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COHORT PROFILE

Cohort Profile: The Health2006 cohort, Research Centre for Prevention and Health

Betina H Thuesen,[1]* Charlotte Cerqueira,[1] Mette Aadahl,[1] Jeanette Frost Ebstrup,[1] Ulla Toft,[1] Jacob P Thyssen,[2] Runa Vavia Fenger,[1] Lars-Georg Hersoug,[1] Jesper Elberling,[3] Oluf Pedersen,[4,5,7] Torben Hansen,[5,6] Jeanne Duus Johansen,[2] Torben Jørgensen[1] and Allan Linneberg[1]

[1]Research Centre for Prevention and Health, Copenhagen University Hospital Glostrup, The Capital Region of Denmark, Denmark, [2]National Allergy Research Centre, Department of Dermato-Allergology, Copenhagen University Hospital Gentofte, Denmark, [3]Danish Research Centre for Chemical Sensitivities, Gentofte University Hospital, University of Copenhagen, Copenhagen, Denmark, [4]Hagedorn Research Institute and Steno Diabetes Centre, Gentofte, Denmark, [5]The Novo Nordisk Foundation Centre for Basic Metabolic Research, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark, [6]Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark and [7]Faculty of Health Sciences, University of Aarhus, Aarhus, Denmark

*Corresponding author. Research Centre for Prevention and Health, Glostrup University Hospital, Nordre Ringvej 57, build. 84/85, DK-2600 Glostrup, Denmark. E-mail: betina.heainsbaek.thuesen@regionh.dk

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Introduction

The Health2006 cohort was set up to address research questions dealing with lifestyle-related chronic diseases such as coronary heart disease, diabetes, musculoskeletal disorders, asthma, allergy, chronic lung diseases and mental disorders. The participants in the Health2006 cohort were drawn as a random sample from the background population aged 18–69 years living in the south-western part of the greater Copenhagen area. A total of 3471 persons (participation rate of 44.7%) entered the study and participated in a health examination between June 2006 and June 2008. Five-year follow-up examinations are ongoing. Two questionnaires were completed by all participants, covering a broad range of questions about symptoms and diagnoses of diseases, physical activity, smoking, alcohol, eating habits, perceived stress, five-factor personality traits, mental problems, quality of life, socioeconomic variables and many other issues. The physical examination included measurements of cardio-respiratory fitness, muscle strength, lung function, allergy and anthropometric measures. In addition, collection of blood samples was used for genotyping and measurements of metabolic and nutritional biomarkers.

Why was the cohort set up?

Since 1964, general population-based cohorts have been examined at the Research Centre for Prevention and Health (RCPH). The first study, initiated in 1964 by Leif Hagerup, investigated coronary risk factors in 50-year-olds.[1] Since then, several new cross-sectional and prospective cohort studies have been performed at the RCPH and these cohorts were recently described.[2] The Health 2006 study was initiated by principle investigators Allan Linneberg and Torben Jørgensen to continue the collection of data and obtain biological material for the biobank for future research. The Health2006 study aimed to address research questions dealing with lifestyle-related chronic diseases. The main focus of most previous studies at the RCPH was on coronary heart disease (CHD) and diabetes risk factors. The Health2006 study was also designed to cover CHD-related health issues, but in contrast to most previous studies, the Health2006 study was designed to investigate chronic disease in a broader sense. Besides CHD and diabetes, the study focused on asthma, allergy, chronic lung diseases, eczemas, chemical intolerance, musculoskeletal disorders, osteoporosis and mental disorders. In addition, the aim was to create a solid foundation for future research by assessing a number of phenotypic descriptions of the individuals. The phenotypic descriptions cover five components:

- Morphological component, which comprises measures as regards weight, amount of fat, fat distribution, bone density and calcium metabolism (PTH, Ca^{++}, D-vitamin).
- Cardio-respiratory component, which comprises general fitness (maximal or submaximal fitness tests), blood pressure, pulse and lung function.

- Muscle component, which comprises muscle power and strength.
- Mental component, which comprises personality, intelligence, social network, coping characteristics, vulnerability, general self-efficacy and anxiety of the individual, and stress hormones.
- Metabolic components, which comprises a number of biomarkers within different areas [e.g. lipid metabolism (cholesterol, free fatty acids, apolipoproteins), glucose metabolism (glucose, insulin, C-peptide, proinsulin) and thyroid metabolism (thyroid-stimulating hormone, free thyroxine 3 and 4 and anti-thyroperoxidase)].

The main questionnaire on lifestyle factors and general health used in this cohort is also used in the more recent Health2008 ($n = 795$) and Health2010 ($n = 1522$) cohorts. In addition, most procedures from the physical examination in Health2006 are also included in these cohorts. Since the participants in the Health2008 and Health2010 cohorts are drawn from the same background population as the Health2006 cohort, data from the Health2006 can be supplied with corresponding data from the recent cohorts to achieve more power for some research questions. For example, in genetic studies it is also possible to use data from the Health2006 cohort in combination with data from some of our older cohorts like the Inter99 cohort or the Monica cohorts. However, one should then be aware that there might be disagreements between the wordings used in the questionnaires and that the procedures used at the physical examinations may have changed over time. It is also important to note that a small number of individuals may by chance have been included in more than one cohort since the cohorts are random samples drawn from the same background population. By combining data from the Health2006 cohort with data from other of our cohorts it is possible to identify participants who are found in more than one cohort.

Who is in the cohort?

The participants in the Health2006 cohort were drawn as a random sample from the background population aged 18–69 years, living in 11 municipalities in the south-western part of the greater Copenhagen area. In February 2006, a sample of 7931 persons with Danish citizenship and born in Denmark was obtained from the Danish Central Personal Register, Ministry of Internal Affairs. Of the 7931 persons in the sample, 161 were not eligible for invitation because of, for example, death or emigration, and hence 7770 persons were invited by mail to participate in the study. The invitation included information on the physical examination and a short description of the tests that were going to take place. A total of 3471 persons (44.7%) entered the study and participated in the health examinations at the RCPH, which took place between June 2006 and June 2008. Participants were asked to meet fasting at RCPH at the day of examination, and to refrain from smoking at least 1 h prior to the examination. In addition, users of antihistamine medication were asked not to use their medication 3 days prior to the examination and users of inhaled (inhalers) medications for lung disease were asked to avoid use of the inhalers on the day of examination. Pregnant women were excluded. A written informed consent form was obtained from all participants and the study was approved by the Ethical Committee of Copenhagen County (KA-20060011) and the Danish Data Protection Agency. In addition, the study was registered at www.clinical.trials.com (Unique ID: KA20060011).

To evaluate potential differences between responders and non-responders, the entire study population ($n = 7770$) was linked to central registries. As illustrated by Table 1, non-responders differed significantly from responders with respect to socio-demographic characteristics, education and use of health services. Responders were older, had a higher educational level and had a higher personal income than non-responders. A higher proportion of men and individuals with low socioeconomic position defined by information on the main source of personal income was seen among non-responders and they were more often living alone than the responders. Information from the National Patient Registry showed that the prevalence of hospitalization among non-responders was significantly higher than among responders (Table 1). In addition, non-responders had significantly more days of hospitalization (Wilcoxon rank test $P = 0.031$, data not shown). On the other hand, data from the Danish Prescription Registry showed that the prevalence of use of prescription drugs and the prevalence of more than one annual contact with general practitioners were higher among responders than non-responders (Table 1). Also, responders purchased a higher number of daily doses of prescription drugs during the year 2005 than non-responders and the general practitioner's fee paid for by the National Health Service was higher among responders than non-responders (Wilcoxon rank test $P = 0.033$ and $P < 0.0001$ respectively, data not shown). These significant differences between responders and non-responders must be taken into consideration when results from the Health2006 study are discussed, and especially if characteristics of the participants are used to generalize on a population level.

How often have they been followed up?

A 5-year follow-up examination of all participants in the Health2006 cohort has been initiated in 2011 and is scheduled to terminate in November 2012. In addition, the national registers will be used to follow the

Table 1 Register-based characteristics of responders and non-responders

Characteristic	Measure	Responders ($n = 3471$)	Non-responders ($n = 4299$)	Test for difference between responders and non-responders
Sex	Men	44.7%	53.9%	$P < 0.0001$
Age	Mean	49.4 years	45.7 years	$P < 0.0001$
Education	Prevalence of persons with middle school as highest educational level[a]	22.6% (776/3442)	36.1% (1529/4236)	$P < 0.0001$
	Prevalence of persons with higher education[a]	6.3% (215/3442)	4.1% (174/4236)	$P < 0.0001$
Family status	Prevalence of persons living alone (with or without children)[b]	20.7% (720/3471)	34.0% (1460/4299)	$P < 0.0001$
Socioeconomic position	Prevalence of persons with a low socioeconomic position[c]	6.5% (226/3471)	13.7% (288/4299)	$P < 0.0001$
Income	Mean[d]	305,184 dkr	260,381 dkr	$P < 0.0001$
Prevalence of hospitalization	One or more days during year 2005	9.0%	10.4%	$P = 0.031$
Prevalence of use of prescription drugs	One or more daily doses during year 2005	70.4%	64.8%	$P < 0.0001$
Prevalence of contacts to general practitioners	One or more contacts during year 2005	87.2%	80.4%	$P < 0.0001$

All register information relates to the calendar year 2005 where the random sample of potential participants was obtained from the Danish Central Personal Register, Ministry of Internal Affairs.
[a]Based on information from the national register of education.
[b]Based on information from the Denmark Statistics.
[c]Low socioeconomic position defined as being unemployed and dependent on benefit payments.
[d]Gross income.

participants and to evaluate potential differences between those who attend the re-examinations and those who have been lost to follow-up. Due to the high quality and extended use of nation-wide registries in Denmark, only potential emigrants will be lost due to follow-up in the national registries.

What has been measured?

The data collected from the Health2006 cohort are summarised in Table 2.

Questionnaires

Two questionnaires were answered by all participants in the Health2006: a main questionnaire on lifestyle factors and general health and a supplementary questionnaire on mental health. The main questionnaire will be available in an English version by February 2013. Participants answered a broad range of questions about symptoms and diagnoses of diseases, perceived stress,[3] five-factor personality traits,[4] mental problems, lifestyle, quality of life, socioeconomic variables and many other issues. The main questionnaire included validated questions for assessment of upper and lower airways symptoms as well as atopic dermatitis and hand eczema.[5–7]

The main questionnaire was also used for assessment of physical activity. Participants were asked to categorize themselves into one of four groups of leisure time activity.[8] In addition, all participants answered a more detailed questionnaire on physical activity by filling in the amount of time spent in different physical activity MET (metabolic equivalent) intensity levels during leisure time and commuting and at work.[9] The activities also included sleep and sedentary behaviour, e.g. TV-viewing and sitting during work, and provide detailed information on the type, duration and intensity of physical activity. A 24-hMET-score[10] can be calculated by multiplying time spent on an activity level by an assigned MET-value and adding the activity levels. The questionnaire is a revised version of the Physical Activity Scale that has previously been validated against activity diary and objective measures such as accelerometry and maximum oxygen uptake.[11,12]

Dietary intake was measured using a self-administered 48-item food frequency questionnaire (FFQ). From this the Dietary Quality Score (DQS) was calculated. Briefly, the DQS was developed as a crude index of the overall quality of dietary habits. The score was based on questions regarding the intake of fruits, vegetables, fish and different types of fat. The FFQ and the development and validation of the DQS have previously been described in detail.[13]

Table 2 Summary of data collected

Anthropometric measures and assessment of obesity	Height, weight, waist and hip circumference, impedance and intraperitoneal fatness
Fitness and muscle strength	Cardio-respiratory fitness, hand-grip strength, lower leg extension power (in a subgroup only), 24-h MET score, sitting time
Lung function measurements	FEV_1, FVC, FE_{NO}
Measurement of allergy	Specific serum IgE (cat, dog, birch, house dust mite), skin prick test, patch testing
Metabolic and nutritional biomarkers	Blood: glucose, insulin, glycated haemoglobin, lipids (cholesterols and triglycerides), 25-hydroxy vitamin D_3, albumin, calcium, folate, vitamin B_{12}, creatinine, alanine transaminase, ferritine, anti-thyroperoxidase parathyroid hormone, thyroid-stimulating hormone and free thyroxine.
	Urine: albumin, creatinine and sodium
Genetics	20 000 single nucleotide polymorphisms
Cardiovascular function	Systolic and diastolic blood pressure, resting pulse
Mental health	Perceived stress, five-factor personality traits, mental problems, quality of life
Diet	48-item food frequency questionnaire, Dietary Quality Score
Other questionnaire-based information	Symptoms and diagnoses of diseases, smoking, alcohol, socioeconomic status

Anthropometric measures and assessment of obesity

Height and weight were measured wearing light clothes and no shoes. Waist circumference (WC) was measured directly on the body surface midway between the lower rib margin and the iliac crest. The hip circumference was measured over light clothing at the widest girth of the hip. Additionally, all participants underwent measurement of impedance (body fat) and intraperitoneal fatness (assessed by ultrasound).

Fitness and muscle strength

The health examination included estimation of cardio-respiratory fitness by a performance-based progressive step test, the Danish step test (www.health-calc.com/fitness-tests/the-danish-step-test). The step test has been validated against a Wattmax test,[14] an indirect maximal ergometer cycle test based on workload. Muscle fitness was measured by hand grip strength in all participants using a Jamar® dynamometer (Sammons Preston Rolyan, Chicago, IL, USA). In addition, lower leg extension power was measured in a sub-sample ($n = 438$) of the participants by using a leg-extensor power rig (Medical Engineering Unit, University of Nottingham Medical School, Nottingham, UK).[15]

Lung function measurements

Lung function was measured by spirometry according to international standards[16] using the SpiroUSB (Micro-Medical Ltd, Rochester, UK). In addition, lower airway inflammation, as reflected by exhaled nitrogen oxide (FE_{NO}), was measured according to international guidelines[17] by using the hand-held Niox-Mino (Aerocrine AB, Stockholm, Sweden). FE_{NO} is an accepted biomarker of allergic asthma and lower airways inflammation[18] and oxidative stress.[19] Lung function measurements in the Health2006 have previously been described in more detail.[5,6]

Measurement of allergy

Measurement of specific IgE in serum is considered the gold standard for assessment of type I respiratory allergy in large-scale epidemiological studies. In the Health2006, all serum samples were analysed for the four most important inhalant allergens [birch, grass, cat and house dust mite (*Dermatophagoides pteronyssinus*)] by using the ADVIA Centaur® assay (Siemens, Deerfield, IL,US)[20]. Furthermore, skin prick test reactivity against a panel of 10 inhalant allergens was performed on 2393 consecutive participants by using the Solu-prick (ALK-Abelló A/S, Hørsholm, Denmark).

A total of 3460 persons were patch tested for measurement of type IV allergy. Patch testing was performed by using panel 1 and 2 from the standardised ready-to-apply Thin-layer Rapid Use Epicutaneous (TRUE)-test® (Mekos Laboratories, Hillerød, Denmark).[21,22] Directions to apply the patch test panels to the upper back 2 days before examination were mailed together with the patch tests. At the day of examination, they were read and photographed 1-1.5 h after removal by trained healthcare personnel. Photos were later reviewed by experts in dermatology. This was done to secure that the International Contact Dermatitis Research Group (ICRDG) criteria were used.[23] Contact allergy was defined as a positive (at least grade 1+ according to ICRDG) patch test reaction to at least one allergen or mixes of haptens.

Biobank

Fasting venous blood samples from all participants were taken on the day of examination and were left to coagulate for 2 h. The serum was then separated by centrifugation at 3000 r.p.m. for 10 min and frozen immediately afterward. Serum samples from all participants were stored in the biobank at RCPH (at both -20°C and −80°C) for future analyses of biomarkers. The buffy coat was frozen for DNA extraction, and later genomic DNA was extracted using a Qiagen AutoPure LS system. In addition, the biobank contains urine samples from all participants.

Metabolic and nutritional biomarkers

Fasting blood samples were analysed for glucose, insulin, glycated haemoglobin (HbA1c) and lipids (cholesterols and triglycerides), and urine samples for urine albumin/creatinine ratio at the Steno Diabetes Center. In addition, serum levels of 25-hydroxy vitamin D_3 (25-OH-D_3), albumin, calcium, folate, cobalamine (vitamin B_{12}), creatinine, alanine transaminase (ALAT), ferritine, anti-thyroperoxidase (anti-TPO), parathyroid hormone (PTH), thyroid-stimulating hormone (TSH) and free thyroxine (fT4) were measured at the Institute of Clinical Chemistry and Laboratory Medicine, University of Medicine, Greifswald, Germany.

Genetics

The following genetic variations have been genotyped: the two most common filaggrin null mutations in Caucasians R501X and 2282del4[7,24] and the three GST mutations (GSTP1, GSTT1 and GSTTM1). The study is part of the LuCamp study (www.LuCamp.org), in which about 20 000 single nucleotide polymorphisms (SNPs) have been genotyped in all participants of the Health2006 cohort. In addition, an aliquot of DNA from all participants is stored at KBiosciences (www.kbiocience.co.uk) for further rapid genotyping of SNPs by the PCR KASPar genotyping system (KBiosciences, Hoddesdon, UK).

What has been found?

Some characteristics of the participants are illustrated in Table 3. In addition to the descriptive data shown in Table 3, some results from the Health2006 study have previously been published. These publications have mainly focused on hand eczema, contact allergy, atopic dermatitis, rhinitis, airway symptoms, lung function and chemical intolerance.[5,6,25–28] Exposure to environmental tobacco smoke has been associated with decreased lung function, respiratory symptoms and rhinitis symptoms whereas no associations were found between other sources of indoor air pollution and lung function, allergic or respiratory symptoms.[5,6] Data from the Health2006 cohort have also demonstrated a decreased prevalence of nickel allergy[26,27] after the Danish nickel regulation initiative and a modest decrease in contact allergy to a wide panel of allergens.[28] Mutations in the filaggrin gene are also the topic of a number of publications. Filaggrin null mutations have been associated with increased contact sensitization to nickel and other chemicals, increased risk of hand eczema[7] and with increased serum levels of vitamin D.[29] In addition, filaggrin null mutations have been shown to modify the effects of smoking on the risk of asthma.[30] Mental fitness in relation to cardiovascular biomarkers was the main aim in a new PhD project including a study investigating the personality-perceived stress relation and a study investigating the personality-leisure time sitting time (LTST) relation. All five dimensions of the five-factor personality traits associated with perceived stress and with LTST and all associations found were mediated by coping measured as general self-efficacy.[31,32] The Health2006 has also contributed to the discovery of new genetic loci determining the risk of atopic dermatitis,[33] and a series of papers in genetic epidemiology are in progress. A complete list of references based on data wholly or partly based on data from the Health2006 study is available on our webpage at http://www.regionh.dk/fcfs/Menu/.

What are the main strengths and weaknesses?

The main strengths of this study are the objective measurements of muscle strength, cardio-respiratory fitness, lung function, allergy and biomarkers of chronic diseases in combination with questionnaire-data-based information on a wide range of lifestyle factors. Another major strength of this study is the possibility of linkage to national registries, whereby data from clinical examinations and questionnaires can be associated with register-based information, e.g. future diagnoses of chronic disease. As illustrated in Table 1, register data for non-responders also are available on, for example, use of prescription drugs, hospital episodes and mortality, which makes it possible to compare responders with non-responders. Another strength of this study is the biological material stored in our biobank that offers the opportunity to perform specialized measurements on different biomarkers in the future.

The main weaknesses of the Health2006 study are the relatively low rate of participation and the documented differences between responders and non-responders that may limit the validity of generalizations made from Health2006 results. These differences should also be considered when discussing potential bias of associations found in data from the study. Furthermore, the size of the population does not allow us to study rare outcomes.

Table 3 Characteristics of participants in the Health2006 cohort

BMI ($n = 3469$)	Mean	25.9 kg/m^2
	Underweight (<18.5 kg/m^2)	1.9%
	Normal (⩾18.5-25 kg/m^2)	45.9%
	Overweight (⩾25-30 kg/m^2)	36.2%
	Obese (⩾30 kg/m^2)	16.1%
Waist circumference ($n = 3468$)	Mean (♂/♀)	95.1/ 83.5 cm
	Obese (♂: >102 cm, ♀: >88 cm)	29.3%
Waist-to-hip ratio ($n = 3467$)	Mean (♂/♀)	0.94 / 0.82
	Obese (♂: ⩾0.90, ♀: ⩾0.85)	46.9%
Smoking (self-reported) ($n = 3437$)	Daily smokers	22.5%
	Occasional smokers	3.3%
	Ex-smokers	32.5%
	Never smokers	41.8%
Alcohol (self-reported) ($n = 3426$)	No drinking within last 12 months	5.3%
	>7 (women)/14 (men) units/week	31.5%
Diet (self-reported)[a] ($n = 3430$)	Unhealthy	6.9%
	Average	69.3%
	Healthy	23.8%
Physical activity, leisure time	Sedentary	18.5%
(self-reported) ($n = 3433$)	Low activity	60.5%
	Medium/high activity	20.9%
Blood pressure ($n = 3470$) (mmHg)	Mean (systolic/diastolic)	130/82
	Systolic >140 and/or diastolic >90	30.2%
Total cholesterol ($n = 3450$)	Mean	5.3 mmol/l
	>5 mmol/l	59.1%
Fasting plasma glucose[c]	Mean	5.4 mmol/l
($n = 3271$)	>7 mmol/l	1.8%
Plasma HbA1c[c]	Mean	5.4
($n = 3281$)	⩾6.5%	0.7%
Self-reported doctor-diagnosed	Diabetes ($n = 3423$)	3.9%
	CVD[b] ($n = 3453$)	6.4%
	Depression ($n = 3413$)	11.4%
	Asthma ($n = 3413$)	10.8%
	Hayfever ($n = 3405$)	17.9%
Self-rated health (SF12) ($n = 3431$)	'Fair' or 'poor'	8.7%

BMI, body mass index.
[a]Based on Dietary Quality Score, developed as a crude index of the overall quality of the dietary habits. The score was based on questions regarding the intake of fruits, vegetables, fish and different types of fat.
[b]Stroke, heart attack and/or other heart disease.
[c]Among participants not reporting doctor-diagnosed diabetes.

Can I get hold of data and where can I find more?

Access to data and biological material for research projects can be granted by the board of the RCPH. Any application must be accompanied by a research protocol that must comply with Danish regulations on ethical approval and data protection. Data are presently available only in Danish. However, relevant data from the Health2006 cohort will be translated if data are included as part of international studies. For more information, please contact principal

investigator Allan Linneberg (e-mail: allan.linneberg@regionh.dk) or visit our webpage at http://www.regionh.dk/fcfs/Menu/.

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Conflict of interest: None declared

KEY MESSAGES

- The Health2006 cohort has provided interesting findings in the field of asthma, allergy and eczema in addition to genetic studies dealing with mutations in the filaggrin gene associated with skin barrier function.
- A decreased prevalence of nickel allergy was observed in Health2006 participants after the introduction of nickel regulations in Denmark during the 1990s.
- All five dimensions of the five-factor personality traits were associated with perceived stress and with leisure-time sitting-time in the Health2006 cohort. In both cases the associations were mediated by coping measured as general self-efficacy.
- The Health2006 cohort has contributed to the discovery of new genetic loci determining the risk of atopic dermatitis, and a series of papers in genetic epidemiology including data from the Health2006 cohort are in progress.

References

[1] Hagerup LM. Coronary heart disease risk factors in men and women. From the population study in Glostrup, Denmark. *Acta Med Scand Suppl* 1974;**557:**1–116.
[2] Osler M, Linneberg A, Glumer C, Jorgensen T. The cohorts at the Research Centre for Prevention and Health, formerly 'The Glostrup Population Studies'. *Int J Epidemiol* 2011;**40:**602–10.
[3] Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav* 1983;**24:**385–96.
[4] Costa PT Jr, McCrae RR. Domains and facets: hierarchical personality assessment using the revised NEO personality inventory. *J Pers Assess* 1995;**64:**21–50.
[5] Hersoug LG, Husemoen LL, Sigsgaard T, Madsen F, Linneberg A. Indoor exposure to environmental cigarette smoke, but not other inhaled particulates associates with respiratory symptoms and diminished lung function in adults. *Respirology* 2010;**15:**993–1000.
[6] Hersoug LG, Husemoen LL, Thomsen SF, Sigsgaard T, Thuesen BH, Linneberg A. Association of indoor air pollution with rhinitis symptoms, atopy and nitric oxide levels in exhaled air. *Int Arch Allergy Immunol* 2010;**153:**403–12.
[7] Thyssen JP, Carlsen BC, Menne T *et al*. Filaggrin null mutations increase the risk and persistence of hand eczema in subjects with atopic dermatitis: results from a general population study. *Br J Dermatol* 2010;**163:**115–20.
[8] Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. *Circulation* 1968;**38:**1104–15.
[9] Andersen LG, Groenvold M, Jorgensen T, Aadahl M. Construct validity of a revised Physical Activity Scale and testing by cognitive interviewing. *Scand J Public Health* 2010;**38:**707–14.
[10] Ainsworth BE, Haskell WL, Leon AS *et al*. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc* 1993;**25:**71–80.
[11] Aadahl M, Jorgensen T. Validation of a new self-report instrument for measuring physical activity. *Med Sci Sports Exerc* 2003;**35:**1196–02.
[12] Aadahl M, Kjaer M, Kristensen JH, Mollerup B, Jorgensen T. Self-reported physical activity compared with maximal oxygen uptake in adults. *Eur J Cardiovasc Prev Rehabil* 2007;**14:**422–28.
[13] Toft U, Kristoffersen LH, Lau C, Borch-Johnsen K, Jorgensen T. The Dietary Quality Score: validation and association with cardiovascular risk factors: the Inter99 study. *Eur J Clin Nutr* 2007;**61:**270–78.
[14] Aadahl M, Zacho M, Linneberg A, Thuesen BH, Jorgensen T. Comparison of the Danish step test and the watt-max test for estimation of maximal oxygen uptake: the Health2008 study. *Eur J Prev Cardiol* 2012; doi:10.1177/2047487312462825.
[15] Aadahl M, Beyer N, Linneberg A, Thuesen BH, Jorgensen T. Grip strength and lower limb extension power in 19–72-year-old Danish men and women: the Health2006 study. *BMJ Open* 2011;**1:**e000192.
[16] Miller MR, Hankinson J, Brusasco V *et al*. Standardisation of spirometry. *Eur Respir J* 2005;**26:**319–38.

[17] ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. *Am J Respir Crit Care Med* 2005;**171:**912–30.
[18] Deykin A. Targeting biologic markers in asthma—is exhaled nitric oxide the bull's-eye? *N Engl J Med* 2005; **352:**2233–35.
[19] Dalsgaro OJ, Vestbo J. Oxidativt stress og genetiske polymorfismer ved KOL [Oxidative stress and genetic polymorphism in COPD]. *Ugeskr Laeger* 2002;**164:**4056–61.
[20] Petersen AB, Gudmann P, Milvang-Gronager P *et al*. Performance evaluation of a specific IgE assay developed for the ADVIA centaur immunoassay system. *Clin Biochem* 2004;**37:**882–92.
[21] Kreilgard B, Hansen J, Fischer T. Chemical, pharmaceutical and clinical standardization of the TRUE Test caine mix. *Contact Dermatitis* 1989;**21:**23–27.
[22] Wilkinson JD, Bruynzeel DP, Ducombs G, Frosch PJ, Gunnarsson Y, Hannuksela M *et al*. European multicenter study of TRUE Test, Panel 2. *Contact Dermatitis* 1990;**22:** 218–25.
[23] Wilkinson DS, Fregert S, Magnusson B *et al*. Terminology of contact dermatitis. *Acta Derm Venereol* 1970;**50:**287–92.
[24] Thyssen JP, Johansen JD, Linneberg A *et al*. The association between null mutations in the filaggrin gene and contact sensitization to nickel and other chemicals in the general population. *Br J Dermatol* 2010;**162:**1278–85.
[25] Thyssen JP, Johansen JD, Menne T, Nielsen NH, Linneberg A. Effect of tobacco smoking and alcohol consumption on the prevalence of nickel sensitization and contact sensitization. *Acta Derm Venereol* 2010;**90:**27–33.
[26] Thyssen JP, Linneberg A, Menne T, Nielsen NH, Johansen JD. The association between hand eczema and nickel allergy has weakened among young women in the general population following the Danish nickel regulation: results from two cross-sectional studies. *Contact Dermatitis* 2009;**61:**342–48.
[27] Thyssen JP, Johansen JD, Menne T, Nielsen NH, Linneberg A. Nickel allergy in Danish women before and after nickel regulation. *N Engl J Med* 2009;**360:** 2259–60.
[28] Thyssen JP, Linneberg A, Menne T, Nielsen NH, Johansen JD. Contact allergy to allergens of the TRUE-test (panels 1 and 2) has decreased modestly in the general population. *Br J Dermatol* 2009;**161:**1124–29.
[29] Thyssen JP, Thuesen B, Huth C *et al*. Skin barrier abnormality caused by filaggrin (FLG) mutations is associated with increased serum 25-hydroxy vitamin D concentrations. *J Allergy Clin Immunol* 2012;**130:**1204–07.
[30] Berg ND, Husemoen LL, Thuesen BH *et al*. Interaction between filaggrin null mutations and tobacco smoking in relation to asthma. *J Allergy Clin Immunol* 2012;**129:** 374–80.
[31] Ebstrup JF, Eplov LF, Pisinger C, Jorgensen T. Association between the Five Factor personality traits and perceived stress: is the effect mediated by general self-efficacy? *Anxiety Stress Coping* 2011;**24:**407–19.
[32] Ebstrup JF, Aadahl M, Eplov LF, Pisinger C, Jorgensen T. Cross-Sectional Associations Between the Five Factor Personality Traits and Leisure-Time Sitting-Time: The Effect of General Self-Efficacy. *J Phys Act Health* 2012; (Epub ahead of print).
[33] Paternoster L, Standl M, Chen CM *et al*. Meta-analysis of genome-wide association studies identifies three new risk loci for atopic dermatitis. *Nat Genet* 2012;**44:**187–92.