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以降のページは雑誌／図書等に掲載された論文となりますので
「研究成果の刊行に関する一覧表」をご参照ください。

Ⅴ. モノグラフ

MONOGRAPH

The First Wave

November, 1997～April, 2000

National Institute for Longevity Sciences Longitudinal Study of Aging

NILS-LSA

I. Objectives and Overview of the NILS-LSA

I. Objectives and Overview of the NILS-LSA

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1) Background and outline of the NILS-LSA

The life expectancy of the Japanese population is the longest in the world. Both the absolute number and relative percentage of the elderly population in Japanese society is rapidly increasing. In 2020, the percentage of the elderly population in Japan will be the largest in the world. Along with these changes, various medical and care-giving problems for the elderly patient have arisen. Longevity science, with the goal that all of elderly people can live a long life with physical and mental health should be promoted in Japan.

Human aging is associated with many factors, including not only physical and physiological factors but also social and psychological factors. Thus, research into human aging requires many kinds of examinations and specialists in various areas. In addition, human aging research requires long-term study in which the same subjects are measured repeatedly to observe age-related changes. However, the number of researchers and budget for studies on gerontological and geriatric epidemiology are limited. It has been very difficult in Japan to start and to continue a large-scale and comprehensive longitudinal study of aging, despite a rapid increase in the elderly population.

In 1995, a new national research institute of aging in Japan, the National Institute for Longevity Sciences (NILS) was established and in 1997 the NILS-LSA (NILS – Longitudinal Study of Aging) started. The participants in the NILS-LSA of the first wave were 2,267 randomly selected men and women aged 40 to 79 years from the NILS area. They will be examined every two years. Six to seven participants are now examined every day at the NILS-LSA examination center. The aging process is assessed by detailed questionnaires and examinations including clinical evaluation, body composition and anthropometry, physical functions, nutritional analysis, and psychological assessments. The data from the study will be useful to investigate the causes of geriatric diseases and health problems in the elderly such as depression, mental disturbance, restriction of ADL, low nutrition and physical activity. The data will also be useful to prevent these diseases and health problems in the elderly.

2) Progress of the NILS-LSA

In 1990, projects of "Comprehensive Research on Aging and Health" were started by the Ministry of Health and Welfare to promote longevity sciences in commemoration of the 60th year in the reign of Emperor Showa. A research group for a longitudinal study on aging was organized as one of these projects. Indices on aging were evaluated, the methodology for the longitudinal study was assessed, and many problems in actual longitudinal follow-ups using existing cohorts were analyzed by this research group in order to start a new comprehensive longitudinal study of aging in Japan. A pilot longitudinal study on aging started in 1992. A manual of the many procedures used in the study was published in 1996.

In July 1995, the National Institute for Longevity Sciences (NILS) was established as the leading national research center for aging and geriatric research in Obu city in the suburbs of Nagoya. In 1996, the Laboratory of Long-term Longitudinal Studies was established in the Department of Epidemiology to start a new longitudinal study of aging in Japan.

Various equipment necessary for geriatric research, such as magnetic resonance imaging (MRI) and peripheral quantitative computed tomography (pQCT) were set up in the NILS, and a special examination center for longitudinal study was established in the Chubu National Hospital. Physicians, psychologists, nutritionists, epidemiologists, and exercise physiologists were assigned to the Laboratory of Long-term Longitudinal Studies and the Department of Epidemiology.

In October 1997, a trial run of the examinations led by local volunteers started, and in November 1997, the NILS-LSA began as a large-scale and comprehensive longitudinal study of aging in Japan. Every day, six or seven participants were examined at the NILS-LSA Examination Center. The first wave of the examination finished in April 2000, 2267 men and women had completed the examinations. All participants will be examined every two years. The second wave of the examination started in April 2000. The total number of examined variables is over 1,000, including various areas of gerontology and geriatrics such as medical examinations, anthropometry, body composition, physical functions, physical activities, psychological assessments, nutritional analysis and molecular epidemiology.

3) Objectives of the NILS-LSA

1. Main purpose

Systematic observation and description of the process of normal aging in humans.

(1) To quantify normal and successful aging.

(2) To determine the reference values in normal aging process by longitudinal observation.

2. Additional purpose

(1) To find out early markers of age-related diseases.

(2) To clarify molecular genetic factors of aging and geriatric diseases.

(3) To find out factors associated with longevity.

(4) To examine the effects of life-style, stress, life events and disease on aging process.

(5) To separate normal aging and age-related disease.

(6) To assess the influence of age on progressive changes of various diseases.

(7) To determine predictors of age at death and risk factors for diseases as well as institutionalization and loss of independence.

(8) To include various tests applied to the same subjects to determine whether aging is physiologically and psychologically interactive and continuous processes or aging is the end result of multiple independent processes.

(9) To examine regional difference on factors of longevity and relationship among life-style, aging and disease in Japan, and

(10) To examine race difference by international comparative study.

(11) To assess social and economical changes with age in the elderly.

(12) To develop indices of biological age.

(13) To prepare basic population for the research of clinical and social medicine.

4) Research area

For the detailed and comprehensive examinations at the NILS, the research area was determined to be in the neighborhood of the NILS, that is Obu city (population 70,000) and Higashiura town (population 40,000) (Fig. 1). This area is located in the south of Nagoya, and is a big city bedroom town and also industrial area of the Toyota group, but still has many orchards and farms, having both urban and rural characteristics.

This research area is geographically located at the center of Japan, and the climate is almost average for Japan. We examined the representativeness of the area via national postal questionnaire of prefecture-stratified random samples of 3,000 households from all prefectures in Japan, and showed that the life-style of this area was the most typical of all areas in Japan. It is expected that the results of examinations in this area will represent the average in Japan.

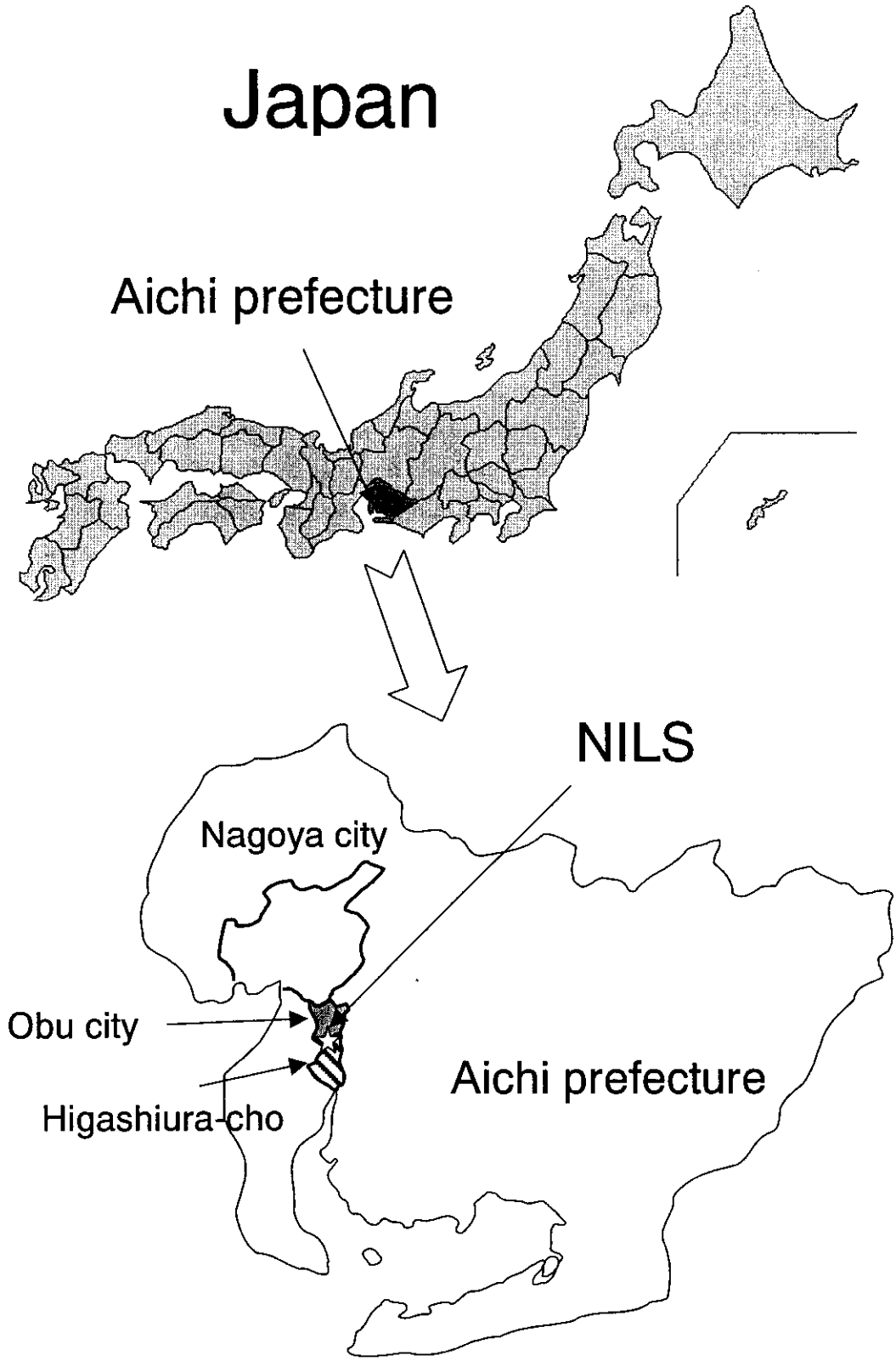

Fig. 1 Research area of the NILS-LSA

5) Subjects

The subjects of the NILS-LSA were men and women residents of 40 to 79 years old. They were stratified by both age and gender, and randomly selected from resident registrations in cooperation with the local governments (Obu city and Higashiura town). The number of men and women is to be the same to test gender difference. Age at the base line is to be 40 to 79 years and the number of participants in each decade (40s, 50s, 60s, 70s) is to be the same. The total number of participants will be 2400, that is 300 men and 300 women for each decade. They will be followed up every two years. Random samples of the same number of dropout participants will be recruited except the participants over 79 years old. The male and female participants aged 40 years will be also newly recruited every year.

Recruitment and follow up of volunteers will be much easier than with random samples. However, volunteers generally tend to be rich, highly educated, and interested in health. Observation of these volunteers would produce results for economically and socially upper class people who are very healthy and live long. Examinations in random samples are necessary to observe the aging process of ordinary Japanese who live ordinary lives.

6) Implementation of the study

Selected men and women who are assigned to the next month's examination are invited by mail to an explanatory meeting that is held twice a month, once on Sunday and once on Monday (Fig. 2, 3). At the explanatory meeting, procedures for each examination and the importance of the continuation to follow up are fully explained. Participants are limited to those who understand all examination procedures and sign their names on a written form (informed consent).

The Department of Epidemiology of the NILS is taking the initiative for all examinations and investigations. All participants are examined from 9 am to 5 pm at a special examination center within a facility at the Chubu National Hospital located next door to the NILS (Fig. 4). To examine 2,400 men and women in two years, that is 1,200 men and women per year, six or seven participants are to be examined each day, 4 days a week from Tuesday to Friday, 200 days (50 weeks) a year. Taking advantage of the fact that all participants can be examined at a center, detailed examinations including not only medical evaluations, but also examinations of exercise physiology, body composition, nutrition, and psychology can be tested. Each examination is to be extensive and most up-to-date, aiming at the internationally highest level. The follow up period is to be up to 30 years, but we hope to get significant longitudinal results within 5 to 10 years. The first wave examination was finished by April 2000, and 2267 male and female participants had completed their examinations. The second wave examination was started.

Information from the examinations that will be helpful to manage the health of participants is returned to individual participants as a report from the NILS-LSA.

Age and gender distribution of participants (the first wave of the NILS-LSA)

Age	Male	Female	Total
40 – 49	291	282	573
50 – 59	282	279	561
60 – 69	283	285	568
70 – 79	283	282	565
Total	1,139	1,128	2,267

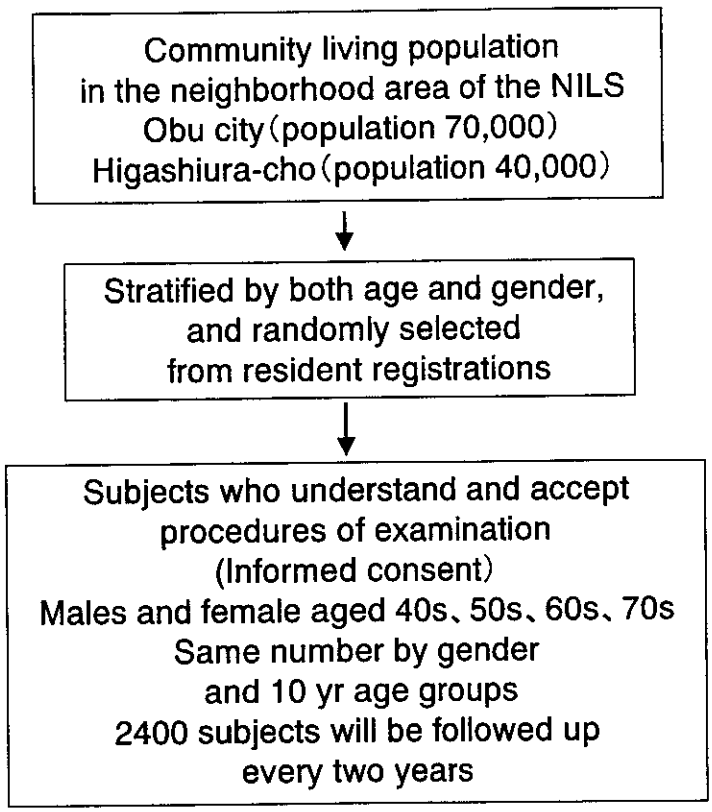

Fig. 2 Selection of the subjects in the NILS-LSA.

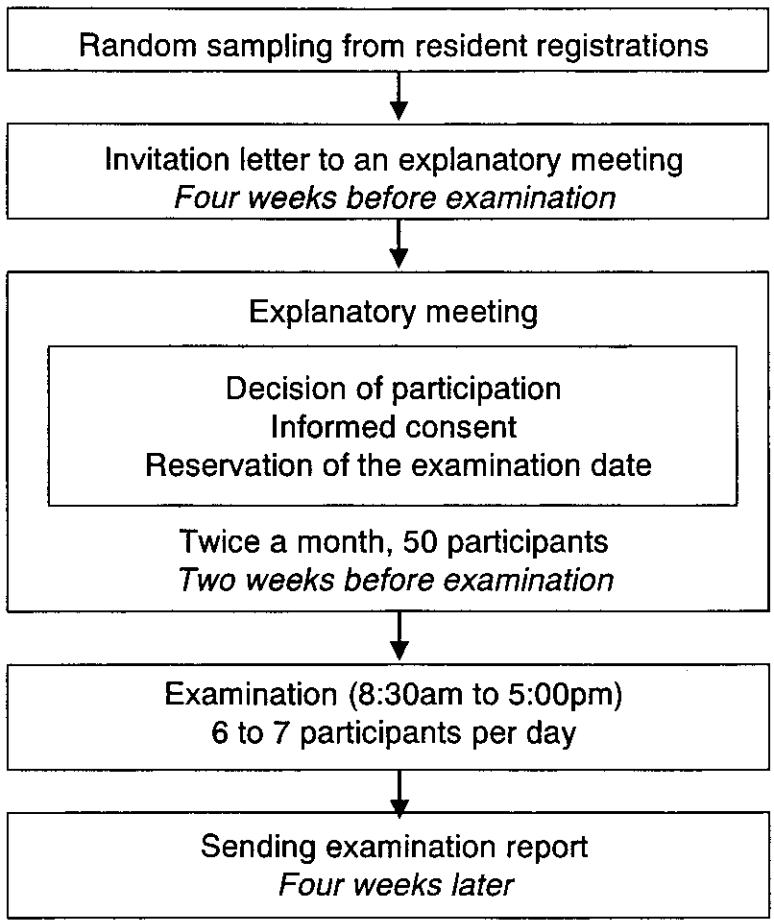

Fig. 3 Examination schedule in the NILS-LSA.

7) Informed consent

Participation in the examinations totally depends on free will, without any enforcement, and refusal to participate has no disadvantage; All participants are fully informed of the following items. Only subjects who understand and accept examination procedures, and sign their names to a written form to participate in the study (informed consent) are included. This informed consent includes; (1) purpose of the study; (2) detailed procedures for each examination; (3) gene analysis; (4) preservation of blood, urine and DNA samples for future examinations; (5) to send examination report to the participants; (6) to keep secret personal data from the examination. The Ethical Committee of the Chubu National Hospital has already approved all procedures of the NILS-LSA.

8) Examinations and tests

The normal aging process is assessed by detailed examinations including clinical evaluation, sensory aging, body composition and anthropometry, physical functions, nutritional analysis, and psychological tests (Table 1).

Table 1. The first wave examinations and tests in the NILS-LSA

Health related questionnaire

Self-rated Health (SRH), Medical history, Clinical symptoms, Medical care, Life style, Personal history (job, marriage, education, etc.), Family history, Environment, Alcohol, Smoking, Social and economical back ground

Routine clinical evaluations

Physical examination

Blood pressure

Blood chemistry

GOT, GPT, gamma-GTP, Total protein, Albumin, LDH, Alkaline phosphates, Chorine esterase, Uric acid, Urea nitrogen, Creatinine, Calcium, Total cholesterol, Trigrlyceride, HDL-cholesterol, Lipid peroxide, Fasting glucose, HbA1c, Insulin, Vitamin A, Serum sialic acid, Fe, Cu, Mg, Zn, free T3, free T4, TSH, DHEA-S

CBC: Red cell count, White cell count, Hb, Hematocrit, Platelet count

Urine analysis: Protein, Sugar, Urobilinogen, Ketone, pH, Occult blood, Hemoglobin, Nitrite

Sensory aging

Visual system

Visual acuity: near vision (33 cm), distant vision (5 m), Kinetic visual Acuity, Refraction, Visual field, Retinal camera, Intraocular pressure, Color perception, Stereoscopic vision, Contrast sensitivity, Quantitative test of lens opacity

Auditory system

Audiometry (air and bone), Middle ear functions (Impedance audiometry)

Skin sensory system

Quantitative sensory test (Neurometer), Skin discrimination test

Medical examinations

ECG (Automatic ECG analyzer)

Cardiac ultrasonic tomography

Pulse wave (digital plethysmography)

Pulmonary functions (spirometer)

Blood oxygen saturation (Pulse oxymeter)

Dual energy X-ray Absorptiometry (DXA)

Lumbar spine, Right and left femur neck, Total bone density, Body fat (total and segmental fat)

High Quality Peripheral Quantitative CT (pQCT)

Radial bone mineral density

Intima-media thickness of carotid artery

Head MRI (Magnetic resonance imaging system)

DNA phenotype and disease markers

Alzheimer's disease

Apolipoprotein E phenotype, Protease phenotype, Peptidase activity and inhibitors, beta-amyloid peptide concentration accumulative beta-amyloid autoantibody, DLST phenotype, Mitochondria CCO

Stroke and arteriosclerosis

Angiotensin converting enzyme (ACE) phenotype, Platelet-activating factor acetylhydrase activity (PAF-AH) and phenotype

Osteoporosis

Transforming growth factor beta 1 (TGF-b1) phenotype, Osteocalcin, Bone alkaline phosphatase, Aminoterminal cross-links of type I collagen (urine)

Obesity and diabetes

CCK-A receptor phenotype, beta 3-adrenaline receptor phenotype, Leptin, Sex hormones (testosterone, free testosterone, estradiol, sex hormone binding globulin)

Prostate hypertrophy

Alpha-1 adrenaline receptor phenotype

Aging

Mitochondria 5178 phenotype

Body Composition

Body fat measurement

Air displacement plethysmography (BOD POD), Bioelectrical impedance

body fat measurement, Dual energy X-ray Absorptiometry (DXA)

Body fluid measurement (Bioimpedance spectroscopy)

Ultrasonic tomography

Intrabdominal fat, Muscle thickness, Subcutaneous fat thickness

Anthropometric measurements

Physical function

Exercise test system

Grip strength, Sit-ups, Trunk flexion, Static balance, Leg extension power, Isometric leg strength, Reaction time.

10m Walking test (pitch, step length, speed),

3-D motion analysis system (four cameras and two force plates)

Stabilometer (with eye-open and eye-closed conditions)

Physical activity questionnaire

Electric pedometer (7 days average)

Psychological tests

Interview

Cognition (MMSE, WAIS-R), Life events, Stress, Basic ADL (Katz Index)

Questionnaire

Depression (CES-D, GDS), Personality (Self-esteem, EPSI, Locus of control, Attitude toward death), Social environment (Social support, Social network), Family relations, Subjective well-being (LSI-K, SWLS), Stress coping, Instrumental ADL

Nutrition analysis

Food and nutrition Intake

Nutrition Diary (3 days) using scales and disposable camera

Food frequency questionnaire

Dietary habit questionnaire