

# Establishing a Comprehensive Anti-aging Research Center: Experiences and Challenges

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## Research article

**Keywords:** anti-aging, research center, establishing, experience, challenge

**Posted Date:** May 28th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-29136/v1>

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# Abstract

**Introduction:** Age-related diseases have become the leading causes of morbidity and mortality worldwide. Anti-aging researches both at the population and individual levels are still urgently needed. Establishing comprehensive anti-aging research centers is crucial to advancing anti-aging researches. However, few studies have shown guidelines for establishing a comprehensive anti-aging research center. We aim to describe the establishment of a comprehensive anti-aging center, summarize the initial experiences, and discuss limitations, strengths and challenges.

**Methods:** The establishment contains three phases (from October, 2017 to January, 2020), the first phase is assessing the need for anti-aging research by reviewing relevant literatures and investigating the elderly population. The second phase is interpreting the aging-related policies by searching and analyzing China's aging-related policies in recent years on government websites. The third phase is completing the protocol of establishing the center, raising funds for the establishment of the center and selecting the adequate equipment.

**Results:** In phase one, we find improving strategies at the population and individual levels are still needed. Through establishing elderly cohort, we find that many elderly people are with high risk factors of aging. In phase two, we find many age-related policies have been unveiled. In phase three, we complete the protocol of establishing the center based on the results of phase one and two. We also have raised funds and selected equipment for the center.

**Conclusion:** With limited guideline for establishing a comprehensive anti-aging research center, the experience in this paper might help other institutions to build anti-aging research center or program.

**KEY WORDS:** anti-aging; research center; establishing; experience; challenge

## Introduction

Population aging is one of the most important global social trends in the 21st century. The most immediate result of aging is an increase in the incidence of age-related diseases<sup>1</sup>. It is well known that chronic non-communicable diseases have been the major contributors to the disease burden, among which age-related diseases such as diabetes, cardiovascular disease, and cancer diseases have become the leading causes of morbidity and mortality worldwide<sup>2-9</sup>. Moreover, these diseases could not only affect the life quality of the elderly, but also the family members who take care them<sup>10</sup>. So how to prevent the age-related diseases and how can people achieve the condition of healthy aging? Further exploration of improving anti-aging strategies is important for human health.

At present, multiple anti-aging researches are in development, and some of them have shown considerable promise for slowing down aging or reducing the incidence of age-related diseases. It appears that enhancing autophagy<sup>11, 12</sup>, eliminating senescent cell<sup>13, 14</sup>, transfusing plasma from young individuals<sup>15, 16</sup>, and stem cell therapy<sup>17, 18</sup> are promising interventions to help individuals get conditions

of healthy aging. However, many of them are pre-clinical studies which still need critical assessment in clinical trials to confirm their efficacy. Moreover, some interventions that could be very useful in clinical settings might not even reduce the risk of age-related diseases at the population level. This may because implementing such interventions at population level should consider not only biological and medical factors but also socioeconomic and political factors. There is no doubt that interventions aimed at reducing the risk of diseases are superior to therapeutic methods. And it is cheaper and easier to prevent diseases through health strategies and policies. So we aim to establish a comprehensive anti-aging research center focusing on the anti-aging programs/researches both at the population and individual levels. In this paper, we will describe the establishment of this center, summarize the initial experiences, and discuss limitations, strengths, and challenges.

## Methods

This comprehensive anti-aging research center was first proposed in October, 2017, and preliminarily completed in January, 2020. In the development of any research center, the most important starting point is to define the center's mission. The mission statement of this center is to slow down aging, reduce the incidence of age-related diseases, and help the elderly maintaining a better physical and mental health. The establishment of the program is completed in three phases. The first phase: assessing the anti-aging need; the second phase: interpreting the aging-related policies; the third phase: completing the protocol for establishing the anti-aging research center. A specific committee composed of the big data evidence-based decision-making department (department A), the policy transformation department (department B), and the experimental and clinical research department (department C) is assigned the above missions (Fig. 1).

## Phase 1 : Assessing the Anti-aging Need

In this phase, members of department A assess the need for anti-aging research mainly by reviewing relevant literature and investigating the elderly population.

### Reviewing

Search databases such as PubMed, Web of Science, China National Knowledge Infrastructure (CNKI), and Wanfang Data to evaluate the current situation and the prospect of anti-aging researches.

*Investigating.* Establish the elderly cohort to collect self-assessment information of the elderly's health through questionnaires. The information include: age, sex, BMI, defecation, bradymasesis, sedentariness, physical exercise, sleep, chronic disease, smoking and drinking. The inclusion criteria: 1) 60–90 years old; 2) informed consent. The exclusion criteria: the elderly who can't complete the questionnaire.

## Phase 2: Interpreting the Aging-related Policies

In this phase, members of department B interpret China's aging-related policies in recent years by searching and analyzing information on government websites.

# Phase 3: Completing the Protocol of Establishing the Center

In this phase, members of department C are required to complete the protocol of establishing the anti-aging research center based on the results of phase 1 and phase 2. Then raise funds for the establishment of the center and select the adequate equipment.

The researches involved in the establishment of the center have been approved by the Ethics Committee of Shanghai East Hospital, Tongji University School of Medicine.

## Results

### Execution of the Phase 1

*Reviewing:* According to review and summarize researches of anti-aging in databases. We find that the anti-aging interventions can be divided into three categories depending on how they are implemented: drug interventions, non-drug interventions, and other interventions (Table 1). For drug interventions and other interventions, the main benefits might include opportunities to extend human life cycle, reduction of age-related diseases, and improving the quality of life. Moreover, these results have been mostly verified by animal evidence-based clinical studies. However, when it comes to promotion at the population level, drug interventions still have the following problems: lack of human clinical trials, high costs of some drugs, and ethical issues. For non-drug interventions, they are cheaper and easier to operate, as they are non-invasive and appear to have minimal side effects. Moreover, these interventions can be used not only as important applications of anti-aging interventions at the individual level, but also to bring greater benefits to public health strategies at population-level. However, these non-drug interventions lack evidence of large-scale clinical trials. Stem cell therapy and plasma therapy are two “special drug interventions”, they require clinical trials for safety and efficacy. Therefore, given the multifactorial nature of aging, it is urgently important to develop anti-aging programs based on integrating the above interventions, which is also conducive to the formulation of the most appropriate anti-aging interventions at the population and individual level.

Table 1  
Anti-aging interventions

Drug intervention	Non-drug intervention	Other intervention
<b>Autophagy enhancer</b>  Such as Everolimus, IR-58, Metformin, Niclosamide, Prazosin, Pifithrin- $\alpha$ , PREP inhibitor, Perifosine, Rapamycin, Resveratrol, Rottlerin, Rottlerin, Spermidine, Torin1, Verapamil, Valproic acid, Xestospongine B	<b>Intermittent fasting/caloric</b>  16/8 method: fasting every day for 14–16 hours by restricting daily eating window to 8–10 hours;  5:2 plan: a cycle of standard eating for 5 consecutive days followed by a restricted calorie intake (500–600 calories/day) in the next 2 days ;  Eat-stop diet: once or twice 24-hour fast per week ;  Warrior diet: starvation during the day and eating a huge meal (feasting) at night;  Alternate day fasting ;	<b>Stem cell therapy</b>  Intracerebral transplantation or peripheral injection of a variety of stem cells including mesenchymal stem cells (MSCs), neural stem cells (NSCs) or glial-restricted progenitors (GRPs)
<b>Senolytics</b>  Such as Dasatinib, Fisetin, Geldanamycin, Navitoclax, Piperlongumine, Panobinostat, Quercetin	<b>Physical Exercise</b>  Structured, individualized, and continue PE programs for longer durations	<b>Plasma therapy</b>  Infusion of plasma collected from younger individuals
<b>Other drugs</b>  Curcumin  Astragalus membranaceus	<b>Improving bad habits</b>  Smoking, bad diet, alcohol consumption, lack of sleep, stress, sun exposure, environmental pollution, etc.	

## Investigating

We establish an elderly cohort with a sample size of 840 (Table 2). Among them, more than a half are underweight (BMI  $\leq 18.5$ ) or overweight (BMI  $\geq 24$ ), 18.45% have defecation difficulty, 43.33% have bradymesis, 36.07% are sedentary, 27.5% have no regular physical exercise, 28.57% have sleep disorder, 77.26% have one or more chronic disease, 18.81% have the habit of smoking, 10.83% have the habit of drinking. All of these factors may affect aging directly or indirectly. So there is a need for public health policies to slow aging and reduce the incidence of age-related diseases.

Table 2  
Information of the elderly cohort

	N	%
Age		
60–69	380	45.24
70–79	364	43.33
80–89	89	10.6
≥ 90	7	0.83
Sex		
male	352	41.9
female	488	58.1
BMI		
≤18.5	25	2.98
≥ 18.5, and ≤24	349	41.55
≥ 24,and≤28	359	42.74
≥ 28	107	12.74
Defecation difficulty		
Yes	155	18.45
No	685	81.55
Bradymasesis		
Yes	364	43.33
No	476	56.67
Sedentariness (≥90 min,per time)		
Yes	387	36.07
No	453	53.93
Regular physical exercise		
Yes	609	72.5
No	231	27.5
Sleep disorder		

	N	%
Yes	240	28.57
No	600	71.43
Chronic disease		
Yes	649	77.26
No	191	22.74
Smoking		
Yes	158	18.81
No	682	81.19
Drinking		
Yes	91	10.83
No	749	89.17

## Execution of the Phase 2

### Policies

Since the Chinese government has initiated the building of a healthy China and a community with shared future for mankind, a number of policies to deal with aging has been unveiled. Most recently, the government unveiled a medium and long-term plan for responding proactively to population aging. The plan requires establishing the basic institutional framework for tracking population aging by 2022<sup>19</sup>. By the middle of the century, a mature institutional arrangement that meets the needs of a great modern socialist country should be put into place. It deploys the specific task of coping with the aging population from five aspects. Firstly, it calls for improving the national income distribution system, steadily increasing the pension reserves and establish a fairer and more sustainable social security system. Secondly, it requires improving the quality of new members of the labor force, establishing a lifelong learning system for senior citizens, and striving to achieve fuller employment and create better quality jobs. Thirdly, according to the plan, a high-quality health service system including health education, disease prevention and treatment, rehabilitation nursing, long-term nursing and hospice care should be established. Fourthly, the plan also values the application of technology in responding to population aging including strengthening the development of assistive technologies for senior citizens. Fifthly, it also calls for fostering a social environment in which senior citizens are respected, cared for, and live happily in their later years. The legal system will be improved to protect the lawful rights and interests of senior citizens<sup>19</sup>. Therefore, the importance to address the challenge of aging has been increasingly recognized by the Chinese government, and the anti-aging researches will be actively supported.

# Execution of the Phase 3

Protocol: We have completed the protocol of establishing the anti-aging research center based on the results of phase 1 and phase 2. In addition, the protocol also contained the directions of the programs/researches to be carried out later and the specific design requirements of the them. Moreover, in the process of starting up the research center, we have accomplished the following things: 1) In order to support the finance of the center, we have submitted our protocol to relevant departments and applied for special funds. At present, we have obtained financial support from Shanghai Pudong Municipal Health Commission, National Natural Science Foundation, and National Key Research and Development Program of China. 2) In order to support the work of the center, we have invited relevant medical or research institutions to participate in the construction of the center. At present, we have cooperated with 5 hospitals, 13 community health service centers and one stem cell research institute. 3) In order to support the communication of the center, we have invited experts in the field of aging to join the special expert groups to give regular lectures in the future.

## Equipment

Considering the equipment demand and cost performance, the existing equipment is mainly purchased from Siemens (Germany) and Tsinghua Tongfang (China). They are used to detect aging and age-related diseases. We have also established a mature medical cosmetology team and psychological counseling team. In addition, we have cooperated with Beijing CapitalBio Technology Co., Ltd. to carry out gene testing, immunohistochemical testing, gut microbiota testing, etc. At the same time, we are working with the stem cell institute to conduct stem cell anti-aging research in the future.

*Roles and responsibilities:* Department A is mainly responsible for: 1) Conducting literature research from the perspective of public health based on the evidence-based concept, assisting Department C to determine the direction of anti-aging researches in the future; 2) Based on big data, retrospective data analysis and prospective cohort construction are combined to solve the identification of aging and refined diagnosis and treatment interventions, providing data analysis support for slowing down aging and reducing the incidence of age-related diseases.

Department B is mainly responsible for: 1) Communicating with Department A and Department C to evaluate the research results and evidence quality; 2) Publishing research results through professional channels, showing research results through non-professional mass media, and assisting the government in formulating relevant anti-aging policies.

Department C is mainly responsible for: 1) Establishing cooperative relationship with other research institutions; 2) Cooperate with community health service centers to carry out researches on anti-aging at the population level; 3) Provide a complete database of elderly population for Department A and improve the anti-aging strategies based on the analysis results of Department A (Fig. 2).

## Discussion

In this paper, we report for the first time on the steps of starting up a comprehensive anti-aging research center. This might provide reference value for the construction of other anti-aging center. The establishment of our center is still in progress and will continue to be improved in the following work.

Although the problem of aging is common all over the world, it is particularly pressing for China. The absolute number of elderly people ( $\geq 65$  years old) in China is the largest in the world with 167 million, accounting for 12% of the total population in 2019, and will rise to almost 400 million by 2050, accounting for 26% of the total population<sup>20</sup>. Meanwhile, China has increasingly recognized the vital need to address the aging challenge, and has proactively proposed the “Healthy China 2030” plan. Healthy ageing is not only the absence of disease, but also the maintenance of functional ability throughout the life.

Our center is established to respond to the increasingly serious crisis of aging and age-related diseases worldwide. One of the focuses of the center is to carry out anti-aging research at the population level. At the same time, we also focus on formulating precise anti-aging programs for individuals. Currently, physical exercise and caloric restriction are the two main interventions against aging at the population level<sup>21, 22</sup>. But these population-level interventions haven't been universally acknowledged as effective in humans, factors like the genetic background and the phase of life when it occurs might also influence the outcomes<sup>23–27</sup>. For example, regular physical activity is less effective for individuals with physical disability, especially for those with low income. Another example is restricting calories in the elderly, which can lead to loss of muscle mass<sup>22</sup>. Moreover, the elderly might confront different age-related health problems, just as the results of our results. So simply relying on physical exercise and caloric restriction to improve the anti-aging effect at the population level is not enough. Interventions at the individual level might be useful in population sub-groups when the population-level interventions are not feasible or controversial. Therefore, more well-conducted randomized controlled trials are still needed to assess the effect of these anti-aging strategies.

When launching a research center, especially when the research theme of the center are associated with many disciplines, it should be implemented by a well-structured and multidisciplinary team. In this center, our team includes not only experts in the field of aging, but also experts in statistics, public health, and policy transformation. Meanwhile, we cooperate with medical teams in hospitals and community health service centers to carry out comprehensive anti-aging research at the population level. The experience in the establishment of a center is of great help for other centers. Although programs/ researches of anti-aging have become the focus of researches, there is no standard guideline for establishing anti-aging research centers. So the above described method is suggested. Moreover, we also compare the establishing guidelines with other kind centers. For example, a study<sup>28</sup> reported a comprehensive six-step for the establishment of a new extracorporeal membrane oxygenation (ECMO) center: planning, developing, implementing, sustaining, evaluating, and moving forward. Recently, Assy J et al.<sup>29</sup> established a ECMO center with limited resources by following the six-step guidance. This showed the

importance of developing guidelines for the establishment of specific center. There are many similarities between their steps and ours. For example, their first step is “planning”, which includes the identification of key personnel, the assessment of needs, and the development of a strategic plan; Their second step is “developing”, which requires the clear designation of human and organizational resources, as well as the acquisition of appropriate equipment. The information contained in these steps is also reflected in our construction process. However, since they are the centers of ECMO, and our center covers a variety of program/researches related to anti-aging, their guidelines for implementing, sustaining, and evaluating are different from ours.

This study also have some limitations. Firstly, since the establishment of this research center has just been completed, and the anti-aging programs/researches have just started, the value of the center cannot be evaluated by the results of these anti-aging studies. In addition, there may be other difficulties or problems in the process of conducting each anti-aging programs, such as the efficiency of policy transformation, the evaluation and the promotion degree of the research results, which all need to be actively dealt with in the following work.

## **Conclusion**

With limited guideline for establishing a comprehensive anti-aging research center, the experience in this paper might help other institutions to build their own anti-aging research center or program.

## **Declarations**

## **Ethics approval and consent to participate**

The researches involved in the establishment of the center have been approved by the Ethics Committee of Shanghai East Hospital, Tongji University School of Medicine. All participants were informed consent.

## **Availability of data and material**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## **Competing Interests**

The authors declare no competing interests.

## **Funding**

This work was supported by Important Weak Subject Construction Project of Pudong Health and Family Planning Commission of Shanghai (Grant No. PWZbr2017-06); National Natural Science Foundation of China (71774116, 71904145); and National Key Research and Development Program of China (SQ2018YFC130057). They provided financial support in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

## Author Contributions

XC wrote the manuscript; XC and JG created the figures; JG and JH revised the manuscript; XC, JG, JH, SG, QL, YZ, and HY collected the data and conducted the literature; ZW and HJ devised the study.

## Acknowledgements

Not Applicable

## Consent to publication

Not applicable.

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Figures

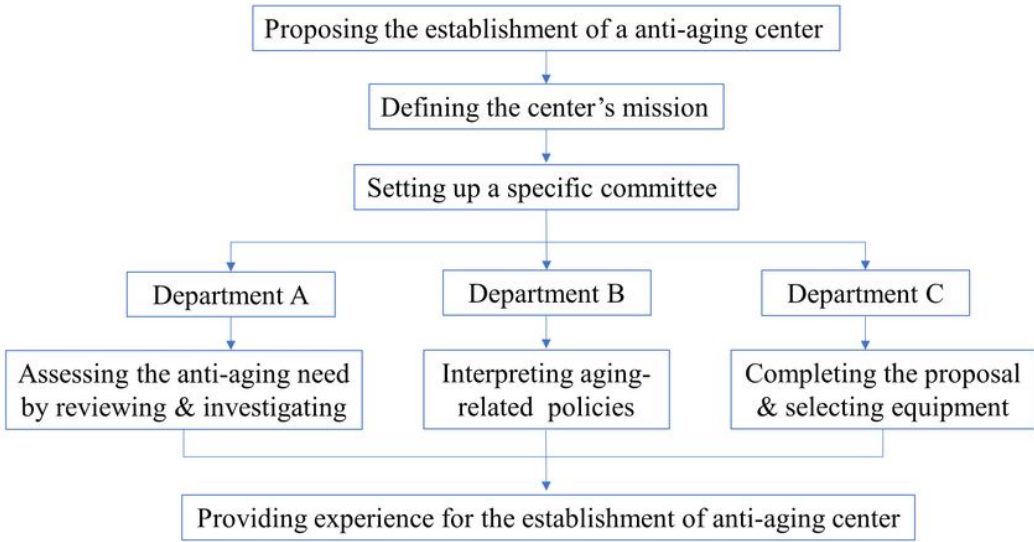
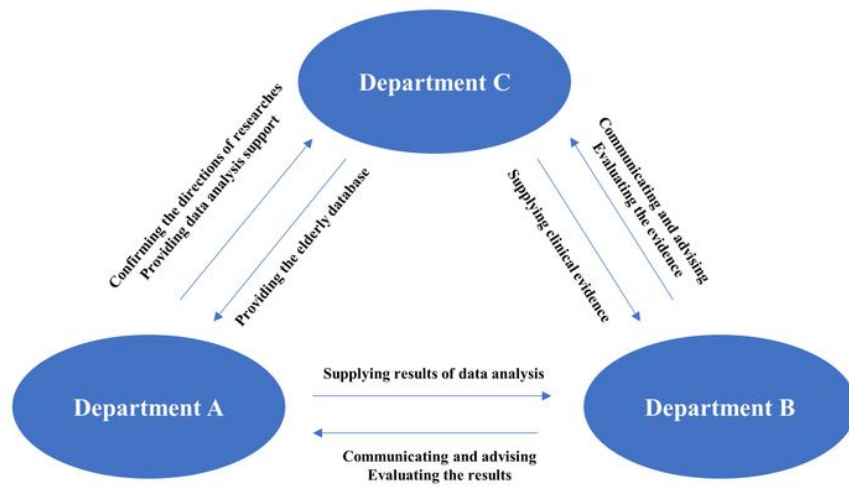


Figure 1

The flow chart



**Figure 2**

Roles and responsibilities of three departments