figure 3). This is due in part to the elimination of a practice pathway that allowed practicing physicians to become certified without completing fellowship training. But more concerning is the continuing lack of interest in graduating students and residents in geriatric medicine. Figure 3 shows the large gap between the number of geriatricians needed vs. the supply (Fig. 3A) and the number of offered fellowship positions vs. the number of positions filled for geriatric fellows (Fig. 3B). The number of academic geriatricians continues to decline as well ⁴. A number of alternatives to fill the clinical void have been proposed including geriatric competencies for all medical students ⁵ and residents in Internal Medicine and Family Medicine ⁶. However, these approaches do not address the research needs for clinical and translational investigators. While the elimination of the second year (and thus the research component) of geriatric training in 1998 was an attempt to increase the popularity of the specialty, it had essentially no effect (Fig. 3C). The change may have even subliminally sent the message that Geriatrics is not a research-based specialty and there have been calls to return Geriatrics training to two years – with the second year primarily focused on research. Redesign of the Geriatrics Training curriculum has been championed by some who advocate extending Geriatrics training to 2–3 years for academic programs and would place Geriatrics training on par with all other Internal Medicine subspecialties – all of which require at least two years of fellowship training.^{6a}

Successful Junior Faculty Development Programs for Aging Translational Research—New models of support have been championed in the last two decades to develop a cadre of research professionals focused in aging and the care of aged adults to address the paucity of researchers in geriatrics. These programs, public, private, local, regional, national, disease-specific and -nonspecific span the training spectrum from student to resident to post-doctoral positions to faculty appointments. There is not enough room to exhaustively outline these programs in this manuscript, but several junior faculty programs specifically created to enhance *translational* research in aging will be reviewed to assess critical factors of success. Though threatened by recent financial challenges in the public and private sector, these award programs are still active at present and provide an avenue for interested faculty to move into this important arena. Their conceptual foundation rests on the need to draw investigators from across the biomedical spectrum into the field of aging, and to “gerontologize” translational research – i.e. expand it to every NIH institute rather than limit understanding of the importance of aging, multimorbidity and functional outcomes to the NIA.

Paul B. Beeson Career Development Awards—The Paul B. Beeson Career Development Awards in Aging Research Program was named after the first Director of the National Institute on Aging (NIA) and began in 1994 “to foster the independent research careers of clinically trained investigators whose research will enhance the health and quality of life of older Americans” ⁷. The program also works to strengthen research in aging at

institutions where Beeson awardees hold faculty appointments, and to translate research into treatment and prevention strategies. The Beeson Program began as a private foundation-sponsored endeavor funded by the John A. Hartford Foundation, the Commonwealth Fund, The Atlantic Philanthropies, the Starr Foundation, and an anonymous donor. In 2004, it became a public-private partnership with the NIA becoming a cosponsor. The Beeson Awards are now administered through the NIA K mechanism: Mentored Clinical Scientist Development (K08) award or the Patient-Oriented Research Career Development (K23) award with private foundation dollars enhancing the number and amount of the award, sponsoring annual alumni meetings, and other events (e.g. occasional Beeson symposia at the American Geriatrics Society Annual Meeting). The NIA, the National Institutes of Health (NIH) Office of Dietary Supplements, the American Federation for Aging Research (AFAR), and as of 2010, the National Institute of Mental Health and the National Institute of Neurological Disorders and Stroke co-administer the Beeson Program. Though administered as a K award, Beeson awardees receive much greater funding for the research component than typical NIH K awards – thus, the Beeson is a “super-K,” and one can apply to convert an early K08 or K23 to a Beeson if it is appropriately aging-focused.

The effect of the Beeson Program on individuals⁸ and institutions⁷ has been recently reviewed, and the impact undeniably positive. Awardees span at least 40 institutions with scholars doing research in >30 areas of high impact for the health of older adults. Only five of 139 Beeson Scholars reported from 1994–2008 had left academics. Seventy-one percent of Beeson awardees received subsequent research funding directly stemming from their work under the Beeson Program, and 91% have served as mentors to medical students, residents, fellows and/or junior faculty focused in aging research, and there have been major impacts on geriatric research and education documented at “Beeson-impacted” institutions⁷.

T. Franklin Williams Scholars (TFWS) and Dennis W. Jahnigen Scholars (DWJS) Programs—These two ‘sister’ programs are closely linked and aim to integrate geriatric aging research into the specialties of Internal Medicine (TFWS; <http://www.im.org/AcademicAffairs/Aging/TFWS/Pages/default.aspx>) or the surgical and related specialties (DWJS; <http://specialists.americangeriatrics.org/jahnigen/apply/default.php>). Both programs began about 2002 and were originally funded by The John A. Hartford Foundation and Atlantic Philanthropies, Inc. The TFWS Program is administered by the Association of Specialty Professors and its partner Internal Medicine specialty societies, and the DWJS is administered by The American Geriatrics Society through its Surgical and related specialties Section. From 2002–2010 the programs worked through individual societies and their junior faculty support programs to co-fund promising investigators very early in their career – often *before* the applicant was competitive for a K award. Thus, these awards often served as a pre-K award in contrast to the Beeson Program. Both the TFWS and DWJS programs evolved to a public-private partnership with NIA in 2011 called the Grants for Early Medical and Surgical Specialists in Aging Research (GEMSSTAR) Program.

GEMSSTAR is a highly innovative partnership for clinical scientists very early in their career. Having completed specialty training junior faculty with an interest in aging or geriatric illnesses within their specialty are eligible apply for an R03 two year award through an NIA-sponsored, annually issued RFA. Geriatricians reaching out to a research field

within specialty medicine or surgery/related field are also eligible. If the applicant receives an R03 score in the potentially fundable range, they are then invited to put together a Professional Development Plan (PDP) that can be sponsored by a TFWS or DWJS partner, or another matching entity (foundation, institution, CTSA, etc). Receipt of the R03 is contingent upon acquiring matching funds to support the PDP which involves mentoring in both one's specialty and geriatrics/aging.

Like the Beeson Program, the goals and success of the TFWS/DWJS/GEMSSTAR programs is undeniable as outlined in recent publications^{9–11}. Each program has named just over 100 scholars since inception with return on investment running for both programs running about 5 to 1 based on awarded extramural research funding to TFWS or DWJS even given their very junior status¹⁰ and unpublished data from AGS and ASP).

Claude D Pepper Older Americans Independence Centers (OAICs) Research Career Development Cores (RCDC)—The NIA sponsors 13 OAICs

(www.peppercenters.org) focus on preventing disability and maintaining independence for older adults; an RCDC is a required component. The RCDC provides junior faculty support for research within the OAIC mandate typically using intensive mentoring by multiple mentors, group support, writing groups/pre-submission review of grants and papers, and success of these individuals as a key component of evaluation for renewal. Critically, RCDC supported faculty are immediately surrounded by an infrastructure of other key cores in the OAIC – though specific cores vary from across centers each must have a pilot studies core and most include some type of clinical research core, data management and statistics, sample/data repositories and sharing options, instrument libraries or other key core areas of expertise. Each institution with an OAIC has extensive programs in aging research in which the OAIC plays a key role.

What do these programs have in common? First and foremost, they create a community of researchers that share experiences, time, talent and support. There are many mentored programs (K awards and VA CDAs for example) but the mentoring is local and specific. Beeson, DWJS/TFWS and OIACs share a common bond across institutions, within and between specialties, and have multiple opportunities to network throughout the year. They see each other several times a year at their specialty society meetings, the AGS and/or Gerontological Society of America (GSA) meetings. In addition there are specific meetings annually for: OAICs that has more than half the program focused on junior faculty, and the Beeson/TFWS/DWJS programs all support alumni meetings where scholars present their science among peers, discuss triumphs, pitfalls and shared success, and there are career development sessions for each stage in the progression of academic faculty.

Second, the shared NIH/Public domain provides both an imprimatur of excellence for junior researchers, and an avenue to demonstrate excellence. Supported faculty members are immediately recognized as experts in their field and have opportunities to shine at an early age. There are often few, and occasionally no, other specialty experts with a focus in aging – one of the most important topics in medicine today. But importantly, these individuals come from their specialty, and recognized as specialists rather than geriatricians merely “visiting” a specialty. This provides a “Trojan horse” approach bringing geriatrics to specialty fields.

For example, it's much more likely that a cardiologist will seek out or happen across a chapter in a cardiology text or symposium at a cardiology meeting focusing on geriatric cardiology than go out of his/her way to find a geriatric text book to read a chapter of geriatric cardiology. There is a legitimacy or "street cred" of a specialist that understands the specialist world, underwent a fellowship in a specialty and has inside access to specialty society education committees, research committees, program selection committees, etc.

Third, dual function means twice as many opportunities to be chosen as a speaker for national meetings, get invited to author texts, and it allows for dual assignment of grant applications. Importantly, this is not, and cannot be seen to be, a lack of focus. It is an important aspect of bridging the gap.

Finally, these programs have been successful because of the pride of the alumni from these programs, and their desire to recruit and mentor those who follow. Once named a Beeson, TFWS, DWJS, or OAIC RCDC scholar, they are recognized as such for life and they have tremendous pride in their named program. They are not an anonymous K or VA CDA awardee, they are part of fraternity/sorority with deep ties. They look out for each other, follow each other's careers, recruit to the programs with enthusiasm and mentor those who answer the call.

In the opinion of the author, these critical aspects have contributed heavily to the success of these programs; most alumni of these programs are still in academics, engaged in research and finding funding success even in tough times. These programs, and others like them, will need to continue, and can serve as a blueprint for other programs needed to meet the workforce challenges required for translational research in aging.

The success of these junior faculty programs is undeniable. On average, Beeson/TFW/DWJ/GEMSSTAR/OAIC RCDC Scholars with 3–10 years of opportunity since initiating their award have garnered about a 5-fold return on investment based on federal and private funding awarded after being named a scholar (unpublished data; Association of Specialty Professors and American Geriatrics Society). Just a few examples of key advances spearheaded by these individuals – within only a few years of their first faculty appointment – include: quality outcome measures for older surgical patients,^{11a,11b} identification of a novel, intra-mitochondrial renin angiotensin system important in aging,^{11c} a more accurate definition of COPD in seniors than can be achieved with current guidelines by recognizing age-related variability,^{11d} and the introduction of frailty and functional status to more accurately select senior transplant recipients vs. age alone.^{11e,11f,17}

II. Translational Aging Resources

Animal Resources—There are a number of important animal resources for aging research primarily maintained and catalogued by the NIA (<http://www.nia.nih.gov/research/scientific-resources>). A number of rodent resources are available including mice and rats across the age spectrum of various strains, F1 crosses and calorie restricted animals (Table). In addition, a tissue bank of specimens is available. All investigators with an aging-focused grant are eligible to access these resources, but pricing and priority access vary depending on availability of specimens/strains and NIA grantee vs. other grant support. Other options

for rodents include retired breeders from several manufacturers, however, investigators are cautioned that retired males often fight when repaired in housing and may require individual cages. Females that have produced multiple litters have substantial variation from nulliparous females for some biologic systems (e.g. immunology).

In addition to rodent animals and tissues, nonhuman primate (NHP) resources are also available through the NIA (<http://ipad.primate.wisc.edu>). When compared to rodents, nonhuman primates better model a number of critical issues in aging research – in particular, NHPs have more human-like joints and movement that may better simulate arthritis, functional decline and sarcopenia than rodent models (e.g. ^{12–16}). Recently, functional assessments that mimic physical performance measures in humans have been demonstrated to decline with age in NHPs, an important step forward for translational models of functional decline and frailty ¹⁶.

A number of other animal resources are available and outlined in detail at <http://www.nia.nih.gov/research/scientific-resources>.

Cohorts/Populations—The NIA and other NIH institutes have invested heavily in a number of large cohorts either directly to follow aging in the long-term (e.g. Baltimore Longitudinal Study of Aging (BLSA), Health Aging and Body Composition (Health ABC)), disease-focused in an aging-related area (e.g. Multi-ethnic Study on Atherosclerosis (MESA), Cardiovascular Health Study (CHS), or in specific groups that have now entered geriatric ages (e.g. Women’s Health Initiative (WHI)). Other important surveys provided critical data in aging cohorts (e.g. Health and Retirement Survey). These are summarized in a number of websites with access information and specimen repositories (<http://nihlibrary.ors.nih.gov/nia/ps/niadb.asp>, <http://www.nia.nih.gov/research/dbsr/publicly-available-datasets>, <http://www.icpsr.umich.edu/icpsrweb/NACDA/>).

Networks—Six NIA-funded networks exist in aging research: Alzheimer’s Diseases Centers of Excellence – aimed at Alzheimer’s and other dementia research (<http://www.nia.nih.gov/alzheimers/alzheimers-disease-research-centers>); The Claude D. Pepper Older Americans Independence Centers (OAICs) – focused on preserving/restoring physical function and independence (www.peppercenters.org); Nathan Shock Centers – for basic biology of aging research (<http://www.nia.nih.gov/research/dab/nathan-shock-centers-excellence>); Roybal Centers – focused on psychosocial issues in aging (<http://www.nia.nih.gov/research/dbsr/edward-r-roybal-centers-translation-research-behavioral-and-social-sciences-aging>); Centers on the Demography and Economics of Aging (<http://www.nia.nih.gov/research/dbsr/centers-demography-and-economics-aging>), and Minority Resource Centers for Aging Research (RCMARs) (<http://www.nia.nih.gov/research/dbsr/resource-centers-minority-aging-research-rcmar>). In general, these are institutionally-focused centers that include core services, pilot funding and junior faculty development programs, but minimal/modest inter-institutional cooperative research, though this is changing slowly (see **Culture Change** below). The Veterans Affairs (VA) system also has the Geriatric Research Educational and Clinical Centers (GRECCs) that provide similar support core, mentoring and pilot support. Though not specifically directed at research, the John A. Hartford Centers of Excellence ([*Transl Res.* Author manuscript; available in PMC 2015 May 01.](http://www.jhartfound.org/grants-strategy/centers-</p>
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of-excellence-in-geriatric-medicine-and-training-national-program-o) administered through the American Federation for Aging Research (AFAR; <http://www.afar.org/research/centers/>) have also provided mentoring and salary support for junior faculty in geriatrics, though this is being phased out as JAHF strategic plans transitions toward developing models of care and clinical impact.

Finally, PCORI has issued RFAs to establish research sites for two types of networks. Clinical Research Data Networks (<http://www.pcori.org/funding-opportunities/funding-announcements/clinical-data-research-networks-cdrn-improving-infrastructure-for-conducting-patient-centered-outcomes-research-pcor/>) and Patient Powered Research Networks (<http://www.pcori.org/funding-opportunities/funding-announcements/patient-powered-research-networks-pprn-improving-infrastructure-for-conducting-patient-centered-outcomes-research-pcor/>). The stated goal of these two networks, which have not yet been reviewed or funded at the time of this writing, is to improve the capacity to conduct comparative effectiveness research (CER) efficiently, by “creating a large, highly representative electronic data infrastructure for conducting clinical outcomes research.”

Tools and Toolboxes—The NIH Toolbox is a recently released, multidimensional set of brief measures assessing cognitive, emotional, motor and sensory function across the lifespan from ages 3–85. The underlying principle leading to the NIH Toolbox was a need for a standard set of measures that could be used across diverse study designs and settings to assess neurological and behavioral function over time. This facilitates the study of functional changes across the lifespan, including evaluating intervention and treatment effectiveness. Many resources in the toolbox are free, but fees may apply for use of the NIH Toolbox in projects not funded by NIH.

The Patient-Reported Outcomes Measurement Information System (PROMIS®; <http://www.nihpromis.org/>) is a free resource and was developed as part of the NIH Roadmap initiative to provide validated patient reported outcomes for clinical research and practice. PROMIS® uses both computer adaptive testing and traditional “paper and pencil” instruments in global health, physical function, fatigue, pain, sleep/wake function, emotional distress, and social health. Currently, the PROMIS® network consists of 12 research sites and 3 administrative centers that are developing tools in several new domains and performing validation studies in new and existing domains. PROMIS® provides a unique resource in four key areas: 1. Comparability—measures have been standardized across common domains, metrics and conditions; 2. Reliability and Validity—all metrics for each domain have been rigorously reviewed and tested; 3. Flexibility—PROMIS can be administered in a variety of ways or formats; 4. Inclusiveness—PROMIS is designed to reach across all study populations regardless of literacy, language, physical function or life course.

Cultural Changes Required to Accelerate Translational Research in Aging: Embracing Complexity

If there is a single word that separates aging research from other types of translational research it would probably be *complexity*. As previously noted, the typical older adult rarely

presents with a single disease, and often doesn't even have a predominant illness – more often than not, multiple chronic conditions are present. This conflicts with the general paradigm for biomedical research – isolating a single factor/mechanism/disease to ensure that any intervention or experimental result can be clearly attributed in a causal pathway. If we are to truly affect health outcomes for older adults through translational research we must embrace complexity in every aspect.

In six recent meetings that brought multiple NIH institutes/centers together with NIA officials to set research agendas in specific areas several common themes emerged that show how far we must go to really embrace complexity^{17–22}. First, animal models for most diseases that predominately appear in old age (e.g. interstitial pulmonary fibrosis, chronic kidney disease) typically employ 2–4 month old rodents rather than aged animals – presumably due primarily to expense. Rarely, are experiments done in outbred rodents; rarer still are animal models employing common co-morbidities (e.g. studying stroke in animals with chronic kidney disease or heart failure), and almost never is multi-morbidity employed in animal studies. Further, animal studies rarely focus on anything but death/life as an outcome when much more relevant outcomes for seniors are disability/functional impairment. Simple changes in study design (inclusion of exercise tolerance in a heart failure model rather than survival as the only outcome) would go a long way toward accomplishing relevant outcomes for aging studies.

Clinical studies have many of the same challenges. Overly restrictive inclusion/exclusion criteria limit enrollment of older adults, usually in the name of simplifying study design and/or reducing needed sample size. Appropriately addressing healthcare in aging means research in subjects with multiple co-existing conditions. For example, the relative risk for disability is increased 2.3-fold in those with heart disease, 4.3-fold for those with arthritis, but 13.6-fold for those with both²³. It is impossible to ignore these issues when conducting translational geriatric research without nearly assuring failure when that research moves from simple, age-focused animal or human models into the heterogenous senior population, but most disease-oriented, specialty researchers do not consider these issues in their study design.

Important strategies that could help such studies without interfering with critical aspects of clinical trial design and internal validity should be employed. An example might be harmonization of critical functional assessments that would add very little (< 10 minutes) to overall participant burden, but allow valid meta-analyses and cross-study comparisons by using a uniform battery of physical performance measures (e.g. Short Physical Performance Battery (SPPB), Mini-Cog, Trails). A recent paper emphasizing global health outcomes to include in studies of those with multimorbidity is another example²⁴. This approach is particularly important if we are to realize the power of EMRs and other clinical data to advance the care of older adults. What if the vital signs for all patients 65 or 70 years and over included a timed up-and-go (TUG) and/or SPPB? These measures require strict standardization and training when used as major endpoints in clinical trials in much the same way blood pressure (BP) measurement must be standardized when it is a major outcome. However, just like BP, the TUG or SPPB measures can be very easily assessed in clinical situations by nurse's aides who are doing vital signs, would take < 5 minutes to

complete, provide important geriatric outcomes in large clinical datasets, and allow EMR-triggered reminders to practitioners as to who may benefit from physical therapy/home safety evaluations/fall prevention programs/etc.

An additional challenge that, if met, would greatly enhance translational research in aging, would be to harness the power of existing, but loosely affiliated centers of excellence by organizing them into true research networks that share protocols and enrollment across centers. This type of integration has become a major focus of the CTSA, and there is a small, but growing focus on aging research within the CTSA network (see <https://www.ctsacentral.org/ic> for details).

A parallel strategy might be to focus the efforts of NIA-funded centers by transforming them into more cohesive networks. While this has occasionally taken place for individual projects (e.g. Lifestyle Interventions and Independence for Elders (LIFE <https://www.thelifestudy.org/public/index.cfm>)), if aging research is to be the next critical area of research excellence it will take a cooperative group structure such as those formed in cancer or HIV. The Cancer Cooperative Groups and the AIDS Clinical Trials Groups (ACTGs) transformed research in those illness-based networks and in many cases moved the illness from an absolute death sentence 25–30 years ago into a chronic illness that rarely causes death if well managed. Like many of the suggestions outlined in this paper, it would clearly take additional resources over/above those currently allocated to the NIA-sponsored or VA-sponsored networks to function in this way. But if we ask ourselves, “where would we be in the care of HIV patients without the ACTGs and other cooperative groups?” and want to achieve similar results when addressing the care of older, multi-morbid adults, it will take a similar effort. Advances in data management and harmonization of data measures outlined previously would allow this much more economically than would have been possible just a few decades earlier.

Review Panel Expertise in Aging and Multi-morbidity

Probably the single most important resource needed to enhance translational research in aging would not add a single dime to the total cost of research. Proposals that focus on aging and embrace complexity are frequently panned in study sections throughout the NIH and the VA unless they are study sections specifically constituted to review aging research. However, proposals on heart failure, kidney disease, health outcomes and utilization, cancer, infection, wound healing, muscle atrophy, obesity, and many other conditions are reviewed across disease focused panels with very little or often no expertise in aging, even though these conditions disproportionately affect seniors. Thus, these review panels don't know to ask for functional outcomes rather than only mortality as an outcome of interest, they fail to require the use of appropriately aged animals that mimic the age of onset in humans, they don't allow, let alone demand, inclusion or stratification in key areas (age, specific common co-morbidities) in disease-specific proposals. Worse yet, when such review panels see protocols that do take into account appropriate complexity they are often labeled as unfocused and not mechanistic enough rather than being recognized for their attempt to model the human condition. A common call to have aging expertise on review panels across institutes should be a major focus to support aging research – the Trans-NIH Geroscience

Interest Group (<http://sigs.nih.gov/geroscience/Pages/default.aspx>) is a potential avenue to affect this change. Two small changes could allow us to put our collective “toe in the water;” 1) require that animal studies of diseases that disproportionately affect seniors use an appropriate age span to ensure the physiology of aging is part of the experimental design, and 2) specific emphasis on the most common dyads/triads of concordant illnesses as a way to begin embracing complexity across NIH ICs and review panels.

Conclusion

There is a large and growing population of older adults who disproportionately experience illness, declining function and disability, and consume the majority of health care resources. If we are to appropriately respond to the challenge of providing the most effective and efficient health care for this group of adults, we will need to address common obstacles that limit the applicability of the current research paradigm and allow a new paradigm to not only emerge, but flourish (Table 2). Key issues include the need to utilize and expand the workforce trained in aging research; augment specific resources in animal models, clinical cohorts, tools/toolboxes and research networks; harmonize measures and outcomes to unleash the power of large data sets and EMRs; and, most importantly, start the long process of culture change within the community of science to embrace the complexity that is needed to truly mimic the milieu required to study disease prevention and treatment for seniors.

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Fig. 1.

Increasing population of old and very old persons in the U.S. Reproduced from http://www.aoa.gov/Aging_Statistics/future_growth/future_growth.aspx

Fig 2.

Reproduced from Federal Interagency Forum on Aging-Related Statistics. Older Americans 2012: Key Indicators of Well-Being. Federal Interagency Forum on Aging-Related Statistics. Washington, DC: U.S. Government Printing Office. June 2012.

3A

FIGURE 1-1 Projected number of needed geriatricians.

SOURCE: Alliance for Aging Research, 2002. Copyright 2002 by the Alliance for Aging Research.

3B.

FIGURE 4-1 First-year geriatric medicine fellowship positions, available and filled.

SOURCE: ADGAP, 2007b.

3C.

FIGURE 4-3 Numbers of physicians newly certified in geriatric medicine, 1988-2004.

SOURCE: ADGAP, 2005.

Fig 3.

3A. Projected need and actual supply of geriatricians. Reproduced with permission from IOM (Institute of Medicine). 2008.

Retooling for an aging America: Building the health care workforce. Washington, DC: The National Academies Press.

3B. The number of Geriatrics first year fellowship positions available and filled. Reproduced with permission from IOM (Institute of Medicine). 2008. Retooling for an aging America: Building the health care workforce. Washington, DC: The National Academies Press.

3C. The number of board certified geriatricians fell dramatically once the practice pathway was eliminated (i.e. practice experience qualified one to sit for the ABIM certification exam - ACGME-approved fellowship training was not needed prior to 1994). Changing the requirement for fellowship training from two years to one has had very little impact. Reproduced with

permission from IOM (Institute of Medicine). 2008. Retooling for an aging America: Building the health care workforce. Washington, DC: The National Academies Press.

Table 1

Strains of rodents available through the NIA Aging Rodent Colony (<http://www.nia.nih.gov/research/dab/aged-rodent-colonies-handbook/available-strains>).

Inbred Rats:	Fischer 344 (F344) Brown Norway (BN)
Hybrid Rats:	F344xBN F1 (F344BN)
Inbred Mice:	BALB/cBy CBA C57BL/6 DBA/2
Hybrid Mice:	CB6F1 (BALB/cBy × C57BL/6) B6D2F1 (C57BL/6 × DBA/2) - reduced to entries every 4th month
Caloric Restricted Rats:	F344 (males only) F344BN F1 (males only) Last Entry for CR/AL Rats: DOB 8/12
Caloric Restricted Mice:	C57BL/6 B6D2F1 (males only)

Table 2

Major obstacles that impede translational research in aging and suggested, high priority approaches to overcome these limitations. For details, the reader is referred to refs 17–23 for examples of research agendas in specific fields that employ these strategies.

Obstacle	High Priority Suggested Approaches
<ul style="list-style-type: none"> Lack of well-trained researchers in aging 	<ul style="list-style-type: none"> Refocus geriatric training to emphasize research on par with other medical specialties (i.e. re-expand to a 2–3 year fellowship in geriatrics) Continue/Expand programs that engage non-geriatricians in aging research
<ul style="list-style-type: none"> Inappropriate animal models used for illnesses that most commonly occur in older age 	<ul style="list-style-type: none"> Funding agencies should require use of aged animals in models of congestive heart failure, lung fibrosis, stroke, etc Expansion of aged animal resources by suppliers (e.g. facilitated by major suppliers recording exact age of retired breeders) Focus on most common dyads/triads of concurrent illness as a means to expand research models while minimizing effects on internal validity
<ul style="list-style-type: none"> Inadequate inclusion of outcomes as/more relevant than death 	<ul style="list-style-type: none"> Inclusion of functional outcomes, disability in animal studies Healthspan measures included in animal models <i>Appropriately powered</i> clinical trials to include outcomes most relevant to seniors (preservation/return of functional capacity, universal health outcomes)
<ul style="list-style-type: none"> Limited cohorts with adequately characterized aging phenotypes 	<ul style="list-style-type: none"> Extension of follow-up for key population and disease-based cohorts to include geriatric outcomes (e.g. dementia, disability) Harmonization of functional assessments within clinical electronic records
<ul style="list-style-type: none"> Cultural rejection of complexity in science 	<ul style="list-style-type: none"> Inclusion of aging-focused researchers on standing review panels across NIH, VA and other major funders Specific calls for research inclusive of co- and multi-morbidity Development/refinement of universal health measures for individuals and populations