

に限るべきで、意図的であっても予後を悪化させる可能性があることが示されている⁷⁾。

薬物療法

1. ホルモン

筋肉の蛋白質合成に関わる同化ホルモンであるテストステロン、成長ホルモン(GH)、インスリン様成長ホルモン-1(IGF-1)、dehydroepiandrosterone(DHEA)は、加齢により低下する。ホルモン補充療法は抗加齢対策として、理にかなっている。しかしながら、閉経女性に対するエストロゲン補充療法が、Women's Health Initiative(WHI)の結果、心血管疾患の減少や認知機能の改善を認めず、逆に発癌、血栓症の増加を起こすことが発表され、ホルモン補充療法の実施は困難になると予想される。ちなみに、エストロゲン補充療法による筋肉量増加効果は、示されていない。

テストステロンは、筋肉量を増やすという効果においては、最も有望視されている。しかしながら、医学的、社会的により重要な効果、たとえば、転倒・骨折の減少、施設入所の減少、ADLの改善などについては明らかではない。男性の性腺機能低下症症例では、テストステロン治療により、筋肉の機能改善や骨量の維持効果、男性としての性的特徴の発現などがみられるが、加齢による生理的なホルモン低下に対して、薬物的濃度のテストステロンの長期的投与は、有害な効果を引き起こし得る。実際、テストステロンにより、冠動脈疾患、前立腺癌、過粘稠度症候群(高ヘマトクリットによる)を起こす可能性があり、現時点では、筋肉量を増やすという観点からのテストステロン投与に正当性は認められない。

GH、IGF-1の筋肉量ならびに筋力の増加に対する効果の評価は一定しておらず、長期的な投与による危険性についても、明らかでない。高齢者では、GH、IGF-1の補充が、手根管症候群、女性化乳房、浮腫、関節痛を引き起こすことが報告されている。

2. ビタミンD

ビタミンDの筋力増強作用が、近年注目されている。Bischoffらは、ビタミンD投与が転倒を予防するとの報告をしており、主に筋力増強作用によるものとしている⁸⁾。ビタミンD欠乏によって生じる骨軟化症では筋力低下が主症状にあり、ビタミンDの補充により筋力低下は劇的に改善するとのことである。ビタミンD欠乏時には、II型筋線維の障害が起こるとされる。多くの高齢者において、慢性的なビタミンD欠乏があることがわかってきており、骨粗鬆症に対する対策とあわせて、ビタミンDの投与がSarcopeniaの予防、治療となる可能性がある。

まとめ

以上総合すると、Sarcopenia対策には、レジスタントトレーニングを中心として、十分なカロリーと蛋白質の摂取をすすめるとともに、ビタミンDなどのサプリメントを摂取することである。さらには、活動的な社会生活を持続し、肉体的だけでなく、精神的にも健康な生活を心がけることが、ホルモン、サイトカインの複雑なネットワークが引き起こしていると考えられるSarcopeniaの予防になる可能性がある。Sarcopenia対策において、健康な高齢者へのアプローチと虚弱者、慢性疾患罹患者もしくは超高齢者へのアプローチは必然的に異なるであろうが、いずれにせよ包括的なチームアプローチが必須と思われる。

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Geriatric Medicine 8月号予告

特集 アンチエイジングの新しい動向①—サプリメントを中心に—

巻頭言

1. イチョウ葉
2. CoQ₁₀
3. ソバポリフェノール
4. L-カルニチン
5. DHA
6. 金線蓮
7. 大豆イソフラボン
8. 植物ステロール
9. 抗酸化サプリメント

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Case Study

紅麹(天然スタチン)

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Short Topics

1. シリマリン
2. 大豆サポニン

(株)ファンケル中央研究所 宮田 智
(株)ファンケル中央研究所 小野衣里日

Round Table Discussion

「アンチエイジングの新しい動向—サプリメントを中心に—」

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(予定者・敬称略)

IV. モノグラフ

第3次調査

MONOGRAPH

The Third Wave

May, 2002~May, 2004

National Institute for
Longevity Sciences
Longitudinal Study of Aging

NILS-LSA

- I. Objectives and Overview of the NILS-LSA
- II. Background Examinations
- III. Medication
- IV. Food and Nutrition
- V. Bone Mineral Density
- VI. Blood and Urine Analysis
- VII. Psychological Examinations
- VIII. Visual and Auditory Examinations
- IX. Physiological Examinations
- X. Physical Function Tests and Physical Activities
- XI. Anthropometry and Body Composition
- XII. Head MRI
- XIII. Oral examinations

I. Objectives and Overview of the NILS-LSA

I. Objectives and Overview of the NILS-LSA

- 1) Background and outline of the NILS-LSA**
- 2) Progress of the NILS-LSA**
- 3) Objectives of the NILS-LSA**
- 4) Research area**
- 5) Subjects**
- 6) Implementation of the study**
- 7) Informed consent**
- 8) Examinations and tests**
- 9) Future of the NILS-LSA**
- 10) Staff**

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 have arisen. Longevity science, with the goal that all of elderly people can live a long life with good 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 as a research facility in Chubu National Hospital 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 males and females aged 40 to 79 years randomly selected from the NILS area. They will be examined every two years and now the third wave examination is carrying out. Six to seven participants were 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.

In March 2004, Chubu National Hospital and NILS were reorganized to establish National Center for Geriatrics and Gerontology as a new national facility for research and medical care. There are six National Centers for Advanced and Specialized Medical Care in Japan. Other National Centers are located in five areas; Cancer Center in Chuo-ku, Tokyo and in Kashiwa-shi, Chiba, Cardiovascular Center in

Suita-shi, Osaka, Center of Neurology and Psychiatry in Kodaira-shi, Tokyo and Ichikawa-shi, Chiba, International Medical Center in Shinjuku-ku, Tokyo, and Center for Child Health and Development in Setagaya-ku, Tokyo. They provide advanced medical care and conduct researches in each special medical area.

Chubu National Hospital was reorganized as National Hospital for Geriatric Medicine. NILS was also reorganized to cover more area of geriatrics and gerontology. The number of department increased from 8 to 13. A new research section, the Section of Nutritional Epidemiology was added to the Department of Epidemiology and the Laboratory of Epidemiology for the Aged was reorganized to the Section of Preventive Epidemiology.

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 of aging was organized as one of these projects. Indices of 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 geriatrics 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 equipments 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 was conducted, and in November 1997, the NILS-LSA began as a large-scale and comprehensive longitudinal study of aging in Japan. From Tuesday to Friday in every week, six or seven participants were examined at the NILS-LSA Examination Center. In the first wave of the examination finished in April 2000, 2,267 males and females had completed the examinations. All participants will be examined every two years. The second wave of the examination started in April 2000 and finished in May 2002. Total number of participants of the second wave examination was 2,259. From May 2002, the third wave examination started. The third examination finished in May 2004, and 2,378 participants were examined. The fourth wave examination started in June 2004 (Fig. 1). The number of examined variables was 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.

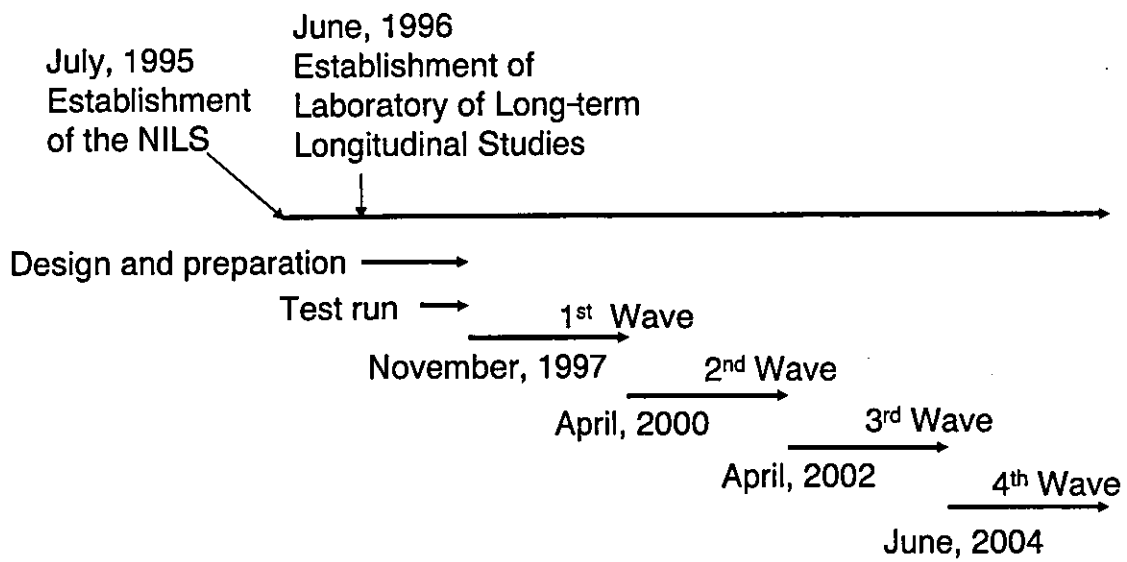


Fig. 1 Progress of the NILS-LSA

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 examine race difference by international comparative study
- (9) To assess social and economical changes with age in the elderly
- (10) To develop indices of biological age
- (11) To prepare basic population for the research of clinical and social medicine

4) Research area

The NILS-LSA is a facility-based study using various equipments including MRI, DXA and pQCT for the detailed and comprehensive assessments of aging and geriatric disease. The facility of examinations is located at the NILS. Thus, the research area was determined to be in the neighborhood of the NILS, that is Obu city (population 79,000) and Higashiura town (population 48,000) (Fig. 1). This area is located in the south of Nagoya, and is a 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 Japanese average. 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 found 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 Japan.

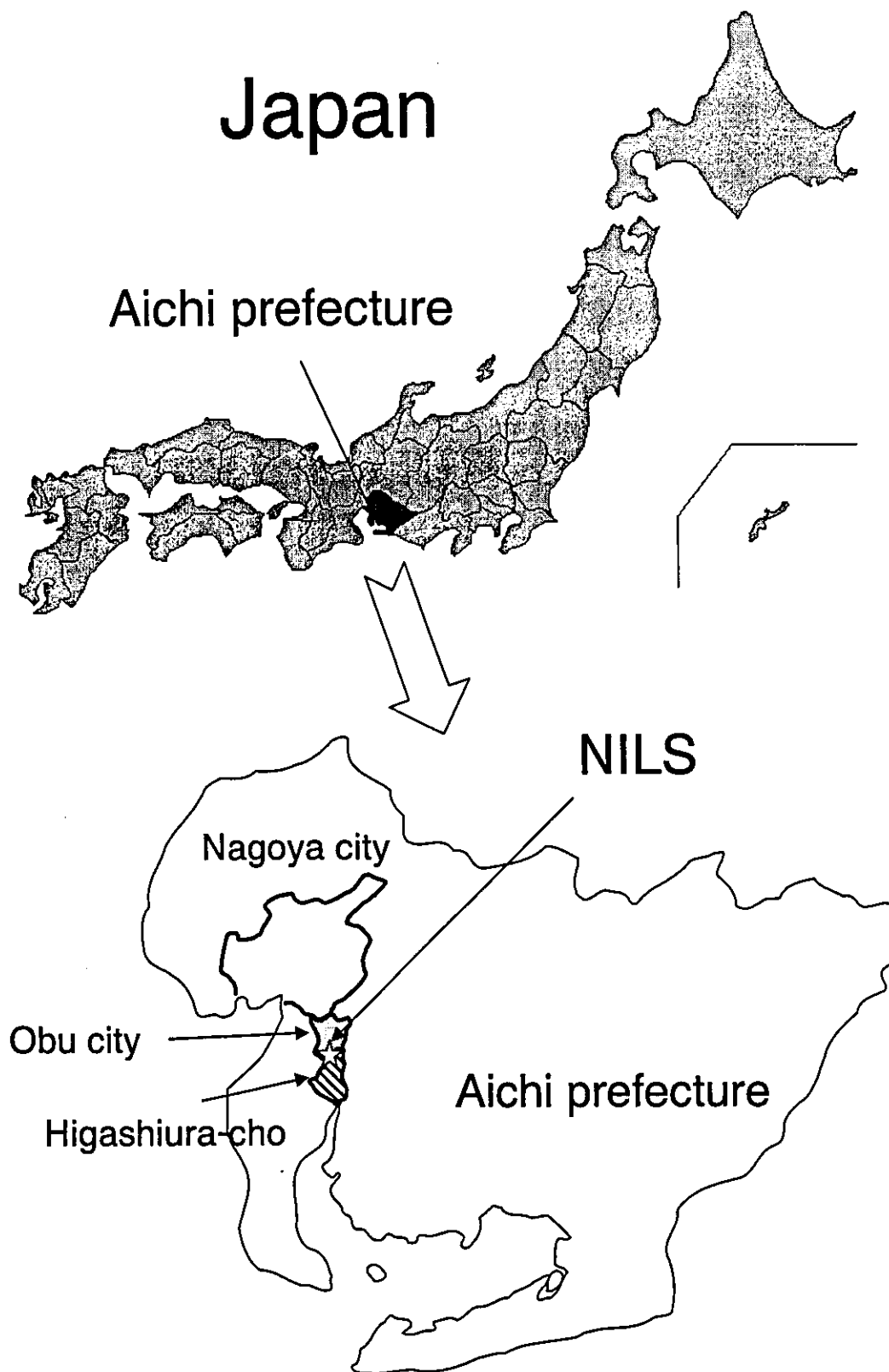


Fig. 2 Research area of the Nils-LSA

5) Subjects

The subjects of baseline examination of the NLS-LSA were males and females aged 40 to 79 years old. The population of Obu city and Higashiura town was stratified by both age and gender, and randomly selected from resident registrations in cooperation with the local governments (Fig.3). The number of males and females was to be equal to test gender difference, and the number of participants in each decade (40s, 50s, 60s, 70s) was also to be equal. The total number of participants was to be 2,400, that is 300 males and 300 females for each decade. They will be followed up every two years. Age and gender-matched 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 (Fig.4). Table 1 shows age and gender distribution of the participants in the first wave examination. Table 2 shows age and gender distribution of the second wave participants. Eighty percent subjects of the first wave examination participated the second wave examination (Table 3). The third wave examination was finished in May, 2004. The number of participants in the third wave was 2,378. Age and gender distribution of the third wave participants was shown in Table 4. About 72 percent of the first wave examination participants came back for the third wave examination (Table 5) and 84 percent of the second wave participants came back for the third wave examination (Table 6).

Recruitment and follow up of volunteers would be much easier than with random samples. However, these samples generally tend to be interested in health, and observation of these samples would produce biased results. Examinations in random samples are necessary to observe the aging process of ordinary Japanese who live ordinary lives.

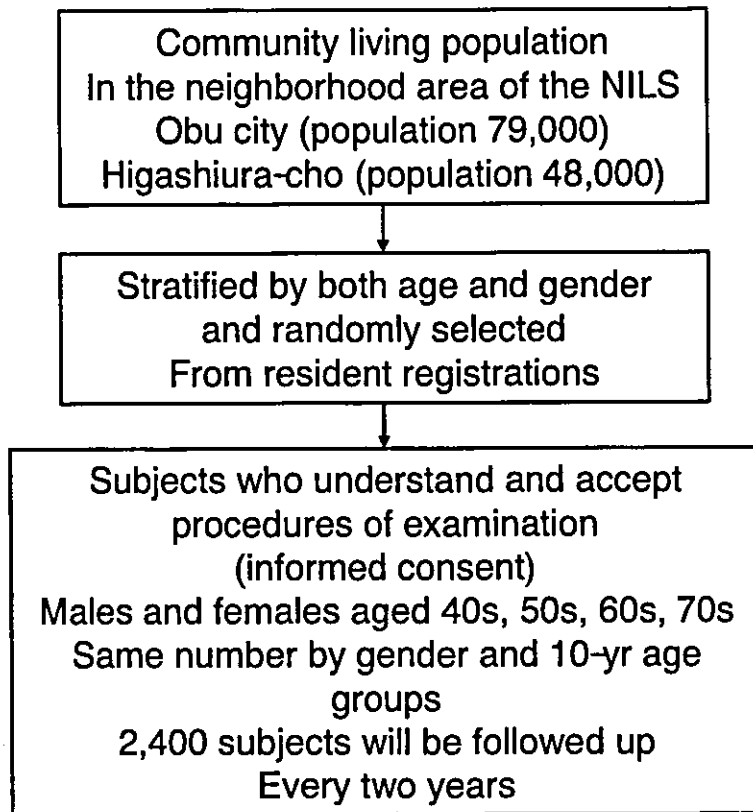


Fig. 3 Selection of the subjects in the NLS-LSA.

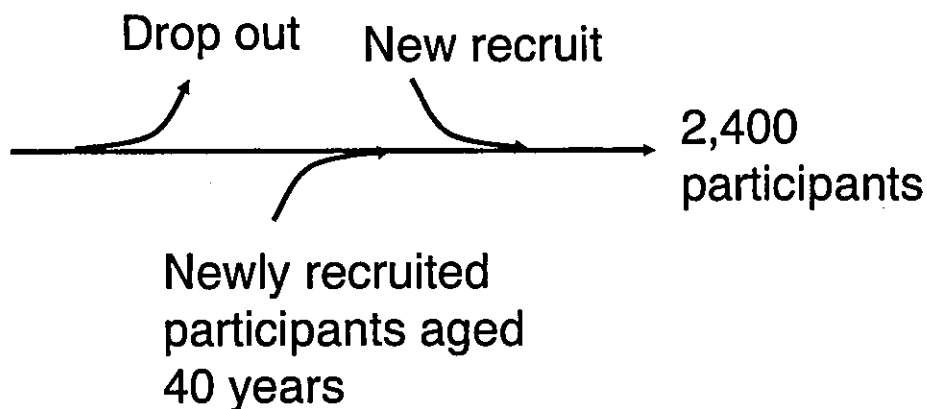


Fig. 4 NLS-LSA as a dynamic cohort

Table 1. Age and gender distribution of the first wave participants

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

Table 2. Age and gender distribution of the second wave participants

Age	Male	Female	Total
40 - 49	273	261	534
50 - 59	296	284	580
60 - 69	291	271	562
70 - 79	275	269	544
80 -	17	22	39
Total	1,152	1,107	2,259

Table 3. Number of males and females who participated both the first and second wave examinations

	Male	Female	Total
First wave	1,139	1,128	2,267
First and second wave	944	869	1,813
Percentage	82.9%	77.0%	80.0%

Table 4. Age and gender distribution of the third wave participants

Age	Male	Female	Total
40 - 49	266	294	560
50 - 59	331	285	616
60 - 69	297	286	583
70 - 79	267	275	542
80 -	43	34	77
Total	1,204	1,174	2,378

Table 5. Number of males and females who participated both the first and third wave examinations

	Male	Female	Total
First wave	1,139	1,128	2,267
First and third wave	848	783	1,631
Percentage	74.5%	69.4%	71.9%

Table 6. Number of males and females who participated both the second and third wave examinations

	Male	Female	Total
Second wave	1,152	1,107	2,259
Second and third wave	977	926	1,903
Percentage	84.8%	83.6%	84.2%

6) Implementation of the study

Randomly selected males and females who were assigned to the examination were invited by mail to an explanatory meeting that was held (Fig. 5). At the explanatory meeting, procedures for each examination and the importance of continuation to follow up were fully explained. Participants were limited to those who accept examination procedures and sign their names on a written form (informed consent).

The Department of Epidemiology of the NILS was taking the initiative for all examinations and investigations. The participants were examined from 8:30 am to 5 pm at a special examination center within a facility at the the NILS. To examine 2,400 males and females in two years, that is, 1,200 males and females per year, six or seven participants were to be examined each day, four 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 the center, detailed examinations including not only medical evaluations, but also examinations of exercise physiology, body composition, nutrition, and psychology can be done. Each examination was to be extensive and most up-to-date, aiming at keeping the internationally highest level. The follow up period is to be up to 30 years, but we hope to get initial significant longitudinal results within 5 to 10 years.

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

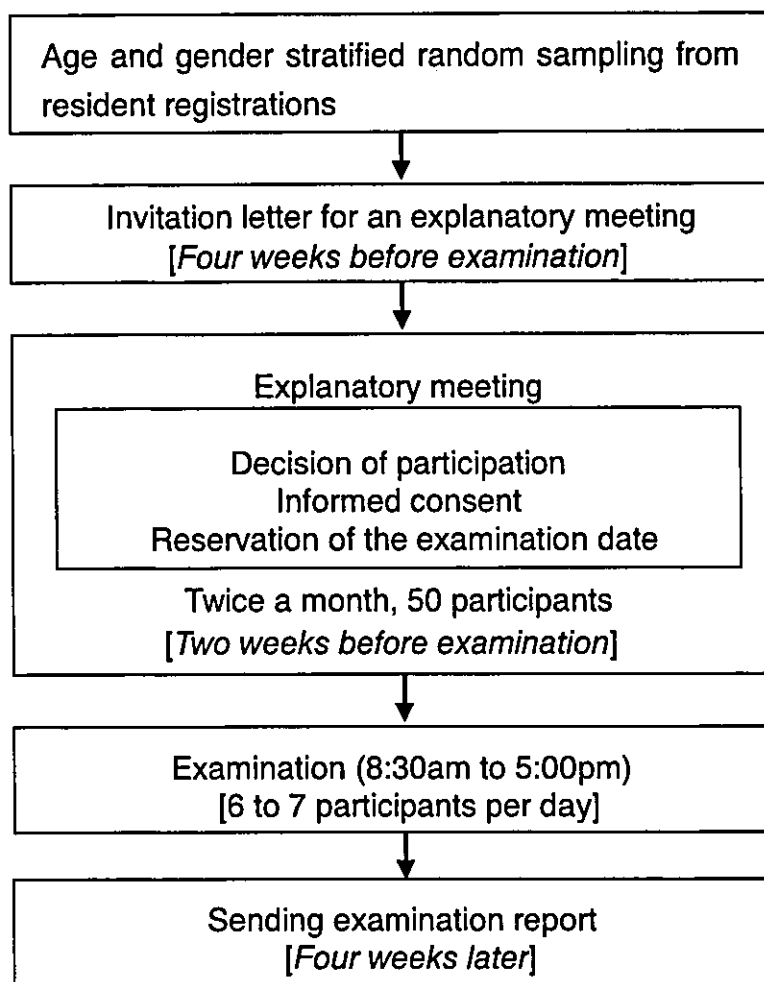


Fig. 5 Examination schedule in the NLS-LSA.