

RESEARCH PAPER

Ethical concerns in aging research: perspectives of global frontline researchers

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This study investigated the ethical landscape of aging research amid the increasing global focus on extending the human lifespan and health span. Our global survey of 180 researchers across 38 jurisdictions revealed divergent perceptions of aging, a consensus regarding the feasibility of delaying aging, and multiple perspectives regarding lifespan extension. The present findings underscore a paradigm shift toward inclusive and ethically sound research, emphasizing the need for an approach that strikes a balance between basic and clinical research. In addition, this study highlighted key ethical concerns in aging research, including the effects of misleading advertising, potential inequality in access to aging interventions, and risks pertaining to the extrapolation of research findings from lower-model organisms to humans. The insights presented in this paper call for an integrated approach for overcoming the complex ethical and societal challenges in aging research to ensure responsible and equitable advancements in this burgeoning field.

aging | ethical landscape | ethics | surveys and questionnaires

INTRODUCTION

As the 21st century unfolds, the dynamics of aging and its effects on society are becoming increasingly significant. The rise in life expectancy, which constitutes a triumph of modern medical and societal advances, has brought aging research into sharp focus. This field, once peripheral, now stands at the forefront of biomedical exploration, driven by a substantial increase in recent decades in the global population of individuals aged ≥ 60 years, which is expected to account for 22% of the total global population by 2050 (World Health Organization, 2022). This demographic shift, coupled with a tripling of the global population of individuals aged >80 years between 2020 and 2050, has catalyzed a paradigm shift in aging research, which has moved from symptom-focused research to aging mechanism-focused research (World Health Organization, 2022). This shift has led to the exploration of aging interventions—including pharmaceuticals, gene therapy, regenerative medicine, and immunotherapy—with several interventions having already progressed to clinical trials (Nielsen et al., 2022). In addition, the evolution of research tools such as genome sequencing and data science has further enriched this field. However, this rapid advancement has brought with it various ethical and societal challenges, and the complexity of these challenges encompasses scientific, metaphysical, and

socioeconomic dimensions, necessitating comprehensive understanding and careful navigation.

In light of the aforementioned information, the present study sought to outline the ethical landscape of aging research by analyzing the perceptions of frontline researchers worldwide. Recognizing the diversity in ethical values due to cultural, economic, and social factors, we explored how these values shape researchers' approaches to aging research and its societal implications. Awareness of the global perspective is essential for developing a balanced and inclusive approach to tackling the ethical dilemmas posed by advancements in aging research. As we stand on the cusp of a new era in this field, alignment of scientific progress with ethical and societal considerations is imperative to ensure responsible and equitable advancements in aging research.

Era of aging research

The 20th century witnessed a considerable increase in the global life expectancy, rising from an average of 55.1 to 83.9 years throughout that century; this rise was propelled by advancements in technology, education, the economics, and medical care (Scott, 2021). In addition, this demographic shift was accompanied by a rapid increase in the global population, particularly that of the elders. The global population of individuals aged

>60 years, which was 12% of the total global population in 2015, is expected to increase to 22% of the total global population by 2050 (World Health Organization, 2022). Furthermore, also by 2050, the population of individuals aged ≥ 80 years is projected to reach approximately 426 million (World Health Organization, 2022). These changes have promoted aging research, particularly studies regarding healthy aging. Consequently, pharmaceutical companies, private enterprises, and individual investors are increasingly investing in aging research. At the same time, multiple countries—including the United States, Brazil, Singapore, Pakistan, and Ghana—have implemented national initiatives to foster and guide aging research, having recognized its growing importance (World Health Organization, 2015). These initiatives reflect a global acknowledgment of the need to address the challenges and opportunities presented by population aging.

Over the preceding three decades, the focus of aging research has undergone a paradigm shift. Although researchers in this field initially focused on studying the symptoms and effects of aging, they are now exploring the mechanisms that drive aging phenotypes (Cai et al., 2022a; Zhang et al., 2022a; Zhang et al., 2022b). This shift marks a crucial development in the field and has opened avenues for a wide range of innovative aging interventions, including pharmaceuticals, gene therapy, regenerative medicine, immunotherapy, and lifestyle modifications for health promotion (Cai et al., 2022b; Campisi et al., 2019; Sun et al., 2022; Wu et al., 2024). Some of these interventions have advanced to clinical trials, and this progression underscores their potential viability and effectiveness. Additional factors propelling the field forward include advancements in research tools and methodologies. Cutting-edge techniques such as genome sequencing, sophisticated computer modeling, data science, and longitudinal data collection from specific populations have been instrumental in the progress of aging research. For example, Liu et al. (2023) demonstrated that endogenous retroviruses can mitigate cellular senescence, tissue degeneration, and, to some extent, organismal aging. In addition, Sun et al. (2023) revealed that chitinase-1-positive microglia drive aging in the spinal motor neurons of primates. These methodological advancements have not only enhanced the precision and depth of aging research but also expanded its scope and implications.

Collectively, the developments indicate the dawn of a new era in aging research. Nevertheless, as this field continues to evolve, key health and societal challenges remain to be overcome. The convergence of scientific innovation, strategic policy-making, and societal demand has positioned aging research at the forefront of biomedical science, holding the promise of transformative effects on human health and longevity.

Ethical and social concerns

The field of aging research is burgeoning thanks to technological advancements and potential therapeutic interventions. However, despite its apparent promise, this field poses a unique set of ethical and social challenges that can be categorized into three distinct but interconnected dimensions: scientific considerations, metaphysical concerns, and socioeconomic implications.

Central to the ethical discourse is the scientific aspect of aging research. Although numerous interventions in this field have progressed to clinical trials, the field remains in the nascent stage.

Findings from most studies regarding aging require rigorous validation, including the assessment of potential adverse effects of proposed interventions. Furthermore, the ideal timing for initiating interventions and the appropriate frequency of interventions remain unclear (Belsky et al., 2017), and this lack of clarity intensifies safety, ethical, and social concerns pertaining to these interventions. The main challenge lies in navigating these scientific uncertainties while upholding ethical integrity and social responsibility.

The metaphysical dimension explores the philosophical underpinnings of life extension and aging research. Central themes include the morality of extending the human lifespan, the concept of aging as an invariant aspect of life, and the notion of dominating nature through scientific interventions. Responses to related philosophical questions vary widely depending on diverse economic, social, cultural, and religious factors. For instance, some researchers view the extension of human life as a threat to the established life cycle and personal identity (Lesser, 2005), whereas others argue that it can enhance people's quality of life by increasing opportunities for enriching experiences and pleasure (Horrobin, 2006). This division among researchers highlights the difficulty of resolving metaphysical concerns in aging research and the need for a nuanced and culturally sensitive approach.

Aging research has profound demographic, economic, and sociocultural implications. Although some researchers have anticipated overpopulation due to lifespan extension, others expect lifespan extension to delay demographic shifts (Gavrilov and Gavrilova, 2001). Goldman et al. (2013) highlighted that the extension of the human lifespan may strain social welfare and health-care systems. Conversely, Scott (2021) advocated the potential of longevity dividends through major shifts in individual behaviors, corporate strategies, and government policies. Socially and culturally, an increase in the human lifespan or health span may change individuals' perceptions of older adults, alter the structure of society, and foster age-based prejudice and discrimination (President's Council on Bioethics, 2003). Moreover, such an increase may lead to social injustice, particularly unequal access to effective aging interventions, which may exacerbate health disparities, particularly in developing countries (Glannon, 2002).

In addition, researchers have highlighted numerous inter-related ethical concerns, such as recruiting and obtaining informed consent from older participants in clinical trials, collecting human biopsy samples, and establishing biobanks (Seppet et al., 2011). Aging research may also involve the handling of sensitive personal data, such as information regarding participants' genetics and physical states (e.g., poor health, weaknesses, and vulnerabilities); thus, the protection of individual privacy is crucial. Furthermore, the aging intervention industry may resort to false and misleading advertisements to sell unproven and unauthorized interventions (e.g., stem cell-based interventions) to consumers (Rubin, 2022).

In summary, aging research is a field fraught with complex ethical considerations encompassing scientific, metaphysical, and socioeconomic domains. Addressing these challenges requires a multifaceted approach that seeks to balance scientific advancement with philosophical wisdom, social justice, and economic pragmatism. As this field evolves, continual ethical reflection and dialogue are imperative to navigate these intricate domains.

Global survey on ethical and social concerns in aging research

To clarify the ethical and social concerns in aging research and to facilitate the establishment of a relevant governance framework, this study explored the perspectives of global frontline researchers with abundant expertise in aging interventions. Unlike previous studies, the present study specifically targeted the recruitment of researchers with a profound understanding of the technology involved in aging interventions.

RESULTS AND DISCUSSION

In this study, the respondents' responses were weighted on the basis of their jurisdiction, sex, age, laboratory role, years of research experience, and area of research. Despite a modest response rate of 1.98%, the survey successfully captured the diverse perspectives of 180 unique respondents spanning 38 jurisdictions. The geographical diversity of this study—with substantial participation from the United States, China, the United Kingdom, Italy, Spain, and Canada—enriched the global relevance of our findings.

The respondent cohort primarily comprised seasoned researchers, with 47.78% aged >50 years and 28.89% aged 41–50 years. This age distribution suggests that our data predominantly reflect the perspectives of experienced professionals with a deep understanding of the complexities inherent in aging research. Of the 180 respondents, 118 (65.56%) were principal investigators (PIs)—a role typically associated with extensive experience and leadership in research endeavors. This high representation of PIs was complemented by a lower, yet significant, representation of other academicians—including professors, assistant professors, and postdoctoral fellows—collectively accounting for 7.22% of all the respondents. Approximately 61.67% of the respondents had >10 years of relevant experience; this high proportion underscores the depth of expertise and insight informing the present survey results.

Our comprehensive survey of the global aging research community revealed a nuanced panorama of perspectives related to the ethical ramifications of aging research. The results indicated a consensus among researchers who do not categorize aging as a disease but acknowledge its crucial role as a risk factor for various diseases. General agreement was noted regarding the potential of aging interventions to halt the aging process, the efficacy of preventive interventions, and the need for international cooperation, among other aspects. However, basic and clinical researchers differed in terms of their perspectives regarding the practicality of significantly extending the human lifespan.

Global perceptions of aging: disease or natural decline?

Our survey revealed that several aging-related perspectives varied significantly across the respondents. Of the 180 respondents, 146 (81.11%) disagreed with the characterization of aging as a disease (Figure 1; Q1). This view aligns with traditional definitions, where aging is regarded as a natural, physiological process characterized by a gradual decline in age-specific fitness components (Rose, 1990). Only 24 respondents (13.33%) agreed with the characterization of aging as a disease, and a further 13 respondents (7.22%) strongly agreed with this characterization.

These findings are pivotal because they reveal the current concept of aging among researchers: aging is predominantly perceived not as a pathological condition but as a natural element of life's trajectory.

The survey results unveiled key themes related to the contemporary discourse on aging research. The predominant perception of aging as a natural process rather than a disease may influence the direction of related research and the development of interventions. The findings indicate a focus on managing aging as a part of life rather than combating it as a pathological condition. This perspective may have profound implications for how aging research is funded, conducted, and applied in clinical settings.

Consensus on delaying aging and combating disease

Our survey revealed a strong consensus among the respondents that aging in humans can be effectively delayed through specific interventions; 133 respondents (73.89%) agreed and 56 (31.11%) of the total strongly agreed with this statement (Figure 1; Q2). Furthermore, 144 respondents (80.01%) concurred that the incidence of aging-related diseases can be markedly reduced through scientific interventions (Figure 1; Q3). These findings indicate a widespread belief in the potential of biomedical research to improve quality of life during the aging process and mitigate associated health challenges.

The respondents' strong belief in the efficacy of interventions to delay aging and to reduce the incidence of aging-related diseases indicates a promising outlook for the field. However, it also raises questions about the ethical and practical considerations of such interventions. For instance, what are the potential societal implications of substantially extending the human lifespan? In addition, how would such interventions be made accessible and equitable across populations?

Debate over extending the human lifespan

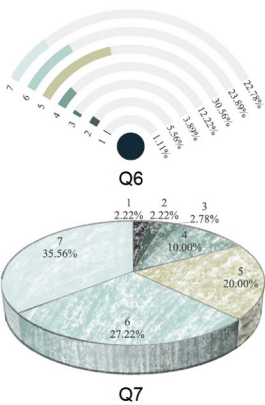
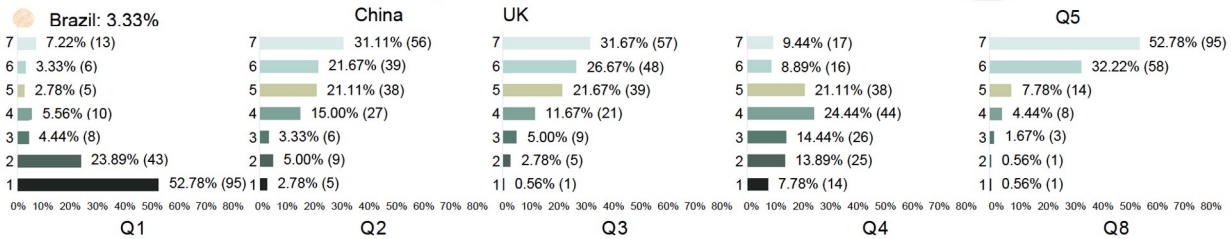
The present survey revealed a spectrum of opinions regarding the possibility of extending the human lifespan beyond its current known limit (approximately 122 years) (Blagosklonny, 2021). Although some of the respondents expressed optimism, 44 (24.44%) held neutral perspectives on this matter (Figure 1; Q4). This divergence reflects the ongoing debate in the scientific community regarding the limits of the human lifespan and the feasibility of substantially extending it through scientific advancements. The varying opinions regarding the possibility of extending the human lifespan beyond its current limits point to an area of uncertainty and active exploration in the field. In addition, this variation suggests that despite optimism regarding the potential of aging research, researchers also recognize the current limitations of such research and the associated need for further scientific breakthroughs.

Sex differences in aging research

Approximately 93.33% of the respondents agreed the statement “sex differences between males and females should be included in important scientific considerations for aging research” (Figure 1; Q5). This overwhelming consensus, with 105 (58.33%) of the respondents expressing strong agreement, indicates a crucial shift in the scientific community's attitude. We found that the sex

Empirical Analysis: A Global Survey

- USA: 15.00%
- China: 11.11%
- UK: 10.00%
- Italy: 8.89%
- Spain: 8.89%
- Canada: 6.11%
- Portugal: 4.44%
- Brazil: 3.33%



- Q1: Aging is a disease.
- Q2: Human aging can be delayed through specific interventions.
- Q3: The incidence of human aging-related diseases can be significantly reduced by scientific aging interventions.
- Q4: With progress made in aging research, future aging interventions could enable the maximum life expectancy of humans to exceed 122 years.
- Q5: Sex differences between males and females should be included in important scientific considerations for aging research.
- Q6: Individuals can undergo aging-related medical interventions prior to the appearance of signs of aging.
- Q7: The problem of equity in the application of future technologies or products should be considered in the experimental design stage for medical interventions in aging research.
- Q8: Advancing aging research requires active international collaboration.

Figure 1. Global survey on ethical and social concerns in aging research. Responses to the first eight questions (Q1–Q8) of the questionnaire.

of the respondents had no significant effect on their responses to Q5, with males having a mean response of 6.28 and females having a mean response of 6.34 ($P=0.716$, which is greater than 0.05). This finding indicates broad recognition of the need to account for sex differences in aging studies. Historically, the predominant focus on males in aging research because of various factors has led to sex bias (Plevkova et al., 2020). Nevertheless, our results indicate growing awareness of this problem and its potential effects on the validity and applicability of research findings. This shift in perspective may translate into more comprehensive and inclusive aging research, ultimately benefiting a broader demographic.

Preventive approaches in aging interventions

Regarding the clinical translation of aging interventions, 139 of the respondents (77.23%) agreed with the following statement: “individuals can undergo aging-related medical interventions before the appearance of signs of aging” (Figure 1; Q6). A total of 55 (30.56%) of the respondents expressed slight agreement. This proactive approach, backed by a considerable proportion of the surveyed researchers, underscores a shift toward early detection and intervention strategies to prevent the negative effects of aging; the focus is on not only understanding the mechanisms of aging but also identifying and applying biomarkers relevant to different phases of the life cycle to determine optimal times for

initiating interventions (Ren et al., 2023). For instance, scientists have developed a comprehensive framework for exploring the biomarkers of aging and have comprehensively analyzed the classifications and clinical applications of these biomarkers (Moqri et al., 2023; Zheng et al., 2024). Similarly, the Aging Biomarker Consortium and colleagues established expert consensus on the biomarkers of brain, heart, vascular, skeletal, and liver aging by synthesizing data from literature reviews and insights from scientists and clinicians (Aging Biomarker Consortium et al., 2023a; Aging Biomarker Consortium et al., 2023b; Aging Biomarker Consortium et al., 2024; Aging Biomarker Consortium et al., 2023c; Aging Biomarker Consortium et al., 2023d; Aging Biomarker Consortium et al., 2023e). These consensus comprehensively evaluate the aging biomarkers of vital organs by three categories: functional, structural, and humoral categories. These advancements suggest a shift toward a preventive approach to aging in health care, which may fundamentally alter the management of aging and its associated conditions.

Equity and accessibility in aging interventions

Of the 180 respondents, 149 (82.78%) agreed that considering equity when developing aging interventions is important, and 64 (35.56%) expressed strong agreement with this idea (Figure 1; Q7). These findings reflect growing consciousness within the

scientific community of the social responsibility of researchers. Emphasis on equitable access, particularly for low-income populations, highlights a commitment to ensuring that advancements in aging research translate into benefits for all sections of society. This perspective could shape future research and development strategies and thus could facilitate the development of affordable and accessible aging interventions.

Need for international collaboration

Of the 180 respondents, 167 (92.78%) advocated active international collaboration in aging research (Figure 1; Q8). This strong consensus suggests recognition of aging as a global challenge transcending national borders. In addition, this emphasis on collaboration reflects an understanding that global resources, knowledge, and expertise must be pooled to effectively manage the complexities of aging. Such an approach aligns with humanitarian principles and underscores the universal nature of aging; the implementation of such an approach could improve the robustness and global applicability of research findings.

Differences in perspectives between basic and clinical researchers

The respondents were stratified on the basis of four factors: designation (PIs vs. non-PIs), age (researchers aged >50 years vs. those aged ≤50 years), research experience (researchers with >10 years of experience vs. those with ≤10 years of experience), and research type (basic vs. clinical researchers). No significant between-group differences were observed in the mean scores for any of the first eight questions (P value>0.05), indicating general consensus among the groups. However, notable differences in perspectives, particularly in responses to questions related to the potential of aging interventions (Q2 and Q4), were observed between the basic and clinical researchers (Table 1).

Generally, the basic and clinical researchers agreed with the following statement: “human aging can be delayed through specific interventions” (Q2). However, the clinical researchers expressed stronger agreement than did the basic researchers (mean scores: 5.69 and 5.04, respectively). This difference may be attributable to the direct involvement of clinical researchers in applying findings from aging research, which may lead them to believe more strongly in the feasibility and immediate relevance of aging interventions. Generally, the respondents expressed uncertainty about the possibility of extending the human lifespan beyond its established limits (Q4). However, the basic researchers exhibited a higher level of confidence in this potential than did the clinical researchers (mean scores: 4.39 and 3.66, respectively). This difference may be attributable to the relatively exploratory nature of basic research, which may encourage an optimistic outlook regarding the possibility of breakthroughs. By contrast, clinical research, which often deals with the realities of aging-related diseases and patient care, may encourage a more conservative stance influenced by the current limitations in effective treatments for aging-related chronic conditions.

Our findings highlight a gap between the optimism of basic researchers and the pragmatism of clinical researchers. More specifically, basic research drives innovation and expands our understanding of what might be possible, whereas clinical translation grounds these findings in the reality of current medical practice and patient care. The cautious optimism of

clinical researchers may stem from their firsthand experience of the complexities and challenges of translating basic research findings into effective clinical interventions. More specifically, this experience may temper clinical researchers’ expectations regarding the immediate applicability of aging interventions. By contrast, the high optimism of basic researchers may fuel the continual pursuit of groundbreaking discoveries in aging research. These findings suggest that a balanced approach integrating insights from both basic and clinical research is needed for developing realistic, effective, and ethically sound aging interventions. The difference in perspectives between basic and clinical researchers may guide future aging research; thus, dialogue and collaboration between basic and clinical researchers must be promoted. Such collaboration may facilitate holistic understanding of the challenges and possibilities of extending the human lifespan and health span.

Our findings revealed nine ethical concerns in aging research (Q9–Q17). Using the K-means clustering algorithm with the silhouette method ($K=3$), we categorized these concerns on the basis of their mean scores. This analytical approach, akin to an ethical risk assessment, enabled us to systematically classify these concerns into three distinct categories (Table 2): crucial ethical concerns (Category A), relatively important ethical concerns (Category B), and ethical concerns lacking consensus (Category C).

Category A: crucial ethical concerns

The predominant ethical concerns observed in this study, as indicated by 87.78% of the respondents, were related to the potential negative effects of false advertising about aging interventions. The field’s focus on extending the human lifespan is associated with a risk of unrealistic public expectations fueled by hype and unsubstantiated claims. This problem is largely attributable to premature commercialization and private investment strategies that may prioritize profit over scientific integrity. Such practices may erode public trust and have unintended social consequences.

Another major concern in this category is the exacerbation of social inequity due to unequal access to aging interventions. The disparity across populations in terms of technological accessibility, often influenced by global wealth distribution, poses a pivotal ethical dilemma. This so-called technology gap not only pertains to the availability of aging interventions but also extends to the knowledge and resources required for the effective use of such interventions. These ethical concerns must be prioritized for shaping the governance and policy frameworks of aging research. Addressing the primary concerns in Category A is imperative for maintaining public trust and ensuring equitable access to advancements in the field.

Category B: relatively important ethical concerns

In this category, ethical concerns revolve around the direct transference of aging interventions tested in animal models to human subjects. The researchers surveyed in this study expressed apprehension about relying on low-grade evidence from animal studies, which may compromise patient health. The respondents were cautious about the administration of aging interventions before the assessment of biological markers of aging. To the best of our knowledge, no sensitive and reliable criteria are available for evaluating the efficacy of aging interventions. Thus, effective biomarkers of aging must be explored to validate the efficacy of aging assessments and to

Table 1. Perspectives of researchers stratified by multiple factors

Issues	Groups ^{a)}							
	PI	Non-PI	>50 years old	≤50 years old	>10 years	≤10 years	Basic research	Clinical translation
Q1	Mean ^{b)} : 2.25	Mean: 2.13	Mean: 2.19	Mean: 2.22	Mean: 2.06	Mean: 2.43	Mean: 2.38	Mean: 2.04
	SD: 1.85	SD: 1.82	SD: 1.89	SD: 1.78	SD: 1.69	SD: 2.04	SD: 2.02	SD: 1.62
	P ^{c)} =0.684		P=0.892		P=0.207		P=0.228	
Q2	Mean: 5.53	Mean: 5.03	Mean: 5.49	Mean: 5.24	Mean: 5.36	Mean: 5.36	Mean: 5.69	Mean: 5.04
	SD: 1.53	SD: 1.66	SD: 1.52	SD: 1.65	SD: 1.63	SD: 1.52	SD: 1.57	SD: 1.55
	P=0.0501		P=0.303		P=0.994		P^{d)}=0.00577	
Q3	Mean: 5.65	Mean: 5.44	Mean: 5.49	Mean: 5.66	Mean: 5.58	Mean: 5.58	Mean: 5.74	Mean: 5.42
	SD: 1.36	SD: 1.37	SD: 1.41	SD: 1.32	SD: 1.43	SD: 1.26	SD: 1.35	SD: 1.37
	P=0.314		P=0.404		P=0.988		P=0.122	
Q4	Mean: 4.04	Mean: 3.97	Mean: 4.07	Mean: 3.97	Mean: 4.05	Mean: 3.97	Mean: 4.39	Mean: 3.66
	SD: 1.68	SD: 1.71	SD: 1.68	SD: 1.69	SD: 1.71	SD: 1.65	SD: 1.66	SD: 1.64
	P=0.78		P=0.687		P=0.773		P=0.00369	
Q5	Mean: 6.36	Mean: 6.18	Mean: 6.20	Mean: 6.38	Mean: 6.38	Mean: 6.16	Mean: 6.38	Mean: 6.22
	SD: 1.11	SD: 1.12	SD: 1.23	SD: 1.00	SD: 0.99	SD: 1.28	SD: 1.00	SD: 1.21
	P=0.311		P=0.27		P=0.227		P=0.341	
Q6	Mean: 5.35	Mean: 5.16	Mean: 5.35	Mean: 5.22	Mean: 5.17	Mean: 5.46	Mean: 5.36	Mean: 5.21
	SD: 1.48	SD: 1.33	SD: 1.34	SD: 1.51	SD: 1.48	SD: 1.33	SD: 1.37	SD: 1.49
	P=0.393		P=0.555		P=0.172		P=0.461	
Q7	Mean: 5.69	Mean: 5.65	Mean: 5.71	Mean: 5.64	Mean: 5.77	Mean: 5.52	Mean: 5.68	Mean: 5.66
	SD: 1.42	SD: 1.44	SD: 1.53	SD: 1.32	SD: 1.45	SD: 1.38	SD: 1.31	SD: 1.53
	P=0.854		P=0.741		P=0.259		P=0.929	
Q8	Mean: 6.36	Mean: 6.08	Mean: 6.16	Mean: 6.35	Mean: 6.31	Mean: 6.19	Mean: 6.34	Mean: 6.18
	SD: 0.93	SD: 1.23	SD: 1.18	SD: 0.91	SD: 1.03	SD: 1.07	SD: 0.91	SD: 1.17
	P=0.126		P=0.235		P=0.469		P=0.317	

a) The significance of between-group differences were analyzed through *t* testing. b) Data are presented as mean and standard deviation (SD) values for each group, and *P* values obtained through *t* testing are described in Sex differences in aging research part. c) The original hypothesis was that the mean values of the two groups of each factor would be equal. This hypothesis was rejected if between-group differences were significant (*P* value<0.05). d) Significant differences are highlighted in bold.

Table 2. Ethical concerns in aging research (ranks and classifications)

Rank	Mean	Specific ethical concern	Category
1	5.85	Q12: There are many misleading advertisements relating to aging interventions, particularly exaggerating the effect; these impede progress in research and the industry.	A. Crucial ethical concerns
2	5.78	Q14: Potential inequities in the future application of aging intervention technologies may lead to a further widening gap in life expectancy between the rich and the poor.	
3	5.05	Q11: Rapid application of aging research findings to humans based on experimental evidence in lower model organisms alone may increase the risk of damage to health.	B. Relatively important ethical concerns
4	4.96	Q16: The public misunderstands the current state of aging research.	
5	4.80	Q10: Certain aging intervention technologies, in the absence of biomarkers for scientific assessment of aging, have entered the stage of clinical trials or even application.	
6	4.59	Q15: Genetic studies of aging involve a large amount of human genetic data, which may lead to risks such as the leakage of human genetic information or personal medical data.	C. Ethical concerns lacking consensus
7	4.32	Q9: Experimental animals used for aging research are more likely to have their welfare infringed upon due to longer feeding periods and higher requirements for feeding conditions.	
8	4.19	Q13: The future widespread application of aging intervention technologies may lead to an increase in the number of older people, which may increase the risk of social discrimination against older adults or younger people.	
9	3.85	Q17: Older adults are more involved as participants in clinical research on aging; this comes with greater difficulty in protecting the rights and interests of participants compared with those in other biomedical fields.	

identify the early signs of aging-related diseases. Another ethical concern was related to the protection of participants’ genetic information and medical data in aging research; this concern highlights the sensitivity of personal information and the risks associated with its handling. The concerns in Category B, although not as immediately pressing as those in Category A,

require careful consideration and rigorous validation to prevent harm to individuals.

Category C: ethical concerns lacking consensus

No clear consensus emerged for the remaining ethical concerns (Q9, Q13, and Q17). These concerns, although controversial,

underscore the complexity and evolving nature of ethical decision-making in aging research. The lack of consensus suggests a need for ongoing dialogue and engagement with a broader range of stakeholders—including researchers, ethicists, policymakers, and the public—to navigate these concerns.

Our findings suggest that the establishment and enforcement of legislation and regulation are pivotal in addressing the concerns surrounding aging research and interventions. Given the complex nature of this field, we recommend refining the current legal frameworks and policies to prevent regulatory oversights. Such action is particularly crucial in specialized domains such as cell and gene therapies. Accordingly, we must formulate guidelines that delineate the regulatory scope and clarify the boundaries of permissible activities. In addition, the current laws should be revised to impose stricter penalties for deceptive marketing practices. To improve transparency and minimize confusion, information disclosure systems, such as a centralized registry for clinical research, may be introduced. Furthermore, to mitigate potential inequity, strategic policies should be enacted. Such policies may include offering free licenses for certain technologies and encouraging developing nations to participate in patent pools. Such measures would ensure that aging interventions are not only safe and effective but also ethically accessible to all segments of society (Peng et al., 2023).

CONCLUSION

Our comprehensive survey of the global aging research community revealed a nuanced panorama of perspectives related to the ethical ramifications of aging research. The results indicated a consensus among researchers who do not categorize aging as a disease but acknowledge its crucial role as a risk factor for various diseases. General agreement was noted regarding the potential of aging interventions to halt the aging process, the efficacy of preventive interventions, and the need for international cooperation, among other aspects. However, basic and clinical researchers differed in terms of their perspectives regarding the practicality of significantly extending the human lifespan.

The ethical concerns identified in the present study were organized into three categories according to the respondent-perceived significance of these concerns and the levels of consensus related to these concerns within the scientific community. The crucial ethical concerns involved deceptive marketing related to aging interventions and the potential exacerbation of social inequity due to disparate access to such interventions. The relatively important ethical concerns were related to the use of lower-model organisms, misconceptions among the public, the discovery of effective biomarkers, and the unauthorized disclosure of participants' genetic information. Overall, this study highlights the importance of integrating ethical considerations into aging research to enhance the positive impact of such research and to create an environment conducive to the well-being of individuals in all age groups in an ethical and inclusive manner.

METHODS

Questionnaire development

We comprehensively searched the Web of Science and PubMed

databases for relevant studies regarding the ethics of aging research. We identified key ethical concerns in aging research that garnered attention from the scientific community. In addition, through discussions with leading researchers in the field, we summarized major scientific, ethical, and social concerns. These concerns were then translated into a structured questionnaire addressing 17 distinct problems: eight related to research and clinical translation and nine related to potential ethical and social implications (Supporting Information; Page 1).

Questionnaire format

The questionnaire is presented in English in the Appendix. Each response was rated on a 7-point Likert scale with endpoints ranging from 1 (*strongly disagree*) to 7 (*strongly agree*) to allow for nuanced expression of opinions.

Questionnaire distribution and data collection

Recognizing the high degree of diversity in the field of aging research, we targeted a broad audience for our survey. The questionnaire was distributed to 9,077 researchers globally; these researchers were identified through their publications in nine leading journals focused on aging research (Supporting Information; Page 2). Responses were collected between August 19 and October 19, 2022; during this period, three reminders were sent to the identified researchers to encourage participation.

Data analysis

The survey responses were analyzed in three stages. The first stage was an initial analysis; for the responses to the first eight questions (Q1–Q8), we systematically calculated mean scores, standard deviations, and other statistical measures to understand general trends (Supporting Information; Page 3). In the second stage, major ethical risks were identified; specifically, we ranked the responses to the subsequent nine questions (Q9–Q17) to derive a list of ethical risks as perceived by the participants. Finally, in the third stage, the identified ethical concerns were categorized; for this purpose, we used the K-means clustering algorithm with the silhouette method ($K=3$) to categorize the nine ethical concerns into three distinct groups on the basis of their mean scores.

Compliance and ethics

The author(s) declare that they have no conflict of interest.

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Supporting information

The supporting information is available online at <https://doi.org/10.1007/s11427-024-2650-y>. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accuracy and content remains entirely with the authors.

References

Aging Biomarker Consortium, Bao, H., Cao, J., Chen, M., Chen, M., Chen, W., Chen,

- X., Chen, Y., Chen, Y., Chen, Y., et al. (2023a). Biomarkers of aging. *Sci China Life Sci* 66, 893–1066.
- Aging Biomarker Consortium, Jia, Y.J., Wang, J., Ren, J.R., Chan, P., Chen, S., Chen, X.C., Chhetri, J.K., Guo, J., Guo, Q., et al. (2023b). A framework of biomarkers for brain aging: a consensus statement by the Aging Biomarker Consortium. *Life Med* 2, lnad017.
- Aging Biomarker Consortium, Jiang, M., Zheng, Z., Wang, X., Chen, Y., Qu, J., Ding, Q., Zhang, W., Liu, Y.S., Yang, J., et al. (2024). A biomarker framework for liver aging: the Aging Biomarker Consortium consensus statement. *Life Med* 3, lnad004.
- Aging Biomarker Consortium, Suo, J., Gan, Y., Xie, Y., Xu, S., Wang, J., Chen, D., Chen, L., Deng, L., Feng, S., et al. (2023c). A framework of biomarkers for skeletal aging: a consensus statement by the Aging Biomarker Consortium. *Life Med* 2, lnad045.
- Aging Biomarker Consortium, Zhang, L., Guo, J., Liu, Y., Sun, S., Liu, B., Yang, Q., Tao, J., Tian, X.L., Pu, J., et al. (2023d). A framework of biomarkers for vascular aging: a consensus statement by the Aging Biomarker Consortium. *Life Med* 2, lnad033.
- Aging Biomarker Consortium, Zhang, W., Che, Y., Tang, X., Chen, S., Song, M., Wang, L., Sun, A.J., Chen, H.Z., Xu, M., et al. (2023e). A biomarker framework for cardiac aging: the Aging Biomarker Consortium consensus statement. *Life Med* 2, lnad035.
- Belsky, D.W., Caspi, A., Cohen, H.J., Kraus, W.E., Ramrakha, S., Poulton, R., and Moffitt, T.E. (2017). Impact of early personal-history characteristics on the Pace of Aging: implications for clinical trials of therapies to slow aging and extend healthspan. *Aging Cell* 16, 644–651.
- Blagosklonny, M.V. (2021). No limit to maximal lifespan in humans: how to beat a 122-year-old record. *Oncoscience* 8, 110–119.
- Cai, Y., Song, W., Li, J., Jing, Y., Liang, C., Zhang, X., Zhang, W., Liu, B., An, Y., et al. (2022a). The landscape of aging. *Sci China Life Sci* 65, 2354–2454.
- Cai, Y., Ji, Z., Wang, S., Zhang, W., Qu, J., Belmonte, J.C.I., and Liu, G.H. (2022b). Genetic enhancement: an avenue to combat aging-related diseases. *Life Med* 1, 307–318.
- Campisi, J., Kapahi, P., Lithgow, G.J., Melov, S., Newman, J.C., and Verdin, E. (2019). From discoveries in ageing research to therapeutics for healthy ageing. *Nature* 571, 183–192.
- Gavrilov, L.A., and Gavrilova, N.S. (2001). The reliability theory of aging and longevity. *J Theor Biol* 213, 527–545.
- Glannon, W. (2002). Identity, prudential concern, and extended lives. *Bioethics* 16, 266–283.
- Goldman, D.P., Cutler, D., Rowe, J.W., Michaud, P.C., Sullivan, J., Peneva, D., and Olshansky, S.J. (2013). Substantial health and economic returns from delayed aging may warrant a new focus for medical research. *Health Affairs* 32, 1698–1705.
- Horrobin, S. (2006). The value of life and the value of life extension. *Ann New York Acad Sci* 1067, 94–105.
- Lesser, H.A. (2005). Dementia and personal identity. In: Hughes, J., Louw, S., and Sabat, S.R., eds. *Dementia: Mind, Meaning, and the Person*, International Perspectives in Philosophy & Psychiatry. Oxford: Oxford Academic.
- Liu, X., Liu, Z., Wu, Z., Ren, J., Fan, Y., Sun, L., Cao, G., Niu, Y., Zhang, B., Ji, Q., et al. (2023). Resurrection of endogenous retroviruses during aging reinforces senescence. *Cell* 186, 287–304.e26.
- Mogri, M., Herzog, C., Poganik, J.R., Justice, J., Belsky, D.W., Higgins-Chen, A., Moskalev, A., Fuellen, G., Cohen, A.A., Bautmans, I., et al. (2023). Biomarkers of aging for the identification and evaluation of longevity interventions. *Cell* 186, 3758–3775.
- Nielsen, J.L., Bakula, D., and Scheibye-Knudsen, M. (2022). Clinical trials targeting aging. *Front Aging* 3, 820215.
- Peng, Y., Ding, L., Song, M., Xiao, Z., Lv, J., and Liu, G.H. (2023). Acting on ethics and governance of aging research. *Trends Mol Med* 29, 419–421.
- Plevkova, J., Brozmanova, M., Harsanyiiova, J., Sterusky, M., Honetschlager, J., and Buday, T. (2020). Various aspects of sex and gender bias in biomedical research. *Physiol Res* 69, S367–S378.
- President's Council on Bioethics. (2003). Age-retardation: scientific possibilities and moral challenges. Staff Working Paper. Washington: President's Council on Bioethics.
- Ren, J., Song, M., Zhang, W., Cai, J.P., Cao, F., Cao, Z., Chan, P., Chen, C., Chen, G., Chen, H.Z., et al. (2023). The Aging Biomarker Consortium represents a new era for aging research in China. *Nat Med* 29, 2162–2165.
- Rose, M.R. (1990). *Evolutionary Biology of Aging*. New York: Oxford University Press.
- Rubin, R. (2022). From positive to negative to positive again—the mystery of why COVID-19 rebounds in some patients who take paxlovid. *JAMA* 327, 2380.
- Scott, A.J. (2021). Achieving a three-dimensional longevity dividend. *Nat Aging* 1, 500–505.
- Seppet, E., Pääsuke, M., Conte, M., Capri, M., and Franceschi, C. (2011). Ethical aspects of aging research. *Biogerontology* 12, 491–502.
- Sun, S., Li, J., Wang, S., Li, J., Ren, J., Bao, Z., Sun, L., Ma, X., Zheng, F., Ma, S., et al. (2023). CHIT1-positive microglia drive motor neuron ageing in the primate spinal cord. *Nature* 624, 611–620.
- Sun, Y., Li, Q., and Kirkland, J.L. (2022). Targeting senescent cells for a healthier longevity: the roadmap for an era of global aging. *Life Med* 1, 103–119.
- World Health Organization. (2015). *World Report on Ageing and Health*. September 29, 2015. Available from URL: <https://www.who.int/publications-detail-redirect/9789241565042>.
- World Health Organization. (2022). *Ageing and Health*. October 1, 2022. Available from URL: <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>.
- Wu, R., Sun, F., Zhang, W., Ren, J., and Liu, G.H. (2024). Targeting aging and age-related diseases with vaccines. *Nat Aging* 4, 464–482.
- Zhang, J., Yin, J., Heng, Y., Xie, K., Chen, A., Amit, I., Bian, X., and Xu, X. (2022a). Spatiotemporal Omics-Refining the landscape of precision medicine. *Life Med* 1, 84–102.
- Zhang, Y., Liu, X., Klionsky, D.J., Lu, B., and Zhong, Q. (2022b). Manipulating autophagic degradation in human diseases: from mechanisms to interventions. *Life Med* 1, 120–148.
- Zheng, Z., Li, J., Liu, T., Fan, Y., Zhai, Q.C., Xiong, M., Wang, Q.R., Sun, X., Zheng, Q. W., Che, S., et al. (2024). DNA methylation clocks for estimating biological age in Chinese cohorts. *Protein Cell* doi: 10.1093/procel/pwae011.