

Jaana Keto

THE MIDDLE-AGED SMOKER IN HEALTH CARE

*PRIMARY HEALTH CARE USE, CARDIOVASCULAR
RISK FACTORS, AND PHYSICIAN'S HELP
IN QUITTING*

UNIVERSITY OF OULU GRADUATE SCHOOL;
UNIVERSITY OF OULU,
FACULTY OF MEDICINE;
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IN HEALTH CARE**

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and physician's help in quitting

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Abstract

The research focus for smoking and public health has typically been on serious smoking diseases such as cancer and coronary thrombosis, which typically require treatment in a hospital setting at an older age. In this thesis, primary health care utilisation and cardiovascular risk factors according to smoking status were studied in a younger cohort: at age 46 in the Northern Finland Birth Cohort of 1966. Primary health care costs of smokers vs. never-smokers were 28% higher for men and 21% higher for women. Signs of elevated risk of metabolic syndrome and cardiovascular disease were visible: smokers had 20% higher triglycerides, slightly larger waist-to-hip ratio, and type 2 diabetes prevalence was twice as high among smokers than never-smokers after adjustment for covariates. The calculated ten-year risk of a cardiovascular event was twice as high for smokers vs. either never-smokers, former smokers or recent quitters. These results should be seen as early warning signals in primary health care, and cost-effective actions should be taken to prevent later multimorbidity – smoking cessation aid by a physician is very cost effective. Only a minority of smokers receive cessation support from a physician, even though the majority of them wish to quit. In order to understand this discrepancy, a survey was conducted on physicians and smoking cessation. Physicians thought it was their responsibility to try to get the patient to quit, but practical measures to treat smoking dependence were rare. The most commonly reported restrictions for smoking cessation work – lack of time and functional treatment paths – could be addressed by administration and management. The attitudes and experiences of Finnish physicians were in line with the WHO recommendation to improve smoking cessation services and integrate them into health care: 80% were in favour of more resources being directed to smoking cessation services, and less than one third thought that smoking cessation was even somewhat well organised in the Finnish health care system.

Keywords: cardiovascular risk factors, health care costs, middle-age, NFBC 66, physicians, primary health care, smoking, smoking cessation

Keto, Jaana, Keski-ikäinen tupakoitsija terveydenhuollossa. Perusterveydenhuollon käyttö, sydän- ja verisuonitautien riskitekijät, sekä lääkärin apu tupakoinnin lopettamisessa

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Tiivistelmä

Tupakoinnin terveys- ja talousvaikutusten tarkastelu keskittyy usein myöhemmällä iällä sairaala- hoitoa vaativiin tupakkasairauksiin kuten syöpään ja sepelvaltimotautiin. Tässä väitöskirjassa tarkastellaan tupakoinnin ja perusterveydenhuollon käytön sekä sydän- ja verisuonitautien riskitekijöiden yhteyttä nuoremmassa otoksessa: 46 vuoden iässä Pohjois-Suomen vuoden 1966 syntymäkohortissa. Perusterveydenhuollon vuosittaiset kustannukset olivat tupakoivilla korkeammat kuin tupakoimattomilla: miehillä 28% ja naisilla 21%. Merkkejä kohonneesta metabolisen oireyhtymän ja sydän- ja verisuonitautien riskistä oli havaittavissa: tupakoivien triglyseridit olivat 20% korkeammat, heidän lantio-vyötärösuhteensa oli hieman suurempi kuin tupakoimattomilla, ja tyypin 2 diabetes oli heillä kaksi kertaa yleisempää taustamuuttujien vakioinnin jälkeen. Arvioitu riski saada vakava sydän- tai verisuonitapahtuma seuraavan kymmenen vuoden kuluessa oli tupakoivilla kaksi kertaa suurempi kuin heillä, jotka joko eivät olleet ikinä tupakoineet, olivat aiemmin tupakoineet, tai jotka olivat hiljattain lopettaneet. Perusterveydenhuollon tulisi nähdä nämä ilmiöt varhaisina varoitussignaaleina ja ryhtyä kustannusvaikuttaviin toimenpiteisiin myöhemmän multimorbiditeetin ehkäisemiseksi – lääkärin antama tuki tupakoinnin lopettamisessa on erittäin kustannusvaikuttavaa. Vaikka suurin osa tupakoitsijoista haluaa lopettaa, vain vähemmistö saa siihen tukea lääkäriltä. Tämän epäsuhdan ymmärtämiseksi tehtiin kyselytutkimus lääkäreille tupakastavieroituksesta. Lääkärit näkivät velvollisuudekseen yrittää saada tupakoiva potilas lopettamaan, mutta käytännön toimet tupakkariippuvuuden hoitamiseksi olivat harvinaisia. Yleisimmin raportoidut esteet vieroitustyölle – aikapula ja puutteelliset hoitopolut – ovat hallinnon ja johdon ratkaistavissa. WHO:n mukaan Suomella on parantamisen varaa lopettamisen tukipalveluissa ja tupakkariippuvuuden hoidon integroimisessa terveydenhuoltojärjestelmään. Tästä väitöskirjasta käy ilmi, että suomalaisten lääkäreiden asenteet ja kokemukset ovat linjassa WHO:n ohjeistuksen kanssa: 80% kannatti lisäresurssien ohjaamista lopettamispalveluihin ja alle kolmanneksen mielestä tupakastavieroitus toteutui edes jokseenkin hyvin suomalaisessa terveydenhuoltojärjestelmässä.

Asiasanat: kustannukset, NFBC 66, perusterveydenhuolto, Pohjois-Suomen syntymäkohortti, sydän- ja verisuonisairaudet, tupakastavieroitus, tupakointi

Preface

Are we living in a post-fact era? Not if you look at how popular evidence-based leadership and management is in the social and health care sector, where real-world data is increasingly utilised in decision-making. The sources of real-world data vary from discharge registers to disease-specific databases and population cohorts, such as the Northern Finland Birth Cohort of 1966 (NFBC 66), an internationally renowned dataset that has so far served as material for some thousand articles published in international peer-reviewed journals. The NFBC 66, alongside with a survey on Finnish physicians and tobacco, served as the data sources for this thesis.

It has been a pleasure and a great learning experience to work with people from different organisational cultures, all sharing the common interest to gain more information about Finnish smokers in health care. A sincere thank you to all my co-authors: Hanna Ventola, Jari Jokelainen, Docent Kari Linden, Dr. Tero Ylisaukko-oja, Dr. Juha Auvinen, and Professor Sirkka Keinänen-Kiukaanniemi; to my supervisor Professor Markku Timonen; to Professor Tiina Laatikainen and Professor Jaakko Kaprio for their thorough efforts in pre-examining this thesis; to Professor Solja Niemelä and Docent Miika Linna for acting as my steering committee; and to everyone else who participated in this project. Finally, I would like to express my gratitude to the members of the NFBC 66 who have patiently filled questionnaires and taken part in clinical examinations since they were born, as well as to the 1 141 Finnish physicians who took part in our Finnish Physicians and Tobacco 2012 study.

Jaana Keto

Helsinki, November 2017

Abbreviations

AvoHilmo	Finnish patient register for primary health care
BMI	Body Mass Index
CI	Confidence Interval
e.g.	exempli gratia
EU	European Union
HDL	High-Density Lipoprotein
Hilmo	Finnish patient register for secondary health care
i.e.	id est
LDL	Low-Density Lipoprotein
NFBC 66	Northern Finland Birth Cohort of 1966
NNTB	Number Needed to Treat to Benefit
RR	Risk Ratio
SCORE	Systematic Coronary Risk Evaluation
SD	Standard Deviation
VLDL	Very Low-Density Lipoprotein
WHO	World Health Organisation

List of original publications

This thesis is based on the following publications, which are referred throughout the text by their Roman numerals:

- I Keto, J., Ventola, H., Jokelainen, J., Timonen, M., Linden, K., Ylisaukko-oja T., Keinänen-Kiukaanniemi S., & Auvinen, J. (2017). Primary health care utilisation and its costs among middle-aged smokers. *European Journal of Health Economics*, 18(3), 351-360. doi:10.1007/s10198-016-0793-2.
- II Keto, J., Ventola, H., Jokelainen, J., Linden K., Keinänen-Kiukaanniemi S., Timonen M., Ylisaukko-oja T., & Auvinen, J. (2016). Characterization of cardiovascular disease risk factors in relation to smoking behaviour and history: a population-based cohort study. *Open Heart*, doi:10.1136/openhrt-2015-000358.
- III Keto, J., Jokelainen, J., Timonen, M., Linden, K., & Ylisaukko-oja T. (2015). Physicians discuss the risks of smoking with their patients, but seldom offer practical cessation help. *Substance Abuse Treatment, Prevention, and Policy*, 10, 43. doi:10.1186/s13011-015-0039-9.
- IV Keto, J., Jokelainen, J., Linden, K., Ylisaukko-oja T., & Timonen, M. (2015). Yleislääketieteen erikoislääkärien kokemat esteet tupakasta vieroituksessa. *Yleislääkäri*, 4, 23-26.

Additional, previously unpublished data are also presented in this thesis.

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1 Literature review

Leaves of the tobacco plant have been chewed and smoked in the Americas for some 7 000 years, both as part of rituals, but also for recreational purposes (Gilman & Xun 2004). Once the American continents and tobacco had been discovered by Europeans in the 16th century, tobacco consumption quickly spread to Europe. At first, tobacco was thought to have positive health effects, and it was used to balance the humoralist system of the patient, as was typical medical practice at the time. The medical practice of treating patients with tobacco smoke enemas, for instance, didn't go out of fashion until the 19th century, when the nicotine found in tobacco was discovered to be a cardiac poison in animal experiments (Gilman & Xun 2004). However, the main method of tobacco consumption hasn't ever been enemas; tobacco has been smoked in a pipe or later as cigarettes, which is the predominant method of consumption in the Western world today, and thus the focus of this thesis. Tobacco has been consumed also in the form of chewing tobacco and snus, both the dry and the moist kind. The modern nicotine industry offers several user interfaces for nicotine, such as electronic cigarettes.

1.1 Smoking in the society

1.1.1 Controversies on the health effects of smoking

It is now known that smoking is detrimental to health, not only in the form of increased lung cancer rates, but also by elevating risk of cardiovascular death, chronic obstructive pulmonary disease (COPD), infertility, proneness to infections, and slower recovery rates from surgery and bone fractures et cetera (Surgeon General 2014). Even at the introduction of tobacco to Europeans, not everyone held a positive view. The early opponents of smoking started a debate that wouldn't be settled until 400 years later, when the causal relationship between smoking and serious illnesses was scientifically proved. As is the case today, the original arguments against smoking ranged from concern of the smoker's health to moralism and socio-economic concerns. King James I himself wrote a treatise on the subject in 1604 titled *A Counterblaste To Tobacco*, in which he wrote:

Have you not reason then to bee ashamed, and to forbear this filthie noveltie, so basely grounded, so foolishly received and so grossely mistaken in the right use thereof? In your abuse thereof sinning against God, harming your selves

both in persons and goods, and raking also thereby the markes and notes of vanitie upon you: by the custome thereof making your selves to be wondered at by all forraine civil Nations, and by all strangers that come among you, to be scorned and contemned. A custome lothsome to the eye, hatefull to the Nose, harmefull to the braine, dangerous to the Lungs, and in the blacke stinking fume thereof, neerest resembling the horrible Stigian smoke of the pit that is bottomelesse (King James I of England 1604).

First formal statistical evidence of the connection between smoking and lung cancer was published in Germany between the first and second world wars, leading to a negative public stance towards smoking in the 1930s Germany (Proctor 2001). In the global medical community, widespread evidence-based concerns about the adverse health effects of smoking started to arise in the late 1940s and early 1950s (Doll & Hill 1950). The British Doctors' Study was one of the first large epidemiological studies on smoking and health, and its key result – that cigarette smoking caused lung cancer – was published in 1954 (Doll & Hill 1954). This finding didn't bring an end to controversies: in the early 1960s, one third of physicians in the United States weren't convinced of the relationship between smoking and lung cancer (Proctor 2012). Finally, in 1964, the United States Surgeon General's office released a report on the subject, kicking off actions against tobacco globally (Surgeon General's Advisory Committee on Smoking and Health 1964). Several lawsuits against the tobacco industry were filed in the United States, and in 1998, a master settlement agreement was reached between large tobacco companies and the attorneys general of 46 states. The settlement resulted in tobacco companies agreeing to cease certain tobacco marketing practices, as well as to pay annual payments to compensate for some of the medical costs of smoking-attributable illnesses.

Smoking prevalence

There are major differences in smoking prevalence even within the European Union (WHO n.d.). Smoking prevalence in Finland has been on a constant decline for decades, and the current prevalence – 15% in 2017 – places Finland well under the latest global and European means from 2015 (table 1) (WHO n.d., National Institute for Health and Welfare 1978–2014, Murto *et al.* 2010–2017). The difference in smoking prevalence between men and women in European countries varies from

the 1.25-fold difference in Germany to the 3.5-fold difference in Latvia, smoking prevalence always being higher among men than women (WHO n.d.).

Table 1. Daily smoking prevalence among adults in 2015 and in Finland in 2017 (WHO n.d., Murto *et al.* 2010–2017).

Area	Smoking prevalence men	Smoking prevalence women
Europe	39%	19%
Finland	16%	13%
Western Pacific	49%	3%
Eastern Mediterranean	36%	3%
Americas	23%	13%
South-East Asia	32%	3%
Africa	24%	2%
Global	36%	7%

Smoking and health differences

In Finland, there is a slight difference in smoking prevalence between men (16%) and women (13%) (Murto *et al.* 2010–2017). The difference is much bigger between socioeconomic groups: in 2014, smoking was five times more common among unemployed Finns than upper white-collar workers (fig. 1) (Helldán & Helakorpi 2015). While the total smoking prevalence has declined in Finland, the polarisation in smoking habits according to socioeconomic status has increased over the years (National Institute for Health and Welfare 1978–2014, Heloma *et al.* 2012). This is the case in most developed countries (European Commission 2013).

Health differences have been a key theme of the European Commission as well as the Finnish government for some years now (Government programmes of Finland 1917–2015, European Commission 2013). While there are marked differences in life expectancy according to sex in the EU, they are topped by differences according to socioeconomic status (European Commission 2013). In Finland, the absolute difference in life expectancy between men and women – 5.6 years for children born in 2015 – is above the EU average (European Commission 2013). The absolute difference in life expectancy is even bigger when the comparison is based on income level instead of sex: on average, Finnish men from the highest income quintile live 11.4 years longer than men from the lowest quintile (Martikainen *et al.* 2014). It has been estimated that smoking along with excess alcohol use explains 60% of the life expectancy difference between men from the

lowest and the highest income quintile (Martikainen *et al.* 2012). While the difference in life expectancy between socioeconomic groups has increased in Finland since the late 1980s, this increase is mainly explained by polarisation of smoking and drinking behaviour (Martikainen *et al.* 2012).

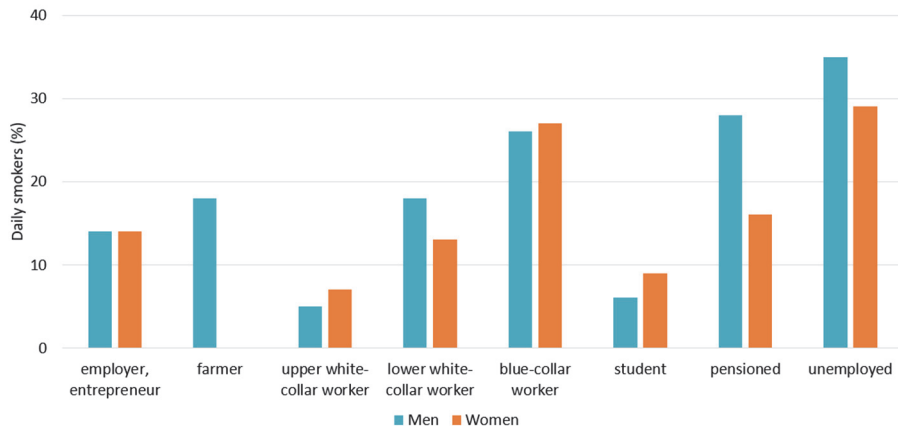


Fig. 1. Smoking prevalence according to socioeconomic status in Finland in 2014 (Helldán & Helakorpi 2015).

1.1.2 Public actions against tobacco

The World Health Organisation (WHO) has campaigned against smoking since it became apparent that smoking is a main threat to public health. The WHO Framework Convention on Tobacco Control (FCTC) was entered into force in 2005, and has since become one of the most widely adopted treaties in United Nations history (WHO FCTC n.d.). WHO has launched a series of reports that track the status of the tobacco epidemic and the impact of local interventions implemented to stop it (WHO 2017). The report has a particular focus on tobacco taxation and prices. Taxation is in fact the earliest form of public actions against tobacco, as the opposition of King James I towards tobacco led to every pound of tobacco imported to England being taxed heavily since 1616 (King James of England n.d.). In modern day Europe, the tobacco directives of the European Union guide local legislation on the sales and advertisement of tobacco products. The first tobacco directives from 1989 focused on warning labels and have gotten more

comprehensive and strict since. The latest directive was adapted in 2014, and despite law suits from tobacco companies, has remained intact.

The World Bank has described six policies that should be prioritised in a comprehensive tobacco control programme: 1) price increases through higher taxes on cigarettes and other tobacco products; 2) bans/restrictions on smoking in public and work places; 3) better consumer information, including public information campaigns, media coverage, and publicising research findings; 4) comprehensive bans on the advertising and promotion of all tobacco products, logos and brand names; 5) large, direct health warning labels on cigarette boxes and other tobacco products; and 6) treatment to help dependent smokers stop, including increased access to medications (Joossens & Raw 2017). WHO has a nearly similar MPOWER-list: Monitor tobacco use and prevention policies; Protect people from tobacco smoke; Offer help to quit tobacco use; Warn about the dangers of tobacco; Enforce bans on tobacco advertising, promotion and sponsorship; and Raise taxes on tobacco (WHO 2008a).

Actions against tobacco in health care

While smoking is seen as a social issue, it is also a medicalised phenomenon: there are ICD-10 codes for smoking and nicotine addiction. As smoking status is a crucial factor in both primary and secondary prevention as well as the treatment of several diseases, the health care sector has a motive for decreasing smoking prevalence. A systematic approach where detection and treatment of smoking dependence is integrated into the health care system is recommended by WHO (WHO 2008). Utilisation of treatment paths has gained popularity globally in the past few years: the physician can refer their patient to a tobacco clinic, a tobacco nurse, or a support group, for instance (WHO 2017). Clinical treatment guidelines offer tools for the physician in helping the patient to quit smoking (Fiore *et al.* 2008, NICE 2008, Duodecim 2012).

Actions against tobacco in Finland

The state of Finland has taken strong measures to decrease smoking prevalence: the first tobacco law is from 1976 and has been regularly updated since, and taxation of tobacco products has been getting stricter over the years (Finlex 2016, Linnakangas & Juanto 2016). Indeed, when member states of the European Union were assessed according to their actions against tobacco as recommended by the

World Bank, Finland was on 6th place out of 35 states (Joossens & Raw 2017). However, in the subcategory measuring treatment of smoking dependence, Finland scored only 5 points out of 10. In other words, smoking is strongly discouraged by taxation and prohibitions, but there is room for improvement in supporting and helping people who wish to quit smoking.

1.2 Smoking and cardiovascular disease

Most premature deaths in developed countries are due to cardiovascular disease, which is the most common cause of death also in Finland (Statistics Finland n.d.). Smoking is the main completely preventable cause of cardiovascular disease as some 10% of cardiovascular deaths are attributable to smoking, and cardiovascular events are the most common type of smoking-attributable deaths (Rigotti & Clair 2013, GBD 2015 Tobacco collaborators *et al.* 2017). Up to 80% of heart disease, stroke, and type 2 diabetes could be prevented by eliminating smoking and other adverse lifestyle habits (Mendis *et al.* 2011). Current European guidelines acknowledge this, and highlight the importance of smoking cessation in prevention of cardiovascular disease (Piepoli *et al.* 2016). The current status of both primary and secondary prevention of cardiovascular disease in Europe has been investigated in the EUROASPIRE study since 1995 (Kotseva *et al.* 2009, Kotseva *et al.* 2016). According to the EUROASPIRE reports, smoking cessation support in cardiovascular prevention is underutilised. For instance, nearly half of European smokers who experience a serious coronary event – for which smoking is a risk factor – continue to smoke six months after the event (Kotseva *et al.* 2016). Successful smoking cessation after a myocardial infarction, for instance, would reduce coronary mortality by 46% (Wilson *et al.* 2000). The risk of cardiovascular disease reverts to the same level with never-smokers ten years after quitting (Honjo *et al.* 2010).

1.2.1 Sex, smoking, and cardiovascular disease

Smoking elevates the risk of cardiovascular deaths more for women than for men (Rigotti & Clair 2013). For instance, the hazard ratio of death from stroke is 3.2 (99% CI 2.2–4.7) for female smokers vs. female never-smokers, while the hazard ratio is 1.7 (99% CI 1.0–2.8) for smoking vs. never-smoking men (Jha *et al.* 2013). It remains unclear to which extent the observed differences between men and women in smoking-associated cardiovascular risk are due to unadjusted, gender-

skewed associations of smoking and other cardiovascular risk behaviour, to which extent to different smoking habits, and to which extent to possible differences in biological sensitivity to some of the compounds in cigarette smoke (Jha *et al.* 2006, Jha *et al.* 2013, Rigotti & Clair 2013, Peters *et al.* 2014).

1.2.2 Mechanisms of smoking-induced cardiovascular events

Smoking has been found to both have an independent effect on cardiovascular risk, and to elevate some of the other risk factors present in cardiovascular risk assessment algorithms: it increases the risk of type 2 diabetes and has an adverse effect on blood lipid and lipoprotein profile, and possibly elevates also blood pressure (Rigotti & Clair 2013). Of these two categories, the independent effect is considered more significant than that mediated by an increase in other risk factors (Rigotti & Clair 2013). The exact mechanisms underlying cigarette smoke-induced atherosclerosis, arterial thrombosis, and their clinical manifestations as cardiovascular disease are only partially understood. The main compounds behind the increase in cardiovascular event risk are reactive oxygen species, carbon monoxide, and nicotine, alongside with other inflammatory and cytotoxic compounds of cigarette smoke (Rigotti & Clair 2013). Some of the key mechanisms by which these compounds induce cardiovascular events are described below.

Reactive oxygen species

Reactive oxygen species induce cardiac remodeling, which can be seen as left ventricular hypertrophy and atrial fibrosis, increasing the risk of stroke. Oxidative stress caused by systemic oxygen free radicals causes systemic and local inflammation, which is seen as an elevation in levels of C-reactive protein and peripheral leucocytes, in addition to other proinflammatory cytokines, which promote arterial thrombosis (Libby *et al.* 2002, Varela-Carver *et al.* 2010). Proinflammatory and cytotoxic cytokines can also weaken vasomotor functions, which results in thickening of the arterial wall and intima media, reduced ability to expand and contract vessels, as well as increased arterial stenosis (Libby *et al.* 2002, Puranik & Celermajer 2003). Reactive oxygen species also increase levels of plasma fibrinogen, leading to enhanced coagulability (Rigotti & Clair 2013).

Carbon monoxide

Carbon monoxide found in cigarette smoke decreases oxygen availability, leading to a decline in myocardial oxygen supply, and ultimately myocardial ischemia (Benowitz 2003). The body can compensate for the decrease in oxygen availability by increasing red blood cell mass, which in turn enhances coagulability (Benowitz 2003). Another consequence of reduced oxygen availability is an increase in levels of proinflammatory and cytotoxic cytokines (Puranik & Celermajer 2003).

Nicotine

Nicotine stimulates the release of adrenal medulla hormones, which modifies cardiac output by increasing heart rate, ventricular contractility, and blood pressure. These changes may lead to cardiac ischemia or stroke (Benowitz 2003, Csordas & Bernhard 2013, Cohen & Townsend 2009, McManus & Liebeskind 2016).

1.2.3 Smoking and other cardiovascular risk factors

Clinical cardiovascular risk assessment tools typically include smoking status, body mass index (BMI, kg/m²), high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides, blood pressure, and type 2 diabetes status (SCORE project group 2003, D'Agostino *et al.* 2008, Vartiainen *et al.* 2016).

Smoking, BMI, and visceral adipose tissue

On average, smokers have a lower BMI than never-smokers or former smokers (Lahti-Koski *et al.* 2002, Harris *et al.* 2016). This is caused by several mechanisms that can be divided to a) behavioural factors and b) nicotine-mediated changes in appetite and lipometabolism (Harris *et al.* 2016). However, a slightly lower BMI doesn't necessarily protect smokers from metabolic disease: based on a review of cross-sectional studies, smokers are in fact likely to have more visceral adipose tissue (Harris *et al.* 2016). A Mendelian randomisation meta-analysis on nearly 150 000 European participants arrived at a similar conclusion: smoking was associated with an increase in waist circumference and waist-to-hip ratio (Morris *et al.* 2015). A Finnish population-based study on 5 833 subjects studied the association of smoking status and BMI on visceral fat accumulation (Tuovinen *et al.* 2016). Among overweight and obese women, heavy smokers or ex-smokers had

bigger waist circumferences and were thus more susceptible for diabetes and cardiovascular disease than their never-smoking peers (Tuovinen *et al.* 2016).

Based on a meta-analysis of smoking cessation trials, quitting is often followed by an increase in weight; most of the increase happens within the first year after quitting with a mean weight gain of 4–5 kg; the corresponding increase in BMI in the five years following quitting is 1.14 kg/m² (Aubin *et al.* 2012, Harris *et al.* 2016). Weight gain is similar regardless of type of pharmacotherapy used to support cessation (Aubin *et al.* 2012). The accumulation of visceral adipose tissue caused by smoking seems to be rather slowly reversible: in a cross-sectional study on 5 697 Korean males, the increase in metabolic disease markers, such as visceral adipose tissue, plasma triglyceride levels, and hyperglycaemia reverted to the level of never-smokers in approximately 15 years after quitting (Matsushita *et al.* 2011). Another study looked at clinical endpoints instead of disease markers, linking data of 52 819 American participants of the National Health Interview Survey with the National Death Index (Siahpush *et al.* 2014). The study concluded that overweight or even obese ex-smokers had a lower risk of cardiovascular or other smoking-related diseases than normal-weight smokers (Siahpush *et al.* 2014).

Smoking and blood lipids & lipoproteins

A meta-analysis on the association of smoking and blood lipids & lipoproteins utilised data from large cohort studies from 1966 to 1987 that examined the effects of smoking and other modifiable risk factors on cardiovascular disease (Craig *et al.* 1989). The analysis concluded that smokers, on average, have higher values of serum LDL (10.4%), total cholesterol (3.0%), and triglycerides (9.1%), alongside with lower HDL values (5.7%) than non-smokers. The effect sizes were dose-dependent. Results from more recent studies in different settings are in line with these findings (Cullen *et al.* 1998, Gosset *et al.* 2009, Slagter *et al.* 2013, Rampure *et al.* 2016, Zhao *et al.* 2017).

In a German cross-sectional study with 30 908 participants with a mean age of 41 for men and 37 for women, LDL, total cholesterol, and triglycerides were all significantly increased in smokers vs. non-smokers: the increase in LDL was 1.4% for male and 2.0% for female smokers; the increase in total cholesterol was 0.9% for male and 5.5% for female smokers; and the increase in triglycerides was 15% for male and 12% for female smokers. Conversely, HDL was lower for smokers: by 6.4% for male and 6.7% for female smokers (Cullen *et al.* 1998).

The details of the reversibility of smoking-associated increases in blood lipid and lipoprotein values is unclear; the most consistent evidence is for HDL, which has been shown to significantly and quickly increase after smoking cessation (Maeda *et al.* 2003, Forey *et al.* 2013). These were also the conclusions of a review on smoking cessation studies that assessed changes in cholesterol and triglycerides after quitting (Campbell *et al.* 2008).

Smoking, blood pressure and heart rate

Smoking causes a transient increase in blood pressure and heart rate, during which the likelihood of stroke is elevated (Cohen & Townsend 2009, McManus & Liebeskind 2016). However, the long-term effects of smoking on blood pressure remain unclear: in some studies there have been no notable difference in blood pressure according to smoking status; in some studies smokers have had slightly higher, in some studies slightly lower blood pressure than never-smokers (Rigotti & Clair 2013). An English cross-sectional study on 33 860 participants concluded that in the inspected cohort, any independent chronic effect of smoking on blood pressure was small, and dependent of sex, age, and alcohol intake (Primatesta *et al.* 2001). In an equally sized German set of cohorts, smokers of both sexes had a 2% lower blood pressure compared with their non-smoking peers (Cullen *et al.* 1998). More recently, the associations of smoking status with blood pressure and resting heart rate were studied in a Mendelian randomisation meta-analysis of 23 population-based studies (Linneberg *et al.* 2016). The results suggested a clearly elevated heart rate among smokers, amplified by heaviness of smoking: those who smoked 20 cigarettes a day had a 7 beats/minute higher heart rate than never-smokers. Such an association was not found for blood pressure (Linneberg *et al.* 2016).

Smoking and type 2 diabetes

A meta-analysis of cohort studies on smoking and risk of type 2 diabetes concludes that the two are heavily associated (Willi *et al.* 2007). The association is dose-dependent: in the meta-analysis risk ratio was 1.61 (95% CI 1.43-1.80) for heavy smokers vs. never-smokers, and 1.29 (95% CI, 1.13-1.48) for lighter smokers vs. never-smokers. Also former smokers are at an increased risk of diabetes (RR 1.23; 95% CI 1.14-1.33). The reasons for this phenomenon are not entirely clear, but it is known that nicotine use leads to both insulin resistance and decreased insulin

secretion by several mechanisms, at least some of which are reversible with smoking cessation (Harris *et al.* 2016).

1.3 The costs of smoking to society

1.3.1 The costs of smoking are distributed to many payers

Annual costs of treating serious smoking-attributable diseases have been estimated to be 40.87 billion euros in Europe, and approximately 353 billion euros globally (Effertz & Mann 2013, Goodchild *et al.* 2017). Besides treatment of smoking-attributable disease, smoking causes also indirect costs, for instance in the form of absence from work and loss of productivity. These indirect costs raise the total global annual cost of smoking to approximately 1 202 billion euros (Goodchild *et al.* 2017). There may be indirect costs also for the smoker, as smoking seems to be negatively related to one's long-term labour market outcomes (Böckerman *et al.* 2014).

In a welfare state such as Finland, the costs of smoking are distributed to many payers. The costs of smoking can be divided to primary and secondary health care costs, supported living services and other forms of social care for the seriously ill, medicinal costs, sickness allowances, and other transfer payments (Seppälä & Pekurinen 2014). Based on a Finnish estimate, direct health care costs account to approximately 40% of the total costs of smoking to a welfare state (Vähänen 2015).

1.3.2 Smoking and primary health care utilisation

The treatment of serious smoking-related illnesses or their risk factors is usually started in primary health care in middle-age, and then continued in secondary care in late working age or after retirement if the risk actualises into a serious event. Also, the complications of these disorders are again treated in primary care after patients are discharged from the corresponding secondary care unit. Furthermore, besides serious smoking illnesses, smokers have an increased risk of also less immediately life-threatening illnesses – such as respiratory infections, depression, and musculoskeletal problems – which are more commonly treated in primary health care. The onset of such illnesses is usually earlier in life than for serious smoking-related illnesses. In terms of public economy, these seemingly minor health issues are highly relevant, as they are the most common reasons for absence

from work in many developed countries, including Finland (European Foundation for the Improvement of Living and Working Conditions 2010). Smoking makes the patient also more susceptible to post-operative complications, and it slows down the healing of wounds, which add up to the burden of smoking on primary health care (Silverstein 1992).

Primary health care in Finland

In Finland, primary health care consists of treatment given in community health centres, occupational health care clinics, or private practices – in other words, outside hospitals. Secondary care is currently organised by selected hospital districts, while primary care is organised by municipalities. In 2017, Finland is on the verge of a social and health care reform which will most likely result in both primary and secondary health care being organised by counties. One aim of the reform is to simplify the current multi-payer model so that most of the costs of both primary and secondary health care, as well as social and medicinal costs will be covered by the state (Ministry of Social Affairs and Health n.d.).

Smoking status, primary health care utilisation and costs

The smoking-attributable fraction of primary health care utilisation of a person is difficult to estimate: Smoking elevates the risk of several health issues that are treated in primary health care, but primary health care is also involved in the treatment of many life-threatening smoking diseases in the form of preventative work, follow-ups and treatment of complications. As a result, in order to study the relationship of smoking status and primary health care utilisation, one needs to have person-specific data on smoking status and actual visits to primary health care. While time-stamped information about visits to health care professionals exists in many countries in the form of treatment registers or insurance claim databases, reliable information about smoking status isn't readily available. Even though there is an ICD-10 code for tobacco use and nicotine dependence, smoking status is rarely recorded on patient records, let alone updated. One way to overcome this challenge is to utilise a smaller sample of people whose smoking status can be mapped by a questionnaire or biomonitoring.

In a study conducted in Japan on a cohort of 43 408 people aged 40–79, after adjustment for age, physical functioning, alcohol consumption, BMI, and average time spent walking, there were no significant differences in outpatient care costs

according to smoking status (Izumi *et al.* 2001). Interestingly, in a German study on 3 071 adults aged 32–81 current smokers had a lower odds ratio (0.69) for visits to the physician than never-smokers after adjustments for age, sex, education, alcohol consumption and physical activity (Wacker *et al.* 2013). On the other hand, in both studies smokers had more hospital stays and their total health care costs were higher than those of never-smokers (Izumi *et al.* 2001, Wacker *et al.* 2013). An Australian group hypothesised that smokers could have a higher threshold for seeking preventative care, something that could lead to higher secondary care costs in later life (Jorm *et al.* 2012). In the study population of 254 382 people aged 45 and over, current smokers were slightly less likely to use primary care services, especially the kind they had to pay for themselves (Jorm *et al.* 2012). The authors had adjusted the results for income, level of education and region of residence, among others, to account for predisposing and access-related differences.

In some studies, also primary health care costs have been higher among smokers. In a cross-sectional study from Spain with some 500 participants aged 45–74, smokers had approximately two more annual visits to a primary health care physician, translating to 28% higher costs (Suárez-Bonel *et al.* 2015). According to the Great Britain General Household Survey, smokers over the age of 16 had a relative risk of 1.18 for general practitioner consultations (Callum *et al.* 2010). A study on some 10 000 working-age Northern Americans showed that the costs for inpatient and ambulatory care were 21% higher for ever-smokers; ambulatory care wasn't reported separately (Sturm 2002).

In studies where only total health care utilisation and its costs have been mapped without analysing primary care separately, the relative share of secondary care costs of elderly smokers with serious smoking-attributable diseases may be great (Sturm 2002, Fishman *et al.* 2003). When only primary care use has been investigated, a wide age distribution may complicate interpretation of the results. Indeed, authors of previous studies have suggested that the effect of age on excess medical costs associated with smoking should be further studied (Izumi *et al.* 2001, Fishman *et al.* 2003).

Former smoking and health care utilisation

Studies that have included former smokers as a separate group in their analyses suggest that former smokers utilise more health care services than never-smokers, and sometimes even more than current smokers (Fishman *et al.* 2003, Callum *et al.* 2010, Jorm *et al.* 2012, Vals *et al.* 2013). This could be partially explained by recent

quitters seeking help for withdrawal symptoms, and there is evidence of respiratory symptoms being more common shortly after quitting, but these symptoms are usually short-lived (Brown *et al.* 1991, Willemse *et al.* 2004). Thus, a more likely explanation for high rates of health care utilisation among former smokers is the fact that sicker smokers are more likely to quit than healthy smokers (Beard *et al.* 2013). In other words, a smoker who frequently meets health care professionals is more likely to receive smoking cessation encouragement and help from health care professionals, and also to be more motivated to quit (Beard *et al.* 2013). The peak in health care utilisation and costs seems to be highest recently after quitting. In a study on 723 middle-aged patients from Washington, the total health care costs of former smokers were twice as high as those for never-smokers and 1.5 times as high as those for current smokers within one year of quitting, after which they sunk below the cost level of smokers – yet permanently remaining higher than those of never-smokers (Fishman *et al.* 2003). These results should be generalised with caution, as the number of subjects in this study was rather low, and every participant had the same health care provider. Also in a much larger Australian study focusing on primary health care use, former smokers used more primary care services than never-smokers, especially if they had quit less than five years ago (Jorm *et al.* 2012). In an Estonian study based on three cross-sectional surveys, past smoking was associated with increased visits to primary health care among men, but not women (Vals *et al.* 2013).

Primary health care's share of costs of smoking

According to European reports from the past decade, the share of smoking-attributable health care costs that falls into primary health care varies from 13% to 27% (Philips & Bloodworth 2009, Callum *et al.* 2010, Vähänen 2015). In these estimates health care costs have consisted of a) primary health care costs, b) secondary health care costs (i.e. hospital admissions), and c) prescription/drug costs. The notable variance between studies is partially explained by differences in age-specific smoking prevalence and unit costs in each setting, but there are notable differences also in methodology (Philips & Bloodworth 2009, Callum *et al.* 2010, Vähänen 2015). Smoking-related health care costs in a population are usually estimated by a disease-based approach, which utilises age- and sex-specific epidemiological information about a) the smoking-attributable factor of selected diseases, b) smoking prevalence, c) size of inspected population, d) and the estimated health care costs of treating one patient with said illness (Sung *et al.*

2011). Especially estimates of the smoking-attributable factors of illnesses can differ greatly. For instance, Vähänen *et al.* used rather conservative estimates, and arrived at a conclusion that primary health care covered 13% of smoking-attributable health care costs. On the other hand, Callum *et al.* and Philips & Bloodworth used survey data on primary health care visits of smokers vs. non-smokers in their model to estimate the excess primary health care use caused by smoking, arriving at a much higher figure.

1.4 Physicians and smoking cessation

1.4.1 Smoking dependence

Smoked tobacco is classified as one of the most addictive commonly used drugs, with an addiction potential comparable to cocaine (Nutt 2007). However, electronic cigarettes and other smokeless nicotine products with high addiction potential are also gaining popularity, making the term tobacco dependence seem somewhat outdated. Nicotine addiction would cover chemical addiction to all nicotine products, but the term leaves out the behavioural components of smoking dependence. Most smokers end up being dependent of smoking, but some develop much stronger chemical addiction to nicotine than others (Laviolette 2004, Korpi *et al.* 2015). The English version of the ICD-10 classification uses the term nicotine dependence, while the Finnish version refers to a dependence syndrome caused by “using tobacco.” It should also be noted that the Finnish language doesn’t differentiate between dependence and addiction. In this thesis, the term smoking dependence is preferred, but other terms are also used if referring specifically to nicotine addiction, for instance.

Biochemical basis of nicotine addiction

A key component of smoking dependence is neurobiological addiction to nicotine (Laviolette 2004, Mustonen 2004, Korpi *et al.* 2015). In the central nervous system, the ventral tegmental area in particular, nicotine binds to nicotinic acetylcholine receptors, resulting in the release of catechol amines, namely dopamine and acetylcholine, activating the mesolimbic dopamine pathway (fig. 2). This is further reinforced by concomitant alcohol use (Adams 2017). Nicotine is also a modulator of serotonin and endogenous opioids. Long-term nicotine use results in an increase

in the amount and affinity of nicotinic receptors and changes in the endogenous opioid system. These changes in gene expression and the neurochemical, neurophysiological, and structural features of various brain cell populations are the root cause of nicotine withdrawal symptoms (Korpi *et al.* 2015). Some people are more susceptible to nicotine addiction than others – this is in part due to differences in the genetic sequence contributing to differences in density, distribution, and subtypes of receptors (Loukola *et al.* 2014, Korpi *et al.* 2015, Cross *et al.* 2017). Some of these differences are age- and sex-specific (Cross *et al.* 2017).

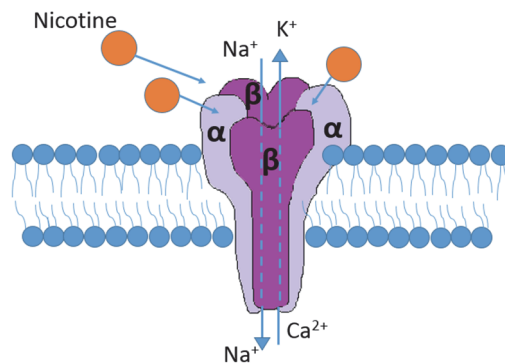


Fig. 2. Nicotine binding to $\alpha 4\beta 2$ nicotinic acetylcholine receptor, opening the ion channel. Image based on International Union of Basic and Clinical Pharmacology.

1.4.2 Health care professionals in smoking cessation

WHO recommends integration of nicotine dependence diagnosis and treatment into the health care system (WHO 2008a). The way nicotine dependence treatment is organised varies from country to country: in some countries there are privately or publicly run smoking cessation clinics; in some countries smoking cessation nurses at community health care centres play a big role; some rely on quitline services (Raw *et al.* 2009). Finland has been shown to have suboptimal availability of smoking cessation services (WHO 2017, Joossens and Raw 2017). Despite a national recommendation to improve organisation of smoking cessation services, in 2012 many health care centres lack even the most simple form of a treatment path: having a point person for smoking cessation (Raw *et al.* 2009, National Institute for Health and Welfare 2013).

Effectiveness of cessation support delivered by health care professionals

According to Cochrane reviews, the likelihood of successful smoking cessation is highest when pharmacotherapy is combined with support from a physician (Stead *et al.* 2015, Stead *et al.* 2016). Even a brief recommendation by the physician to quit increases the likelihood of successful quitting by 66%, and a more intensive discussion further raises the effect (Stead *et al.* 2013). A more structured discussion can also improve the outcome: using motivational interview technique instead of usual care or brief advice seems to yield better results (Lindson-Hawley *et al.* 2015).

Reviews conclude that tobacco interventions by dentists, other dental professionals, and nurses – especially if their main role is in health promotion or smoking cessation – can also help patients quit smoking (Carr & Ebbert 2012, Rice *et al.* 2013). While specialised nurses often play a key part in smoking cessation, some of the most effective smoking cessation aid is not accessible at a nurse's reception, as withdrawal medication is available by prescription only (Cahill *et al.* 2013). Also, a physician is needed for dose adjustments of other medication after smoking cessation: dosing may need to be reduced by up to 50% because of drug interactions, especially CYP1A2 induction caused by components of cigarette smoke (Zevin & Benowitz 1999, Kroon 2007).

Pharmacotherapy for smoking cessation

Several pharmacological methods have proven to improve the chances of quitting (Cahill *et al.* 2013). Over-the-counter nicotine replacement therapy is available in several forms, varying from oral sprays to nicotine patches. The number needed to treat to benefit (NNTB) with nicotine replacement therapy is 23 (95% CI 20–25) according to meta-analysis (Cahill *et al.* 2016). Prescription medication indicated for alleviating nicotine withdrawal symptoms comprises of varenicline and bupropion, which are referred to as withdrawal medication in this thesis. Of these, varenicline acts as both an agonist and an antagonist in the nicotinic acetylcholine receptors, with a NNTB of 11 (95% CI 9–13) according to meta-analysis (Cahill *et al.* 2016). The effects of bupropion are thought to be mediated mainly by metabolic changes of dopamine and noradrenaline. The NNTB for bupropion in smoking cessation is 22 (95% CI 18–28) (Cahill *et al.* 2016). In some countries, such as Finland, also off-label nortriptyline is used for smoking cessation. Use of a low-cost nicotinic receptor partial agonist, cytisine, is common especially in Russia and Eastern Europe (Rigotti 2014, Cahill *et al.* 2016).

1.4.3 Do physicians help their patients with smoking cessation?

Treatment guidelines on smoking cessation state that it is the responsibility of every physician and dentist to discuss their patient's smoking habits at least once a year (Fiore *et al.* 2008, NICE 2008, Duodecim 2012). However, this recommendation doesn't seem to be carried out in practice.

Patient perspective

In a European study on secondary cardiovascular prevention practices, 89% of smokers who had experienced a serious coronary event reported having received verbal recommendation to quit after the event, but only 19% reported being advised to attend a smoking cessation clinic or to use a pharmacological quitting aid (Kotseva *et al.* 2016). In the national adult tobacco survey from 2010, only 51% of American smokers reported that a physician had advised them to quit within the past year (Danesh *et al.* 2014). The number was a somewhat lower 39% in a Finnish study from 2014 (Helldán & Helakorpi 2015).

Physician's perspective

When physicians' activity in helping their patients quit is assessed, a significant discrepancy becomes apparent between the patients' and the physicians' perspective: depending on the study, 85–95% of physicians report consistently asking whether their patient smokes, and recommending quitting to them (Association of American Medical Colleges 2007, Pipe *et al.* 2009). When physicians have been asked how often they deliver more practical help, such as helping the patient make a personal quitting plan, referring the patient to a smoking cessation professional, prescribing withdrawal medication, or recommending nicotine replacement therapy, activity rates drop, and are more in line with those reported by patients (Association of American Medical Colleges 2007, Pipe *et al.* 2009, Stead *et al.* 2009, Schauer *et al.* 2016). This phenomenon was visible also in a systematic review of smoking cessation surveys directed to physicians from 16 countries (Bartsch *et al.* 2016). The review categorised activities according to the 5A strategy of smoking cessation counselling: "Ask" (ask all patients about tobacco use), "Advise" (advise all tobacco users to quit), "Assess" (assess the willingness to quit), "Assist" (assist with quitting), and "Arrange" (arrange follow-up) (Fiore *et al.* 2008). According to the review, 65% of physicians reported compliance with

the “Ask” strategy, and 63% with “Advise” (Bartsch *et al.* 2016). As in previous studies, activity rates were lower for the more practical categories: 36% were compliant with the “Assess” strategy, 44% with “Assist”, and 22% with “Arrange” (Bartsch *et al.* 2016).

1.4.4 Factors affecting physicians’ activity in offering smoking cessation help

Who gives and who receives smoking cessation help?

Judging on self-reported data by both physicians and patients, there are several factors affecting the probability of receiving help with smoking cessation. Patient characteristics have been shown to matter: heavy smokers and those who already present smoking-related symptoms are more likely to receive help (Stead *et al.* 2009, Bock *et al.* 2012). The physician’s own characteristics also matter: physicians who are smokers, or those who believe discussing smoking would be awkward or harmful for the patient–physician relationship are less likely to offer help (Lancaster & Stead 2008, Stead *et al.* 2009, Pipe *et al.* 2009).

Attitudes on the role of the physician in helping their patients quit seem to have changed greatly in the past two decades. For instance, the percentage of Norwegian general practitioners who felt it was embarrassing to ask people about their smoking dropped by nearly 50% within a few years at the turn of the millennium, while the belief that assisting patients with smoking cessation is a part of the physician’s role gained popularity (Stead *et al.* 2009). In 1999, one third of Finnish general practitioners felt that physicians don’t have the right to take the initiative to inform patients about the positive or negative effects of their lifestyle, and 43% felt uncomfortable informing patients about the potential risks of smoking (Helgason & Lund 2002). One fifth felt that helping people with smoking cessation wasn’t part of their job (Helgason & Lund 2002). Smoking cessation attitudes of Finnish physicians were mapped again in 2006 as a part of the Lääkäri ja tupakka 2006 study, but the results haven’t been published (Jousilahti *et al.* 2007, Hokkinen *et al.* 2009). The great country-to-county variation in attitudes and treatment practices on smoking and smoking cessation highlight the role of local research as a means to improve the quality of smoking cessation services (Stead *et al.* 2009).

Self-reported restrictions for helping patients quit smoking

One of the most commonly reported restrictions for helping patients quit smoking is inadequate tools. This is presented as insufficient resources and organisational structures such as treatment paths, and limited education and training for physicians on the subject (Association of American Medical Colleges 2007, Stead *et al.* 2009). A meta-analysis on the effectiveness of smoking cessation training showed that training programmes help health care professionals both identify smokers and increase the number of patients who successfully quit smoking (Carson *et al.* 2012).

While smoking cessation aid is one of the most cost-effective actions a physician can take, physicians still find lack of time a main restriction for providing smoking cessation help. Perceived lack of time seems to play a bigger part in Europe than in the United States of America (Association of American Medical Colleges 2007, Stead *et al.* 2009). Conversely, the significance of reimbursement of time spent on smoking cessation aid is lower in Europe, and there is substantial variation even within the European Union, but it should be noted that the effectiveness of financial incentive models for improving quality of primary health care hasn't been well-studied (Association of American Medical Colleges 2007, Stead *et al.* 2009, Scott *et al.* 2011). International comparisons on smoking cessation should be made with caution, as phrasing of questions differs between studies, as do the characteristics of patients the targeted physicians treat (Association of American Medical Colleges 2007, Stead *et al.* 2009, Bock *et al.* 2012).

Smoking in the medical profession

The personal smoking status and history of the physician can affect their smoking cessation practices: It has been shown that physicians who smoke are less active in helping their patients quit (Lancaster & Stead 2008). On the other hand, if a physician has previously smoked, they can be less disillusioned about the issue, not exaggerating the difficulty of quitting as they have first-hand experience of successful smoking cessation (Alakoski *et al.* 2006).

In many developed countries such as the United States of America, Canada, United Kingdom, Australia, and most Scandinavian countries, smoking in the medical profession has declined much faster than in the corresponding general population, reaching a prevalence of < 10% by the mid 1990's (Smith & Leggat 2007). In Southern and Eastern Europe smoking prevalence within the medical

profession is still high. The most recent results published in English are from the early 2000's, when smoking prevalence in countries such as Greece, Italy, Estonia, Bosnia & Herzegovina, and France was 20–40% among local physicians (Smith & Leggat 2007). As for developing countries such as China and India, smoking in the medical profession seems to be even more common. Interestingly, in these countries, smoking is more common among younger than older physicians, whereas the opposite is true in developed countries (Smith & Leggat 2007). Differences in smoking prevalence according to the physician's sex were generally in line with genderisation of smoking in the corresponding general populations (WHO n.d.).

Smoking in the Finnish medical profession

Considering the size of the medical profession in a country, some of the largest studies on physicians and smoking have been conducted in Finland (Barengo *et al.* 2003, Smith & Leggat 2007, Hokkinen *et al.* 2009). Smoking habits of Finnish physicians have been mapped since smoking became a serious medical theme in the 1960's in studies independent of each other. Since 2001, the studies have included questions on smoking cessation related attitudes and practices (Barengo *et al.* 2003). The changes in physicians' smoking habits between the 1970's and the 2000's have been similar to those in the general working-age population with approximately similar level of education, but the baseline prevalence was lower for physicians (fig. 3) (Hokkinen *et al.* 2009, Helakorpi *et al.* 2010).

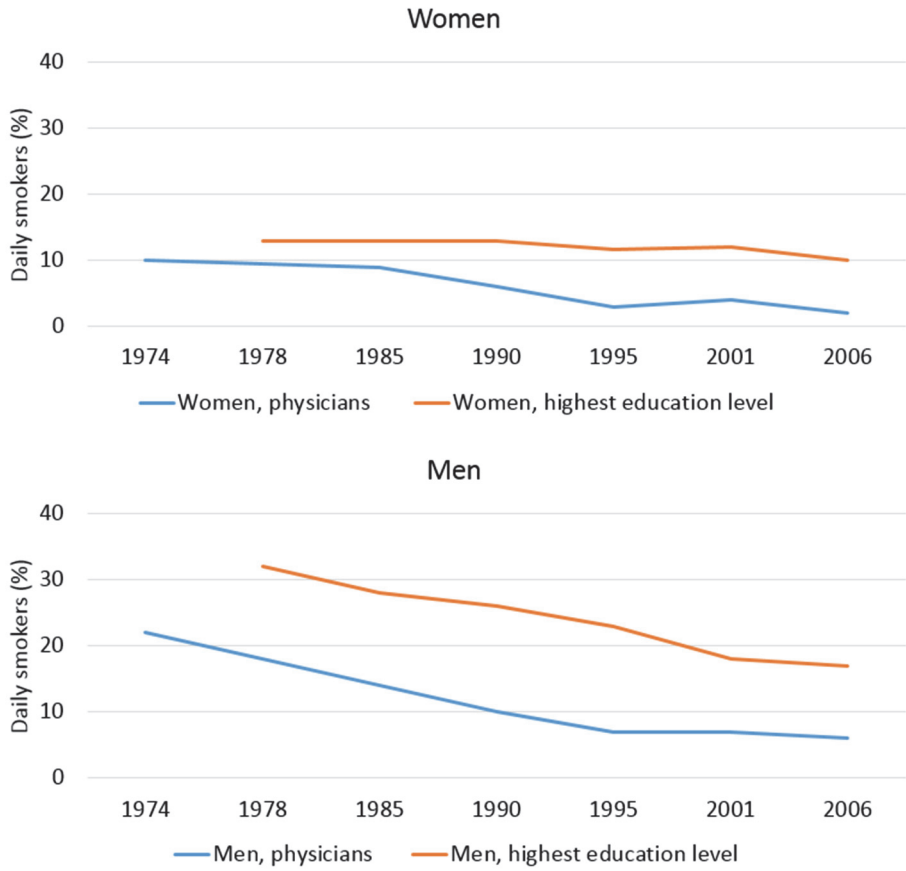


Fig. 3. Smoking prevalence over time in the Finnish medical profession and the the general 25–64 year-old population with the highest education (13+ years) (Hokkinen *et al.* 2009, Helakorpi *et al.* 2010).

2 Aims

Smoking is associated with multimorbidity leading to increased use of health care services (Fiore *et al.* 2008, Taylor *et al.* 2010, Suárez-Bonel *et al.* 2015, Vähänen 2015, Goodchild *et al.* 2017). Physicians play a key role in recognising these high-risk patients and helping them decrease their morbidity and premature mortality by providing smoking cessation aid (Fiore *et al.* 2008, Piepoli *et al.* 2016, Stead *et al.* 2016). The aim of this thesis was to approach this theme by providing information about the middle-aged Finnish smoker in health care: how much do they utilise primary health care services (I), what is their clinical profile in terms of cardiovascular risk factors (II), and how Finnish physicians help their patients with quitting (III and IV).

Smoking and primary health care utilisation at age 46 (I)

The main focus of previous research and discussion on the health economics of smoking has been on serious tobacco illnesses such as cancer and cardiovascular events, usually treated in older age mainly in a hospital setting (Effertz & Mann 2013, Goodchild *et al.* 2017). However, smokers are also at an increased risk of illnesses with an earlier age of onset. These less dramatic illnesses, such as infection proneness and musculoskeletal problems are treated mainly in a primary care setting. Also, the prevention of serious smoking-related events is often initiated in primary health care in working age in the form of treating cardiovascular risk factors. Previous studies that have looked into smoking and primary health care utilisation have typically had a wide age distribution, and they have been conducted in societies with health care systems different from that in Finland, and with bigger income differences (Izumi *et al.* 2001, Sturm 2002, Fishman *et al.* 2003, Callum *et al.* 2010, Jorm *et al.* 2012, Vals *et al.* 2013, Suárez-Bonel *et al.* 2015, World Bank n.d.). The aim of this study was to inspect whether the burden of smoking on the human body could be reflected in primary health care utilisation already at age 46 in the Northern Finland Birth Cohort of 1966 (NFBC 66).

Smoking and cardiovascular risk factors at age 46 (II)

Smoking is above all an independent risk factor for cardiovascular disease, but it also affects other cardiovascular risk factors (Rigotti & Clair 2013). The effect of smoking on risk factors such as serum lipids and lipoproteins, and type 2 diabetes,

as well as the reversibility of these changes has been studied before, but the results remain non-consistent especially for cholesterol (Craig *et al.* 1989, Green & Harari 1995, Maeda *et al.* 2003, Bakhru & Erlinger 2005, Campbell *et al.* 2008). This may partially be due to the wide age distributions and thus different lengths of exposure to cigarette smoke in previous studies, as many of the adverse effects of smoking have been proven to be dose-dependent (Craig *et al.* 1989, Willi 2007, Spijkerman *et al.* 2014). The aim of this study was to inspect cardiovascular risk factors at age 31 and 46 in the NFBC 66 according to smoking status and history.

Finnish physicians and smoking cessation (III and IV)

Smoking cessation is one of the most effective means of both primary and secondary prevention of cardiovascular disease and many other illnesses (Bullen 2008, Mendis *et al.* 2011, Piepoli *et al.* 2016). Nearly one fifth of the Finnish adult population are smokers, and the majority of them wants to quit (Helldán & Helakorpi 2015, Murto *et al.* 2010–2017). The help of a physician greatly increases the likelihood of successful smoking cessation (Stead *et al.* 2015, Stead *et al.* 2016). However, only 39% of Finnish smokers report having discussed smoking with their physician within the past year (Helldán & Helakorpi 2015). Also, while Finland is a model country for reducing smoking by heavy taxation according to WHO standards, there is room for improvement in smoking cessation services (WHO 2017, Joossens & Raw 2017). A physician's perspective is needed to understand this discrepancy. Such information needs to be up-to-date and local as previous studies have shown that smoking-related attitudes, measures taken to help patients with quitting, as well restrictions for providing smoking cessation help vary greatly depending on where and when the study was conducted (Association of American Medical Colleges 2007, Pipe *et al.* 2009, Stead *et al.* 2009, Bartsch *et al.* 2016, Schauer *et al.* 2016). The aim of this study was to investigate:

- a) How Finnish physicians feel about smoking and smoking cessation related issues
- b) What measures Finnish physicians take to help their patients quit smoking
- c) Common features of Finnish physicians active in smoking cessation and
- d) What is restricting Finnish physicians from being more active in helping their patients quit smoking.

3 Methods

3.1 Cohort study on smoking, primary health care utilisation, and cardiovascular risk factors (I, II)

Primary health care utilisation and costs (I) and cardiovascular risk factors (II) according to smoking status was investigated in a cross-sectional study with the Northern Finland Birth Cohort of 1966 at age 46. Self-reported data on smoking status from the 46-year follow-up, alongside with self-reported data on primary health care utilisation from the year preceding the 46-year follow-up was utilised. Cardiovascular risk factors were measured at the 46-year clinical health inspection. Previously unpublished results on cardiovascular risk factors at age 31 according to smoking status are based on the 31-year clinical health inspection and self-reported smoking status at age 31. The sections of the health questionnaire that were utilised in this study are presented in Appendices A (smoking status) and B (health care utilisation).

The Northern Finland Birth Cohort of 1966 (NFBC 66)

The NFBC 66 comprised originally 96% of the live-born children in the two northernmost provinces of Finland with an expected date of birth in 1966 ($n = 12\ 058$) (Rantakallio 1988). Members of the birth cohort have been followed up by both questionnaires and clinical examinations since before their birth. The latest data collection took place in 2012, when members of the cohort were 46 years old. The Ethical Committee of the Northern Ostrobothnia Hospital District has approved the Northern Finland Birth Cohort study (§94/2011), which was performed according to the 1983 Declaration of Helsinki. More information about the project and the 31- and 46-year-old data collections, including the research questionnaires can be found from the project site (<http://www oulu.fi/nfbc/node/19663>).

3.1.1 Smoking status and primary health care utilisation (I)

Primary health care utilisation was assessed for sub-groups based on smoking status: current smokers, ex-smokers, and never-smokers (appendix A and B, fig. 4). Primary health care was defined as services provided by the community health centre, occupational health care, or a private practice. Self-reported primary health care use during the year preceding the 46-year-old check-up was divided to visits to a) the physician regardless of speciality, b) the dentist, c) mental health professionals (including psychiatrists and psychologists in an outpatient setting), and d) other primary health care professionals (such as nurses and oral hygienists). Information on smoking status and primary health care utilisation was available for 4 997 participants.

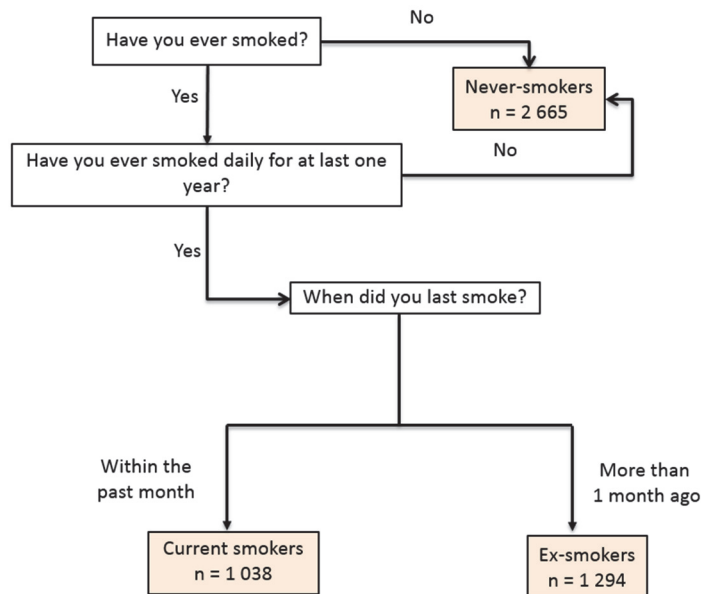


Fig. 4. Sub-groups according to smoking behaviour in study I.

Calculation of primary health care costs

A mean cost for each of the four categories of primary health care was calculated by using the standard unit cost report by the National Institute for Health and Welfare (Kapiainen *et al.* 2014). Annual health care costs were calculated by multiplying the mean cost for each service category with the self-reported number of visits. Costs are reported as mean annual costs (EUR/person) for each sub-group.

Statistical methods

The unadjusted mean annual primary health care utilisation was calculated and analysed for current smokers, ex-smokers, and never-smokers. The Kruskal–Wallis test was used and 95% confidence intervals were calculated (Kruskal & Wallis 1952). The Mann–Whitney U test was used in bivariate analyses between groups with different smoking status, i.e. never-smokers vs. ex-smokers and never-smokers vs. current smokers (Mann & Whitney 1947). To assess the impact of smoking status, the negative binomial hurdle model was applied for health care utilisation and its costs (R Documentation n.d.). Utilisation of mental health care services and its costs were analysed by using a zero-inflated negative binomial model (Greene 1994). The zero-inflated negative binomial model or the negative binomial hurdle models are the recommended models for data that contains an excessive number of zeros. Akaike’s information criterion (AIC) and Vuong test were used to identify the best model (Akaike 1973, Vuong 1989). All analyses were conducted separately for men and women. The Mann–Whitney U test with continuity correction was used when analysing the differences in primary health care utilisation between men and women. To account for possible confounding factors in need and likeliness to seek primary health care services, the risk ratios for primary health care use for never-smokers vs. current smokers, and never-smokers vs. ex-smokers were adjusted for BMI alone, and also for BMI together with education. A p-value of less than 0.05 was considered statistically significant. The analyses were performed using the open-source software package R, version 3.1.2 (<https://cran.r-project.org/web/packages>).

3.1.2 Smoking status and cardiovascular risk factors (II)

Cardiovascular risk factors were compared between sub-groups based on smoking status mapped at the 46-year follow-up: current smokers, recent quitters, former smokers, and never-smokers (II, fig. 5). The investigated risk factors were body mass index (BMI), waist circumference (cm), hip circumference (cm), waist-to-hip ratio (WHR), total cholesterol, HDL, LDL, triglycerides, systolic blood pressure (BP), diastolic blood pressure, use of antihypertensive medication, use of lipid-profile lowering medication, and diagnosed type 2 diabetes. To estimate the clinical significance of possible differences in risk factors between the sub-groups, the ten-year risk of a cardiovascular event (Framingham algorithm) and cardiovascular death (SCORE algorithm) was also calculated as a mean for each sub-group. Information on smoking status and clinical risk factors was available for 5 974 participants.

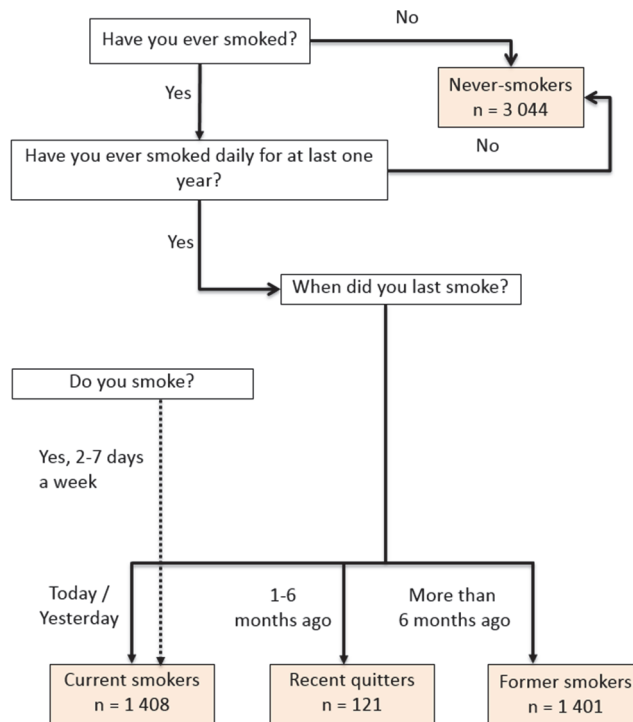


Fig. 5. Sub-groups according to smoking behaviour in study II, based on self-reported answers at 46-year follow-up.

Data collection

During the clinical examinations at the 31-year and 46-year follow-ups, the participants gave blood samples and underwent physical examinations, anthropometry and blood pressure determination performed by a trained study nurse or physician. Information on smoking history and status, diagnosed type 2 diabetes, and use of antihypertensive and lipid-profile lowering medication was acquired by a questionnaire (<http://www.oulu.fi/nfbc/node/19663>).

Physical examinations

Weight and height, as well as waist and hip circumference, were measured with the participants wearing light underwear. Body height and weight were measured to an accuracy of 0.1 cm and 0.1 kg, respectively. Based on these measurements, BMI was calculated. If clinical information on measured BMI was missing, the BMI derived from self-reported height and weight as marked on the questionnaire was used.

The waist-to-hip ratio (WHR) was also calculated. Systolic and diastolic blood pressure was measured on the right arm of the seated participants using an automated oscillometric blood pressure device (Omron Digital Automatic Blood Pressure Monitor Model M10-IT) and an appropriately sized cuff. The mean of two lowest values out of three measurements was recorded as blood pressure. Serum total cholesterol, HDL, LDL, and triglycerides were determined from fasting samples. All plasma samples were analysed in a University Hospital of Oulu laboratory according to a standardised protocol.

Statistical methods

Distributions of continuous variables are expressed as means \pm standard deviation (SD), and categorical variables as numbers and percentage of proportions. Log transformation was used to normalise the skewness of the distributions. The χ^2 test was used for cross tabulation of class variables, and analysis of variance (ANOVA) or analysis of covariance (ANCOVA) were used to study the association between smoking status and continuous cardiovascular risk factors (Pearson 1900, Keppel 1991). Logistic regression analysis was used to examine the association between smoking status and categorical cardiovascular risk factors. Post-hoc analyses between the sub-groups were performed using multiple-comparison Dunnett's test,

and current smokers were used as control group (Dunnett 1955). All analyses were performed separately for men and women. BMI and the use of antihypertensive medication or lipid-profile lowering medication, as appropriate, were controlled in multivariate analysis. A p-value of less than 0.05 was considered statistically significant. Statistical analyses were conducted using the open-source software package R, version 3.1.0 (<https://cran.r-project.org/web/packages>).

3.1.3 Changes in cardiovascular risk factors between ages 31 and 46 according to smoking history

An additional analysis on changes in cardiovascular risk factors between ages 31 and 46 according to smoking history was performed. Self-reported data on smoking and clinical data on cardiovascular risk factors from both 31- and 46-year follow-ups were utilised (fig. 6).

The sub-groups analysed were 1) never-smokers, 2) those who had smoked at some point but quit before the 31-year follow-up, 3) those who had smoked at 31 but quit before the 46-year follow-up, and 4) those who had smoked regularly, nearly daily for at least a year at both 31- and 46-year follow-ups, i.e. long-time smokers. Once missing clinical data on BMI was supplemented by using the BMI marked on the questionnaires, and new or relapsed smokers were excluded from the analyses, 3 376 people were left eligible for analysis. Changes in the following risk factors were calculated for the sub-groups: total cholesterol, HDL, LDL, triglycerides, systolic blood pressure, and diastolic blood pressure.

Statistical methods

The independent-sample t-test was used to test changes in risk factors between the 31- and 46-year follow ups (O'Mahony 1986). Analysis of covariance (ANCOVA) was used to examine the association between belonging to one of these sub-groups and size of changes in cardiovascular risk factors between the 31- and 46-year follow-ups (Keppel 1991). Unadjusted results are presented. A p-value of less than 0.05 was considered statistically significant. Statistical analyses were conducted using the open-source software package R, version 3.1.0 (<https://cran.r-project.org/web/packages>).

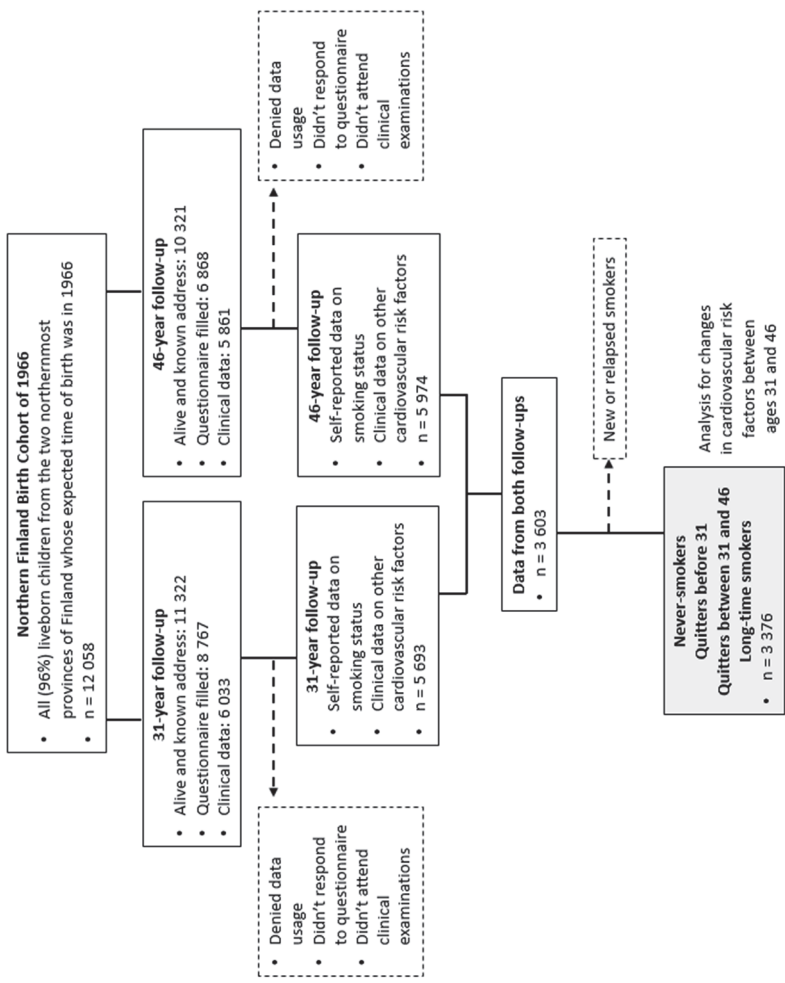


Fig. 6. Sample flow chart for analysis on changes in cardiovascular risk factors between ages 31 and 46.

3.2 Survey on Finnish physicians and smoking cessation (III and IV)

Smoking cessation related attitudes, experiences and practices of Finnish physicians were mapped in the Finnish Physicians and Tobacco 2012 study (III). A link to an electronic survey was sent to 7 800 physicians from fields most relevant to smoking cessation: general practice, occupational health care, obstetrics and gynecology, surgery, respiratory diseases and allergology, internal medicine and cardiology, psychiatry, and oncology. Out of the targeted physicians, 1 141 physicians responded to the survey (response rate 15%). This corresponds to approximately 5 % of the entire Finnish medical profession, and 8% of specialised physicians (The Finnish Medical Association n.d.). While specialists were targeted, also some general practitioners responded to the survey (fig. 7). Response rates in this study and previous studies on Finnish physicians and smoking cessation in proportion to the size of the medical community are presented in figure 8. The demographics of the respondents are presented in table 2. According to statistics provided by the Finnish Medical Association, the responders represented the Finnish medical profession very well in terms of age, sex, and hospital district (data on file, The Finnish Medical Association n.d.).

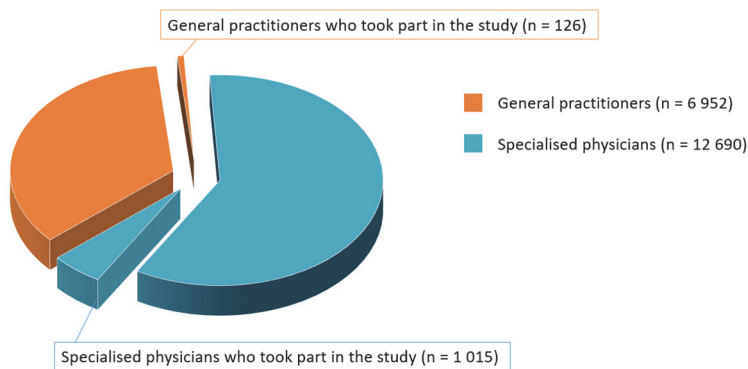


Fig. 7. The working-age Finnish medical profession divided to specialists and general practitioners in 2012. The sub-segments represent the physicians who took part in the Finnish Physicians and Tobacco 2012 study (III and IV).

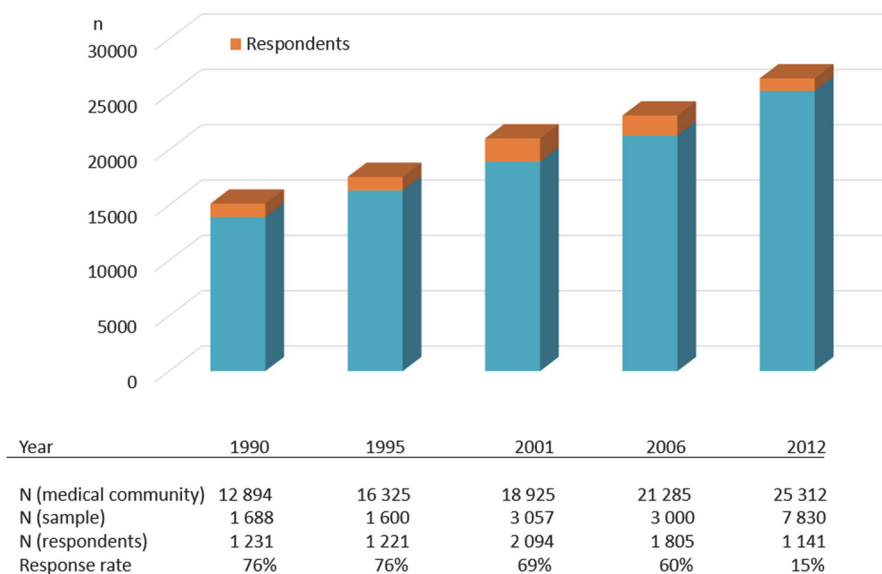


Fig. 8. Number of respondents and response rate in independent studies on Finnish physicians and smoking cessation in proportion to the size of the medical community (Barengo *et al.* 2003, Hokkinen *et al.* 2009, The Finnish Medical Association n.d.) (III and IV).

Table 2. Description of the study sample (III).

Attribute	n (%)
Place of work	
Primary health care	600 (52.6)
Secondary health care	466 (40.8)
Other (non-clinical work) ¹	75 (6.6)
Total	1 141 (100)
Specialists vs. general practitioners	
General practitioner	126 (11.0)
Specialist	1 015 (89.0)
Sex	
Male	481 (42.2)
Female	660 (57.8)
Smoking status (self-reported)	
Daily smoker	25 (2.2)
Occasional smoker	60 (5.3)

¹Respondents were excluded from analyses concerning clinical work.

Survey on smoking cessation work

In the survey, physicians were asked to report their smoking cessation related attitudes, experiences and practices. A total of 10 smoking cessation practices were mapped, for which a four-point grading system was applied: performing the activities “nearly always” (3 points), “often” (2 points), “sometimes,” (1 points) and “never” (0 points). When analysing the results, smoking cessation practices were divided to a) conversation and b) practical help, and a total score for both categories was calculated for each respondent. “Conversation” consisted of recommending cutting down the number of cigarettes smoked, discussing the health risks related to smoking, recommending quitting, marking smoking status on the patient records, and asking how often the patient smokes. “Practical help” consisted of prescribing withdrawal medication, recommending nicotine replacement therapy, helping the patient make a plan to quit smoking, and providing information on smoking cessation methods. The mapped practices are key activities from treatment guidelines for smoking cessation, and carrying them out could thus be seen as adhering to guidelines (Fiore *et al.* 2008, NICE 2008, Duodecim 2012). The questionnaire can be found in Appendix C. Similar studies with nearly identical questionnaires have been previously carried out both in Finland and other countries as well, enabling chronological and international comparison (Barengo *et al.* 2003, Hokkinen *et al.* 2009, Pipe *et al.* 2009).

Association of attitudes, experiences, and delivering smoking cessation aid

Association between delivering smoking cessation aid and agreement with the following smoking-cessation related claims was investigated:

- I am familiar with the local treatment guidelines for smoking dependence
- I have succeeded in my efforts to affect my patients’ smoking
- My current knowledge and skills are sufficient for giving advice to patients who wish to quit
- Additional health care resources should be directed to smoking cessation
- It is the physician’s responsibility to try to get the patient to quit smoking
- Smoking is one of the most significant public health issues in Finland

Those who had answered either “completely agree” or “somewhat agree” were considered to agree, and those who had answered either “completely disagree” or “somewhat disagree” were considered to disagree with the claims.

Restrictions for smoking cessation work

To further understand why only a minority of smokers report having discussed smoking with their physician, a sub-study was performed on restrictions for smoking cessation work as experienced by physicians specialised in general medicine (IV). A total of 1 141 Finnish physicians responded to the survey, 270 (24%) of whom had specialised in general medicine. This sub-sample represented 15% of general medicine specialists in Finland at the time of the study (The Finnish Medical Association n.d.). In this thesis, results will be presented also for all respondents regardless of specialty (previously unpublished data).

Statistical methods

Distributions of continuous variables are expressed as means and standard deviations (SD), and categorical variables as proportions. Pair-wise comparisons of continuous variables between groups were tested using the Mann–Whitney U-test, and categorical data was tested with χ^2 or Fisher’s exact test, as appropriate. Exploratory principal components analysis (PCA) was initially used to explore the dimension structure of the consultation activities. Promax rotation was applied. The scree plot and total-variance-explained variability criteria were used to specify the retained factor. This analysis produced two sub-scales: a) the conversation scale (5 items; each scored from 0 to 3) and b) the practical help scale (4 items; each scored from 0 to 3). The action “refer patient to another health care provider, such as a nurse or specialist clinic” that was mapped in the survey remained alone in the PCA analysis, and was therefore excluded from the two sub-scales. The total variance explained was 72%. A polychoric correlation matrix was used in the PCA. Reliability of the factor solution was determined by calculating internal consistency using Cronbach’s alpha with a corresponding 95% confidence interval (CI). All statistical tests were two-tailed, and p-values < 0.05 were considered statistically significant. Statistical analysis was performed using the R software environment, version 3.0.0 (<https://cran.r-project.org/web/packages>).

4 Results

4.1 Smoking and primary health care utilisation (I)

Unadjusted primary health care utilisation at age 46 in the NFBC 66 is presented in table 3. At age 46, current smokers of both sexes utilised primary health care services more than people who had never smoked. This meant approximately one annual extra visit to primary health care for both sexes. Male smokers were also more likely to be high utilisers of primary health care (≥ 8 annual visits) than ex-smokers or never-smokers.

4.1.1 Past smoking and primary health care utilisation

Both female and male ex-smokers utilised primary health care services more than never-smokers (table 3). Female ex-smokers were also the sub-group with the highest percentage of high utilisers of primary health care.

4.1.2 Primary health care utilisation by service type

BMI was adjusted for when studying the association of smoking status and primary health care utilisation by service type (fig. 9). The increase in primary health care use among smokers was mostly due to higher number of visits to the dentist or to the physician (fig. 9). When the results were adjusted for both BMI and education level, the results remained statistically significant for visits to the dentist (both sexes) and visits to the physician (women only). The percentage of people with at least one visit within the past year to a mental health care professional was higher among current smokers than other groups, especially in men (8.4% among current male smokers, 3.7% among male never-smokers, $p < 0.001$).

4.1.3 Sex and primary health care utilisation

Women used more primary health care services than men in corresponding sub-groups, regardless of the type of service provided. Women had approximately two more annual visits to primary health care compared to men in each sub-group.

Table 3. Utilisation of different types of primary health care services at age 46 in the NFBC 66. Results are unadjusted. (I)

Variable	Men			Women			p-value
	Never-smokers n = 1 016	Ex-smokers n = 628	Current smokers n = 499	Never-smokers n = 1 649	Ex-smokers n = 666	Current smokers n = 539	
Total use of primary health care services							
Visits (mean/inhabitant)	5.54	6.22	6.70	7.59	8.44	8.65	0.015 ¹
95% CI for visits (mean)	(5.12-5.96)	(5.73-6.71)	(6.02-7.39)	(7.18-7.99)	(7.81-9.06)	(7.66-9.63)	
Visits to the physician							
Visits (mean/inhabitant)	1.97	2.31	2.20	2.67	3.02	2.99	0.258
95% CI for visits (mean)	(1.83-2.11)	(2.09-2.53)	(1.96-2.45)	(2.55-2.85)	(2.78-3.27)	(2.70-3.27)	
Visits to the dentist							
Visits (mean/inhabitant)	1.27	1.43	1.67	1.64	1.70	1.98	0.065
95% CI for visits (mean)	(1.17-1.38)	(1.29-1.57)	(1.47-1.87)	(1.55-1.73)	(1.55-1.84)	(1.78-2.19)	
Visits to mental health professionals							
Visits (mean/inhabitant)	0.24	0.20	0.50	0.43	0.68	0.79	0.080
95% CI for visits (mean)	(0.12-0.35)	(0.10-0.30)	(0.26-0.74)	(0.31-0.56)	(0.42-0.95)	(0.44-1.14)	
Visits to other primary health care professionals							
Visits (mean/inhabitant)	2.06	2.28	2.33	2.81	3.04	2.89	0.129
95% CI for visits (mean)	(1.78-2.34)	(1.99-2.56)	(1.91-2.75)	(2.54-3.09)	(2.67-3.40)	(2.27-3.52)	
High utilisation of primary health care ≥ 8 visits/year (%)	21.4	26.6	27.9	32.7	40.1	35.8	0.003 ²

¹p<0.05, ²p < 0.01, ³p < 0.001, Mann-Whitney U test.

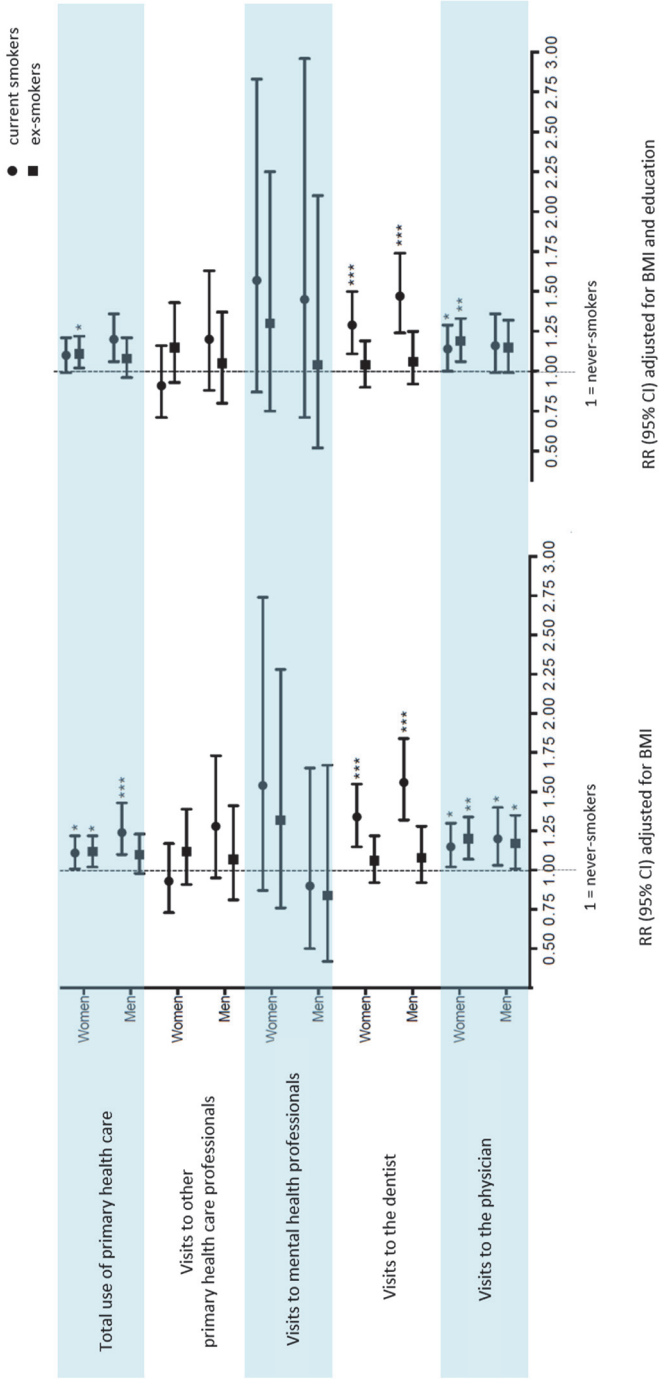


Fig. 9. Annual utilisation of primary health care in sub-groups based on smoking status at age 46 in the NFBC 66. Results are presented with adjustments for BMI alone and BMI together with education level. Never-smokers are used as a reference to ex-smokers and current smokers. RR risk ratio, CI confidence interval, *P < 0.05, **P < 0.01, *P < 0.001. Wilcoxon rank sum test. (I)**

4.1.4 Primary health care costs

Annual primary health care costs in EUR/person at age 46 are presented in figure 10. The costs are adjusted for BMI. For currently smoking men, annual primary health care costs were 28% higher compared with never-smokers (fig. 10). For women, the difference was 21%. This difference corresponds to approximately 100 € annual extra costs per smoker.

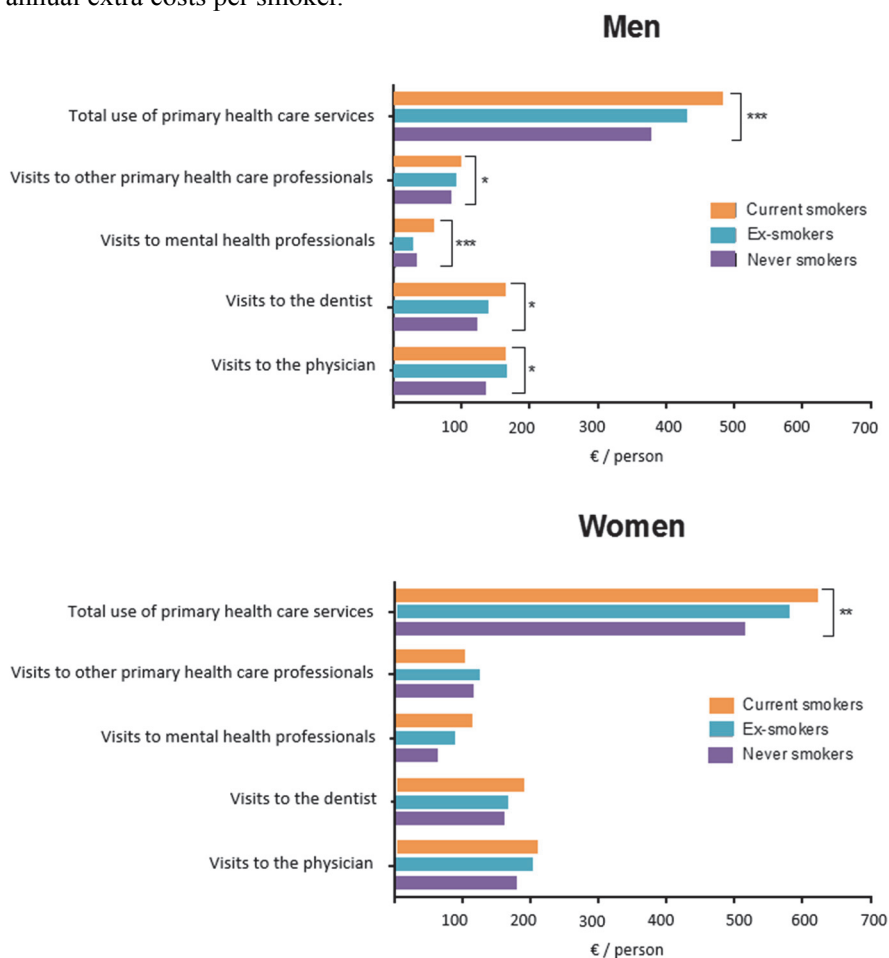


Fig. 10. Annual primary health care costs in Euros/inhabitant from the year preceding the 46-year follow-up in the NFBC 66. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, negative binomial hurdle model. Results were adjusted for BMI. (I)

4.2 Smoking and cardiovascular risk factors (II)

4.2.1 Cardiovascular risk factors in the NFBC 66 at age 46

Mean cardiovascular risk factors at age 46 in the NFBC 66 cohort are presented in table 4. The mean values of the cohort exceed recommendations for BMI, waist circumference, waist-to-hip ratio, total cholesterol, LDL, and for men, also for diastolic blood pressure (WHO 2008b, Catapano *et al.* 2016).

Table 4. Mean cardiovascular risk factors for NFBC 66 at age 46. (II)

Variable	Men	Women	Recommendation ¹
	NFBC 1966	NFBC 1966	
n	2 736	3 238	-
Age (years)	46.6±0.6	46.6±0.6	-
Current smokers, n (%)	743 (27.5)	665 (20.3)	no smoking
Recent quitters, n (%)	64 (2.3)	57 (1.8)	-
Former smokers n (%)	707 (25.8)	694 (21.4)	-
Never smokers n (%)	1 222 (44.7)	1 822 (56.0)	-
Use of antihypertensive medication (%)	18.5	16.6	-
Use of hypolipidemic medication (%)	6.9	2.3	-
Type 2 diabetes (%)	3.0	2.6	-
BMI (SD)	27.3±4.3	26.5±5.2	< 25
Waist (cm) (SD)	97.5±11	87.3±13.1	≤ 94 (men) ≤ 80 (women)
Waist-to-hip ratio (SD)	0.98±0.06	0.87±0.06	≤ 0.9 (men) ≤ 0.85 (women)
Total cholesterol (mmol/L) (SD)	5.54±1.0	5.18±0.85	< 5
HDL (mmol/L) (SD)	1.40±0.33	1.67±0.39	> 1.0 (men) ² > 1.2 (women) ²
LDL (mmol/L) (SD)	3.74±0.94	3.24±0.86	< 3
Triglycerides (mmol/L) (SD)	1.49±0.96	1.08±0.58	< 1.7 ²
Systolic blood pressure (mm Hg) (SD)	128.2±13.9	118.51±15.5	< 130
Diastolic blood pressure (mm Hg) (SD)	86.5±10.2	82.4±10.7	< 85
Framingham risk score (%) (SD)	9.4±5.1	3.7±2.6	-

¹WHO 2008b, Catapano *et al.* 2016. ²No recommendation, but known to indicate lower risk.

4.2.2 Smoking status and other cardiovascular risk factors

There were statistically significant ($p < 0.05$) differences for most cardiovascular risk factors between sub-groups (table 5). However, these differences were so small between former smokers, recent quitters, and those who had never smoked that the difference in calculated ten-year risk of a cardiovascular event for these sub-groups was less than 1%. This was true for both men and women. For current smokers, the calculated risk was approximately two-fold compared with the other sub-groups.

Cardiovascular risk profile of a smoker vs. never-smoker

Smokers had higher triglycerides (20% for women, 21% for men) and LDL (4% for women and men), and lower HDL (7% for women, 5% for men) than their never-smoking peers. Male smokers had also higher total cholesterol (2%). Smokers had slightly higher blood pressure (0.5-1%) than never-smokers. Smokers had higher BMI than never-smokers (4% for women, 1% for men), and never-smokers had the smallest waist-to-hip ratio when BMI was adjusted for. Type 2 diabetes prevalence was more than twice as common among smokers vs. never-smokers (2.3-fold difference for women, 2.2 for men). Use of antihypertensive medication was more common among smokers than never-smokers (1.4-fold difference for women, $p = 0.007$; 1.02 for men, $p = 0.015$). Use of lipid-profile lowering medication was more common among female smokers than never-smokers (1.9-fold difference, $p = 0.041$).

Table 5. Cardiovascular risk factors in the NFBC 66 at the 31-year follow-up according to smoking status. Results are presented as mean \pm standard deviation unless otherwise specified. *Independent-sample t-test. Previously unpublished data.

Variable	Men				Women				p-value
	Current smokers	Recent quitters	Former smokers	Never-smokers	Current smokers	Recent quitters	Former smokers	Never-smokers	
n	743	64	707	1222	665	57	694	1822	
BMI (kg/m ²)	27.2 \pm 4.5	27.5 \pm 4.0	27.9 \pm 4.0	26.8 \pm 4.0	27.1 \pm 5.4	26.8 \pm 5.7	26.9 \pm 5.4	26.1 \pm 5.1	<0.001
Waist (cm)	98.3 \pm 12.3	99.6 \pm 10.9	99.0 \pm 11.6	95.8 \pm 11.3	89.2 \pm 13.6	89.0 \pm 15.0	88.5 \pm 13.5	85.9 \pm 12.4	<0.001 ¹
Waist-to-hip ratio	0.995 \pm 0.1	0.997 \pm 0.1	0.986 \pm 0.1	0.969 \pm 0.1	0.881 \pm 0.1	0.879 \pm 0.1	0.870 \pm 0.1	0.862 \pm 0.1	<0.001 ¹
Total cholesterol ^{3,4} (mmol/L)	5.6 \pm 1.0	5.5 \pm 1.0	5.6 \pm 1.0	5.5 \pm 1.0	5.2 \pm 0.9	5.1 \pm 0.7	5.1 \pm 0.8	5.2 \pm 0.8	0.521 ^{1,2}
HDL cholesterol ³ (mmol/L)	1.35 \pm 0.3	1.36 \pm 0.3	1.41 \pm 0.3	1.42 \pm 0.3	1.58 \pm 0.4	1.77 \pm 0.4	1.66 \pm 0.4	1.69 \pm 0.4	<0.001 ^{1,2}
LDL cholesterol (mmol/L)	3.81 \pm 1.0	3.69 \pm 0.9	3.80 \pm 0.9	3.66 \pm 0.9	3.34 \pm 1.0	2.98 \pm 0.9	3.21 \pm 0.8	3.22 \pm 0.8	0.002 ^{1,2}
Triglycerides (mmol/L)	1.7 \pm 1.0	1.4 \pm 0.6	1.5 \pm 1.0	1.4 \pm 0.9	1.2 \pm 0.6	1.1 \pm 0.6	1.1 \pm 0.6	1.0 \pm 0.5	<0.001 ^{1,2}
Systolic BP ^{3,4} (mmHg)	127.1 \pm 13.8	126.4 \pm 13.3	129.5 \pm 13.4	128.1 \pm 14.2	117.5 \pm 15.1	116.8 \pm 16.1	117.5 \pm 15.4	119.1 \pm 15.1	0.016 ^{1,2}
Diastolic BP (mmHg)	86.3 \pm 10.2	86.1 \pm 9.5	87.8 \pm 9.8	85.9 \pm 10.3	82.6 \pm 11.1	81.2 \pm 11.8	81.6 \pm 10.7	82.6 \pm 10.5	0.110 ^{1,2}
Type 2 diabetes (%) ³	4.0	0	4.2	1.8	4.2	3.5	3.0	1.8	<0.001 ¹
Framingham risk score (%)	14.7 \pm 6.0	7.4 \pm 2.3	8.1 \pm 2.2	7.5 \pm 3.4	5.9 \pm 3.9	3.0 \pm 2.1	3.2 \pm 1.9	3.3 \pm 1.9	<0.001 ¹

¹BMI or ²use of antihypertensive and lipid-profile lowering medication was adjusted for when testing for differences between groups (ANOVA/ANCOVA).

³Included in Framingham risk score. ⁴Included in SCORE risk score. HDL, high density lipoprotein; LDL, low density lipoprotein; BP, blood pressure. The values are presented as mean \pm SD unless otherwise indicated.

4.2.3 Changes in cardiovascular risk factors between ages 31 and 46 according to smoking history

Changes in smoking status over time

Changes in smoking status in the NFBC 66 between ages 31 and 46 are presented in fig. 11. Of those who were smokers at 31, 44% had quit smoking by the age of 46. Of those who had quit smoking before the age of 31, 84% remained non-smokers at the age of 46. Of those who were never-smokers at the age of 31, 94% were still never-smokers at the 46-year follow-up.

Cardiovascular risk factors at age 31

Cardiovascular risk factors at age 31 according to smoking status are presented in table 6 (previously unpublished data). Male smokers had higher triglyceride and lower HDL values than other sub-groups. They also had a smaller hip circumference but a bigger waist-to-hip ratio, and lower systolic and diastolic blood pressure than the other sub-groups. Female smokers had lower total cholesterol and HDL values than other sub-groups. They also had a larger waist circumference, and lower systolic and diastolic blood pressure than the other sub-groups.

Changes in cardiovascular risk factors between ages 31 and 46

An analysis on changes in cardiovascular risk factors between ages 31 and 46 according to smoking history was performed for those members of the birth cohort who had taken part in both 31- and 46-year follow-ups (both clinical examinations and questionnaire on smoking) (table 6, previously unpublished data). Diastolic blood pressure, total cholesterol, and LDL increased with age between the 31 and 46-year follow-ups in all sub-groups of both sexes. For men, there was also an increase in triglycerides for all sub-groups, but in women a statistically significant change in triglycerides was seen only for long-time smokers. There was a decrease in HDL for male long-time smokers, never-smokers, and those who had quit between ages 31 and 46. For women, there was a decrease in HDL for long-time-smokers, never-smokers, and those who had quit before the age of 31.

Size of changes in cardiovascular risk factors according to smoking history

While most risk factors were higher at age 46 than age 31 regardless of smoking history, there were differences in the size of these changes. The biggest increases in risk factors were observed among the largest subgroups: long-time smokers and those who had quit smoking between ages 31 and 46. The differences between subgroups were statistically significant among men for HDL and diastolic blood pressure. In women, the differences were statistically significant for total cholesterol, HDL, LDL, triglycerides, and diastolic blood pressure.

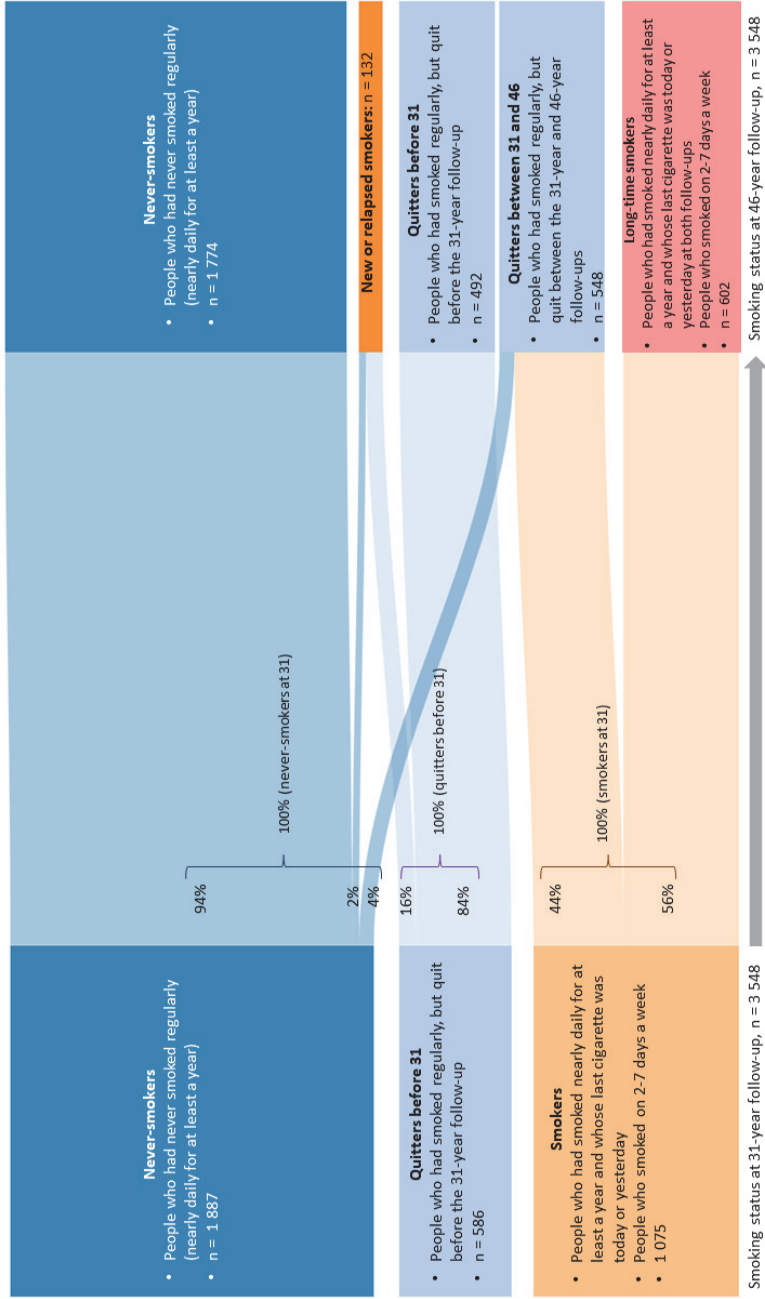


Fig. 11. Smoking trends in the NFBC 66 between the 31- and 46-year follow-ups.

Table 6. Cardiovascular risk factors in the NFBC 66 at the 31-year follow-up according to smoking status. Results are presented as mean \pm standard deviation unless otherwise specified. ¹Independent-sample t-test. Previously unpublished data.

Variable	Men				Women				p-value ¹
	Smokers	Recent quitters	Former smokers	Never-smokers	Smokers	Recent quitters	Former smokers	Never-smokers	
n	991	67	334	1172	830	92	431	1776	
BMI	25.08 \pm 3.71	25.51 \pm 3.07	25.56 \pm 3.38	24.95 \pm 3.18	24.39 \pm 4.89	24.00 \pm 5.42	24.12 \pm 4.03	23.88 \pm 4.29	0.122
Waist	88.63 \pm 10.21	89.78 \pm 8.89	89.51 \pm 9.69	88.10 \pm 8.86	79.50 \pm 12.72	79.83 \pm 12.79	78.80 \pm 10.25	77.95 \pm 11.13	0.042
Waist-to-hip ratio	0.914 \pm 0.06	0.912 \pm 0.05	0.912 \pm 0.06	0.904 \pm 0.06	0.817 \pm 0.08	0.810 \pm 0.06	0.812 \pm 0.06	0.806 \pm 0.08	0.051
Total cholesterol	5.21 \pm 1.00	5.26 \pm 1.23	5.22 \pm 1.02	5.18 \pm 1.00	4.83 \pm 0.91	4.93 \pm 0.80	4.94 \pm 1.00	4.98 \pm 0.99	0.024
HDL	1.36 \pm 0.32	1.36 \pm 0.30	1.42 \pm 0.31	1.45 \pm 0.32	1.63 \pm 0.38	1.74 \pm 0.30	1.71 \pm 0.39	1.73 \pm 0.38	<0.001
LDL	3.22 \pm 0.90	3.24 \pm 1.04	3.23 \pm 0.90	3.20 \pm 0.89	2.74 \pm 0.79	2.74 \pm 0.81	2.80 \pm 0.84	2.80 \pm 0.81	0.388
Triglycerides	1.45 \pm 0.96	1.37 \pm 0.88	1.25 \pm 0.63	1.22 \pm 0.77	1.09 \pm 0.55	0.99 \pm 0.40	1.05 \pm 0.64	1.04 \pm 0.56	0.156
Systolic BP	128.38 \pm 12.25	128.40 \pm 14.04	130.45 \pm 12.03	130.56 \pm 12.38	118.24 \pm 12.54	119.47 \pm 11.05	119.52 \pm 10.96	120.14 \pm 12.14	0.015
Diastolic BP	78.61 \pm 10.75	79.94 \pm 12.13	80.91 \pm 10.96	80.32 \pm 11.67	72.96 \pm 11.23	74.87 \pm 9.11	73.96 \pm 9.55	74.97 \pm 10.91	0.002

4.3 Finnish physicians and smoking cessation (III)

4.3.1 Attitudes and experiences of physicians on smoking and smoking cessation

A total of 1 141 physicians took part in the Finnish Physicians and Tobacco 2012 study. When those respondents who didn't do clinical work were excluded from analysis concerning clinical work (n = 75), 1 066 physicians remained eligible. Nearly all (97%) respondents were of the opinion that smoking is among the most significant public health issues in Finland, and that it is the physician's responsibility to try to get their patient to quit smoking (93%). Some 22% found their knowledge and skills insufficient for giving advice to patients who wish to quit smoking (fig. 12). Some 72% of the respondents were not familiar with the local treatment guidelines for smoking cessation.

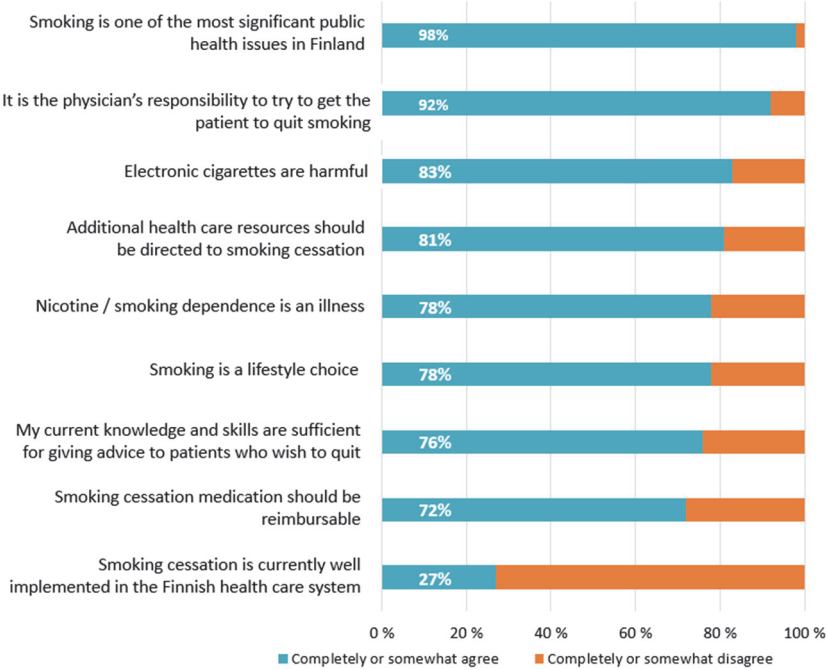


Fig. 12. Smoking-related attitudes and experiences of Finnish physicians in 2012, n = 1 066. (III)

4.3.2 Smoking cessation aid by Finnish physicians

When Finnish physicians were asked how often they perform smoking cessation related activities, a majority of respondents reported that they nearly always 1) ask how often the patient smokes, 2) mark the patient's smoking status in the patient records, or 3) recommend quitting to the patient (fig. 13). Discussing health risks related to smoking “nearly always” was also relatively common, as was recommending cutting down the number of cigarettes smoked. These smoking cessation related activities were classified as “conversation.” Activity rates were much lower for giving “practical help” in quitting, such as prescribing withdrawal medication, which was done nearly always by 4% of the respondents.

4.3.3 Factors associated with delivering smoking cessation aid

The respondents were scored on how often they had smoking cessation related conversations and how often they delivered practical quitting help. The association of these activity scores and the physician's attitudes was studied (fig. 14). Physicians who felt confident about their smoking cessations skills and knowledge were more active in providing practical help with smoking cessation than their colleagues who found their skills insufficient. Finding it the physician's responsibility to try to make their patient quit was also positively associated with providing practical smoking cessation help, as was previous success with affecting patients' smoking habits, finding smoking one of the most significant public health issues, familiarity with local treatment guidelines for smoking cessation, and thinking that additional resources should be directed to smoking cessation. The same factors were also associated with an increase in smoking-related conversations, but the effect was smaller.

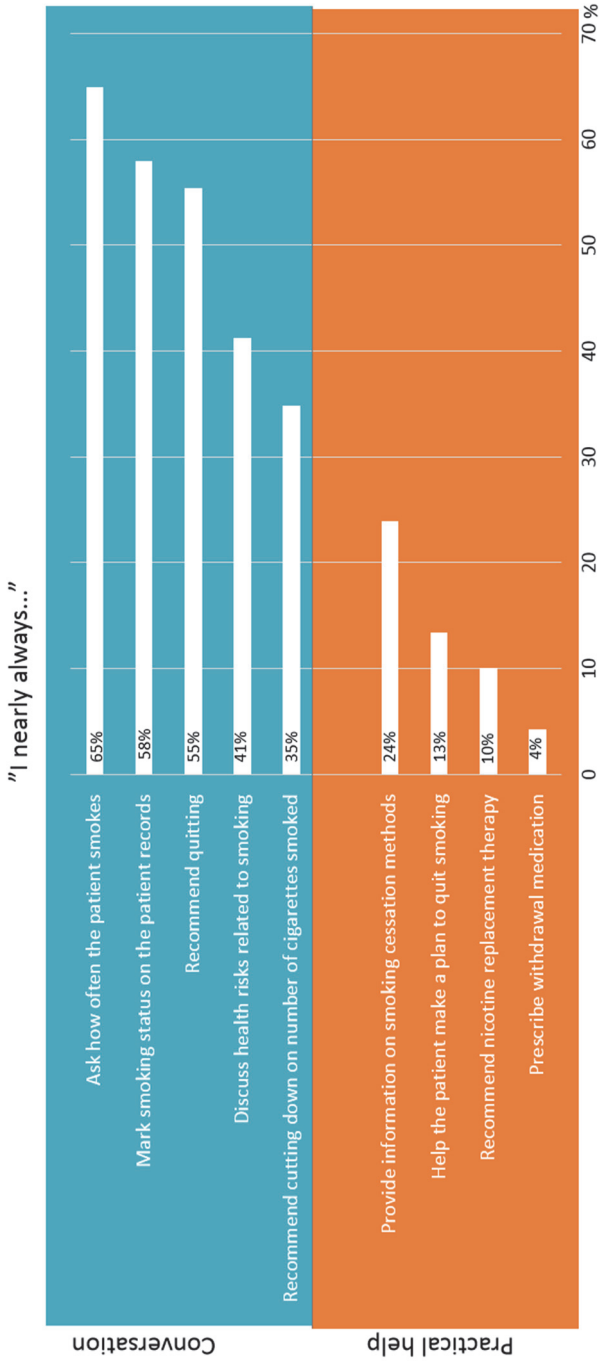


Fig. 13. Smoking cessation help offered by Finnish physicians in 2012. Percentages of respondents who reported taking the following actions "nearly always." n = 1 066, degrees of freedom = 1 for all items, *p < 0.05 (χ² test). (III)

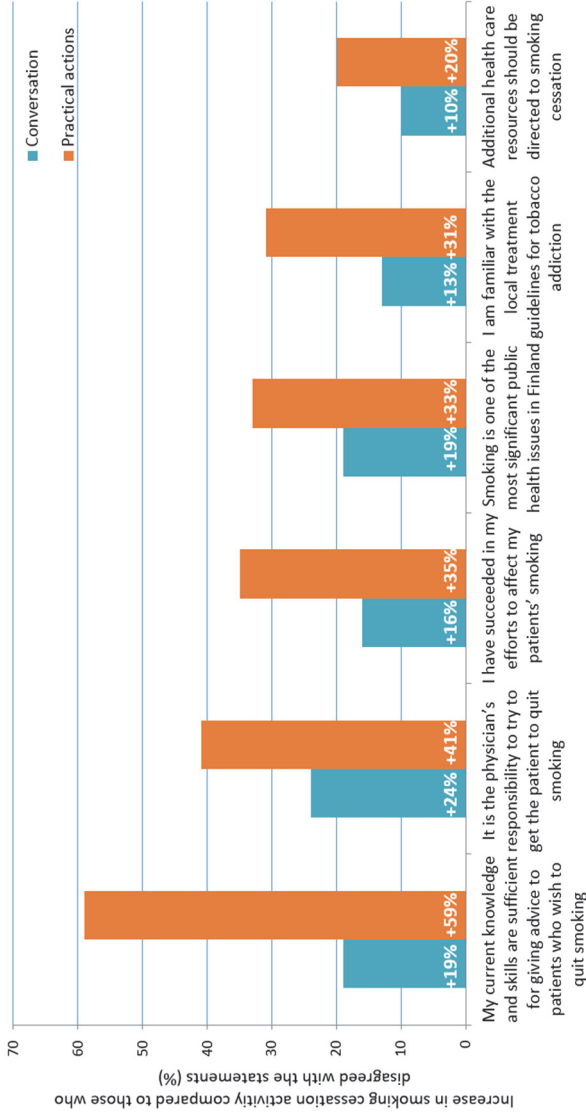


Fig. 14. The effect of positive attitudes and experiences on smoking cessation activity. The reference (0%) is the activity level of physicians who disagree with the claims. $p < 0.005$ (Mann–Whitney U-test) for all items, $n = 1066$. (III)

4.4 Restrictions for smoking cessation work as experienced by Finnish physicians (IV)

Some 71% of Finnish general medicine specialists who took part in the study and 70% of all respondents regardless of their specialty felt that there were restrictions for their smoking cessation work. The most commonly reported restriction was lack of time, reported by 64% of general medicine specialists and 51% of all respondents. Additionally, 11% of general medicine specialists felt that they didn't have sufficient tools for offering smoking cessation aid, translating to a lack of knowledge in the subject. This was a restriction for 9% of all respondents. The self-reported restrictions of general medicine specialists were in line with those of all respondents (fig. 15). The restrictions experienced by physicians specialised in general medicine have been published in article IV.

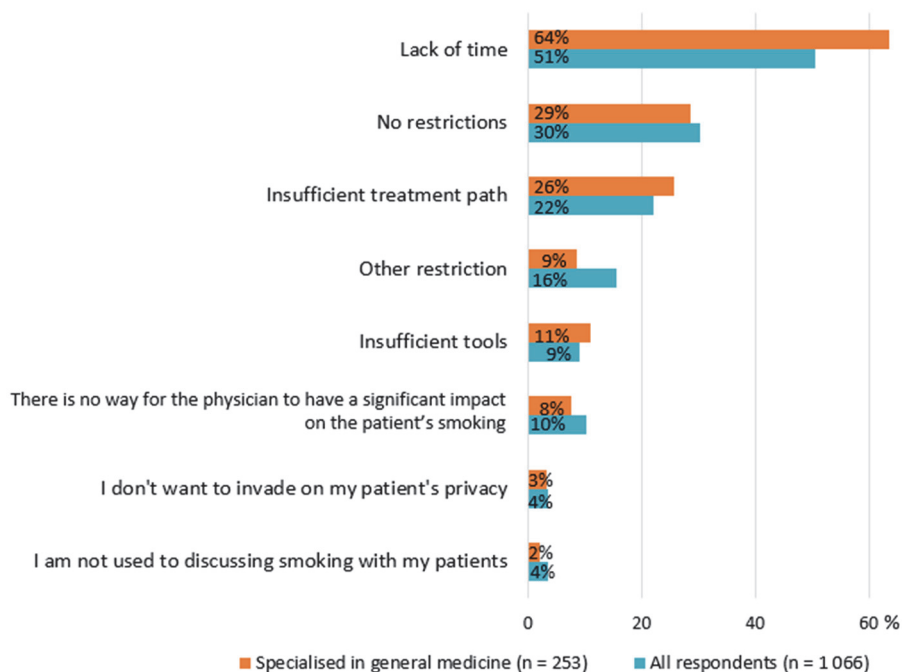


Fig. 15. Restrictions for smoking cessation as experienced by Finnish physicians in 2012. Based on original article IV and previously unpublished data.

Organisation of smoking cessation services

The possibility to refer the patient to a smoking cessation expert either within or outside one's organisation is presented in figure 16. A treatment path was available for 21% of general medicine specialists, and out of these respondents, 60% found the path non-functional. Out of all respondents, a treatment path was available for 19%, and 53% of them found it non-functional.

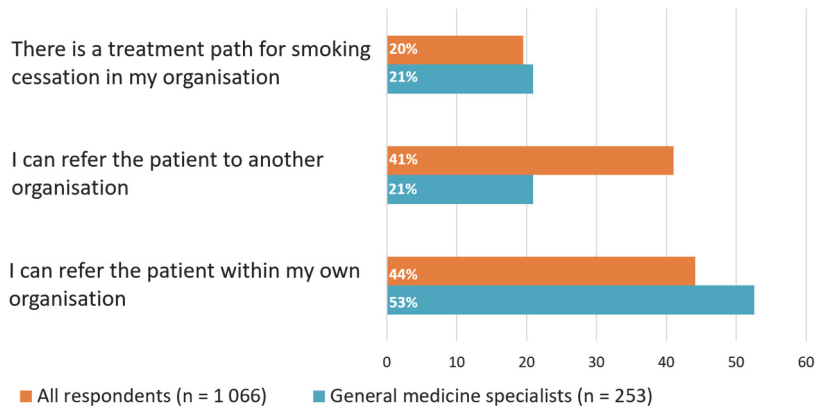


Fig. 16. Organisation of smoking cessation services at the workplace of Finnish physicians in 2012. Based on original article IV and previously unpublished data.

5 Discussion

5.1 Smoking is associated with increased primary health care utilisation already in middle age

Smoking is known to be a key risk factor for cardiovascular disease and cancer, the most common causes of death in developed countries such as Finland (Fiore *et al.* 2008, Statistics Finland, WHO, Office of the Surgeon General 2014). The economic consequences of treating serious smoking illnesses have been well studied and reported (Vähänen 2015, Vitikainen *et al.* 2006, Effertz & Mann 2013, Goodchild *et al.* 2017). However, smoking has adverse, but less drastic health effects already before these serious illnesses require acute treatment in secondary care. The results presented in this thesis suggest that the accumulation of these less drastic smoking-related health problems can be seen as a clear increase in the use of primary health care services already in middle age.

The increased primary health care utilisation of smokers is of similar magnitude as in a Spanish study from 2015, and as the increase of total health care utilisation observed in American studies (Sturm 2002, Fishman *et al.* 2003, Suárez-Bonel *et al.* 2015). However, previous studies have sometimes ended at different conclusions as well: in some studies, current smokers have used less or as much primary care or outpatient services as non-smokers (Izumi *et al.* 2001, Jorm *et al.* 2012, Vals *et al.* 2013). For instance, in an Australian study on 254 382 people aged 45 and over, current smokers were slightly less likely to use primary care services, especially the kind they had to pay for themselves (Jorm *et al.* 2012). The authors had adjusted the results for income, level of education and region of residence, among others, to account for predisposing and access-related differences. However, the result is likely to reflect a difference in health care utilisation culture rather than a difference in the actual need for primary health care services. This is backed by the finding that Australian 40–59-year-olds with multimorbidity are 1.71 times more likely to be current smokers than non-smokers (Taylor *et al.* 2010). In a Spanish study the probability of being a high healthcare-cost individual was more than doubled in smokers even after adjusting for hypertension, diabetes, and dyslipidemia (Suárez-Bonel *et al.* 2015). Smoking has been found to increase the risk of later multimorbidity more than any other risk factor in initially disease-free people also in a Finnish setting (Wikström *et al.* 2015).

5.1.1 Why do middle-aged smokers have more visits to physicians and dentists?

The NFBC 66 questionnaire doesn't include questions about the reasons behind visits to primary health care professionals. This information could have been obtained by linking the data with patient registers, but at the time of this study, the Finnish centralised patient register for primary health care (AvoHilmo) had just been set up and had limited coverage. One can, however, speculate. Judging from how smoking is known to affect the incidence of diseases and health issues common in middle age, it is likely that key reasons behind visits to the primary health care physician were musculoskeletal problems, respiratory problems, and infections (Brown *et al.* 1991, Willemse *et al.* 2004, Office of the Surgeon General 2014). It should be noted that these are also the most common reasons for sick leave (European Foundation for the Improvement of Living and Working Conditions 2010). As for reasons behind the increased visits to the dentist, likely causes are periodontitis and other problems with oral connective tissue. The carcinogenic components of cigarette smoke are detrimental to dental health, increasing the risk of periodontitis, which in turn is associated with systemic health issues, such as depression and cardiovascular disease (Bergström 1989, Beck & Offenbacher 2005, Rosania *et al.* 2009). The association between smoking status and primary health care use seemed to be strongest for visits to the dentist, as the association remained highly statistically significant even after adjusting for both BMI and education level. The studied sample of 46-year-old smokers probably suffered from a cluster of interconnected, smoking-related health issues, which are likely to manifest themselves as cardiovascular events in later life if the root cause is not treated.

5.1.2 Smoking and mental health care utilisation

Smoking prevalence is much higher among patients with mental health issues than in the general population: 40% of mental health care patients are smokers (Lasser *et al.* 2000). Due to heavy multimorbidity, smokers suffering from mental health issues have an up to 25 years shorter life expectancy than the general population, and approximately 40% of smoking-attributable deaths occur among people with mental health issues (Lasser *et al.* 2000, Williams & Ziedonis 2004, Colton & Manderscheid 2006). Thus, people suffering from mental health problems are

likely to be high utilisers of not only mental health care services, but other forms of primary health care as well (Leskelä *et al.* 2015).

Based on previous literature, it could be expected that also in the NFBC 66 smokers would be more likely to utilise mental health services (Lasser *et al.* 2000). While male smokers were more than twice as likely to have visits to mental health professionals than their never-smoking peers, the statistical significance was lost once the results were adjusted for BMI. These results should be interpreted with caution for several reasons: The confidence intervals of risk ratios for visiting mental health professionals in primary care were much bigger than for the other service types. Also, it could be that high utilisers of mental health care had dropped out from the NFBC 66 study, leading to people with mental health issues being underrepresented in the present results. Furthermore, self-reported health care utilisation is less reliable if the patient suffers from mental health problems (Bhandari & Wagner 2016).

5.1.3 Also past smoking is associated with increased primary health care utilisation

Previous research has shown that there is a peak in health care utilisation after quitting smoking (Fishman *et al.* 2003, Callum *et al.* 2010, Jorm *et al.* 2012, Vals *et al.* 2013). This peak is most likely due to the fact that smokers who are the sickest and thus in the greatest need of medical attention are most likely to quit (Beard *et al.* 2013, Rosella *et al.* 2014). Also in the sample studied in this thesis, ex-smokers used primary health care services more than never-smokers. The finding remained statistically significant for women after adjusting for BMI or BMI together with education level. Female ex-smokers were also most likely to be high utilisers of primary health care. As for why this phenomenon was weaker for men is probably due to the same cultural and behavioural reasons as for why men in general utilise health care services less than women (Luoto *et al.* 2003).

5.1.4 Costs of smoking to the primary health care sector

Smoking was associated with a 21% increase in total primary health care costs in 46-year-old women when compared with never-smokers, the increase being 28% for men. As for costs caused by visits to a physician in primary health care, the increase was 22% for women and 21% for men – similar percentages than in a recent Spanish study with a mean age of 56 years (Suárez-Bonel *et al.* 2015). A

United Kingdom study on adults over 16 years of age arrived at a slightly lower estimate: smoking was attributable for 11% of all adult general practitioner consultation costs (Callum *et al.* 2010). The study relied on a similar approach as the one used here, but the respondents were asked to report their primary health care utilisation from only the past 0.5 to 3 months (Callum *et al.* 2010). The National Institute for Health and Welfare in Finland has estimated that only 0.6% of costs for physicians' appointments in primary health care are attributable to smoking, even when one fifth of the population are smokers (Vähänen 2015). This highlights the fact that the role of smoking on a person's health and the corresponding health care costs is age-sensitive. For certain population segments – such as 46-year-old adults – the role of smoking in primary health care costs can be significant. A disease-based model with conservative estimates of smoking-attributable factors may result in an underestimation of the role of smoking on primary health care costs.

5.2 Smokers have higher cardiovascular risk factors already in middle-age

In this cross-sectional study, already 31-year-old smokers showed signs of slightly higher cardiovascular risk factors than never-smokers. Also the increase in many risk factors between ages 31 and 46 was typically larger among those who had been smokers at age 31. At the age of 46, there were statistically significant differences in most cardiovascular risk factors between smokers, recent quitters, former smokers, and never-smokers. The difference was most substantial for triglycerides and prevalence of type 2 diabetes. The difference in calculated ten-year risk of a cardiovascular event was less than 1% between recent quitters, former smokers, and never-smokers – in other words, those whose binary smoking status in the risk assessment algorithms was non-smoker. This result reflects the relative similarity in cardiovascular risk factors between these non-smoking groups from a clinical point of view.

5.2.1 Smoking and type 2 diabetes

Of the risk factors investigated, the biggest difference between sub-groups was observed for type 2 diabetes. Type 2 diabetes prevalence was two-fold for current smokers versus never-smokers in both sexes after adjusting for BMI. While a dose-

dependent association of smoking and type 2 diabetes has been established before, the association hasn't been as strong as the one observed here – most likely due to more thorough adjustments of cardiovascular risk behaviour and differences in heaviness of smoking (Willi 2007, Spijkerman *et al.* 2014). In a meta-analysis of 25 prospective studies, a pooled, adjusted relative risk in smokers for diabetes was 1.44 (Willi 2007). In a large European case-cohort study the hazard ratios of type 2 diabetes for smokers vs. never-smokers were 1.43 for men and 1.13 for women independent of age, education, center, physical activity, and alcohol, coffee, and meat consumption (Spijkerman *et al.* 2014). A Finnish prospective study on 41 372 subjects with a mean follow-up of 21 years also showed that smoking increased the risk of type 2 diabetes at all levels of BMI and physical activity, with an adjusted hazard ratio of 1.57 for men smoking 20 cigarettes per day or more, and a corresponding hazard ratio of 1.87 for women (Patja *et al.* 2005).

Quitting may have a positive effect on diabetes, as insulin sensitivity has been shown to improve with smoking cessation (Harris *et al.* 2016). In this study and previous studies as well, former smokers have been shown to be at an increased risk of type 2 diabetes compared to never-smokers, with the exception of Finnish women in the study by Patja *et al.* (Patja *et al.* 2005, Spijkerman *et al.* 2014). Even if type 2 diabetes isn't cured by smoking cessation, the risk of coronary heart disease has been shown to decrease to the same level with diabetic never-smokers ten years after quitting (Al-Delaimy *et al.* 2002).

5.2.2 Smoking and blood lipids & lipoproteins

While literature isn't very consistent on the effect size of smoking on lipids and lipoproteins, previous studies have, on average, shown bigger differences in LDL and smaller differences in triglycerides between smokers and never-smokers than the ones observed here (Craig *et al.* 1989, Cullen *et al.* 1998, Gosset *et al.* 2009, Slagter *et al.* 2013, Rampure *et al.* 2016, Zhao *et al.* 2017). Many studies have had wide age distributions, which may blur the results as older smokers have been exposed to cigarette smoke for a longer time and may be heavier smokers. It seems that triglyceride levels are rather sensitive to smoking already at a younger age, which was visible in the NFBC 66 as well: smokers had clearly higher triglycerides at age 46, and male smokers already at age 31. Also a previous study showed a dose-dependent, reversible effect of smoking on triglycerides even when age was adjusted for (Bakhru & Erlinger 2005).

As the differences in HDL and LDL were small among subgroups, few conclusions can be drawn about the effects of smoking cessation on them. Smokers had lower HDL already at age 31, and men who quit between the 31- and 46-year follow-ups showed signs of improvements in HDL between these time points, but the effect was very small. In previous studies HDL has typically quickly increased after smoking cessation, but the evidence for improvements in LDL and triglycerides has been contradictory (Green & Harari 1995, Maeda *et al.* 2003, Bakhru & Erlinger 2005, Campbell *et al.* 2008). Overall, risk factors were higher at age 46 for most subgroups, although the changes were typically slightly bigger for those who had been smokers at age 31.

The observed 20% difference in triglycerides between 46-year-old current smokers and never-smokers draws attention to the basic mechanisms of atherosclerosis: in the atherosclerotic process triglycerides of different sizes get stuck in the intima of blood vessels, causing an inflammatory reaction and thickening of the vessel walls. The observed elevation is clinically significant: the mean level of triglycerides was 1.7 mmol/l in male smokers, meaning that the average male smoker fulfilled one of the conditions for metabolic syndrome already at the age of 46 – which in turn is associated with developing cardiovascular disease and diabetes (Beilby 2004).

5.2.3 Smoking and visceral fat accumulation

Smokers have abnormal triglyceride and VLDL metabolism especially at the site of adipose tissue, which has been partially attributed to a decrease in lipoprotein lipase activity (Campbell *et al.* 2008). On the other hand, lipoprotein lipase activity is regulated by insulin, and several studies have confirmed insulin resistance among smokers (Campbell *et al.* 2008, Harris *et al.* 2016). These changes can result in the accumulation of visceral fat, as well as elevated VLDL and triglycerides (Campbell *et al.* 2008, Morris *et al.* 2015). The associations of smoking, visceral fat accumulation, triglycerides, and type 2 diabetes were visible also in this study: the most notable cardiovascular risk elevations among smokers were on type 2 diabetes and triglycerides, and smokers had a bigger waist-to-hip ratio than never-smokers.

Smoking cessation has been shown to have positive, but rather slow effects on the amount of visceral fat (Harris *et al.* 2016). Also in this study, former smokers had a slightly smaller waist-to-hip ratio than current smokers already at the age of 31, but the difference was small. While the waist-to-hip ratio may improve with

smoking cessation, BMI typically increases by 1.14 kg/m² within five years following smoking cessation; a difference of this magnitude in BMI was observed in the NFBC 66 for former male smokers vs. current smokers (Harris *et al.* 2016). Interestingly, smokers had a higher BMI than never-smokers in this study, while consensus is that smokers have a lower BMI than never-smokers (Harris *et al.* 2016).

5.3 Finnish physicians think it's their responsibility to try to get their patient to quit, but seldom deliver practical help

Guidelines for smoking cessation highlight the role of the physician in motivating their patient to quit, and in helping them reach this goal (Fiore *et al.* 2008, NICE 2008, Duodecim 2012). Whether Finnish physicians are familiar with these guidelines and follow their main principles is presented in study III. The majority of Finnish physicians reported that they almost always ask whether their patient smokes or not. They even encourage their patients to quit, although not as often as the international average of 90% among non-smoking physicians (Pipe *et al.* 2009). However, activity rates were dramatically lower for telling patients *how* they should quit and for providing cessation aid. For instance, American physicians were six times more active in prescribing withdrawal medication already in 2006, and in the international study by Pipe *et al.* the mean was nearly eight times higher than in this study (Association of American Medical Colleagues 2007, Pipe *et al.* 2009). Overall activity rates were higher also in an international review according to which 44% of physicians assist their patients with quitting, and 22% arrange follow-ups (Bartsch *et al.* 2016). Still, compared to a similar study conducted in Finland ten years previously in 2001, there was a notable raise in cessation activity (Barengo *et al.* 2003). In 2001, only 13% of Finnish physicians reported always recommending quitting even when the patient didn't bring up the subject themselves or have an illness related to smoking (Barengo *et al.* 2003.) A similar discrepancy between the attitudes and practices of physicians on smoking cessation has been noticed also in other countries (Nobile *et al.* 2014, Harutyunyan 2017).

Even though physicians seemed relatively active in bringing up the subject of smoking with their patients, this result doesn't necessarily reflect reality. There is a big discrepancy between how often Finnish smokers report that their physician has advised them to quit and how often physicians report giving such advice (Helldán & Helakorpi 2015). This could be due to a selection bias or social desirability influences, which may affect how honestly both smokers and physicians answer

questions on the subject. The latter explanation is supported by the obvious cognitive dissonance visible in the present results: almost all respondents thought that smoking is among the most significant public health issues in Finland, and that it is the physician's responsibility to try to get the patient to quit smoking, but only a minority had familiarised themselves with the local guidelines for smoking cessation, or acted according to them.

5.3.1 Common traits of physicians who deliver smoking cessation aid

Common traits of physicians active in delivering smoking cessation aid have been studied before (Association of American Medical Colleagues 2007, Pipe *et al.* 2009, Stead *et al.* 2009). It has been shown, for instance, that if a physician smokes, they are less likely to support their patient with smoking cessation (Pipe *et al.* 2009). This shouldn't be a restriction for smoking cessation in Finland, as smoking is extremely rare among Finnish physicians. According to the results presented in this thesis, only 2% of Finnish physicians smoked daily in 2012, which is globally the lowest prevalence so far recorded for physicians (Pipe *et al.* 2009). The prevalence had come down from 2006, when smoking prevalence of Finnish physicians was 6% for men and 2% for women, and from 2001, when 7% and 4% of Finnish male and female physicians, respectively, were daily smokers (Barengo *et al.* 2003, Hokkinen *et al.* 2009). There must thus be other reasons for why only 39% of Finnish smokers report that their physician has advised them to quit within the past year (Helldán & Helakorpi 2015).

In this thesis, it has been shown that being active in delivering smoking cessation aid was positively associated especially with 1) having read the local treatment guidelines for smoking cessation, 2) having confidence in one's own smoking cessation skills, and 3) previous success with helping patients quit smoking. Previous research has also shown that physicians who score low in tests measuring knowledge on smoking cessation are twice as likely to think that patients usually fail to quit (Stead *et al.* 2009). It seems apparent that finding out about the effective means of smoking cessation and actively using them on patients is followed by good results and a feeling of success, encouraging the physician to actively help patients with quitting in the future as well. This virtuous circle begins with the physician getting acquainted with effective withdrawal methods and the subject of smoking cessation. Finnish national guidelines for smoking cessation

were first published in November 2002 (Duodecim 2012). By the end of the year 2006, two-thirds of Finnish physicians had at least heard of the guidelines, and a decade later in 2012 the proportion was 82% (Hokkinen *et al.* 2009, Ylisaukko-oja *et al.* 2014). Still, even in 2012, less than one third of respondents had familiarised themselves with the guidelines either thoroughly or in outline (Ylisaukko-oja *et al.* 2014).

Finding it the physician's responsibility to try get the patient to quit smoking was also heavily associated with being active in delivering smoking cessation aid, and most respondents agreed with the claim. Attitudes on the physician's role in smoking cessation had drastically changed in 13 years: in 1999, one third of Finnish general practitioners felt that physicians don't have the right to take the initiative to inform patients about the positive or negative effects of their lifestyle, 43% felt uncomfortable informing patients about the potential risks of smoking, and one fifth felt that helping people with smoking cessation wasn't part of their job (Helgason & Lund 2002).

5.3.2 Experienced restrictions for delivering smoking cessation aid

A key aim of this thesis was to gain local information about what physicians themselves see as restrictions for smoking cessation work at their reception. Lack of time turned out to be the most common problem, reported by more than half of the respondents. In an international study from 2009, only 16% of respondents reported lack of time as one of the three most important restrictions for helping patients quit smoking (Pipe *et al.* 2009). An American study from 2006 came closer to the Finnish situation: in the study, limited time was a significant barrier for 41% of the respondents (Association of American Medical Colleagues 2007).

Lack of well-functioning treatment paths and insufficient tools, i.e. lack of knowledge in smoking cessation methods were among the most common restrictions. This was also reflected in the self-reported smoking cessation activities: physicians encouraged their patients to quit smoking, but were less active in delivering practical help to their patients. It's possible that Finnish physicians are increasingly self-critical about their smoking cessations skills: the proportion of respondents who felt that their skills and knowledge in smoking cessation were inadequate was slightly higher than ten years prior (22% vs. 15%) (Barengo *et al.* 2003). In a similar study on Finnish dentists, the most commonly reported restriction was lack of knowledge in smoking cessation methods, lack of time taking second place (Grönholm *et al.* 2017).

Overall, the most commonly reported restrictions were external and could be solved by administrative measures, while in previous studies the most common barriers have been attributed to the patient or the patient–physician relationship: patient motivation and willpower, the belief that only few smokers succeed in quitting, and especially in Finland the belief that physicians don't have the right to bring up smoking (Helgason & Lund 2002), Association of American Medical Colleagues 2007, Pipe *et al.* 2009, Stead *et al.* 2009).

5.4 Strengths and limitations

5.4.1 Studies I and II

Design

Study I used self-reported data to assess differences in primary health care utilisation according to smoking status. This approach may produce a more realistic estimate of smoking-related primary health care costs than a disease-based approach, where the smoking-attributable factor of diseases treated in primary health care utilisation is often rather conservative (Philips & Bloodworth 2009, Callum *et al.* 2010, Sung *et al.* 2011, Vähänen 2015). Also, previous studies on smoking and primary health care utilisation have typically had a higher mean age and a wider age distribution, while the present study focused on 46-year-olds alone. In study I, people who had quit smoking more than one month ago were combined into ex-smokers in order to get bigger subgroups; information about health care utilisation wasn't available for everyone who took part in the 46-year-old follow-up. A future prospect would be to further stratify these ex-smokers into recent quitters and former smokers in order to investigate the time-dependency of increased primary health care utilisation among ex-smokers in the NFBC 66.

Study II was designed to provide information on cardiovascular risk factors according to smoking status at the age of 46. The incidence of cardiovascular events wasn't studied as the number of cardiovascular events would have been very small in such a relatively young population (Vartiainen *et al.* 2016, D'Agostino *et al.* 2008, SCORE project group 2003). A longer follow-up is needed for gaining such information. From previous studies, it is known that while most clinical risk factors elevated by smoking are reversible, even a relatively short period of smoking has

some permanent effects on the human body, which can be witnessed as changes in DNA methylation (Lee & Pausova 2013, Piepoli *et al.* 2016). Whether such molecular changes are clinically relevant in terms of cardiovascular risk actualisation, a more thorough investigation on the association between cardiovascular event rates and smoking history is called for. If the NFBC 66 was to be utilised in future research on smoking-related cardiovascular risk assessment, the present sub-groups of quitters before 31 and quitters between ages 31 and 46 could be further divided according to time since quitting, time spent as smokers, and heaviness of smoking. However, it might prove difficult to gain adequately powered samples, as the different ex-smoker sub-groups used in study II were already rather small, some 200 persons each. With a decrease in sub-group size, the reliability of smoking history would be even more critical for the validity of the results – smoking status in the NFBC 66 hasn't so far been validated by biomarkers of smoking such as CO or cotinine.

Overall, the longitudinal nature of the NFBC 66 could be further utilised. The changes in risk factors between ages 31 and 46 offer prospects for future studies that could look into the effects of different adjustments – for instance, a change in BMI could be an important confounding factor for coincidental changes in blood lipids and lipoproteins.

Previous studies have suggested that if smoking has a long-term effect on blood pressure, the effect is very small (Cullen *et al.* 1998, Primates *et al.* 2001). Unsurprisingly, this study arrived at similar results. In future studies, it might be interesting to inspect heart rate as well as blood pressure (Linneberg *et al.* 2016).

Data sources

The longitudinal NFBC 66 research project stands out from many other real world data sources both qualitatively and quantitatively: it comprised originally 96% of the live-born children in the two northernmost provinces of Finland with an expected date of birth in 1966 (n = 12 058). Some loss to follow-up has happened: response rate was 67% at the 46-year follow-up. Clinical examinations have been carried out by trained research personnel, and plasma samples were analysed in a University Hospital of Oulu laboratory according to a standardised protocol. The cohort is described in more detail at <http://www oulu.fi/nfbc/node/44315>. Data on health care utilisation was self-reported, as the national patient register for primary health care had low coverage when the study took place.

Information on smoking was entirely self-reported, and wasn't validated by biomonitoring, such as cotinine or carbon monoxide measurements (Connor *et al.* 2009). Especially answers to the more specific questions on tobacco smoke exposure, such as how many daily cigarettes one used to smoke before quitting may not be very reliable (Bhandari & Wagner 2016). Due to this concern, the definition of a never-smoker didn't include the usual condition of less than 100 cigarettes smoked, but was defined as never having smoked almost daily for at least a year. Thus, the group of never-smokers may have included occasional smokers. Also, given the fact that in earlier studies some of the self-reported never-smokers or former smokers had actually been smoking to at least some extent, our results on the burden of smoking in middle-age people are most likely rather an underestimation than an overestimation of the real-life situation (Connor *et al.* 2009). The self-reported smoking prevalence in 2012 in the age group of 45–54 in Northern Finland was 17% or 26% for men and 14% or 17% for women in two Finnish studies (Borodulin *et al.* 2013, Helldán *et al.* 2013). However, definite conclusions about the validity of smoking status in the NFBC 66 should not be drawn based on this comparison, as the sample sizes were rather small in the other studies (Borodulin *et al.* 2013, Helldán *et al.* 2013). These previous studies are also susceptible to a similar response bias as studies I and II: people who are interested in their health are more likely to attend. Insights of this phenomenon in the NFBC 66 could be inspected by studying the risk characteristics at age 31 of those who later dropped out of the study.

Methods

In study I, health care utilisation results were presented as both unadjusted, adjusted for BMI, and adjusted for BMI together with education level. The adjustments affected the statistical significance of the results for some service types, but had only a small effect on the trends found: smokers used more primary health care services than never-smokers. Some previous studies have adjusted the results also for depression and mental well-being, physical activity and/or alcohol consumption – a future prospect would be to do this for the NFBC 66 as well (Izumi *et al.* 2001, Jorm *et al.* 2012, Wacker *et al.* 2013).

In study II, BMI was the only confounding factor that was adjusted for, as a high BMI is known to correlate with many habits that increase cardiovascular risk and could be expected to co-exist with smoking, such as a sedentary lifestyle, an

unbalanced diet, and excess alcohol consumption (Lahti-Koski *et al.* 2002). Some of these confounding factors have been mapped in the NFBC 66 questionnaires, but the reliability of answers to these questions was not considered as high as that of BMI from clinical examinations and education level from a national registry. If, however, this information was utilised in a future study, it could be used to assess patterns of cardiovascular risk behaviour in the cohort. This would also bring valuable information about the validity of BMI as a master adjustor for confounding cardiovascular risk behavior.

Epidemiological data shows that smoking elevates the risk of cardiovascular events more for women than for men, but the exact reasons and their significance for this phenomenon remain unclear (Jha *et al.* 2006, Rigotti & Clair 2013, Jha *et al.* 2013, Peters *et al.* 2014). In this thesis, male smokers had typically higher cardiovascular risk factors than female smokers, but statistical significance was not assessed. The relative differences in risk factors and the calculated ten-year risk of a cardiovascular event between never-smokers and current smokers were similar for both sexes. A future prospect would be to perform a sensitivity analysis for sex instead of doing all the analyses separately for both sexes as was done in this thesis; this could be done for both studies I and II. Combining the sexes would also result in bigger sub-groups according to smoking status, which might raise the statistical significance of the results. The possible differences between sexes in self-reported heaviness of smoking in the NFBC 66 at age 46 could also be investigated.

A future prospect would be to adjust the Framingham score results of study II for smoking status to inspect to which extent the two-fold elevation in estimated 10-year risk of a cardiovascular event for smokers vs. other sub-groups is due to a difference in the binary smoking status parameter, and to which extent to an elevation in the other parameters. Also, a presentation of the proportions of the NFBC 66 who exceeded recommendations for each risk factor might make public health priorities more visible.

5.4.2 Studies III and IV

Design

Similar studies with nearly identical questionnaires have been previously carried out both in Finland and other countries, enabling chronological and international comparison (Barengo *et al.* 2003, Hokkinen *et al.* 2009, Pipe *et al.* 2009). A wide spectrum of smoking cessation related items was covered, allowing thorough

analyses of both the attitudes and the practical aspects of smoking cessation in the Finnish health care system from the physicians' point of view. The cessation methods mapped are in line with the local treatment guidelines for smoking cessation, allowing interpretations on adherence to the guidelines based on reported cessation aid (Duodecim 2012).

Data sources

A link to the survey was sent to a random sample of physicians who had given the Finnish Medical Association permission to use their e-mail address for research purposes. According to statistics provided by the Finnish Medical Association, the respondents represented the Finnish medical profession very well in terms of age, sex, and hospital district (The Finnish Medical Association n.d.). This is a definite strength of the study, as previous studies on the subject have often utilised convenience samples, raising the issue of sample bias (Smith & Leggat 2007). Also, the respondents represented 5% of the entire Finnish medical profession, and 8% of specialised physicians (The Finnish Medical Association n.d.). In most studies on physicians and smoking cessation, sample sizes are rather small considering the number of active physicians in each country, resulting in questionable coverage and representability. For instance, many studies conducted in the United States of America have a sample size of some hundreds or thousands, while there are some 800 000 practicing physicians in the country (Association of American Medical Colleagues 2007, Stead *et al.* 2009). With a response rate of 15%, a possibility for some selection bias remains in this study as well: respondents who consider the subject of smoking cessation important are likely to be overrepresented in the sample.

While electronic surveys have many advantages over traditional methods, obvious limitations are a generally lower response rate and the respondents' reduced willingness to use time on the survey (Czaja & Blair 2005, Shih & Fan 2009). As previous studies on Finnish physicians and smoking cessation have been conducted by mailed paper questionnaires, a decrease in response rate was to be expected, and it was compensated by a larger number of targeted physicians. This was a successful strategy: while the response rate was lower than in previous studies, the number of respondents remained fairly similar (Barengo *et al.* 2003, Hokkinen *et al.* 2009). Still, the coverage and representability of the studies has systematically decreased due to the Finnish medical community nearly doubling in size between 1990 and 2012 (The Finnish Medical Association n.d.).

6 Practical conclusions

Alarm signals of multimorbidity in smokers already at the age of 46

In this cross-sectional study of the NFBC 66 at age 46, smokers had higher cardiovascular risk factors than never-smokers, most notably triglycerides and type 2 diabetes. The finding that 46-year-old smokers had 28% (men) or 21% (women) higher primary health care costs than never-smokers challenges previous, more conservative estimates about the smoking-attributable fraction of primary health care use. Increased visits to primary health care and elevated cardiovascular risk factors in middle age can be seen as early alarm signals of metabolic syndrome, multimorbidity and the more drastic events many smokers encounter later in life: cardiovascular events, cancer, and COPD (Taylor *et al.* 2010, Wikström *et al.* 2015).

The role of smoking prevalence in cardiovascular mortality on a population level has become more emphasised as blood pressure and lipid values have improved (Ford *et al.* 2007, Pereira *et al.* 2013, Jousilahti *et al.* 2016, Burke *et al.* 2017). Smoking was the greatest clearly detectable – and eliminable – cardiovascular risk factor in the NFBC 66 at age 46. While other risk factors were either within recommendations or slightly higher than ideal, smoking prevalence was 28% for men and 20% for women. On average, smoking reduces lifespan by 10 years, much more than hypertension does (Doll *et al.* 2004, Jha *et al.* 2013, Makridakis & DiNicolantonio 2014). This should be considered when planning and carrying out primary prevention of cardiovascular disease. In Eastern Finland, a decline in male smoking from 32% to 29% between 2008 and 2012 in the study sample was estimated to explain some 17% of the coinciding decline in coronary heart disease mortality (Jousilahti *et al.* 2016). Even seemingly small differences in smoking prevalence can thus have significant effects on public health.

Room for improvement in smoking cessation services

Smoking cessation services are a key means of primary prevention of cardiovascular disease, but half of Finnish physicians working in fields relevant to smoking cessation felt that lack of time was restricting them from aiding their patients with quitting. While Finland, according to global and European reports, is a model country in terms of making smoking inconvenient by heavy taxation and restricting where one can smoke, there is room for improvement in the treatment of smoking dependence (WHO 2017, Joossens & Raw 2017). Finnish physicians

agree: 80% were in favour of more resources being directed to smoking cessation services, and less than one in three thought that smoking cessation was at least somewhat well organised in the Finnish health care system. While physicians were fairly inactive in treating smoking dependence themselves, they still thought that patients should have access to cessation aid in the health care sector. However, treatment paths for smoking cessation were available for only some respondents, and over half of those respondents who had a treatment path felt that it was non-functional. According to WHO reports, the availability of smoking cessation services has globally improved, but not in Finland since the survey presented here took place (WHO 2013, WHO 2017). An assessment by The Association of European Cancer Leagues shows that between 2010 and 2016, the smoking addiction treatment score of Finland improved with only one point from 4 to 5 on a scale from 0 to 10 (Joossens & Raw 2011, Joossens & Raw 2017). At the same time, Cyprus and Latvia improved their treatment score by 4 points, and five other European countries increased their score by either 3 or 2 points (Joossens & Raw 2011, Joossens & Raw 2017).

Investments on smoking cessation are some of the most cost-effective actions in the health care sector (Cromwell *et al.* 1997, Vitikainen *et al.* 2006). Developing smoking cessation services would be in line with a key goal of the Finnish government: reducing health differences, which are to a significant extent due to differences in smoking habits and excess alcohol consumption (Martikainen *et al.* 2014, Finnish Government n.d.). The government seems to acknowledge this, as one of its key goals is to increase the availability of drug services (Finnish Government n.d.). Prevention-related cost-effectiveness is a hot topic in Finland at the moment, as the country is on the verge of a social and health care reform. The reform will most likely result in shifting from the current multi-payer model to a situation where most of the costs of both primary and secondary health care, as well as social and medicinal costs will in the future be covered by one payer, the state (Ministry of Social Affairs and Health n.d.). Cost effectiveness and value effectiveness of the health care sector can thus be expected to be of increasing importance. According to Finnish physicians, perceived lack of time and functional treatment paths are the most important reasons for why they are not reducing smoking-attributable health problems by offering smoking cessation aid. These are issues than can be addressed by health care administration and managers ensuring that physicians have adequate referral options and other resources in smoking cessation.

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Appendices

Appendix A: Form for reporting smoking behaviour in the NFBC 66 study
(translated from Finnish)

Appendix B: Form for reporting health care utilisation in the NFBC 66 study
(translated from Finnish)

Appendix C: Questionnaire for Finnish Physicians and Tobacco 2012 study
(translated from Finnish)

Appendix A: Form for reporting smoking behaviour in the NFBC 66 study

1. Have you ever smoked in your life?

- 1 no (*→ jump to question 45*)
- 2 yes, I started at age I____I____I

2. Have you ever smoked regularly? (= nearly daily for at least a year)

- 1 no
- 2 yes, I have smoked regularly for I____I____I years

3. If you have quit smoking, at which age did you quit?

age I____I____I

4. Do you currently smoke?

- 1 7 days a week
- 2 5 - 6 days a week
- 3 2 - 4 days a week
- 4 1 day a week
- 5 occasionally
- 6 never

5. When did you last smoke?

(If you smoke regularly, mark option 1)

- 1 yesterday or today
- 2 2 days - 1 month ago
- 3 1 month – 6 months ago
- 4 7 months -11 months ago
- 5 1 – 5 years ago, *jump to question 45*
- 6 6 – 10 years ago, *jump to question 45*
- 7 Over 10 years ago, *jump to question 45*

6. How many cigarettes on average do you smoke or used to smoke daily before you quit? (answer each question; if you don't smoke a certain product, mark 0)

- 1 filtered cigarettes I ___ I ___ I a day
- 2 other type of cigarettes I ___ I ___ I a day
- 3 pipes I ___ I ___ I a day
- 4 cigars I ___ I ___ I a day

7. Do you use moist snus or chewing tobacco?

- 1 never
- 2 occasionally
- 3 yes, regularly

8. How many hours a day do you spend in a space where you have to breath cigarette smoke caused by other people? (if none, mark 0)

I ___ I ___ I hours

Appendix B: Form for reporting health care utilisation in the NFBCS66 study

1. How many times, within the past year, have you visited:
(if none, mark 0)

In a community health centre

Physician	<input type="text"/>	<input type="text"/>	times
Nurse	<input type="text"/>	<input type="text"/>	times
Psychologist	<input type="text"/>	<input type="text"/>	times
Physiotherapist	<input type="text"/>	<input type="text"/>	times
Dentist	<input type="text"/>	<input type="text"/>	times
Oral hygienist	<input type="text"/>	<input type="text"/>	times
Other health care professional	<input type="text"/>	<input type="text"/>	times

In occupational health care

Physician	<input type="text"/>	<input type="text"/>	times
Nurse	<input type="text"/>	<input type="text"/>	times
Psychologist	<input type="text"/>	<input type="text"/>	times
Physiotherapist	<input type="text"/>	<input type="text"/>	times

Special care (= disability services, e.g. Tahkokangas service centre)

Physician	<input type="text"/>	<input type="text"/>	times
Nurse	<input type="text"/>	<input type="text"/>	times
Psychologist	<input type="text"/>	<input type="text"/>	times
Physiotherapist	<input type="text"/>	<input type="text"/>	times
Dentist	<input type="text"/>	<input type="text"/>	times
Oral hygienist	<input type="text"/>	<input type="text"/>	times
Other health care professional	<input type="text"/>	<input type="text"/>	times

Elsewhere

Hospital polyclinic	_ _	times
Private physician	_ _	times
Physician housecall	_ _	times
Private dentist	_ _	times
Private oral hygienist	_ _	times
Private physiotherapist	_ _	times
Mental health office / psychiatric polyclinic	_ _	times
Addiction treatment unit	_ _	times
Other social or health care unit where? _____	_ _	times
Natural therapist / alternative treatment provider	_ _	times

Appendix C: Questionnaire for Finnish Physicians and Tobacco 2012 study

1. Where do you primarily work?

- Community health centre
- Hospital
- Occupational health care
- Private practice (other than occupational health care)
- Administration
- Education, Research
- Other, what?

2. Which Finnish health care district do you work in at the time being?

3. How many patients per day do you see on an average basis?

4. How much time do you have for a single patient, on an average basis? (in minutes)

5. Your age?

6. Your gender?

7. Are you a specialist or a general practitioner?

8. Which field of medicine are you specialised in?

- general practice
- obstetrics and gynecology
- urology
- pulmonary disease and allergology
- cardiology
- internal medicine
- surgery
- psychiatry
- cancer
- occupational health
- other, what?

9. Do you smoke (cigarettes, cigars, or pipe)?

- No
- Yes, daily
- Yes, occasionally

10. Have you smoked regularly in some point of your life?

- No
- Yes

11. When did you quit?

- Less than 6 months ago
- 6-11 months ago
- 1-2 years ago
- More than 2 years ago

12. Do you use moist snus?

- No
- Yes, daily
- Yes, occasionally

13. What is your opinion on the following claims?

	Completely agree	Somewhat agree	Somewhat disagree	Completely disagree
Smoking is one of the most significant public health issues in Finland				
Smoking is a lifestyle choice				
Nicotine / smoking addiction is an illness				
Moist snus is harmful				
Electronic cigarettes are harmful				
Additional health care resources should be directed to smoking cessation				
Smoking withdrawal medication should be reimbursable				

14. Comments on the claims above:

15. What is your opinion on the following claims?

	Completely agree	Somewhat agree	Somewhat disagree	Completely disagree
It is the physician's responsibility to try to get the patient to quit smoking				
Smoking cessation is currently well implemented in the Finnish health care system				
Smoking cessation is currently well implemented in my own special field				
Smoking cessation is implemented better in my own special field than other fields of medicine				
My current knowledge and skills are sufficient for giving advice to patients who wish to quit				

16. Comments on the claims above:

17. In which situations do you ask your patient questions about their smoking / quitting? (You may choose multiple options)

- During the first appointment, if possible
- For the first time during later appointments
- I get back to the subject after the first time the issue has been discussed
- If the patient has an illness relating to smoking
- If the patient is pregnant
- I don't ask my patients questions about their smoking

18. How often do you go through the next procedures when discussing quitting with your patient?

(Smoking cessation is not an on-label indication for nortriptyline. However, nortriptyline has been included in this questionnaire because it is listed as a suitable drug for smoking cessation in the “Käypä hoito” guidelines.)

	Nearly always	Often	Sometimes	Never
I ask my patient how often they smoke				
I make a note of my patient's smoking status in the patient records				
We discuss the health risks of smoking				
I recommend quitting to the patient				
I recommend the patient to cut down on smoking				
I help the patient to make a plan for quitting				
I provide the patient with information on different smoking cessation methods				
I recommend nicotine replacement therapy				
I prescribe the patient withdrawal medication (bupropion, varenicline, nortriptyline)				
I refer the patient to another health care professional (e.g. a nurse, a pharmacist)				

19. Which non-pharmacological means do you use to support the smoking cessation of your patient? (You may choose multiple options)

- A follow-up appointment with a physician
- A follow-up appointment with a nurse
- A support group for smoking cessation
- Written support material for the patient
- Online support material for the patient
- A support phone line for quitters (e.g. Stumppi)
- Refer to a pharmacist
- Other, what?

20. Do you, at least occasionally, use pharmacological means (nicotine replacement therapy, varenicline, bupropion, nortriptyline) to help your patients with smoking cessation?

(Smoking cessation is not an on-label indication for nortriptyline. However, nortriptyline has been included in this questionnaire because it is listed as a suitable substance for smoking cessation in the “Käypä hoito” recommendation.)

- Yes
- No

21. How often do you use the following pharmacological means to help your patient quit smoking?

	Nearly always	Often	Occasionally	Never
Nicotine replacement therapy (band-aid, chewing gum, tablet, sublingual administration, inhalator)				
Varenicline				
Bupropion				
Nortriptyline				

22. How do the following factors affect your use of nicotine replacement therapy (band-aid, chewing gum, tablet, sublingual administration, inhalator) in smoking cessation?

	Has a significantly positive effect	Has a somewhat positive effect	Has a somewhat negative effect	Has a significantly negative effect	Cannot say
Efficacy					
Side effects and safety					
Previous experience or knowledge about the product					
Usability for the patient					
Over-the-counter vs. prescription medication					
Price					

23. How do the following factors affect your use of varenicline in smoking cessation?

	Has a significantly positive effect	Has a somewhat positive effect	Has a somewhat negative effect	Has a significantly negative effect	Cannot say
Efficacy					
Side effects and safety					
Previous experience or knowledge about the product					
Usability for the patient					
Over-the-counter vs. prescription drugs					
Price					

24. How do the following factors affect your use of bupropion in smoking cessation?

	Has a significantly positive effect	Has a somewhat positive effect	Has a somewhat negative effect	Has a significantly negative effect	Cannot say
Efficacy					
Side effects and safety					
Previous experience/knowledge about the product					
Usability for the patient					
Over-the-counter vs. prescription drugs					
Price					

25. How do the following factors affect your use of nortriptyline in smoking cessation?

	Has a significantly positive effect	Has a somewhat positive effect	Has a somewhat negative effect	Has a significantly negative effect	Cannot say
Efficacy					
Side effects and safety					
Previous experience/knowledge about the product					
Usability for the patient					
Over-the-counter vs. prescription drugs					
Price					

26. Other comments regarding pharmaceuticals used in smoking cessation:

27. How well would you say you have succeeded in your attempts to affect the smoking habits of your patients?

- Excellent success
- Rather good success
- Rather bad success
- Very bad success
- I don't try to affect the smoking habits of my patients
- Cannot say

28. Open text field:

29. Which factors restrict the conversation you have with your patient on smoking cessation? (You may choose multiple options)

- I am not used to discussing smoking
- I don't want to intrude on the patient's privacy
- There is no way for the physician to have a significant effect on the patient's smoking habits
- Lack of time
- Insufficient treatment path
- Insufficient tools
- Other factor, what?
- There are no restricting factors

30. How do the practical aspects of referring the patient to a smoking cessation professional work in your organisation?

	Yes	No
You can refer the patient within your own organisation		
You can refer the patient to another organisation		
There is a treatment path for smoking cessation in your organisation		

31. If there is a treatment path for smoking cessation in your organisation, do you think it works?

- Yes
- No

32. If you refer your patients to a smoking cessation professional, where is it typically to?

33. Which sources have you used to gain information on smoking cessation? (You may choose multiple options)

- Discussion with colleagues
- The Finnish “Käypä hoito” treatment guidelines
- International treatment guidelines
- Scientific journals
- Educational events organised by the pharmaceutical industry
- Educational events organised by others
- Online health care databases (e.g. Terveystieto)
- Web pages provided by the pharmaceutical industry
- Other than medical web pages (e.g. Google, Wikipedia)
- Medical sales presentations

34. The following questions (34-37) concern the Finnish “Käypä hoito” treatment guidelines for smoking cessation. The recommendation has been updated on January 19th 2012. How have you familiarised yourself with the guidelines?

- I have familiarised myself with the guidelines thoroughly
- I have familiarised myself with the guidelines in outline
- I have browsed the guidelines
- I have heard of the guidelines, but haven’t familiarised myself with them
- I am not familiar with the guidelines

35. Have the guidelines changed how you treat your patients?

- Yes
- No

36. How would you describe your use of the “Käypä hoito” treatment guidelines for smoking cessation?

	Completely agree	Somewhat agree	Somewhat disagree	Completely disagree
I follow the “Käypä hoito” guidelines				
Following the “Käypä hoito” guidelines yields good results				
It is easy to follow the “Käypä hoito” guidelines in my daily work				

37. Other comments concerning the “Käypä hoito” guidelines or this questionnaire:

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- IV Keto J, Jokelainen J, Linden K ym. Yleisläketieteen erikoislääkärien kokemat esteet tupakasta vieroituksessa. *Yleislääkäri* 2015;4:23-26.

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- I429. Männikkö, Niko (2017) Problematic gaming behavior among adolescents and young adults : relationship between gaming behavior and health
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- I440. Hagnäs, Magnus (2018) The association of cardiorespiratory fitness, physical activity and ischemic ECG findings with coronary heart disease-related deaths among men
- I441. Huhtaniska, Sanna (2018) The association between antipsychotic and benzodiazepine use with brain morphology and its changes in schizophrenia
- I442. Sundquist, Elias (2018) The role of tumor microenvironment on oral tongue cancer invasion and prognosis

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