

BMJ Open Protocol of a research project ‘Projections of the burden of disease and disability in Finland – health policy prospects’ using cross-sectional health surveys and register-based follow-up

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To cite: Paalanen L, Härkänen T, Tolonen H. Protocol of a research project ‘Projections of the burden of disease and disability in Finland – health policy prospects’ using cross-sectional health surveys and register-based follow-up. *BMJ Open* 2019;9:e029338. doi:10.1136/bmjopen-2019-029338

► Prepublication history for this paper is available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2019-029338>).

Received 22 January 2019
Revised 24 April 2019
Accepted 28 May 2019



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ABSTRACT

Introduction With the rapid ageing of the population in Europe, reliable estimates of the future development of the disease and disability burden as well as healthy life years in the older sections of the population are crucial. Meanwhile, the future prospects of the health and functional ability of the working-aged population are critical. The aims of the *Projections of the burden of disease and disability in Finland – health policy prospects* research project are to provide information about the long-term consequences of health-related behaviours of the population and to project the potential improvement of the burden of disease and disability based on realistic scenarios about the development of risk behaviours in the total population and its subgroups.

Methods and analysis The analyses will be based on data from representative cross-sectional and longitudinal health examination surveys (HESs) conducted between 1972 to 2017 in Finland, and register data from several national administrative registers. Included HESs (FINRISK Surveys from 1972 to 2012, Mini-Finland Survey from 1978 to 1980, the Health 2000/2011 Surveys and the FinHealth 2017 Study) provide abundant information about biological and behavioural risk factors and the health and morbidity of the population. The modifiable risk factors used as predictors include hypertension, hyperlipidaemia, obesity, diabetes, physical inactivity, smoking, alcohol use and unfavourable diet. The main outcomes are ischaemic heart disease, cerebrovascular diseases, lung cancer, chronic obstructive pulmonary disease, Alzheimer’s disease and diabetes. Within the project, novel projection techniques of data-driven Bayesian hierarchical models to provide robust and comparable estimates will be developed.

Ethics and dissemination The prevailing legislation and regulations have been followed for all surveys. Surveys since 1997 have been approved by the respective Ethics Committees covering the scope of this project. A written informed consent was obtained from participants since 1997. The outputs of the project will include 8 to 10 scientific papers in peer-reviewed journals.

INTRODUCTION

With the rapid ageing of the population in Europe, healthcare systems are facing

Strengths and limitations of this study

- All included surveys included physical measurements and laboratory samples in addition to self-reported data.
- The linkage of survey data with administrative registers enables the use of comprehensive follow-up data.
- Statistical methods for health projections will be developed in the project, and estimated intervention effects on risk behaviours and their consequences obtained from literature on randomised clinical trials will be incorporated in different scenario projections.
- Comparison of different scenarios on the population level or in subgroups provides insight into optimal decision-making in public health policy.
- Although the questionnaires and measurements have been kept as similar as possible throughout the study years, methodological differences across the surveys may limit the comparability of data.

increasing demand and patient load. Therefore, reliable estimates of the future development of the disease and disability burden as well as healthy and disease-free life years in the older sections of the population are crucial. At the same time, the future prospects of the health and functional ability of the working aged population are of critical importance as they must provide the necessary financial resources and manpower for maintaining and caring for the older population.

Non-communicable diseases (NCD) are the leading cause of mortality globally. About 71% of all deaths are related to NCDs, with cardiovascular disease (CVD) (eg, coronary heart disease, stroke), cancers, respiratory diseases and diabetes being the most frequent causes of NCD deaths.¹ NCDs are also responsible for 28% of premature mortality, deaths under age of 70 years, in high-income countries. CVD, diabetes, cancers and chronic

obstructive pulmonary disease (COPD) are among the most important causes of hospitalisations and absences from work.²

The burden of disease estimates for Finland for 2016 reported by the WHO in collaboration with the Institute of Health Metrics and Evaluation, include ischaemic heart disease (IHD), Alzheimer's disease, cerebrovascular diseases and lung cancer within the top 10 causes of both disability adjusted life years (DALYs) and years of life lost (YLLs) to premature mortality (<http://ghdx.healthdata.org/gbd-2016>). For years lived with disability (YLDs) also diabetes was on the top-10 list (<http://www.healthdata.org/finland>). Thus, this group of potentially preventable NCDs poses a serious challenge to the economies of most countries and is responsible for remarkable economic burden to all European countries.³

A body of evidence indicates that lifestyles such as smoking, diet, alcohol use and physical activity have a major influence on health and longevity. The 10 leading risk factors contributing to the burden of disease in Finland are dietary habits, hypertension, obesity, alcohol and drug use, smoking, high fasting plasma glucose, high cholesterol, low physical activity and low glomerular filtration rate and low bone mineral density. It has been shown that adherence to a healthy lifestyle is associated with a lower risk of mortality. The relative risk of all-cause mortality declines proportionate to a higher number of healthy lifestyle factors.⁴ Lifestyles also make a large contribution to inequalities in health and functioning.^{5,6}

Researchers from the EPIC-Norfolk prospective population study found that the combination of four behavioural risk factors, smoking, physical inactivity, alcohol drinking and low fruit and vegetable consumption, predicted a four-fold difference in the risk of dying over an average period of 11 years for middle-aged and older people.⁷ They also showed that the risk of death, particularly from CVD, decreases as the number of positive health behaviours increases. Results from the Healthy Ageing: a Longitudinal study in Europe (HALE) project indicated that adherence to a Mediterranean diet, non-smoking, moderate alcohol use and any physical activity among elderly were associated with a more than 50% lower rate of all-cause and cause-specific mortality.⁸ Lifestyle factors such as smoking, physical activity and obesity are also shown to be associated with healthy and disease-free life expectancy. In a recent large multi-cohort study, people with none of these three lifestyle-related risk factors were shown to have on average 8 years longer life expectancy in good health between the ages 50 and 75 years, compared with people with at least two of the three risk factors.⁹ Similarly, the European Society of Cardiology European Action on Secondary and Primary Prevention by Intervention to Reduce Events survey has shown that a large proportion of people at high risk for CVD have uncontrolled blood pressure, lipids and diabetes demonstrating the need for more effective prevention.¹⁰

Evidence based health policy planning requires the best available information on the future development of

the main public health problems and how to influence this development. Ideally, health projections should take into account the history and current levels of health and its determinants as well as potential scenarios for changes in the health determinants in the total population and subgroups. Health projections based on different scenarios concerning the amenable determinants of public health have been produced, based on the Global Burden of Disease data or using the so called IMPACT model for coronary heart disease.¹¹⁻¹³ However, the data sources available in Finland are much richer than those used in the Global Burden of Disease estimates. They can be used to improve the accuracy of the projections. In particular, the national health examination surveys with mortality and morbidity follow-up and re-examinations studies provide a unique data source which allows the projections to make use not only of the current levels of the risk factors but also the population and individual level changes from the past.

In 2017, a research project called the *Projections of the burden of disease and disability in Finland – health policy prospects (PoDDy-HePo)* was launched. The project was started in the end of 2017 and will be carried out until 2021. The overall aim of the project is to provide information about the long-term consequences of health related behaviours of the population and to what extent can the projected development of the burden of disease and disability be improved according to realistic scenarios about the development of risk behaviours in the total population and its subgroups. This information will help local, national and international governments and other policymakers to develop policies to address the growing problems of NCDs and inequalities, and to increase healthy life expectancy.

Making use of the wealth of relevant data sources available in Finland and novel statistical techniques, the project will provide up-to-date information about the prevalence of major chronic disease risk factors and the burden of disease, and health projections under different risk factor and policy scenarios in the Finnish population and its subgroups. Such data are highly relevant for policymakers and other stakeholders working in the field of public health and especially on prevention of chronic diseases. Statistical methods, which will be developed in the project, should be directly applicable to other countries with a comprehensive health monitoring system, such as Denmark, UK and the Netherlands. We will apply flexible statistical methods to account for interactions and non-linearities. For example, the random forest or non-parametric Bayesian methods allow combining time-to-event data obtained from registers with categorical or continuous variables commonly collected in surveys. The results will also facilitate the improvement of health projections in countries with less comprehensive health monitoring data.

METHODS AND ANALYSIS

The analyses of the PoDDy-HePo project will be based on existing data from cross-sectional and longitudinal health examination surveys (HESs) conducted between 1972 to 2017 in Finland, and register data from several administrative registers. Included HESs are based on random samples of the general population. They provide abundant information about biological and behavioural risk factors, and the health and morbidity of the population.

The project has two aims:

1. Estimation of the proportion of ill health attributable to modifiable risk factors, where the objectives are to
 - ▶ understand determinants of the health inequalities and their changes over time, and to assess the contribution of modifiable risk factors to these inequalities;
 - ▶ assess the impact of modifiable risk factors and their combinations to mortality and DALYs; and
 - ▶ assess the impact of modifiable risk factors and their combinations on healthy life expectancy and disability and disease-free life years.
2. Providing projections of the incidence, prevalence and number of cases of major chronic disease and disability measures under different scenarios in the whole population and its subgroups. For this aim, the objectives are to
 - ▶ assess and document the strengths and weaknesses of available projection methods;
 - ▶ prepare statistical methods for projecting incidence, prevalence, life expectancy and expected healthy life years and the number of diseased individuals accounting for birth cohort differences and trends;

- ▶ account for sampling, parameter, model and prediction uncertainties in the projections using, for example, Bayesian predictive distributions or multiple imputation techniques;
- ▶ assess existing knowledge from randomised clinical trials (RCT) about intervention effects; and
- ▶ provide projections on health outcomes and risk factors.

Health examination survey data

The following population-based HESs among the adult Finnish population form the basis for the PoDDy-HePo project: FINRISK Surveys from 1972 to 2012,¹⁴ Mini-Finland Survey (MFS) from 1978 to 1980,¹⁵ the Health 2000/2011 Surveys^{16 17} and the FinHealth 2017 survey.¹⁸ Information from repeated measurements on the same persons is available from the Mini-Finland Health Survey and the Health 2000/2011 re-examinations.

All these HESs included health examinations with physical measurements, blood pressure measurements and laboratory samples as well as a self-administered questionnaire and/or interviews resulting in comprehensive information about health and functioning, diseases, health behaviours and living conditions. Covered age groups, numbers of participants and participation rates are given in [table 1](#). The covered core topic areas in questionnaires or interviews and included physical measurements are given in [tables 2–3](#). The laboratory samples of all surveys included at least blood collection, and key biomarkers, such as serum total cholesterol, have been determined for all surveys.

Table 1 Age groups, number of participants and participation rate in the National FINRISK studies 1972 to 2012, the Mini-Finland Health Survey (MFS), Health 2000/2011 surveys and the FinHealth 2017 survey

	Age groups (years)	Participants, health examination (n)	Participants, questionnaire or interview only (n)	Participation rate, total (%)*
FINRISK 1972	25–59	10938	-	88
FINRISK 1977	30–64	10199	-	90
FINRISK 1982	25–64	9347	-	82
FINRISK 1987	25–64	6479	-	82
FINRISK 1992	25–64	6051	-	76
FINRISK 1997	25–64†	8446	-	73
FINRISK 2002	25–64†	8798	782	71
FINRISK 2007	25–74	6258	1735	67
FINRISK 2012	25–74	5827	597	65
MFS 1978–1980	30+	7217	486	96
Health 2000	30+	6354	1061	93
Health 2011	29+	4729	1174	74
FinHealth 2017	18+	5957	841	69

*Because of differences in age groups the participation rates are not directly comparable between the surveys.

†In some areas 25–74.

Table 2 Core topic areas in questionnaires and interviews of the National FINRISK study cohorts (FR) 1972 to 2012, Mini-Finland Health Survey (MFS), Health 2000, Health 2011 and FinHealth 2017 surveys relevant for the PoDDy-HePo project

Topic area	FR 1972	FR 1977	FR 1982	FR 1987	FR 1992	FR 1997	FR 2002	FR 2007	FR 2012	MFS 1978–1980	Health 2000	Health 2011	FinHealth 2017
Topics in questionnaires and interviews													
Activities of daily living	x	x	x	x	x	x	x	x	x	x	x	x	*
Alcohol use	x	x	x	x	x	x	x	x	x	x	x	x	x
Blood pressure	x	x	x	x	x	x	x	x	x	x	x	x	x
Cholesterol	x	x	x	x	x	x	x	x	x	x	x	x	x
Cognitive functioning										x	x	x	x
Diabetes	x	x	x	x	x	x	x	x	x	x	x	x	x
Diet	x	x	x	x	x	x	x	x	x	x	x	x	x
Family history of cardiovascular diseases	x	x	x	x	x	x	x	x	x	x	x	†	x
Food frequency questionnaire							x		x		x		x
General health	x	x	x	x	x	x	x	x	x	x	x	x	x
Healthcare use	x	x	x	x	x	x	x	x	x	x	x	x	x
Heart disease history	x	x	x	x	x	x	x	x	x	x	x	x	x
Household composition	x	x	x	x	x	x	x	x	x	x	x	x	x
Injuries and accidents				x	x	x	x	x	x	x	x	x	x
Medication use	x	x	x	x	x	x	x	x	x	x	x	x	x
Mental health	x	x	x	x	x	x	x	x	x	x	x	x	x
Need and use of help							x				x	x	x
Need and use of rehabilitation											x	x	‡
Physical activity	x	x	x	x	x	x	x	x	x	x	x	x	x
Physical functioning	x	x	x	x	x	x	x	x	x	x	x	x	x
Psychosocial factors				x	x	x	x	x	x	x	x	x	x
Quality of life	x	x	x	x	x	x	x	x	x	x	x	x	x
Reproductive health				x	x	x	x	x	x	x	x	x	x
Self-reported height and weight	x	\$				x					\$	x	x
Sleep	x	x					x		x		x	x	x
Smoking and tobacco use	x	x	x	x	x	x	x	x	x	x	x	x	x
Socio-economic status	x	x	x	x	x	x	x	x	x	x	x	x	x

Continued

Table 2 Continued

Topic area	FR 1972	FR 1977	FR 1982	FR 1987	FR 1992	FR 1997	FR 2002	FR 2007	FR 2012	MFS 1978-1980	Health 2000	Health 2011	FinHealth 2017
Symptoms of health problems	x	x	x	x	x	x	x	x	x	x	x	x	x
Unemployment and pension	x	x	x	x	x	x	x	x	x	x	x	x	x
Weight history	x	x	x	x	x	x	x	x	x	x	x	†	x
Work ability, working conditions								x	x	x	x	x	x

*Only among subjects aged 70+years.

†Information available for the majority of subjects from the Health 2000 survey.

‡Question on attending physiotherapy on a doctor's referral during the past 12 months.

§Only weight was asked in FINRISK 1977 study and Health 2000 survey.

Note, the number and format of questions under each topic may have varied across the survey years. PoDDy-HePo, Projections of the burden of disease and disability in Finland – health policy prospects.

National cross-sectional HESs, called the **FINRISK surveys**, were conducted among the general Finnish population every 5 years in selected geographical areas between 1972 to 2012.¹⁴ Each time an independent stratified random sample was drawn from the National Population Information System. The sample sizes varied between 7927 to 13500 persons (altogether 98977 persons).

The **Mini-Finland Health Survey (MFS, 1978 to 1980)** involved a representative sample of the Finnish population.¹⁵ The sample size was 8000 persons. A total of 1278 participants from the MFS survey were invited to participate in a re-examination in connection to the Health 2000 Survey and 89% agreed. In 2011 to 2012, those 920 subjects still alive were invited to participate in a second re-examination in connection to the Health 2011 Survey and 81% agreed.

The **Health 2000 Survey**, carried out in 2000 to 2001, covered a representative sample of the Finnish population.¹⁶ Health examination was conducted in the age group 30 years and older (sample size 8028). In the age group 18 to 29 years (sample size 1894) only a questionnaire was administered. The 8022 persons selected to the Health 2000 Survey and living in Finland in 2011 were invited to take part in a re-examination, **Health 2011**.¹⁷ They were at least 29 years of age in 2011. Also a new sample (n=1994) was selected from the age group 18 to 28 years.

In 2017, a comprehensive nationally representative HES, the **FinHealth 2017 Survey**, was conducted (sample size 12 037).¹⁸

In addition to the foregoing surveys among the general adult population in Finland, data from the **Migrant Health and Well-being Study (Maamu)** will be used in some substudies.¹⁹ The Maamu Study was carried out in Finland among three migrant groups in 2010 to 2012. The sample size was 3000 persons of whom 1510 (50%) participated in the health examination.

Administrative register data

All Finnish residents have a unique personal identity code (PIC), which enables linkage of different data sources such as survey data to administrative registers. In the PoDDy-HePo project, comprehensive register-based data including (a) background information, (b) disease history and (c) follow-up data on disease outcomes, mortality and causes of death, will be utilised. Furthermore, the information about population structure and estimated demographic changes required for the projections will be obtained from the Statistics Finland.

All cross-sectional HESs described earlier, have been linked to the national administrative registers using the PIC with the exception of the MFS. The administrative registers that will be used are

- ▶ **Care Register for Healthcare:** dates and diagnoses of hospitalisations (<https://www.thl.fi/fi/web/thlfi-en/statistics/information-on-statistics/register-descriptions/care-register-for-health-care>)
- ▶ **Causes of death register:** date and cause of death (http://www.stat.fi/meta/til/ksyyt_en.html)

Table 3 Physical measurements and tests of the National FINRISK study cohorts (FR) 1972 to 2012, Mini-Finland Health Survey (MFS), Health 2000, Health 2011 and FinHealth 2017 surveys relevant for the PoDDy-HePo project

Measurement or test	FR 1972	FR 1977	FR 1982	FR 1987	FR 1992	FR 1997	FR 2002	FR 2007	FR 2012	MFS 1978–1980	Health 2000	Health 2011	FinHealth 2017
Audiometry											x		
Arm circumference			x	x	x	x	x	x	x		x	x	x
Blood pressure	x	x	x	x	x	x	x	x	x	x	x	x	x
Body composition			x								x	x	x
Cognitive functioning										x	x	x	x
Electrocardiography							x*			x	x	x	
Height and weight	x	x	x	x	x	x	x	x	x	x	x	x	x
Lung function										x	x	x	
Oral health										x	x	x*	
Physical activity monitor (accelerometry)									x*			x*	x*
Physical functioning or fitness test					x*	x*	x*	x*	x*	x	x	x	x
Postural balance						x*					x	x	
Pulse		x	x	x	x	x	x	x	x	x	x	x	x
Standard physical status by physician										x	x	x	
Skin fold thickness										x			
Visual acuity													
Waist and hip circumferences			x	x	x	x	x	x	x		x	x	x

*Only for a subsample.

†Only waist was measured in Health 2011 survey.

PoDDy-HePo, Projections of the burden of disease and disability in Finland – health policy prospects.

- ▶ **Socio-demographic data** from Statistics Finland.
- ▶ **Registers of the Social Insurance Institution:** entitlement to specifically reimbursed medications due to specific chronic conditions, sickness absence, work disability pensions, purchase of medicines by anatomical therapeutic chemical (ATC) code (http://www.kela.fi/web/en/statistics-by-topic_statistics-on-reimbursement-entitlements-in-respect-of-medicines)
- ▶ **Finnish Cancer Register:** date and diagnoses of cancers (<http://www.cancer.fi/syoparekisteri/rekisterointi/rekisteriseloste>)
- ▶ **Population Register Centre:** geographical information (geographical coordinates) of the place of residence and the examination centres (<http://vrk.fi/en/population-information-system>)

The MFS has been linked only to Care register for healthcare, Causes of death register and registers of the Social Insurance Institution.

Predictors

The modifiable risk factors used as predictors include hypertension, hyperlipidaemia, obesity, diabetes, physical inactivity, smoking, alcohol use and unfavourable diet. These risk factors are associated with most of the diseases selected as the main outcomes of the project.

Marital status and education will be used as the main socio-demographic and socio-economic indicators. The possible correlation and interaction of these indicators with other relevant background factors will be considered in the analyses of each substudy individually.

Outcomes

The focus will be on IHD, cerebrovascular diseases, lung cancer, COPD, Alzheimer's disease and diabetes. These diseases were selected as they were among the top 10 causes of DALYs and years of life lost due to premature mortality, premature mortality, physical and cognitive disability and multi-morbidity by previous Global Burden of Disease estimates.²⁰ Diabetes is included as both a predictor and outcome as it is a risk factor for several diseases listed as outcomes and, on the other hand, diabetes will also be examined as a disease outcome within the project. Cancers will not be in the focus of this project as there is another ongoing project called Prospective Cancer Meta Cohort Study (METCA) on the causes of cancer and cancer burden in Finland with which our study groups collaborates (<https://cancerregistry.fi/research/research-themes/the-causes-of-cancer-and-cancer-burden/>).

The burden of disease will be estimated using indicators introduced by the WHO in collaboration with the Institute for Health Metrics and Evaluation.²¹ DALYs, YLLs and YLDs will be calculated using the algorithms by WHO and the Institute for Health Metrics and Evaluation. Disability weights updated in 2016 will be used (<http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights>).

The population attributable fractions are calculated to estimate the contribution of risk factors to burden of disease and disability.²²

Projections

In previous studies, a variety of projection methods, such as microsimulation methods²³ and the IMPACT model¹² have been commonly used to dynamically project not only the changes in the health outcomes of interest but also in the risk factors. Some of these methods do not account for different sources of uncertainty for example in parameter estimates in Dynamic Modeling for Health Impact Assessment (DYNAMO-HIA).²⁴ Existing software tools for projections usually utilise only point estimates of model parameters, thus projections based on small datasets can underestimate the uncertainty in the projections. Another common problem in projections has been the overly simple assumptions of total eliminations of a risk factor. In PoDDy-HePo project, we aim to utilise the strengths of these methods and to overcome these limitations by applying estimates obtained from RCT literature and Bayesian inference²⁵ which can accommodate various forms of uncertainty in analysis.²⁶ We will also account for individual trends in risk factors as well as demographic changes. We will also account for for example informative censoring due to mortality, which can depend on same risk factors as morbidity and act as a competing risk.

Within the project, novel projection techniques of data-driven Bayesian hierarchical models to provide robust and comparable estimates will be developed. Hierarchical models are needed not only to handle repeated measures but also geographical clustering of the sampling designs in some of the survey datasets in combining different survey datasets, which have been restricted to selected geographical areas in Finland. The novel methods will allow a natural way to incorporate different sources of uncertainty in projections including the large proportion of missing data and expert knowledge based on for example, literature about randomised clinical trials.

Non-response adjustment will be applied to prevalence and trend estimates as well as to the calculations of population attributable risks and projections. Information about the characteristics, risk factors and health status of the non-participants to the health examination surveys will be obtained from the sampling frame and through record linkage to administrative registers. Experience gained in the Non-participation in health examination surveys project (NoPaHES, <http://www.ehes.info/nopahes>) will be used for non-participation adjustment. Multiple imputation, data augmentation and weighting techniques will be applied to handle missing data which originate from loss-to-follow-up, item non-response and missing-by-design.²⁷ The same approaches can be used for dealing with measurement errors.

Patient and public involvement

Patients and the public were not involved in the design or planning of the study. The surveys were carried out among the general population.

Table 4 Ethical permissions for the National FINRISK Studies 1972 to 2012, the Mini-Finland Health Survey (MFS), Health 2000/2011 surveys and the FinHealth 2017 Survey from ethical committees

Survey	Year of data collection	Ethical committee	N.°
FINRISK 1972–1992	1972, 1977, 1982, 1987, 1992	<i>Not required at the time of the survey</i>	–
FINRISK 1997	1997	Ethical issues' committee of the National Public Health Institute (KTL)	38/96
FINRISK 2002	2002	Ethical committee for research in epidemiology and public health at the Hospital District of Helsinki and Uusimaa (HUS)	558/E3/2001
FINRISK 2007	2007	Coordinating ethics committee for the Helsinki and Uusimaa Hospital District	299/EO/06
FINRISK 2012	2012	Coordinating ethics committee for the Helsinki and Uusimaa Hospital District	162/13/03/00/2011
MFS	1978–1980	<i>Not required at the time of the survey</i>	–
Health 2000	2000	National Public Health Institute's ethical committee and the Ethical committee for research in epidemiology and public health at the Hospital District of Helsinki and Uusimaa (HUS)	407/E3/2000
Health 2011	2011	Coordinating ethics committee for the Helsinki and Uusimaa Hospital District	45/13/03/00/11
FinHealth 2017	2017	Coordinating ethics committee for the Helsinki and Uusimaa Hospital District	37/13/03/00/2016

ETHICS AND DISSEMINATION

All included surveys have followed the prevailing legislation and regulations of the time when they were conducted. Surveys since 1997 have been approved by the respective Ethics Committees at the time when the surveys were conducted (table 4). These ethical approvals cover the scope of this project. A written informed consent was obtained from survey participants, except for the early surveys which were conducted before the current legislation on medical research and the Helsinki Declaration. The participants of these early surveys were fully informed, they participated in the surveys voluntarily and the use of the data for medical and public health research was explained to them. These data can be used on the basis of the law on the National Institute for Health and Welfare (THL), which has a statement about the use of archived material (Act on the National Institute for Health and Welfare (668/2008)). Permissions for the record linkage have been obtained from relevant register owners.

The outputs of the project will include 8 to 10 scientific papers. The results will be disseminated through scientific publications, social media and conference or workshop presentations. Besides the scientific community, one of the key objectives is making the results available for the planning and evaluation of health policies.

Contributors HT is the principle investigator of this study and has been mainly responsible for its conception. LP was responsible for drafting the manuscript in collaboration with HT. As the responsible statistician of the project TH provided methodological expertise for this study and critically commented the manuscript.

Funding This work was supported by the Academy of Finland (grant number 307907).

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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