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Cohort Profile: A natural population cohort study on long-lived adults: West China Longevity and Aging Procedure (WCLAP)

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Cohort Profile: A natural population cohort study on long-lived adults: West China Longevity and Aging Procedure (WCLAP)

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ABSTRACT

Purpose: The West China Longevity and Aging Procedure cohort study (WCLAP) aims to provide guidance for older adults in western China with the aim of improving quality of life, reducing the burden of family care, summarizing the characteristics of longevity lifestyles, building a Chinese-longevity-population biobank, and exploring the mechanisms underlying population aging.

Participants: Since the establishment of the WCLAP research baseline in 2018, a population of 1,537 adults aged 80 years and above, living in the community, have been enrolled in the program as research participants. Of these, 231 are aged 100 years and above. Participants are followed up every year.

Finding to data: WCLAP data is collected in 5 hospital research sub-centers strategically located adjacent to the national "Longevity Townships" of Chengdu Ziyang, Leshan, Yibin, and Pengshan. Data collection included a comprehensive assessment of the participant's health (including physical, psychological, social, common chronic disease assessments), instrumental tests (body composition and muscle percentage), and the collection of biomedical-biobank samples (include blood, urine, feces, hair, and urine).

Future plans: Through the annual cohort follow-up, survival-related information is collected at a group level. Analysis of biological samples facilitates biological characterization at the microscopic level through proteomics, metabolomics, genomics, and other techniques. Baseline data, group-level follow-up data, and microbiological examination data are integrated together to provide an evaluation tool, exploring sarcopenia, disability, dementia, caregiver burden, aging biomarkers, and other influencing factors.

Registration: The WCLAP was approved by the Medical Ethics Committee of the West China Hospital of Sichuan University (Reference Number: 2018-463), and registered with the China Clinical Trial Registration Center (Registration number:

ChiCTR1900020754).

Keywords: Natural population; Long-lived adults; Cohort study; Sarcopenia; Frailty; Dementia.

INTRODUCTION

The increasing age of the population has become one of the main factors affecting the quality of life globally. As the elderly population increases, age-related chronic conditions contribute to the global healthcare burden and are anticipated to become the next global public health challenge[1] There is much research ongoing to determine how best to achieve healthy aging, improve quality of life in old age, and reduce the burden on family caregivers of elderly disabled relatives. As such, a great investment is being driven into the field of aging health in various countries. In 2018, the population of people aged over 64 surpassed that of children under 5 for the first time. By 2050, it is predicted that nearly 20% of the world's population will be over 65[2]. Consequently, the workforce in social production is likely to face increased life pressure and social responsibility. It is important to establish a balance between social burden and social productivity, and a good strategy is required to achieve this.

In 2000, China was acknowledged to have an aging society. A national survey conducted by the National Bureau of Statistics reported China's elderly population (defined as those aged 60 and over) to have reached 249 million at the end of 2018, comprising 17.9% of the total population; with those aged 65 and over numbering 167 million, accounting for 11.9% of the total population[3]. This rate of aging is projected to increase further to 24.7% in the next 25 years[4]. In 2010, Chinese scholars reported the total number of people over 60 to be 178 million, accounting for 13.32% of the total population and predicted that by 2030, this will reach 359 million. By 2050, the total number of people over 60 is estimated to reach 448 million, accounting for about 40% of the total population, with a serious impact on quality of life[5, 6]. In the future, with further advancements in technology and human intelligence, China is expected to face more severe consequences from this aging society.

The elderly population of longevity townships in China has different behavioral characteristics to those in Europe and America, including the variety and structure of dietary intake, economic level, educational background, psychological health (anxiety, depression), the provision of family care, and physical activity. The present research

aims to focus on the behavioral characteristics associated with high-quality survival and longevity of the elderly population in China's longevity areas. This will be achieved by assessing the lifestyles at a large scale and the biological multi-omics at the microscopic scale. This study aims to summarize the characteristics associated with longevity in this special population of elderly Chinese people. By starting from the concept of primary prevention, this study aims to characterize behaviors associated with a long and healthy and longevity life, providing government departments with evidence supporting public health primary prevention strategies. Conversely, through the testing and analysis of biological samples with the help of metabolomics, proteomics, and other methods, biomarkers of healthy aging will be identified to provide a basis for the future development of anti-aging drugs and the treatment of age-related diseases.

COHORT DESCRIPTION

Study design and setting

The design and baseline of WCLAP were formed in 2017 and 2018, respectively, with the plan of conducting an annual cohort follow-up. WCLAP was designed to be a prospective dynamic cohort study across 4 medical and health institutions in the National Longevity Region in western China. From October 10, 2018, to December 1, 2019, WCLAP successively established baseline research subcenters in five longevity regions in western China; Chengdu (The West China Hospital of Sichuan University), Ziyang (Ziyang Zhonghua Hospital), Leshan (The First People's Hospital of Leshan City), Meishan (Pengshan Traditional Chinese Medicine Hospital of Meishan City), and Yibin (The Second People's Hospital of Yibin City). The data collected by each sub-center were collated at the West China Hospital of Sichuan University (WCHSCU). All biological samples were collected according to standardized operational processes and stored in the biological specimen bank of the West China Hospital of Sichuan University.

Ethnical approval

The WCLAP was approved by the Medical Ethics Committee of the West China Hospital of Sichuan University (Reference Number: 2018-463), and registered with the China Clinical Trial Registration Center (Registration number: ChiCTR1900020754).

Data collection

Data collection comprised (1) the completion of a questionnaire survey, (2) a full physical examination, and (3) biological specimen collection and laboratory tests.

The design of the questionnaire was based on the National Health and Aging Trends Study (NHATS) created by the Johns Hopkins University[7] and applied to the population of western China. The contents of the questionnaire survey comprised basic demographic characteristics, social activity, family longevity, health and disease status, lifestyle behaviors, and evaluation scales. Before the formal use of the questionnaire, our team carried out pre-test among the old adult in the community to continuously verify the reliability and validity of the questionnaire, and finally confirmed the final version of the questionnaire tool.

The physical examination included measures of grip strength, pace, body mass index (BMI), blood pressure, skinfold thickness at the triceps, the sit-up test, and body composition. Before data collection, all test instruments were calibrated according to manufacturer guidelines.

Biological specimen collection for laboratory testing included blood, urine, stool, saliva, and hair. Subjects were provided with a free routine screening of their blood and urine samples within one month of their physical examination.

Study subjects

Participants were recruited from the National Longevity Region in Western China. The

eligibility criteria were as follows:

1. Participants agreed to participate in the study and signed an informed consent form.

2. Participants were aged 80 years old or older (according to their identification card).

3. Participants had lived in the locality for at least 1 year.

4. Participants were willing and able to cooperate with the evaluator in the local language to complete the 30-minute evaluation.

Exclusion criteria:

1. Unwillingness to sign the informed consent form, complete all assessment content independently.

2. The presence of metal implants in the body, such as stents, artificial joints, pins, plates, or cardiac pacemakers.

3. Being under the age of 80 (according to their identification card).

4. Having a life expectancy of under 6 months (diagnosed by medical institution).

Sampling method

A multi-stage cluster sampling method was used as follows:

1. The study population comprised the population of elderly adults across the varied topography and landforms of the national longevity area in western China, including hills, basins, mountains, and plains.

2. Given the two factors of the geographical environment and the extent of the national longevity areas, four cities in western China were selected as sub-centers for the study, namely Meishan, Ziyang, Yibin, and Leshan.

3. Given the influence of many factors, including the convenience of transport routes, the willingness of municipal/county/village-level government bodies to cooperate, the

sizes of local populations, the distances between collection points and local sub-centers, and local acceptance of modern medicine, districts were selected adjacent to each sub-center. These were Pengshan District (adjacent to Meishan City), Yanjiang District (adjacent to Ziyang City), Cuiping District (adjacent to Yibin City), and Shizhong District (adjacent to Leshan City).

4. In each of the above districts, a number of towns (10 towns from Pengshan,17 towns from Yanjiang, 12 towns from Cuiping, 12 towns from Shizhong) were randomly selected based on factors such as accessibility, population size and structure.

5. Data collection was conducted at each research site, facilitated by preliminary communication with government departments, sub-centers, and community organizations at all levels of the project site, to initiate social mobilization and publicity for the study. Residents of each of the selected towns were invited to voluntarily participate in the study. Our team will provide each participant with free medical examination service (about 90 USD) and long-term health follow-up service (free hospital referral service will be provided if necessary) as compensation.

Baseline evaluation

The baseline assessment was completed in 2019, whereby 1,546 elderly adults participated. The baseline assessment included the survey, biological sample collection, and physical examination as detailed above.

The questionnaire included basic personal information, information about social and support networks, social microenvironment, religious beliefs, family longevity, chronic disease, health self-assessment, eating habits, household drinking water, smoking status, alcohol/tea intake, physical exercise, and daily and leisure activity. This was achieved using validated assessment tools, and where possible those designed specifically for use in elderly populations; Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL), Clinical Frailty Scale, Social Support Rating Scale (SSRS), Pittsburgh Sleep Quality Index (PSQI), the short form of the multi-nutritional assessment (MNA-SF), mini mental-state exam (MMSE), the Generalized Anxiety

Disorder questionnaire (GAD-7) and the Geriatric Depression Scale (GDS-15). The questionnaire contents are detailed in Table 1.

Table 1: The main contents of the questionnaire survey

Questionnaire Frame	Content Description
Basic personal information	Name, gender, age, ID number, place of birth, length of local residence, local residential address, telephone number (her/himself + relatives), Educational background, nationality, language (minority language), main occupation before 60 years old, etc..
Social network & support	Childbirth (number of sons and daughters), family situation, family financial control, family respect, home care, family function, neighbor/friend relationship, support and assistance, marriage/spouse situation, etc.
SRSS Scale	Social support evaluation, including friends, neighbors, family, asking for help, talking, etc.
Social microenvironment	Family living area, source of income, annual family income, and economic satisfaction.
Religious belief	Religious type, religious activities
Longevity Family Survey	Long-lived relatives, family history of genetic disease
History of chronic disease	Types of chronic diseases, hospitalization, medical insurance, medical expenses in the past year, satisfaction with medical conditions, timely medical treatment, etc.
Health self-assessment	Limitation of activity, physical state, emotional state, pain, self-feeling, etc.
Eating habits	The number of meals per day, the amount of food, the

	combination of meals, whether or not breakfast, salt intake, cooking methods, eating speed, taste preference and dietary intake structure/frequency/type.
MNA-SF Scale	BMI, psychology, calf circumference, mid-arm circumference diet, etc.
Household drinking water	Type/source of drinking water.
Smoking	Smoking history, age of first smoking, cigarette type, smoking cessation history, smoking status of family members, second-hand smoke inhalation status.
Alcohol intake	Drinking history, first drinking age, drinking frequency and type.
Tea intake	Whether to drink tea now and in the past, age of first drinking, tea type, daily intake (ml).
Physical exercise	Whether physical exercise is performed now and in the past, age at physical exercise start and end.
Daily & Leisure activity	Housework, farming, raising poultry, reading, playing mahjong, TV, radio, chat in teahouses, etc.
ADL Scale	Daily living ability assessment, including eating, walking, dressing, bathing, etc.
IADL Scale	Instrumental assessment of activities of daily living, including cooking, taking medicine, shopping, calling, etc.
Frail Scale	Fatigue, endurance, walking, illness, weight loss.
PSQI Scale	Sleep assessment
MMSE Scale	Cognitive function assessment, including orientation, memory, attention, calculation, meeting ability, language ability.

GAD-7 Scale	Anxiety assessment, including nervousness, worry, irritability, fear, etc.
GDS-15 Scale	Depression assessment, including feelings of helplessness, memory, getting help, difficulty, boredom, emptiness, etc.

Note: SSRS,Social Support Rating Scale ;MNA-SF, Mini Nutritional Assessment-Short Form;ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living;PSQI, Pittsburgh Sleep Quality Index;MMSE, Mini-mental State Examination ;GAD-7, Generalized Anxiety Disorder-7; GDS-15, Geriatric Depression Scale-15.

Biological samples were collected from participants, and in return they received a free routine blood and urine screening including liver and kidney function tests. All specimens were pre-processed on the day of collection. For convenience, samples were labelled with the participant's basic information, including their sample number, name, gender, and age. All specimens except hair specimens were stored temporarily at 4°C before being moved (using dry ice to ensure ultra-low temperature refrigeration throughout the transportation) to the main -80°C storage facility at the Biological Specimen Bank of West China Hospital of Sichuan University. The description of the specimen pre-processing procedure and long-term storage conditions at each sub-center are shown in Table 2.

Table 2: Specimen pre-processing procedure and long-term storage conditions

Sample Type	Pre-Process Standard Method	Storage Condition
Blood	2 tubes (5ml/tube) of blood per person were collected, which had been centrifuged by 3500 rpm in 15 minutes, and divided into 8 EP tubes (2 tubes of albuginea and 6 tubes of plasma).	-80℃ ultra-low temperature refrigerator.

Urine	On the day of collection, the urine was divided into 2 EP tubes (2 ml and 15 ml each) at room temperature.	-80℃ ultra-low temperature refrigerator.
Stool	Take a small amount, place in the preservation solution, and mix well.	-80℃ ultra-low temperature refrigerator.
Saliva	Centrifuge, 2500 rpm, 1 minute, the supernatant and residue were placed in two 5ml pointed EP tubes.	-80℃ ultra-low temperature refrigerator.
Hair	Put 10-20 hairs (10 cm/piece) in a sealed bag.	Store at room temperature.

Note: All EP tubes are suitable for ultra-low temperature storage.

A full physical examination was conducted to characterize the basic physical fitness level and incidence of age-related disease (such as sarcopenia) in the study population. The procedure for the full physical examination is shown in Table 3.

Table 3: Physical examination procedure

	Item	Description
Physical condition	Height	Stand up straight, measure 2 times in a row, and ask about last year's weight
	Weight	Take off the coat and other heavy clothes, repeat the measurement twice.
	Upper arm circumference	Measure the circumference of the upper arm at the midpoint of the line between the shoulder and the elbow, repeat the

		measurement twice.
	Triceps skinfold thickness	Use a cortical thickness gauge to measure the fat thickness at the midpoint of the shoulder and elbow joint, repeat the measurement twice.
	Calf circumference	Keep leg upright, measure the circumference of the thickest part of the calf, repeat the measurement twice.
	Waist circumference	Measure the waist circumference at a point 2 cm above the belly button, repeat the measurement twice.
	Hip circumference	The circumference between the symphysis pubis and the most convex part of the back gluteus maximus, repeat the measurement twice.
	Knee height	The length between the knee joint and the heel, repeat the measurement twice.
	Finger distance	The length between the index fingers of both hands, repeat the measurement twice.
Disease related condition	Blood pressure& Pulse	After sitting and resting for 2-5 minutes, start the measurement, record the diastolic and systolic blood pressure (electronic sphygmomanometer), and repeat the measurement twice.
	Electrocardiogram bioelectrical impedance	After confirming that there is no metal in the participant's body, use INBODY S10

	analysis (BIA)	(BioSpace, Seoul, Korea) to measure the BIA data, enter the participant's information into the host, adopt a sitting posture, and connect all limbs with electrodes. No talking is allowed during the measurement.
	Gait speed (s/m)	Measure the pace of the participants and calculate the pace (seconds/meter) at the start and end times of 3 segments of 4 meters.
	Grip strength	Ask the participant's habit of using hands and test the grip strength of both hands twice.
	Balance test	Participants were tested for balance in three stances, including feet side by side, staggered feet, and front and rear feet. Each stance held for 10 seconds was deemed qualified.
	Blood sugar	Fingertip blood sugar test.
	Sit-up ability tests	Participants hold their shoulders, complete 1 and 5 consecutive sit-up tests respectively, and record the completion status (whether it can be completed and when it is completed).

Measurement of key variables

Mental state and cognitive assessment

The assessment of the psychological state mainly comprised the evaluation of anxiety and depression in participants using the GAD-7 and GDS-15 assessment tools, respectively. The GAD-7 comprises 7 questions to assess the participant's generalized anxiety in the past 2 weeks. The GAD-7 scale[8] is scored from 0 to 21, with a higher

score representing a more severe anxiety level. The evaluation standards are 0-4 points signifying a normal level, 5-9 points for mild anxiety, 10-14 points for moderate anxiety, and 15-21 points signifying severe anxiety. The GDS-15 scale[9] is used in the evaluation of depression in elderly adults over the past week. The scale consists of 4 questions that are scored directly and 11 reverse-scored questions. Again, a higher score represents the more severe depression. The evaluation standards are 0-4 signifying a normal level, 5-8 for mild depression, 9-11 for moderate depression, and 12-15 signifying severe depression.

Considering the characteristics of China's elderly population, such as low education level, poor economic level, and the need for an assessment that was easy to administer, this study used the MMSE[10] to evaluate cognitive function. The MMSE scale evaluates participants' orientation, memory, recall ability, language ability, attention, and calculation ability through 30 questions. The highest achievable score is 30, with scores of 0-26 points representing cognitive dysfunction.

Sarcopenia

Following the recommendations of the "Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment", the assessment of sarcopenia in used this study mainly comprised the measurement of grip strength, pace, and Bioelectrical Impedance Analysis (BIA; Inbody S10, BioSpace, Seoul, Korea). Previous studies have shown no statistical differences between the use of magnetic resonance imaging (MRI) and BIA for the assessment of sarcopenia[11]. Muscle mass was defined using the appendicular skeletal muscle mass index (ASMI), calculated similarly to BMI, using the formula, appendicular skeletal mass (ASM) / height^2. A threshold of 7.0 kg/m^2 in men and 5.7 kg/m^2 in women was considered to signify low muscle mass. Low grip strength for men and women was defined as 26 kg and 18 kg, respectively[12]. The participant's usual walking speed was measured over 4 m, with a gait speed of less than 0.8 m/s considered to signify sarcopenia[13].

Activities of daily life

Participants' daily living activity assessment used health self-assessment measures (body, emotion, feeling) together with the ADL (level of basic self-care) and IADL (ability to use basic appliances) scales[14]. Based on previous research findings, we additionally used some simple, independently-designed health self-evaluation questions covering the previous month of the participant's life condition, including overall self-evaluation, limitations of the ability to undertake activity, the impact of health status on daily life, the impact of emotional status on daily life, pain status, self-assessed psychological state, the influence of health and mental state on daily social interaction, and other issues.

The ADL scale assesses participants' ability to take care of themselves by asking the ability of participants to defecate, urinate, groom, use the toilet, eat, move, dress, use the stairs, and bathe. The full scale of the scale comprises 100 points, with 100 points representing perfect ability with no need to rely on others; 61-99 points representing a mild dysfunction, but basically having the ability to take care of themselves; 41-60 points representing moderate dysfunction, and needing some help; 21-40 points representing severe dysfunction and needing to be dependent on others; and less than 20 points representing complete dependence on others.

The IADL scale comprehensively evaluates the participants' ability to use basic appliances. The evaluation content includes cooking, housework, taking medicine, walking, shopping, financial management, using the telephone, and washing clothes. The scale has a maximum score of 16, with a score of less than 8 indicating impaired instrumental life ability.

Sleep quality

The PSQI scale[15] is used to evaluate the sleep of participants through sleep quality, the time taken to fall asleep, duration of sleep, sleep efficiency, sleep disorders, use of hypnotic drugs, and daytime dysfunction. The scale has a maximum score of 21 points, with a score of 0-5 representing the best sleep quality; 6-10 good sleep quality; 11-15 average sleep quality; and 16-21 poor sleep quality. In addition, we also asked questions

about “siesta”/napping and the Sleep Self-Assessment.

Medical history and social support

Participants were asked to provide a full medical history of chronic diseases (diagnosed by professional medical institutions), including cardiovascular and cerebrovascular diseases, respiratory diseases, nervous system diseases, hearing disorders, bone and joint diseases, liver and kidney diseases, and incontinence. The assessor asked about the symptoms experienced, including whether the participant was ill, the number of years they experienced the illness, and the treatment undertaken.

The SSRS[16] was used to evaluate the social support of the participants through factors such as the social interaction between the participants and friends, neighbors, family members, and social groups. The maximum score of this scale is 40 points, with a higher score representing better social support. A score of 30-40 was considered to represent a good degree of social support; a score of 20-29 a general degree of social support; and a score of less than 20 a lower degree of social support. In addition, we investigated the family microenvironment, including the housing structure, family economic control/discourse power, family respect, family decision-making, family support, family conflict response, and spousal relationship.

Nutrition and behavior

The MNA-SF[17] was used to conduct a nutritional assessment. This assessment tool consists of two sections, with all participants completing the first section and participants only progressing to the second section if they scored less than 11 points on the first, indicating possible malnutrition. A combined score (scores from both sections added together) of greater than 24 points was interpreted as a good nutritional status; 17-23.5 points was interpreted as a risk of malnutrition; and a score of less than 17 indicated the definite presence of malnutrition.

In addition, based on the characteristics of the traditional Chinese diet and previous research findings, we independently designed a series of survey questions related to

eating habits, diet types, and the frequency with which they ate certain foods. The survey of eating habits included the number of meals per day, meal times, the amount eaten at each meal, the types of food eaten at each meal (meat and vegetables), breakfast, flavorings, cooking methods, and speed of eating. Dietary content was assessed by asking how frequently (i.e. daily, 3-5 times a week, 1-2 times a week, 1-3 times a month, or never) participants consumed grains, vegetables, fruits, meat, eggs, seafood, dairy products, vegetable oil, animal oil, nuts, candy, cakes, etc.

Participant behavior was captured by asking about smoking, alcohol intake, tea intake, physical labor, and leisure activities. Participants were asked whether they smoke (at least one cigarette per day for more than 6 months), for how many years, what type of cigarettes, how many cigarettes per day, whether they had attempted to quit smoking, whether they experienced second-hand smoke inhalation, and how often. Similarly, alcohol consumption was defined as drinking alcohol at least once a week. Participants were asked at what age they started drinking alcohol, their drinking frequency, type of alcohol consumed, and the volume of a single drink. Participants were asked if they drank tea frequently (more than 3 times a week), whether their habits had been different in the past, the age they started drinking tea, the type of tea, and the amount of tea consumed daily.

Manual labor was assessed by asking participants whether they undertake moderate or severe manual labor, the number of days they did this per week, and the number of hours per day. Leisure activities were captured including growing vegetables, raising poultry, raising pets, reading books and newspapers, educational activities (Mahjong, etc.), watching television or listening to the radio, socializing in tea houses, etc.

Follow-up

The follow-up tool was designed taking into account the characteristics/results of the baseline data (October 2018-December 2019), key issues (frailty, cognition, disability, sarcopenia, psychology, etc.), and follow-up methods (phone or face-to-face follow-up). In 2020, the follow-up work needed to incorporate further external factors such as

COVID-19, and the government's policy response. The initial plan was to conduct a telephone follow-up with all participants recruited at baseline. Later, depending on the COVID-19 situation in China, it may be possible to conduct an in-person follow-up.

The telephone follow-up comprised a phone call of no longer than 10 minutes. For any participants who had died, the investigator recorded the date of death, cause of death, and other information, and comforted the family members of the deceased. For participants with the wrong phone number, the investigator tried to contact their family members or community staff to minimize the rate of loss to follow-up. For participants who were temporarily unavailable/busy, the investigator re-attempted contact on at least 5 occasions at different times of the working day/week/weekend. Telephone follow-up investigators were mostly medical college students, and all received comprehensive training.

Following completion of the telephone follow-up on all participants recruited at baseline, the attrition rate of the study was assessed. Then, according to the sample size requirements of the prospective dynamic cohort study, new participants were recruited to join the cohort, in line with the recruitment criteria outlined above.

Data quality control and management

Due to the participants being over 80 years old, and the locations of longevity areas being typically in marginal mountainous areas, this study chose to conduct data capture using paper questionnaires. Paper questionnaires were verified on the day of data collection. 30-50% of the questionnaires were randomly selected for verification by two independent investigators on the same day. Any missing or ambiguous responses were confirmed by the investigator telephoning the participant.

The database was established using Epidata3.0. Independent double entry was used, and the two independent databases were compared using the "consistency check" function of the software. Any inconsistencies between the two databases were modified on a case-by-case basis until the two databases were completely consistent.

All biological specimens were pre-processed and marked on the day of collection

(adding marking information, such as name, gender, age, and code, etc., based on the original barcode and QR code of each cryopreservation tube), and stored in the ultra-low temperature refrigerator Medium (-80 degrees Celsius). The transport conditions of biological specimens in intra-city were with the help of a transfer box, which was kept at 4 degrees Celsius to avoid hemolysis of biological specimens; for the transfer of biological specimens between cities, dry ice was used to maintain an ultra-low temperature environment, and the entire process of transport had a temperature control record; all biological specimens According to ethical requirements, were stored in the biological specimen bank of West China Hospital of Sichuan University for long-term preservation. At the same time, after each transfer was completed, whether it was intra-city transfer or inter-city transfer, random inspections (1-3%) of the location information of cryopreservation tubes were required to ensure that the storage location of biological specimens will not change due to the transfer work. (Change, move and loss of storage location information, etc.).

All evaluation results would be fed back to the person or family members within one month, laying a good foundation of trust for the next follow-up work.

The Principal Investigator (PI) has overall responsibility for data management, including data storage, application, and use. The data management plan follows guidance on medical ethics, fairness, and bias. Therefore, before using the data, the data was de-identified by removing sensitive information such as the fields of participant name, gender, age, identification number, and home address.

PATIENT AND PUBLIC INVOLVEMENT

No patient involved.

STATISTICAL STRATEGY AND FINDINGS TO DATE

Data analyses were conducted using SPSS version 22.0 and R 3.6.1. Descriptive statistical analyses were conducted on longevity-related characteristics and medical

examination data to provide percentages, means, and standard deviations. For interrogation of independent samples by region, gender, ages, and disease, chi-squared tests were used. If the conditions for using chi-squared tests were not met, the Fisher test was used instead. For variables such as scores on any of the psychometric or behavioral scales, the rank-sum test was used.

Participant characteristics are displayed in Table 4.

Table 4: Participant characteristics

Characteristics	All (n=1537)	Men (n=643)	Women (n=894)	P value	Missing number
Age(years), mean(±SD)	88.7 (7.36)	87.7 (6.39)	89.40 (7.91)	<0.001	1
80-85	682 (44.4)	295 (46.0)	387 (43.3)	<0.001	1
86-90	293 (19.1)	142 (22.1)	151 (16.9)		
91-99	328 (21.4)	150 (23.4)	178 (19.9)		
≥100	233 (15.2)	55 (8.6)	178 (19.9)		
Ethnics, n (%)					3
Han	1530 (99.7)	639 (99.7)	891 (99.8)		
Others	4 (0.3)	2 (0.4)	2 (0.2)		
Educational level, n (%)				<0.001	6
No formal education	915 (59.8)	232 (36.3)	683 (76.6)		
Elementary school	432 (28.2)	281(44.0)	151 (16.9)		
Middle school	98 (6.4)	66 (10.3)	32 (3.6)		
Technical secondary school	35(2.3)	23(3.6)	12(1.3)		
High school and above	51 (3.3)	37(5.8)	14 (1.6)		
Status of spouse, n (%)				<0.001	20
Alive	512 (33.8)	352(55.3)	160 (18.2)		
Divorced	5 (0.3)	2 (0.3)	3 (0.3)		

Widowed		1000 (65.9)	282 (44.3)	718 (81.5)		
Annual household income per capita, n (%)						8
< 1000 rmb/year		77(5.0)	32(5.0)	45(5.1)		
1000-3000 rmb/year		299(19.6)	121(18.9)	178(20.0)		
3001-6000 rmb/year		257(16.8)	101(15.8)	156(17.5)		
6001-8000 rmb/year		104(6.8)	41(6.4)	63(7.1)		
8001-10000 rmb/year		75(4.9)	29(4.5)	46(5.2)		
> 10000 rmb/year		582 (38.1)	269 (42.1)	313 (35.2)		
Unknown		135 (8.8)	46 (7.2)	89 (10.0)		
Anthropometric measures						
Height (cm)		148.4 (10.7)	156.1 (7.7)	142.8 (8.9)	<0.001	12
Weight(kg)		49.4 (10.4)	54.3 (9.8)	45.9 (9.4)	<0.001	12
BMI (kg/m^2)		22.3 (3.7)	22.2 (3.3)	22.4 (4.0)	<0.001	15
Underweight (<18.5)		201 (13.2)	62 (9.7)	139 (15.7)		
Normal (18.5–24.0)		863 (56.7)	391 (61.2)	472 (53.4)		
Overweight (24.0-27.9)		356 (23.4)	158 (24.7)	198 (22.4)		
Obese (> 28.0)		103 (6.8)	28 (4.4)	75 (8.5)		
Grip strength		17.5 (11.2)	22.2 (11.0)	14.0 (10.0)	<0.001	47
4-meter gait speed		0.58 (0.23)	0.63 (0.22)	0.58 (0.23)	<0.001	103
Life-styles						
Drinking	Yes	435 (28.4)	329 (51.4)	106 (11.9)	<0.001	6
tea history	No	1096 (71.6)	311 (48.6)	785 (88.1)		
Drinking	Yes	476 (31.1)	196 (46.2)	180 (20.2)	<0.001	6
alcohol history	No	1055 (68.9)	344 (53.8)	711 (79.8)		
Smoking history	Yes	429 (28.1)	332 (52.1)	97 (10.9)	<0.001	9

	No	1099 (71.9)	305 (47.9)	794 (89.1)		
Scale evaluation						
ADL scale result		93.3 (14.3)	95.3 (12.0)	91.9 (15.6)	<0.001	17
Good (100 points)		934 (61.7)	443 (70.0)	491(55.7)		
Mild dysfunction (>60)		514 (33.9)	170 (26.9)	344 (39.0)		
Moderate dysfunction (41-60)		36 (2.4)	12 (1.9)	24 (2.7)		
Severe dysfunction (21-40)		17 (1.1)	4 (0.6)	13 (1.5)		
Completely disabled (<20)		14 (0.9)	4 (0.6)	10 (1.1)		
IADL scale result		11.4 (4.6)	12.1 (4.2)	10.9 (4.9)	<0.001	16
Good function (≥8)		1214 (79.8)	542 (85.6)	672 (75.7)		
Impaired function (< 20)		307 (20.2)	91 (14.4)	216 (24.3)		
MMSE scale result		16.3 (8.1)	19.0 (7.7)	14.3 (7.7)	<0.001	174
normal		151 (11.1)	100 (17.3)	51 (6.5)		
Cognitive Impairment		1212 (88.9)	478 (82.7)	734 (93.5)		

STRENGTHS AND LIMITATIONS OF THIS STUDY

Strengths

The first multi-center study conducted in the elderly Chinese people living in Longevity Townships.

Exploring longevity-related behaviors in western China, and characterizing chronic diseases incident in this population (sarcopenia, disability, mild cognitive impairment; MCI, frailty, etc.) and the present prevalence of these diseases.

Establishing a biological sample bank of people living in these areas, and plan to find and verify longevity-related biomarkers by multi-omics.

Limitations

Much of the data is collected through self-report, creating a potential for recall bias. To counter this, data evaluators underwent comprehensive training, but there may still be investigator bias in the evaluation stage.

The target population of this research is elderly adults, so a selective survival bias may exist in the disease epidemiological aspects of the research, as may the loss to follow-up bias.

COLLABORATION

Welcome geriatric medicine and longevity related researchers through our center website (http://www.wchscu.cn/scientific/clinical/platform/55440.html) for more data information (Database name: A natural cohort study of the old adult), if researchers have any requirements, you can also contact us by E-Mail (hxncrcg@163.com) for more details and cooperation.

FUTURE DETAILS

It is planned to continue to carry out annual participant follow-up and collection of biological samples. Participants in the existing cohort will be followed up continuously, and new participants will be recruited into the prospective dynamic cohort study based on maintaining a constant sample size (i.e. to compensate for dropout). Participants who did not have the opportunity to contribute biological samples at the baseline time point will be followed up as soon as possible, and annual sample collections will occur as appropriate.

Biological samples (blood, urine, saliva, stool) from participants will be analyzed using proteomics, metabolomics, and other techniques as outlined above. Results from these analyses will then be combined with the questionnaire and physical examination data to identify biomarkers of longevity, healthy lifestyle factors, and health-related factors.

The findings of these complex analyses will be exploited for any factors that can be translated into community benefit. With reference to China's aging society, non-pharmaceutical health intervention and promotion programs will be explored and formulated with the intention of meeting the needs of the current and future Chinese population. We will propose primary prevention measures suitable for community health promotion, which will be beneficial for a healthy lifestyle, incorporating what we have learned about the behaviors of the elderly Chinese inhabitants of Longevity Townships.

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CONTRIBUTORS

All the authors have made important contributions to this paper and have provided potential intellectual support for this cohort profile.

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Disclaimer

Our sources of funding had no role in the design of cohort profile, and will not be any impact on data collection, analysis, writing and decision to submit or publish the research results.

COMPETING INTERESTS

None.

PATIENT AND PUBLIC INVOLVEMENT STATEMENT

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

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Cohort Profile: A natural population cohort study on long-lived adults: West China Longevity and Aging Procedure (WCLAP)

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Cohort Profile: A natural population cohort study on long-lived adults: West China Longevity and Aging Procedure (WCLAP)

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ABSTRACT

Purpose: The West China Longevity and Aging Procedure cohort study (WCLAP) aims to provide guidance for older adults in western China with the aim of improving quality of life, reducing the burden of family care, summarizing the characteristics of longevity lifestyles, building a Chinese-longevity-population biobank, and exploring the mechanisms underlying population aging.

Participants: Since the establishment of the WCLAP research baseline in 2018, a population of 1,537 adults aged 80 years and above, living in the community, have been enrolled in the program as research participants. Of these, 231 are aged 100 years and above. Participants are followed up every year.

Finding to data: WCLAP data is collected in 5 hospital research sub-centers strategically located adjacent to the national "Longevity Townships" of Chengdu Ziyang, Leshan, Yibin, and Pengshan. Data collection included a comprehensive assessment of the participant's health (including physical, psychological, social, common chronic disease assessments), instrumental tests (body composition and muscle percentage), and the collection of biomedical-biobank samples (include blood, urine, feces, hair, and urine).

Future plans: Through the annual cohort follow-up, survival-related information is collected at a group level. Analysis of biological samples facilitates biological characterization at the microscopic level through proteomics, metabolomics, genomics, and other techniques. Baseline data, group-level follow-up data, and microbiological examination data are integrated together to provide an evaluation tool, exploring sarcopenia, disability, dementia, caregiver burden, aging biomarkers, and other influencing factors.

Registration: The WCLAP was approved by the Medical Ethics Committee of the West China Hospital of Sichuan University (Reference Number: 2018-463), and

registered with the China Clinical Trial Registration Center (Registration number: ChiCTR1900020754).

Keywords: Natural population; Long-lived adults; Cohort study; Sarcopenia; Frailty; Dementia.

STRENGTHS AND LIMITATIONS OF THIS STUDY

Strengths

The first multi-center study conducted in the elderly Chinese people living in Longevity Townships.

Exploring longevity-related behaviors in western China, and characterizing chronic diseases incident in this population (sarcopenia, disability, mild cognitive impairment; MCI, frailty, etc.) and the present prevalence of these diseases.

Establishing a biological sample bank of people living in these areas, and plan to find and verify longevity-related biomarkers by multi-omics.

Limitations

Much of the data is collected through self-report, creating a potential for recall bias. To counter this, data evaluators underwent comprehensive training, but there may still be investigator bias in the evaluation stage.

The target population of this research is elderly adults, so a selective survival bias may exist in the disease epidemiological aspects of the research, as may the loss to follow-up bias.

Data availability statement

Data are available on reasonable request. All data relevant to the study are available on reasonable request to the corresponding author.

INTRODUCTION

The increasing age of the population has become one of the main factors affecting the quality of life globally. As the elderly population increases, age-related chronic conditions contribute to the global healthcare burden and are anticipated to become the next global public health challenge[1]. There is much research ongoing to determine how best to achieve healthy aging, improve quality of life in old age, and reduce the burden on family caregivers of elderly disabled relatives. As such, a great investment is being driven into the field of aging health in various countries. In 2018, the population of people aged over 64 surpassed that of children under 5 for the first time. By 2050, it is predicted that nearly 20% of the world's population will be over 65[2]. Consequently, the workforce in social production is likely to face increased life pressure and social responsibility. It is important to establish a balance between social burden and social productivity, and a good strategy is required to achieve this.

In 2000, China was acknowledged to have an aging society. A national survey conducted by the National Bureau of Statistics reported China's elderly population (defined as those aged 60 and over) to have reached 249 million at the end of 2018, comprising 17.9% of the total population; with those aged 65 and over numbering 167 million, accounting for 11.9% of the total population[3]. This rate of aging is projected to increase further to 24.7% in the next 25 years[4]. In 2010, Chinese scholars reported the total number of people over 60 to be 178 million, accounting for 13.32% of the total population and predicted that by 2030, this will reach 359 million. By 2050, the total number of people over 60 is estimated to reach 448 million, accounting for about 40% of the total population, with a serious impact on quality of life[5, 6]. In the future, with further advancements in technology and human intelligence, China is expected to face more severe consequences from this aging society.

The elderly population of longevity townships in China has different behavioral characteristics to those in Europe and America, including the variety and structure of

dietary intake, economic level, educational background, psychological health (anxiety, depression), the provision of family care, and physical activity. The present research aims to focus on the behavioral characteristics associated with high-quality survival and longevity of the elderly population in China's longevity areas. This will be achieved by assessing the lifestyles at a large scale and the biological multi-omics at the microscopic scale. This study aims to summarize the characteristics associated with longevity in this special population of elderly Chinese people. By starting from the concept of primary prevention, this study aims to characterize behaviors associated with a long and healthy and longevity life, providing government departments with evidence supporting public health primary prevention strategies. Conversely, through the testing and analysis of biological samples with the help of metabolomics, proteomics, and other methods, biomarkers of healthy aging will be identified to provide a basis for the future development of anti-aging drugs and the treatment of age-related diseases.

COHORT DESCRIPTION

Study design and setting

The design and baseline of WCLAP were formed in 2017 and 2018, respectively, with the plan of conducting an annual cohort follow-up. WCLAP was designed to be a prospective dynamic cohort study across 4 medical and health institutions in the National Longevity Region in western China. From October 10, 2018, to December 1, 2019, WCLAP successively established baseline research subcenters in five longevity regions in western China; Chengdu (The West China Hospital of Sichuan University), Ziyang (Ziyang Zhonghua Hospital), Leshan (The First People's Hospital of Leshan City), Meishan (Pengshan Traditional Chinese Medicine Hospital of Meishan City), and Yibin (The Second People's Hospital of Yibin City). The data collected by each sub-center were collated at the West China Hospital of Sichuan University (WCHSCU). All biological samples were collected according to standardized operational processes

and stored in the biological specimen bank of the West China Hospital of Sichuan University.

Ethnical approval

The WCLAP was approved by the Medical Ethics Committee of the West China Hospital of Sichuan University (Reference Number: 2018-463), and registered with the China Clinical Trial Registration Center (Registration number: ChiCTR1900020754).

Data collection

Data collection comprised (1) the completion of a questionnaire survey, (2) a full physical examination, and (3) biological specimen collection and laboratory tests.

The design of the questionnaire was based on the National Health and Aging Trends Study (NHATS) created by the Johns Hopkins University[7] and applied to the population of western China. The contents of the questionnaire survey comprised basic demographic characteristics, social activity, family longevity, health and disease status, lifestyle behaviors, and evaluation scales. Before the formal use of the questionnaire, our team carried out pre-test among the old adult in the community to continuously verify the reliability and validity of the questionnaire. The internal consistency was determined from Cronbach's alpha calculation. Our questionnaire had a Cronbach's alpha of 0.91, and finally was confirmed the final version.

The physical examination included measures of grip strength, pace, body mass index (BMI), blood pressure, skinfold thickness at the triceps, the sit-up test, and body composition. Before data collection, all test instruments were calibrated according to manufacturer guidelines.

Biological specimen collection for laboratory testing included blood, urine, stool, saliva,

and hair. Subjects were provided with a free routine screening of their blood and urine samples within one month of their physical examination.

Study subjects

Participants were recruited from the National Longevity Region in Western China. The eligibility criteria were as follows:

1. Participants agreed to participate in the study and signed an informed consent form.

2. Participants were aged 80 years old or older (according to their identification card).

3. Participants had lived in the locality for at least 1 year.

4. Participants were willing and able to cooperate with the evaluator in the local language to complete the 30-minute evaluation.

Exclusion criteria:

1. Unwillingness to sign the informed consent form, complete all assessment content independently.

2. The presence of metal implants in the body, such as stents, artificial joints, pins, plates, or cardiac pacemakers.

3. Being under the age of 80 (according to their identification card).

4. Having a life expectancy of under 6 months (diagnosed by medical institution).

Sampling method

A multi-stage cluster sampling method was used as follows:

1. The study population comprised the population of elderly adults across the varied topography and landforms of the national longevity area in western China, including

hills, basins, mountains, and plains.

2. Given the two factors of the geographical environment and the extent of the national longevity areas, four cities in western China were selected as sub-centers for the study, namely Meishan, Ziyang, Yibin, and Leshan.

3. Given the influence of many factors, including the convenience of transport routes, the willingness of municipal/county/village-level government bodies to cooperate, the sizes of local populations, the distances between collection points and local sub-centers, and local acceptance of modern medicine, districts were selected adjacent to each sub-center. These were Pengshan District (adjacent to Meishan City), Yanjiang District (adjacent to Ziyang City), Cuiping District (adjacent to Yibin City), and Shizhong District (adjacent to Leshan City).

4. In each of the above districts, a number of towns (10 towns from Pengshan,17 towns from Yanjiang, 12 towns from Cuiping, 12 towns from Shizhong) were randomly selected based on factors such as accessibility, population size and structure.

5. Data collection was conducted at each research site, facilitated by preliminary communication with government departments, sub-centers, and community organizations at all levels of the project site, to initiate social mobilization and publicity for the study. Residents of each of the selected towns were invited to voluntarily participate in the study. Our team will provide each participant with free medical examination service (about 90 USD) and long-term health follow-up service (free hospital referral service will be provided if necessary) as compensation.

Baseline evaluation

The baseline assessment was completed in 2019, whereby 1,546 elderly adults participated. The baseline assessment included the survey, biological sample collection, and physical examination as detailed above.

The questionnaire included basic personal information, information about social and

support networks, social microenvironment, religious beliefs, family longevity, chronic disease, health self-assessment, eating habits, household drinking water, smoking status, alcohol/tea intake, physical exercise, and daily and leisure activity. This was achieved using validated assessment tools, and where possible those designed specifically for use in elderly populations; Activities of Daily Living (ADL)[8-10], Instrumental Activities of Daily Living (IADL)[9, 10], Clinical Frailty Scale[11, 12], Social Support Rating Scale (SSRS)[13], Pittsburgh Sleep Quality Index (PSQI)[14, 15], the short form of the multi-nutritional assessment (MNA-SF)[16, 17], mini mental-state exam (MMSE)[18, 19], the Generalized Anxiety Disorder questionnaire (GAD-7)[20] and the Geriatric Depression Scale (GDS-15)[21]. The questionnaire contents are detailed in Table 1.

Table 1: The main contents of the questionnaire survey

Questionnaire Frame	Content Description
Basic personal information	Name, gender, age, ID number, place of birth, length of local residence, local residential address, telephone number (her/himself + relatives), Educational background, nationality, language (minority language), main occupation before 60 years old, etc..
Social network & support	Childbirth (number of sons and daughters), family situation, family financial control, family respect, home care, family function, neighbor/friend relationship, support and assistance, marriage/spouse situation, etc.
SRSS Scale	Social support evaluation, including friends, neighbors, family, asking for help, talking, etc.

Social microenvironment	Family living area, source of income, annual family income, and economic satisfaction.
Religious belief	Religious type, religious activities
Longevity Family Survey	Long-lived relatives, family history of genetic disease
History of chronic disease	Types of chronic diseases, hospitalization, medical insurance, medical expenses in the past year, satisfaction with medical conditions, timely medical treatment, etc.
Health self-assessment	Limitation of activity, physical state, emotional state, pain, self-feeling, etc.
Eating habits	The number of meals per day, the amount of food, the combination of meals, whether or not breakfast, salt intake, cooking methods, eating speed, taste preference and dietary intake structure/ frequency/ type.
MNA-SF Scale	BMI, psychology, calf circumference, mid-arm circumference diet, etc.
Household drinking water	Type/source of drinking water.
Smoking	Smoking history, age of first smoking, cigarette type, smoking cessation history, smoking status of family members, second-hand smoke inhalation status.
Alcohol intake	Drinking history, first drinking age, drinking frequency and type.

Tea intake	Whether to drink tea now and in the past, age of first drinking, tea type, daily intake (ml).
Physical exercise	Whether physical exercise is performed now or in the past, age at physical exercise start and end.
Daily & Leisure activity	Housework, farming, raising poultry, reading, playing mahjong, TV, radio, chat in teahouses, etc.
ADL Scale	Daily living ability assessment, including eating, walking, dressing, bathing, etc.
IADL Scale	Instrumental assessment of activities of daily living, including cooking, taking medicine, shopping, calling, etc.
Frail Scale	Fatigue, endurance, walking, illness, weight loss.
PSQI Scale	Sleep assessment
MMSE Scale	Cognitive function assessment, including orientation, memory, attention, calculation, meeting ability, language ability.
GAD-7 Scale	Anxiety assessment, including nervousness, worry, irritability, fear, etc.
GDS-15 Scale	Depression assessment, including feelings of helplessness, memory, getting help, difficulty, boredom, emptiness, etc.

Note: SSRS, Social Support Rating Scale; MNA-SF, Mini Nutritional Assessment-Short Form; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living; PSQI, Pittsburgh Sleep Quality Index; MMSE, Mini-mental State Examination; GAD-7, Generalized Anxiety Disorder-7; GDS-15, Geriatric Depression Scale-15.

Biological samples were collected from participants, and in return they received a free routine blood and urine screening including liver and kidney function tests. All specimens were pre-processed on the day of collection. For convenience, samples were labelled with the participant's basic information, including their sample number, name, gender, and age. All specimens except hair specimens were stored temporarily at 4°C before being moved (using dry ice to ensure ultra-low temperature refrigeration throughout the transportation) to the main -80°C storage facility at the Biological Specimen Bank of West China Hospital of Sichuan University. The description of the specimen pre-processing procedure and long-term storage conditions at each sub-center are shown in Table 2.

Table 2: Specimen pre-processing procedure and long-term storage conditions

Sample Type	Pre-Process Standard Method	Storage Condition
Blood	2 tubes (5ml/tube) of blood per person were collected, which had been centrifuged by 3500 rpm in 15 minutes, and divided into 8 EP tubes (2 tubes of albuginea and 6 tubes of plasma).	-80℃ ultra-low temperature refrigerator.
Urine	On the day of collection, the urine was divided into 2 EP tubes (2 ml and 15 ml each) at room temperature.	-80℃ ultra-low temperature refrigerator.
Stool	Take a small amount, place in	-80℃ ultra-low temperature

	the preservation solution, and mix well.	refrigerator.
Saliva	Centrifuge, 2500 rpm, 1 minute, the supernatant and residue were placed in two 5ml pointed EP tubes.	-80℃ ultra-low temperature refrigerator.
Hair	Put 10-20 hairs (10 cm/piece) in a sealed bag.	Store at room temperature.

Note: All EP tubes are suitable for ultra-low temperature storage.

A full physical examination was conducted to characterize the basic physical fitness level and incidence of age-related disease (such as sarcopenia) in the study population. The procedure for the full physical examination is shown in Table 3.

Table 3: Physical examination procedure

	Item	Description
Physical condition	Height	Stand up straight, measure 2 times in a row, and ask about last year's weight
	Weight	Take off the coat and other heavy clothes, repeat the measurement twice.
	Upper arm circumference	Measure the circumference of the upper arm at the midpoint of the line between the shoulder and the elbow, repeat the measurement twice.
	Triceps skinfold	Use a cortical thickness gauge to measure

	thickness	the fat thickness at the midpoint of the shoulder and elbow joint, repeat the measurement twice.
	Calf circumference	Keep leg upright, measure the circumference of the thickest part of the calf, repeat the measurement twice.
	Waist circumference	Measure the waist circumference at a point 2 cm above the belly button, repeat the measurement twice.
	Hip circumference	The circumference between the symphysis pubis and the most convex part of the back gluteus maximus, repeat the measurement twice.
	Knee height	The length between the knee joint and the heel, repeat the measurement twice.
	Finger distance	The length between the index fingers of both hands, repeat the measurement twice.
Disease related condition	Blood pressure& Pulse	After sitting and resting for 2-5 minutes, start the measurement, record the diastolic and systolic blood pressure (electronic sphygmomanometer), and repeat the measurement twice.
	Electrocardiogram bioelectrical impedance	After confirming that there is no metal in the participant's body, use INBODY S10 (BioSpace, Seoul, Korea) to measure the

	analysis (BIA)	BIA data, enter the participant's information into the host, adopt a sitting posture, and connect all limbs with electrodes. No talking is allowed during the measurement.
	Gait speed (s/m)	Measure the pace of the participants and calculate the pace (seconds/meter) at the start and end times of 3 segments of 4 meters.
	Grip strength	Ask the participant's habit of using hands and test the grip strength of both hands twice.
	Balance test	Participants were tested for balance in three stances, including feet side by side, staggered feet, and front and rear feet. Each stance held for 10 seconds was deemed qualified.
	Blood sugar	Fingertip blood sugar test.
	Sit-up ability tests	Participants hold their shoulders, complete 1 and 5 consecutive sit-up tests respectively, and record the completion status (whether it can be completed and when it is completed).

Measurement of key variables

Mental state and cognitive assessment

The assessment of the psychological state mainly comprised the evaluation of anxiety and depression in participants using the GAD-7 and GDS-15 assessment tools, respectively. The GAD-7 comprises 7 questions to assess the participant's generalized anxiety in the past 2 weeks. The GAD-7 scale is scored from 0 to 21, with a higher score representing a more severe anxiety level. The evaluation standards are 0-4 points signifying a normal level, 5-9 points for mild anxiety, 10-14 points for moderate anxiety, and 15-21 points signifying severe anxiety[22]. The GDS-15 scale is used in the evaluation of depression in elderly adults over the past week. The scale consists of 4 questions that are scored directly and 11 reverse-scored questions. Again, a higher score represents the more severe depression. The evaluation standards are 0-4 signifying a normal level, 5-8 for mild depression, 9-11 for moderate depression, and 12-15 signifying severe depression[23].

Considering the characteristics of China's elderly population, such as low education level, poor economic level, and the need for an assessment that was easy to administer, this study used the MMSE to evaluate cognitive function. The MMSE scale evaluates participants' orientation, memory, recall ability, language ability, attention, and calculation ability through 30 questions. The highest achievable score is 30, with scores of 0-26 points representing cognitive dysfunction[24].

Sarcopenia

Following the recommendations of the "Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment", the assessment of sarcopenia in used this study mainly comprised the measurement of grip strength, pace, and Bioelectrical Impedance Analysis (BIA; Inbody S10, BioSpace, Seoul, Korea). Previous studies have shown no statistical differences between the use of magnetic resonance imaging (MRI) and BIA for the assessment of sarcopenia[25]. Muscle mass was defined using the appendicular skeletal muscle mass index (ASMI), calculated similarly to BMI, using the formula, appendicular skeletal mass (ASM) / height^2. A

threshold of 7.0 kg/m^2 in men and 5.7 kg/m^2 in women was considered to signify low muscle mass. Low grip strength for men and women was defined as 26 kg and 18 kg, respectively[26]. The participant's usual walking speed was measured over 4 m, with a gait speed of less than 0.8 m/s considered to signify sarcopenia[27].

Activities of daily life

Participants' daily living activity assessment used health self-assessment measures (body, emotion, feeling) together with the ADL (level of basic self-care) and IADL (ability to use basic appliances) scales[8-10]. Based on previous research findings, we additionally used some simple, independently-designed health self-evaluation questions covering the previous month of the participant's life condition, including overall self-evaluation, limitations of the ability to undertake activity, the impact of health status on daily life, the impact of emotional status on daily life, pain status, self-assessed psychological state, the influence of health and mental state on daily social interaction, and other issues.

The ADL scale assesses participants' ability to take care of themselves by asking the ability of participants to defecate, urinate, groom, use the toilet, eat, move, dress, use the stairs, and bathe. The full scale of the scale comprises 100 points, with 100 points representing perfect ability with no need to rely on others; 61-99 points representing a mild dysfunction, but basically having the ability to take care of themselves; 41-60 points representing moderate dysfunction, and needing some help; 21-40 points representing severe dysfunction and needing to be dependent on others; and less than 20 points representing complete dependence on others.

The IADL scale comprehensively evaluates the participants' ability to use basic appliances. The evaluation content includes cooking, housework, taking medicine, walking, shopping, financial management, using the telephone, and washing clothes. The scale has a maximum score of 16, with a score of less than 8 indicating impaired instrumental life ability[9].

Sleep quality

The PSQI scale is used to evaluate the sleep of participants through sleep quality, the time taken to fall asleep, duration of sleep, sleep efficiency, sleep disorders, use of hypnotic drugs, and daytime dysfunction. The scale has a maximum score of 21 points, with a score of 0-5 representing the best sleep quality; 6-10 good sleep quality; 11-15 average sleep quality; and 16-21 poor sleep quality. In addition, we also asked questions about “siesta”/napping and the Sleep Self-Assessment[28].

Medical history and social support

Participants were asked to provide a full medical history of chronic diseases (diagnosed by professional medical institutions), including cardiovascular and cerebrovascular diseases, respiratory diseases, nervous system diseases, hearing disorders, bone and joint diseases, liver and kidney diseases, and incontinence. The assessor asked about the symptoms experienced, including whether the participant was ill, the number of years they experienced the illness, and the treatment undertaken.

The SSRS was used to evaluate the social support of the participants through factors such as the social interaction between the participants and friends, neighbors, family members, and social groups[29]. The maximum score of this scale is 40 points, with a higher score representing better social support. A score of 30-40 was considered to represent a good degree of social support; a score of 20-29 a general degree of social support; and a score of less than 20 a lower degree of social support. In addition, we investigated the family microenvironment, including the housing structure, family economic control/discourse power, family respect, family decision-making, family support, family conflict response, and spousal relationship.

Nutrition and behavior

The MNA-SF was used to conduct a nutritional assessment[30]. This assessment tool consists of two sections, with all participants completing the first section and

participants only progressing to the second section if they scored less than 11 points on the first, indicating possible malnutrition. A combined score (scores from both sections added together) of greater than 24 points was interpreted as a good nutritional status; 17-23.5 points was interpreted as a risk of malnutrition; and a score of less than 17 indicated the definite presence of malnutrition.

In addition, based on the characteristics of the traditional Chinese diet and previous research findings, we independently designed a series of survey questions related to eating habits, diet types, and the frequency with which they ate certain foods. The survey of eating habits included the number of meals per day, meal times, the amount eaten at each meal, the types of food eaten at each meal (meat and vegetables), breakfast, flavorings, cooking methods, and speed of eating. Dietary content was assessed by asking how frequently (i.e. daily, 3-5 times a week, 1-2 times a week, 1-3 times a month, or never) participants consumed grains, vegetables, fruits, meat, eggs, seafood, dairy products, vegetable oil, animal oil, nuts, candy, cakes, etc.

Participant behavior was captured by asking about smoking, alcohol intake, tea intake, physical labor, and leisure activities. Participants were asked whether they smoke (at least one cigarette per day for more than 6 months), for how many years, what type of cigarettes, how many cigarettes per day, whether they had attempted to quit smoking, whether they experienced second-hand smoke inhalation, and how often. Similarly, alcohol consumption was defined as drinking alcohol at least once a week. Participants were asked at what age they started drinking alcohol, their drinking frequency, type of alcohol consumed, and the volume of a single drink. Participants were asked if they drank tea frequently (more than 3 times a week), whether their habits had been different in the past, the age they started drinking tea, the type of tea, and the amount of tea consumed daily.

Manual labor was assessed by asking participants whether they undertake moderate or severe manual labor, the number of days they did this per week, and the number of

hours per day. Leisure activities were captured including growing vegetables, raising poultry, raising pets, reading books and newspapers, educational activities (Mahjong, etc.), watching television or listening to the radio, socializing in tea houses, etc.

Follow-up

The follow-up tool was designed taking into account the characteristics/results of the baseline data (October 2018-December 2019), key issues (frailty, cognition, disability, sarcopenia, psychology, etc.), and follow-up methods (phone or face-to-face follow-up). In 2020, the follow-up work needed to incorporate further external factors such as COVID-19, and the government's policy response. The initial plan was to conduct a telephone follow-up with all participants recruited at baseline. Later, depending on the COVID-19 situation in China, it may be possible to conduct an in-person follow-up.

The telephone follow-up comprised a phone call of no longer than 10 minutes. For any participants who had died, the investigator recorded the date of death, cause of death, and other information, and comforted the family members of the deceased. For participants with the wrong phone number, the investigator tried to contact their family members or community staff to minimize the rate of loss to follow-up. For participants who were temporarily unavailable/busy, the investigator re-attempted contact on at least 5 occasions at different times of the working day/week/weekend. Telephone follow-up investigators were mostly medical college students, and all received comprehensive training.

Following completion of the telephone follow-up on all participants recruited at baseline, the attrition rate of the study was assessed. Then, according to the sample size requirements of the prospective dynamic cohort study, new participants were recruited to join the cohort, in line with the recruitment criteria outlined above.

Data quality control and management

Due to the participants being over 80 years old, and the locations of longevity areas

being typically in marginal mountainous areas, this study chose to conduct data capture using paper questionnaires. Paper questionnaires were verified on the day of data collection. 30-50% of the questionnaires were randomly selected for verification by two independent investigators on the same day. Any missing or ambiguous responses were confirmed by the investigator telephoning the participant.

The database was established using Epidata3.0. Independent double entry was used, and the two independent databases were compared using the "consistency check" function of the software. Any inconsistencies between the two databases were modified on a case-by-case basis until the two databases were completely consistent.

All biological specimens were pre-processed and marked on the day of collection (adding marking information, such as name, gender, age, and code, etc., based on the original barcode and QR code of each cryopreservation tube), and stored in the ultra-low temperature refrigerator Medium (-80 degrees Celsius). The transport conditions of biological specimens in intra-city were with the help of a transfer box, which was kept at 4 degrees Celsius to avoid hemolysis of biological specimens; for the transfer of biological specimens between cities, dry ice was used to maintain an ultra-low temperature environment, and the entire process of transport had a temperature control record; all biological specimens According to ethical requirements, were stored in the biological specimen bank of West China Hospital of Sichuan University for long-term preservation. At the same time, after each transfer was completed, whether it was intra-city transfer or inter-city transfer, random inspections (1-3%) of the location information of cryopreservation tubes were required to ensure that the storage location of biological specimens will not change due to the transfer work. (Change, move and loss of storage location information, etc.).

All evaluation results would be fed back to the person or family members within one month, laying a good foundation of trust for the next follow-up work.

The Principal Investigator (PI) has overall responsibility for data management, including data storage, application, and use. The data management plan follows

guidance on medical ethics, fairness, and bias. Therefore, before using the data, the data was de-identified by removing sensitive information such as the fields of participant name, gender, age, identification number, and home address.

PATIENT AND PUBLIC INVOLVEMENT

No patient involved.

STATISTICAL STRATEGY AND FINDINGS TO DATE

Data analyses were conducted using SPSS version 22.0 and R 3.6.1. Descriptive statistical analyses were conducted on longevity-related characteristics and medical examination data to provide percentages, means, and standard deviations. For interrogation of independent samples by region, gender, ages, and disease, chi-squared tests were used. If the conditions for using chi-squared tests were not met, the Fisher test was used instead. For variables such as scores on any of the psychometric or behavioral scales, the rank-sum test was used.

Participant characteristics are displayed in Table 4.

Table 4: Participant characteristics

Characteristics	All (n=1537)	Men (n=643)	Women (n=894)	P value	Missing number
Age(years), mean(±SD)	88.7 (7.36)	87.7 (6.39)	89.40 (7.91)	<0.001	1
80-85	682 (44.4)	295 (46.0)	387 (43.3)	<0.001	1
86-90	293 (19.1)	142 (22.1)	151 (16.9)		

91-99	328 (21.4)	150 (23.4)	178 (19.9)		
≥100	233 (15.2)	55 (8.6)	178 (19.9)		
Ethnics, n (%)					3
Han	1530 (99.7)	639 (99.7)	891 (99.8)		
Others	4 (0.3)	2 (0.4)	2 (0.2)		
Educational level, n (%)				<0.001	6
No formal education	915 (59.8)	232 (36.3)	683 (76.6)		
Elementary school	432 (28.2)	281(44.0)	151 (16.9)		
Middle school	98 (6.4)	66 (10.3)	32 (3.6)		
Technical secondary school	35(2.3)	23(3.6)	12(1.3)		
High school and above	51 (3.3)	37(5.8)	14 (1.6)		
Status of spouse, n (%)				<0.001	20
Alive	512 (33.8)	352(55.3)	160 (18.2)		
Divorced	5 (0.3)	2 (0.3)	3 (0.3)		
Widowed	1000 (65.9)	282 (44.3)	718 (81.5)		

Annual household income per capita, n (%)					8
< 1000 rmb/year	77(5.0)	32(5.0)	45(5.1)		
1000-3000 rmb/year	299(19.6)	121(18.9)	178(20.0)		
3001-6000 rmb/year	257(16.8)	101(15.8)	156(17.5)		
6001-8000 rmb/year	104(6.8)	41(6.4)	63(7.1)		
8001-10000 rmb/year	75(4.9)	29(4.5)	46(5.2)		
> 10000 rmb/year	582 (38.1)	269 (42.1)	313 (35.2)		
Unknown	135 (8.8)	46 (7.2)	89 (10.0)		
Anthropometric measures					
Height (cm)	148.4 (10.7)	156.1 (7.7)	142.8 (8.9)	<0.001	12
Weight(kg)	49.4 (10.4)	54.3 (9.8)	45.9 (9.4)	<0.001	12
BMI (kg/m^2)	22.3 (3.7)	22.2 (3.3)	22.4 (4.0)	<0.001	15
Underweight (<18.5)	201 (13.2)	62 (9.7)	139 (15.7)		
Normal (18.5–24.0)	863 (56.7)	391 (61.2)	472 (53.4)		
Overweight (24.0-27.9)	356 (23.4)	158 (24.7)	198 (22.4)		
Obese (> 28.0)	103 (6.8)	28 (4.4)	75 (8.5)		

Grip strength		17.5 (11.2)	22.2 (11.0)	14.0 (10.0)	<0.001	47
4-meter gait speed		0.58 (0.23)	0.63 (0.22)	0.58 (0.23)	<0.001	103
Life-styles						
Drinking	Yes	435 (28.4)	329 (51.4)	106 (11.9)	<0.001	6
tea history	No	1096 (71.6)	311 (48.6)	785 (88.1)		
Drinking	Yes	476 (31.1)	196 (46.2)	180 (20.2)	<0.001	6
alcohol history	No	1055 (68.9)	344 (53.8)	711 (79.8)		
Smoking history	Yes	429 (28.1)	332 (52.1)	97 (10.9)	<0.001	9
	No	1099 (71.9)	305 (47.9)	794 (89.1)		
Scale evaluation						
ADL scale result		93.3 (14.3)	95.3 (12.0)	91.9 (15.6)	<0.001	17
Good (100 points)		934 (61.7)	443 (70.0)	491(55.7)		
Mild dysfunction (>60)		514 (33.9)	170 (26.9)	344 (39.0)		
Moderate dysfunction (41-60)		36 (2.4)	12 (1.9)	24 (2.7)		
Severe dysfunction (21-40)		17 (1.1)	4 (0.6)	13 (1.5)		

Completely disabled (<20)	14 (0.9)	4 (0.6)	10 (1.1)		
IADL scale result	11.4 (4.6)	12.1 (4.2)	10.9 (4.9)	<0.001	16
Good function (≥8)	1214 (79.8)	542 (85.6)	672 (75.7)		
Impaired function (< 20)	307 (20.2)	91 (14.4)	216 (24.3)		
MMSE scale result	16.3 (8.1)	19.0 (7.7)	14.3 (7.7)	<0.001	174
normal	151 (11.1)	100 (17.3)	51 (6.5)		
Cognitive Impairment	1212 (88.9)	478 (82.7)	734 (93.5)		

COLLABORATION

Welcome geriatric medicine and longevity related researchers through our center website (http://www.wchscu.cn/scientific/clinical/platform/55440.html) for more data information (Database name: A natural cohort study of the old adult), if researchers have any requirements, you can also contact us by E-Mail (hxncrcg@163.com) for more details and cooperation.

FUTURE DETAILS

It is planned to continue to carry out annual participant follow-up and collection of biological samples. Participants in the existing cohort will be followed up continuously, and new participants will be recruited into the prospective dynamic cohort study based on maintaining a constant sample size (i.e. to compensate for dropout). Participants who did not have the opportunity to contribute biological samples at the baseline time point will be followed up as soon as possible, and annual sample collections will occur as appropriate.

Global aging problem has been coming. How to improve the longevity and quality of life is a great challenge for modern medicine, biology and sociology. Centenarians are an important model to study longevity and "healthy aging". The project will conduct experiments on gene and protein levels of centenarians from blood samples to explore the mechanism of longevity and aging, and provide a theoretical basis for the prevention and treatment of aging-related diseases, which would be reasonable for extension of life and realization of healthy aging.

Frailty syndrome is a systemic change, which companions with multi-system dysfunction, especially the decline of capacity of physiological reserve in neuromuscular, metabolic and immune systems in the elderly. Frailty could reduce the ability to fight stress and significantly increasing the risk of adverse events in the elderly. In order to evaluate the diagnostic accuracy of frailness, the selection, detection, validation and clinical application of biomarkers representing different stages of frailness based on biological theory were established from the perspective of genomics and epigenetics.

We are going to further explore the biological mechanisms of elderly health aging, reveal changes in the longevous elderly, discover some novel important longevity-related genes and their related functions and signal path, from genomics, apparent genome, transcriptome, proteomics, metabolomics, microbic genomics level. Furthermore, confirmatory researches need to be extensive based on biomarkers associated with longevity among population. In combination with animal models, anti-aging drugs, cells and other therapeutic strategies would be discovered.

The findings of these complex analyses will be exploited for any factors that can be translated into community benefit. With reference to China’s aging society, non-pharmaceutical health intervention and promotion programs will be explored and formulated with the intention of meeting the needs of the current and future Chinese population. We will propose primary prevention measures suitable for community

health promotion, which will be beneficial for a healthy lifestyle, incorporating what we have learned about the behaviors of the elderly Chinese inhabitants of Longevity Townships.

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Disclaimer

Our sources of funding had no role in the design of cohort profile, and will not be any impact on data collection, analysis, writing and decision to submit or publish the research results.

COMPETING INTERESTS

None.

PATIENT AND PUBLIC INVOLVEMENT STATEMENT

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

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