ENHANCING RELIABILITY IN ANTI-AGING RESEARCH: A CALL FOR ADHERENCE TO REPORTING STANDARDS

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Abstract
The global rise in the elderly population accentuates the importance of addressing challenges associated with aging, including comorbidities and declining physical function. Variability in the aging process emphasizes the potential for evidence-based biomedical innovations. Robust trials for anti-aging interventions become vital as public interest grows. Despite promising biomedical innovations, practical implementation encounters social and ethical challenges. Ensuring credibility in anti-aging research requires collaboration with biogerontology-focused journals and peer reviewers. This opinion piece delves into the unique aspects and challenges of anti-aging research and the pivotal role of adherence to reporting standards in advancing healthy aging initiatives.

Keywords: aging; research; reliability; reporting standards.

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Key Messages for Research and Practice

• The aging population worldwide is anticipated to undergo a significant increase by 2050, underscoring the importance of tackling challenges associated with aging and advancing initiatives for promoting healthy aging.

• As interest in anti-aging interventions grows, conducting robust trials to assess health span and resilience becomes crucial.

• Despite promising evidence-based biomedical innovations in anti-aging research, practical implementation faces social and ethical challenges.

• To maintain the credibility of anti-aging research, involving biogerontology-focused journals and peer reviewers is essential. Proposing a dedicated ethical organization to collaborate with researchers, establish guidelines, and achieve a consensus on reporting standards is imperative.
Presently, 11% of the global population is aged 60 and above, and projections indicate a rise to 22% by 2050 [1]. The increased life expectancy of the population and the aging process introduces age-related challenges, marked by the prevalence of multiple comorbidities and a decline in physical functioning among this group [2]. Recognizing this, the World Health Assembly endorsed the Decade of Healthy Ageing (2020-2030) to improve the well-being of older individuals [3].

The process of aging exhibits variability among different species, individuals, organs, tissues, cells, and subcellular compartments, and the field of anti-aging research has promise for the development of evidence-based biomedical innovations that can enhance individual well-being [4]. While anti-aging research holds promise, its application faces social and ethical challenges [5]. This opinion piece underscores the importance of upholding credibility in anti-aging research through adherence to reporting standards.

**The Current Landscape in Antiaging Research**

Gerontology is a scientific field that examines the biological, social, psychological, and policy-related dimensions of aging. It is distinct from geriatric medicine, a subspecialty of medicine that treats the illnesses and clinical issues common to the elderly [6]. Biogerontology involves investigating the biological foundations of aging and its linked diseases [4].

One key aim of biogerontological research is to apply the insights gained from basic research to develop new approaches such as diets, drugs, or other medical interventions. These endeavors aim to prevent and treat human diseases while promoting healthy aging and longevity.

Although interventions demonstrating positive results in animal models exist for addressing the aging process, their applicability to humans remains uncertain. Identifying biomarkers linked to age and morbidity becomes essential to ensure a successful translation, given the complexities involved in conducting longitudinal trials [7].

As gerontology expands, public interest is on the rise. For example, a study in a dermatology clinic found that over fifty percent of patients actively seek anti-aging therapies, with nearly two-thirds expressing keen interest in future interventions [8].

**Unique aspects of anti-aging research**

Clinical trials targeting aging face challenges in determining the right age groups for interventions and potential side effects [7], in addition to challenges with obtaining regulatory approval, designing studies, and defining study outcomes in a clinically meaningful manner [9]. Critical considerations include balancing the selection of the study population, involving both sexes, considering sex-specific pathways in aging biology, and considering whether targeting healthy older adults for primary prevention or frail, multimorbid individuals with a higher risk tolerance for secondary prevention trials [10]. Adjusting inclusion criteria to allow mild chronic conditions could be beneficial [9].

A long-term, double-blind, placebo-controlled trial is essential to evaluate aging processes comprehensively [9]. However, the variable under study, the extension of quality lifespan, is influenced by numerous factors, posing ethical dilemmas in obtaining reliable trial data due to the difficulty in eliminating confounding variables [10].

Essential for advancing human trials are surrogate markers for lifespan and health span that must show correlations with aging and treatment response [7]. Currently, suggested biomarkers, such as c-reactive protein (CRP) for inflammation and insulin-like growth factor-1 (IGF-1) for metabolism, are complemented by the advent of artificial intelligence-driven predictors, offering optimism for more precise measurements of the aging process, with careful consideration given to biomarker selection.

In antiaging research, there’s potential to draw inspiration from oncology, where the FDA employs an «accelerated approval» process, which allows provisional approval based on Phase 2 data and offers a possible model for studying fundamental aging processes [9]. The rationale behind provisional approval is the belief that the potential benefits outweigh the associated risks, especially when efficacy is evident in significant clinical outcomes. This framework enables a more streamlined advancement, presenting an alternative to the traditional and lengthier Phase 3 trials.

**The Crucial Role of Reporting Standards in anti-aging research**

Applying established ethical and professional standards to all scientific research activities can help reduce research misconduct and improve scientific evidence.
The irreproducibility of scientific results is influenced by various factors, encompassing flaws in experimental design, statistical analyses, and inadequate reporting [11]. Research integrity, ethics, and responsible conduct training are some ways to achieve these goals [12]. The importance of rigorous reporting standards cannot be overstated in biogerontological research, as they form the bedrock of transparent and reliable scientific communication.

Ensuring exceptional quality in randomized clinical trials (RCTs) is paramount, especially in anti-aging research with high stakes. These trials should not just meet but exceed reporting standards like CONSORT [13]. to ensure reproducibility and reliability for patients.

Open science, promoting collaborative and transparent research with freely accessible data, holds promise in gerontological research by implementing preregistration for transparency and credibility, specifying data collection, analysis plans, and criteria for data exclusion [14].

**Challenges and barriers to anti-aging research**

The quest for impactful publications and insufficient training in experimental design and statistics can result in rushed experiments, increased error rates, and selective reporting, highlighting the crucial need for comprehensive education and tools to enhance scientific rigor [11]. The methods section in many manuscripts often lacks sufficient detail, impeding critical review and replication [11]. Overcoming these hurdles requires transparent reporting, detailed experimental design, improved statistical rigor, and rigorous peer review in anti-aging research.

In anti-aging research studies, the reliability and interpretation of outcomes are profoundly influenced by participant adherence to the prescribed interventions. Martens et al. conducted a randomized, double-blind, placebo-controlled, crossover clinical trial focusing on oral supplementation with nicotinamide riboside (NR) to improve cardiovascular and physiological functions associated with aging in healthy middle-aged and older adults [15]. The study emphasizes the critical role of adherence, with exceptional rates exceeding 95% for both NR and placebo capsules, showcasing the protocol’s robustness. The observed tolerability and safety of NR, combined with a minimal dropout rate (less than 10%) due to side effects during NR treatment, underscores the importance of participant compliance in mitigating potential adverse events. The study’s ability to derive meaningful conclusions showing trends in cardiovascular health benefits relies on these high adherence rates. In essence, participant adherence is a pivotal factor shaping the internal validity of anti-aging research, enabling researchers to discern the true impact of interventions and enhancing the credibility of outcomes in the pursuit of understanding and modulating the aging process.

An example of an anti-aging study adhering to rigorous guidelines is the Targeting Ageing with Metformin (TAME) trial. Supported by the American Federation for Aging Research, it collaborates with the FDA to designate a composite of age-associated conditions as an approved medication target. The trial’s primary objective is to explore metformin’s potential to delay the onset of major age-related diseases and extend health span [16].

In biogerontology, challenges arise when research standards are not adhered to, impacting the interpretation of results and compromising the reliability of key findings. An example is seen in a study investigating the role of chronic inflammation in accelerating aging, where concerns arose due to a significant amount of unreferenced overlap with multiple articles that raised questions about the evidence’s robustness, ultimately leading to the article’s retraction [17].

Another example is the research article on genetic signatures of exceptional longevity, initially published in Science, that was retracted due to significant setbacks [18]. The study, which investigated the genetic contribution to healthy aging through a genome-wide association study of 1055 centenarians and 1267 controls, presented a genetic model with 150 single-nucleotide polymorphisms (SNPs) predicting exceptional longevity with 77% accuracy. Unfortunately, technical errors in the Illumina 610 array and inadequate quality control resulted in false positive SNPs, prompting a reevaluation, and the revised analysis showed substantial changes from the original publication.

Such incidents emphasize the importance of adherence to rigorous research methodologies to ensure the integrity and reliability of findings to understand the complexities of aging processes.

**Conclusions and Recommendations**

Aging research encounters challenges in study design, inclusion complexities, and statistical power. Regulatory approval for aging-related indications adds complexity, requiring both sexes’ inclusion and meaningful outcome definition. Recognizing the pivotal role of biogerontology-focused journals and peer reviewers is crucial for shaping and expanding anti-aging research.
They should assess scientific merit and adherence to ethical standards, ensuring transparent reporting. Journals must retract papers not meeting stringent standards, reinforcing a commitment to research integrity. Unique considerations in anti-aging research require a dedicated, ethical organization collaborating with researchers to establish guidelines. Achieving a consensus on reporting standards is imperative for transparent and robust reporting. Through these efforts, assurance is provided that exploring and manipulating the aging process is grounded in powerful science, paving the way for significant advancements in healthy aging. It’s a shared responsibility to uphold the integrity of the collective endeavor to enhance human life’s quality and span.

**REFERENCES**


