# Smoking cessation patterns in patients with established coronary heart disease
# Entwicklung des Rauchverhaltens bei Patienten*innen mit Koronarer Herzerkrankung


Doctoral thesis for a medical doctoral degree
at the Graduate School of Life Sciences,
Julius-Maximilians-Universität Würzburg,
Section Clinical Sciences
submitted by

**David Johannes Göttler**
from
Nürnberg

Würzburg, 2020

**Submitted on:** **……**

## Members of the Thesis Committee:

**Chairperson:** **Univ.-Prof. Dr. med. N. Schlegel**

**Primary Supervisor:** **Prof. Dr. med. Stefan Störk**

**Supervisor Second:** **Prof. Dr. med. Peter U. Heuschmann**

**Supervisor Third:** **Prof. Dr. med. Dr. phil. Hermann Faller**

**Date of Public Defence:** **……**

**Date of Receipt of Certificates:** **……**

# Index of contents

# Summary


## Background

Tobacco smoking is accountable for more than one in ten deaths in patients with cardiovascular disease. Thus, smoking cessation has a high priority in secondary prevention of coronary heart disease (CHD). The present study meant to assess smoking cessation patterns, identify parameters associated with smoking cessation and investigate personal reasons to change or maintain smoking habits in patients with established CHD.

## Methods

Quality of CHD care was surveyed in 24 European countries in 2012/13 by the fourth European Survey of Cardiovascular Disease Prevention and Diabetes. Patients 18 to 79 years of age at the date of the CHD index event hospitalized due to first or recurrent diagnosis of coronary artery bypass graft, percutaneous coronary intervention, acute myocardial infarction or acute myocardial ischemia without infarction (troponin negative) were included. Smoking status and clinical parameters were iteratively obtained a) at the cardiovascular disease index event by medical record abstraction, b) during a face-to-face interview 6 to 36 months after the index event (i.e. baseline visit) and c) by telephone-based follow-up interview two years after the baseline visit. Parameters associated with smoking status at the time of follow-up interview were identified by logistic regression analysis. Personal reasons to change or maintain smoking habits were assessed in a qualitative interview and analyzed by qualitative content analysis.

## Results

One hundred and four of 469 (22.2%) participants had been classified current smokers at the index event and were available for follow-up interview. After a median observation period of 3.5 years (quartiles 3.0, 4.1), 65 of 104 participants (62.5%) were classified quitters at the time of follow-up interview. There was a tendency of diabetes being more prevalent in quitters vs non-quitters (37.5% vs 20.5%, p=0.07). Higher education level (15.4% vs 33.3%, p=0.03) and depressed

mood (17.2% vs 35.9%, p=0.03) were less frequent in quitters vs non-quitters. Quitters more frequently participated in cardiac rehabilitation programs (83.1% vs 48.7%, p<0.001). Cardiac rehabilitation appeared as factor associated with smoking cessation in multivariable logistic regression analysis (OR 5.19, 95%CI 1.87 to 14.46, p=0.002). Persistent smokers at telephone-based follow-up interview reported on addiction as wells as relaxation and pleasure as reasons to continue their habit. Those current and former smokers who relapsed at least once after a quitting attempt, stated future health hazards as their main reason to undertake quitting attempts. Prevalent factors leading to relapse were influence by their social network and stress. Successful quitters at follow-up interview referred to smoking-related harm done to their health having had been their major reason to quit.

**Interpretation**

Participating in a cardiac rehabilitation program was strongly associated with smoking cessation after a cardiovascular disease index event. Smoking cessation counseling and relapse prophylaxis may include alternatives for the pleasant aspects of smoking and incorporate effective strategies to resist relapse.

# Zusammenfassung

**Einleitung**

Bei Patienten*innen mit kardiovaskulären Erkrankungen ist mehr als einer von zehn Todesfällen auf Tabakrauchen zurückzuführen. Daher ist Rauchentwöhnung ein wichtiger Aspekt der Sekundärprävention der koronaren Herzerkrankung. In dieser Studie wurde der Verlauf des Rauchverhalten von Patienten*innen mit bekannter koronarer Herzerkrankung erfasst, Einflussfaktoren für Tabakabstinenz untersucht und die persönlichen Beweggründe zur Änderung oder Beibehaltung des Rauchverhaltens analysiert.

**Methoden**

Die Güte der Behandlung der koronaren Herzerkrankung wurde in 24 Europäischen Staaten in den Jahren 2012/13 im Rahmen des vierten European Survey of Cardiovascular Disease Prevention and Diabetes erfasst. Eingeschlossen wurden Patienten*innen zwischen 18 und 79 Jahren zum Zeitpunkt des kardiovaskulären Indexereignisses. Als kardiovaskuläres Indexereignis wurde eine stationäre Behandlung aufgrund der folgenden Erst- oder Rezidiv Diagnosen definiert: Koronararterien-Bypass, perkutane Koronarintervention, akuter Myokardinfarkt und akute myokardiale Ischämie ohne Infarkt (Troponin negativ). Rauchgewohnheiten und klinische Parameter wurden bei Patienten*innen im Studienverlauf wiederholt erhoben: a) Anhand der Behandlungsunterlagen während des kardiovaskulären Indexereignis, b) während eines persönlichen Interviews 6-36 Monate nach dem Indexereignis (i.e. Baseline Untersuchung) und c) im Rahmen eines telefonischen Follow-Up Interviews zwei Jahre nach der Baseline Untersuchung. Einflussfaktoren für Tabakabstinenz zum Zeitpunkt des telefonischen Follow-Up Interviews wurden über logistische Regressionsmodelle ermittelt. Die persönlichen Beweggründe das individuelle Rauchverhalten beizubehalten oder zu ändern wurden im Rahmen eines qualitativen Interviews erhoben und mithilfe der qualitativen Inhaltsanalyse ausgewertet.

**Ergebnisse**

104 von 469 (22,2%) Studienteilnehmer*innen wurden zum Zeitpunkt des Indexereignisses als Raucher*innen klassifiziert und nahmen an dem Follow-Up Interview teil. 65 von 104 (62,5%) dieser Raucher*innen gaben median 3,5 Jahre (Quartilen 3,0; 4,1) nach dem kardiovaskulären Indexereignis an mit dem Rauchen aufgehört zu haben. Es gab eine Tendenz zu höheren Prävalenzen von Diabetes bei nicht mehr Rauchenden im Vergleich zu weiterhin Rauchenden (37,5% vs. 20,5%; p=0,07). Höherer Bildungsgrad (15,4% vs. 33,3%; p=0,03) und Symptome einer depressiven Verstimmung (17,2% vs. 35,9%; p=0,03) waren bei nicht mehr Rauchenden seltener als bei weiterhin Rauchenden. Nicht mehr Rauchende nahmen überdurchschnittlich häufig an einem kardialen

Rehabilitationsprogramm teil (83,1% vs. 48,7%; p<0,001). Kardiale Rehabilitation war ein signifikanter Einflussfaktor auf Tabakabstinenz in der multivariaten logistischen Regression (OR 5,19; 95% Konfidenzintervall 1,87-14,46; p=0,002). Weiterhin Rauchende berichteten von Sucht sowie von Entspannung und Freude als Gründe nach wie vor zu rauchen. Diejenigen aktiven und ehemaligen Raucher*innen, welche mindestens einmal einen Rückfall nach einem Aufhörversuch erlebten, gaben Sorgen vor den gesundheitlichen Folgeschäden des Rauchens als Hauptgrund für Aufhörversuche an. Ihr soziales Umfeld und Stress waren häufige Gründe für Rückfälle. Ehemalige Raucher*innen berichteten von bereits eingetretenen gesundheitlichen Problemen, welche sie mit dem Rauchen in Verbindung gebracht hatten, als treibende Kräfte um nachhaltig abstinent sein zu können.

**Interpretation**

Die Teilnahme an einem kardialen Rehabilitationsprogramm war bei Patienten*innen mit kardiovaskulärer Erkrankung deutlich mit dem Verzicht auf Tabakrauchen assoziiert. Beratung zur Raucherentwöhnung und Rückfallprophylaxe könnten Alternativen für die, in der subjektiven Wahrnehmung, angenehmen Aspekte des Rauchens bieten und effektive Strategien zur Vermeidung von Rückfällen berücksichtigen.

# 1. Background

## 1. 1. Introduction

### 1. 1. 1. Topic

Tobacco smoking is a pivotal global risk factor and among the top priority targets for prevention of morbidity and mortality [*1*]. Cardiovascular diseases (CVD) are a leading concern of global health: 17.92 million CVD deaths (95% confidence interval 17.59 to 18.28 million CVD deaths) were estimated for the year 2015 [*2*]. Tobacco smoking is accountable for more than one in ten deaths in patients with CVD [*3*]. Smoking cessation offers a mortality benefit after myocardial infarction: thirteen smokers need to quit to save one life [*4*]. Thus, smoking cessation is an essential and evidence-based part of CVD prevention in clinical practice [*5*]. Following an acute cardiac event, about one of two prior smokers quit smoking [*6*]. Cardiac rehabilitation programs, absence of depressed mood and coronary surgery were associated with smoking cessation in previous studies [*7*, *8*]. The present study analyses smoking cessation patterns in patients after an acute cardiac index event. Elements of this thesis have recently been published by Goettler *et al* at BMC Cardiovascular Disorders [*9*].

### 1. 1. 2. EuroAspire IV

Germany participated in the fourth EuroAspire survey and the EuroAspire follow-up initiative (EuroAspire: European Action on Secondary and Primary Prevention by Intervention to Reduce Events). EuroAspire IV investigated, whether the Joint European Societies guidelines on secondary prevention of CVD were implemented in clinical practice and gathered data on lifestyle, comorbidities and therapeutic approaches of CHD patients in 24 European countries. Patients 18-79 years of age after coronary artery bypass graft, percutaneous coronary intervention, acute coronary infarction or acute coronary ischemia without infarction (troponin negative) were included [*10*].

### 1. 1. 3. Approach

A questionnaire on smoking cessation habits was implemented in the German EuroAspire IV follow-up interview. Questions on quantifiable variables allowed

analysis of objective parameters associated with smoking cessation. Open ended questions asking for the patients' reasons to change or maintain smoking behavior allowed qualitative analysis of subjective perceptions regarding smoking habits.

## 1. 2. Scientific background

### 1. 2. 1. Tobacco smoking

The World Health Organization (WHO) stated the German prevalence of current tobacco smoking in 2010 was 27.9% (males 31.6%; females 24.4%) [*11*]. In 2013 smoking caused 6.1 million preventable deaths and 143.5 million Disability adjusted life years (DALYs) globally [*1*]. Approximately 0.6 million deaths were due to environmental tobacco smoke exposure (ETS) [*1*]. The disease burden attributable to smoking was distributed in descending order to cardiovascular diseases, chronic respiratory diseases and cancer [*1*]. According to Doll *et al* smoking male British doctors faced a two- to threefold increased all-cause mortality rate compared to their non-smoking colleagues [*12*]. However, the excess mortality risk was halved by smoking cessation at 50 years of age and nearly reversed by cessation at 30 years of age [*12*].

According to Ambrose *et al* the respective hazards were predominantly mediated by an increased level of oxidative stress next to decreased nitric oxide generation and bioavailability in both the endothelial cell and the thrombocyte [*13*]. Tobacco smoking triggered vasomotor dysfunction, increased inflammation and induced modification in the lipid profile, fueling the process of atherosclerosis. Platelet dysfunction, alteration of antithrombotic and pro-thrombotic factors and alteration in fibrinolysis caused by smoking increased the risk of thrombosis and thromboembolism [*13*]. Some advantages of smoking cessation may occur almost immediately, possibly those associated with thrombocyte function, others may take longer [*13*].

Tobacco smoking is a global concern. The WHO Framework Convention on Tobacco Control was the first evidence-based public health initiative which resulted in an international treaty negotiated by WHO and accepted by the majority of member states in 2003 [*14*]. The World Health Assembly published in

2013 the “Global Action Plan for the prevention and control of non-communicable diseases” containing the goal of a 30% relative reduction in the prevalence of tobacco smoking in persons above 15 years of age [*15*]. Many countries, including Germany, are not on track with these target, some even at risk for worsening trends, hence sustained and joint efforts are needed to curtail the global tobacco epidemic [*11*, *16*].

### 1. 2. 2. Coronary heart disease

Coronary heart disease / ischemic heart disease (CHD, IHD) was the leading single cause of CVD mortality causing 8.92 million deaths (95%CI 8.75 to 9.12 million deaths) as estimated for the year 2015 [*2*]. Furthermore, CHD was the leading cause of morbidity causing 150.2 million DALYs as estimated for the year 2013 [*17*]. The cardiovascular risk factors smoking, blood pressure, body-mass index and fasting plasma glucose were among the top 5 risk factors of all-cause mortality in most countries in 2013 [*1*]. CHD is a disease of the blood vessels supplying the heart muscle. It presents with unstable angina pectoris, acute myocardial infarction (AMI) or sudden cardiac death. Symptoms may be pain or discomfort in the center of the chest, the left shoulder, jaw or back (i.e. angina pectoris) and difficulties in breathing or shortness of breath (i.e. dyspnea). Additional vegetative reactions involve nausea and vomiting, breaking into a cold sweat, faintness and paleness. Females are more likely to present with dyspnea and vegetative symptoms, whereas males are more likely to present with angina pectoris [*18*].

Atherosclerosis is the underlying concept of CHD pathophysiology [*19*]. The micro-pathologic correlate of atherosclerosis is the atherosclerotic plaque, a formation of cells, cell detritus, proteins and lipids inside the arterial blood vessel wall. The normal muscular artery contains three layers: the inner layer (tunica intima), with a monolayer of endothelial cells above a basement membrane, that is in contact with the blood flow; the middle layer (tunica media), with smooth muscle cells embedded in an extracellular matrix; and the outer layer (adventitia) with mast cells, nerve endings and micro-vessels. Stimuli such as pro-inflammatory mediators, high blood pressure and dyslipidemia induce an “activation” of the endothelial monolayer, involving overexpression of leukocyte

adhesion molecules. The development of atherosclerosis includes the adhesion of white blood cells to the activated endothelial cells, migration of these leukocytes into the intima, maturation of monocytes to tissue macrophages and finally – by lipid uptake – to foam cells. Maturation of the initial atherosclerotic lesions include further changes in endothelial permeability leading to entry and accumulation of lipids, inflammatory cells and smooth muscle cells in the intima. In advanced lesions necrotic cores develop in the central region of the plaque. Subsequent increase in the stable plaque's volume leads to slowly progressive stenosis in the corresponding vessel. Clinical manifestation of the stenosis in the coronary arteries reflects a relative deficit of the blood flow causing angina pectoris, dyspnea and/or vegetative symptoms. The most hazardous complication of advanced atherosclerotic lesions is considered thrombosis: the rupture of the instable plaque's fibrous cap frees blood coagulation components and pro-coagulative tissue factors from the plaque's interior, thus triggering thrombus formation. The thrombus may occlude the vessel at its place of origin (i.e. thrombosis) or further downstream (i.e. thromboembolism) causing an acute myocardial infarction when effectually occluding a vessel of the coronary system [*19*].

A substantial part of CHD morbidity and mortality may be susceptible to comprehensive prevention efforts. According to Geoffrey Rose, prevention efforts encouraging "biological normality" such as smoking cessation have a safe and profound effect on the population as a whole and an even larger effect on individuals with clinically manifest CHD [*20*]. The European Society of Cardiology (ESC) published guidelines on CVD prevention in clinical practice since 1994 [*5*, *21-26*]. Primary prevention focused on persons without clinical manifestations of CHD. Current evidence strongly recommends adequate and regular physical activity, a healthy diet with low amounts of salt and saturated fats, abstinence from tobacco and alcohol and maintaining a healthy body weight [*5*]. Secondary prevention aims at patients with already established CHD. Recommendations added to the ones above are: target an appropriate average blood pressure, maintain low levels of total cholesterol and low-density lipoprotein, use adequate drug therapy and avoid the onset of diabetes [*5*]. Concrete therapy goals and

cardio-protective drug recommendations were defined according to age, overall cardiovascular risk profile and comorbidities, respectively [*5*]. To monitor the achievement of guideline implementation and enable subsequent evaluation since 1996, the EuroAspire (European Action on Secondary and Primary Prevention through Intervention to Reduce Events) cross-sectional surveys have reported on clinical practice in secondary prevention of CHD in Europe using comparable methodology over time [*10*, *27-29*]. Underlying determinants of disease, “the causes of the causes”, have been identified. Some of them are beyond the traditional reach of medical professionals targeting major forces of social, economic and cultural change: globalization, urbanization, climate change and population ageing [*18*, *30*, *31*].

### 1. 2. 3. Tobacco smoking, smoking cessation and coronary heart disease

Tobacco smoking is associated with the onset and progress of CHD: in an international case-control study with 15,152 cases and 14,820 controls the odds to suffer an AMI in current vs never-smokers was tripled (OR 2.95, 95%CI 2.72 to 3.20; adjusted for age and sex) [*32*]. Referring to the SCORE project the 2016 ESC guideline on Cardiovascular Disease prevention stated that the 10-year fatal cardiovascular risk was approximately doubled in smokers with CHD compared to non-smokers with CHD [*5*, *25*, *33*]. General smoking prevalence is correlated with CHD mortality: between 1981 and 2000 CHD mortality rates in England and Wales decreased substantially due to evidence-based treatment options and risk factor control and 48% of this decrease was estimated attributable to smoking [*34*]. In the same period comparable trends of falling CHD mortality due to improved treatment and risk factor control were observed in the USA, there, the risk reduction attributable to smoking was estimated 12% [*35*].

In observational studies the onset of CHD is associated with smoking cessation. In the four EuroAspire surveys approximately half of current smokers during the index hospitalization stopped smoking afterwards [*6*, *36*]. Dawood *et al* reported a 46% quitting rate in patients six month after AMI in the USA [*8*]. A study from the Mayo Clinic, Minnesota, reported a 37% rate of successful quitting after percutaneous coronary intervention [*37*]. “Teachable moments” or “cues to action” like the onset, recurrence or acute progress of CHD may induce change

in smoking behavior [*38*]. Several factors associated with smoking cessation in patients after an acute cardiac event were identified: e.g. age, ethnic origin, smoking intensity (i.e. pack years), level of education, coronary surgery performed, depressed mood or participation in a cardiac rehabilitation program [*7*, *8*, *37*, *39-41*].

### 1. 2. 4. Qualitative exploration of smoking habits

Qualitative research methods, based on textual interpretation and quantitative research methods, based on statistical analysis, may complement each other [*42*]. Knowledge on personal perception of smoking habits in high risk populations is still limited, but nevertheless essential to attain a satisfactory understanding of smoking cessation patterns and develop adequate smoking cessation interventions [*43*]. A study of 20 current and former smokers aged older than 65 years in Scotland stated that former smokers stopped smoking mainly due to health-related considerations and experienced successful cessation as beneficial to their well-being afterwards [*43*]. Persistent smokers reported some positive associations with smoking (e.g. relaxation, enjoyment) though the majority was aware of the health hazards (e.g. respiratory problems, heart disease) and described themselves being addicted [*43*]. Although 13 of 20 study participants in an another study of 20 current smokers above 50 years of age were suffering from severe chronic diseases such as cancer or CHD, the majority indicated “beneficial” qualities of smoking such as better management of tiredness and stress, relaxation, enjoyment and being an important part of their social activities [*44*]. Only 6 of 20 participants were well informed about the health hazards of smoking, remarkably, they had the highest level of education among all study participants [*44*].

The Health-believe model was developed to study and predict health-related behaviors [*45*]. It consists of four dimensions that are presented with examples for smokers with established CHD. 1) *Perceived susceptibility* is the individual perception of risk to develop a specific health problem like experiencing recurrent myocardial infarction. 2) *Perceived severity* is the perceived seriousness of a possible health problem and its consequences like the awareness of a life threat due to sudden cardiac death or physical handicap due to heart failure. 3)

*Perceived benefits* of a certain health-promoting behavior like reduced risk of recurrent AMI due to smoking cessation in patients with established CHD reflect the assessment of quality and efficacy of a given recommendation. 4) *Perceived barriers* like fear of withdrawal symptoms or social isolation from smoking friends may impede behavior change [*46*, *47*]. The personal threat perceived by the combination of susceptibility and severity may be the motivation for behavior change which occurs, if the perceived benefits predominate the perceived barriers [*46*]. This process may be triggered by a cue to action like the acute onset or progress of CHD when the patient feels self-confident of achieving behavior change [*47*].

## 1. 3. Study objectives

### 1. 3. 1. Aims

The primary objective was to design and realize the telephone-based follow-up interview of the German arm of the EuroAspire IV survey in Würzburg. Data on disease specific re-hospitalization and mortality rates and on recent diagnosis of chronic diseases such as diabetes mellitus, chronic kidney disease, transient ischemic attack/stroke and cancer were collected. The sub-study presented in this thesis aimed to describe and evaluate smoking cessation patterns of high-risk individuals with established CHD in a comprehensive approach with quantitative and qualitative elements.

### 1. 3. 2. Research questions

1) What percentage of current smokers during a CHD index hospitalization continues to smoke, quits smoking, relapses after a quitting attempt and/or successfully quits smoking until the telephone-based follow-up interview?
2) Which determinants of demography, relevant comorbidities and secondary prevention efforts influence the chance of successful cessation?
3) Are there differences in these determinants between never-smokers, former smokers, current smokers (undertaking at least one quitting attempt) and ever-smokers (never undertaking a quitting attempt)?

4) Which factors (positive as relaxation or pleasure; negative as addiction or fear of withdrawal symptoms) drive smoking continuation or relapse after a quitting attempt?
5) What motivates a person (e.g. life event, health issue, financial reason) to undertake a quitting attempt or stop smoking?
6) Have such reasons prevented never-smokers to start smoking in the first place?

### 1. 3. 3. Assumptions

Based on current evidence, the prevalence of current smoking at index event was assumed approximately 25% and the rate of subsequent cessation approximately 50% (*refer to 1. 2.* ). Older age, higher levels of education, cardiac surgery, absence of depressed mood and attending a cardiac rehabilitation program were supposed to be associated with successful cessation. The individual decision to change or maintain smoking behavior was assumed strongly depending on the ambivalence between personal perception of benefits and harms related to tobacco smoking, influenced by the individual's social network.

# 2. Methods

## 2. 1. Study population

EuroAspire IV was an international cross-sectional survey conducted at 78 centers in 24 European countries between May 2012 and April 2013. Within each country, one or more geographical areas with defined populations were selected and all hospitals serving this population identified. A sample of one or more hospitals (or all hospitals) of that area was selected. Thus, any inhabitant within the area presenting with acute coronary symptoms or requiring revascularization in form of elective or emergency percutaneous coronary intervention or coronary artery bypass graft had approximately equal chances of being included in the study. Detailed information on the EuroAspire IV study methodology has been provided previously [*10*]. Würzburg is a rural area in Lower Franconia and acted as the German study coordination center in the fourth EuroAspire survey. Two hospitals providing acute treatment for coronary artery disease participated in the study: University Hospital of Würzburg (Department of Cardiovascular Surgery and Department of Medicine I) and Klinik Kitzinger Land (Department of Medicine). Participants were retrospectively identified for study interview from the hospitals' digital information systems and consecutively invited by up to three postal letters according to the following inclusion criteria applicable to the index event (*refer to Figure 1*):

- First or recurrent clinical diagnosis of CHD at index event defined by: elective or emergency coronary artery bypass graft (CABG), elective or emergency percutaneous coronary intervention (PCI), acute myocardial infarction (AMI) or acute myocardial ischemia without infarction (AMIsch; troponin negative)
- Age 18 to 79 years at the date of the cardiovascular index event
- Index event more than 6 months and less than 3 years before the scheduled date of baseline visit
- Admission to the University Hospital of Würzburg or the Klinik Kitzinger Land

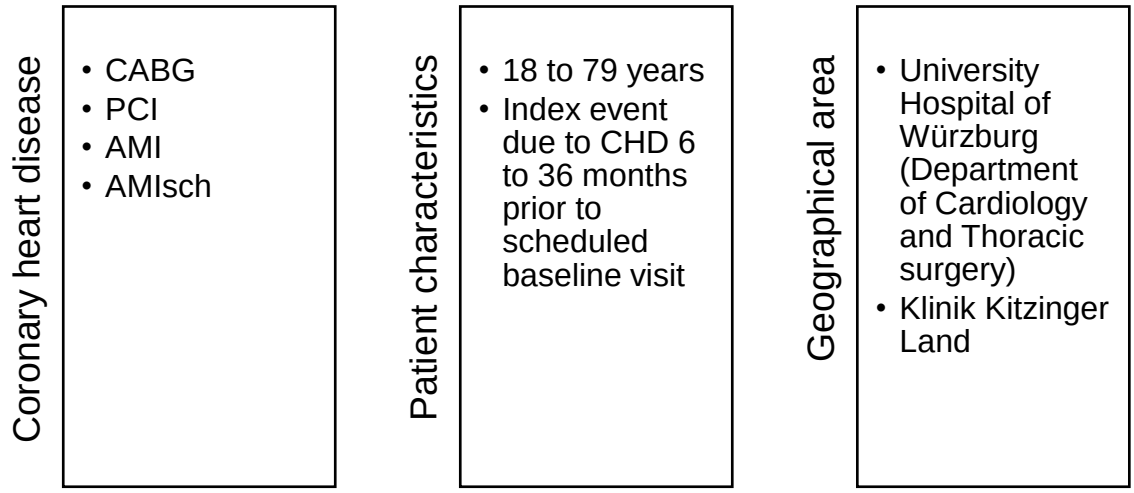


Figure 1 Participants' inclusion criteria

Participants were excluded if they were unable or unwilling to provide consent, died during index hospitalization or if coronary artery disease had not been confirmed.

For the telephone-based follow-up interview all persons participating at baseline visit were included. Participants were called up to ten times on different days and hours. If the participant was unavailable a message explaining the call's purpose and a request for call-back were left on the answering machine. In case the phone number was not valid anymore, public resources (i.e. internet and telephone books) were searched for alternatives. If no valid number was available or the researcher had unsuccessfully called ten times, information on vital status was obtained from public residents' registration offices. Participants who were not reachable, denied participation over the phone or had died prior to telephone-based follow-up interview were excluded from subsequent analyses of follow-up data.

## 2. 2. Study design

The study was designed as a cohort study with data acquisition at three time points (*refer to Figure 2*).

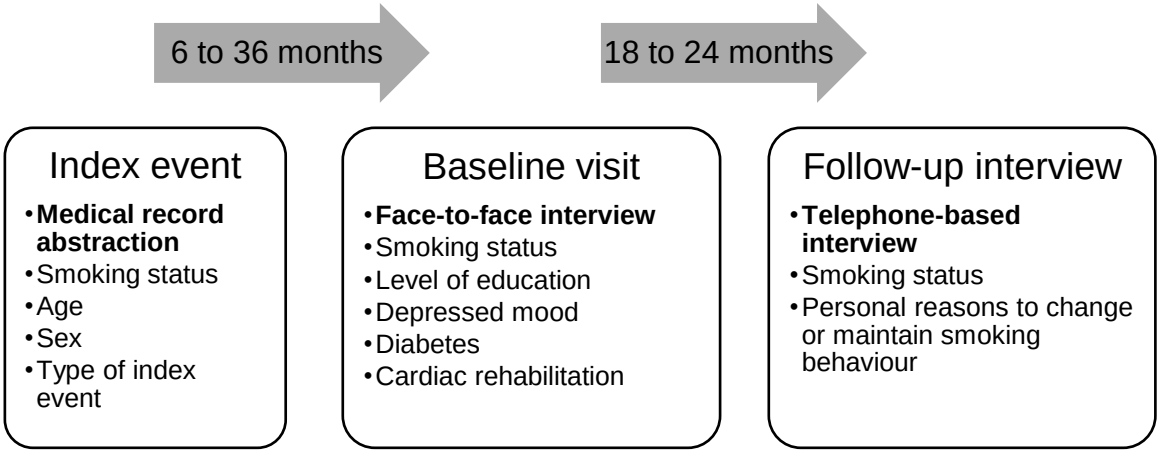


Figure 2 Process of data acquisition

### 2. 2. 1. Index event

Study participants were recruited after the index event. When informed consent had been obtained, trained research staff retrospectively extracted the predefined sets of information from medical records in the hospitals' digital information system using a standardized paper-based questionnaire. Data were collected in the following modules: demography (age, sex, ethnic origin), index event (date, type and further details of the index event), comorbidities at admission and at discharge (hypertension, hyperlipidemia, diabetes, chronic kidney disease, heart failure, smoking status, alcohol abuse, drug abuse and psychiatric disorders). Furthermore, measurements during the hospital stay (e.g. height, weight, blood pressure, heart rate and laboratory data), detailed information on discharge medication and data on subsequent planned or already performed procedures (e.g. CABG, PCI, planned readmission) were also registered.

### 2. 2. 2. Baseline visit

Baseline visit was conducted at least six months and at most three years after the index event. Trained research staff from the Institute of Clinical Epidemiology and Biometry (ICE-B), University of Würzburg and the Comprehensive Heart Failure Center (CHFC), University Hospital of Würzburg, carried out data acquisition according to the standardized international EuroAspire IV protocol.

During a structured personal interview data was collected on the following modules: socio-demography (e.g. age, sex, ethnic origin, education, situation of work), further and former development of CHD (e.g. recurrent admission, hospitalization prior to the index event), lifestyle (smoking, diet, physical exercise), comorbidities (e.g. arterial hypertension, hyperlipidemia, diabetes, chronic kidney disease, heart failure), cardiac rehabilitation, current medication and the participant's knowledge on risk factor control and treatment goals. Device-based measurements (e.g. electrocardiography and echocardiography) and blood analysis (e.g. fasting plasma glucose [PG] and glucose measurement 2-hours after oral glucose loading [2hPG]) were done. The participants answered several questionnaires including the "Hospital Anxiety and Depression Scale" (HADS). Data acquisition for index event and baseline visit was paper-based and subsequently entered electronically via web data entry.

#### 2. 2. 3. Follow-up interview

The telephone-based follow-up interview was performed 18 to 24 month after the baseline visit. The follow-up questionnaire was published recently [*9*]. Data on vital status and readmission to a hospital due to recurrent CABG, PCI or AMI, as well as comorbidities, current smoking behavior and personal reasons to change or maintain smoking habits were collected. Assessment of smoking behavior included intensity and duration of smoking, time to first cigarette in the morning, detailed information on quitting attempts and relapses and open-ended questions on the participant's personal reasons to change or maintain smoking behavior (*refer to 2. 6.* ). The follow-up questionnaire was implemented in a Microsoft Access database, i.e. data were not recorded on paper but directly entered electronically.

## 2. 3. Definitions

#### 2. 3. 1. Smoking status

Current smoking was defined by self-report at each time-point of investigation and confirmed by breath Carbon monoxide (CO) via smokerlyzer >10 ppm at baseline visit. Smoking status was not documented for 59 participants in the medical record. To minimize drop-outs due to missing data, two variables from

different time points were combined to define the variable smoking status at index event:

- Smoking status according to the medical record at index event
- Self-reported smoking one months prior to the index event, as asked retrospectively at baseline visit (*refer to Table 1*).

Table 1 Definition of binary smoking status

| Time point | Smoking status definition | Data source |
|---|---|---|
| **Index event** | Self-reported smoking according to the medical record at index event **or** self-reported smoking one month prior to the index event according to face-to-face interview at baseline visit | Medical record<br>Baseline interview |
| **Baseline visit** | Self-reported smoking **or** breath CO >10 ppm at baseline visit | Baseline interview<br>Smokerlyzer |
| **Follow-up interview** | Self-reported smoking at telephone-based follow-up interview | Follow-up interview |

Furthermore, for 469 patients who participated throughout the whole study period an extended smoking status variable at index event was defined (*refer to Table 2*). All study participants were asked both at baseline visit and at telephone-based follow-up interview, if they had ever smoked **or** had ever undertaken a quitting attempt. At index event those non-smokers consistently reporting never-smoking, were considered never-smokers. Accordingly, those smokers who did not report any quitting attempt prior to the index event were considered ever-smokers.

Table 2 Definition of extended smoking status at index event

| **Extended smoking status definition at index event** | | **Data source** |
|---|---|---|
| Former smoker | Self-reported non-smoking according to the medical record at index event **and** self-reported non-smoking one month prior to the index event according to face-to-face interview at baseline visit | Medical record<br>Baseline interview |
| Never-smoker | Self-reported never-smoking according to the medical record at index event **and** self-reported never-smoking one month prior to the index event according to face-to-face interview at baseline visit | Medical record<br>Baseline interview |
| Current Smoker | Self-reported smoking according to the medical record at index event **or** self-reported smoking one month prior to the index event according to face-to-face interview at baseline visit | Medical record<br>Baseline interview |
| Ever-smoker | Classified current smoker at index event **and** retrospectively did not report any period of non-smoking prior to the index event | Medical record<br>Baseline interview<br>Follow-up interview |

### 2. 3. 2. Demography

Age was calculated as difference between the date at index event or telephone-based follow-up interview and birth date, respectively. In quantitative analyses regarding the primary endpoint age at index event was presented. For qualitative exploration age at telephone-based follow-up interview was presented. The participants' gender was documented in the medical record. At baseline visit study participants reported their highest level of formal education. High school completed, college/university completed and post-graduate degree were considered high education level. No formal schooling, less than primary school, primary school completed, secondary school completed and intermediate between secondary level and university training such as technical training were defined low education level.

### 2. 3. 3. Coronary heart disease and comorbidities

The cardiac event leading to the index event was used for classification (i.e. CABG, PCI, AMI, or AMIsch). Diabetes was defined according to ESC 2013/ADA 2012 criteria by PG ≥7.0 mmol/l **or** 2hPG ≥11.1 mmol/l as assessed at baseline visit [*26*]. Depressed mood was investigated using the German version of the HADS questionnaire at baseline visit. The sub-test on depression uses seven

items addressing depressive symptoms on an ordinal scale. Since all items have values ranging 0 to 3, the test for depression has a maximum score of 21. Presence of depressed mood was defined with a sum score of eight or more [*48*].

#### 2. 3. 4. Cardiac rehabilitation

At baseline visit all participants were asked, if they had been advised to attend a cardiac prevention or cardiac rehabilitation program within three months of discharge following the index event. Subsequently, the frequency of participation was assessed. Cardiac rehabilitation was counted as “participation”, if the participant had attended at least half of the recommended sessions of a cardiac rehabilitation program. Data on duration and type of cardiac rehabilitation program (center-based vs home-based) were not systematically assessed. In Germany, cardiac rehabilitation programs are usually center-based with a duration of three to four weeks.

#### 2. 3. 5. Heavy Smoking Index

The Heavy Smoking Index (HSI) is an abridged version of the Fragerström Test for Nicotine Dependence [*49*]. It combines the two items number of cigarettes smoked per day and time to first cigarette in the morning. With a sensitivity of 79.5% and a specificity of 96.5% it allows evaluating nicotine dependence in a time-saving manner. HSI was assessed at telephone-based follow-up interview and was presented for current smokers at follow-up interview as well as (retrospectively) for former smokers at follow-up interview, referring to the last week before they had quit smoking.

## 2. 4. Data management

Central data management was carried out by the EURObservational Research Programme at the European Heart House in Nice, France. Via web-based data entry data were collected electronically using explicit identification numbers for each country, center and participant. Data were checked for completeness, internal consistency and accuracy. All data were stored under National Data Protection Regulations. Thereafter, a copy of the German data set was sent to the research group in Würzburg.

Data management in Germany was carried out in a cooperation project between ICE-B and CHFC by trained local staff. Follow-up data were collected and stored in two separate Microsoft Access data bases. The first included personal data, containing name, sex, address, telephone numbers and details on phone calls (date and hour of last phone call, number of calling attempts) for each participant. This database was necessary to organize and carry out the telephone-based follow-up interview and to reliably identify the person answering the phone as the correct study participant. The second database was used for the follow-up questionnaire. The unique identification number allowed linking both data bases. Personal information such as name, sex, address and telephone number were never connected to any other data sets containing health related information. Regular checks for completeness and plausibility were run. Recruitment strategy, data acquisition and data storage were authorized by the data protection officer at the University of Würzburg.

A pilot study with 23 persons, who were excluded because coronary heart disease had not been confirmed during the index event, was performed prior to the main data acquisition process to test and optimize study methodology.

## 2. 5. Outcome measure

Smoking status at telephone-based follow-up interview upon current smokers at index event was defined as the primary endpoint. Subsequently, the influence of age, sex and coronary surgery at index event, as well as education, diabetes, depressed mood and cardiac rehabilitation on smoking status at telephone-based follow-up interview was investigated. The variable selection procedure was based on clinical relevance and published literature (*refer to 1. 2. 3. )*. Successful quitters were compared to persistent smokers using statistical tests as described in the following (*refer to 2. 8.* ).

## 2. 6. Qualitative data acquisition and interviewing technique

Qualitative interviews were performed with all 469 study participants at telephone-based follow-up interview by the main researcher (DG) to gain insights into the participants' perspective towards smoking habits and smoking cessation. At that time DG was a fourth-year medical student without practical experience in

qualitative interviewing. He was aided by co-researchers, who were thoroughly experienced in qualitative research. The interviewing technique may have improved during the scientific process; as recommended an open dialog in the research team throughout the study process was carried out to address the challenge of internal consistency and trustworthiness of the findings [*50*].

Qualitative interviews were conducted via telephone after the other telephone-based follow-up questions regarding re-hospitalization, comorbidities, symptom severity of CHD and information on smoking habits. A directed qualitative content analysis approach was used [*51*]: each interview began with one standardized open-ended question asking for reasons to change or maintain smoking behavior and proceeded with one standardized closed question asking for more details regarding predefined key concepts developed from prior research (*refer to Table 3 and 1. 2. 4.* ). If a current or former smoker had reported a quitting attempt additional open-ended and closed questions regarding the quitting attempt and subsequent relapse were asked, respectively. Never-smokers were asked to talk about whether they had specific reasons to never start smoking. Interviews were neither audiotaped nor transcribed verbatim but aggregated in writing in German language. Qualitative quotes were cited with pseudonymized identification numbers (pID) respecting privacy issues and enabling external validation on reasonable request. Depending on the participants' responses the length of aggregated transcripts ranged from short statements such as "myocardial infarction" (pID 1) over "colleagues in Munich had lung cancer, together we agreed to stop" (pID 2) to longer explanations such as "I fell of a 1.6m high ladder, had to go to hospital for 14 days, had a severe concussion and stopped smoking afterwards" (pID 3); examples from reasons to quit. Documented study data consisted of episodes with nearly verbatim transcripts and condensed responses resulting in an abstraction level of meaning unit or condensed meaning unit [*50*]. Hence, the qualitative analysis process already started during data acquisition.

Table 3 Qualitative interview questions at follow-up interview

| Smoking status | Open-ended question | Closed question |
|---|---|---|
| Current smoker | Would you please try to describe your most important reasons to smoke? | Are there reasons you consider positive, such as pleasure, joy or relaxation or even reasons you consider negative, such as addiction or fear of withdrawal symptoms? |
| Current smoker or former smoker that reported a quitting attempt | Would you please try to describe the reasons why you tried to stop smoking at that time? | Did health risks for you or others, financial issues or important life events influence your decision?<br>Only if a disease/diagnosis was mentioned: Did you consider this (disease/diagnosis) life threatening? |
| Current smoker or former smoker that reported a quitting attempt | Would you please try to describe the reasons why you restarted smoking at that time? | Has there been an extraordinary situation or event? |
| Former smoker | Would you please try to describe the reasons why you stopped smoking definitely? | Did health risks for you or others, financial issues or important life events influence your decision?<br>Only if a disease/diagnosis was mentioned: Did you consider this (disease/diagnosis) life threatening? |
| Never-smoker | Would you please try to describe the reasons why you never started smoking? | Did health risks for you or others, financial issues or important life events influence your decision? |

## 2. 7. Qualitative content analysis

According to the participants' smoking status three research questions were formulated (*refer to 1. 3. 2.* ). Qualitative content analysis was organized step wise (*refer to Figure 3*) with inductive and deductive elements to accomplish best possible trustworthiness of results and conclusions [*52*]. Five units of analysis were defined:

- Reasons to continue smoking
- Reasons to undertake quitting attempts
- Reasons to relapse after a quitting attempt
- Reasons to quit
- Reasons to never start smoking

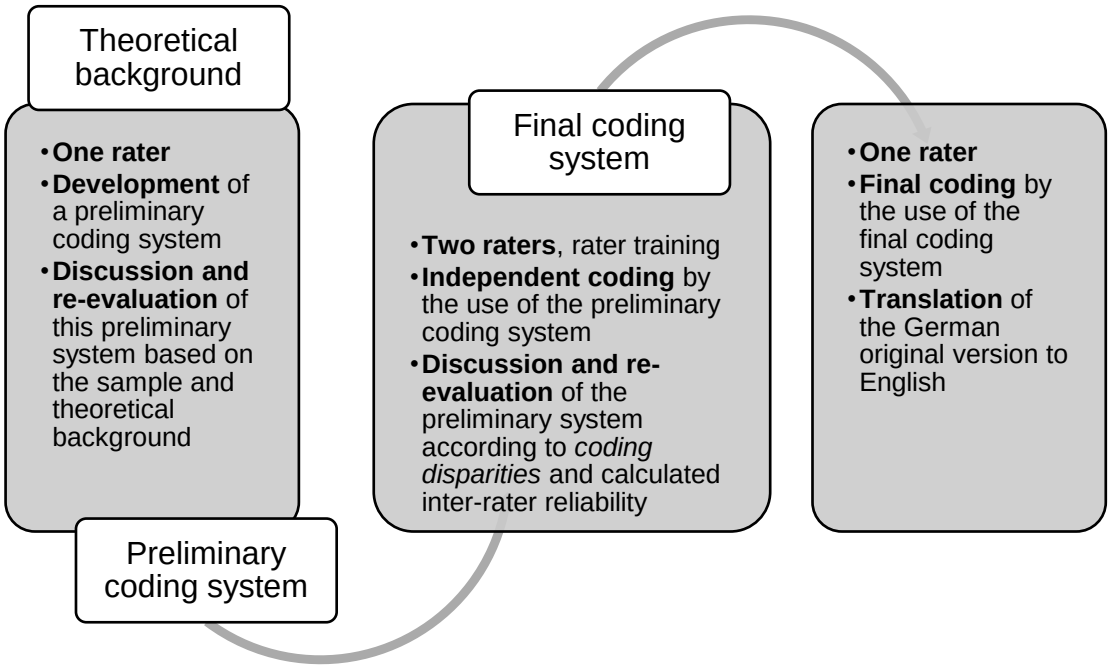


Figure 3 Process of qualitative content analysis

Codes, categories and themes were equally defined for reasons to continue smoking / relapse after a quitting attempt and reasons to undertake quitting attempts / stop smoking to enable comparisons. Reasons to never start smoking were analyzed separately. A meaning unit was defined as a single word, words or sentences "containing aspects related to each other through their content and context" [*50*] (*refer to Table 4*).

Table 4 Examples of meaning unit, condensed meaning unit and code

| **Meaning unit** | **Condensed meaning unit** | **Code** |
|---|---|---|
| It is easier to relax with the smoking (pID 4) | Relaxing | Relaxation |
| Appetite and craving had been there, (…) and then I fell back in my old daily grind (pID 5) | Feeling of craving | Addiction |

In the first step the same researcher who performed the interviews (DG) read through a random sample of 40 answers per question several times to get an overview of the data. This sample size was *a priori* considered to be detailed enough to touch on the most important aspects of all questions and small enough thus allowing subsequent analytical steps as described in the next paragraph.

Based on this initial sample a preliminary coding system was established with methods of condensation (i.e. a process of shortening data while still preserving the core) and abstraction (i.e. describing data by creating codes, categories and themes on a higher level of interpretation; *refer to Table 5*) [*50*]. The preliminary coding system contained the following:

- Code (defined as a label for a condensed meaning unit)
- Coding rule (further explanations to discriminate between similar codes)
- Category (descriptive level of summary)
- Theme (interpretative level of summary)

Table 5 Examples of codes, categories and themes

| **Unit of analysis** | **Reasons to continue smoking**<br>**Reasons to relapse after a quitting attempt** | | | |
|---|---|---|---|---|
| **Theme** | **Positive reasons** | | **Negative reasons** | |
| **Category** | Relaxation | Pleasure | Addiction | Stress |
| **Codes** | Smoking calms me down<br>I imagine winding down | Tastefulness<br>Feeling of happiness | Addiction<br>I felt a desire to smoke again | Stress<br>Road accident |

Codes were defined binary (yes/no) using Microsoft Access 2010 software. To ascertain discrimination each reason to change or maintain smoking behavior (i.e. meaning unit) was labelled with one code only. If more than one meaning unit per unit of analysis was identified, each meaning unit was labelled with one distinct code. Using the input from the research team the preliminary coding system was theoretically evaluated and modified.

Secondly, another rater (AR) was involved to increase the coding system's quality. After detailed rater training based on the first 40 responses and subsequent discussion on how to interpret and use the codes and coding rules of the preliminary coding system, both raters (DG and AR) coded another random sample of 40 responses per question independently according to the preliminary coding system. Inter-rater reliability (Cohen's kappa) was calculated and disparities were discussed face-to-face afterwards. An exception to this process formed the first unit of analysis, i.e. reasons to continue smoking: due to the small

number of current smokers at telephone-based follow-up interview who were available for the qualitative interview (n=41), the entire sample was used to establish the preliminary coding system for this unit of analysis and rater training was considered of disadvantage. Subsequently, coding by the second rater (AR) was done with the same sample and without *a priori* rater training. From 38 categories 33 (87%) scored Cohen's kappa >0.8 (considered very good) and 36 (95%) scored Cohen's kappa >0.7 (considered good) (*refer to Supplemental Table 13*). Owing to the high level of agreement in both inter-rater reliability and face-to-face discussion only one coding rule in the first unit of analysis (reasons to continue smoking) was slightly modified: participants who reported reducing their level of stress by smoking a cigarette were consistently coded as "stress" and not as "relaxation". Hence, consensus among both raters and co-researchers was reached and due to excellent performance of the preliminary coding system, the final coding system was established (*refer to 7. 1. 2.* ).

The final coding system for reasons to continue smoking / reasons to relapse after a quitting attempt consisted of three themes and eight categories (*refer to Figure 4*). Most categories had an affective component that was either positive or negative. Neutral reasons such as boredom or habit were mentioned infrequently and therefore subsumed in the category "spontaneous".

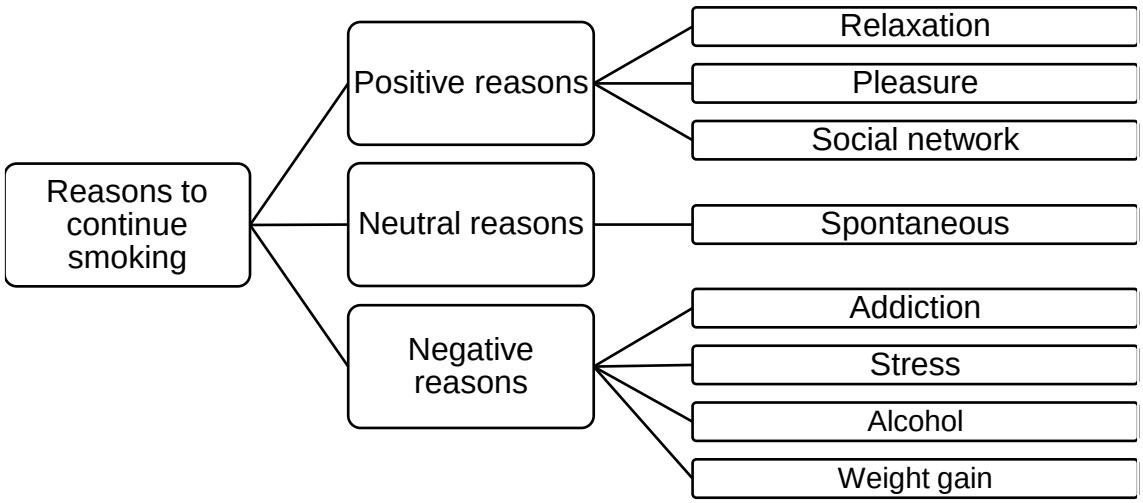


Figure 4 Coding system for reasons to continue smoking and reasons to relapse after a quitting attempt

The final coding system for reasons to undertake quitting attempts / reasons to quit consisted of five categories with relation to health reasons and four categories with relation to personal and social reasons (*refer to Figure 5*).

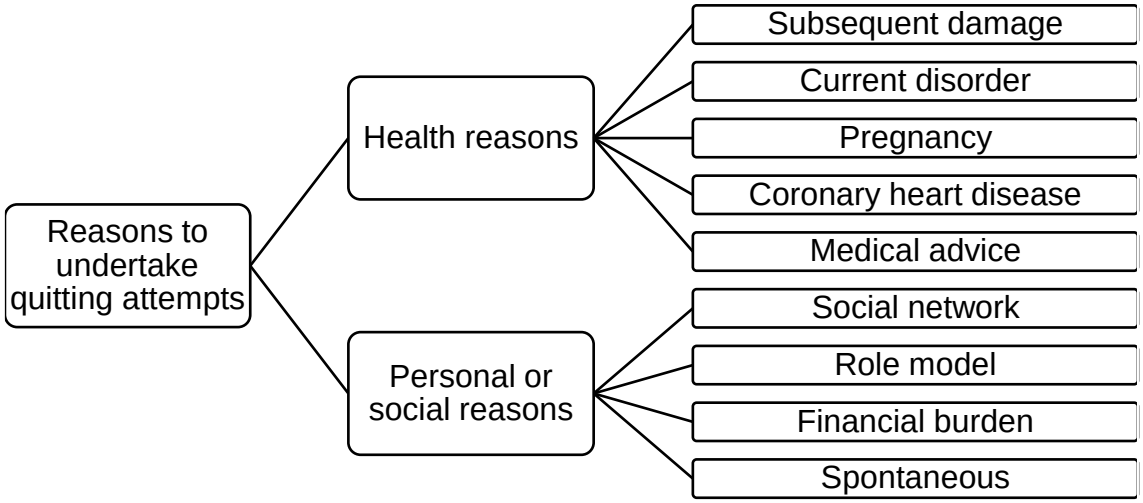


Figure 5 Coding system for reasons to undertake quitting attempts and reasons to quit

The final coding system for reasons to never start smoking consisted of two themes and seven categories (*refer to Figure 6*). Some were comparable to themes and categories used in other units of analyses (subsequent damage, social network, financial burden).

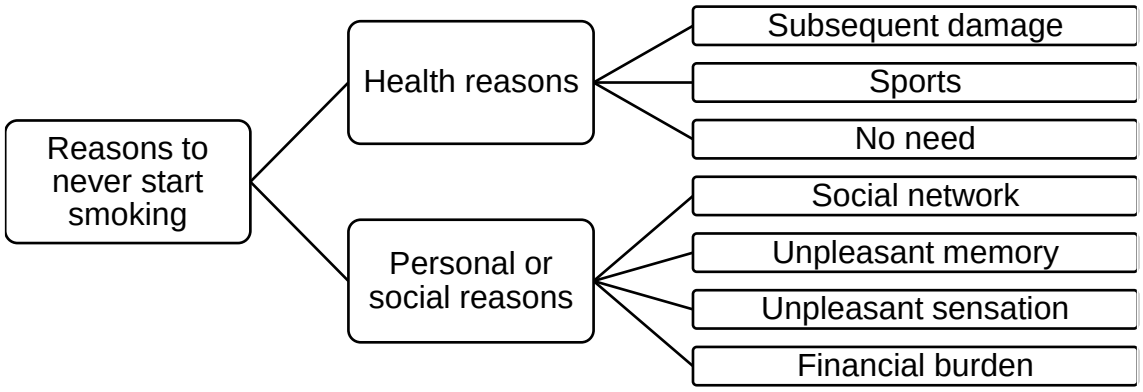


Figure 6 Coding system for reasons to never start smoking

One rater (DG) recoded the meaning units involved in the coding system's development process and coded all remaining data according to the final coding system. As overall inter-rater-reliability was considered very good and as regular

re-evaluation during the development was done, one rater was assumed adequate. Data acquisition, establishment of the coding system, final coding and content analysis were executed in German language. Results were translated by DG to English language afterwards. In results every unit of analysis is presented by demographic data of the sample, frequency of themes and categories, qualitative quotes and differences between sex and age groups.

## 2. 8. Data analysis

Current smokers at index event were compared stratified by smoking status at telephone-based follow-up interview (non-smoker vs smoker and accordingly successful quitter vs persistent smoker). All participants were compared stratified by smoking status at index event (never-smoker vs former smoker vs current smoker vs ever-smoker). Continuous normally distributed variables were presented as mean ± standard deviation (SD) and analyzed by Student's t-test or ANOVA, as appropriate. Non-normal distribution was assumed if Shapiro-Wilks test indicated $p<0.05$. Such variables were presented as median with interquartile range and analyzed by Mann-Whitney U-test or Kruskal-Wallis H-test, as appropriate. Nominal variables were presented as frequency with percentage and analyzed by Fisher's exact test or Pearson's chi-square test, as appropriate.

A multivariable binary logistic regression model was built to illustrate effect sizes. Results were presented as odds ratio (OR) with 95% confidence interval of the odds ratio (95%CI) and p-values. Nagelkerke's R-squared was calculated to quantify goodness of fit. The model was constructed block-wise: 1) sociodemographic variables (age, sex, education level) and 2) comorbidities (CABG at index event, diabetes or depressed mood at baseline visit) and 3) participation in a cardiac rehabilitation program after the index event. Descriptive statistics were utilized in a mixed methods approach to illustrate differences between sexes and age groups for qualitative categories [*53*]. All analyses were performed using IBM SPSS Statistics, version 23.0 (IBM Corporation, NY, USA). Two-tailed p-values $<0.05$ were considered statistically significant.

## 2. 9. Literature search

A structured search of the literature was performed in PubMed and WebOfScience. The main search algorithm implemented (smoking cessation patterns **and** coronary heart disease **and** cohort study) **or** (EuroAspire **and** (smoking **or** principal results **or** comparison)), including a variety of relevant alternative notations. Subsequently, reference lists of appropriate studies were looked up. Detailed questions such as cut-off values for the HADS questionnaire, the global burden of disease study or qualitative study methodology were searched additionally.

## 2. 10. Ethics

The study conforms with the Declaration of Helsinki. The Ethics Committee of the Medical Faculty of the University of Würzburg approved EuroAspire IV as well as the EuroAspire IV follow-up interview (ethics committee vote 58/12). Each participant gave written informed consent to participate at baseline visit and permission to be contacted by telephone for follow-up interview after identification through the hospitals' digital information system and prior to data extraction from the medical record. Denied participation or withdrawal of consent did not influence the participants' medical care in any way. Recruitment strategy, data acquisition and data storage were authorized by the data protection officer at the University of Würzburg.

# 3. Results

## 3. 1. Study sample

In the German EuroAspire IV survey 1380 persons were invited to participate between August 2012 and March 2013. Of those, 536 (38.8%) were interviewed in the baseline visit and 469 (34.0%) at telephone-based follow-up interview, respectively. 124 of 536 (23.1%) patients were categorized as current smokers at the index event. Of those, 104 participated at the telephone-based follow-up interview, thus contributing to primary endpoint analyses. 469 persons participated in the qualitative interview (*refer to Figure 7*). Elements of this thesis have recently been published by Goettler *et al* at BMC Cardiovascular Disorders [*9*].

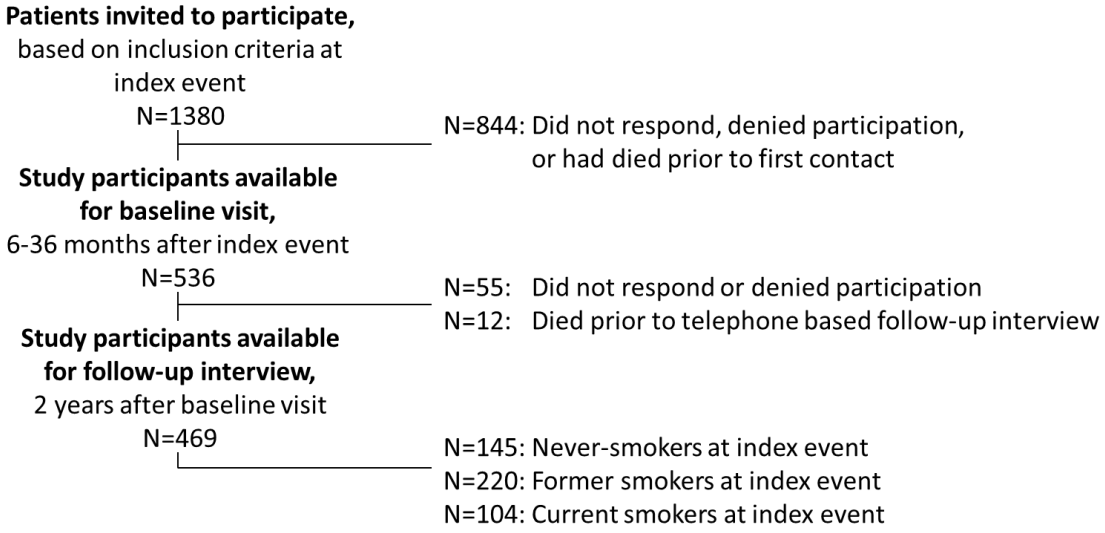


Figure 7 Flow chart

The median total observation time (quartiles) between index event and telephone-based follow-up interview was 3.6 years (2.9, 4.2) for all 469 participants at telephone-based follow-up interview. For 104 current smokers at index event the median time (quartiles) between index event and baseline visit was 1.8 years (1.3; 2.4) and time between baseline visit and telephone-based follow-up was 1.8 years (1.7; 1.8). Median total observation time for current smokers at index event was 3.5 years (3.0, 4.1). As compared with smokers at

index event participating in the telephone-based follow-up interview (n=104), non-participating smokers (n=20) were more often diabetic and more often smokers at the baseline visit (all p<0.05*, refer to Supplemental Table 19*).

## 3. 2. Smoking cessation pattern

3. 2. 1. Descriptive findings

Baseline data of the entire study population at baseline interview (n=536) has been provided previously [*54*]. At telephone-based follow-up interview, 65 of 104 (62.5%) current smokers at index event reported smoking cessation. Of those, 59 of 65 (90.8%) stopped smoking prior to the baseline visit. Relapse as well as late cessation also occurred (*refer to Figure 8*).

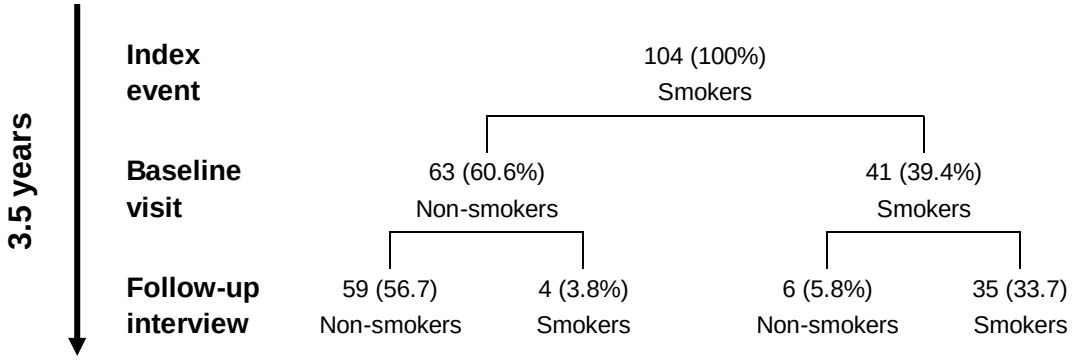


Figure 8 Frequency of smoking cessation in smokers with CHD at index event [*9*]

As reported at baseline visit 67 (64.2%) smokers at index event were provided verbal advice to stop smoking after hospital discharge and 27 (26.3%) participants were provided written information material. Recommendations to use supportive drug therapy were rarely reported (nicotine replacement therapy 16.8%, Bupropion 0% or Vareniclin 0%). A reduction in smoking intensity since hospital discharge was reported by 26 of 41 (68.4%) current smokers at the baseline visit. Cigarettes smoked per day were not documented in medical records.

Participation in a cardiac rehabilitation program within three months after the index event was recommended to 76 of 104 (73.1%) current smokers at index event. Of those, 73 (96.1%) reported attending more than half of the recommended sessions. Among participants in a cardiac rehabilitation program,

67 of 73 (91.8%) received training documents 69 (95.5%) participated in supervised exercise programs, 71 (97.3%) in health promotion workshops, 62 (84.9%) in stress modification and relaxation interventions and 14 (19.2%) participated in dedicated smoking cessation programs. Reporting a quitting attempt prior to admission for the index event was associated with a higher participation rate in cardiac rehabilitation programs (smokers at index event who reported a quitting attempt vs smokers who did not report a quitting attempt; 76.5% vs 58.3%, p<0.001).

Fourteen of 104 (13.5%) current smokers at index event had a CABG procedure, 7 (50.0%) due to AMI (2 ST- elevation myocardial infarction [STEMI], 3 non-ST-elevation myocardial infarction [NSTEMI], 2 not documented) and 7 (50.0%) due to AMIsch. Five of 14 (35.7%) CABG procedures were emergencies. Eighty-two of 104 (78.8%) current smokers at index event had a PCI procedure, 54 (65.9%) due to AMI (36 STEMI, 18 NSTEMI) and 28 (34.1%) due to AMIsch. Fifty-two of 82 (63.4%) PCI procedures were documented as emergencies. Eight of 104 (7.7%) current smokers at index event received conservative treatment (neither PCI nor CABG). Fifty-seven of 104 (54.8%) current smokers at index event had already been hospitalized due to CABG, PCI, AMI or AMIsch *prior to* the index event that lead to including in the present study.

### 3. 2. 2. Univariable analysis

The comparison of non-smokers vs smokers at telephone-based follow-up interview among smokers at index event was considered the primary endpoint analysis. The group of current smokers at index event was approximately 60 years old and predominantly male. Duration of hospitalization ranged between 1 and 15 days (*refer to Supplemental Table 20*). Neither age, nor sex, nor coronary surgery during index event had a statistically significant association with subsequent smoking status (*refer to Table 6*).

Table 6 Current smokers at index event* (n=104) stratified by their smoking status reported median 3.5 years later [*9*]

| | **Total** | **Non-smokers at follow-up interview** | **Smokers at follow-up interview** | |
|---|---|---|---|---|
| | **N=104** | **N=65 (62.5%)** | **N=39 (37.5%)** | **P-value** |
| **Demography** | | | | |
| Age at index event, years | 59.1±9.0 | 59.5±9.0 | 58.5±9.1 | 0.61 |
| Female sex | 16 (15.4) | 11 (16.9) | 5 (12.8) | 0.58 |
| High education level[#] | 23 (22.1) | 10 (15.4) | 13 (33.3) | 0.03 |
| **Comorbidities** | | | | |
| Type of index event: CABG | 14 (13.5) | 10 (15.4) | 4 (10.3) | 0.46 |
| Diabetes at baseline visit [a] | 32 (31.1) | 24 (37.5) | 8 (20.5) | 0.07 |
| Depressed mood at baseline visit [b] | 25 (24.3) | 11 (17.2) | 14 (35.9) | 0.03 |
| **Intervention** | | | | |
| Cardiac rehabilitation program after index event [c] | 73 (70.2) | 54 (83.1) | 19 (48.7) | <0.001 |

Data are n (percent), mean±SD, or median (quartiles) and p-values by asymptomatic Pearson's Chi-Squared test or independent sample t-test, as appropriate.

*Index event occurred 6-36 months prior to baseline visit, and telephone-based follow-up occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up interview was 3.5 years (n=104).

[#]High school completed, college/university completed, postgraduate degree.

CABG, coronary artery bypass graft.

[a] Data missing for 1 participant.

[b] Data missing for 1 participant.

[c] n=3 (2.9%) of 104 participants reported a cardiac rehabilitation program had been recommended but less than half of the recommended sessions were attended. The distribution among non-smokers vs smokers at follow-up interview was equal.

Diabetes and absence of depressed mood was associated with higher quitting rates. High education level was associated with lower quitting rates at follow-up interview, by contrast smoking status at index event was not associated with high educational level (smokers vs non-smokers at index event, 22.1% vs 21.1%, p=0.82) [*9*]. Participation in a cardiac rehabilitation program was strongly associated with smoking cessation at follow-up interview (*refer to Figure 9*).

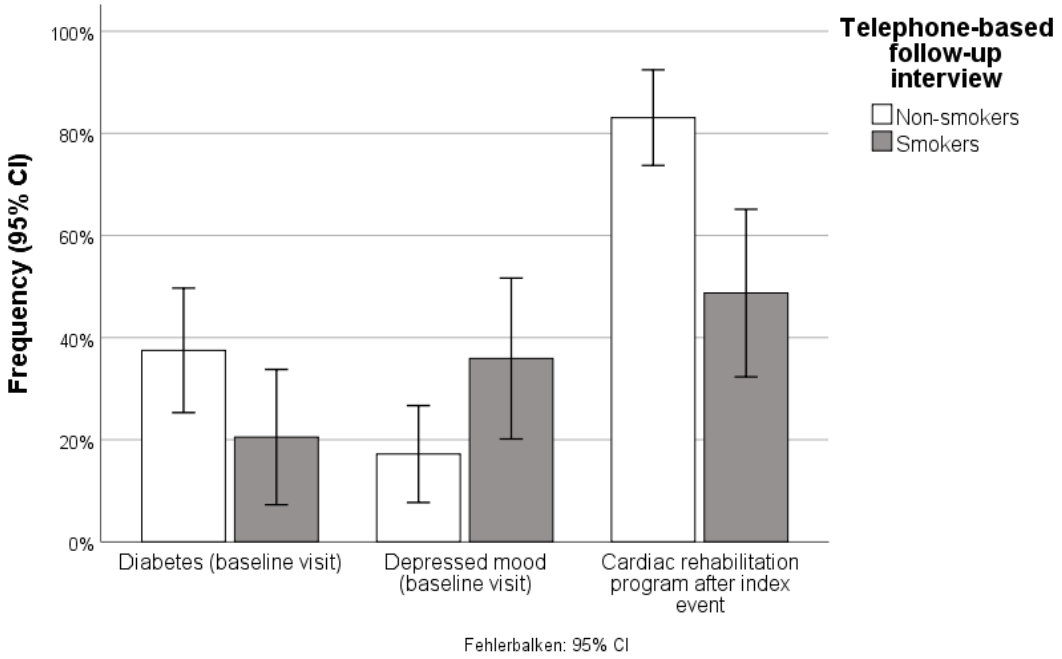


Figure 9 Factors associated with smoking cessation median 3.5 years after a cardiovascular index event (in n=104 patients smoking at the index event)

Any environmental tobacco smoke (ETS) exposition was reported by 19 of 41 (48.7%) persistent smokers vs 9 of 65 (13.8%) successful quitters at the telephone-based follow-up interview. Logistic regression analysis showed an association of ETS with increased rates of persistent smoking (OR 6.3, 95%CI 2.4-17.0, p<0.001; adjusted for age and sex). In the subgroup of smokers at index event who reported ETS at baseline visit and did not participate in a cardiac rehabilitation program (n=12), the rate of persistent smoking was 91.7% (*refer to Figure 10*) [*9*].

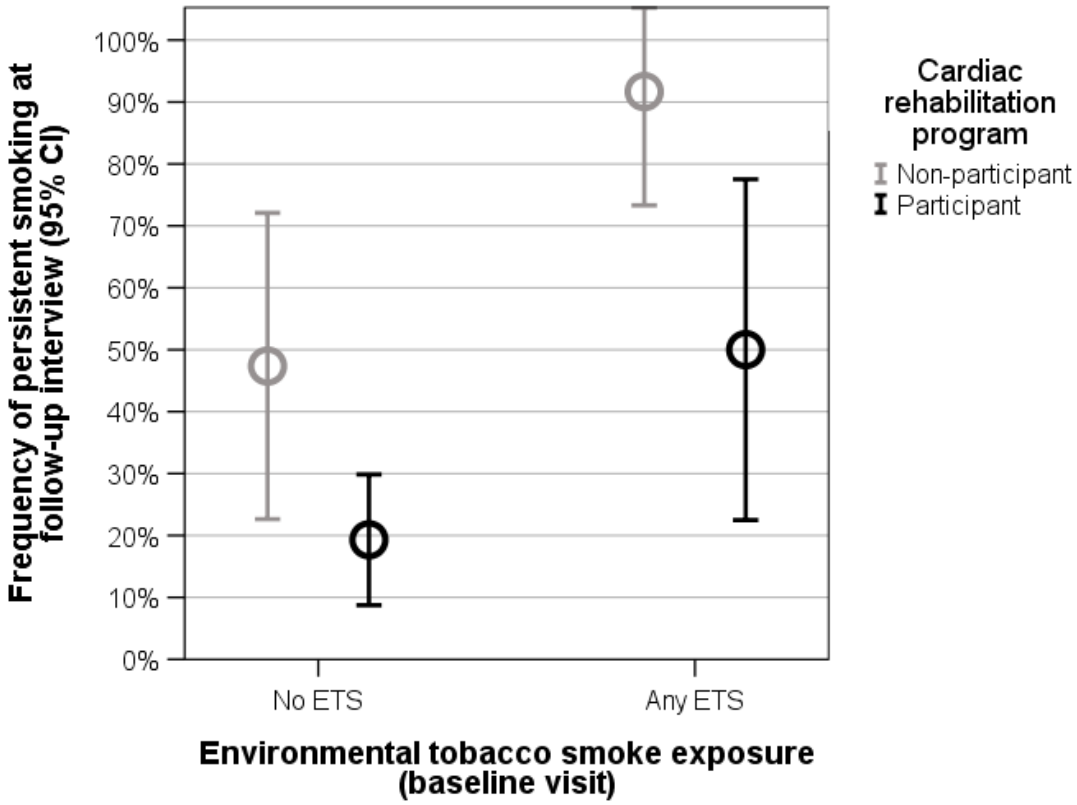


Figure 10 Frequency of persistent smoking median 3.5 years after a cardiovascular index event (in n=104 patients smoking at the index event) stratified by ETS exposure and participation in a cardiac rehabilitation program

### 3. 2. 3. Multivariable analysis

A block-wise multivariable logistic regression model was built to identify factors associated with smoking status at the telephone-based follow-up interview.

Table 7 Factors associated with smoking cessation median 3.5 years after a cardiovascular index event (block-wise multivariable logistic regression in n=104 patients smoking at the index event) [*9*]

| | **Block 1** | | **Block 2** | | **Block 3** | |
|---|---|---|---|---|---|---|
| Nagelkerke's R squared | 0.067 | | 0.165 | | 0.284 | |
| | OR (95%CI) | P | OR (95%CI) | P | OR (95%CI) | P |
| **Demography** | | | | | | |
| Age at index event* | 1.02 (0.97-1.07) | 0.40 | 1.01 (0.96-1.06) | 0.66 | 1.03 (0.97-1.08) | 0.36 |
| Female sex | 1.05 (0.32-3.44) | 0.94 | 1.09 (0.31-3.89) | 0.89 | 1.28 (0.34-4.77) | 0.71 |
| High education level[#] | 0.34 (0.13-0.91) | 0.03 | 0.37 (0.13-1.03) | 0.06 | 0.39 (0.13-1.17) | 0.09 |
| **Comorbidities** | | | | | | |
| No CABG vs CABG | | | 1.12 (0.28-4.52) | 0.87 | 0.63 (0.15-2.68) | 0.53 |
| Diabetes at baseline [a] | | | 2.53 (0.93-6.86) | 0.07 | 2.56 (0.89-7.34) | 0.08 |
| Depressed mood at baseline [b] | | | 0.32 (0.12-0.87) | 0.03 | 0.37 (0.13-1.08) | 0.07 |
| **Intervention** | | | | | | |
| Rehabilitation program | | | | | 5.19 (1.87-14.46) | 0.002 |

OR, odds ratio; 95% CI, 95% confidence interval; P, P-value; CABG, coronary artery bypass graft.

*OR per year.

[#]High school completed, college/university completed, postgraduate degree.

[a] Data missing for 1 participant.

[b] Data missing for 1 participant.

Age and sex were not associated with smoking status at telephone-based follow-up interview, nor was CABG vs other treatment (PCI or conservative therapy) and present diabetes. In the age-adjusted model (block 1) high education level was associated with lower rates of smoking cessation. When the model was extended for comorbidities (block 2), presence of depressed mood was associated with lower rates of smoking cessation. After adjustment for cardiac rehabilitation program (block 3) higher education level (OR 0.39, 95%CI 0.13-1.17, p=0.09) and presence of depressed mood (OR 0.37, 95%CI 0.13-1.08, p=0.07) lost significance. Participation in a cardiac rehabilitation program remained the only

factor associated with successful smoking cessation in patients with established CHD who were smoking at the time of index event (OR 5.19, 95%CI 1.87-14.46, p=0.002). Goodness of fit (Nagelkerke's R-squared) increased accordingly when adding explanatory variables although the explained variance remained small ($R^2$: 6.7%, 16.5%, 28.4% block 1, 2, 3, respectively). Additional variables potentially further elucidating the acuity of the index event (i.e. emergency vs elective admission and ischemia vs infarction) were not associated with smoking cessation (*refer to Supplemental Table 22 and Supplemental Table 23*) [*9*].

### 3. 2. 4. Extended smoking status

At index event 145 of 469 (30.9%) participants were classified never-smokers, 220 (46.9%) former smokers, 68 (14.5%) current smokers and 36 (7.7%) ever-smokers (*refer to Table 8*).

Table 8 Study participants at index event* participating at follow-up interview (n=469) stratified by extended smoking status at index event

| | **Total** | **Never-smokers at index event** | **Former smokers at index event** | **Current smokers at index event** | **Ever-smokers at index event** | **P-value** |
|---|---|---|---|---|---|---|
| | **N=469 (100%)** | **N=145 (30.9%)** | **N=220 (46.9%)** | **N=68 (14.5%)** | **N=36 (7.7%)** | **-** |
| **Data** | | | | | | |
| Age at index event, years | 65.6±8.8 | 68.2±7.9 | 67.0±7.7 | 59.4±8.3 | 58.5±10.3 | <0.001 |
| Female sex | 81 (17.3) | 38 (26.2) | 27 (12.3) | 10 (14.7) | 6 (16.7) | 0.007 |
| Depressed mood at baseline [a] | 80 (17.2) | 21 (14.6) | 34 (15.7) | 16 (23.5) | 9 (25.7) | 0.19 |
| Cardiac rehabilitation [b, c] | 239 (51.1) | 66 (45.8) | 100 (45.5) | 52 (76.5) | 21 (58.3) | <0.001 |
| **Smoking** | | | | | | |
| At index event | 104 (22.2) | 0 (0) | 0 (0) | 68 (100) | 36 (100) | - |
| At baseline visit | 51 (10.9) | 1 (0.7) | 9 (4.1) | 18 (**26.5**) | 23 (**63.9**) | - |
| At follow-up interview | 46 (9.8) | 0 (0) | 7 (3.2) | 16 (23.5) | 23 (63.9) | - |

Data are n (percent), mean±SD or median (quartiles) and p-values by asymptotic Pearson's Chi-Squared test or ANOVA, as appropriate.

*Index event occurred 6-36 months prior to baseline visit and telephone-based follow-up interview occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up interview was 3.6 years (n=469).

[a] Data missing for 5 participants.

[b] Data missing for 1 participant.

[c] n=6 (1.3%) of 468 participants (data missing for 1 participant) reported a cardiac rehabilitation program had been recommended but less than half of the recommended sessions were attended. The distribution among non-smokers vs smokers at follow-up interview was equal.

Thirty-eight of 145 (26.2%) never-smokers were female, whereas females were less frequent in the other sub-groups. Seven of 220 (3.2%) former smokers at index event reported a relapse at telephone-based follow-up interview. Ever-smokers and current smokers were younger and tended to show depressed

mood more often than never- and former smokers. Ever-smokers and current smokers were reported more frequently having attended a cardiac rehabilitation program than never- and former smokers. Persistent smoking at telephone-based follow up interview was more frequent in ever-smokers than current smokers (**63.9% vs 26.5%, p<0.001**). Thirteen of 23 (56.5%) ever-smokers at follow-up interview reported a quitting attempt between index event and telephone-based follow-up interview. Hence, 94 of 104 (90.4%) ever- or current smokers at index event reported either smoking cessation or an attempt to quit after a CHD index event.

## 3. 3. Qualitative interview

Qualitative data was collected and analyzed for all 469 participants of the German EuroAspire IV follow-up survey. Results were presented in English language for each unit of analysis separately, albeit the coding system was identical for two pairs of units, respectively.

### 3. 3. 1. Reasons to continue smoking

Forty-one of 46 (89.1%) current smokers at telephone-based follow-up interview explained their reasons for persistent smoking. Of these, 36 (92.3%) participants were classified light or moderate smokers at follow-up interview. Duration of smoking was 39.2±11.9 (mean±SD) years. Exposure to ETS was frequently reported, especially at home. At least one quitting attempt was reported by 31 (75.6%) participants (*refer to Table 9).*

Table 9 Current smokers at telephone-based follow-up interview* (n=41)

| | | | |
|---|---|---|---|
| Age at follow-up, years | 62.5±9.3 | Female sex | 6 (14.6) |
| Duration of smoking until follow-up interview, years | 39.2±11.9 | Intensity of smoking at follow-up interview, cigarettes/day | 10 (4, 20) |
| ETS exposure at baseline visit | | Heavy Smoking Index at follow-up interview | |
| At work | 5 (12.2) | Light smoker | 21 (53.8) |
| At home | 17 (41.5) | Moderate smoker | 15 (38.5) |
| At other locations | 5 (12.2) | Heavy smoker | 3 (7.7) |
| Ever undertaking a quitting attempt | 31 (75.6) | Age at beginning of the longest quitting attempt, years | 53.5±12.2 |

Table 9 Current smokers at telephone-based follow-up interview* (n=41) (continuation)

| Time to first cigarette in the morning | | Duration of the longest quitting attempt | |
|---|---|---|---|
| <5 min | 3 (7.5) | ≤3 months | 14 (45.2) |
| 5 min to <30 min | 10 (25.0) | 3 months to ≤6 months | 2 (6.5) |
| 30 min to <60 min | 7 (17.5) | 6 months to ≤12 months | 6 (19.4) |
| ≥60 min | 20 (50.0) | >12 months | 9 (22.0) |

Data are n (percent), mean±SD or median (quartiles), as appropriate.

*Index event occurred 6-36 months prior to baseline visit and telephone-based follow-up occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up was 3.9 years (n=41).

Relaxation, pleasure and social network were considered to have a positive connotation and at least one positive reason was reported by 25 (61.0%) participants. Addiction and stress were considered to have a negative connotation and least one negative reason was reported by 22 (53.7%) participants. Spontaneous was considered to have a neutral connotation and was reported by 7 (17.1%) participants (*refer to Figure 11)*. Both positive and negative reasons were reported by 12 (29.3%) participants, only positive reasons by 13 (31.7%) participants and only negative reasons by 10 (24.4%) participants. Descriptive statistics showed no significant differences between sexes or age groups (*refer to Supplemental Table 24 and Supplemental Table 25*).

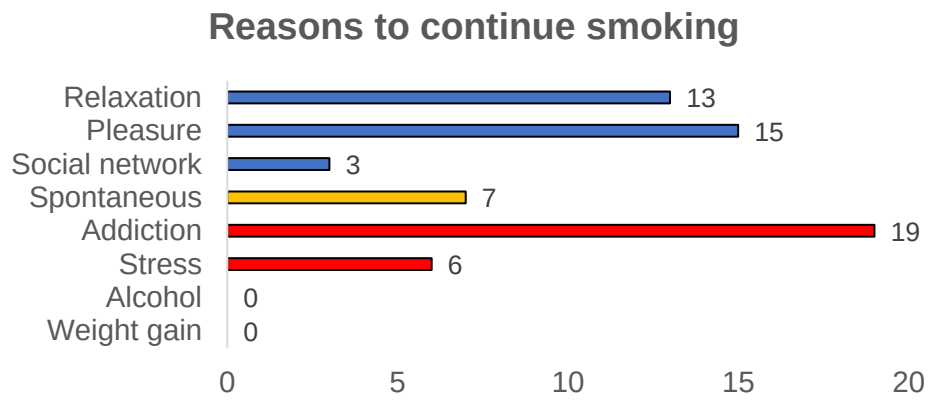


Figure 11 Reasons to continue smoking (absolute frequency) as reported by 41 persistent smokers at telephone-based follow-up interview. Reasons considered to have a positive conotations were coloured in blue, a neutral conotations in gold and a negative conotations in red.

Addiction was reported by 19 (46.3%) persistent smokers at follow-up interview and frequently coded when participants used the word “addicted” to describe themselves or reported addictive behaviors such as craving or withdrawal symptoms.

- “Addiction” (pID 6)
- “It is the pure dependence, there is this burning desire to smoke. I hope the addiction will vanish.” (pID 7)
- “I have tried a lot of times [to stop], but it doesn’t work. Every time I try to stop, I am grumpy” (pID 8)

The sensation of pleasure and/or well-being was reported by 15 (36.6%) participants.

- “It serves me to maintain my joy in life” (pID 9)
- “For me smoking is a stimulant” (pID 10)
- “It is a beautiful ritual after a meal or after breakfast” (pID 11)

A relaxing and/or calming component of smoking was coded for 13 (31.7%) participants. Statements referring to the reduction of stress through smoking were **not** coded into the category relaxation.

- “Relaxation” (pID 9)
- “I imagine winding down” (pID 7)
- “It is easier to relax with smoking” (pID 4)

### 3. 3. 2. Reasons to undertake quitting attempts

Quitting attempts were reported by 152 participants (*refer to Table 10*). Of these, 33 (21.7%) participants were current smokers at telephone-based follow-up interview, 119 (78.3%) participants were former smokers and 143 (94.1%) participants explained their reasons to undertake quitting attempts. Details about their **longest** quitting attempt were retrospectively assessed. The age at initiation of the longest quitting period ranged from 16 years to 73 years (median 38 years). Sixty-seven of 143 (46.9%) related the quitting attempt to the context of a specific illness and 30 of 67 (44.8%) experienced this illness life-threatening.

Table 10 Current or former smokers at telephone-based follow-up interview* who reported quitting attempts (n=152)

| | |
|---|---|
| Age at follow-up interview, years | 66.3±9.1 |
| Female sex | 18 (11.8) |
| Current smoker at follow-up interview | 33 (21.7) |
| Age at initiation of longest quitting attempt, years | 38 (30, 50) |
| Duration of the longest quitting attempt | |
| ≤3 months | 37 (24.3) |
| 3 months to ≤6 months | 23 (15.1) |
| 6 months to ≤12 months | 31 (20.4) |
| >12 months | 61 (40.1) |
| Undertook a quitting attempt due to an illness that was considered life-threatening (refers to patients who reported an illness as trigger to attempt quitting) | 30 of 67 (44.8) |
| Undertook a quitting attempt from one day to the next | 123 (80.9) |

Data are n (percent), mean (SD) or median (quartiles), as appropriate.

*Index event occurred 6-36 months prior to baseline visit and telephone-based follow-up occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up was 3.6 years (n=152).

Subsequent damage, current disorder, pregnancy, coronary heart disease and medical advice were considered health-related and at least one health-related reason was reported by 110 (76.9%) participants. Social network, role model, financial burden and spontaneous were considered personal or social reasons and at least one personal/social reason was reported by 66 (46.2%) participants (*refer to Figure 12*). Both health-related and personal/social reasons were reported by 34 (23.8%) participants, only health-related reasons by 76 (53.1%) participants and only personal/social reasons by 32 (22.4%) participants. Younger age groups reported CHD more frequently (24.6% vs 16.4% vs 0.0%, p=0.01; for <60 years, 60-69 years, ≥70 years). 6 of 16 females (37.5%) reported pregnancy as reason to undertake a quitting attempt. For further details *refer to Supplemental Table 26 and Supplemental Table 27.*

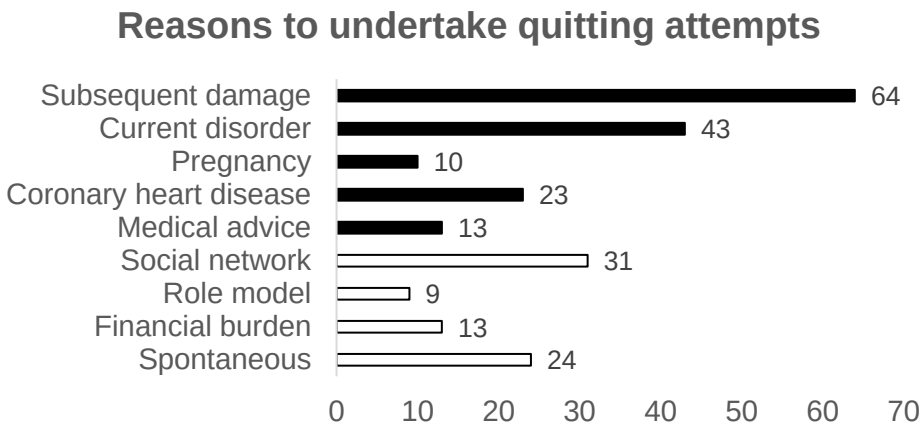


Figure 12 Reasons to undertake quitting attempts (absolute frequency) as reported by 143 current or former smokers at telephone-based follow-up interview who reported quitting attempts. Reasons considered health-related were coloured in black and reasons considered personal/social in white.

Subsequent damage reported by 64 (44.8%) persons was the leading category in reasons to relapse. Participants regularly reported affective thoughts of anxiety and fear as well as arguments and decisions based on rational arguments.

- “I feared the sequelae” (pID 12)
- “Rational thought to live a little bit healthier” (pID 13)
- “It was mainly health reasons. I saw a lot of older smokers” (pID 14)
- “Alcohol and smoking deranged my blood count and I wanted to end both” (pID 15)
- “My father was a heavy smoker and had severe peripheral artery disease. I had to see him suffering and decided to stop” (pID 16)

Current disorder reported by 43 (30.1%) persons was the second leading cause. Symptom severity inside this category showed a spectrum from coughing or sports problems and dyspnea on to agony:

- “Severe coughing fits” (pID 14)
- “I had pneumonia” (pID 17)
- “I couldn’t get on top of a mountain on the golf course, experienced severe dyspnea and felt unwell” (pID 18)
- “I was afraid of death” (pID 19)

Third in frequency was the influence of the social network reported by 31 (21.7%) participants. Shared decision making with spouses, friends or colleagues and social pressure of spouses or children were frequently coded into this category:

- “My wife complained that I am smelling of smoke” (pID 20)
- “It was a collective decision of my wife and myself” (pID 21)
- “Jokingly a friend of mine called me ill-looking and added this may be due to my smoking. Vanity really got me and I stopped it” (pID 22)
- “My handball trainer was a downright smoking enemy” (pID 23)

### 3. 3. 3. Reasons to relapse after a quitting attempt

The profile of 152 smokers who reported a quitting attempt but relapsed afterwards has been presented in *Table 10*. Of these, 147 of 152 (96.7%) persons explained their reasons to relapse. Relaxation, pleasure and social network were considered to have a positive connotation and at least one positive reason was reported by 84 (57.1%) participants. Addiction and stress were considered to have a negative connotation and least one negative reason was reported by 77 (52.4%) participants. Spontaneous was considered to have a neutral connotation and was reported by 30 (20.4%) participants (*refer to Figure 13)*. Both positive and negative reasons were reported by 33 (22.4%) participants, only positive reasons by 51 (34.7%) participants and only negative reasons by 44 (29.9%) participants. The categories pleasure (17.5% vs 6.9% vs 3.1%, p=0.06) and addiction (15.8% vs 13.8% vs 0.0%, p=0.07) showed a non-significant trend towards younger age groups (<60 years, 60-69 years, ≥70 years, respectively). Men reported less often stress as reason to relapse (26.4% vs 50.0%, p=0.04) than women (*refer to Supplemental Table 28 and Supplemental Table 29*).

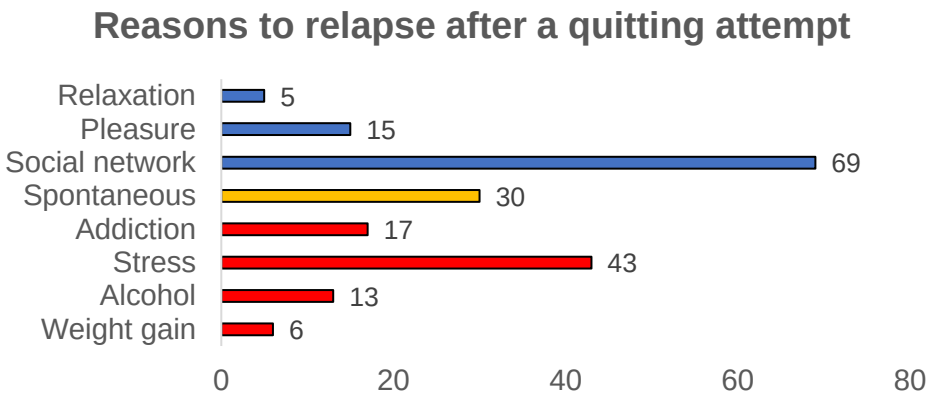


Figure 13 Reasons to relapse after a quitting attempt (absolute frequency) as reported by 147 current or former smokers at telephone-based follow-up interview who reported quitting attempts. Reasons considered to have a positive conotations were coloured in blue, a neutral conotations in gold and a negative conotations in red.

Influence of the social network was reported by 69 (46.9%) participants. Two important subcategories emerged: fellow smokers (i.e. friends, colleagues or family members) offering the currently non-smoking participant a cigarette and shared decision-making with fellow former smokers.

- “You sit together with others, someone offers you a cigarette and you smoke again” (pID 24)
- “During a long journey by car my wife bought me cigarettes to do me a favor” (pID 21)
- “After the heart attack: together with a colleague, who was a former smoker as well, I decided that just one cigarette or cigar per week would be ok. Slowly we started again” (pID 25)

Forty-three (29.3%) participants described situations of moderate to advanced stress, frequently associated with the participants’ professional work. Some participants reported, although it was not specifically asked for it, that smoking would not help coping with stress (e.g. pID 34, pID 7, pID 70), others reported it might help (e.g. pID 63, pID 64, pID 65) and some mentioned it would help (e.g. pID 66, pID 67, pID 68). When people explained that they were offered a cigarette in a stressful situation, stress was coded next to social network.

- “New job. Lots of stress” (pID 26)

- “There was an argument with my boss, to deal with the stress I asked a colleague to give me a cigarette and began again” (pID 15)
- “Divorce, we argued the right of child custody” (pID 27)
- “My mother had died and we argued the heritage” (pID 28)
- “I had a car accident. The accident perpetrator offered me a cigarette” (pID 29)

Reasons with a neutral connotation were subsumed in the third frequent category spontaneous (n=30, 20.4%). Oftentimes, participants reported to afresh buy themselves cigarettes without any stimulus or because of boredom.

- “I just tried [a cigarette] and already began again” (pID 30)
- “Out of pure boredom” (pID 31)
- “I sat in front of the TV, drove to the kiosk and got cigarettes again” (pID 32)
- “The health risks lost their meaning for me. I had a feeling of ‘who cares’” (pID 33)

3. 3. 4. Reasons to quit

At telephone-based follow-up interview 276 of 276 (100%) former smokers reported their reasons to quit. Of these, 213 (77.2%) participants had quit prior to the index event. Intensity of smoking as well as time to first cigarette in the morning and HSI were retrospectively assessed at telephone-based follow-up interview referring to one week prior to smoking cessation (*refer to Table 11*). Duration of smoking and exposure to ETS were assessed at baseline visit. A quitting attempt prior to successful cessation was reported by 119 (43.1%) former smokers. Smoking cessation was achieved from one day to the next by 255 (92.4%) former smokers. One hundred and seventy-two (62.3%) participants referred to an illness (among other arguments) as main reason to stop smoking. Of these, 79 of 172 (45.9%) associated a life-threatening episode in this context.

Table 11 Former smokers at telephone-based follow-up interview* (n=276)

| | | | |
|---|---|---|---|
| Age at follow-up, years | 70 (63, 75) | Female sex | 37 (13.4) |
| Age at smoking cessation, years | 47 (32, 56) | Current smoker at index event | 63 (22.8) |
| Duration of smoking, years | 21 (10, 34) | Intensity of smoking[#], cigarettes/day | 15 (8.5, 20) |
| Ever undertaken a quitting attempt | 119 (43.1) | Age at beginning of the longest quitting attempt, years | 38 (16, 73) |
| Time to first cigarette in the morning[#] | | Duration of the longest quitting attempt | |
| <5 min | 23 (8.4) | ≤3 months | 23 (19.3) |
| 5 min to <30 min | 43 (15.6) | 3 months to ≤6 months | 21 (17.6) |
| 30 min to <60 min | 55 (20.0) | 6 months to ≤12 months | 25 (21.0) |
| ≥60 min | 148 (53.8) | >12 months | 50 (42.0) |
| Heavy smoking index | | ETS exposure at baseline visit | |
| Light smoker | 135 (52.3) | At work | 5 (1.8) |
| Moderate smoker | 75 (29.1) | At home | 13 (4.7) |
| Heavy smoker | 48 (18.6) | At other locations | 9 (3.3) |
| Quit smoking due to an illness that was considered life-threatening (refers to patients who reported an illness as trigger to quit smoking) | | | 79 of 172 (45.9) |
| Quit smoking from one day to the next | | | 255 (92.4) |

Data are n (percent), mean (SD) or median (quartiles), as appropriate.

HSI: Heavy Smoking Index; ETS: environmental tobacco smoke

[#]Retrospectively assessed for the week prior to quitting.

*Index event occurred 6-36 months prior to baseline visit and telephone-based follow-up occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up was 3.5 years (n=276).

Subsequent damage, current disorder, pregnancy, coronary heart disease and medical advice were considered health-related and at least one health-related reason was reported by 216 (78.3%) participants. Social network, role model, financial burden and spontaneous were considered personal or social reasons and at least one personal/social reason was reported by 115 (41.7%) participants (*refer to Figure 14*). Both health-related and personal/social reasons were reported by 55 (19.9%) participants, only health-related reasons by 161 (58.3%) participants and only personal/social reasons by 60 (21.7%) participants. Financial burden was less frequent in the middle age group: 14.9% vs 4.5% vs 9.9%, p=0.05 (<60 years, 60-69 years, ≥70 years, respectively). Men non-

significantly reported less often on present health problems (code: “current disorder”) than women (42.7% vs 59.5%, p=0.06). For further details *refer to Supplemental Table 30 and Supplemental Table 31.*

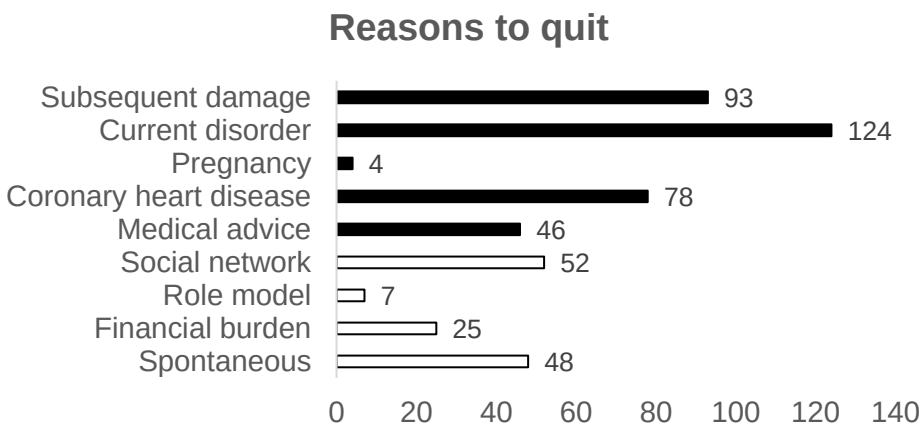


Figure 14 Reasons to quit (absolute frequency) as reported by 276 current or former smokers at telephone-based follow-up interview. Reasons considered health-related were coloured in black and reasons considered personal/social in white.

Current disorder was the most frequently coded category for reasons to quit reported by 124 (44.9%) participants. Three subcategories were identified: Disorders which the participant associated with smoking, such as nausea (e.g. pID 55), loss of energy in sports (e.g. pID 44), dyspnea (e.g. pID 57) or circulatory problems (e.g. pID 56). Health problems forcing the participant to stop smoking for a limited period such as common cold (e.g. pID 58), flu (e.g. pID 59), tooth extraction (e.g. pID 36) or dizziness (e.g. pID 60) followed by voluntary and sustained abstinence. And severe medical conditions such as stroke (e.g. pID 61), lung surgery (e.g. pID 29) or heart attack (e.g. pID 62). When participants reported that friends, spouses or medical personal advised them to stop smoking during an episode of acute illness, social network or medical advice were coded additionally, respectively:

- “Smoker’s cough, phlegm, very awkward” (pID 34)
- “After a party-weekend I felt really bad – nausea and so on – and decided to stop drinking and smoking” (pID 35)
- “A tooth of mine was extracted, thus I had to stop smoking for three days and decided not to restart again” (pID 36)

- “The heart attack and the associated feelings of mortal danger – I was reanimated four times – empowered me to quit” (pID 37)

Subsequent damage was reported by 93 (33.7%) participants. The category consisted of either fear of sequelae or a rational decision based on information or self-experience.

- “Due to information on the harmfulness of smoking” (pID 38)
- “There were sick people standing outside the hospital, smoking. I watched them carefully and it showed me the sequelae of smoking quite plainly – I hoped to do better without smoking” (pID 39)
- “I did not want to die and therefor stopped smoking” (pID 40)
- “Fear of recurrent infarction” (pID 41)

CHD was mentioned by 78 (28.3%) participants. Relations to the heart, angina pectoris, myocardial infarction or ischemia, PCI or CABG were coded into this category. CHD was often related to further medical conditions and/or medical advice; these were coded in current disorder, subsequent damage or medical advice, as appropriate.

- “I have been in medical treatment for massive angina pectoris” (pID 42)
- “The heart attacks. I did not want to die of a heart attack” (pID 43)
- “CABG. Emergency room. Smoking ban” (pID 69)

### 3. 3. 5. Reasons to never start smoking

Table 12 Never-smokers at telephone-based follow-up interview* (n=140)

| | | |
|---|---|---|
| Age at follow-up, years | | 71.8±7.9 |
| Female sex | | 35 (25.0) |
| Environmental tobacco smoke exposure at baseline visit: | At work | 4 (2.9) |
| | At home | 0 (0) |
| | At other locations | 2 (1.4) |

Data are n (percent), mean (SD) or median (quartiles), as appropriate.

*Index event occurred 6-36 months prior to baseline visit and telephone-based follow-up occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up was 3.7 years (n=140).

One hundred and forty of 145 (96.6%) self-reported never-smokers reported their reasons to avoid smoking initiation. They were more than 70 years on average and 35 (25.0%) were females. Exposure to ETS was low (*refer to Table 12*). Subsequent damage, sport and no need for smoking were considered health-related and at least one health-related reason was reported by 90 (64.3%) participants. Social network, unpleasant memory, unpleasant sensation and financial burden were considered personal or social reasons and at least one personal/social reason was reported by 98 (70.0%) participants (*refer to Figure 15*). Both health-related and personal/social reasons were reported by 48 (34.3%) participants, only health-related reasons by 42 (30.0%) participants and only personal/social reasons by 50 (35.7%) participants. There was a non-significant trend in younger age groups to report more often on unpleasant memories: 39.1% vs 40.8% vs 22.1%, p=0.07 (<60 years, 60-69 years, ≥70 years, respectively). Men reported less frequently on subsequent damage (13.3% vs 34.3%, p<0.01) and on unpleasant sensations (13.3% vs 40.0%, p<0.01), but more frequently on sports (12.4% vs 0.0%, p=0.03) as reasons to never start smoking than women (*refer to Supplemental Table 32 and Supplemental Table 33*).

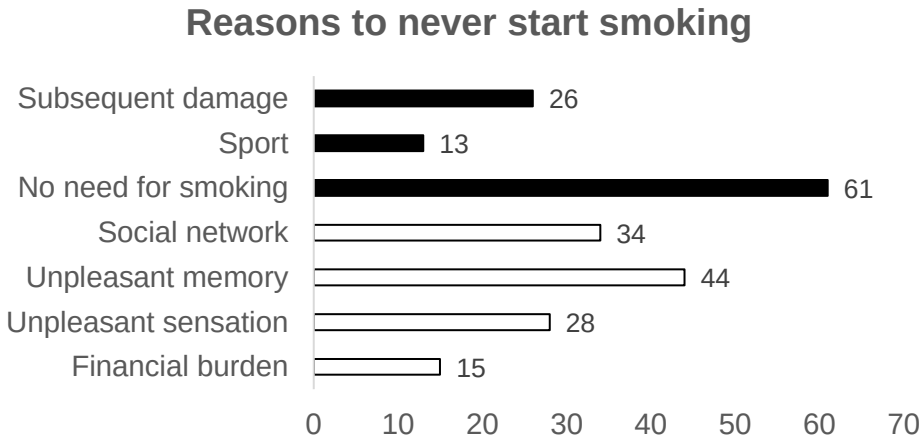


Figure 15 Reasons to never start smoking (absolute frequency) as reported by 140 never-smokers at telephone-based follow-up interview. Reasons considered health-related were coloured in black and reasons considered personal/social in white.

The most frequent category “no need” comprised a group of 61 (43.6%) participants that never had any interest in tobacco products.

- “I never had a need to smoke” (pID 45)
- “No interest in smoking” (pID 46)
- “It never tasted good to me” (pID 47)

The second frequent category “unpleasant memory” mentioned by 44 (31.4%) participants contained more personal details. Codes were given when memories with negative connotations associated with smoking were mentioned. Negative emotions and symptoms – often nausea –the participants had experienced during a smoking attempt and health problems of family members associated with tobacco smoking were identified as subcategories.

- “I smoked once for one day. Afterwards I felt nausea for eight days and never again perceived a need [to smoke]” (pID 48)
- “My father was a heavy smoker and died from lung cancer” (pID 49)
- “My father was a chain smoker and I passively smoked as well. In smoky rooms, I experienced coughs and dyspnea” (pID 50)

Influence of the social network was coded for 34 (24.3%) participants. On the one hand, participants reported to be in social networks of non-smokers, on the other hand, some received advice to never start using tobacco products from current or former smokers.

- “There were no smokers amongst my friends” (pID 51)
- “Smoking was frowned upon by sports persons” (pID 52)
- “The whole clan [family] didn’t smoke” (pID 53)
- “Our father was a heavy smoker who advised us sons to never smoke” (pID 54)

# 4. Discussion

## 4. 1. Major findings

One hundred and twenty-four of 536 (23.1%) persons were classified current smokers at admission for the CHD index event. Of these, 104 participated at telephone-based follow-up interview and 65 of 104 (62.5%) current smokers reported smoking cessation median 3.5 years after a cardiovascular disease index event. Age, sex and coronary surgery at index event were not associated with smoking cessation in this cohort. Whereas, higher education level and presence of depressed mood showed associations with lower rates of smoking cessation and presence of diabetes and attending a cardiac rehabilitation program were associated with higher rates of smoking cessation. After multivariable adjustment, only participation in a cardiac rehabilitation program remained significant [*9*].

Most persistent smokers stated themselves addicted, rather unable to quit smoking than unwilling. Nevertheless, the consumption of tobacco products was also associated with joyful experiences such as relaxation and pleasure. Quitting attempts and subsequent relapses were common among current and former smokers in this cohort. Most former smokers quit smoking prior to the index event. Unsuccessful quitters referred frequently on future and current health hazards as well as social influence as reason to undertake a quitting attempt. Subsequent relapse was also associated with social influence and the perceived level of stress. Successful quitters reported on current and severe health conditions such as CHD as reasons to quit. One third of participants in this cohort never smoked until telephone-based follow-up interview. Health related arguments were sparsely named as reasons to never start smoking. Half of never-smokers reported not having had any desire to smoke.

## 4. 2. Methods

The study design with data acquisition at three time-points provided prospective follow-up data over a period of median 3.5 years for current smokers at index admission / 3.6 years for all participants available at telephone-based follow-up

interview. Data of a very high-risk population of smokers with established CHD were obtained to provide answers to predefined research questions (*refer to 1. 3. 2.* ). Variable definitions were based on published literature and clinical relevance. Smoking status was not documented in the medical record of 59 of 469 (12.6%) study participants. Hence, it had to be assessed retrospectively and may be susceptible to recall bias (*refer to 2. 3. 1.* ). The small study sample did not allow to test every variable of scientific interest and clinical relevance. Hence, a subset that seemed most relevant was presented. Univariable study analyses showed differences between persistent smokers and successful quitters. Furthermore, a three-block binary logistic regression model was built to estimate and quantify determinants associated with smoking status at telephone-based follow-up interview. The literature search via a structured search algorithm and additional searches for specific questions offered insight in the scientific context.

Qualitative study methodology aimed to add valuable information to facilitate a broader understanding of the participants' smoking habits: a directed qualitative content analysis approach was applied [*51*]. It was organized step wise with inductive and deductive elements to accomplish best possible trustworthiness of results and conclusions. This method was preferable in situations where either the object of interest is too complex to allow predefining a questionnaire without losing valuable information and/or previous research and theory is available but sparse [*52*]. A total of 747 qualitative quotes were processed through a well performing coding system. In order to "let the text speak" [*50*] detailed information on demographic data and qualitative quotes were provided enabling readers to draw their own conclusions. Not having audiotaped the interviews was a methodological weakness. Nevertheless, these data seemed unique in their horizontal extend.

## 4. 3. Smoking cessation pattern

### 4. 3. 1. Smoking rate and cessation rate

Smoking rates at CHD index event ranged between 15-25% and smoking cessation rates following an acute cardiac event or procedure ranged between 50-65% in comparable studies such as EuroAspire IV [*10*], PREMIER [*8*], OASIS

[*55*] and a study from Olmsted County, Minnesota [*40*]. In the past decade smoking rates at admission due to CHD and smoking cessation rates following hospital discharge seemed to be stagnating, in women below fifty years of age even increasing [*6*, *36*]. The recent EuroAspire V survey (participants included 2016–2017) did not show substantial improvements regarding tobacco smoking [*56*]. In conformity with the WHO Framework Convention on Tobacco Control national and international policy makers implemented anti-smoking legislation initiatives [*14*]. Subsequently, reduced rates of hospital admission due to acute coronary syndrome and mortality benefits regarding illnesses associated with tobacco smoking were observed as Frazer *et al* indicated [*57*]. Similar trends were reported in Germany, but reduced hospital admission rates due to ST-elevation myocardial infarction following the implementation of anti-smoking initiatives were above all evident in non-smokers [*58*].

There are smoking cessation guidelines for tobacco use and dependence providing comprehensive evidence for the use of the medical advice, behavioral therapy and adequate supportive drug therapy as well as interventions on the health system level [*59*, *60*]. These evidence-based treatment recommendations were infrequently reported in this cohort: the medical advice to quit smoking was reported by 64.2% of current smokers at index event, written training material was offered to 26.3% and pharmacotherapeutic support was recommended to only 16.8%. A systematic Cochrane review analyzed the effect of any form of nicotine replacement therapy compared to control: the odds of smoking cessation increased by 50-66% (RR 1.58, 95%CI 1.50 to 1.66) [*61*]. These findings were in accordance with other European studies indicating that smoking cessation counselling and pharmacotherapy of nicotine dependence were underused in clinical practice [*10*, *62*].

The benefits of smoking cessation include a decrease in all-cause mortality, non-fatal myocardial infarction, better quality of life and less economic burden for the health care system: A systematic review and meta-analysis reported bisecting the odds of death after AMI by smoking cessation (OR 0.54, 95%CI 0.46 to 0.62) [*4*]. However, pooled European data of all countries participating in EuroAspire IV showed no association of smoking cessation with survival in the follow-up

period [*63*]. Accordingly, in a prospective cohort study in Xi'an, China with 35 years of follow-up recent quitters compared to persistent smokers had no significant reduction in all-cause mortality (quit 2–7 years prior to follow-up; RR 0.89, 95%CI 0.63 to 1.16) [*64*]. But long-term quitters (quit 8 years or more prior to follow-up; RR 0.64, 95%CI 0.46 to 0.90) and never-smokers (RR 0.53, 95%CI 0.42 to 0.65, p-Value for trend p<0.001) had a significant reduction in all-cause mortality [*64*]. In the OASIS trial odds of recurrent AMI in patients after acute coronary syndromes were halved by smoking cessation (OR 0.57, 95%CI 0.36 to 0.89) [*55*]. Furthermore, persistent smoking was an independent predictor of major adverse cardiac and cerebrovascular events in patients after PCI (hazard ratio [HR] 1.4, 95%CI 1.1 to 1.7, p=0.02) [*65*]. Smoking cessation after a cardiac event was associated with increased quality of life as described in several studies [*66*, *67*]. Remarkably, the most intensive and expensive smoking cessation interventions were those most salutary- and cost-effective [*68*, *69*].
Hence, smoking cessation was a pivotal guideline recommended and achievable therapy target in patients with established CHD, but several barriers to smoking cessation needed to be addressed. Due to a perceived lack of training the majority of German general practitioners reported low engagement in smoking cessation counseling [*70*]. Australian general practitioners reported a patient's "lack of motivation" as important barrier to smoking cessation advice in primary care [*71*]. Qualitative content analysis revealed the positive aspects of smoking and the impact of spouses, friends and colleagues on risk to relapse after a quitting attempt. In the present study environmental tobacco smoke exposure may have been another barrier to smoking cessation.

#### 4. 3. 2. Demography

##### 4. 3. 2. 1. Age

Results of the present study regarding the participants' age conformed with some, but not all comparable studies including current smokers after acute coronary syndrome. Participants in our sample were older than the European average in EuroAspire IV (65.6±8.8 years vs 62.5±9.6 years), but current smokers at index event were younger than average (59.1±9.0 years) [*10*]. Older age of current smokers at hospital admission was not associated with smoking status at

telephone-based follow-up interview (successful quitters vs persistent smokers; 59.5±9.0 years vs 58.5±9.1 years, p=0.61). This conformed with observations made by Dawood *et al* (54.5±10.3 vs 53.5±9.9 years, p=0.27) and Chow *et al* (59.2±10.5 vs 58.3±10.8 years, p-value not published), but differed from results published by Sochor *et al*: age of current smokers at PCI 55.8±10.7 years; odds ratio of smoking cessation at 12 month follow-up OR 1.44 per decade, 95%CI 1.17 to 1.77, p<0.001 [*8*, *40*, *55*]. For the group of current smokers between 50 and 70 years of age, surviving an acute coronary syndrome, the influence of age seemed unclear in the smoking cessation process.

#### 4. 3. 2. 2. Sex

Current smokers at index event were predominantly male in this cohort (15.4% females) and female sex was not associated with smoking cessation at telephone-based follow-up interview (successful quitters vs persistent smokers; 16.9% vs 12.8% females, p=0.78). Comparable studies of Dawood *et al* and Chow *et al* reported higher rates of females (33.3% and 22.0%, respectively) and no differences between sex groups regarding smoking cessation at follow-up alike [*8*, *55*].

#### 4. 3. 2. 3. Education

As stated in *1. 3. 3.* higher levels of education were assumed to be associated with successful cessation. Surprisingly, in this cohort of 104 pre-CHD-event smokers, persistent smokers at telephone-based follow-up interview had a higher average education level than successful quitters. Though, after adjustment for cardiac rehabilitation program in multivariable regression there was no significant association. By contrast, smoking status at index event was not associated with higher educational level. Supporting this finding, a Chinese study including young male adult smokers showed higher levels of education, defined by ≥ senior college or university, associated with higher levels of current smoking, despite a better knowledge on tobacco related health hazards [*72*]. In a study including current smokers at the time of hospitalization for acute myocardial infarction, Dawood *et al* reported no significant differences in the proportion of patients with more than a high school degree in successful quitters vs persistent smokers 6-month post-AMI (47.3% vs 43.2%, p=0.31) [*8*]. Carabello *et al* suggested, that

longer education periods and higher education levels increase the odds of smoking cessation and decrease the odds of relapse among otherwise healthy youth and adult smokers [*39*]. Pooled European data from EuroAspire IV reported higher education levels to be associated with subsequent smoking cessation in men but not in women [*73*]. In this cohort high educational level was defined by high school completed, college/university completed or postgraduate degree. Differing definitions of higher education level are used in the context of CHD: e.g. more than primary school [*74*], more than high school [*39*] or three ordinal categories such as primary, secondary and tertiary education [*73*, *75*]. Applying more than primary school as definition for high education level, the association in our cohort vanished as 103 of 104 pre-CHD-event smokers of the German EuroAspire IV cohort had more than primary school leaving qualification. It is generally acknowledged that education is a key element in prevention strategies and patients with lower levels of education may benefit from more attention. Nevertheless, the present findings showing higher school-leaving qualification associated with lower rates of smoking cessation are a reason for concern [*9*].

#### 4. 3. 3. Coronary heart disease and comorbidities

##### 4. 3. 3. 1. Coronary heart disease

Coronary surgery was applied to 14 of 104 (13.5%) current smokers at index event. CABG vs non-CABG, infarction vs ischemia and emergency vs elective procedures were not associated with smoking cessation in this cohort. Hammal *et al* reported on smoking status at 1-year follow-up of 2584 current smokers (18.4% CABG) at hospital admission for CHD: successful smoking cessation was less frequently among patients treated with medical treatment alone as well as with medical treatment plus PCI, compared to medical treatment plus CABG (47.6% vs 57.4% vs 74.3%, $p<0.001$) [*7*]. In the present cohort, all 14 of 14 (100%) CABG patients participated in a cardiac rehabilitation program, whereas 59 of 90 (65.6%) non-CABG patients participated in such a program (*refer to Supplemental Table 21*). Secondary prevention efforts should encourage all CHD patients to use smoking cessation expertise and participate in cardiac rehabilitation programs, regardless of their treatment option.

#### 4. 3. 3. 2. Diabetes

There was a non-significant trend of diabetes influencing smoking status at telephone-based follow-up interview in this cohort. Antismoking efforts may have been more intense for diabetic patients although frequency of diabetes did not differ significantly between non-participants and participants of cardiac rehabilitation programs (25.8% vs 33.3%, p=0.30). Data from the APPROACH registry showed no differences in frequency of diabetes between successful quitters and persistent smokers one year after the angiographic diagnosis of coronary artery disease (20.1% vs 19.0%, p=0.5) [*7*].

#### 4. 3. 3. 3. Depressed mood

Depressive symptoms were shown to be associated with cardiovascular risk factors such as smoking, unhealthy food choices, low physical activity and nonadherence to cardio-protective drugs [*76*]. At baseline visit, 25 of 104 (24.2%) current smokers at index event showed depressed mood, according to the HADS questionnaire's subscale on depression. Subsequently, successful quitters at follow-up were less likely to present with depressed mood than persistent smokers. In multivariable regression analysis presence of depressed mood was significantly associated with persistent smoking when adjusted for age, sex, education level, coronary surgery and diabetes, but lost variance after adjustment for cardiac rehabilitation program. The percentage of patients with depressed mood was lower in never-smokers and former smokers at index event (14.6% and 15.7%, respectively). Dawood *et al* reported that 24.0% of current smokers with hospitalization due to AMI showed depressive symptoms post hospital discharge using a comparable method (PHQ-9 score ≥10) [*8*]. There, successful quitters 6 months post discharge presented less often with depressive symptoms than persistent smokers (17.9% vs 30.9%, p<0.001) and depressive symptoms remained a significant predictor of persistent smoking in multivariable regression analysis [*8*]. Farris *et al* studied a sample of 111 adult daily smokers investigating the differences of smokers with and without present psychopathology: 40.5% of participants met criteria for past-year psychological diagnosis, most frequently were emotional disorders (anxiety/depression) and substance use disorders. Those smokers with any psychopathology showed significantly higher intensity

of demand and more willingness to pay higher prices compared to those without, which may result in higher barriers to successful quitting [*77*].

The influence of depressed mood on CHD may include further mechanisms than exclusively behavioral risk factor modification. Evidence suggested that depressive patients with CHD varied in several aspects from non-depressive patients with CHD. Depressive CHD patients seemed to have: higher inflammatory biomarkers (e.g. interleukin-6 and C-reactive protein), impaired vascular function, increased platelet activity, hypothalamic-pituitary-adrenal axis dysfunction, reduced heart rate variability (suggesting autonomic dysregulation) and higher risk of non-adherence to medical treatment regimens and secondary prevention offers (such as cardiac rehabilitation programs and lifestyle modifications) [*76*, *78*].

Some depressive patients used smoking as self-medication. Freedland *et al* reported that smoking improved mood in some cases but worsened it in others [*79*]. Successful cessation or periods of quitting attempts *per se* were not associated with the onset of depressed mood, but in patients who once suffered a major depression prior to a quitting attempt, nicotine abstinence was associated with recurrence of depressive symptoms [*79*]. The existing co-prevalence of smoking and depressed mood may even have been due to shared etiology: evidence supposed a genetic predisposition to both smoking and depressed mood [*79*]. Albeit it remained unknown weather routine screening for psychosocial risk factors lead to less future cardiac events, the negative influence of depressed mood on both smoking cessation and CHD is usually accepted. Stringently, efforts in the treatment of comorbid depression were recommended and may facilitate smoking cessation [*5*].

#### 4. 3. 4. Cardiac rehabilitation program

Participation in a cardiac rehabilitation program was significantly associated with smoking cessation median 3.5 years after a cardiac event in this cohort (*refer to Table 7*). Of 104 current smokers at index event, 76 (73.1%) were advised to attend a cardiac rehabilitation program and 73 (70.2%) did so. Whereas, former and never-smokers less frequently attended a cardiac rehabilitation program (45.8% and 45.5%, respectively). From the entire EuroAspire IV population of

7998 patients (24.4% females), 50.7% were advised to participate in a cardiac rehabilitation program and 81.3% of those attended at least half of the recommended sessions; hence, on the European average 41.2% of eligible patients participated in a cardiac rehabilitation program [*10*]. Furthermore, in the European cohort older patients and pre-event smokers were (among others) less likely to be advised to attend a cardiac rehabilitation program [*80*]. These differences were not observed in this subgroup of German participants in EuroAspire IV. A registry study on patients who underwent PCI in Olmsted County, Minnesota, USA, reported 40% of the cohort participated in a cardiac rehabilitation program after hospital discharge [*81*]. In the previous EuroAspire III survey 44.8% of 8845 interviewed patients reported having been advised to attend a cardiac rehabilitation program and 81.4% of those did so (i.e. 36.5% of all eligible patients attended) [*82*]. In the present cohort, current smokers who reported at least one quitting attempt before the index event more frequently reported having been advised to attend a cardiac rehabilitation program than ever-smokers who did not report a quitting attempt (76.5% vs 58.3%, $p<0.001$). If medical staff had prioritized patients with potentially higher chances to change their smoking behavior, this may implicate a selection bias overestimating the true effect of participation in a cardiac rehabilitation program on chances to quit smoking in this analysis. All 14 patients who had a CABG procedure attended a cardiac rehabilitation program whereas only 65.6% of non-CABG study participants did. Age, sex, level of education and diabetes were not significantly associated with attendance in a cardiac rehabilitation program in this cohort (*refer to Supplemental Table 21*). Cardiac rehabilitation program referral rates in Europe remained suboptimal but were possibly slightly increasing; corresponding rates in Germany were higher than average, especially in smokers [*10*].

The main aims of cardiac rehabilitation programs were to reduce all-cause and cardiovascular mortality, morbidity and re-hospitalization rates, increase quality of life and at the same time be cost-effective [*5*]. Additionally, exercise-based programs have demonstrated to have direct beneficial effects *per se* on the heart and coronary system including improvements in endothelial function of coronary vessels [*83*]. Comprehensive programs included exercise training, risk factor

education, behavior change and/or psychological support [*5*]. There were programs in specialized cardiac rehabilitation clinics, home-based programs with daily contact to a rehabilitation facility and alternative programs such as tele-rehabilitation [*5*, *84*]. Based on evidence from systematic reviews and meta-analyses, exercise-based cardiac rehabilitation was a pivotal recommendation for patients post a cardiac event [*41*, *85*]. The recent Cochrane review of exercise-based cardiac rehabilitation for CHD of 63 randomized controlled trials including 14.486 patients with CHD reported that exercise-based cardiac rehabilitation programs reduced cardiovascular mortality compared with usual care (RR 0.74, 95%CI 0.64 to 0.86) and overall re-hospitalization (RR 0.82, 95%CI 0.70 to 0.96); however, there was no significant reduction in all-cause mortality (RR 0.96, 95%CI 0.88 to 1.04) or the risk of recurrent AMI, CABG or PCI [*86*]. There was evidence for improvements in quality of life and cost-effectiveness of exercised-based cardiac rehabilitation [*86*]. Taylor *et al* reported the beneficial effects of exercise-based cardiac rehabilitation programs were to 58% attributable to changes in the main cardiovascular risk-factors (i.e. smoking, lipids, blood pressure); 24% of the total mortality risk reduction was accountable to reduced smoking [*87*]. In the present study the association of participation in a cardiac rehabilitation program with subsequent smoking cessation was strong (OR 5.19, 95%CI 1.87-14.46, p=0.002). According to results from the PREMIER registry, recommendation to attend a cardiac rehabilitation programs increased the likelihood of smoking cessation (OR 1.80, 95%CI 1.17 to 2.75) [*8*]. A retrospective cohort study of 2306 consecutive patients after PCI from Olmsted County, Minnesota, USA, reported an even stronger odds ratio to quit smoking successfully in patients who attended a cardiac rehabilitation program compared to those who did not (OR 3.17, 95%CI 2.05 to 4.91, p<0.001) [*40*]. A previous systematic Cochrane review and meta-analysis of 8940 patients also stated that exercise-based cardiac rehabilitation programs increased chances of successful quitting compared to usual care (OR 1.56, 95%CI 1.21 to 2.00) [*41*]. In European data of all countries participating in EuroAspire IV successful quitters were more likely to report recommendation to and participation in a cardiac rehabilitation program [*74*]. This cohort's association between participation in a cardiac

rehabilitation program and successful cessation seemed overestimated when compared to published literature [*9*]. This may have been due to a selection bias of highly motivated smokers who already tried quitting smoking prior to the index event. Furthermore, overall goodness of fit according to Nagelkerke's R squared was low (*refer to Table 7*), reflecting the complexity of predicting behavioral change adequately.

A limitation of this study was, that there was no information available on the type (center-based vs home-based), length and intensity of the cardiac rehabilitation programs attended. In general, inpatient cardiac rehabilitation programs were most common in Germany [*88*]. A center-based vs home-based approach and intensity of an exercise intervention was not significantly associated with outcomes such as mortality, morbidity, behavior changes, secondary prevention targets and drug adherence [*86*, *89*]. These findings support the importance of cardiac rehabilitation programs in secondary prevention of CHD.

#### 4. 3. 5. Extended smoking status

It was *a priori* expected that the onset or recurrence of acute CHD may have more impact on the subsequent smoking behavior of study participants if there had been a certain ambivalence regarding tobacco products prior to the hospital admission. Therefore, a broader smoking status variable was established distinguishing 1) never-smokers who consistently reported never smoking, 2) former smokers who quit smoking prior to hospital admission, 3) current smokers who reported current smoking and at least one quitting attempt prior to hospital admission and 4) ever-smokers who reported current smoking and nary a quitting attempt prior to hospital admission. There was a significant difference in subsequent smoking habits: two thirds of ever-smokers reported smoking at telephone-based follow-up interview, whereas only one quarter of current smokers did (63.9% vs 26.5%, $p<0.001$). Higher attendance in a cardiac rehabilitation program of current vs ever-smokers may offer a partial explanation. According to the Health belief model a preexisting ambivalence of the positive and negative aspects of tobacco smoking prior to the onset of a severe disease may lead to successful cessation when a cue to action opens the "teachable window" [*38*, *47*]. This may encourage physicians to repeatedly ask for smoking

habits and offer comprehensive advice according to smoking cessation guidelines [*5*, *60*]. Future research may implement this broader view of smoking status to widen the understanding of some smokers' ambivalence towards their habit.

## 4. 4. Qualitative exploration

4. 4. 1. Persistent smoking and relapse after a quitting attempt

In this cohort of patients with established CHD, there were 39 pre-CHD-event smokers who persisted and seven former smokers who relapsed smoking until telephone-based follow-up interview. Addiction, pleasure, relaxation, stress, the social network and neutral reasons as boredom or habit were mentioned as reasons to persist smoking. The different categories in the present study seemed to be linked through ambivalence and mood. To enable smoking cessation, the vicious relation of smoking as a positive stimulant that "serves […] to maintain […] joy in life" (pID 9), on the one hand and quitting as the origin of craving, boredom and associated bad mood on the other hand, seemed pivotal. The Health Belief Model states the consideration of attempting a behavior change is "pulled by positive forces and repelled by negative forces" [*46*, *90*]. But more than one fifth of current smokers at telephone-based follow-up interview reported solely negative reasons to continue smoking. Nevertheless, these participants were unable to quit. Thus, admitting tobacco smoking inheriting aspects of a highly addictive abuse disorder seems reasonable [*59*]. Kerr *et al* studied a smaller sample of 20 senior current and former smokers addressing their health beliefs and cues to action in more vertical deepness: the present results, unique in their horizontal extend, agree with their statements of tobacco smoking being an addictive behavior and smoking cessation an assumed loss of relaxation and pleasure [*43*]. Another qualitative study on twenty-two long-term older smokers with arterial disease focused on the relationship older smokers had established towards their habit: there was considerable heterogeneity over the perceived dependency towards tobacco products. On the one hand, addiction, either assumed due to self-report or due to dependent consumption patterns, built up a barrier to quit smoking. On the other hand, a group of assumed non-dependent

smokers described another barrier to quitting: their positive relationship to smoking as a functional part of their everyday live, regarding the material circumstances and isolating aspects of old age [*91*]. There are multiple recommendations available to encourage smoking cessation; from the WHO Framework Convention on Tobacco Control and social cognitive theory, on to the most recent guidelines of smoking cessation therapy and secondary prevention after the onset of CHD [*5*, *14*, *59*, *92*]. Physicians may offer smoking cessation counseling to support the individual without injuring his or her autonomy.

The hazard of relapse accompanies each former smoker beginning with the first day of quitting [*93*]. The health-related reasons having had led to previous cessation attempts lost their influence on some of our study participants. Smoking friends, colleagues or even family members offering the former smoker “just one cigarette” (pID 25) were mentioned frequently as reason to relapse. A qualitative study among twenty Greek-Australian smokers above 50 years of age investigated the role of the social network: in accordance with our findings family members and friends were influential both on ushering quitting attempts and on seducing relapse [*94*]. In the present study the influence of the social network was frequently named as reason to relapse, but sparsely referred to as reason to undertake a quitting attempt or as reason to quit successfully (47% vs 22% vs 19%, respectively). Stress seemed to lower the barriers of relapse. The relationship between smoking, stress and negative affects is a complex phenomenon that exceeds the scope of this discussion. Briefly Kassel *et al* argued, given the circumstance that findings regarding nicotine’s effects on negative mood and stress from both human and animal research were inconsistent, bidirectional effects seemed less informative than mediator and moderator-based approaches. Hence, thinking about the relationship resulting of the individual’s contextual influence factors (e.g. social interactions, cognitive challenge, benign distraction) and individual differences (e.g. gender, ethnicity, negative affectivity) rather than interdependent causality of smoking, stress and negative mood, may be the prioritized way of understanding the phenomenon [*95*]. Subsequently, one fifth of statements were coded as without any objective stimulus or because of pure boredom. Only 12% stated having relapsed due to

nicotine dependence. But there were clues for addictive behavior in the leading categories (i.e. social network, stress): e.g. participants frequently relapsed for a long period of time after having smoked “just one cigarette” together with friends and after smoking a cigarette in a stressful situation the habit returned to the daily routine. In contrast to the reasons for persistent smoking, positive categories, such as relaxation or pleasure, were reported sparsely as reasons to relapse.

These findings may extend the knowledge for enhancing relapse prophylaxis strategies; maintenance, as Prochaska and DiClemente proposed, is an active stage of behavior change [*96*]. To aid a current smoker attempting to quit, situations facilitating relapse may be *a priori* discussed and adequate preventive support to cope with these situations provided.

#### 4. 4. 2. Quitting attempts and successful quitting

Possible cues to action motivating the study participants to undertake quitting attempts were identified. Surprisingly, health related reasons, subsumed in the categories subsequent damage and current disorder, clearly outweighed personal/social reasons such as the social network and financial issues. This imbalance was even more distinct in reasons to quit than in reasons to undertake quitting attempts. Furthermore, affective personal experience of current health problems and smoking related sequelae seemed to predominate over rational health education and advertisement. The social network, although *a priori* considered being a stronger influence factor than observed, nevertheless, was referred to third in frequency to undertake quitting attempts and fourth to quit successfully.

The importance of health problems and the influence of family members and friends (i.e. social network) as cue to action stands in concordance with published findings by Kerr *et al* [*43*]. In a qualitative study in older smokers of Greek-Australian origin, knowledge on the harmfulness of smoking and benefits of smoking cessation in general was low; significantly, this study’s title was, “I have never experienced any problem with my health. So far, it hasn’t been harmful (…)” [*44*]. Consequently, health problems were not that influential on the participants smoking behavior, some even reported on beneficial effects of smoking on breathing or prevention of subsequent sequelae such as cancer. The

authors stated that in “populations where smokers lack knowledge of the benefits of smoking cessation and have a positive perception of the benefits of smoking, cessation challenges will be maximized” [*44*]. Hence, participants in the present study might have perceived their personal experiences more influential than any health education, but without their *a priori* knowledge and understanding of the harmfulness of smoking the awareness of smoking being related their personal experiences might have been different.

In comparison of reasons to undertake quitting attempts and reasons to quit, the age of successful quitting was ten years above the age at beginning of the longest quitting attempt. Almost every second quitter reported at least one quitting attempt prior to his or her successful smoking cessation. Especially a severe disease the individual associated with a life threat such as coronary heart disease seemed to open a teachable window for behavior change [*38*]. Quitting attempts and successful quitting were common in adult and senior life. As the interviewing technique focused on horizontal extend rather than vertical deepness, some important aspects of smoking cessation, such as support from the primary care sector, access to smoking cessation programs or questions aiming at self-efficacy, were not covered. Indeed, the present study may support the discussion about smokers’ health beliefs and smoking cessation by providing an insight into the subjective, spontaneously given reasons to change or maintain smoking behavior of some hundred individuals of a very high-risk population.

#### 4. 4. 3. Smoking prevention

There are studies investigating smoking initiation and maintenance among youth and young adults [*97*, *98*]. As the present study offered the unique opportunity to study a large group of all-time never-smokers with established CHD, retrospective investigation of their reasons to never start smoking was done to identify possible barriers to smoking initiation. One third of our study participants reported to be never-smokers. The most frequent theme “no need” offered little information regarding possible preventive issues, but raised the assumption, that some individuals were unsusceptible to smoking initiation regardless of the circumstances. Health related arguments and financial concerns seemed of less importance than the abstract idea of absent susceptibility to tobacco products.

“Unpleasant memories” provided insights in the origin of some participants emotionally negative connotations to smoking: although approximately 70 years of age, one third of never-smokers lively described youth memories of smoking related feelings and symptoms, such as nausea or coughing as well as images of smoking related ill health of family members as possible reasons to never having started smoking regularly. As discussed before the “social network” played a key role in driving relapse, while simultaneously anti-smoking influence seemed associated with tobacco abstinence. To the authors knowledge this is the first study investigating older never-smoking CHD patients’ reasons to resist smoking initiation.

## 4. 5. Strengths and Limitations

Like in other EuroAspire surveys, a selected geographical area was chosen [*10*]. Furthermore, in accordance with the overall trend of declining response rates in epidemiologic surveys participation at baseline interview was low [*99*]. Hence, other CHD populations may differ in demographic and clinical parameters and unmeasured confounding may be present. Explained variance in the logistic regression model was low, but the sample size was too small to include further comorbidities and parameters of smoking cessation. Medical records did not offer the information of smoking duration and intensity (i.e. pack years) prior to index admission. This information was retrospectively assessed, but due to recall bias it could not reliably be used. As smoking is a major risk factor for CHD morbidity and mortality pack years should be documented in medical discharge documents [*12*]. Attendance in a cardiac rehabilitation program was not randomly assigned. The association of participation in a cardiac rehabilitation program on successful smoking cessation might have been overestimated in this study. Nevertheless, there was a substantial effect in accordance with current evidence. The qualitative interviews were neither audiotaped nor transcribed verbatim. Limited by time the interviewing technique could not cover all aspects of scientific interest. Strengths of the present study include, that one single researcher conducted all interviews and the number of qualitative samples was far more extensive than usual. The high performance of the coding system and the independent evaluation by a second rater during the step-wise development approach may

contribute to the trustworthiness of the findings. Further strengths of this survey include the use of predefined standardized methods including standard operation procedures, medical record extraction sheets, questionnaires and centralized laboratory analyzes. By applying personal interviews, comorbidities and risk factors were assessed in more detail than in comparable studies relying on discharge documents alone. Smoking cessation was studied in a small but high-risk cohort of patients with established CHD.

# 5. Conclusion

In the present study the prevalence of smoking at admission due to a cardiac event and the rate of persistent smoking median 3.5 years afterwards were high. Guideline recommended and evidence-based treatment options for smoking cessation such as medical advice and nicotine replacement therapy were infrequently reported. Cardiac rehabilitation was strongly associated with subsequent smoking cessation in this cohort. Coverage of cardiac rehabilitation remained incomplete. Nevertheless, the participation rate was higher than the European average, particularly in the subgroup of current smokers at a CHD index event. Personal reasons to quit smoking included social and health related aspects. Most persistent smokers reported ambivalent feelings towards their habit. Physicians may be encouraged to further implement smoking cessation counseling and referral to cardiac rehabilitation programs in their daily routine to enhance secondary prevention after an acute cardiac event.

# 6. References


1. G. B. D. Risk Factors Collaborators, Forouzanfar MH, Alexander L, Anderson HR, Bachman VF, Biryukov S, Brauer M, Burnett R, Casey D, Coates MM *et al*: **Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013**. *Lancet.* 2015; 386(10010):2287-2323. *https://doi.org/10.1016/S0140-6736(15)00128-2*.

2. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, Ahmed M, Aksut B, Alam T, Alam K *et al*: **Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015**. *J Am Coll Cardiol.* 2017; 70(1):1-25. *https://doi.org/10.1016/j.jacc.2017.04.052*.

3. Ezzati M, Henley SJ, Thun MJ, Lopez AD: **Role of smoking in global and regional cardiovascular mortality**. *Circulation.* 2005; 112(4):489-497. *https://doi.org/10.1161/CIRCULATIONAHA.104.521708*.

4. Wilson K, Gibson N, Willan A, Cook D: **Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies**. *Arch Intern Med.* 2000; 160(7):939-944. *https://doi.org/10.1001/archinte.160.7.939*.

5. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corra U, Cosyns B, Deaton C *et al*: **2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR)**. *Eur Heart J.* 2016; 37(29):2315-2381. *https://doi.org/10.1093/eurheartj/ehw106*.

6. Kotseva K, De Bacquer D, Jennings C, Gyberg V, De Backer G, Ryden L, Amouyel P, Bruthans J, Cifkova R, Deckers JW *et al*: **Time Trends in Lifestyle, Risk Factor Control, and Use of Evidence-Based Medications in Patients With Coronary Heart Disease in Europe: Results From 3 EUROASPIRE Surveys, 1999-2013**. *Glob Heart.* 2017; 12(4):315-322 e313. *https://doi.org/10.1016/j.gheart.2015.11.003*.

7. Hammal F, Ezekowitz JA, Norris CM, Wild TC, Finegan BA, Approach Investigators: **Smoking status and survival: impact on mortality of continuing to smoke one year after the angiographic diagnosis of coronary artery disease, a prospective cohort study**. *BMC Cardiovasc Disord.* 2014; 14(1):133. *https://doi.org/10.1186/1471-2261-14-133*.

8. Dawood N, Vaccarino V, Reid KJ, Spertus JA, Hamid N, Parashar S, Premier Registry Investigators: **Predictors of smoking cessation after a myocardial infarction: the role of institutional smoking cessation programs in improving success**. *Arch Intern Med.* 2008; 168(18):1961-1967. *https://doi.org/10.1001/archinte.168.18.1961*.

9. Goettler D, Wagner M, Faller H, Kotseva K, Wood D, Leyh R, Ertl G, Karmann W, Heuschmann PU, Störk S *et al*: **Factors associated with smoking cessation in patients with coronary heart disease: a cohort analysis of the German subset of EuroAspire IV survey**. *BMC Cardiovascular Disorders.* 2020; 20(1):152. *https://doi.org/10.1186/s12872-020-01429-w*.

10. Kotseva K, Wood D, De Bacquer D, De Backer G, Ryden L, Jennings C, Gyberg V, Amouyel P, Bruthans J, Castro Conde A *et al*: **EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries**. *Eur J Prev Cardiol.* 2016; 23(6):636-648. *https://doi.org/10.1177/2047487315569401*.

11. World Health Organization: **WHO global report on trends in tobacco smoking 2000-2025 - First edition.** *World Health Organization, Geneva, Switzerland.* 2015. Available at [*https://www.who.int/*]. Accessed 02.12.2016.

12. Doll R, Peto R, Boreham J, Sutherland I: **Mortality in relation to smoking: 50 years' observations on male British doctors**. *BMJ.* 2004; 328(7455):1519. *https://doi.org/10.1136/bmj.38142.554479.AE*.

13. Ambrose JA, Barua RS: **The pathophysiology of cigarette smoking and cardiovascular disease: an update**. *J Am Coll Cardiol.* 2004; 43(10):1731-1737. *https://doi.org/10.1016/j.jacc.2003.12.047*.

14. World Health Organization: **WHO Framework Convention on Tobacco Control.** *Geneva, Switzerland.* 2003. Available at [*https://www.who.int/*]. Accessed 30.11.2016.

15. World Health Organization: **Global Action Plan for the Prevention and Control of NCDs 2013-2020.** *World Health Organization, Geneva, Switzerland.* 2013. Available at [*https://www.who.int/*]. Accessed 20.11.2018.

16. Bilano V, Gilmour S, Moffiet T, d'Espaignet ET, Stevens GA, Commar A, Tuyl F, Hudson I, Shibuya K: **Global trends and projections for tobacco use, 1990-2025: an analysis of smoking indicators from the WHO Comprehensive Information Systems for Tobacco Control**. *Lancet.* 2015; 385(9972):966-976. *https://doi.org/10.1016/S0140-6736(15)60264-1*.

17. G. B. D. DALYs Hale Collaborators, Murray CJ, Barber RM, Foreman KJ, Abbasoglu Ozgoren A, Abd-Allah F, Abera SF, Aboyans V, Abraham JP *et al*: **Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition**. *Lancet.* 2015; 386(10009):2145-2191. *https://doi.org/10.1016/S0140-6736(15)61340-X*.

18. World Health Organization: **Cardiovascular diseases (CVDs).** 2017. Available at [*https://afro.who.int/health-topics/cardiovascular-diseases*]. Accessed 21.11.2018.

19. Libby P, Ridker PM, Hansson GK: **Progress and challenges in translating the biology of atherosclerosis**. *Nature.* 2011; 473(7347):317-325. *https://doi.org/10.1038/nature10146*.

20. Rose G: **Strategy of prevention: lessons from cardiovascular disease**. *Br Med J (Clin Res Ed).* 1981; 282(6279):1847-1851. *https://doi.org/10.1136/bmj.282.6279.1847*.

21. Pyorala K, De Backer G, Graham I, Poole-Wilson P, Wood D: **Prevention of coronary heart disease in clinical practice. Recommendations of the Task Force of the European Society of Cardiology, European Atherosclerosis Society and European Society of Hypertension**. *Eur Heart J.* 1994; 15(10):1300-1331. *https://doi.org/10.1093/oxfordjournals.eurheartj.a060388*.

22. Wood D, De Backer G, Faergeman O, Graham I, Mancia G, Pyorala K: **Prevention of coronary heart disease in clinical practice: recommendations of the Second Joint Task Force of European and other Societies on Coronary Prevention**. *Atherosclerosis.* 1998; 140(2):199-270. *https://doi.org/10.1016/s0021-9150(98)90209-x*.

23. De Backer G, Ambrosioni E, Borch-Johnsen K, Brotons C, Cifkova R, Dallongeville J, Ebrahim S, Faergeman O, Graham I, Mancia G *et al*: **European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice**. *Eur Heart J.* 2003; 24(17):1601-1610. *https://doi.org/10.1016/s0195-668x(03)00347-6*.

24. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, Dallongeville J, De Backer G, Ebrahim S, Gjelsvik B *et al*: **European guidelines on cardiovascular disease prevention in clinical practice: full text. Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts)**. *Eur J Cardiovasc Prev Rehabil.* 2007; 14 Suppl 2:S1-113. *https://doi.org/10.1097/01.hjr.0000277983.23934.c9*.

25. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, Albus C, Benlian P, Boysen G, Cifkova R *et al*: **European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts)**. *Eur Heart J.* 2012; 33(13):1635-1701. *https://doi.org/10.1093/eurheartj/ehs092*.

26. Authors/Task Force Members, Ryden L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N, Deaton C, Escaned J, Hammes HP *et al*: **ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD)**. *Eur Heart J.* 2013; 34(39):3035-3087. *https://doi.org/10.1093/eurheartj/eht108*.

27. Wood D: **EUROASPIRE. A European Society of Cardiology survey of secondary prevention of coronary heart disease: principal results. EUROASPIRE Study Group. European Action on Secondary Prevention through Intervention to Reduce Events**. *Eur Heart J.* 1997; 18(10):1569-1582. *https://doi.org/10.1093/oxfordjournals.eurheartj.a015136*.

28. Euroaspire II Study Group: **Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries; principal results from EUROASPIRE II Euro Heart Survey Programme**. *Eur Heart J.* 2001; 22(7):554-572. *https://doi.org/10.1053/euhj.2001.2610*.

29. Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U, Euroaspire Study Group: **EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries**. *Eur J Cardiovasc Prev Rehabil.* 2009; 16(2):121-137. *https://doi.org/10.1097/HJR.0b013e3283294b1d*.

30. Braveman P, Gottlieb L: **The social determinants of health: it's time to consider the causes of the causes**. *Public Health Rep.* 2014; 129 Suppl 2:19-31. *https://doi.org/10.1177/00333549141291S206*.

31. Sheiham A: **Closing the gap in a generation: health equity through action on the social determinants of health. A report of the WHO Commission on Social Determinants of Health (CSDH) 2008**. *Community Dent Health.* 2009; 26(1):2-3.

32. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J *et al*: **Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study**. *Lancet.* 2004; 364(9438):937-952. *https://doi.org/10.1016/S0140-6736(04)17018-9*.

33. Conroy RM, Pyorala K, Fitzgerald AP, Sans S, Menotti A, De Backer G, De Bacquer D, Ducimetiere P, Jousilahti P, Keil U *et al*: **Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project**. *Eur Heart J.* 2003; 24(11):987-1003. *https://doi.org/10.1016/s0195-668x(03)00114-3*.

34. Unal B, Critchley JA, Capewell S: **Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000**. *Circulation.* 2004; 109(9):1101-1107. *https://doi.org/10.1161/01.CIR.0000118498.35499.B2*.

35. Danielsen SE, Lochen ML, Medbo A, Vold ML, Melbye H: **A new diagnosis of asthma or COPD is linked to smoking cessation - the Tromso study**. *Int J Chron Obstruct Pulmon Dis.* 2016; 11:1453-1458. *https://doi.org/10.2147/COPD.S108046*.

36. Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U, Euroaspire Study Group: **Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II, and III surveys in eight European countries**. *Lancet.* 2009; 373(9667):929-940. *https://doi.org/10.1016/S0140-6736(09)60330-5*.

37. Hasdai D, Garratt KN, Grill DE, Mathew V, Lerman A, Gau GT, Holmes DR, Jr.: **Predictors of smoking cessation after percutaneous coronary revascularization**. *Mayo Clin Proc.* 1998; 73(3):205-209. *https://doi.org/10.4065/73.3.205*.

38. McBride CM, Emmons KM, Lipkus IM: **Understanding the potential of teachable moments: the case of smoking cessation**. *Health Educ Res.* 2003; 18(2):156-170. *https://doi.org/10.1093/her/18.2.156*.

39. Caraballo RS, Kruger J, Asman K, Pederson L, Widome R, Kiefe CI, Hitsman B, Jacobs DR, Jr.: **Relapse among cigarette smokers: the CARDIA longitudinal study - 1985-2011**. *Addict Behav.* 2014; 39(1):101-106. *https://doi.org/10.1016/j.addbeh.2013.08.030*.

40. Sochor O, Lennon RJ, Rodriguez-Escudero JP, Bresnahan JF, Croghan I, Somers VK, Lopez-Jimenez F, Pack Q, Thomas RJ: **Trends and predictors of smoking cessation after percutaneous coronary intervention (from Olmsted County, Minnesota, 1999 to 2010)**. *Am J Cardiol.* 2015; 115(4):405-410. *https://doi.org/10.1016/j.amjcard.2014.11.020*.

41. Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, Skidmore B, Stone JA, Thompson DR, Oldridge N: **Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials**. *Am J Med.* 2004; 116(10):682-692. *https://doi.org/10.1016/j.amjmed.2004.01.009*.

42. Malterud K: **Qualitative research: standards, challenges, and guidelines**. *Lancet.* 2001; 358(9280):483-488. *https://doi.org/10.1016/S0140-6736(01)05627-6*.

43. Kerr S, Watson H, Tolson D, Lough M, Brown M: **Smoking after the age of 65 years: a qualitative exploration of older current and former smokers' views on smoking, stopping smoking, and smoking cessation resources and services**. *Health Soc Care Community.* 2006; 14(6):572-582. *https://doi.org/10.1111/j.1365-2524.2006.00659.x*.

44. Mohammadnezhad M, Tsourtos G, Wilson C, Ratcliffe J, Ward P: **"I have never experienced any problem with my health. So far, it hasn't been harmful": older Greek-Australian smokers' views on smoking: a qualitative study**. *BMC Public Health.* 2015; 15:304. *https://doi.org/10.1186/s12889-015-1677-6*.

45. Rosenstock IM: **The Health Belief Model and Preventive Health Behavior**. *Health Education Monographs.* 1974; 2(4):354-386. *https://doi.org/10.1177/109019817400200405*.

46. Rosenstock IM: **Historical Origins of the Health Belief Model**. *Health Education Monographs.* 1974; 2(4):328-335. *https://doi.org/10.1177/109019817400200403*.

47. Janz NK, Becker MH: **The Health Belief Model: a decade later**. *Health Educ Q.* 1984; 11(1):1-47. *https://doi.org/10.1177/109019818401100101*.

48. Bjelland I, Dahl AA, Haug TT, Neckelmann D: **The validity of the Hospital Anxiety and Depression Scale. An updated literature review**. *J Psychosom Res.* 2002; 52(2):69-77. *https://doi.org/10.1016/s0022-3999(01)00296-3*.

49. Chabrol H, Niezborala M, Chastan E, de Leon J: **Comparison of the Heavy Smoking Index and of the Fagerstrom Test for Nicotine Dependence in a sample of 749 cigarette smokers**. *Addict Behav.* 2005; 30(7):1474-1477. *https://doi.org/10.1016/j.addbeh.2005.02.001*.

50. Graneheim UH, Lundman B: **Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness**. *Nurse Educ Today.* 2004; 24(2):105-112. *https://doi.org/10.1016/j.nedt.2003.10.001*.

51. Hsieh HF, Shannon SE: **Three approaches to qualitative content analysis**. *Qual Health Res.* 2005; 15(9):1277-1288. *https://doi.org/10.1177/1049732305276687*.

52. Faller H, Gossler S: **Probleme und Ziele von Psychotherapiepatienten. Eine qualitativ-inhaltsanalytische Untersuchung der Patientenangaben beim Erstgespräch [Problems and goals of psychotherapy patients. A qualitative-content analytic study of patient statements at initial assessment]**. *Psychother Psychosom Med Psychol.* 1998; 48(5):176-186.

53. Mayring P: **Qualitative Inhaltsanalyse. Ein Beispiel für Mixed Methods [Qualitative content analysis. One example of mixed methods.]**. In: *Mixed Methods in der empirischen Bildungsforschung.* Edited by Gläser-Zikuda M, Seidel T, Rohlfs C, Gröschner A, Ziegelbauer S. Münster: Waxmann; 2012: 27-36.

54. Tiffe T, Morbach C, Malsch C, Gelbrich G, Wahl V, Wagner M, Kotseva K, Wood D, Leyh R, Ertl G *et al*: **Physicians' lifestyle advice on primary and secondary cardiovascular disease prevention in Germany: A comparison between the STAAB cohort study and the German subset of EUROASPIRE IV**. *Eur J Prev Cardiol.* 2019:2047487319838218. *https://doi.org/10.1177/2047487319838218*.

55. Chow CK, Jolly S, Rao-Melacini P, Fox KA, Anand SS, Yusuf S: **Association of diet, exercise, and smoking modification with risk of early cardiovascular events after acute coronary syndromes**. *Circulation.* 2010; 121(6):750-758. *https://doi.org/10.1161/CIRCULATIONAHA.109.891523*.

56. Kotseva K, De Backer G, De Bacquer D, Ryden L, Hoes A, Grobbee D, Maggioni A, Marques-Vidal P, Jennings C, Abreu A *et al*: **Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry**. *Eur J Prev Cardiol.* 2019; 26(8):824-835. *https://doi.org/10.1177/2047487318825350*.

57. Frazer K, Callinan JE, McHugh J, van Baarsel S, Clarke A, Doherty K, Kelleher C: **Legislative smoking bans for reducing harms from secondhand smoke exposure, smoking prevalence and tobacco consumption**. *Cochrane Database Syst Rev.* 2016; 2:CD005992. *https://doi.org/10.1002/14651858.CD005992.pub3*.

58. Schmucker J, Wienbergen H, Seide S, Fiehn E, Fach A, Wurmann-Busch B, Gohlke H, Gunther K, Ahrens W, Hambrecht R: **Smoking ban in public areas is associated with a reduced incidence of hospital admissions due to ST-elevation myocardial infarctions in non-smokers. Results from the Bremen STEMI Registry**. *Eur J Prev Cardiol.* 2014; 21(9):1180-1186. *https://doi.org/10.1177/2047487313483610*.

59. Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff: **A clinical practice guideline for treating tobacco use and dependence: 2008 update. A U.S. Public Health Service report**. *Am J Prev Med.* 2008; 35(2):158-176. *https://doi.org/10.1016/j.amepre.2008.04.009*.

60. West R, McNeill A, Raw M: **Smoking cessation guidelines for health professionals: an update. Health Education Authority**. *Thorax.* 2000; 55(12):987-999. *https://doi.org/10.1136/thorax.55.12.987*.

61. Stead LF, Perera R, Bullen C, Mant D, Lancaster T: **Nicotine replacement therapy for smoking cessation**. *Cochrane Database Syst Rev.* 2008(1):CD000146. *https://doi.org/10.1002/14651858.CD000146.pub3*.

62. Balfour D, Benowitz N, Fagerstrom K, Kunze M, Keil U: **Diagnosis and treatment of nicotine dependence with emphasis on nicotine replacement therapy. A status report**. *Eur Heart J.* 2000; 21(6):438-445. *https://doi.org/10.1053/euhj.1999.1949*.

63. De Bacquer D, De Smedt D, Kotseva K, Jennings C, Wood D, Ryden L, Gyberg V, Shahim B, Amouyel P, Bruthans J *et al*: **Incidence of cardiovascular events in patients with stabilized coronary heart disease: the EUROASPIRE IV follow-up study**. *Eur J Epidemiol.* 2019; 34(3):247-258. *https://doi.org/10.1007/s10654-018-0454-0*.

64. He Y, Jiang B, Li LS, Li LS, Sun DL, Wu L, Liu M, He SF, Liang BQ, Hu FB *et al*: **Changes in smoking behavior and subsequent mortality risk during a 35-year follow-up of a cohort in Xi'an, China**. *Am J Epidemiol.* 2014; 179(9):1060-1070. *https://doi.org/10.1093/aje/kwu011*.

65. Zhang YJ, Iqbal J, van Klaveren D, Campos CM, Holmes DR, Kappetein AP, Morice MC, Banning AP, Grech ED, Bourantas CV *et al*: **Smoking is associated with adverse clinical outcomes in patients undergoing revascularization with PCI or CABG: the SYNTAX trial at 5-year follow-up**. *J Am Coll Cardiol.* 2015; 65(11):1107-1115. *https://doi.org/10.1016/j.jacc.2015.01.014*.

66. De Smedt D, Clays E, Annemans L, Boudrez H, De Sutter J, Doyle F, Jennings C, Kotseva K, Pajak A, Pardaens S *et al*: **The association between self-reported lifestyle changes and health-related quality of life in coronary patients: the EUROASPIRE III survey**. *Eur J Prev Cardiol.* 2014; 21(7):796-805. *https://doi.org/10.1177/2047487312473846*.

67. Stafford L, Berk M, Jackson HJ: **Tobacco smoking predicts depression and poorer quality of life in heart disease**. *BMC Cardiovasc Disord.* 2013; 13:35. *https://doi.org/10.1186/1471-2261-13-35*.

68. De Smedt D, Kotseva K, De Bacquer D, Wood D, De Backer G, Dallongeville J, Seppo L, Pajak A, Reiner Z, Vanuzzo D *et al*: **Cost-effectiveness of optimizing prevention in patients with coronary heart disease: the EUROASPIRE III health economics project**. *Eur Heart J.* 2012; 33(22):2865-2872. *https://doi.org/10.1093/eurheartj/ehs210*.

69. Cromwell J, Bartosch WJ, Fiore MC, Hasselblad V, Baker T: **Cost-effectiveness of the clinical practice recommendations in the AHCPR guideline for smoking cessation. Agency for Health Care Policy and Research**. *JAMA.* 1997; 278(21):1759-1766. *https://doi.org/10.1001/jama.278.21.1759*.

70. Twardella D, Brenner H: **Lack of training as a central barrier to the promotion of smoking cessation: a survey among general practitioners in Germany**. *Eur J Public Health.* 2005; 15(2):140-145. *https://doi.org/10.1093/eurpub/cki123*.

71. Young JM, Ward JE: **Implementing guidelines for smoking cessation advice in Australian general practice: opinions, current practices, readiness to change and perceived barriers**. *Fam Pract.* 2001; 18(1):14-20. *https://doi.org/10.1093/fampra/18.1.14*.

72. Xu X, Liu L, Sharma M, Zhao Y: **Smoking-related knowledge, attitudes, behaviors, smoking cessation idea and education level among young adult male smokers in Chongqing, China**. *Int J Environ Res Public Health.* 2015; 12(2):2135-2149. *https://doi.org/10.3390/ijerph120202135*.

73. Bruthans J, Mayer O, Jr., De Bacquer D, De Smedt D, Reiner Z, Kotseva K, Cifkova R, Euroaspire IV investigators: **Educational level and risk profile and risk control in patients with coronary heart disease**. *Eur J Prev Cardiol.* 2016; 23(8):881-890. *https://doi.org/10.1177/2047487315601078*.

74. Snaterse M, Deckers JW, Lenzen MJ, Jorstad HT, De Bacquer D, Peters RJG, Jennings C, Kotseva K, Scholte Op Reimer WJM, Euroaspire Investigators: **Smoking cessation in European patients with coronary heart disease. Results from the EUROASPIRE IV survey: A registry from the European Society of Cardiology**. *Int J Cardiol.* 2018; 258:1-6. *https://doi.org/10.1016/j.ijcard.2018.01.064*.

75. Hoebel J, Kuntz B, Kroll LE, Finger JD, Zeiher J, Lange C, Lampert T: **Trends in Absolute and Relative Educational Inequalities in Adult Smoking Since the Early 2000s: The Case of Germany**. *Nicotine Tob Res.* 2018; 20(3):295-302. *https://doi.org/10.1093/ntr/ntx087*.

76. Carney RM, Freedland KE, Miller GE, Jaffe AS: **Depression as a risk factor for cardiac mortality and morbidity: a review of potential mechanisms**. *J Psychosom Res.* 2002; 53(4):897-902. *https://doi.org/10.1016/s0022-3999(02)00311-2*.

77. Farris SG, Aston ER, Zvolensky MJ, Abrantes AM, Metrik J: **Psychopathology and tobacco demand**. *Drug Alcohol Depend.* 2017; 177:59-66. *https://doi.org/10.1016/j.drugalcdep.2017.03.020*.

78. Lichtman JH, Bigger JT, Jr., Blumenthal JA, Frasure-Smith N, Kaufmann PG, Lesperance F, Mark DB, Sheps DS, Taylor CB, Froelicher ES *et al*: **Depression and coronary heart disease: recommendations for screening, referral, and treatment: a science advisory from the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Psychiatric Association**. *Circulation.* 2008; 118(17):1768-1775. *https://doi.org/10.1161/CIRCULATIONAHA.108.190769*.

79. Freedland KE, Carney RM, Skala JA: **Depression and smoking in coronary heart disease**. *Psychosom Med.* 2005; 67 Suppl 1:S42-46. *https://doi.org/10.1097/01.psy.0000162255.55629.9c*.

80. Kotseva K, Wood D, De Bacquer D, Euroaspire Investigators: **Determinants of participation and risk factor control according to attendance in cardiac rehabilitation programmes in coronary patients in Europe: EUROASPIRE IV survey**. *Eur J Prev Cardiol.* 2018; 25(12):1242-1251. *https://doi.org/10.1177/2047487318781359*.

81. Goel K, Lennon RJ, Tilbury RT, Squires RW, Thomas RJ: **Impact of cardiac rehabilitation on mortality and cardiovascular events after percutaneous coronary intervention in the community**. *Circulation.* 2011; 123(21):2344-2352. *https://doi.org/10.1161/CIRCULATIONAHA.110.983536*.

82. Kotseva K, Wood D, De Backer G, De Bacquer D, Euroaspire III Study Group: **Use and effects of cardiac rehabilitation in patients with coronary heart disease: results from the EUROASPIRE III survey**. *Eur J Prev Cardiol.* 2013; 20(5):817-826. *https://doi.org/10.1177/2047487312449591*.

83. Hambrecht R, Wolf A, Gielen S, Linke A, Hofer J, Erbs S, Schoene N, Schuler G: **Effect of exercise on coronary endothelial function in patients with coronary artery disease**. *N Engl J Med.* 2000; 342(7):454-460. *https://doi.org/10.1056/NEJM200002173420702*.

84. Heran BS, Chen JM, Ebrahim S, Moxham T, Oldridge N, Rees K, Thompson DR, Taylor RS: **Exercise-based cardiac rehabilitation for coronary heart disease**. *Cochrane Database Syst Rev.* 2011(7):CD001800. *https://doi.org/10.1002/14651858.CD001800.pub2*.

85. Clark AM, Hartling L, Vandermeer B, McAlister FA: **Meta-analysis: secondary prevention programs for patients with coronary artery disease**. *Ann Intern Med.* 2005; 143(9):659-672. *https://doi.org/10.7326/0003-4819-143-9-200511010-00010*.

86. Anderson L, Thompson DR, Oldridge N, Zwisler AD, Rees K, Martin N, Taylor RS: **Exercise-based cardiac rehabilitation for coronary heart disease**. *Cochrane Database Syst Rev.* 2016(1):CD001800. *https://doi.org/10.1002/14651858.CD001800.pub3*.

87. Taylor RS, Unal B, Critchley JA, Capewell S: **Mortality reductions in patients receiving exercise-based cardiac rehabilitation: how much can be attributed to cardiovascular risk factor improvements?** *Eur J Cardiovasc Prev Rehabil.* 2006; 13(3):369-374. *https://doi.org/10.1097/01.hjr.0000199492.00967.11*.

88. Benzer W: **[Development and importance of outpatient cardiac rehabilitation in German-speaking countries]**. *Dtsch Med Wochenschr.* 2014; 139(27):1427-1432. *https://doi.org/10.1055/s-0034-1370127*.

89. Anderson L, Sharp GA, Norton RJ, Dalal H, Dean SG, Jolly K, Cowie A, Zawada A, Taylor RS: **Home-based versus centre-based cardiac rehabilitation**. *Cochrane Database Syst Rev.* 2017; 6(6):CD007130. *https://doi.org/10.1002/14651858.CD007130.pub4*.

90. Becker MH: **Introduction**. *Health Education Monographs.* 1974; 2(4):326-327. *https://doi.org/10.1177/109019817400200402*.

91. Parry O, Thomson C, Fowkes FG: **Dependent behaviours and beliefs: a qualitative study of older long-term smokers with arterial disease**. *Addiction.* 2001; 96(9):1337-1347. *https://doi.org/10.1046/j.1360-0443.2001.969133713.x*.

92. Bandura A: **Health promotion by social cognitive means**. *Health Educ Behav.* 2004; 31(2):143-164. *https://doi.org/10.1177/1090198104263660*.

93. Hughes JR, Keely J, Naud S: **Shape of the relapse curve and long-term abstinence among untreated smokers**. *Addiction.* 2004; 99(1):29-38. *https://doi.org/10.1111/j.1360-0443.2004.00540.x*.

94. Mohammadnezhad M, Tsourtos G, Wilson C, Ratcliffe J, Ward P: **Understanding socio-cultural influences on smoking among older Greek-Australian smokers aged 50 and over: facilitators or barriers? A qualitative study**. *Int J Environ Res Public Health.* 2015; 12(3):2718-2734. *https://doi.org/10.3390/ijerph120302718*.

95. Kassel JD, Stroud LR, Paronis CA: **Smoking, stress, and negative affect: correlation, causation, and context across stages of smoking**. *Psychol Bull.* 2003; 129(2):270-304. *https://doi.org/10.1037/0033-2909.129.2.270*.

96. Prochaska JO, Velicer WF: **The transtheoretical model of health behavior change**. *Am J Health Promot.* 1997; 12(1):38-48. *https://doi.org/10.4278/0890-1171-12.1.38*.

97. Subramaniam M, Shahwan S, Fauziana R, Satghare P, Picco L, Vaingankar JA, Chong SA: **Perspectives on Smoking Initiation and Maintenance: A Qualitative Exploration among Singapore Youth**. *Int J Environ Res Public Health.* 2015; 12(8):8956-8970. *https://doi.org/10.3390/ijerph120808956*.

98. Hammond D: **Smoking behaviour among young adults: beyond youth prevention**. *Tob Control.* 2005; 14(3):181-185. *https://doi.org/10.1136/tc.2004.009621*.

99. Galea S, Tracy M: **Participation rates in epidemiologic studies**. *Ann Epidemiol.* 2007; 17(9):643-653. *https://doi.org/10.1016/j.annepidem.2007.03.013*.

# 7. Supplemental material

## 7. 1. Methods

### 7. 1. 1. Inter-rater reliability

Supplemental Table 13 Qualitative content analysis: inter-rater reliability (Cohen's kappa) for reasons to continue smoking and reasons to relapse after a quitting attempt

| Category | Cohen's kappa<br>Reasons to continue smoking (n=41) | Cohen's kappa<br>Reasons to relapse after a quitting attempt (n=147) |
|---|---|---|
| **Relaxation** | 0.89 | 0.64 |
| **Pleasure** | 0.95 | 1.00 |
| **Social network** | 0.79 | 0.89 |
| **Spontaneous** | 0.83 | 0.93 |
| **Addiction** | 0.85 | 0.84 |
| **Stress** | 0.91 | 1.00 |
| **Weight gain** | - | 1.00 |
| **Alcohol** | - | 1.00 |

Supplemental Table 14 Qualitative content analysis: inter-rater reliability (Cohen's kappa) for reasons to undertake quitting attempts and reasons to quit

| Category | Cohen's kappa<br>Reasons to undertake quitting attempts (n=143) | Cohen's kappa<br>Reasons to quit (n=276) |
|---|---|---|
| **Subsequent damage** | 0.89 | 0.82 |
| **Current disorder** | 0.79 | 0.90 |
| **Pregnancy** | 1.00 | - |
| **Coronary heart disease** | 0.92 | 1.00 |
| **Medical advice** | 1.00 | 1.00 |
| **Social network** | 0.86 | 1.00 |
| **Role model** | 1.00 | 1.00 |
| **Financial burden** | 1.00 | 0.84 |
| **Spontaneous** | 0.90 | 0.88 |

Supplemental Table 15 Qualitative content analysis: inter-rater reliability (Cohen's kappa) for reasons to never start smoking

| Category | Cohen's kappa<br>Reasons to never start smoking (n=140) |
|---|---|
| **Subsequent damage** | 0.84 |
| **Sports** | 1.00 |
| **No need** | 0.66 |
| **Social network** | 0.81 |
| **Unpleasant memory** | 0.84 |
| **Unpleasant sensation** | 0.76 |
| **Financial burden** | 1.00 |

## 7. 1. 2. Final coding system

Supplemental Table 16 Theme, category, code and coding rule for reasons to continue smoking and reasons to relapse after a quitting attempt

| **Positive reasons** | | |
|---|---|---|
| **Category** | **Code** | **Coding rule** |
| Relaxation | Sedation<br>Relaxation<br>Smoking settles me<br>I imagine winding down | All answers expressing a relaxing or sedating effect of smoking for the participant shall be coded into this category. If relaxation as well as stress is mentioned, both categories shall be coded. If only stress reduction through smoking is mentioned, relaxation shall not be coded. |
| Pleasure | Enjoyment<br>Quality of life<br>Tastefulness<br>Feeling of happiness<br>Ritual | The category pleasure subsumes all answers that attribute a positive stimulating effect to tobacco smoke. Relaxation or sedation is not coded into this category. |
| Social network | Conviviality<br>Someone offered me a cigarette<br>Smoking is/was widely spread in my circle of friends<br>My husband began smoking again and I tasted once<br>Communicative character | Social network contains all aspects regarding the positive convivial character of smoking and situations where someone actively offered a cigarette to the participant. |

Supplemental Table 16 Theme, category, code and coding rule for reasons to continue smoking and reasons to relapse after a quitting attempt (continuation)

| **Neutral reasons** | | |
|---|---|---|
| **Category** | **Code** | **Coding rule** |
| Spontaneous | I just tasted a cigarette again<br>I smoked one cigarette during holidays<br>Habit<br>Routine<br>Boredom | In contrast to pleasure and social network current smoking or relapse because of neutrally connoted reasons (such as boredom, routine or no reason at all) without any influence of others is coded spontaneous. |
| **Negative reasons** | | |
| **Category** | **Code** | **Coding rule** |
| Addiction | Addiction<br>Craving<br>Dependence<br>Withdrawal symptoms<br>I already tried a lot to stop<br>I felt a desire to smoke again | Addiction is coded when the participant reports subjectively to suffer from addiction or describes clinically distinct behaviors such as craving or withdrawal symptoms. Additionally, addiction shall be coded, if participants explain that they are willing but unable to stop smoking. |
| Stress | Stress<br>Death of my wife<br>Road accident<br>The situation burdens me a lot<br>Smoking helps to deal with the stress | This category contains responses, where participants explain to smoke because of the feeling of stress or to deal with stress. If relaxation as well as stress is mentioned, both categories shall be coded. If only stress reduction through smoking is mentioned, only stress shall be coded. |
| Alcohol | Alcohol | If alcohol consumption is mentioned, alcohol shall be coded as additional category. |
| Weight gain | I smoke to prevent weight gain | When participants report that they relapsed smoking to stop weight gain or lose weight this category shall be coded. |

Supplemental Table 17 Theme, category, code and coding rule for reasons to undertake quitting attempts and reasons to quit

| **Health reasons** | | |
|---|---|---|
| **Category** | **Code** | **Coding rule** |
| Subsequent damage | I feared sequela<br>Either I stop now, or it is over<br>I in person feared to fall ill with lung cancer<br>My wife was a heavy smoker and died of a heart attack<br>Smoking is unreasonable | Subsequent damage is a broad category containing explicit sequela linked with smoking on the one hand and nonspecific future health hazards on the other hand. |
| Current disorder | Respiratory problems<br>As I experienced that smoking harmed me at sports, I stopped<br>Herniated disk, I couldn't move<br>Common cold<br>Agony | The category actual disorder subsumes all answers referring to current health problems the participant correlates to smoking. Thereby it is negligible if a clear causality between the complaint and tobacco smoke exists. |
| Pregnancy | My wife was pregnant<br>Pregnancy | Smoking cessation because of own pregnancy or pregnancy of another person shall be coded pregnancy. |
| Coronary heart disease | Heart attack<br>Heart operation<br>PCI<br>Shock of the severe disease<br>Angina pectoris | Coronary heart disease is coded when the participant refers clearly to a diagnosis or procedure of coronary heart disease. |
| Medical advice | Advice of doctors<br>Distinct advice of the medical staff<br>Ear, nose and throat specialist said it's due to smoking | Medical advice is coded when the participants refer to an advice, given by doctors or other medical staff, to stop smoking. |

Supplemental Table 17 Theme, category, code and coding rule for reasons to undertake quitting attempts and reasons to quit (continuation)

| **Personal or social reasons** | | |
|---|---|---|
| **Category** | **Code** | **Coding rule** |
| Social network | My wife blustered<br>My husband told me to stop smoking<br>Others stopped smoking, so I wanted to stop as well<br>The children looked after me to stop smoking<br>It was a collective decision of my wife and me | Social network extends to all levels of shared decision making (friends, spouses or children) and the explicit wish, sometimes resulting in social pressure, of others to stop smoking. |
| Role model | To be a role model for the kids<br>I had little children<br>Birth of my son | If the pressure through others is less important but there is a strong desire of the participant him-/herself to stop smoking because of being role model for others, role model shall be coded. |
| Financial burden | Smoking is illogical and expensive<br>Financial reasons<br>The money was missing | Every time there is referral to the financial burden of smoking, this category shall be coded. |
| Spontaneous | Spontaneous decision<br>I just wanted to stop, generally<br>I sensed no need or desire anymore<br>I didn't feel like smoking anymore, in the end there was no reason<br>This was an addiction I wanted to free myself | When the answer contains comments regarding no concrete cue to action or reason spontaneous shall be coded. |

Supplemental Table 18 Theme, category, code, coding rule for reasons to never start smoking

| **Health reasons** | | |
|---|---|---|
| **Category** | **Code** | **Coding rule** |
| Subsequent damage | I feared sequela<br>Either I stop now, or it is over<br>I feared to fall ill with lung cancer<br>My wife was a heavy smoker and died of a heart attack<br>Smoking is unreasonable | Subsequent damage is a broad category that contains explicit sequela linked with smoking on the one hand and nonspecific health reasons on the other hand. |
| Sports | I was a diligent sportsman and therefor never smoked<br>I was a diligent soccer player and firmly of the opinion that smoking is bad for your health | The category sports contains comments, that attribute negative effects on sportive activities with smoking. |
| No need | I never had a need to smoke<br>I never linked anything positive with smoking<br>I could never enjoy smoking<br>Tobacco smoke was never tasteful for me | No need shall be coded, if the participant explains never ever to have had a need or desire to start smoking regularly. |
| **Personal or social reasons** | | |
| **Category** | **Code** | **Coding rule** |
| Social network | I had no smokers in my circle of friends<br>I the family nobody smokes<br>My father forbid me to smoke from his money<br>Smoking was not common among farmers' daughters | Social network contains comments that refer to the influence of the social network (family, friends or spouses). |
| Unpleasant memory | We had a restaurant in my parental home. There was a lot of smoking.<br>I had many heavy smokers in my family "brown curtains, blue haze in the household". Both my parents died early due to heart disease and my brother suffered from severe COPD<br>I smoked once in my youth, afterwards I had a strong feeling of nausea | When own smoking or smoking of others is correlated to unpleasant experiences of early childhood, youth or adulthood, unpleasant memory shall be coded. |
| Unpleasant sensation | I feel very uncomfortable when people smoke<br>I feared to swallow up the fume.<br>The smell of smoke was always unpleasant for me<br>My eyes tear because of smoking | Are unpleasant feelings or sensations related to the presence of smoking persons in the present, unpleasant sensation shall be coded. |
| Financial burden | Smoking is illogical and expensive<br>Financial reasons<br>The money was missing | Every time there is referral to the financial burden of smoking, this category shall be coded. |

## 7. 2. Results

### 7. 2. 1. Quantitative results

Supplemental Table 19 Current smokers at index event* (n=124) stratified by their participation at telephone-based follow-up interview [*9*]

| | Total | Participants at follow-up interview | Non-participants at follow-up interview | |
|---|---|---|---|---|
| | N=124 | N=104 (83.9%) | N=20 (16.1%) | P-value |
| **Demography** | | | | |
| Age at index admission, years | 59.8±9.1 | 59.1±9.0 | 63.6±9.3 | <0.05 |
| Female sex | 19 (15.3) | 16 (15.4) | 3 (15.0) | 0.97 |
| High education level[#] | 26 (21.0) | 23 (22.1) | 3 (15.0) | 0.47 |
| **Comorbidities** | | | | |
| Current smoker at baseline visit | 54 (43.3) | 41 (39.4) | 13 (65.0) | 0.04 |
| Type of index event: CABG | 18 (14.5) | 14 (13.5) | 4 (20.0) | 0.45 |
| Diabetes at baseline visit [a] | 44 (36.1) | 32 (31.1) | 12 (63.2) | <0.01 |
| Depressed mood at baseline visit [b] | 32 (26.0) | 25 (24.3) | 7 (35.0) | 0.32 |
| **Intervention** | | | | |
| Cardiac rehabilitation program after index event | 86 (69.4) | 73 (70.2) | 13 (65.0) | 0.65 |

Data are n (percent) or mean±SD and p-values by asymptotic Pearson's Chi-Squared test or independent sample t-test, as appropriate.

CABG, coronary artery bypass graft.

*Index event occurred 6-36 months prior to baseline visit, and telephone-based follow-up interview occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up interview was 3.5 years (n=124).

[#]High school completed, college/university completed, postgraduate degree.

[a] Data missing for 1 participant.

[b] Data missing for 1 participant.

Supplemental Table 20 Duration of hospitalization for the index event of current smokers at index event* (n=104) stratified by their smoking status at telephone-based follow-up interview

| | **Non-smokers at follow-up interview** | **Smokers at follow-up interview** | |
|---|---|---|---|
| | **N=65 (62.5%)** | **N=39 (37.5%)** | **P-value** |
| Range, days | 1, 14 | 1, 15 | - |
| Mean (SD), days | 5.7 (3.5) | 4.7 (3.5) | 0.21 |
| Median (quartiles), days | 6 (3, 8) | 4 (1, 7) | - |

Data are (min, max), mean (SD) or median (quartiles) and p-value by independent sample t-test, as appropriate.

*Index event occurred 6-36 months prior to baseline visit, and telephone-based follow-up interview occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up interview was 3.5 years (n=104).

Supplemental Table 21 Current smokers at index event* (n=104) stratified by their participation at a cardiac rehabilitation program

| | Total N=104 | Participants at a cardiac rehabilitation program N=73 (70.2%) | Non-participants at a cardiac rehabilitation program N=31 (29.8%) | P-value |
|---|---|---|---|---|
| **Demography** | | | | |
| Age at index event, years | 59.1±9.0 | 58.5±8.8 | 60.1±9.4 | 0.43 |
| Female sex | 16 (15.4) | 10 (13.7) | 6 (19.4) | 0.55 |
| High education level[#] | 23 (22.1) | 14 (19.2) | 9 (29.0) | 0.31 |
| **Comorbidities** | | | | |
| Type of index event: CABG | 14 (13.5) | 14 (19.2) | 0 (0) | 0.005 |
| Diabetes at baseline visit [a] | 32 (31.1) | 24 (33.3) | 8 (25.8) | 0.30 |
| Depressed mood at baseline visit [b] | 25 (24.3) | 14 (19.4) | 11 (35.5) | 0.07 |
| Current smoker at follow-up interview | 39 (37.5) | 19 (26.0) | 20 (64.5) | <0.001 |

Data are n (percent) or mean±SD and p-values by asymptotic Pearson's Chi-Squared test or independent sample t-test, as appropriate.

CABG, coronary artery bypass graft.

*Index event occurred 6-36 months prior to baseline visit, and telephone-based follow-up interview occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up interview was 3.5 years (n=104).

[#]High school completed, college/university completed, postgraduate degree.

[a] Data missing for 1 participant.

[b] Data missing for 1 participant.

Supplemental Table 22 Clinical data of current smokers at index event* (n=104) stratified by their smoking status reported median 3.5 years later [*9*]

| | **Total** | **Non-smokers at follow-up interview** | **Smokers at follow-up interview** | |
|---|---|---|---|---|
| | **N=104** | **N=65 (62.5%)** | **N=39 (37.5%)** | **P-value** |
| Type of index event: CABG | 14 (13.5) | 10 (15.4) | 4 (10.3) | 0.46 |
| Type of index event: emergency[a] | 65 (63.1) | 41 (64.1) | 24 (61.5) | 0.80 |
| Type of index event: infarction | 61 (58.7) | 41 (63.1) | 20 (51.3) | 0.24 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

CABG, coronary artery bypass graft.

*Index event occurred 6-36 months prior to baseline visit, and telephone-based follow-up interview occurred about 2 years after baseline visit; median observation time between index event and telephone-based follow-up interview was 3.5 years.

[a] Data missing for 1 participant.

Supplemental Table 23 Factors associated with smoking cessation median 3.5 years after a cardiovascular index event (block-wise multivariable logistic regression in n=104 patients smoking at the index event) [*9*]

| | **Block 1** | | **Block 2** | | **Block 3** | |
|---|---|---|---|---|---|---|
| | OR (95%CI) | P | OR (95%CI) | P | OR (95%CI) | P |
| **Demography** | | | | | | |
| Age at index event* | 1.02 (0.97-1.07) | 0.43 | 1.02 (0.97-1.07) | 0.38 | 1.02 (0.98-1.07) | 0.33 |
| Female sex | 1.06 (0.32-3.49) | 0.93 | 1.03 (0.31-3.42) | 0.96 | 1.22 (0.35-4.25) | 0.75 |
| High education level[#] | 0.33 (0.12-0.89) | 0.03 | 0.32 (0.12-0.88) | 0.03 | 0.34 (0.12-0.92) | 0.03 |
| **Clinical data** | | | | | | |
| No CABG vs CABG | 1.72 (0.48-6.21) | 0.43 | 1.70 (0.45-6.41) | 0.43 | 1.69 (0.45-6.37) | 0.44 |
| Elective vs emergency[a] | | | 1.35 (0.56-3.24) | 0.50 | 1.01 (0.37-2.75) | 0.98 |
| Ischemia vs infarction | | | | | 1.80 (0.68-4.80) | 0.24 |

OR, odds ratio; 95%CI, 95% confidence interval; P, P-value; CABG, coronary artery bypass graft.

*OR per year.

[#]High school completed, college/university completed, postgraduate degree.

[a] Data are missing for 1 participant.

## 7. 2. 2. Qualitative results stratified by age group and sex

Supplemental Table 24 Reasons to continue smoking by age group (n=41)

| | **<60 years N=24 (58.5%)** | **60–69 years N=12 (29.3%)** | **≥70 years N=5 (12.2%)** | **P-value** |
|---|---|---|---|---|
| Relaxation | 7 (29.2) | 5 (41.7) | 1 (20.0) | 0.63 |
| Pleasure | 7 (29.2) | 5 (41.7) | 3 (60.0) | 0.39 |
| Social network | 2 (8.3) | 1 (8.3) | 0 (0.0) | 0.80 |
| Spontaneous | 5 (20.8) | 0 (0.0) | 2 (40.0) | 0.10 |
| Addiction | 11 (45.8) | 6 (50.0) | 2 (40.0) | 0.93 |
| Stress | 4 (16.7) | 2 (16.7) | 0 (0.0) | 0.61 |
| Alcohol | 0 (0) | 0 (0) | 0 (0) | - |
| Weight gain | 0 (0) | 0 (0) | 0 (0) | - |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 25 Reasons to continue smoking by sex (n=41)

| | **Male N=35 (85.4%)** | **Female N=6 (14.6%)** | **P-value** |
|---|---|---|---|
| Relaxation | 10 (28.6) | 3 (50.0) | 0.30 |
| Pleasure | 12 (34.3) | 3 (50.0) | 0.46 |
| Social network | 3 (8.6) | 0 (0.0) | 0.46 |
| Spontaneous | 7 (20.0) | 0 (0.0) | 0.23 |
| Addiction | 18 (51.4) | 1 (16.7) | 0.12 |
| Stress | 4 (11.4) | 2 (33.3) | 0.16 |
| Alcohol | 0 (0) | 0 (0) | - |
| Weight gain | 0 (0) | 0 (0) | - |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 26 Reasons to undertake quitting attempts by age group (n=143)

| | **<60 years N=57 (39.9%)** | **60–69 years N=55 (38.5%)** | **≥70 years N=31 (21.7%)** | **P-value** |
|---|---|---|---|---|
| Subsequent damage | 20 (35.1) | 30 (54.5) | 14 (45.2) | 0.12 |
| Current disorder | 21 (36.8) | 13 (23.6) | 9 (29.0) | 0.31 |
| Pregnancy | 5 (8.8) | 5 (9.1) | 0 (0.0) | 0.23 |
| Coronary heart disease | 14 (24.6) | 9 (16.4) | 0 (0.0) | 0.01 |
| Medical advice | 8 (14.0) | 4 (7.3) | 1 (3.2) | 0.20 |
| Social network | 11 (19.3) | 11 (20.0) | 9 (29.0) | 0.53 |
| Role model | 5 (8.8) | 3 (5.5) | 1 (3.2) | 0.56 |
| Financial burden | 5 (8.8) | 4 (7.3) | 4 (12.9) | 0.68 |
| Spontaneous | 7 (12.3) | 10 (18.2) | 7 (22.6) | 0.44 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 27 Reasons to undertake quitting attempts by sex (n=143)

| | **Male N=127 (88.8%)** | **Female N=16 (11.2%)** | **P-value** |
|---|---|---|---|
| Subsequent damage | 57 (44.9) | 7 (43.8) | 0.93 |
| Current disorder | 41 (32.3) | 2 (12.5) | 0.10 |
| Pregnancy | 4 (3.1) | 6 (37.5) | <0.001 |
| Coronary heart disease | 20 (15.7) | 3 (18.8) | 0.76 |
| Medical advice | 12 (9.4) | 1 (6.3) | 0.68 |
| Social network | 27 (21.3) | 4 (25.0) | 0.73 |
| Role model | 8 (6.3) | 1 (6.3) | 0.99 |
| Financial burden | 12 (9.4) | 1 (6.3) | 0.68 |
| Spontaneous | 21 (16.5) | 3 (18.8) | 0.82 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 28 Reasons to relapse after a quitting attempt by age group (n=147)

| | **<60 years N=57 (38.8%)** | **60–69 years N=58 (39.5%)** | **≥70 years N=32 (21.8%)** | **P-value** |
|---|---|---|---|---|
| Relaxation | 0 (0.0) | 4 (6.9) | 1 (3.1) | 0.12 |
| Pleasure | 10 (17.5) | 4 (6.9) | 1 (3.1) | 0.06 |
| Social network | 24 (42.1) | 29 (50.0) | 16 (50.0) | 0.65 |
| Spontaneous | 10 (17.5) | 11 (19.0) | 9 (28.1) | 0.46 |
| Addiction | 9 (15.8) | 8 (13.8) | 0 (0.0) | 0.07 |
| Stress | 17 (29.8) | 19 (32.8) | 7 (21.9) | 0.55 |
| Alcohol | 6 (10.5) | 4 (6.9) | 3 (9.4) | 0.79 |
| Weight gain | 3 (5.3) | 2 (3.4) | 1 (3.1) | 0.85 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 29 Reasons to relapse after a quitting attempt by sex (n=147)

| | **Male N=129 (87.8%)** | **Female N=18 (12.2%)** | **P-value** |
|---|---|---|---|
| Relaxation | 4 (3.1) | 1 (5.6) | 0.59 |
| Pleasure | 14 (10.9) | 1 (5.6) | 0.49 |
| Social network | 64 (49.6) | 5 (27.8) | 0.08 |
| Spontaneous | 27 (20.9) | 3 (16.7) | 0.67 |
| Addiction | 16 (12.4) | 1 (5.6) | 0.40 |
| Stress | 34 (26.4) | 9 (50.0) | 0.04 |
| Alcohol | 12 (9.3) | 1 (5.6) | 0.60 |
| Weight gain | 5 (3.9) | 1 (5.6) | 0.74 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 30 Reasons to quit by age group (n=276)

| | **<60 years N=74 (26.8%)** | **60–69 years N=111 (40.2%)** | **≥70 years N=91 (33.0%)** | **P-value** |
|---|---|---|---|---|
| Subsequent damage | 26 (35.1) | 37 (33.3) | 30 (33.0) | 0.95 |
| Current disorder | 33 (44.6) | 50 (45.0) | 41 (45.1) | 1.00 |
| Pregnancy | 1 (1.4) | 2 (1.8) | 1 (1.1) | 0.91 |
| Coronary heart disease | 25 (33.8) | 33 (29.7) | 20 (22.0) | 0.22 |
| Medical advice | 12 (16.2) | 22 (19.8) | 12 (13.2) | 0.45 |
| Social network | 16 (21.6) | 16 (14.4) | 20 (22.0) | 0.30 |
| Role model | 2 (2.7) | 2 (1.8) | 3 (3.3) | 0.79 |
| Financial burden | 11 (14.9) | 5 (4.5) | 9 (9.9) | 0.05 |
| Spontaneous | 11 (14.9) | 18 (16.2) | 19 (20.9) | 0.55 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 31 Reasons to quit by sex (n=276)

| | **Male N=239 (86.6%)** | **Female N=37 (13.4%)** | **P-value** |
|---|---|---|---|
| Subsequent damage | 82 (34.3) | 11 (29.7) | 0.58 |
| Current disorder | 102 (42.7) | 22 (59.5) | 0.06 |
| Pregnancy | 2 (0.8) | 2 (5.4) | 0.03 |
| Coronary heart disease | 65 (27.2) | 13 (35.1) | 0.32 |
| Medical advice | 41 (17.2) | 5 (13.5) | 0.58 |
| Social network | 43 (18.0) | 9 (24.3) | 0.36 |
| Role model | 7 (2.9) | 0 (0.0) | 0.29 |
| Financial burden | 23 (9.6) | 2 (5.4) | 0.41 |
| Spontaneous | 45 (18.8) | 3 (8.1) | 0.11 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 32 Reasons to never start smoking by age group (n=140)

| | **<60 years N=23 (16.4%)** | **60–69 years N=49 (35.0%)** | **≥70 years N=68 (48.6%)** | **P-value** |
|---|---|---|---|---|
| Subsequent damage | 7 (30.4) | 8 (16.3) | 11 (16.2) | 0.28 |
| Sport | 2 (8.7) | 7 (14.3) | 4 (5.9) | 0.30 |
| No need for smoking | 10 (43.5) | 19 (38.8) | 32 (47.1) | 0.67 |
| Social network | 8 (34.8) | 9 (18.4) | 17 (25.0) | 0.31 |
| Unpleasant memory | 9 (39.1) | 20 (40.8) | 15 (22.1) | 0.07 |
| Unpleasant sensation | 4 (17.4) | 6 (12.2) | 18 (26.5) | 0.16 |
| Financial burden | 1 (4.3) | 4 (8.2) | 10 (14.7) | 0.30 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

Supplemental Table 33 Reasons to never start smoking by sex (n=140)

| | **Male N=105 (75.0%)** | **Female N=35 (25.0%)** | **P-value** |
|---|---|---|---|
| Subsequent damage | 14 (13.3) | 12 (34.3) | <0.01 |
| Sport | 13 (12.4) | 0 (0.0) | 0.03 |
| No need for smoking | 46 (43.8) | 15 (42.9) | 0.92 |
| Social network | 26 (24.8) | 8 (22.9) | 0.82 |
| Unpleasant memory | 37 (35.2) | 7 (20.0) | 0.09 |
| Unpleasant sensation | 14 (13.3) | 14 (40.0) | <0.01 |
| Financial burden | 12 (11.4) | 3 (8.6) | 0.64 |

Data are n (percent) and p-values by asymptotic Pearson's Chi-Squared test.

# Index of figures

# Index of tables

# Index of abbreviations

| | |
|---|---|
| 2hPG | 2-hours post glucose load plasma glucose |
| 95%CI | 95% confidence interval |
| AMI | Acute myocardial infarction |
| AMIsch | Acute myocardial ischemia without infarction |
| AR | A. Rösch |
| CABG | Coronary artery bypass graft |
| CHD | Coronary heart disease |
| CHFC | Comprehensive Heart Failure Center, University of Würzburg and University Hospital of Würzburg |
| CO | Carbon monoxide |
| CVD | Cardiovascular disease |
| DALYs | Disability Adjusted Life Years |
| DG | D. Göttler |
| ESC | European Society of Cardiology |
| ETS | Environmental tobacco smoke |
| EuroAspire | European Action on Secondary and Primary Prevention by Intervention to Reduce Events |
| HADS | Hospital Anxiety and Depression Scale |
| HSI | Heavy smoking index |
| ICE-B | Institute of Clinical Epidemiology and Biometry, University of Würzburg |
| IHD | Ischemic heart disease |
| NSTEMI | Non-ST- elevation myocardial infarction |
| OR | Odds ratio |
| P | P-value |
| PCI | Percutaneous coronary intervention |
| PG | Plasma glucose |
| pID | Pseudonymized identification number |
| SD | Standard deviation |
| STEMI | ST- elevation myocardial infarction |
| WHO | World Health Organization |

# Affidavit

I hereby confirm that my thesis entitled “Smoking cessation patterns in patients with established coronary heart disease” is the result of my own work. I did not receive any help or support from commercial consultants. All sources and / or materials applied are listed and specified in the thesis.

Furthermore, I confirm that this thesis has not yet been submitted as part of another examination process neither in identical nor in similar form.

Nürnberg, 22 April 2020 David Johannes Göttler

# Eidesstattliche Erklärung

Hiermit erkläre ich an Eides statt, die Dissertation „Entwicklung des Rauchverhaltens bei Patienten*innen mit Koronarer Herzerkrankung“ eigenständig, d.h. insbesondere selbständig und ohne Hilfe eines kommerziellen Promotionsberaters, angefertigt und keine anderen als die von mir angegebenen Quellen und Hilfsmittel verwendet zu haben.

Ich erkläre außerdem, dass die Dissertation weder in gleicher noch in ähnlicher Form bereits in einem anderen Prüfungsverfahren vorgelegen hat.

Nürnberg, 22 April 2020 David Johannes Göttler

# Acknowledgements

Thank you to all study participants of the German EuroAspire IV study for offering their valuable time and information. I thank the participating clinics University Hospital of Würzburg and Klinik Kitzinger Land. I express my gratitude to my supervisors Stefan Störk, Peter Heuschmann and Hermann Faller for their guidance, support and patience. I am grateful to Martin Wagner for the good time and instructive discussions. A special thanks to all supporting doctoral students (Kim Nolte, Martin Schich, Valerie Wahl) and research staff (Margret Breunig, Kerstin Eichstädt, Andre Gerhardt, Timo Ludwig, Yvonne Memmel, Anika Quilitzsch, Dominik Schmitt, Theresa Tiffe). I further thank A. Rösch for participating in the qualitative content analysis process as second rater. I thank Anna Fleischer and Vera Dufner for their contribution by regular discussion of and interest in my thesis project. Finally, my heartful appreciation goes to my family and my friends.

Thank you for your great support throughout the years.

# Curriculum vitae

## List of publications

**Peer-reviewed papers**

**Goettler D**, Wagner M, Faller H, Kotseva K, Wood D, Leyh R, Ertl G, Karmann W, Heuschmann PU, Störk S et al: Factors associated with smoking cessation in patients with coronary heart disease: a cohort analysis of the German subset of EuroAspire IV survey. BMC Cardiovascular Disorders. 2020; 20(1):152. https://doi.org/10.1186/s12872-020-01429-w.

Liese JG, Schoen C, van der Linden M, Lehmann L, **Goettler D**, Keller S, Maier A, Segerer F, Rose MA, Streng A: Changes in the incidence and bacterial aetiology of paediatric parapneumonic pleural effusions/empyema in Germany, 2010-2017: a nationwide surveillance study. Clin Microbiol Infect. 2019; 25(7):857-864. https://doi.org/10.1016/j.cmi.2018.10.020.

Streng A, **Goettler D**, Haerlein M, Lehmann L, Ulrich K, Prifert C, Krempl C, Weissbrich B, Liese JG: Spread and clinical severity of respiratory syncytial virus A genotype ON1 in Germany, 2011-2017. BMC Infect Dis. 2019; 19(1):613. https://doi.org/10.1186/s12879-019-4266-y.

**Goettler D**, Streng A, Kemmling D, Schoen C, von Kries R, Rose MA, van der Linden M, Liese JG: Increase in Streptococcus pneumoniae serotype 3 associated parapneumonic pleural effusion/empyema after the introduction of PCV13 in Germany. Vaccine. 2020; 38(3):570-577. https://doi.org/10.1016/j.vaccine.2019.10.056.

Nürnberg, 22 April 2020

David Johannes Göttler