Smoking cessation in people with and without diabetes after acute coronary syndrome

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Abstract

Introduction: People with diabetes smoke at similar rates as those without diabetes, with cardiovascular consequences. Smoking cessation rates were compared between people with and without diabetes one year after an acute coronary syndrome (ACS).

Methods: People with ACS who smoked and were part of an observational prospective multicenter study in Switzerland were included from 2007 to 2017 and followed for 12 months. Seven-day point prevalence abstinence was assessed at 12-months follow-up. Association between diabetes and smoking cessation was assessed using multivariable-adjusted logistical regression model.

Results: 2'457 people with ACS who smoked were included, mean age 57 years old, 81.9% were men and 13.3% had diabetes. At one year, smoking cessation was 35.1% for people with diabetes and 42.6% for people without diabetes (p-value 0.01). After adjustment for age, sex and educational level, people with diabetes who smoked were less likely to quit smoking compared with people without diabetes who smoked (odds ratio (OR) 0.76, 95% confidence interval (CI) 0.59-0.98, p-value=0.037). The multivariable-adjusted model, with further adjustments for personal history of previous cardiovascular disease and cardiac rehabilitation attendance, attenuated this association (OR 0.85, 95% CI 0.65-1.12, p-value=0.255). Among people with diabetes, cardiac rehabilitation attendance was a positive predictor of smoking cessation, and personal history of cardiovascular disease was a negative predictor of smoking cessation.

Conclusions: People with diabetes who smoke are less likely to quit smoking after an ACS and need tailored secondary prevention programs. In this population, cardiac rehabilitation is associated with increased smoking cessation.

Implication section

This study provides new information on smoking cessation following acute coronary syndromes comparing people with and without diabetes. After an ACS, people with diabetes who smoked were less likely to quit smoking than people without diabetes. Our findings highlight the importance of tailoring secondary prevention to people with diabetes.

Introduction

Diabetes and tobacco consumption are two major public health problems. The prevalence of type 2 diabetes is increasing due to an increase in obesity [1,2,3]. According to 20-years projections, one in ten adults will have diabetes worldwide. Currently, in Switzerland 7.7% of the adult population lives with diabetes, 90% of them have type 2 diabetes [2]. Smoking is the leading cause of disability-adjusted life year (DALY) in high social demographic index countries and was responsible for 7.1 millions of death in 2016 worldwide [3]. Nevertheless, it is estimated that more than 25% of the Swiss population uses tobacco [4], and a recent study suggests that this prevalence may be underestimated [5]. In addition, studies show that people who smoke present a 44% increased risk of developing type 2 diabetes [6].

Together, tobacco consumption and diabetes are the strongest risks factors for cardiovascular disease (CVD) and coronary heart disease (CHD) mortality, each of them increasing those risks by more than two folds [7,8]. It is estimated that up to 65% of cardiovascular deaths are caused by the interaction between diabetes and tobacco use [8]. Diabetes and tobacco consumption act synergistically on morbidity and mortality and people with diabetes who smoke are at increased risk of micro- and macrovascular complications, such as acute coronary syndrome (ACS) [9,10]. After a first cardiovascular event, people with diabetes are at particularly increased risk of recurrence, as compared to people without diabetes [11,12]. Among actions to reduce the cardiovascular risk, smoking cessation interventions is the best way to extend life expectancy of people with diabetes [13]. People who smoke, who quit after a myocardial infarction reduce their risk of mortality by 36% compared to those who

continue to smoke [14,15], and it is reasonable to presume that this benefit is similar or even higher among people with diabetes after an ACS.

Unfortunately, people with diabetes still smoke at similar or even higher rates than those without diabetes, and are less motivated to quit smoking [16,17,18]. Although people with diabetes who smoke will greatly benefit from intensive secondary prevention after an ACS, only a minority reaches adequate control of cardiovascular risk factors [19]. Contemporary rates and factors associated with smoking cessation among ACS patients with diabetes remains poorly reported. This study aims to compare smoking cessation rates between people with and without diabetes one year after an ACS taking into account socio-demographic and cardiovascular risk factors, and to determine specific factors associated with smoking cessation among people with diabetes.

Research Design and Methods

Study design and population

This study is a secondary analysis of the Special Program University Medicine-Acute Coronary Syndromes (SPUM-ACS) study, a multicenter prospective observational cohort study of consecutive patients hospitalized with ACS in Switzerland. Initially, the study was designed to identify new biomarkers for coronary heart disease prevention. Details regarding the methods of the SPUM-ACS study have been reported previously [20]. All patients hospitalized with ACS in four university hospitals in Switzerland were invited to participate, except those with severe physical

disability, inability to give consent due to dementia, or life expectancy of less than 1 year for non-cardiac reasons. Inclusion criteria were age ≥18 years, a main diagnosis of ST-elevation myocardial infarction (STEMI) for patients presenting after pain onset, non-ST elevation myocardial infarction (NSTEMI), or unstable angina.

Smoking cessation

At the time of ACS, smoking status was self-reported and was categorized as current, former and never-smokers. Participants were asked by the study investigators if they smoked at the time of inclusion. If they reported not smoking, they were asked if they had smoked in the past, smoking duration as well as the number of cigarettes smoked. Smoking abstinence during follow-up was obtained by contacting patients in a clinical face-to-face, or by telephone depending on the patient's possibilities, visit at 1-year post ACS. Seven-day point prevalence abstinence (abstinence from cigarettes during the 7 days preceding the visit) was assessed and validated with carbon monoxide (CO) in expired air in a subsample of 492 participants. In sensitivity analyses among the 492 people who smoked with validated smoking abstinence by expired air CO, we compared both cutoffs of 10 ppm and 6 ppm for CO, to estimate the risk of misclassification of smoking abstinence [21,22].

Covariables

Data were collected by trained study investigators based on a standardized, web-based case report forms. Diabetes was defined as the use of antidiabetic medication

or was self-reported without distinction between type 1 and type 2. Total cholesterol, HDL-cholesterol and triglycerides levels were analysed locally using standardized dosage methods. LDL-cholesterol was calculated using the Friedewald formula. Medications that were taken prior to hospitalization or prescribed at discharge were also collected. Pre-existing CVD was defined as a previous diagnosis of coronary heart disease, ischemic cerebrovascular disease or peripheral artery disease. Family history of premature CHD was based on patient reports of a coronary event in a first-degree relative younger than 55 years old for men, or younger than 60 years old for women. Education status was dichotomized as having graduated from high school or university or having a lower-level education. Hypertension was defined as a systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or use of blood pressure lowering drugs.

Sample

Overall, 7'429 participants were included in the SPUM-ACS study between May 2007 and January 2017. Among this sample, participants who did not smoke at baseline (n= 4'715), those with an unknown diabetic status at baseline (n=2) and those who did not complete the 1-year follow up (n=255) were excluded. The final sample consisted of 2'457 people who smoked, with ACS, who attended the 1-year follow-up visit (Figure 1). Among them, 2'129 (86.7 %) did not have diabetes and 328 (13.3%) had diabetes.

Statistical analysis

Patients were categorized according to presence of diabetes at hospital admission and reported clinical characteristics in each groups. T-tests and chi-square tests were used for group comparisons. Multivariable-adjusted logistical model were built assessing the association between diabetes and smoking cessation with stepwise adjustments for socio-demographic variables (age, sex, educational level), rehabilitation attendance and pre-existing CVD. The first model was adjusted for age, sex and educational level. In the second model, adjustment for rehabilitation attendance was added. In the third model, further adjustments for pre-existing CVD were added. Two separate univariate logistical models in participants with or without diabetes were built, to assess the influence of socio-demographic variables (age, sex, ethnicity and educational level), health related variables (Body Mass Index (BMI), history of hypertension, history of hypercholesterolemia, pre-existing CVD, family history of CHD, use of antidepressant) and cardiac rehabilitation attendance.

Results

Characteristics of participants

Characteristics of participants are shown in Table 1. Patients with diabetes were older compared with those without diabetes, with a mean age of 60 years vs. 56 year, respectively. The sex ratios were similar in both groups, with almost a fifth of the participants who were women. The large majority of patients were Caucasians. Patients with diabetes were less likely to have a higher educational level compared

with those without diabetes (18.5% vs. 27.9 %, p-value 0.001). Patients with diabetes had a higher BMI than patients without diabetes and were more likely to have a history of hypertension and a history of hypercholesterolemia. Patients with diabetes were also more likely to have a pre-existing CVD (34.1% vs 16.4%, p-value <0.001). Patient with and without diabetes had similar rates of family history of premature CHD and the use of antidepressant was also similar in both groups. Among patients with diabetes, 75% used oral anti-diabetic drugs and 27.1% used insulin. Patients with diabetes were less likely to attend rehabilitation programs compared with patients without diabetes (66% vs. 77.3%, p-value <0.001).

Association between diabetes and smoking cessation

At one year, smoking cessation rates were 41.6% for the entire cohort, 42.6% for patients without diabetes and 35.1% for patients with diabetes, as shown in figure 2 and Table 2. In the sensitivity analyses, among people without diabetes with CO-validated smoking cessation, 5 participants (1.4%) were incorrectly classified as having quit smoking with a CO-cutoff of 10 ppm and 13 participants (3.7%) with a CO-cutoff of 6 ppm. Among people with diabetes, using CO-validated smoking cessation, 1 participant (2.6%) was misclassified as having quit smoking with both CO-cutoffs of 10 and 6 ppm. Table 2 shows the association between diabetes and smoking cessation. In the unadjusted logistical model, people with diabetes who smoked had a significantly lower 1-year smoking cessation rate compared with people without diabetes who smoked, with an odds ratio of 0.73 (95% CI 0.57-0.93). After adjustment for age, sex and educational level, this association was not modified. After further adjustment for rehabilitation attendance, the association

persisted but did not reach statistical significance. Further adjustment for pre-existing CVD decreased the association between diabetic status and smoking cessation. We looked at time trends in smoking cessation from 2007 to 2017 in patients with and without diabetes. We observed some variability in the proportion of quitters but no clear trends over time (p for trend 0.704 for people without diabetes and 0.979 for people with diabetes).

Determinants of smoking cessation in people with diabetes

Factors associated with one-year smoking cessation, by diabetes status, are reported in Figure 3. Among people without diabetes who smoked, men had a significantly higher 1-year smoking cessation rate compared to women. This association between sex and smoking cessation did not reach statistical significance among people with diabetes who smoked. Personal history of pre-existing CVD was associated with lower rate of smoking cessation at one year, both among people with diabetes who smoked and among people without diabetes who smoked. Rehabilitation attendance was associated with higher rates of smoking cessation, both among people with and without diabetes who smoked. The use of antidepressant was statistically associated with lower rate of smoking cessation among people without diabetes who smoked.

Discussion

In this large observational study including people with ACS who smoked, those with diabetes were more prone to continue smoking one year after hospital discharge

than those without diabetes. This association persisted after adjustment for age, gender and education. A variable associated with smoking cessation among patients with diabetes was attendance to a cardiac rehabilitation program. Lower attendance to a rehabilitation program among patients with diabetes compared to those without diabetes may contribute to explain the decrease in smoking cessation rate in this population. Besides, a personal history of previous CVD also lowered smoking cessation rates among patients with and without diabetes.

In this study, people with diabetes who smoke were less likely to quit smoking at 1-year, with a quit rate of 35.1% compared to 42.6% in those without diabetes. These results are consistent with previous findings [19]. Several hypotheses might explain these results. First people with diabetes who smoke may wrongly believe that they will not benefit from smoking cessation and it might discourage them to quit smoking. People with diabetes who smoke are more concerned about weight, dietary adherence and the management of their diabetes [23] but do not consider smoking cessation as a priority [24]. They may not be fully aware of the risks of micro and macrovascular complications linked with tobacco use [25,26]. Indeed, after a diagnosis of diabetes, people will focus on weight loss, lower consumption of saturated fat and lower energy intake but the impact of a new diagnosis of diabetes on smoking cessation is borderline [27]. On the contrary, a new diagnosis of CVD will increase the rates of smoking cessation [27]. Second, the lower smoking cessation rate among people with diabetes who smoke might also be explained by their fear to gain weight [23]. Among people without diabetes, smoking cessation is associated with a reduced cardiovascular and all-cause mortality [28,29]. Even if weight gain associated with smoking cessation increases the short term risk of type 2 diabetes, the

cardiovascular benefit of smoking cessation is not attenuated [28,29]. It has also been demonstrated that, among people with diabetes, smoking cessation is associated with a decreased risk of mortality [30,31]. Less evidence exists however on the specific impact of weight gain after cessation on morbi- mortality in people with diabetes. A recent study, among >170,000 participants with type 2 diabetes, suggested that weight gain after smoking cessation attenuated the benefits regarding cardiovascular disease, but did not attenuate the beneficial effect of smoking cessation with respect to mortality [32]. Third, the information about the benefits of smoking cessation and available options to stop smoking may not be tailored for people with diabetes who smoke [25,33]. People with diabetes may be less likely to be given cessation advice by health professionals [25]. Although smoking cessation therapy and counselling are cost effective and increase the rate of smoking cessation [34], tobacco use has been given less attention than hypertension or hypercholesterolemia in secondary prevention [35]. Fourth, studies have shown that people with diabetes are more likely to suffer from depression [36] and if they smoke, this risk is even higher [37]. Depression has been shown to be a risk factor for persistent smoking after a myocardial infarction [38]. Finally, patients with diabetes are more likely to have a lower socio-economic status [39], which has been showed to be associated to a lower smoking cessation rate after an ACS [40,41]. Financial barriers may contribute to their lower rehabilitation programs attendance.

Patients who continue to smoke after a first ACS may have a higher level of dependence to tobacco, with success rates of smoking cessation decreasing with longer tobacco consumption [42]. They may also be more likely to be “hard core smokers”, a population of people highly addicted to smoking with no intention to

stop, who are less likely to be aware that smoking is linked with negative health consequences [43,44]. Indeed, in this study, a history of previous CVD was associated with lower smoking cessation rate. Previous studies have reported that a personal history of CVD was correlated with a lower smoking cessation rate in secondary prevention [40,45]. An explanation could be that rates of smoking cessation may be higher when the clinical trigger event is perceived as life threatening, which may less be the case when someone already had a cardiac event in the past. A cardiovascular event represents an opportunity to discuss the impact of smoking on health and to motivate smoking cessation. It has been shown that smoking cessation rates are modulated by the type of cardiovascular interventions, with increased cessation rates with more invasive interventions [46]. Similarly, it is possible that the need for cardiovascular rehabilitation, related to more severe ACS, contributes to an increased quit rate. Our results showed that attendance to cardiac rehabilitation was associated with smoking cessation, both in people with diabetes and those without diabetes. This finding supports the notion that rehabilitation programs are effective to increase smoking cessation, taking into account the selection bias that patients attending rehabilitation programs might have a higher socio-economic status.

Low socioeconomic status is a fundamental cause of health disparity, involving lack of several resources, notably money and access to knowledge, needed to maintain health [47]. Socioeconomic status, diabetes and smoking share strong interactions. Tobacco use itself is a risk factor for developing type 2 diabetes [6]. Moreover, people with lower incomes are more likely to have diabetes and to smoke [48]. They are also less likely to control their cardiovascular risks factors after a myocardial infarct, notably regarding smoking cessation and levels of glycated hemoglobin [41]. Lower

incomes are also linked with lower participation rates to lifestyle educational sessions [41]. People with lower socioeconomic status are therefore at high cardiovascular risk and thus require specific management for diabetes and smoking cessation, especially after a first cardiovascular event.

Among people without diabetes, woman had a lower one-year cessation rate after an ACS compared with men. Although not statistically significant, we found a similar association between gender and smoking cessation among people with diabetes. The gender difference may notably be explained by the fact that during their hospital stay, women may be less likely to receive smoking cessation and cardiac rehabilitation advice [49]. Gendered social norms also explains that motivation to smoke and concern about quitting differ between men and women [50]. Women might have less social support, less confidence in their capacity to change their behaviors and more fear of gaining weight after smoking cessation. The association between sex and smoking cessation may not reach significance among people with diabetes because, as previously mentioned, this population may also be less likely to receive smoking cessation advice. The smaller sample size might also explain the non-significant results.

The strengths of this study is that it included a large sample of people who smoked who were prospectively followed after an ACS. However, there are some limitations to acknowledge. There were no information about anti-smoking medication prescribed at discharge, neither about the intensity of smoking cessation counselling received over follow-up. Although the study was multicentric, the sample was quite homogeneous in term of ethnicity with few non-Caucasian participants, thus limiting

its external validity. Finally, smoking cessation was not validated by CO in expired air in all participants. In sensitivity analyses, among people without diabetes, only 1.4% participants would have been incorrectly classified as having quit smoking with a CO-cutoff of 10 ppm and 3.7% with a CO-cutoff of 6 ppm. Among people with diabetes, one participant (2.6%) would be misclassified with both CO-cutoffs of 10 and 6 ppm. This small impact on misclassification would not alter our conclusions.

In conclusion, people with diabetes who smoke are less likely to stop smoking after an ACS than people without diabetes who smoke. This difference of outcome may be explained by a more severe CVD status and limited access to rehabilitation programs of people with diabetes, compared to people without diabetes. People with diabetes who smoke tend to have lower socioeconomic status, contributing to lower rates of smoking cessation after an ACS. This social health disparity underlines the importance of secondary prevention taking into account the specificities of this population, notably their low financial means and poorer access to care. There is a need for tailored secondary prevention programs for people with diabetes, who should be encouraged to follow rehabilitation programs. Further studies, assessing smoking cessation after an ACS among people with diabetes, could contribute to a better understanding of the specific problems and resources among this population regarding smoking cessation, in order to help this population achieve higher smoking cessation rates.

Author Contributions

Ludivine Clement conceived of the article and wrote the manuscript. David Nanchen conceived of the article and wrote the manuscript. Carole Clair conceived of the article and wrote the manuscript. Baris Gencer researched the data and reviewed the manuscript. Olivier Muller researched the data and reviewed the manuscript. Roland Klingenberg researched the data and reviewed the manuscript. Lorenz Räber researched the data and reviewed the manuscript. Christian M. Matter researched the data and reviewed the manuscript. Thomas F. Lüscher researched the data and reviewed the manuscript. Stephan Windecker researched the data and reviewed the manuscript. François Mach researched the data and reviewed the manuscript. Nicolas Rodondi researched the data and reviewed the manuscript.

David Nanchen, Carole Clair and Ludivine Clement are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Declaration of Interest

Prof Lüscher reports receiving research grants to the institution from Abbott, Biosensors, Biotronik, Boston Scientific, Daichi Sankyo, Eli Lilly and Medtronic, and consultant payments from AstraZeneca, Boehringer Ingelheim, Bayer, Merck, and Pfizer, MSD, Roche and Servier. Prof Matter reports receiving grants from MSD, Eli Lilly, AstraZeneca, Roche and Bayer; expert testimony from MSD; payment for lectures from MSD, AstraZeneca, and Roche; and having patents from Mabimmune, CH. Prof Windecker reports receiving research contracts to the institution from Abbott, Biotronik, Boston Scientific, Biosensors, Cordis, Medtronic, St. Jude Medical. Prof Mach has received honoraria for advisory boards and conferences on dyslipidaemia from Amgen, AstraZeneca, BMS, Eli Lilly, MSD, Sanofi, and Pfizer. All other authors report no conflicts of interest.

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Table 1: Baseline characteristics of people who smoke with acute coronary syndrome (ACS), by diabetes status (n=2,457)

	No diabetes N=2'129 (86.7%)	Diabetes N=328 (13.3%)	p-value
Demographics			
Age year (n=2'457), mean (SD*)	56.1 (10.4)	60 (11.2)	<0.001
Women (n=2'457), n (%)	378 (17.8)	66 (20.1)	0.3
Caucasian (n=2'414), n (%)	2'003 (95.8)	292 (90.7)	0.01
Higher education (n=2'256), n (%)	546 (27.9)	55 (18. 5)	0.001
Comorbidities			
Body Mass Index kg/m2 (n=2'429) mean (SD)	26.6 (4.3)	29.0 (5.2)	<0.001
History of hypertension (n=2'457), n (%)	843 (39.6)	231 (70.4)	<0.001
History of hypercholesterolemia (n=2'453), n (%)	1'231 (57.9)	239 (73.1)	<0.001
Pre-existing cardiovascular disease (n=2'455), n (%)	348 (16.4)	112 (34.1)	<0.001
Family history of premature coronary heart disease (n=2'441), n (%)	617 (29.2)	76 (23.4)	0.03
Use of antidepressant (n=1'298), n (%)	143 (13.9)	33 (12.1)	0.439
Use of oral antidiabetics (n=1'298), n (%)	0 (0)	204 (75)	
Use of insulin (n=1'299), n (%)	0 (0)	74 (27.1)	
Preventive measures			
Rehabilitation attendance (n=2'232), n (%)	1'500 (77.3)	192 (66.0)	<0.001

Continuous variable are presented as mean (SD (standard deviation)), and categorial variables are presented as n (%).

Table 2: Association between diabetes status and one-year smoking cessation in unadjusted and multivariable adjusted models

	No diabetes N=2129	Diabetes N=328	P value
Smoking cessation at one year (n=2457), n (%)	907 (42.6)	115 (35.1)	0.01
Unadjusted OR of smoking cessation (95% CI) (n=2'457)	1.00 (ref)	0.73 (0.57;0.93)	0.01
OR of smoking cessation adjusted for age, sex and educational level (95% CI) (n=2'256)	1.00 (ref)	0.76 (0.59;0.98)	0.037
OR of smoking cessation adjusted for age, sex, educational level and rehabilitation attendance (95% CI) (n=2'070)	1.00 (ref)	0.79 (0.60;1.04)	0.093
OR of smoking cessation adjusted for age, sex, educational level, rehabilitation attendance and pre-existing cardiovascular disease (95% CI) (n=2'068)	1.00 (ref)	0.85 (0.65; 1.12)	0.255

Figure 1: Flowchart of the participants

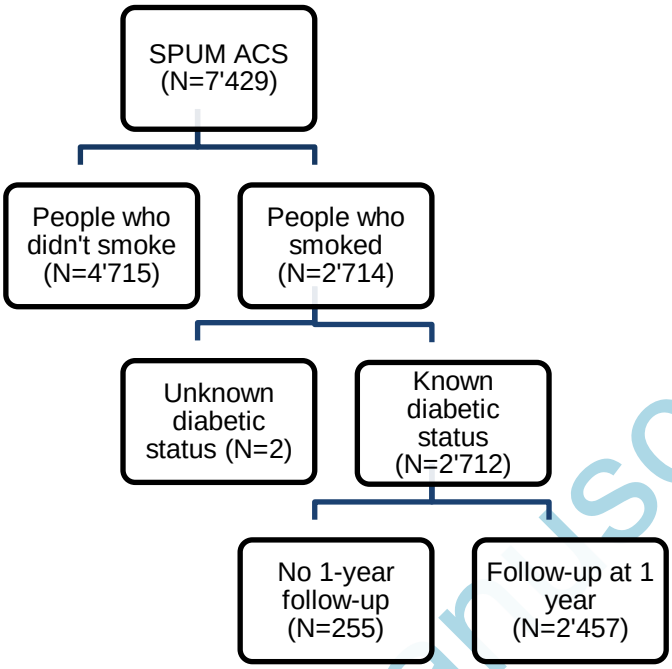


Figure 2: Smoking cessation one year after an acute coronary syndrome in people with and without diabetes

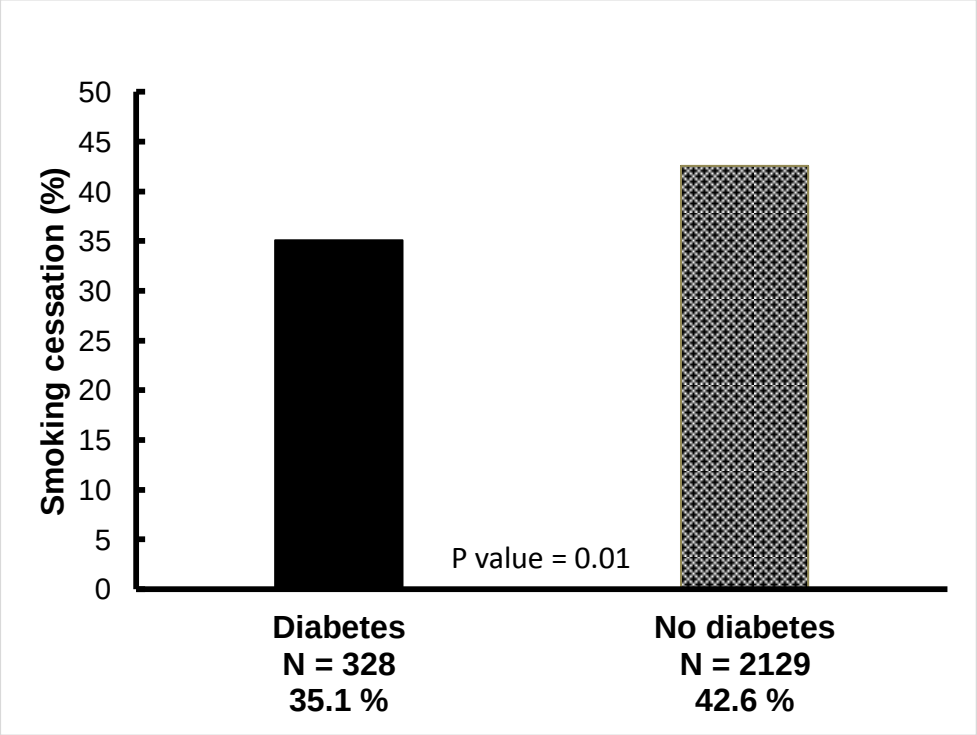
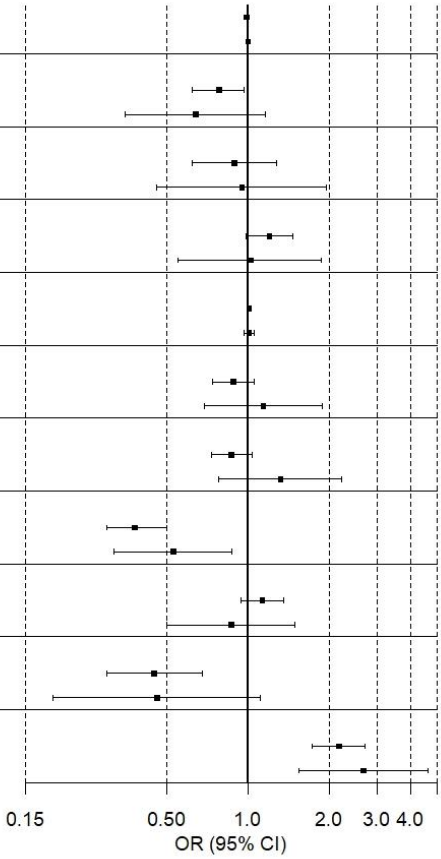


Figure 3: Univariate analyses of variables associated with 1-year smoking cessation after an acute coronary syndrome in people with and without diabetes

Smoking cessation adjusted for	N	OR (95% CI)	P value
Age*			
No diabetes	2'129	0.99 (0.98-1.00)	0.09
Diabetes	328	1.0 (0.98-1.02)	0.81
Sex†			
No diabetes	2'129	0.78 (0.62-0.97)	0.03
Diabetes	328	0.64 (0.35-1.16)	0.14
Ethnicity‡			
No Diabetes	2129	0.89 (0.62-1.28)	0.54
Diabetes	328	0.95 (0.46-1.95)	0.89
Educational level**			
No diabetes	1'959	1.2 (0.98-1.46)	0.08
Diabetes	297	1.02 (0.55-1.87)	0.95
BMI††			
No diabetes	2'103	1.01 (0.99-1.03)	0.26
Diabetes	326	1.01 (0.97-1.05)	0.66
Hypertension history			
No diabetes	2'129	0.88 (0.74-1.05)	0.15
Diabetes	328	1.14 (0.69-1.88)	0.61
Hypercholesterolemia history			
No diabetes	2'126	0.87 (0.73-1.04)	0.13
Diabetes	327	1.32 (0.78-2.22)	0.3
Pre existing CVD			
No diabetes	2'127	0.38 (0.3-0.5)	< 0.001
Diabetes	328	0.53 (0.32-0.87)	0.01
Family history of CHD			
No diabetes	2'116	1.13 (0.94-1.36)	0.21
Diabetes	325	0.87 (0.5-1.49)	0.6
Use of antidepressant			
No diabetes	1'026	0.45 (0.3-0.68)	< 0.001
Diabetes	272	0.46 (0.19-1.11)	0.08
Rehabilitation attendance			
No diabetes	1'914	2.17 (1.73-2.71)	< 0.001
Diabetes	291	2.68 (1.55-4.63)	< 0.001



* For each increase of one unit
† Reference = man
‡ Caucasian vs non-caucasian. Reference = caucasian
** Reference = high educational level = high school or higher
†† For each increase of one unit
BMI = Body Mass Index, CVD = Cardiovascular Disease, CHD = Coronary Heart Disease