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LONGITUDINAL ANALYSIS OF TRENDS IN SMOKING HABITS AND IMPACT OF CHANGES IN SMOKING AND BODY MASS ON LUNG FUNCTION

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CONTENTS

ABBREVIATIONS

ASSAD, Australian Secondary Students'' Alcohol and Drug Survey

BHS, Busselton Health Study

BMI, body mass index

CDC, center for Disease Control and Prevention

COPD, chronic obstructive pulmonary disease

ECRHS, European Community Respiratory Health Survey

FEV_1, forced expiratory volume in 1 second

FVC, forced vital capacity

GBD, global Burden of Disease

GEE, generalised estimating equations

MPOWER, monitoring, protecting, offering, warning, enforcing, raising

SD, standard deviation

TAHS, Tasmanian Longitudinal Health Study

WHO, World Health Organization

WHOFCTC, World Health Organization Framework Convention on Tobacco Control

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SUMMARY

The tobacco epidemic has been the driving force to establish the foundation of the battle against tobacco use and effective public policy measures using simple preventative and targeting strategies against nicotine dependence. However, smoking is still a widespread phenomenon at various forms in recent years and the assessment of smoking trends and behavioral changes will reflect the attributes of impacted age groups to identify smoking prone populations and lead to strategize preventative and recovery systems.

We analyzed the long-term trends in smoking initiation and cessation in order to identify age- and gender specific changes in Australian population over a 70 year timeline, utilizing the data from two longitudinal studies on the general population from the Tasmanian Health Study (TAHS) and the Busselton Health Study (BHS). To determine the effect of both smoking status and weight change on lung function in the general population, we also performed an analysis on lung function outcomes modulated by smoking behavioral changes relative to weight gain over 20 years in the European Community Respiratory Health Survey (ECRHS).

We estimated trends in the rates of smoking initiation (number of incident smokers divided by total time at risk) between 1920 and 1989, by sex and age groups (11-15, 16-20, 21-35 years). The rates of smoking initiation during young adolescence (11-15 years) increased steeply between 1925 and 1980 in females. After being relatively stable, they slightly increased after the 70's also among males. In the same period, the rates showed a completely different trend between males and females during late adolescence (16-20 years): initiation rates in males decreased steeply, whereas they steadily increased in females. Smoking initiation during late adolescence peaked in the '40s for males and decreased afterward, while in females initiation increased until the mid-'70s. These results reflect the shift of smoking trend from boys to girls among teens, and they highlight a sharp increase in smoking initiation among Australian female adolescents during the '70s and '80s that is consistent with information available from Europe.

Our findings also showed that quitters with high weight gain had faster lung function decline compared to quitters with moderate weight gain at older

ages, but not at younger ages, highlighting the importance of early smoking cessation and weight control among quitters.

Using a historical perspective, this longitudinal study documents early signs of the successful implementation of tobacco control measures in the Australian population. It underlines the importance of encourging positive awareness and implementing strategies for early smoking cessation, parallel to promoting prevention and stronger intervention strategies in youth. In addition, empowering and monitoring active and healthy living can improve the outcomes of smoking cessation on lung function trajectories and mitigate the future risk of diseases like asthma and COPD.

1 INTRODUCTION

One of the top historical public health threats of the last century is the tobacco epidemic, also defined as a global non-infectious disease. It has been the driving force to establish the foundation of the battle against tobacco use as a harmful substance.[1]

Tobacco consumption is a challenging topic which is not limited to demographic boundaries with race, gender, level of education, including socio - economic and - environmental diversity regardless of prevention measures. The level of tobacco consumption still shows discrepancies among many countries and relative ethnic backgrounds.[2] In spite of the successful decline in tobacco consumption through public health policies and education, smoking is still the leading cause of avoidable mortality and morbidity, and the compelling modifiable risk factor predominantly in respiratory, cardiovascular, obesity associated diseases as well as a wide range of cancer types according to the Center for Disease Control and Prevention (CDC)[3–7].

Tobacco use is one of the highest global risk factor and it is classified as a substance use related to the cause of indirect deaths among alcohol and addictive substances / illicit drugs (Figure 1). [8] Although the global decline of tobacco smoking demostrates the success of preventative and regulatory policies in public health affairs, first- and second-hand smoking, including chewing tobacco products, are still attributed as the leading worldwide risk factor out of twenty, according to the analysis of Global Burden of Disease, Injuries, and Risk Factor Study (GBD) for 195 countries and territories from 1990 to 2015 (Figure 2).[9]

Figure 1. https://ourworldindata.org/smoking

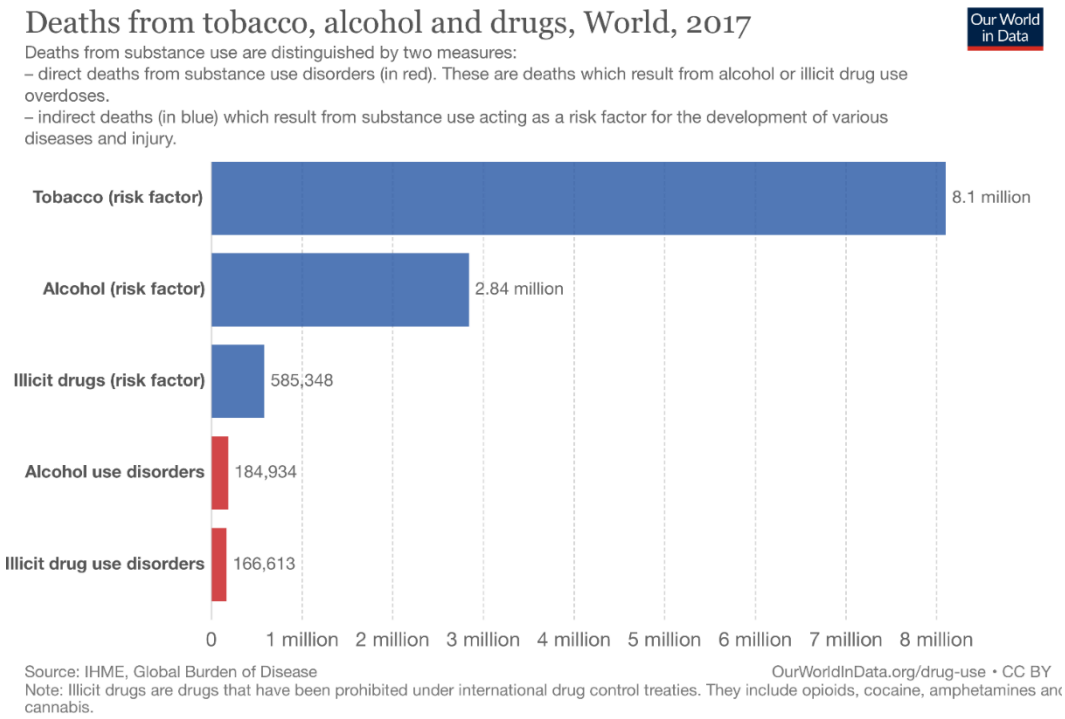
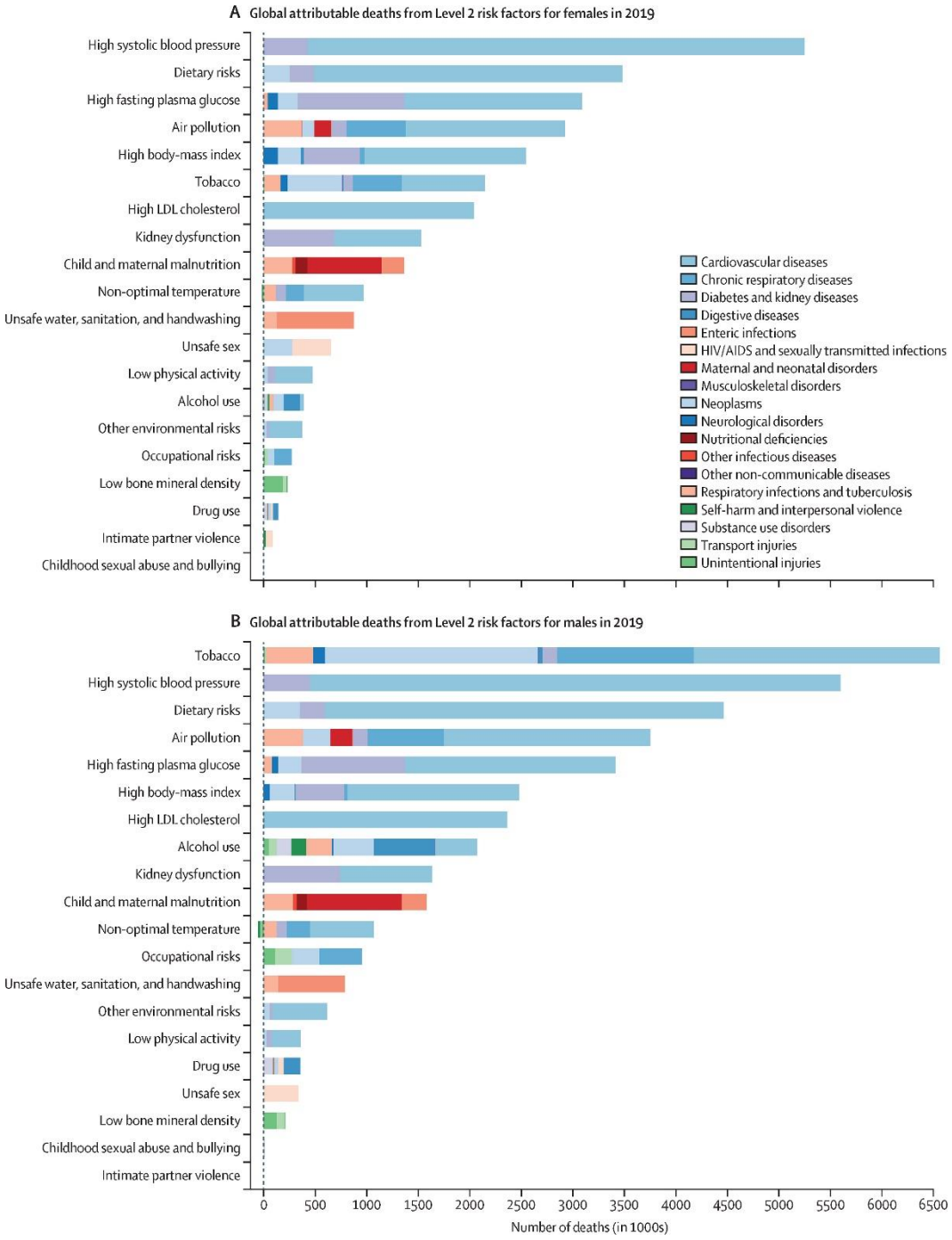


Figure 2. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019



The global prevalence of tobacco consumption was 23.6% in 2018.[10] Tobacco consumption is one of the highest global risk factor and cause of deaths (Figure 1 and Figure 2).[6] The World Health Organization (WHO) reported that 100 million people died worldwide because of the tobacco epidemic in the 20th century, although the premature death rates have successfully decreased.[11] The mortality risk of one billion people is an unprecedented situation in the 21st century. These deaths could be prevented if stringent measures, intervention tools, support and management policies build up against tobacco associated products.[12] In addition, the hidden costs of tobacco associated consumption on health care expenditure can be decreased.[13] Tobacco is still the second globally highest death risk factor.[14]

Monitoring and understanding the trends of tobacco consumption over time and across populations have been the pillars of the WHO organization through the Framework Convention on Tobacco Control (FCTC). WHO implemented one of the most effective guidelines for intervention and prevention, called **MPOWER (M**onitoring, **P**rotecting, **O**ffering, **W**arning, **E**nforcing, **R**aising), which includes six proven tobacco control measures.[15] These measures are:

1. **Monitoring:** It is a forefront application and surveillance to collect and record tobacco product consumption and to facilitate data collection at local and national levels. The criterion includes how recent the data is and whether the data covers the entire population as well as population groups by age, gender, and ethnic backgrounds.
2. **Protecting:** The execution of governmental and public regulations at all levels of implementation of health policies and the establishment of community programs to restrict smoking trends using strong plans and strategies and to provide smoke free air environments at public, work and social places, such as schools and hospitals including at home.
3. **Offering:** To encourage smoking cessation for individuals, provide treatment and therapeutical medical applications through the health care system.

4. **Warning:** To urge individuals towards a more reasonable behaviour change using strong terms and shocking images. Pictorial warnings are strategically placed on cigarette packages. Because most smokers are not fully aware of the health risks related to tobacco consumption.
5. **Enforcing:** To impose inclusive bans and preventative adds against tobacco consumption on all communication tools, multimedia settings, social and public settings.
6. **Raising:** To , Tobacco excise taxes and increase of cigarette prices are mandated to downregulate demand of tobacco consumption and reduce the rates of second hand smoking.

The MPOWER strategies have proven to be successful worldwide, as shown by the declining trend in tobacco use documented in the WHO global reports on smoking since the first edition in 2007. [16]

As regards Australia, The Government Department of Health have been described as a World Leader in tobacco control due to its early adoption of policies and health related initiatives, which have resulted in a long term decline in smoking prevalence.[10,16–18] The present thesis will address the long term trends in smoking initiation and cessation shaping the tobacco epidemic history in Australia, using 70 years of retrospective data. In addition, it will assess the impact of changes in smoking behaviours and weight gain on lung function trajectories among adults in the frame of the Ageing Lungs in European Cohorts (ALEC) study.

1.1 DEFINITION AND HISTORY OF TOBACCO

The genus Nicotiana, a member of the plant family Solanaceae, is characterized by about 100 species and sub-species widely distributed throughout the World. Nicotiana Tabacum and Rustica species are the most widely used species of tobacco production.[12]

First signs of use of tobacco were found in the American continent although knowledge about origin of tobacco use has varied historically.[19] It has been suggested that tobacco is cultivated since 15,000 BC in the American continent [20] and utilized as real and mystical qualities was offered to the gods and

used in religious ceremonies by native americans.[21] After the discovery of the American continent in the 14th century, tobacco was spread to the entire continent of American, and then to Europe. Tobacco first reached Spain and Portugal in Europe, and then Russia and the Middle East.[22–24] The French ambassador Jean Nicot, who also gave his name to nicotine substance, introduced tobacco as a medicine in the palace of France in the fifteenth century.[20] Tobacco was also introduced to Far Eastern countries by Spanish and Portuguese merchant ships in the same century.[25]

Although tobacco was widely used in Europe and other continents as various products such as cigarettes, cigars, pipes and shisha, serial production of cigarette as a tobacco product first has been started in England in the 18th century.[20] Cigarettes are the most widely used among tobacco products, although different forms of tobacco related devices, broadly referred to as electronic cigarettes (vape pen, e-Hookah, Hookah pen) have emerged as alternatives to traditional products.[26,27] The use of thids new array of products is recognized to be in the rise among both adults and adolescents.[28–30]

1.2 CAUSES OF SMOKING INITIATION

The relationship of psychological, physiological, social and environmental factors that influence smoking behaviour and their link to tobacco consumption is still examined in general sub populations using etiological studies.[31] Exposure to smoking and smoking initiation have several socio-cultural and behavioural playgrounds for both adult and young populations. Most smokers start to smoke during adolescence, which is a crucial time period in a person's life span and leads to various health risk behaviors.[32] Despite the persuasive advertisements and promotional strategies on smoking behaviour, family and social influences are often important factors determining who starts smoking, who gives up, and who continues. These factors have an impact on smoking behaviours.[33]

Young people, who are sensitive and open to the promotion and advertisements of new products, are one of the most important target groups of cigarette producers and sellers.[34] Cigarette companies used to provide messages

using the printed and electronic press, as well as movie series aimed at young people, although this type of advertisement is forbidden at present in most countries. Although the adverse consequences of smoking are well known, several aspects related to this habit are attractive for the youth, including social acceptance from older peers. As a consequence, most adolescents are prone to experiment with smoking without realising that they can become nicotine addict after smoking as few as 100 cigarettes (five packs).[35]

The number of friends who smoke is the common risk factor associated to cigarette use. In other words, the greater the numberof friends who smoke, the more likely it is that a non smoker will be come a smoker.[33] Experimentation with cigarettes usually starts during junior high school and it gradually turns into a regular smoking pattern that typically occurs in the early years of high school.[36] Especially among girls cigarette smoking initiated before junior high school has also been correlated with psychological problems.[37] Smoking cigarettes is frequently perceived as a way to reduce body weight among young and adult women.[38] In addition to weight control and suppression of appetite, a number of studies demonstrates that the changes in endogenous sex hormons are also associated with smoking.[39]

Smokers believe that smoking modulates levels of arousal and controls their mood. It is thought that smoking improves concentration, reaction time, and the performance of certain tasks. Smoking cessation causes withdrawal symptoms such as irritability, a depressed mood, restlessness and anxiety. Relief from withdrawal symptoms is probably the primary reason for continuing smoking, although smokers may believe that smoking itself is able to enhance their performance and heighten their mood.[40,41]

1.3 CAUSES OF SMOKING ADDICTION

Addiction is a complex condition, defned as a compulsive seeking, inability to stop consuming a chemical, drug, or to perform an activity even though it causes harmful consequence. Nicotine is the known addictive component of tobacco smoke which induces pleasure and reduces stress and anxiety.[40] It is metabolised quickly, causing blood levels to fall rapidly after dosing, although, nicotine promotes the resting metabolic rate and energy metabolism.[42] People who metabolise nicotine more slowly, and therefore maintain more constant blood levels, tend to be less heavily addicted.[43]

Adolescence is a phase of growth and a time of developmental changes of body which encompasses ages from 10 to 19, and it is defined as the transition period from childhood to adulthood. The brain development continues throughout adolescence,. In parallel, puberty also takes place between age 9 to 14 for girls and age 11 to 16 for boys; pubertal hormones are involved in cognitive and emotional behavioural changes while the maturation of subcortical limbic structures is also affected.[44] The prefrontal cortex of human brain is the last region to mature during adolescence and it is in charge for decision making and involved in attention performance.

Smoking affects both adolescents' and adults' social behaviour. However, the lack of mature cognitive control is a key setback among teens that makes it harder for them to take control of consumption rates, compared to adults, thus creating potential risks for health and mental issues in the future.[45–47] There is evidence that smoking affects changes in synaptic plasticity, which is very important for learning and memory, and that it increases the risk of developing learning difficulties.[48] Research has not yet shown concrete biological factors involved in smoking initiation and addiction contributed genetically and physiologically.

1.4 HARMFUL SUBSTANCES IN CIGARETTES

The tobacco plant belongs to the nightshade family and its leaves are utilized in consumable products once dried and fermented. Tobacco contains a variety of natural substance such as nicotine, nitrosamines, aromatic amines, polycyclic aromatic hydrocarbons, menthol, acetone, ammonia, glycerol, propylene glycol naphthalene, arsenic [14].

Nicotine is classified as an alkaloid. Altough it has not yet proven direct cause of disease and/or cancer, nicotine has an essential role in smoking addiction.[40] Once nicotine is absorbed into the blood stream, adrenal gland and central nervous system are triggered for the expression of a number of hormones, such as adrenaline, which stimulates physiological activities such as heart rate and blood pressure, as well as dopamine, which activates the rewarding behaviour circuit in the brain. Through inhalation of smoke, nicotine is delivered to the brain much more quickly than by other routes of administration: a high concentration arterial bolus of nicotine reaches the brain within 10-16 seconds after each inhalation, which is faster than by intravenous injection.[43] Delivery of repeated doses to the brain is the cause of cigarette addiction.[43]

There are more than 600 ingredients in a cigarette, and around 7000 chemical compounds are generated when it is burned.[40] These substances can be transferred to smoke at the typical combustion temperatures of a cigarette: the temperature of the burning cone can reach up to 900 °C in a cigarette, and the median temperature along the rod is 600 °C. These compounds cause symptoms and disorders in addition to the addictive element of nicotine. Most of the harm correlated with tobacco smoking is owing to the combustion process and exposure to smoke and digestion process.

Carbon monoxide arises from combustion of various tobacco components such as starch, cellulose, sugar, organic acids, esters and a result of the thermal decomposition. Tobacco smoke inhaled consists of mainstream and side-stream. The mainstream includes 5 to 22 mg of carbon monoxide per one cigarette, whereas side-stream smoke includes 9 to 35 mg per cigarette.[49] Carbon monoxide is a very dangerous blood poison.[50] It leads to a disruption in the exchange of

oxygen between blood and endothelial cells through the lungs and creates a stable complex with hemoglobin (carboxyhemoglobin).[51,52]

A number of other toxicants such as nitrogen oxides, acrolein, hydrogen cyanide are known to be present in tobacco. Prominent ones among them are the respiratory irritants ammonia, formaldehyde, and sulfur dioxide. Deposition of irritant agents also shows carcinogenic effects following inhalation of cigarette smoke.[53] Studies have shown that several chemical components of tobacco smoke, including benzene, polonium-210, and vinyl chloride, are carcinogenic in both humans and experimental animals.[54,55] At cellular and molecular level, they cause cell transformations, mutations, and other genetic damage both *in vitro* and *in vivo*.

1.5 HEALTH PROBLEMS CAUSED BY SMOKING

It has been well documented that smoking tobacco products is associated with increased risk or greater severity of respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD), as well as infectious lung diseases such as pneumonia and tuberculosis.[56,57] Smoking increases morbidity and mortality rates by affecting all systems including respiratory, circulatory, gastrointestinal, central and peripheral nervous systems, excretion, hematopoietic and reproductive system.[58–60] Smoking during adolescence shows impact on lung capacity in future, and it increases the probability of development of several lung associated diseases. Second hand smoke has also been related to lower respiratory infections.[61]

The negative effects of smoking on human health were first noticed in the 1930s, when the increase in population smoking was accompanied by alarming disease trends. The highest lung cancer rate in the world was seen in the United Kingdom, rising five times faster than rates for all other cancers in 1930. This leaded to the first scientific studies linking smoking to lung cancer. Five case-control studies testing the hypothesis of smoking as a putative causal factor of lung cancer , this hypothesis were published in 1950.[25,62]

Ernst Wynder showed that cigarette tar caused tumors on the backs of mice in 1953, later on the following year Richard Doll and colleagues

documented that the risk of lung cancer greatly increased among smokers relative to comparable nonsmokers.[63] The growing scientific consensus regarding the relationship between smoking and lung cancer led to the 1962 Royal College Report in the United Kingdom and to the first Surgeon General's Report in the United States in 1964.[58,64] These pivotal documents have concluded that smoking is causally associated with lung cancer, and subsequent reports outlined a long list of diseases caused by smoking. The 1990 Surgeon General's Report focused on the topic of smoking cessation. It documented that successful cessation of tobacco consumption resulted in a reduction in the burden of all smoking-related diseases and was beneficial in lowering mortality at any age. The latest reports documented concerns about the featured smoking devices for nicotine consumption, such as e-cigarettes and vapes.[3,18,59,65]

1.5.1 THE EFFECT OF SMOKING ON LUNG FUNCTION

Mounting evidence from clinical evaluations showed that smoking directly affects the respiratory system and that tobacco consumption is the most common preventable cause of respiratory tract associated disease, symptoms and consequences.[66] Respiratory function testing can demonstrate impaired respiratory function before clinical symptoms become evident, and its results can be used to prevent or reduce the incidence of respiratory diseases.[67–69] Spirometry is a functional assessment of lung capacity and it is a physiological test that measures how an individual inhales or exhales volumes of air as a function of time.[68]

Several studies have looked at the general effects of smoking on the respiratory mechanism among smokers.[14] Beck and colleagues presented the analysis of mean residual lung function by smoking status, sex, and age almost four decades ago. Results indicated a progressive loss of lung function with advancing age in males and females in all smoking phase. Moreover, these age-related trends were related to the amount of consumption.[70] Gold and colleagues have also shown that cigarette smoking is associated with evidence of mild airway obstruction and gradual decline of lung function on forced vital capacity (FVC) and forced expiratory volume in the first second (FEV_1) in adolescents.[71] Rao et al. reported that the average FEV_1 and FEV_1 / FVC values were lower in smokers

than non-smokers in their study.[72] In addition, Sato et al. concluded that smoking was associated with a faster decline in FEV_1, while smoking cessation tended to result in a slower decline in FEV_1.[73] These studies showed significant differences between smokers and non smokers, with a consistent trend for reduced lung function in smokers.

1.5.2 THE EFFECT OF SMOKING ON OBESITY

The effects of nicotine on the digestive system should not be ignored. Smoking was found to be associated with obesity, which is one of the major risks that individuals face during their life.[15,74–76] However, understanding the relationship between smoking and obesity is quite complicated. The idea that cigarette smoking is helpful in controlling body weight has been part of popular/social culture for many years. It has been shown that nicotine reduces body weight by enhancing the resting metabolic rate and suppressing food consumption.[77] Although most studies show a negative relationship between smoking and body weight, it has been reported that cigarette smoking has a minimal impact on weight control among teenagers and young adults.[78]

Concerns about weight have a significant effect on the decision to start smoking and quit smoking especially among women[79] and fear of gaining weight has been cited as a reason for relapse among ex-smokers.[80] Although current smoking is often associated with lower body mass index (BMI), heavy smoking has been found to be associated with higher BMI.[77,79–81]

2 AIM

The assessment of smoking trends and behavioral changes will reflect and monitor the attributes of impacted age groups to identify smoking prone subgroups of the population and may influence decision makers to strategize planning of preventative and recovery public health policies. In addition, it is important to examine the complex interactions between smoking behaviours and weight gain in relation to diseases characterised by an accelerated lung function decline, such as chronic obstructive pulmonary disease and asthma. We believe it will also provide insights for comorbidity with major lung function and tobacco/nicotine consumption associated disorders.

In these longitudinal studies, we strategically pursued two objectives **(i)** to examine the long-term trends in smoking initiation and cessation in order to identify age- and gender specific changes in the Australian population over a 70 years time line in the **T**asmanian **H**ealth **S**urvey (**TAHS**) and **B**usselton **H**ealth **S**urvey (**BHS**), and **(ii)** to assess whether lung function outcomes are modulated by smoking behavioral changes and weight gain status among subjects aged 20-67 years in the **E**uropean **C**ommunity **R**espiratory **H**ealth **S**urvey (**ECRHS**). The analysis originates by the work from Dr. Gabriela Peralta and colleagues, Barcelona Institute for Global Health (ISGlobal), Spain, regarding lung function trajectories in relation to body mass index and weight gain status in adults.[82] In the present study, using information available from the same cohort, I looked into how a range of smoking behaviors affect lung function decline during the life time of participants, and whether weight change modulates this relationship.

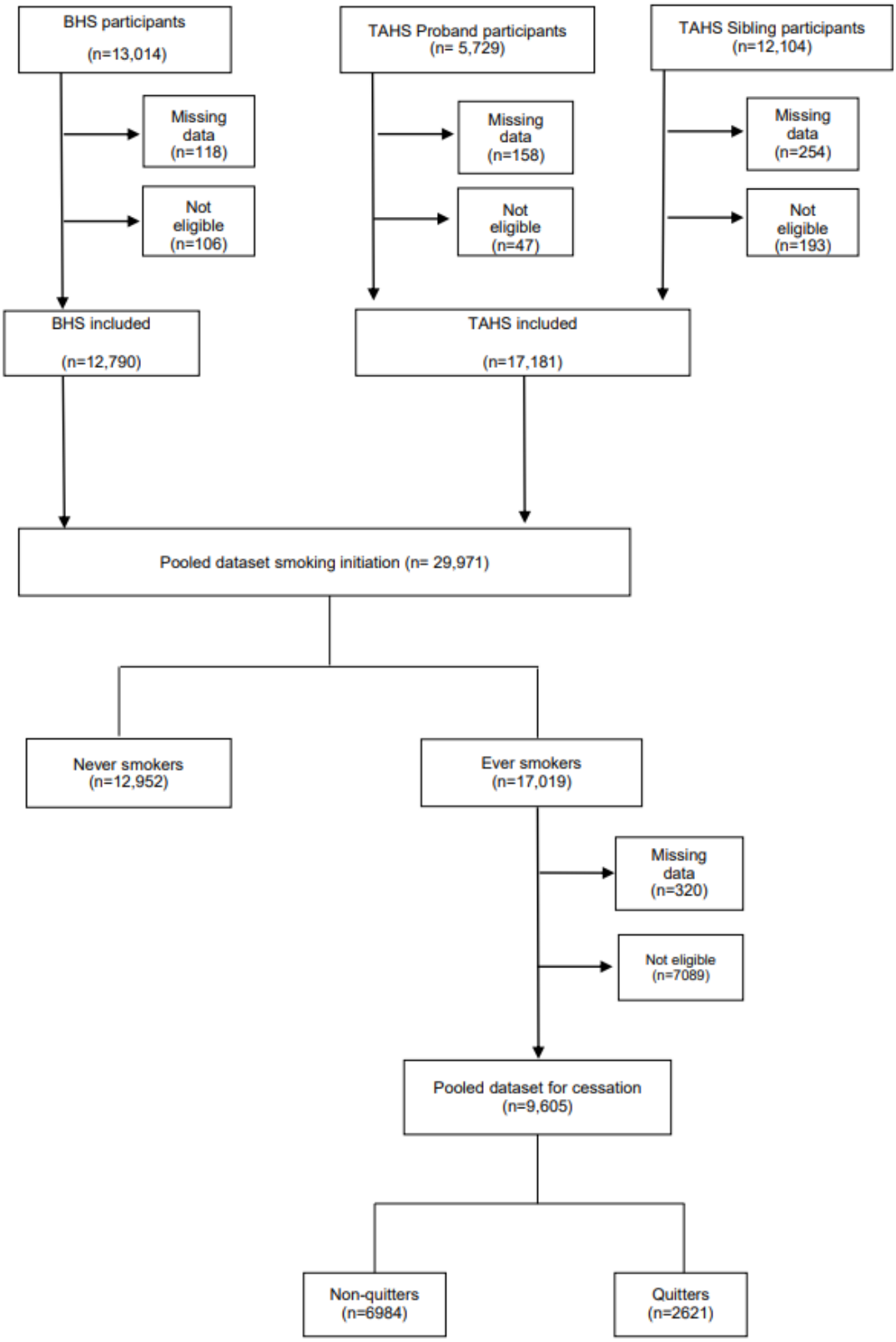
3 TRENDS IN SMOKING INITIATION AND SMOKING CESSATION IN AUSTRALIA OVER 70 YEARS

3.1 STUDY DESIGN AND POPULATION

We obtained data from two longitudinal studies on the general population in Australia. The Tasmanian Longitudinal Health Study (TAHS) investigated all the seven years-old children attending schools in the state of Tasmania in 1968 (the probands cohort) and their siblings.[83] We obtained data on 5,729 probands (participation rate 78.4%) and 12,104 siblings (participation rate 71.6%) who took part in the follow-up studies conducted in 2002 and 2007, respectively. While most subjects (70%) were still living in Tasmania at the time of the follow-up, part of them had moved to Australia (mainly to the eastern coast).[83]

The Busselton Health Study (BHS) comprises a series of cross-sectional surveys undertaken in the shire of Busselton, Western Australia.[84,85] We obtained data from eight time points, namely five surveys conducted between 1966 and 1981 on people aged ≥18 (n=3,394–4,006 subjects per survey), one survey conducted in 1987 on people aged ≥65 (n=1,117), and one survey conducted in 2010-15 on people aged 46-69 (n=5,107). Participation rates ranged from 54% to 91%. Two further waves in 1990 and 2005-07 were not included because they used questionnaire items on smoking that were not comparable to the other waves. For both original studies ethical approval was obtained from the relevant ethics committee. All procedures have conformed to the principles embodied in the Declaration of Helsinki.

Figure 3. Flowchart of BHS and TAHS participants



3.2 DATA ON SMOKING

For TAHS, we derived smoking status from the question "In your lifetime, have you smoked at least 100 cigarettes or equal amounts of cigars, pipes or any other tobacco product?". Age at initiation were based on question "How old were you when you started smoking?" (Table 1).

Table 1. Questionnaire items on smoking.

Study	Smoking Status	Age at initiation	Age at cessation
BHS 1966	Non-Smoker / Ex-Smoker / Smoker ?	Age starting smoking ?	Age ceased smoking?
BHS 1969	Are you a Non-Smoker ( ) Ex-Smoker ( ) Smoker ( )	At what age did you start smoking?	At what age did you stop smoking for good?
BHS 1972 BHS 1975	Which of the following best describes your smoking habits? Non-Smoker ( ) Cigarette Smoker ( ) Ex-Smoker ( ) Pipe Smoker ( ) Cigar Smoker ( )	If applicable, age started	If applicable, age ceased
BHS 1978 BHS 1981 BHS 1987	Have you ever smoked at least one cigarette per day for as long as one month? No ( ) Yes ( ) Do you now smoke at least one cigarette per day? No ( ) Yes ( )	How old were you when you first began to smoke at least one cigarette per day?	How long ago is it since you last smoked at least one cigarette per day?
BHS 2010	Have you ever smoked cigarettes? No ( ) Yes ( ) Do you currently smoke manufactured or hand-rolled cigarettes? No ( ) Yes ( )	At what age did you start smoking?	How old were you when you last stopped smoking?
TAHS PROBANDS TAHS SIBLINGS	In your lifetime, have you smoked at least 100 cigarettes or equal amounts of cigars, pipes or any other tobacco product? NO/YES Do you currently smoke (within the last 4 weeks)?	How old were you when you started smoking?	How old were you when you stopped smoking?

For BHS, subjects who had participated in more than one occasion were only considered once, using *a priori* the first information available to identify age at initiation, and the last information available to identify cessation.[86,87] Slightly different types of questions were available to define smoking status and age at initiation/cessation at distinct study waves (Table 1).

We observed a fair consistency of initiation reported at consecutive study waves regardless of the items used (Table A2). We also found that defining age at smoking uptake using similar questions at consecutive study waves provided consistent results (Table A3).

3.3 STATISTICAL ANALYSIS

We conducted separate analyses for males and females and deleted list wise subjects with missing information on smoking status or age at initiation. We calculated rates of smoking initiation (per 1000/year) retrospectively from childhood to the most recent assessment, as the ratio between the number of incident (new) smokers and total time at risk (person-years). We considered subjects at risk from age 11 to age at initiation, age at the last study, or age 35, which ever came first, since only a minority of subjects reported to uptake smoking outside this age range. We excluded life-long never smokers from the analyses.

We reported crude rates of smoking initiation by decades over the periods 1910–1999, for TAHS and BHS separately, and using the pooled dataset. The analysis of smoking initiation was conducted on all ages combined, and for three separate age groups, which we refer to as young adolescents (11–15 years), late adolescents (16–20 years), and young adults (21–35 years).[86]

We estimated smoothed trends in smoking initiation (with 95% confidence intervals) using generalized linear models and a negative binomial/Poisson outcome distribution, a logarithmic link function, and an offset for log person-years. We modelled period (time) using natural splines with equally spaced inner knots. We selected the number of knots that provided the best fitting according to the Bayesian Information Criterion (BIC). We optimised each analysis by

restricting the period to the years with more than 100 person-years at risk. We adjusted for study group (TAHS probands, TAHS siblings, BHS), age, and age^2 (to account for non-linearity). We performed the statistical analyses using STATA 16 software (Stata Corp. College Station, TX, USA).

3.4 RESULTS

The proportion of women among BHS participants increased in more recent survey waves, ranging from 50.8% in 1966 to 54.8% in 2005-2010 (Table A1). Considering survey waves targeting a similar age range (1966 to 1981), there was a declining trend in the proportion of smokers (from 53.1% to 47.2%) as well as an anticipation of mean age at initiation (from 19.7 to 18.7 years-old). Overall, 13,014 subjects took part in at least one BHS wave (Figure A1), and 2,486 (19.1%) of these individuals participated in the study at multiple time points.

After excluding participants with missing data on smoking status or age at initiation, we included 12,790, 5,524, and 11,657 subjects from BHS, TAHS Probands, and TAHS Siblings, respectively. Figure S1 illustrates the number of subjects contributing data at each BHS wave and in TAHS cohorts. The pooled dataset for the analysis on smoking initiation included 29,971 subjects. Of these, 15,151 (50.6%) were women. Median age was 49 years (Table 2).

Table 2. Characteristics of participants from the general population, who took part in BHS, TAHS Probands and TAHS Siblings. [a]

Study group	BHS [a]	TAHS Probands	TAHS Siblings	Overall
Subjects (n)	12,790	5,524	11,657	29,971
Women (%)	6,817 (53.3)	2,708 (49.0)	5,626 (48.3)	15,151 (50.6)
Birth cohort, year (median, min–max)	1945 (1873-1965)	1961 (1960-1962)	1959 (1936-1968)	1957 (1873-1968)
Age, year (median, min–max)	56 (16-98)	43 (41-45)	49 (39-71)	49 (16-98)
Ever smokers (%)	6,942 (54.3%)	3,261 (59.0%)	6,816 (58.5%)	17,019 (56.8%)
Age at initiation, year (mean±SD)	18.5± 5.7	16.5±3.7	16.6±3.6	17.4±4.7
Total years at risk for initiation (age range 11–35 years)	195,996	77,717	165,646	439,359
Quitters (%)	1,010 (30.7%)	457 (21.7%)	1,154 (27.4%)	2,621 (27.3%)
Age at cessation, year (mean±SD)	43.1±4.4	39.7±2.2	42.2±4.0	42.2±4.1
Total years at risk for cessation (in age range 36–50 years)	34,617	15,296	37,455	87,368

[a] n.(%) of subjects with characteristic or mean±SD.

Smokers were 17,019 (56.8%) and mean age at initiation was 17.4 (SD, 4.7) years. The total time at risk for smoking initiation was 439,359 years.

Table 3. Crude rates of smoking initiation and person-years at risk for males and females, by age group (1910–1999). [a]

	Males		Females	
Age group (years)	Rate (per 1,000/year)	Person-years	Rate (per 1,000/year)	Person-years
11-12	18.7	29,446	9.7	30,109
13-14	53.9	28,022	33.2	29,297
15-16	127.1	24,110	89.6	26,676
17-18	123.9	18,215	98.9	21,899
19-20	61.8	14,406	46.0	18,176
21-22	33.7	12,630	20.2	16,607
23-26	13.3	23,355	10.1	31,359
27-30	6.2	22,114	6.1	29,895
31-35	1.7	26,682	2.3	35,868

[a] calculated using the pooled dataset (TAHS + BHS)

Over the period 1910–1999, rates of smoking initiation were the highest at ages 15–16 for males (127.1 per 1,000/year) and ages 17–18 for females (89.6 per 1,000/year) (Table 3).

Table 4. Crude rates of smoking cessation and person-years at risk for males and females, by age group (1930–2005). [a]

	Males		Females	
Age group (years)	Rate (per 1,000/year)	Person-years	Rate (per 1,000/year)	Person-years
36-37	21.3	10,085	17.8	8,047
38-39	26.6	9,522	23.3	7,698
40-41	41.7	8,585	42.2	7,011
42-43	31.8	7,148	25.7	5,684
44-45	35.5	5,071	28.9	382
46-47	24.9	3,884	24.8	2,858
48-50	43.1	4,198	46.5	2,926

[a] calculated using the pooled dataset (TAHS + BHS)

Crude rates of initiation for males and females are reported in tables 5 and 6, respectively. For each age group and period combination, TAHS and BHS provided consistent rates, which supported data pooling.

Table 5. Crude rates of smoking initiation per 1000/year (and person-years at risk) in males, by age group, cohort and period. [a]

	Age 11-15			Age 16-20			Age 21-35		
	BHS	TAHS	Pooled	BHS	TAHS	Pooled	BHS	TAHS	Pooled
1910-1919	42.2 (2,014)		42.2 (2,014)	148.8 (773)		148.8 (7,73)	61.9 (388)		61.9 (388)
1920-1929	39.4 (3,199)		39.4 (3,199)	131.9 (1,788)		131.9 (1,788)	60.3 (1,061)		60.3 (1,061)
1930-1939	28.4 (3,315)		28.4 (3,315)	135.3 (2,314)		135.3 (2,314)	41.7 (2,376)		41.7 (2,376)
1940-1949	37.6 (2,737)		37.5 (2,744)	173.9 (1,788)		173.9 (1,788)	45.9 (2,674)		45.9 (2,674)
1950-1959	30.6 (4,082)	38.9 (874)	32.1 (4,956)	124.2 (1,917)		124.5 (1,992)	16.5 (2,538)		16.5 (2,542)
1960-1969	37.7 (7,898)	40.2 (8,903)	39.0 (16,801)	120.3 (4,330)	127.6 (2,139)	122.7 (6,469)	16.1 (3,729)	26.8 (411)	17.1 (4,140)
1970-1979	57.6 (4,653)	58.2 (30,383)	58.1 (35,036)	105.3 (4,152)	109.1 (15,203)	108.2 (19,355)	6.8 (7,108)	15.4 (5,654)	10.6 (12,762)
1980-1989		91.2 (1,370)	91.2 (1,370)	70.3 (1,038)	78.7 (8,222)	77.8 (9,260)	5.2 (7,130)	9.4 (28,151)	8.5 (35,281)
1990-1999							1.9 (2,613)	2.5 (20,279)	2.4 (22,892)

[a] cells with less than 100 person-years at risk are omitted

Table 6. Crude rates of smoking initiation per 1000/year (and person-years at risk) in females, by age group, cohort and period. [a]

	Age 11-15			Age 16-20			Age 21-35		
	BHS	TAHS	Pooled	BHS	TAHS	Pooled	BHS	TAHS	Pooled
1910-1919	0.5 (1,993)		0.5 (1,993)	12.6 (1,266)		12.6 (1,266)	3.4 (1,479)		3.4 (1,479)
1920-1929	3.2 (3,419)		3.2 (3,419)	17.2 (2,677)		17.2 (2,677)	6.6 (3,783)		6.6 (3,783)
1930-1939	5.3 (3,784)		5.3 (3,784)	42.8 (3,548)		42.8 (3,548)	13.4 (6,713)		13.4 (6,713)
1940-1949	6.9 (3,162)		6.9 (3,169)	63.8 (3,009)		63.8 (3,009)	16.9 (7,527)		16.9 (7,527)
1950-1959	7.3 (4,382)	8.5 (706)	7.5 (5,088)	62.7 (2,726)		62.3 (2,824)	13.3 (6,549)		13.3 (6,556)
1960-1969	17.6 (9,799)	17.8 (8,431)	17.7 (18,230)	81.4 (6,239)	87.6 (2,317)	83.1 (8,556)	10.2 (6,649)	31.3 (479)	11.6 (7,128)
1970-1979	47.4 (6,011)	51.1 (29,404)	50.5 (35,415)	97.5 (6,039)	111.9 (15,555)	107.9 (21,594)	7.3 (11,327)	13.6 (6,540)	9.6 (17,867)
1980-1989		87.8 (1,287)	87.8 (1,287)	70.9 (1,212)	81.6 (7,723)	80.1 (8,935)	4.9 (10,471)	8.2 (28,606)	7.3 (39,077)
1990-1999							1.8 (3,394)	2.2 (19,406)	2.1 (22,800)

[a] cells with less than 100 person-years at risk are omitted

In the pooled dataset, rates of smoking initiation at ages 16-20 peaked in 1940-49 for males (173,9 per 1,000) and 1970-79 for females (107.9 per 1,000/year), and decreased afterwards. At ages 21-35, rates steadily decreased for males over the period 1910-1999, from 61.9 to 2.4 per 1,000/year, while smoking initiation was less frequent among females. In the age group 11-15 years, rates were relatively stable up to 1970 and increased steeply afterwards for both males and females. They were higher for males than for females throughout the period, except for 1980-1989 when initiation among females almost reached initiation in males (87.8 vs 91.2 per 1,000/year).

Figure 4. Estimated trends in smoking initiation (age 11-35 years, left panel) and smoking cessation (age 36-50 years, right panel) by sex, with 95% confidence intervals. Blue lines: males. Red lines: females.

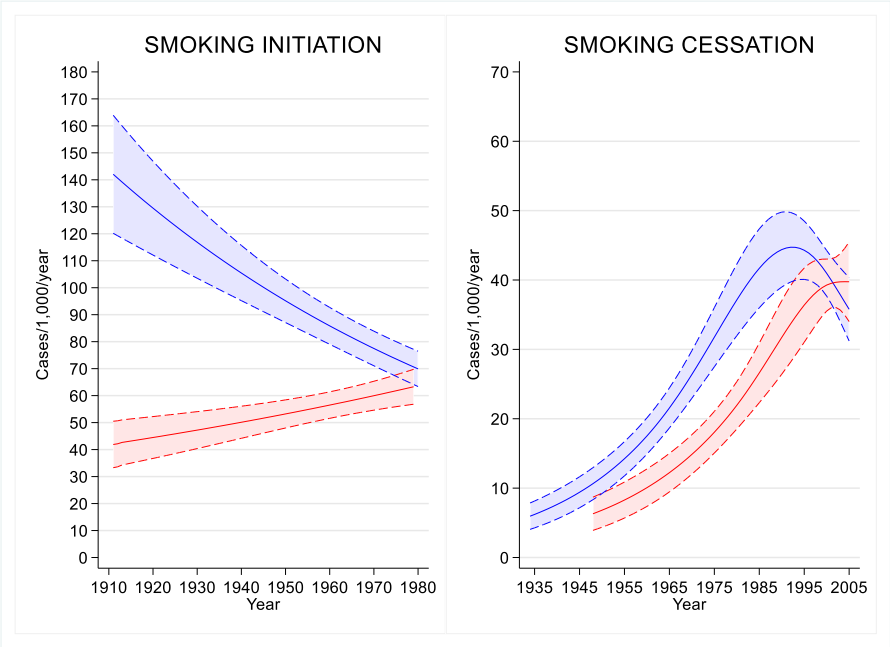
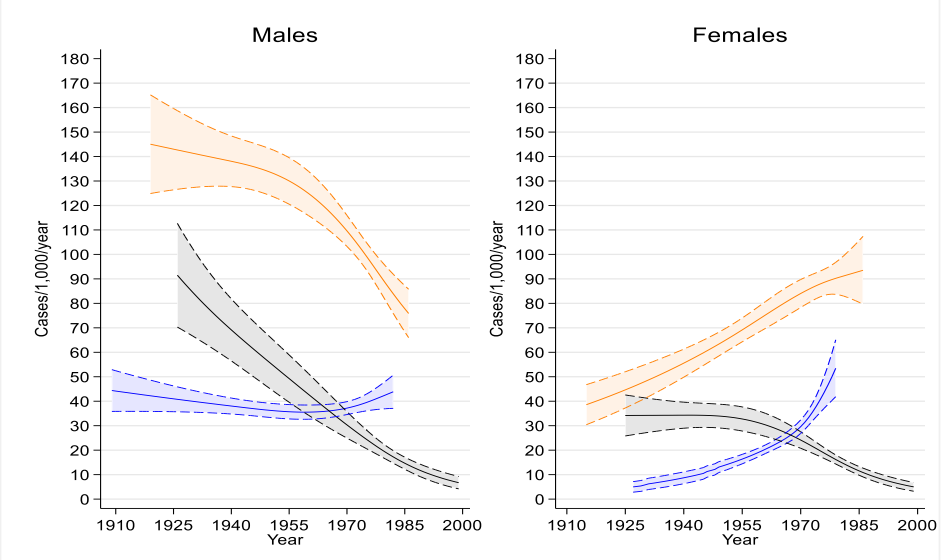


Figure 5. Estimated trends in smoking initiation by sex, with 95% confidence intervals (1908–1999). Blue lines: age 11–15 years. Yellow lines: age 16–20 years. Grey lines: age 21–35 years.



Figures 4 and 5 show adjusted smoothed trends of smoking initiation for males and females. When analysing all ages together (11-35 years), we observed opposite trends in smoking initiation for males (decreasing) compared to females (increasing) (Figure 4, panel left). However, this analysis did not capture the different trends of initiation for early adolescents, late adolescents, and adults (i.e. effect modification by age). In fact, when stratified by age group, estimated trends supported the patterns observed for crude rates (Figure 5), with two exceptions. First, the increasing trend after 1970 among young adolescent males was less evident in the adjusted analysis. Second, among adult females the adjusted analysis suggested a decreasing trend from the 1920s (around 30 per 1,000/year) to the 1990s (around 10 per 1,000/year). These differences are likely due to adjustment for age (removing possible residual confounding within distinct age groups) but also to a restriction of the period (years with less than 100 person-years at the extremes were dropped).

4 IMPACT OF SMOKING BEHAVIOUR CHANGES AND WEIGHT GAIN ON LUNG FUNCTION TRAJECTORIES IN ADULTS

4.1 STUDY DESIGN AND POPULATION

The European Community Respiratory Health Survey (ECRHS) is an international population-based study, which used a standardised protocol to assess the prevalence of asthma and allergic diseases in young adults in many countries. ECRHS measured lung function as well as detailed information on sociodemographic and lifestyle factors between 1990 to 2014.[88] ECRHS I started in 1991–1993 by collecting information on symptoms and exposure to known or suspected risk factors for asthma from representative samples of the population living in the participating centres. A random sample of 1,500 males and 1,500 females aged between 20–44 years was selected from appropriate local sampling frames. Each participant was sent a brief questionnaire (stage 1), and from those who responded, a 20% random sample was selected to undergo a more detailed clinical examination (stage 2).[89]

ECRHS II considered all the subjects who completed stage 1 of ECRHS I, have been selected for stage 2, and had at least their smoking status recorded. Participants in ECRHS II were administered questionnaires and they underwent a clinical examination in 1999-2003, when they were aged 27-57 years. [89] Original participants in ECRHS I stage 2 were then followed-up in 2010-2014 (ECRHS III), when they were aged 39-67 years.[88]

We obtained data on 14,312, 7,801, and 4,342 participants who took part in ECRHS I, II and III, respectively. In order to maximize the use of available information, the present thesis investigated two separate follow-up periods, by using data from the subjects who took part in the follow-up between ECRHS I and II called first period, and from the subjects who took part in the follow-up between ECRHS II and III called second period. A flow chart of the ECRHS is shown in Figure 6.

4.2 DATA ON SMOKING

Information on smoking history was provided by questionnaire at ECRHS I, II and III. Subjects' smoking status was classified as non-smokers, ex-smokers and current smokers at each survey based on the cumulative information provided derived from the questions "Have you ever smoked for as long as a year?"; "Have you stopped or cut down smoking?" and "Do you now smoke, as of one month ago?". For instance, a subject was defined ex-smoker at ECRHS II only if data from ECRHS I and II were consistent with this. Subjects with missing data or inconsistent information were excluded from the analysis. By combining data from baseline and the end of each follow-up period, six categories of change in smoking status were defined. These were never smoker (non smoker at both time points), sustained quitter (ex-smoker at both time points), smoker (smoker at both time points), new smoker (non smoker at baseline and smoker at follow-up), quitter (smoker at baseline and ex-smoker at follow-up), and restarter (ex-smoker at baseline and smoker at follow-up).

4.3 DATA ON WEIGHT CHANGES PROFILES

BMI was calculated as $weight\,(kg)\Big/height\,(m)^2$ at each survey. We computed annual weight change during each follow-up period as the difference between weight measured at baseline and weight measured at the end of a period, divided by the duration of the period in years. Since there are no standard reference values for weight change in adults, we used similar weight change categories as in recent longitudinal population-based studies (including the analysis of ECRHS data by Peralta et al.)[82,90] and defined "stable weight or moderate weight gain" as an increase in weight ≤1 kg/year, and "high weight" gain as an increase in weight >1 kg/year.

4.4 DATA ON LUNG FUNCTION

In the three examinations, forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1), repeatable to 150 mL from at least two of a maximum of five correct manoeuvres that met the American Thoracic Society and European Respiratory Society recommendations, were measured.[68] In ECRHS I and II, centres used different type of spirometers but almost all centres used the same spirometer at ECRHS III. FEV_1/FVC ratio was calculated at each time point.

4.5 STATISTICAL ANALYSIS

We performed separate analyses for the two follow-up periods (ECRHS I-II and ECRHS II-III) including participants who had complete information on lung function, smoking status, weight, sex, age, and height at each period. We described the distribution of lung function outcomes (FEV_1, FVC, FEV_1/FVC Ratio) by smoking behaviour and weight gain status.

Lung function trajectories were modeled by using population-averaged generalized estimating equations (GEE) with Gaussian outcome distribution, identity link function, and a robust variance estimator. We included smoking status as the main explanatory variable, and we stratified by weight gain status after testing the interactions of weight gain with age and smoking status: all the interactions were statistically significant for all lung function parameters (p value <0.001 for all models). GEE models had FEV_1, FVC, and FEV_1/FVC Ratio as the outcome variables. All GEE models had the individuals as the clustering factor (to account for repeated lung function measurements) and unstructured within-cluster correlation. We added sex as a fixed covariate and height, age, age squared, as time-specific covariates in the models. The continuous variables (height and age) were centered at the mean calculated over both periods. Interaction terms between smoking status and age (or age squared) were added to allow for different trajectories of lung function with aging across smoking behaviour groups.

The analyses were performed the statistical analyses using STATA 16 software (Stata Corp. College Station, TX, USA).

4.6 RESULTS

After excluding participants with missing data on smoking status, age, $FEV_{1,}$ FVC we included 14,312, 7,801, and 4,342 subjects from ECRHS I, II, and III, respectively. 6,527 and 4,204 participants were included first and second period respectively. Characteristics of participants are reported in table 7.

Table 7. Characteristics of participants in ECRHS I, II, and III. [a]

Characteristics	ECRHS I	ECRHS II	ECRHS III
N	14,312	7,801	4,342
Sex (Female)	7,268 (50.7%)	3,958 (51.0%)	2,222 (51.1%)
Age in year	33.5±7.2	42.7±7.1	54.3±7.1
Height in cm	1.7±0.1	1.7±0.1	1.7±0.1
Weight in kg	69.5±13.8	74.5±15.3	78.5±16.3
BMI kg/m^2	23.8±3.8	25.6±4.4	27.1±4.8
Smoking Status			
Non-smoker	5,923 (41.4%)	3,373 (44.1%)	1,959 (46.8%)
Ex-smoker	1,347 (9.4%)	1,966 (25.7%)	1,468 (35.1%)
Current smoker	5,447 (38.1%)	2,310 (30.2%)	758 (18.1%)
Second-hand smoker(Yes)	4,198 (29.4%)	1,349 (17.3%)	114 (2.6%)
FEV_1 (L)	3.7±0.8	3.5±0.8	3.0±0.7
FVC (L)	4.5±1.0	4.4±1.0	4.0±0.9
FEV_1/FVC (%)	0.82±0.1	0.80±0.1	0.75±0.1

[a] n. (%) of subjects with characteristic or mean±SD.

Approximately half of the study sample were women. Mean age was 33.5 years at baseline, 42.7 years at the second follow-up and 54.3 years at the last follow-up. The proportion of current smokers decreased at subsequent examinations from 38.1% at ECRHS I to 18.1% at ECRHS III (table 7).

Table 8 represents the distribution of the six categories of smoking behaviours for participants at the first follow-up period. The largest groups were those who remained non-smoker (never smoker), ex-smoker (sustained quitter) or

current smoker (smoker), but 651 (9.9%) gave up smoking between ECRHS I and ECRHS II (quitter), 97 (1.5%) were ex-smokers who restarted (restarted), and 104 (1.6%) were non-smokers who uptook smoking (new smoker). Data for new smokers and restarters were omitted from analysis due to the small numbers.

Table 8: Smoking status at first period (ECRHS I-II). [a]

Smoking status	ECRHS I	ECRHS II	MALES	FEMALES	OVERALL
Never smoker	**Non-Smoker**	**Non-Smoker**	1,401 (44.0%)	1,780 (53.1%)	3,181 (48.7%)
Sustained Quitter	**Ex-Smoker**	**Ex-Smoker**	291 (9.1%)	269 (8.0%)	560 (8.5%)
Smoker	**Smoker**	**Smoker**	1,024 (32.2%)	910 (27.1%)	1,934 (29.6%)
New smoker	**Non-Smoker**	**Smoker**	55 (1.7%)	49 (1.5%)	104 (1.6%)
Quitter	**Smoker**	**Ex-Smoker**	356 (11.2%)	295 (8.8%)	651 (9.9%)
Restarter	**Ex-Smoker**	**Smoker**	53 (1.7%)	44 (1.3%)	97 (1.5%)
Overall			3,180 (48.7%)	3,347 (51.3%)	6,527 (100%)

[a] each cell reports n. of subjects with available data (%).

Table 9: Lung function and BMI change at the first period, according to change in smoking and weight gain status. [a]

Smoking Status		Stable-Moderate Weight in the first period		Weight Gain in the first period	
		N	Mean±SD	N	Mean±SD
Δ FEV_1 (ml/y)	**Never Smoker**	984	-22.0±35.5	267	-22.4±44.7
	Sustained Quitter	171	-20.7±40.3	43	-23.4±55.3
	Smoker	627	-26.8±37.7	145	-33.6±45.9
	Quitter	172	-21.6±31.4	94	-33.1±39.9
ΔFVC (ml/y)	**Never Smoker**	984	-15.3±48.5	267	-17.6±48.0
	Sustained Quitter	171	-12.1±48.1	43	-17.6±61.7
	Smoker	627	-16.9±45.5	145	-20.1±62.6
	Quitter	172	-16.4±37.7	94	-33.4±46.7
Δ FEV_1/FVC Ratio (percentage/y)	**Never Smoker**	984	-2.3±6.0	267	-1.9±5.9
	Sustained Quit	171	-2.3±6.1	43	-2.1±5.0
	Smoker	627	-3.1±5.9	145	-4.1±7.4
	Quitter	172	-1.8±4.5	94	-1.5±4.9
ΔBMI (kg/m^2)/y	**Never Smoker**	984	0.10±0.2	267	0.56±0.2
	Sustained Quit	171	0.04±0.2	43	0.53±0.2
	Smoker	627	0.05±0.2	145	0.56±0.2
	Quitter	172	0.12±0.1	94	0.59±0.3

[a] each cell reports mean±SD or n. of subjects with a characteristic.

Table 9 shows the change in FEV_1, FVC, FEV_1/FVC Ratio and BMI stratified by weight gain and smoking status. Smokers had faster decline in FEV_1 and FEV_1/FVC ratio than never smokers, sustained quitters and quitters, both in the group with stable weight and in the group gaining weight.

Table 10 represents the distribution of the six categories of change in smoking behaviours for participants at the second period follow-up, respectively. During the second follow-up period, the largest groups were those who remained non-smoker (never smoker), ex-smoker (sustained quitter) or current smoker (smoker) but 456 (10.8%) gave up smoking between ECRHS II and ECRHS III (quitter), 79 (1.8%) restarted (restarter), and 28 (0.6%) started smoking (new smoker). Data for new smokers and restarters were omitted from analysis due to the small numbers.

Table 10: Smoking status at second period (ECRHS II-III).[a]

Smoking Status	ECRHS II	ECRHS III	MALES	FEMALES	OVERALL
Never Smoker	**Non-Smoker**	**Non-Smoker**	830 (40.8%)	1,094 (50.4%)	1,924 (45.8%)
Sustained Quitter	**Ex-Smoker**	**Ex-Smoker**	533 (26.2%)	483 (22.3%)	1,016 (24.2%)
Smoker	**Smoker**	**Smoker**	373 (18.3%)	328 (15.1%)	701 (16.7%)
New Smoker	**Non-Smoker**	**Smoker**	15 (0.7%)	13 (0.6%)	28 (0.7%)
Quitter	**Smoker**	**Ex-Smoker**	236 (11.6%)	220 (10.1%)	456 (10.8%)
Restarter	**Ex-Smoker**	**Smoker**	48 (2.4%)	31 (1.4%)	79 (1.9%)
Overall			2,035 (48.4%)	2,169 (51.6%)	4,204 (100%)

[a] each cell reports n. of subjects with available data (%).

Table 11. Lung function and BMI change at second period, according to change in smoking and weight gain status.[a]

Smoking Status		Stable-Moderate Weight in the second period		Gain weight in the second period	
		N	Mean±SD	N	Mean±SD
Δ FEV_1 (ml/y)	**Never Smoker**	691	-40.6±24.0	79	-52.0±27.7
	Sustained Quitter	360	-41.9±23.6	36	-52.5±28
	Smoker	258	-49.1±25.9	33	-60.3±29.8
	Quitter	140	-42.9±26.0	42	-51.8±31.6
ΔFVC (ml/y)	**Never Smoker**	691	-33.5±33.7	79	-46.3±36.5
	Sustained Quitter	360	-33.8±29.5	36	-48.8±31.6
	Smoker	258	-37.7±35.2	33	-57.6±45.2
	Quitter	140	-34.1±29.9	42	-54.3±46.6
Δ FEV_1/FVC Ratio (percentage/y)	**Never Smoker**	691	-3.5±4.4	79	-3.7±3.9
	Sustained Quitter	360	-3.8±3.8	36	-3.9±4.1
	Smoker	258	-4.9±4.4	33	-4.1±6.1
	Quitter	140	-4.2±4.4	42	-2.7±4.9
ΔBMI (kg/m^2)/y	**Never Smoker**	691	0.08±0.2	79	0.51±0.2
	Sustained Quitter	360	0.08±0.2	36	0.53±0.2
	Smoker	258	0.77±0.2	33	0.51±0.2
	Quitter	140	0.12±0.2	42	0.56±0.2

[a] each cell reports mean±SD or n. of subjects with a characteristic.

Table 11 shows the differences of FEV_1, FVC, FEV_1/FVC Ratio and BMI according to smoking status and change in weight. As observed for the first period, smokers had faster decline in lung function than never smokers, sustained quitters and quitters in both weight status.

Figure 6. Estimated trajectories of FEV_1 (L) with 95% confidence intervals, by smoking status and weight change during the follow-up periods between ECRHS I-II and ECRHS II-III.

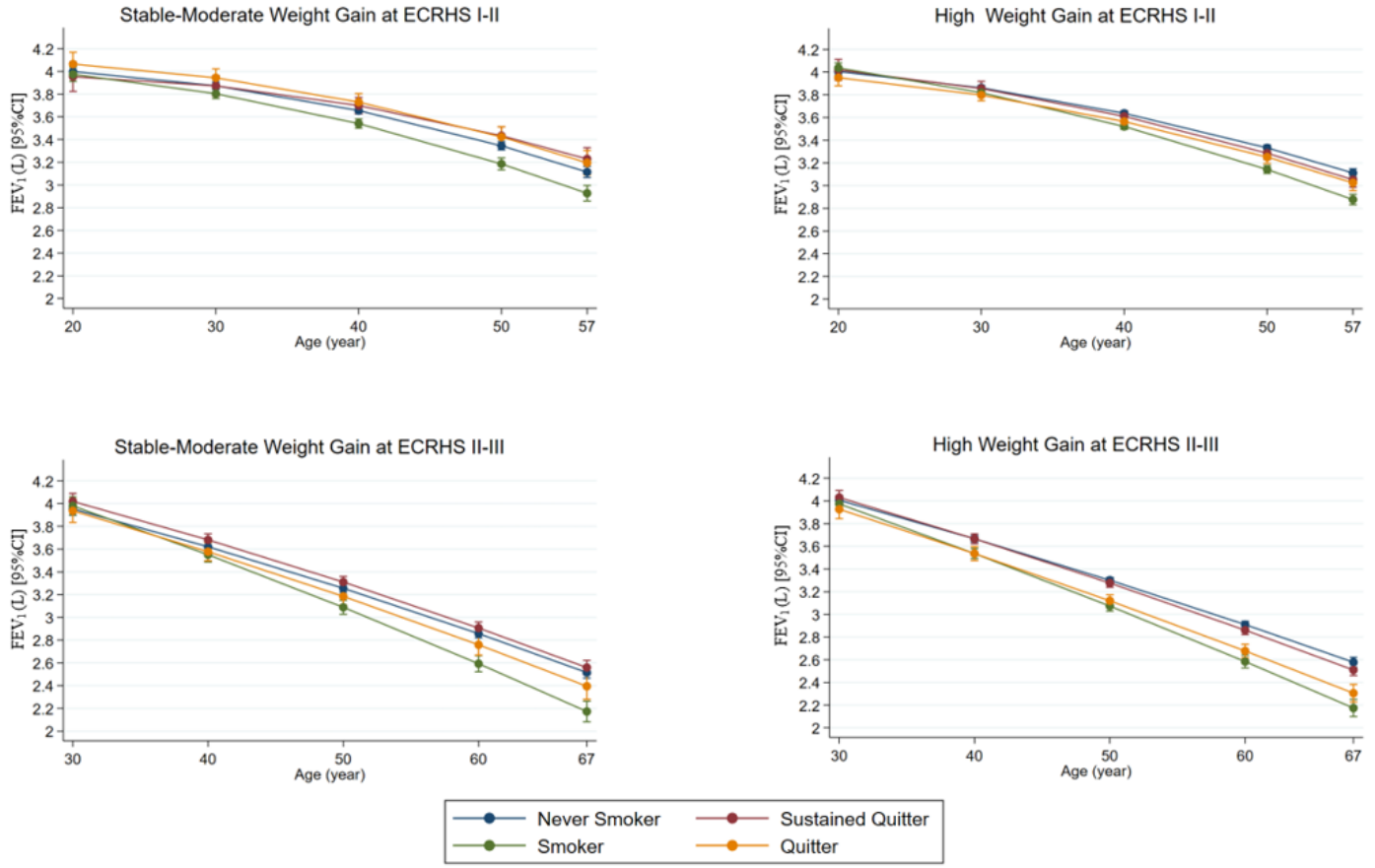


Figure 7. Estimated trajectories of FVC (L) with 95% confidence intervals, by smoking status and weight change during the follow-up periods between ECRHS I-II and ECRHS II-III.

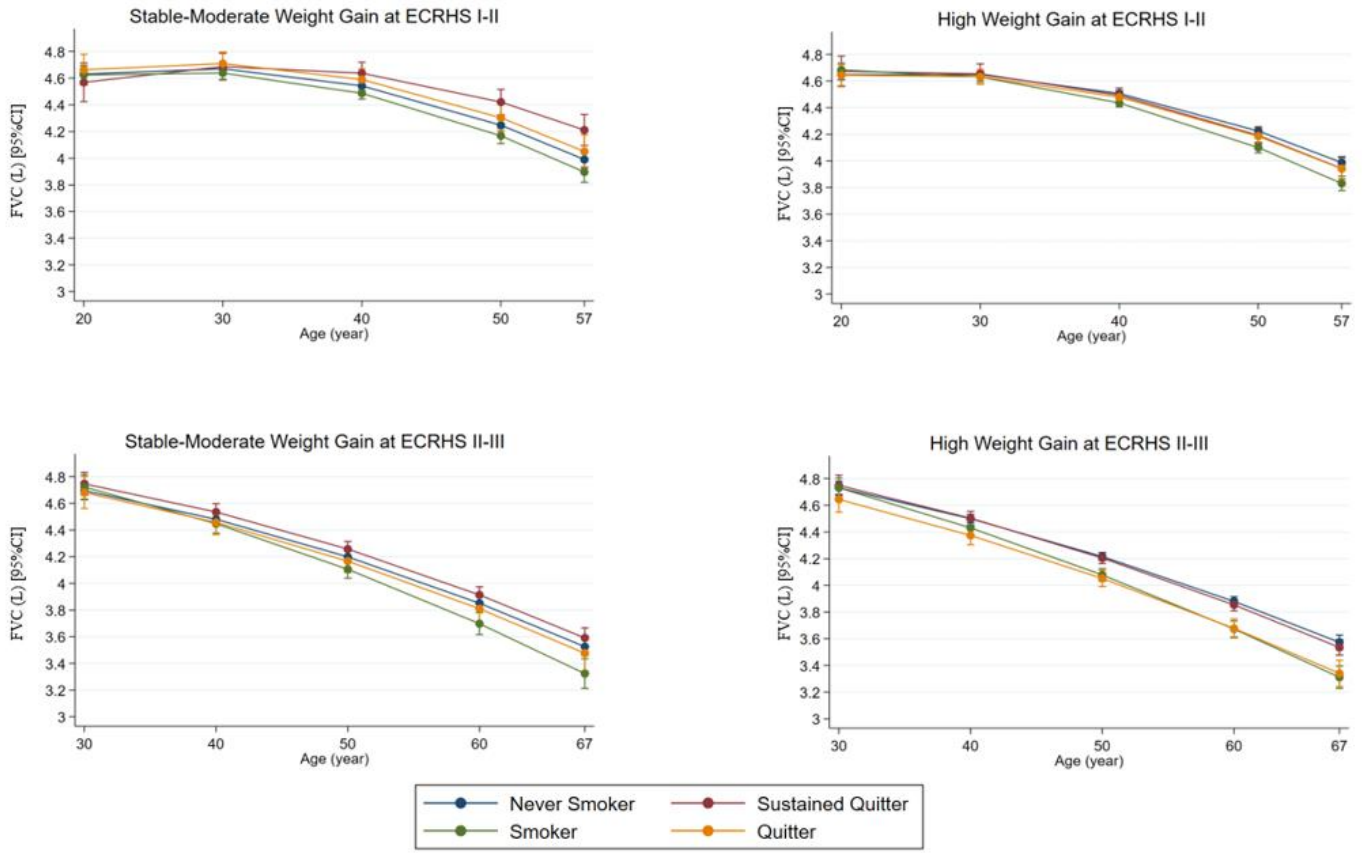
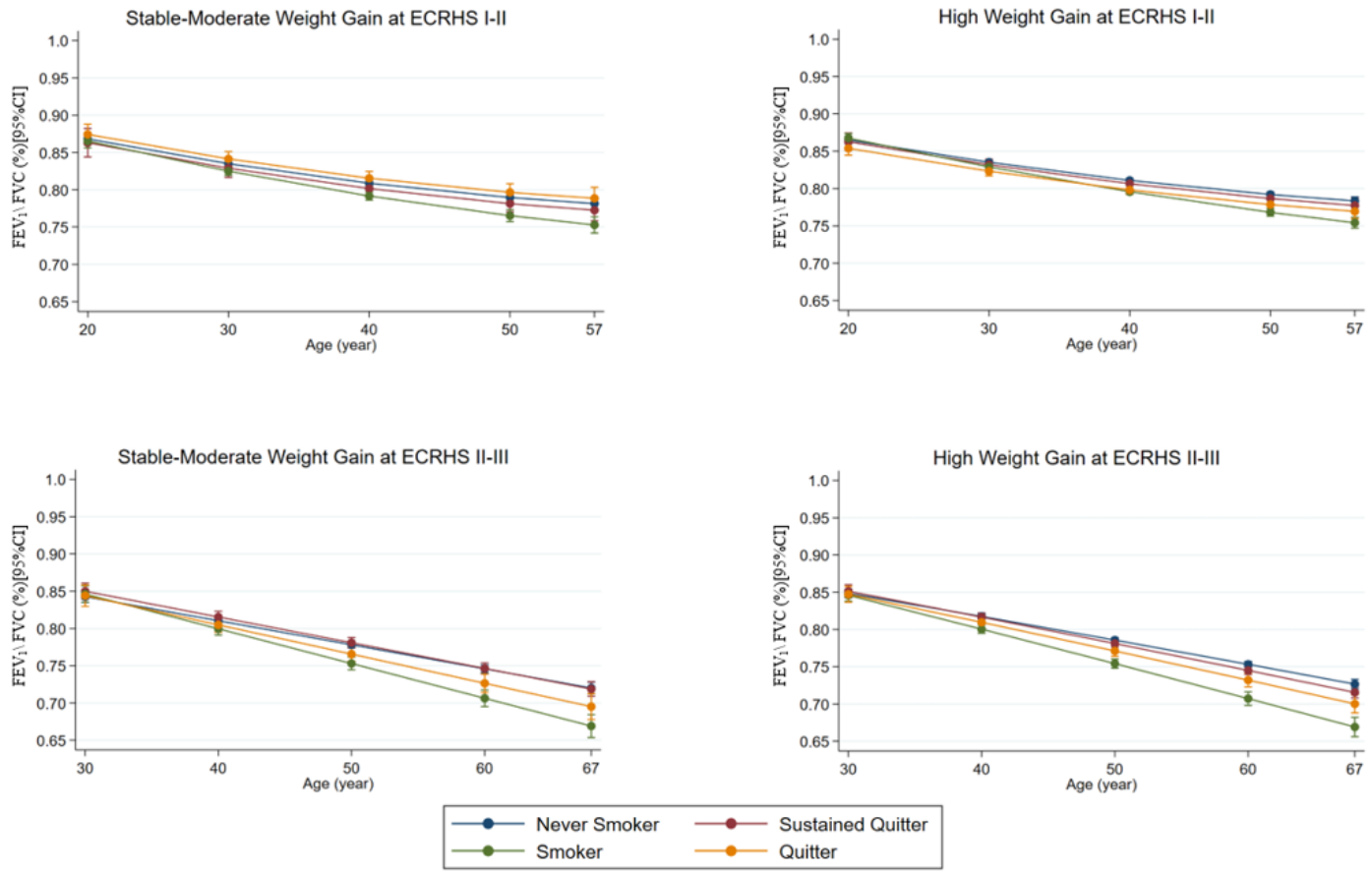


Figure 8. Estimated trajectories of FEV_1/FVC (%) Ratio with 95% confidence intervals, by smoking status and weight change during the follow-up periods between ECRHS I-II and ECRHS II-III.



Figures 6-8 show the estimated trajectories of lung function by smoking behavior during each of the two follow-up periods and for each weight change category. The estimated trajectories of lung function were slower during the first period, when people were younger, compared to the second period. Among smokers, the decline of FEV_1, FVC and FEV_1/FVC ratio was faster than among never smokers, sustained quitters, and quitters, both if they had a stable weight/moderate weight gain and if they had a high weight gain.

The decline in lung function was similar for never smokers and sustained quitters (i.e., people who had quit smoking before the start of a follow-up period) regardless of their weight gain status and during both periods. Quitters had intermediate lung function decline when compared to never smokers and smokers. Nevertheless, quitters had faster lung function decline than sustained quitters (Figure 6-8).

In the first period, the decline of lung function was slower among quitters compared to smokers. In the second period, quitters who had high weight gain had faster decline of FEV_1 and FEV_1/FVC ratio than never-smokers and sustained quitters, while they had an almost similar decline of FVC compared to never-smokers and sustained quitters (Figure 6-8).

5 DISCUSSION

5.1 TRENDS IN SMOKING INITIATION AND SMOKING CESSATION IN AUSTRALIA OVER 70 YEARS

We evaluated time trends in smoking initiation and cessation in two independent samples of the Australian general population in order to identify age- and gender-specific changes of smoking behaviors. The rates of smoking initiation during young adolescence (11-15 years) increased steeply between 1925 and 1980 in females. After being relatively stable, they slightly increased after the 70's also among males. This suggested that smoking behaviors progressively affected more young girls compared to boys in that period. The rates of smoking initiation were highest during late adolescence (16-20 years) for both males and females. Smoking initiation during late adolescence peaked in the '40s for males and decreased afterwards, while in females initiation increased until the mid-'70s. Among young adults (21-35 years), initiation rates decreased for men, whereas they were relatively low and almost stable among women. Woodward et al. documented that smoking prevalence in Australia has declined in men since the 1950s and in women since 1980, which is consistent with our study.[91] Our findings on gender differences in smoking prevalence are consistent with epidemiological literature on smoking in adolescents from European, North America, and global surveys.[92–94]

As for smoking cessation, we observed increased rates among adults (36-50 years) between 1935 and 1990 for both males and females. Smoking cessation peaked in the '90s for males and decreased afterwards, while in females cessation increased until the 2000s. According to the National Drug Strategy Household Survey, the proportion of Australians aged 14 years and over who quit smoking decreased between 1993 and 1995 and then increased until 1998 which is consistent with our results. The proportion of quitters decreased from 26.2% in 2001 to 24.1% in 2010 and 22.8% in 2019.[18]

The smoking initiation decline in young adults is likely the result of the progressive impact of anti-tobacco campaigns, which encompassed the education of current and potential cigarette users about the health risks as well

as increases in the prices of tobacco products. Although the pattern of smoking trends shifted towards young and late adolescents, we should recognize the impact of public strategies taken during 70's and 80's.

Historically, Australia has a remarkable role in cooperating with WHO's Framework Convention on Tobacco Control in order to keep tobacco consumption under control. In 1972, one of the first measures implemented was the introduction of health warnings on cigarette packs. The next strategy employed to decrease the consumption of tobacco between 1973 and 1976 was the phasing out of direct advertising for cigarettes in the electronic media (radio and television). Nonetheless, advertising for cigarette was still allowed in cinemas, sporting events, billboards, and print media until the late 1980s. Restrictions on smoking in public places were established in 1975, starting with the prohibition of smoking on public transport; the number of places with smoking restrictions increased in the late 1980s and the 1990s.[95] With the purpose of restricting tobacco access to adults, the legal age for purchasing cigarettes was increased to 18 in many Australian states, and in the late 1990s it became illegal to sell tobacco to people under 18 years in all Australia.[95] In the early 1990s, prevention of smoking activity has been included in the curriculum of primary and secondary schools across Australia.[96]

In 2011 a WHO report mentioned that smoke-free laws covered 96% of the Australian population by 2008.[5] Figure 10 shows the prevalence of daily smoking among people aged 18 years or older against key tobacco control measures implemented in Australia since 1990: daily smoking decreased from 27.7% in 1990 to 13.8% in 2017-18.[95] Figure 10 emphasizes how long it took to obtain a significant success by implementing and enforcing smoke-free laws, public health measures and civil actions through government regulations against the tobacco epidemic.

Figure 10. Prevalence of daily smoking among people aged 18 years or older in Australia between 1990 and 2017-18. The labels indicate key tobacco control measures implemented during this period.

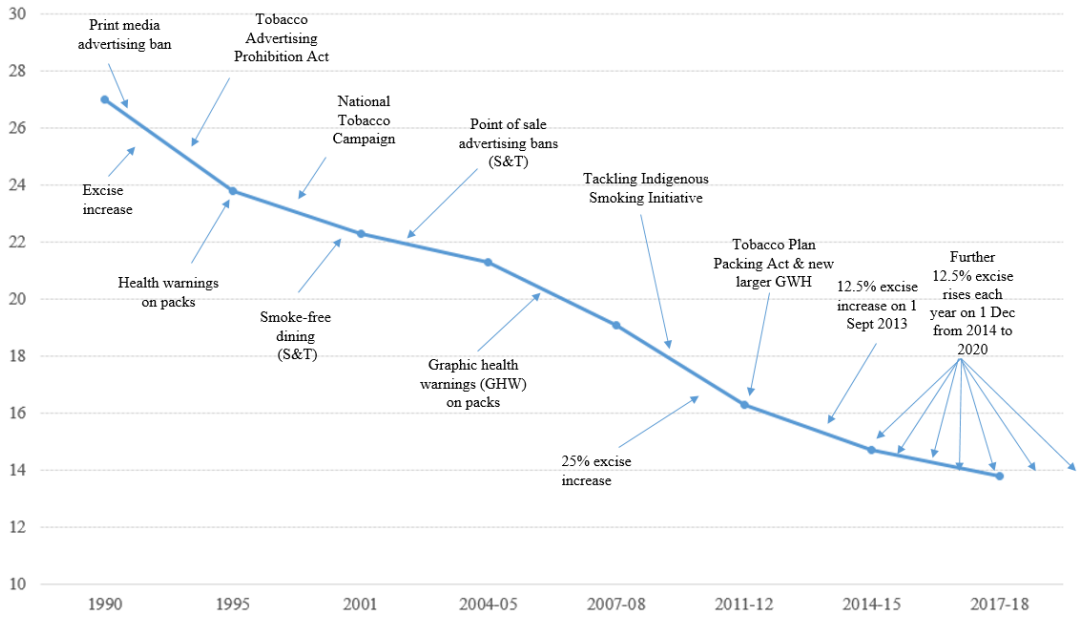


Figure 11. Trends in **s**moking prevalence by sex and age group between 1995 and 2018. Left panel: males. Right panel: women. Blue lines: age 12–15 years. Orange lines: age 16–17 years. Grey lines: age 18 years or older

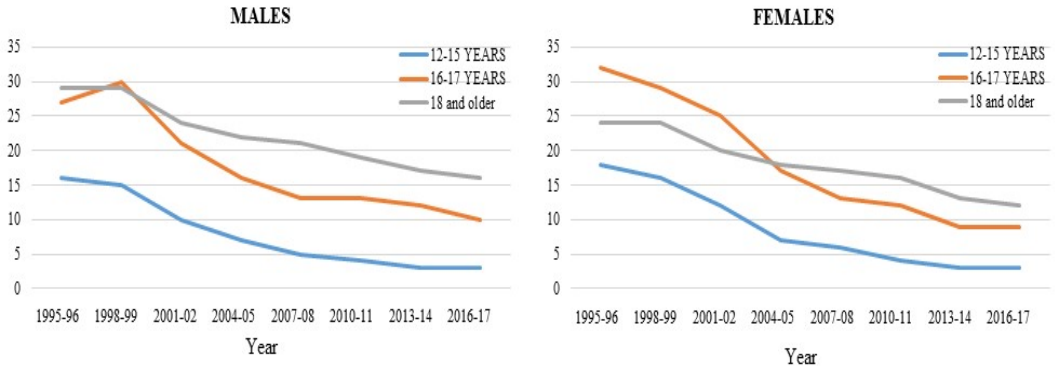


Figure 11 was generated by using a report of the ASSAD 2017 trends in substance use among Australian secondary school students during 1996-2017 and information available from the Australian Bureau of statistics. The prevalence of smoking increased through the 1990s among young adolescents (12-15 years) before rapidly declining from the late 1990s to the late 2000s for both genders (Figure 11). However, the impact of policies had a drastic impact on the decline in females between 12-15 years and 16-17 years starting in the mid-1990s (1995-96), while there was a prolonged delay until 2004-05 and then the prevalence of smoking became similar between females and males from 2007-08.[97,98] The progressive decline of smoking trends in early and late adolescence from the late 1990s to 2016-17 confirms the positive impact of governmental policies.

In 2019, smoking prevalence among Australians aged 18 and over was 14.7% and the prevalence of smoking among people aged 15 was 14.0%.[98] Smokers were motivated to quit or cut back by the cost of tobacco, up from around 1 in 2 (52%) in 2016 and 3 in 5 (58%) in 2019 respectively.[18] Higher cigarette prices, enforced smoking bans in public spaces, intervention strategies, and higher funding levels to tobacco control programs have resulted in major reductions in smoking prevalence.[99] Countries that adopted anti-tobacco initiatives and forefront of scientific research on tobacco control such as Australia, Scandinavia, the UK, and the US have effectively addressed the age group that is at greatest risk of starting smoking.[16,18,95,96,100]

On the other hand, while the prevalence of smoking is declining in the general population, tobacco consumption is still high among people with mental health conditions.[101] In 2019, daily smokers were more than twice as likely to have a high level of psychological distress compared with people who had never smoked (25% compared with 12%, respectively).[18] Mental health conditions associated with stress, anxiety and depression related to social and financial circumstances may also be an important risk factor for smoking initiation. There is evidence that we should not ignore the physical and hormonal changes during adolescence, an age that is prone to psychological and mental health

transformation associated with early puberty onset and adjustment issues in social maturity.[102–105]

Another change in smoking habits is personally rolling cigarettes. 36% of smokers preferred rolling their own cigarettes in 2016, whereas this habit increased to 45% in 2019. The use of e-cigarettes is also becoming more common than smoking manufactured cigarettes.[18,106] The rate of e-cigarette use increased from 8.8% to 11.3% between 2016 and 2019.[18] There was a noticeable increase in the use of e-cigarette across most age groups, especially among young adults. Moreover, it was reported that 20% of non-smokers and 64% of current smokers tried e-cigarettes in the age range 18–24 in 2019.[18] It has to be remarked that there are upcoming threats raised by alternatives to tobacco products like e-cigarettes and vapes, since their short and long-term health consequences are yet to be determined. *The trends in smoking and vaping among young adolescents should be monitored through public health surveillance in order to implement additional policies to further reduce tobacco consumption and prevent addiction issues linked to new nicotine-containing products in the near future.*

5.1.1 STRENGTHS AND LIMITATIONS

One strength of the present study is the extended timeline of seventy years and the separate assessment of age classes and genders, which enabled to identify subgroups of the population where successful tobacco control policies were lagging behind. Moreover, assessing smoking initiation and cessation as two separate events in the individuals' history of smoking provided insights that are generally less appreciable when studying smoking prevalence.

One limitation is that our observational study depends on self-reported information on smoking history and status that was not originally collected to assess smoking trends. However, the agreement between self-reported smoking is usually good in population studies.[107] Individuals might be inaccurate in recalling the timing of past events. Nonetheless, we found that both age at smoking initiation and age at smoking cessation were reported consistently at different BHS time points when they were assessed using identical questions (Table A3, and A4), but also when the questions were different (Tables A2, and A5). Another limitation is that the populations investigated may not be completely representative of the Australian population. The difference in study design betweeen BHS and TAHS is unlikely to be a major source of bias, since we found similar crude rates of smoking initiation and cessation in subgroups that were comparable for sex and age assessed (Table A6, A7, and A8). Moreover, our data could not distinguish among specific tobacco products (boxed vs hand-rolled cigarettes) and we did not have data on newly designed smoking tools (e-cigarettes), which are becoming important sources of nicotine exposure. Finally, relapse is the main challenge when investigating smoking cessation. However, age at cessation reported 3-4 years apart in BHS was fairly consistent (Table A4), which suggests that our results reflect cessation among subjects at a low risk of relapse (Table A5).

5.1.2 CONCLUSION

Our analysis describing the tobacco epidemic in samples of the Australian general population showed that early adolescent females were more likely to smoke than boys in the '70s and '80s, which reflected the shift of smoking behaviors from boys to girls in this age group in that period. Nowadays, Australia is a leading country in the implementation of efficient tobacco control strategies and was one of the first countries to adhere to the WHO's Framework Convention on Tobacco Control. Recent data suggest that rates of smoking initiation declined after the '90s among early adolescents, highlighting a major achievement of the policies implemented over time.[10,16,18] Nonetheless, Australia needs strategies to strengthen cessation in current smokers. In spite of much support for the adult population from many resources, strong and up to date measures and surveillance against smokeless tobacco-related products should be implemented in youth. Along with the prevalence of smoking, we recommend monitoring future trends in smoking initiation and cessation, as this will better inform public health decisors regarding the need of improvement of specific dimensions of tobacco control policies.

5.2 IMPACT OF SMOKING BEHAVIOUR CHANGES AND WEIGHT GAIN ON LUNG FUNCTION TRAJECTORIES IN ADULTS

We provide evidence on how changes in smoking status and weight gain interact affecting outcomes of lung function in adults in the population-based **E**uropean **C**ommunity **R**espiratory **H**ealth **S**urvey (**ECRHS**). Our findings document that weight gain profiles play a role on modulating lung function decline in adults in relation to changes in smoking behaviors.

Many studies have reported that behavioral changes in smoking status affect lung function outcomes.[70,108–114] The relationship between smoking cessation and weight gain in connection with lung function has received less attention.[110–112,115] Our comparative analysis between never smokers and smokers presented a discernible smoking-related acceleration in lung function decline which is consistent with other studies.[116,117] The age-related decline in lung function was similar between never smokers and sustained quitters (who had quit smoking before the start of a follow-up period) regardless of weight gain status and in both periods, which suggests that smokers may catch up the never smoking group if they quit early in life by recovering previous loss of lung function due to smoking.[118–121] Moreover, we found that quitting smoking during a follow-up period was still beneficial, since quitters had intermediate lung function decline when compared to never smokers and sustained smokers. However, lung function among quitters was not as good as lung function among sustained quitters, further stressing the importance of early smoking cessation. Kohansal and colleagues had shown that smoking cessation had a beneficial effect at any age, in spite of the fact that it was more prominent in earlier quitters, and that decline in FEV_1 among smokers who quit before the age of 30 years was similar to that observed in never smokers.[112] We also made a similar observation in our study showing there was an advantage of smoking cessation at early age.

5.2.1 STRENGTHS AND LIMITATIONS

Strengths of this study include the use of large samples from the European population, the width of age distribution covering early to late adulthood, and a long window of observation covering up to twenty years overall.

This study has some limitations. As in many other epidemiological studies, our analysis is based on body weight, which is a poor marker of obesity since it is not able to distinguish between fat mass and fat-free mass, which can change in proportion with age and gender[122,123] and could have different effects on lung function. Unfortunately, bio impedance data were only available at ECRHS III. Given the lack of standard reference values for weight change in adults, weight change status was categorized based on a previous longitudinal study.[90] The results could be affected by potential confounding by, for example, dietary intake, which may affect both body weight and lung function, as data on diet were available only for a small subgroup of the study sample at ECRHS II and III. We did not take smoking intensity into account because the number of smokers was not sufficient enough to be able to compare smoking intensity with lung function changes.

5.2.2 CONCLUSION

Our findings confirm that smoking cessation is beneficial at any age in terms of preventing an accelerated lung function decline. However, cessation at younger ages could be effective in reverting the effects of smoking, since early quitters seemed to catch up the never smokers group in terms of lung function, while late quitters were not able to reach never smokers. Moreover, in the second follow-up period, when subjects were aged 20 to 67 years, quitters who gained more weight were less able to recover their lung function compared to quitters who had a moderate weight gain. Our findings support that weight control may provide an additional benefit in terms of lung function among older adults who quit smoking.

6 FUTURE DIRECTIONS

Tobacco consumption is an undisputable health concern related to many forms of chronic diseases and cancer worldwide and it is still driving force threatening health of individuals by diseases related to nicotine dependence.[3] There is evidence on the adverse effect of tobacco use based not only on social and clinical studies supported through systematic review and large-scale data sets, but also on biomedical, cellular, and molecular biology research.[105] Nonetheless, the addictive nature of nicotine and tobacco is still under inquiry to expose the roots of disease initiation, progression, and epidemic outcomes.[124]

There has been tremendous accomplishment through public education and preventative strategies to target adult and young populations through community and public health policies. However, we are currently facing novel products that contain nicotine and unjustified claims that, by using these products in alternative to standard cigarettes, people will be able to reduce tobacco consumption and the health risks related to smoking.[125] E-cigarettes and vapes are getting increasingly common as replacements of tobacco use, but they also deliver nicotine directly and lead to physical and psychological dependence among adults and youth. Recent studies demonstrate an increase of tobacco use among early adolescents, who are vulnerable to addiction not only by cigarette exposure but also by experimenting novel nicotine containing products. Therefore, we recommend stringent industry regulations and tobacco control strategies to promote the prevention and protection of the youth from smoking exposure, in parallel to the strengthening of cessation programs.

Nicotine intake also shows relation with many mental illnesses including attention deficit hyperactivity disorder, anxiety disorders, and depression as well as addiction. We shall not neglect the impact of mental health status predisposing to smoking initiation in young and adult individuals. In recent years, there has been mounting evidence for the association between smoking behaviour and mental disorders. [126,127]. They are more likely to be at risk than others for developing smoking problems.[128] In Australia individuals suffering from mental disorders were found to be more likely to be smokers, and less likely to quit.[39,126,129] These studies open the window to change the strategies to overcome

smoking cessation. Furthermore, it is not possible to ignore the impact of mental state on smoking initiation within school-aged children and escalation in the use of e-cigarette other than cigarettes.[130,131] Tobacco smoking has been shown to affect neurophysiological and cognitive behaviours within adolescent years, and, a correlation between nicotine dependence and alcohol consumption is also well documented. In addition, tobacco consumption could also affect offspring lungs for next generation through epigenetic modifications.[132]

Tobacco is also a known risk factor for oral cancer, dental caries, adult periodontal diseases and reported to cause congenital defects such as cleft lip and palate in children whose mother consumed tobacco during pregnancy.[133–135] Oral health and dental diseases associated with smoking are to become a potentially important topic of research. In some studies, oral health has taken into count as an incorporated criterion for analysis of lung function decline associated conditions, which are triggered by prolonged oral health problems.[136,137]

In conclusion, it is crucial for people to cease smoking and to abstain from any form of tobacco, including e-cigarette and vape for better health outcomes. From the public health perspective, a number of objectives should be pursued in order to improve healthy living and promote smokeless environments, including:

- Implementing policies and practices to address healthy recovery from smoking behaviours
- Implementing behavioral mental health support and treatments for youth and adults
- Establishing health care providers and surveillance for youth
- Implement active living and healthy eating to improve smoke-free lifestyles by the approach in positive mental attitude
- Promote the benefits of a smokeless lifestyle rather than suppression among youngsters and adults

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APPENDIX A

Trends In Smoking Initiation And Smoking Cessation In Australia Over 70 Years

Figure A1. Distribution of subjects included by study group and year.

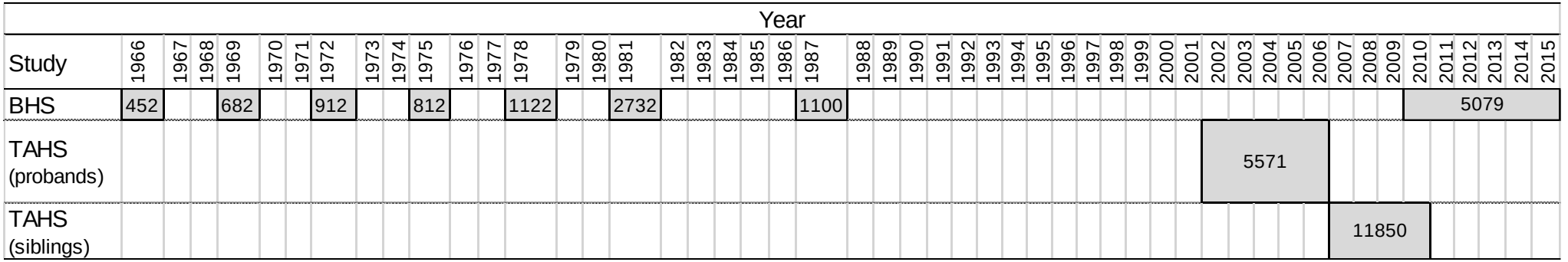

Table A1: Distribution of characteristics of participants in the BHS waves.[a]

	BHS waves							
Characteristics	1966	1969	1972	1975	1978	1981	1987	2010-2015
Number pf participants	3,394	3,680	3,885	3,635	4,006	3,940	1,117	5,107
Participation rate (%)	91%	90%	86%	76%	74%	64%	54%	62%
Women (n, %)	1,723 (50.8)	1,906 (51.8)	2,032 (52.3)	1,947 (53.6)	2,177 (54.3)	2,142 (54.4)	601 (53.8)	2,800 (54.8)
Birth year (median, min-max)	1920 (1873-1946)	1921 (1875-1950)	1925 (1879-1955)	1927 (1881-1959)	1929 (1881-1960)	1930 (1884- 1965)	1915 (1889-1947)	1954 (1944-1964)
Age, year (median, min-max)	46 (20-93)	48 (19-94)	47 (17-93)	48 (16-94)	49 (18-97)	51 (16-97)	73 (40-98)	56 (46-66)
Ever smokers (%)	1,801 (53.1)	1,929 (52.5)	1,871 (48.2)	1,568 (43.4)	1,938 (49.3)	1,852 (47.2)	533 (50.4)	2,696 (53.1)
Age at initiation, year (mean±SD)	19.7±7.3	19.8±7.1	19.2±6.4	18.7±5.6	18.7±5.9	18.7±5.9	19.5±7.3	17.1±3.9
Ex-smokers (%)	514 (7.29%)	636 (31.0%)	670 (32.2%)	614 (33.2%)	989 (48.0%)	1,082 (54.4%)	415 (72.0%)	2,176 (80.2%)
Age at cessation, year (mean±SD)	40.7±15.1	41.0±14.7	41.3±15.1	41.6±14.9	41.6±15.5	41.4±14.9	52.9±14.7	36.4±12.1

[a] n. (%) of subjects with characteristic or mean±SD.

Table A2: Comparison of age at smoking initiation reported using **different** questionnaire items at BHS waves (analysis restricted to the subjects who reported to be ever smokers at both waves under comparison).[a]

1st study wave	2nd study wave	N of smokers	Later initiation at 2nd wave, n (%)	Same age at initiation (±1 year), n (%)	Earlier initiation at 2nd wave, n (%)	Age at initiation at 1st wave, mean±SD	Age at initiation at 2nd wave, mean±SD	Spearman's rank correlation coefficient (p-value)
1969	1972	1,289	16.2% (209)	66.4% (856)	17.4% (224)	19.2±5.8	19.2±6.0	0.82 (<0.001)
1975	1978	916	12.3% (113)	69.3% (636)	18.23% (167)	18.9±5.5	18.7±5.7	0.84 (<0.001)
1981	1990	119	21.1% (25)	68.9% (82)	10.1% (12)	17.0±2.8	17.5±2.9	0.73 (<0.001)
1987	2005	22	31.8% (7)	68.2% (15)	0.0% (0)	21.3±7.3	22.2±6.9	0.95 (<0.001)
2005	2010	265	9.4% (25)	73.6% (195)	17% (45)	17.3±3.2	17.0±3.2	0.73 (<0.001)

[a] n. (%) of subjects with characteristic or mean±SD.

Table A3: Comparison of age at smoking initiation reported using **similar** questionnaire items at BHS waves (analysis restricted to the subjects who reported to be ever smokers at both waves under comparison).[a]

1st study wave	2nd study wave	N of smokers	Later initiation at 2nd wave, n (%)	Same age at initiation (±1 year), n (%)	Earlier initiation at 2nd wave, n (%)	Age at initiation at 1st wave, mean±SD	Age at initiation at 2nd wave, mean±SD	Spearman's rank correlation coefficient (p-value)
1966	1969	1,364	20.4% (278)	62.9% (859)	16.6% (227)	19.4±6.7	19.6±6.5	0.82 (<0.001)
1972	1975	1,010	11.2% (113)	78.0% (788)	10.8% (109)	18.9±5.4	19.0±5.6	0.89 (p<0.001)
1978	1981	1,124	12.6% (142)	73.9% (831)	13.4% (151)	18.8±5.7	18.8±6.1	0.87 (<0.001)
1981	1987	295	18.9% (56)	61.7% (182)	19.3% (57)	19.7±7.1	19.5±7.1	0.87 (<0.001)
1978	1987	267	18.4% (49)	59.9% (160)	21.7% (58)	19.4±6.1	19.4±7.2	0.85 (<0.001)

[a] n. (%) of subjects with characteristic or mean±SD.

Table A4: Comparison of age at smoking cessation reported using similar questionnaire items at BHS waves (analysis restricted to the subjects who reported to be quitters at both waves under comparison).[a]

1st study wave	2nd study wave	N of smokers	Later cessation at 2nd wave, n (%)	Same age at cessation (±1 year), n (%)	Earlier cessation at 2nd wave, n (%)	Age at cessation at 1st wave, mean±SD	Age at cessation at 2nd wave, mean±SD	Spearman's rank correlation coefficient (p-value)
1966	1969	293	23.2% (68)	53.2% (156)	23.6% (69)	40.5±13.9	40.3±13.4	0.93 (<0.001)
1972	1975	303	15.5% (47)	71.9% (218)	12.5% (38)	41.5±14.0	41.7±14.1	0.96 (<0.001)
1978	1981	543	22.7% (123)	56.3% (322)	18.0% (98)	42.3±14.5	42.5±14.4	0.96 (<0.001)
1981	1987	178	26.9% (48)	50.6% (90)	22.5% (40)	49.2±12.8	49.1±13.9	0.89 (<0.001)
1978	1987	151	34.4% (52)	42.4% (64)	23.2% (35)	48.8±12.8	49.1±13.8	0.89 (<0.001)

[a] n. (%) of subjects with characteristic or mean±SD.

Table A5: Comparison of age at smoking cessation reported using **different** questionnaire items at BHS waves (analysis restricted to the subjects who reported to be quitters at both waves under comparison).[a]

1st study wave	2nd study wave	N of smokers	Later cessation at 2nd wave, n (%)	Same age at cessation (±1 year), n (%)	Earlier cessation at 2nd wave, n (%)	Age at cessation at 1st wave, mean±SD	Age at cessation at 2nd wave, mean±SD	Spearman's rank correlation coefficient (p-value)
1969	1972	348	18.4% (64)	62.4% (217)	19.2% (67)	40.3±13.7	40.3±13.2	0.95 (<0.001)
1975	1978	317	27.4% (87)	58.7% (186)	13.9% (44)	42.4±14.0	43.5±14.2	0.95 (<0.001)
1981	2010	40	30.0% (12)	55.0% (22)	15.0% (6)	24.6±4.7	27.5±9.1	0.60 (<0.001)

[a] n. (%) of subjects with characteristic or mean±SD.

Table A6: crude rates of smoking initiation per 1000/year (and person-years at risk) in males, by age group, cohort and period. [a]

Period	Age(years)											
	11-15				16-20				21-35			
	BHS	TAHS Siblings	TAHS Probands	OVERALL	BHS	TAHS Siblings	TAHS Probands	OVERALL	BHS	TAHS Siblings	TAHS Probands	OVERALL
1900-1909	47.2			47.12	106.9			106.9	70.6			70.6
	(763)			(763)	(262)			(262)	(85)			(85)
1910-1919	42.2			42.2	148.8			148.8	61.9			61.9
	(2,014)			(2,014)	(773)			(773)	(388)			(388)
1920-1929	39.4			39.4	131.9			131.9	60.3			60.3
	(3,199)			(3,199)	(1,788)			(1,788)	(1,061)			(1,061)
1930-1939	28.4			28.4	135.3			135.3	41.7			41.7
	(3,315)			(3,315)	(2,314)			(2,314)	(2,376)			(2,376)
1940-1949	37.6			37.5	173.9			173.9	45.9			45.9
	(2,737)			(2,744)	(1,788)			(1,788)	(2,674)			(2,674)
1950-1959	30.6	38.9		32.1	124.2	133.3		124.5	16.5			16.5
	(4,082)	(874)		(4,956)	(1,917)	(75)		(1,992)	(2,538)			(2,542)
1960-1969	37.7	40.2		39.0	120.3	127.6		122.7	16.0	26.8		17.1
	(7,898)	(8,903)		(16,801)	(4,330)	(2,139)		(6,469)	(3,729)	(411)		(4,140)
1970-1979	57.6	60.7	54.9	58.1	105.3	104.7	116.6	108.2	6.8	15.4		10.6
	(4,653)	(17,195)	(13,188)	(35,036)	(4,152)	(9,681)	(5,522)	(19,355)	(7,108)	(5,654)		(12,762)
1980-1989		91.2		91.2	70.3	93.3	50.9	77.8	5.2	8.4	11.2	8.5
		(1,370)		(1,370)	(1,038)	(5,394)	(2,828)	(9,260)	(7,130)	(18,269)	(9,882)	(35,281)
1990-1999									1.9	2.2	2.9	2.4
									(2,613)	(12,016)	(8,263)	(22,892)

[a] cells with less than 100 person-years at risk are omitted

Table A7: crude rates of smoking initiation per 1000/year (and person-years at risk) in females, by age group, cohort and period. [a]

Period	Age(years)											
	11-15				16-20				21-35			
	BHS	TAHS Siblings	TAHS Probands	OVERALL	BHS	TAHS Siblings	TAHS Probands	OVERALL	BHS	TAHS Siblings	TAHS Probands	OVERALL
1900-1909	1.1			1.1	6.2			6.2	3.9			3.9
	(881)			(881)	(482)			(482)	(257)			(257)
1910-1919	0.5			0.5	12.6			12.6	3.4			3.4
	(1993)			(1,993)	(1,266)			(1,266)	(1,479)			(1,479)
1920-1929	3.2			3.2	17.2			17.2	6.6			6.6
	(3,419)			(3,419)	(2,677)			(2,677)	(3,783)			(3,783)
1930-1939	5.3			5.3	42.8			42.8	13.4			13.4
	(3,784)			(3,784)	(3,548)			(3,548)	(6,713)			(6,713)
1940-1949	6.9			6.9	63.8			63.8	16.9			16.9
	(3,162)			(3,169)	(3,009)			(3,009)	(7,527)			(7,527)
1950-1959	7.3	8.5		7.5	62.7	51.0		62.3	13.3			13.3
	(4,382)	(706)		(5,088)	(2726)	(98)		(2,824)	(6,549)			(6,556)
1960-1969	17.6	17.8		17.7	81.4	87.6		83.1	10.2	31.3		11.6
	(9799)	(8,431)		(18,230)	(6,239)	(2,317)		(8,556)	(6,649)	(479)		(7,128)
1970-1979	47.4	50.9	51.4	50.5	97.5	102.0	131.2	107.9	7.3	13.6		9.6
	(6,011)	(16,532)	(12,872)	(35,415)	(6,039)	(10,252)	(5,303)	(21,594)	(11,327)	(6,540)		(17,867)
1980-1989		87.8		87.8	70.9	102.2	41.8	80.1	4.9	6.6	11.4	7.3
		(1,287)		(1,287)	(1,212)	(5,090)	(2,633)	(8,935)	(10,471)	(19,244)	(9,362)	(39,077)
1990-1999									1.8	2.2	2.2	2.1
									(3,394)	(11,542)	(7,864)	(22,800)

[a] cells with less than 100 person-years at risk are omitted

Table A8: Crude rates of smoking cessation per 1000/year (and person-years at risk), by sex, cohort and period.[a]

	Males aged Age 36-50			Females Age 36-50		
	BHS	TAHS	Pooled	BHS	TAHS	Pooled
1930-1939	3.8 (2,076)		3.8 (2,076)	2.48 (403)		2.4 (403)
1940-1949	6.1 (4,750)		6.1 (4,750)	5.8 (1,357)		5.8 (1,357)
1950-1959	13.0 (6,689)		13.0 (6,689)	6.6 (3,162)		6.6 (3,162)
1960-1969	19.9 (5,968)		19.9 (5,968)	9.9 (3,904)		9.9 (3904)
1970-1979	34.8 (2,866)		34.8 (2,866)	19.3 (2,121)		19.3 (2,121)
1980-1989	44.8 (1,872)	30.7 (1,170)	39.4 (3,042)	23.6 (1,438)	28.7 (939)	25.6 (2,377)
1990-1999	32.8 (4,350)	26.6 (13,667)	28.1 (18,017)	31.18 (4,201)	22.2 (11,561)	24.6 (15,762)
2000-2005	40.2 (2,160)	33.4 (14,795)	34.3 (16,955)	44.7 (2,237)	32.5 (13,254)	34.2 (15,491)

[a] cells with less than 100 person-years at risk are omitted

APPENDIX B

Impact of Smoking Behaviour and Weight Gain Changes on Lung Function

Figure B1. Estimated trajectories of FEV_1 decline, by smoking status with 95% confidence intervals. Blue lines: Never Smoker. Red line: Sustained Quitter. Green lines: Smoker. Yellow lines: Quitter.

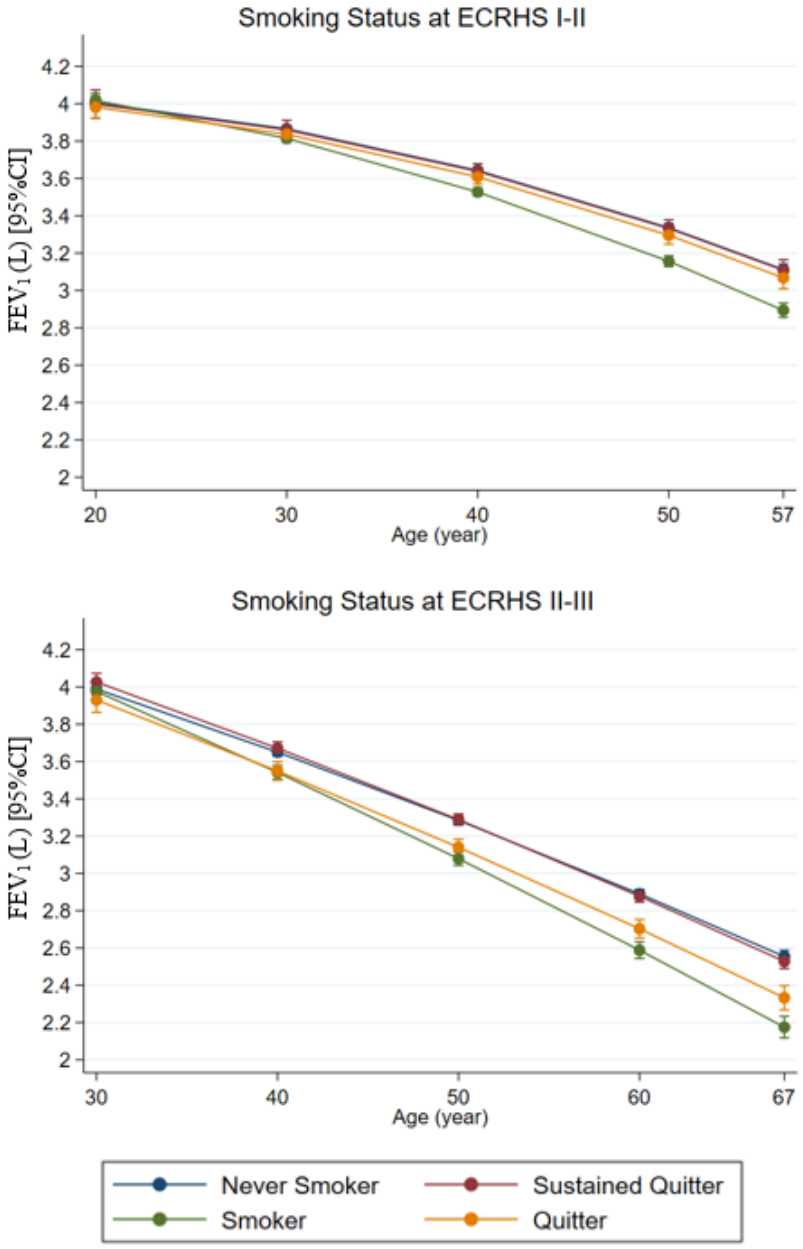

Figure B2. Estimated trajectories of FVC decline, by smoking status with 95% confidence intervals. Blue lines: Never Smoker. Red line: Sustained Quitter. Green lines: Smoker. Yellow lines: Quitter.

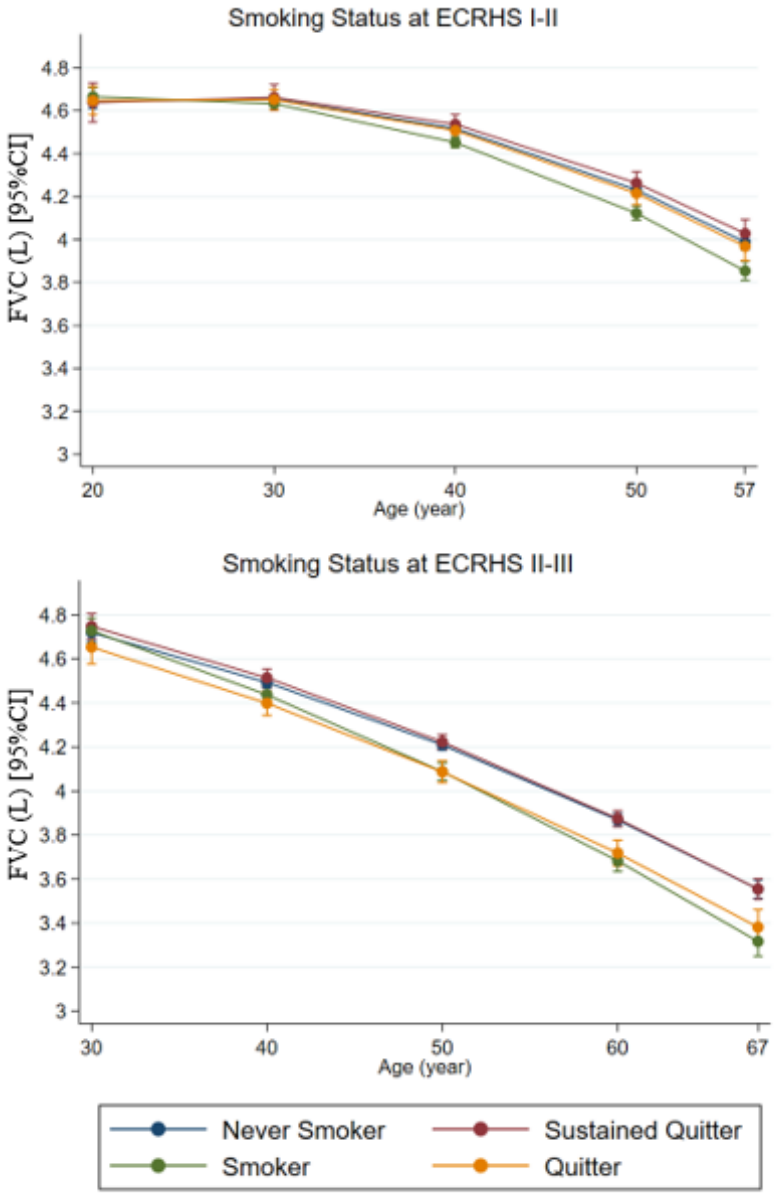

Figure B3. Estimated trajectories of FEV_1/FVC Ratio decline, by smoking status with 95% confidence intervals. Blue lines: Never Smoker. Red line: Sustained Quitter. Green lines: Smoker. Yellow lines: Quitter.

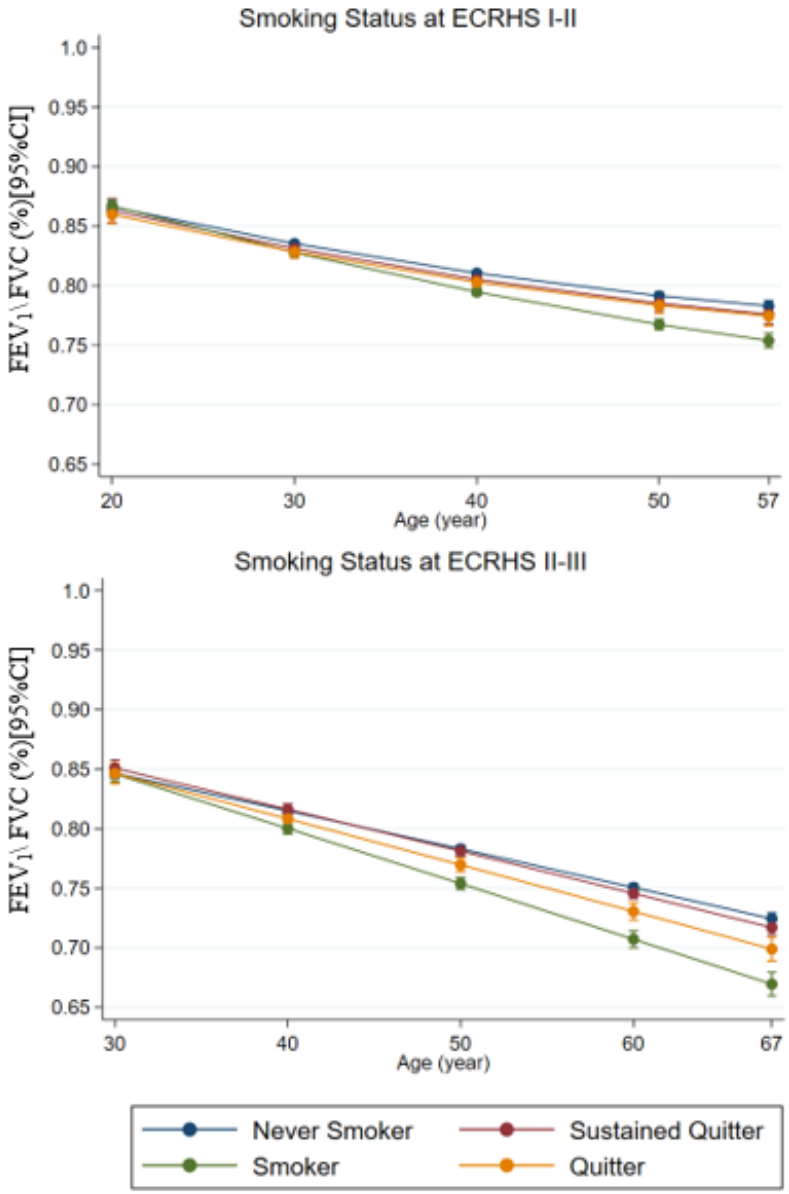

Figure B4. Estimated trajectories of BMI (Body Mass Index) decline, by smoking status with 95% confidence intervals. Blue lines: Never Smoker. Red line: Sustained Quitter. Green lines: Smoker. Yellow lines: Quitter.