

## Long-term effects of systematic smoking cessation counselling during acute coronary syndrome, a multicentre before-after study

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### Summary

**TRIAL DESIGN:** In the Special Program University Medicine-Acute Coronary Syndromes (SPUM-ACS) observational study (clinical trial registration: NCT01000701), a multicentre before-after clinical trial, we assessed 5-year outcome after acute coronary syndrome, comparing a systematic with an opportunistic smoking cessation counselling phase.

**METHODS:** We studied smokers who were hospitalised for acute coronary syndromes (ACS), and we assessed self-reported smoking cessation, incidence of cardiovascular events and mortality 5 years after hospital discharge. In the observational phase, from August 2009 to October 2010, only smokers who requested smoking cessation counselling received it during hospitalisation. In the interventional phase, from November 2010 to February 2012, hospitalised smokers with ACS were systematically offered intensive smoking cessation counselling including four telephone calls within 2 months of discharge. Because of the before-after design, the care givers were aware of study phase. The objective was to assess whether systematic counselling to every smoker with ACS has an impact on the long-term smoking cessation rate, incidence of cardiovascular events and mortality. Missing data on smoking cessation were analysed with multiple imputation. The study was not powered to assess differences in 5-year smoking cessation rates or cardiovascular outcomes.

**RESULTS:** Overall, 458 smokers with ACS were included at baseline (225 during the intervention phase and 233 during the observation phase). At 5 years, 286 (62.4%) reported their smoking status (140 for the intervention phase and 146 for the observation phase) and 51 (11.1%) had died. There was no statistically significant difference in the abstinence rate between the interventional phase (75/140, 54%), and the observational phase (68/146, 47%), with a risk ratio with multiple imputation adjusted for age, sex, education and ACS type of 1.13 (95% confidence interval [CI] 0.84–1.51,  $p = 0.4$ ). The 5-year risk of major acute cardiovascular event was similar in the intervention phase as compared with the observational phase. The multivariate adjusted hazard ratio for all-cause mortality was 0.84 (95% CI 0.45–1.60,  $p = 0.6$ ).

**CONCLUSIONS:** In this controlled long-term interventional study, systematic intensive smoking cessation counselling in all hospitalised smokers with ACS did not increase 5-year smoking cessation rates, nor decrease cardiovascular event recurrence, as compared with opportunistic smoking cessation counselling during hospitalization.

### Introduction

Smoking is an established risk factor for coronary heart disease [1, 2]. Quitting reduces mortality and further cardiac events after acute coronary syndromes (ACS) [3]. Three years after quitting, the risk of recurrent cardiovascular events is decreased to the level of nonsmokers after ACS [4]. It has also been shown that smoking cessa-

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tion counselling is more effective in hospitalised patients with ACS than in the general population [5]. Thus, smoking cessation counselling for ACS patients is universally recommended by cardiovascular disease prevention guidelines [6].

There are several intensities of smoking cessation counselling interventions for smokers [5, 7–9]. Intensive interventions begun in hospital and sustained after discharge are more likely to increase smoking abstinence than less intense interventions [8, 10]. Furthermore, smoking cessation rates increase when smokers are systematically identified and counselled after ACS [11]. We previously demonstrated an increase in uptake of counselling when smokers admitted for ACS were proactively offered motivational interviewing [12]. Even in smokers not motivated to quit, combining systematic in-hospital and telephone counselling sessions over 2 months seemed to increase smoking abstinence at 12 months, but without reaching statistical significance compared with opportunistic counselling [12]. The long-term benefits of systematic smoking interventions at the time of ACS might, however, be greater because repeated exposure to motivational interviewing shortly after an ACS may enhance the decision to quit, although this has been poorly studied. Therefore, we aimed to study the long-term rate of smoking abstinence and incidence of major adverse cardiovascular event (MACE), comparing a systematic smoking cessation counselling intervention with opportunistic smoking counselling.

## Methods

### Study population

We collected data during the 5-year follow-up visit of ACS patients enrolled in the Smoking-ACS study, a clinical trial embedded in the Special Program University Medicine-Acute Coronary Syndromes (SPUM-ACS) observational study (clinical trial registration: NCT01000701) [12, 13]. The SPUM-ACS study is an observational prospective Swiss cohort of patients hospitalised for ACS in four university hospitals in Switzerland. The SPUM-ACS study was designed to assess quality of care after an index ACS and identify new determinants and consequences of coronary heart disease (CHD) [12–15]. The ACS-Smoking study enrolled all smokers hospitalised for ACS between August 2009 and February 2012, at two intervention sites chosen because they had teams providing reactive smoking cessation interventions to hospitalised smokers as a routine standard care [12]. The ACS-Smoking study tested the efficacy on 1-year smoking abstinence of a systematic intensive smoking cessation counselling intervention based on motivational interviewing over opportunistic counselling. In each study phase, participants were followed up over a period of 5 years to assess smoking cessation and recurrence of cardiovascular events.

Inclusion criteria were age  $\geq 18$  years, actively smoking at the time of inclusion, a main diagnosis of ST-segment elevation myocardial infarction (STEMI) for patients presenting after pain onset, non-ST-segment elevation myocardial infarction (NSTEMI), or unstable angina [12, 13]. Exclusion criteria were severe physical disability, inability to give consent owing to dementia, and life expectancy of  $< 1$  year for non-cardiac reasons. [12]

### Smoking abstinence

At time of the index ACS, smoking status was self-reported. Smoking status was categorised into current, former and never-smokers. Active smoking was defined as smoking one cigarette or more per day for the month preceding the hospital stay. At the 5-year follow-up visit, smoking status was assessed during clinical or telephone follow-up visits based on patient's self-reported 7 days abstinence information.

### Intervention

The ACS-Smoking trial compared an observational phase with an interventional phase. During the observational phase, from August 2009 to October 2010, patients were offered an in-hospital smoking cessation intervention only if their healthcare provider requested it (opportunistic counselling). The counselling session did not include follow-up after discharge. The interventional phase ran from November 2010 to February 2012. During this phase, smokers with ACS were systematically offered intensive smoking cessation counselling during their hospital stay and were followed up with up to four counselling phone calls within a two-month period after discharge. This was an intensive systematic approach to delivering smoking cessation counselling. Nicotine replacement therapy was proposed at each counselling sessions, independently of the study phase [12].

### Outcomes

The primary outcome of this study was smoking abstinence at 5 years after the index ACS. The secondary outcomes were incidences of fatal and non-fatal MACE, as well as all-cause mortality over 5 years of follow-up after the index ACS. Incidents clinical events were adjudicated at each study site by medical doctors who reviewed the patient's file. MACE was a combination of cardiovascular mortality and non-fatal MACE was defined as myocardial infarction, stent thrombosis, repeat unplanned revascularisation, cerebrovascular event, or repeat hospitalisation due to angina.

### Covariables

Pre-existing cardiovascular disease was defined as a previous diagnosis of coronary heart disease, ischaemic cerebrovascular disease or peripheral artery disease. Education status was dichotomised as having graduated from "high school or university" or having a lower-level education. Hypertension was defined as a systolic blood pressure  $\geq 140$  mm Hg or diastolic blood pressure  $\geq 90$  mm Hg or use of blood-pressure lowering drugs. Diabetes was either self-reported or diagnosed by the use of anti-hyperglycaemic medication, or a haemoglobin A1c of 6.5% or greater at admission. Hypercholesterolaemia was total cholesterol  $> 5.0$  mmol or 190 mg/dl at admission. Data were entered via standardised, web-based case report forms [12, 16]. At the 5-year visit, we cross checked patient self-reports about medical history, medications and use of nicotine replacement therapy with the information in their medical files.

## Statistical analyses

We reported risk ratio (RR) and its 95% confidence interval (CI) for smoking cessation 5 years after index ACS between the cohorts, taking an intention-to-treat approach. In order to take into account the potential risk of confounding bias in a before-after design, we adjusted for sex, age, education level, and type of ACS (STEMI, NSTEMI, unstable angina) with a Poisson regression method. For survival analyses, all patients were analysed. To deal with the high rate of missing data (24.7%) regarding smoking abstinence at the 5-year follow-up visit, we used a multiple imputation by chained equation. By using the distribution of the observed data, the multiple imputation estimates a set of plausible values for the missing data. Random components are incorporated into these estimated values to reflect their uncertainty. Multiple data sets are created and then analysed individually but identically to obtain a set of parameter estimates [17]. In sensitivity analyses, we also reported results of smoking cessation analyses considering lost to follow-up patients as current smokers.

To compare incidence of 5-year MACE and all-cause mortality between the cohorts, we could not assume proportional hazards as Kaplan Meier curves were crossing. Therefore, we used the flexible parametric modelling for survival analyses (Lambert) for hazard ratios (HRs). We adjusted for sex, age, education level, and type of ACS (STEMI, NSTEMI, unstable angina). In the second model, we further adjusted for history of cardiovascular disease, diabetes, hypertension, hypercholesterolaemia and body mass index (BMI). Potential confounders were determined by biological or clinical plausibility. Participants were followed up until the occurrence of fatal or non-fatal MACE or the end of the study. The SPUM-ACS-Smoking study was initially designed to assess 1-year smoking cessation rates. Therefore, the present study was not powered to demonstrate a difference between groups regarding 5-year smoking cessation rates or incidence of MACE. Statistical significance tests were two-tailed; the alpha level was 0.05. We used Stata version 14.2 (StataCorp LP, College Station, TX, USA) for all statistical analyses.

## Ethics statement

The study was approved by Medical Ethics Committees of each centre (Lausanne, Geneva) and conforms to the ethical guidelines of the 1975 Declaration of Helsinki (Protocol 07-131 for Ethics Geneva and Protocol 106/09 for Ethics Vaud). All patients gave written informed consent to participate.

## Results

Overall, 458 smokers hospitalised with ACS were included in the intervention trial. At 5-year follow-up, 51 (11.1%) had died and 113 (24.7%) were lost to follow-up or refused contact; 286 (62.4%) reported their current smoking status. Eight patients had missing information regarding smoking status although they could be contacted. The lost to follow-up rate was similar in both the observation phase cohort ( $n = 55$ , 23.6%), and in the intervention phase cohort ( $n = 58$ , 25.8%). Because we used multiple imputation by chained equation, 407 smoking status are analysed for the

adjusted risk ratio and 458 for the MACE incidence analysis.

We previously described in detail the characteristics of study participants at the time of the smoking cessation intervention (supplementary table S1 in the appendix) [12]. There was no significant difference between the study groups, except that attendance to cardiovascular rehabilitation was more frequent in the intervention phase cohort than in the observation phase cohort (73% vs 58%) [12]. Patients received more in-hospital intensive counselling and had more frequently nicotine replacement therapy at discharge during the intervention phase than during the observation phase (87% vs 22% and 59% vs 18%, respectively) [12]. At the 5-year visit, in the intervention phase cohort, mean age was 61 years; 20% were women, and 96% had attended at least one medical visit within the last year (table 1). Participants did not differ significantly between cohorts regarding age, gender, medical conditions such as diabetes or hypertension, or drug use. In the intervention phase cohort, 44% of the participants had an education level lower than university compared with 27% in the observation phase cohort.

The 1-year and 5-year smoking cessation rate are reported in the table 2. One year after ACS, 110/214 (51%) quit smoking in the intervention phase cohort, and 94/217 (43%) in the observation phase cohort. After multiple imputation by chained equation, the adjusted risk ratio for stopping was 1.17 (95% CI 0.89–1.54,  $p = 0.3$ ). At 5 years, 75/140 (54%) quit smoking in the intervention phase cohort, and 68/146 (47%) in the observation phase cohort, with an adjusted risk ratio with multiple imputation for stopping of 1.13, which also did not reach statistical significance (95% CI 0.84–1.51,  $p = 0.4$ ). Similar results were obtained in sensitivity analyses considering patients lost to follow-up as current smokers (table S3 in the appendix).

The 1-year and 5-year incidence of fatal and non-fatal MACE are reported in the table 3 and figures 1 and 2.

Compared with the observation phase cohort, patients from the intervention phase cohort had a similar risk of MACE at 1 year, with an unadjusted HR of 1.17 (95% CI 0.70–1.94,  $p = 0.6$ ), and a multivariate adjusted HR of 1.27 (95% CI 0.75–2.15,  $p = 0.4$ ). At 5 years, compared with the observation phase cohort, patients in the intervention phase cohort had a similar risk of MACE with an unadjusted HR of 0.93 (95% CI 0.65–1.32,  $p = 0.7$ ), and a multivariate adjusted HR of 1.04 (95% CI 0.73–1.50,  $p = 0.8$ ). Similar results were found when examining non-fatal MACE only. The multivariate adjusted hazard ratio for all-cause mortality was 0.84 (95% CI: 0.45–1.60,  $p = 0.6$ ) in the comparison of the intervention phase cohort with the observation phase cohort.

## Discussion

In this 5-year follow-up multicentre clinical study of smokers hospitalised for ACS, we found that smoking cessation counselling provided to all smokers at the time of their ACS, as compared with opportunistic counselling, did not increase long-term smoking cessation rates. We reported that about half of smokers were free from tobacco 5 years after their hospitalisation for ACS, with an absolute difference of abstinence of 7% between study groups, which did

**Table 1:**  
Characteristics of patients 5 years after index acute coronary syndrome (ACS), by smoking cessation counselling phase (n = 294).

	5-year follow up		
	Intervention phase cohort (n = 146)	Observation phase cohort (n = 148)	p-Value
Age, years, median (Q1; Q3)	61 (55; 68)	63 (57; 69)	0.09
Female, n (%)	29 (20%)	27 (18%)	0.8
Education level: less than university, n (%)	64 (44%)	40 (27%)	0.002
ACS-type: STEMI	78 (53%)	76 (51%)	0.7
BMI (n = 240), kg/m <sup>2</sup> , median (Q1,Q3)	26.7 (24.2; 30.0)	26.5 (23.7; 30.1)	1.0
Diabetes (n = 246), n (%)	36 (25%)	37 (25%)	0.8
Hypertension <sup>a</sup> (n = 218), n (%)	18 (12%)	22 (15%)	0.9
Hypercholesterolaemia <sup>b</sup> (n = 259), n (%)	36 (25%)	30 (20%)	0.3
At least one medical visit during the last year (n = 287), n (%)	140 (96%)	142 (96%)	0.7
– By primary care physician (n = 275), n (%)	131 (90%)	134 (91%)	0.8
– By cardiologist (n = 279), n (%)	111 (75%)	109 (75%)	1
Use of nicotine replacement therapy to stop smoking since inclusion (n = 143), n (%)	12 (16%)	6 (9%)	0.2
Use of bupropion to stop smoking since inclusion (n = 287), n (%)	1 (1%)	0	NA
Use of vareniclin to stop smoking since inclusion (n = 287), n (%)	0	2 (1%)	NA
Antiaggregant <sup>c</sup> (n = 287), n (%)	136 (93%)	136 (92%)	0.3
Lipid-lowering drugs (n = 287), n (%)	115 (79%)	130 (88%)	0.1
Nitrate drugs (n = 287), n (%)	14 (10%)	20 (14%)	0.4
Anti-hypertensive drugs (n = 287), n (%)	118 (81%)	131 (89%)	0.2

BMI: body mass index; STEMI: ST-segment elevation myocardial infarction

<sup>a</sup> Systolic blood pressure >140 mm Hg in 3 measurements

<sup>b</sup> Total cholesterol >5.0 mmol or 190 mg/dl.

<sup>c</sup> Aspirin, clopidogrel, prasugrel or ticagrelor

**Table 2:**  
Smoking cessation prevalence comparing participants in the smoking cessation intervention phase cohort with the observation phase cohort at 1 year (n = 431) and 5 years (n = 286) after the index acute coronary syndrome (ACS), with or without multiple imputation for missing data.

		Intervention phase cohort	Observation phase cohort	Risk ratio (95% CI)	Adjusted risk ratio (95% CI) <sup>a</sup>	Risk ratio with multiple imputation (95% CI) <sup>b</sup>	Adjusted risk ratio with multiple imputation (95% CI) <sup>a,b</sup>
Smoking cessation	1-year rate	110/214 (51%)	94/217 (43%)	1.19 (0.97–1.45, p = 0.1)	1.17 (0.89–1.55, p = 0.3)	1.19 (0.90–1.56, p = 0.2)	1.17 (0.89–1.54, p = 0.3)
	5-years rate	75/140 (54%)	68/146 (47%)	1.15 (0.91–1.45, p = 0.2)	1.15 (0.82–1.62, p = 0.4)	1.11 (0.84–1.48, p = 0.5)	1.13 (0.84–1.51, p = 0.4)

CI: confidence interval

<sup>a</sup> Adjusted for sex, age, education level and type of ACS.

<sup>b</sup> 12 patients (5 (2%) in intervention phase cohort and 7 (3%) in observation phase cohort) had no smoking status data at 1 year; 114 patients (59 (29%) in intervention phase cohort and 55 (27%) in observation phase cohort) had no smoking status data at 5 years. We used multiple imputation chained equation to estimate a set of plausible values for the missing data. Therefore, 442 datapoints were analysed at 1 year, 407 were analysed at 5 years.

**Table 3:**  
Major adverse cardiovascular events (MACE)<sup>a</sup> and all-cause mortality comparing participants from the intervention phase cohort with the observation phase cohort at 1 year and 5 years after the index ACS using Lambert flexible parametric modelling (n = 458).

		Intervention phase cohort		Observation phase cohort		Unadjusted		Model 1 multivariable adjustment <sup>b</sup>		Model 2 multivariable adjustment <sup>c</sup>	
		Nb events/ patients	Incidence rate, per 100 person-years	Nb events/ patients	Incidence rate, per 100 person-years	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value	Hazard ratio (95%CI)	p-value
MACE	1-year	31/225 (13.8%)	14.3	28/233 (12.0%)	12.4	1.17 (0.70–1.94)	0.6	1.33 (0.79–2.24)	0.3	1.27 (0.75–2.15)	0.4
	5-years	60/225 (26.7%)	6.2	66/233 (28.3%)	6.9	0.93 (0.65–1.32)	0.7	1.09 (0.76–1.55)	0.6	1.04 (0.73–1.50)	0.8
Non-fatal MACE	1-year	27/225 (12.0%)	12.4	25/233 (10.7%)	11.1	1.14 (0.66–1.96)	0.6	1.21 (0.70–2.10)	0.5	1.18 (0.68–2.07)	0.6
	5-years	56/225 (24.9%)	5.8	59/233 (25.3%)	6.1	0.97 (0.67–1.40)	0.9	1.10 (0.76–1.59)	0.6	1.06 (0.73–1.55)	0.8
All-cause mortality	1-year	7/225 (3.1%)	2.9	9/233 (3.8%)	3.7	0.79 (0.29–2.12)	0.6	1.08 (0.39–3.04)	0.9	1.19 (0.39–3.64)	0.8
	5-years	18/225 (9.3%)	1.7	29/233 (13.3%)	2.6	0.64 (0.35–1.15)	0.13	0.89 (0.49–1.62)	0.7	0.84 (0.45–1.60)	0.6

<sup>a</sup> MACE: cardiovascular mortality, myocardial infarction, stent thrombosis, repeat unplanned revascularisation, cerebrovascular event, or repeat hospitalisation due to angina.

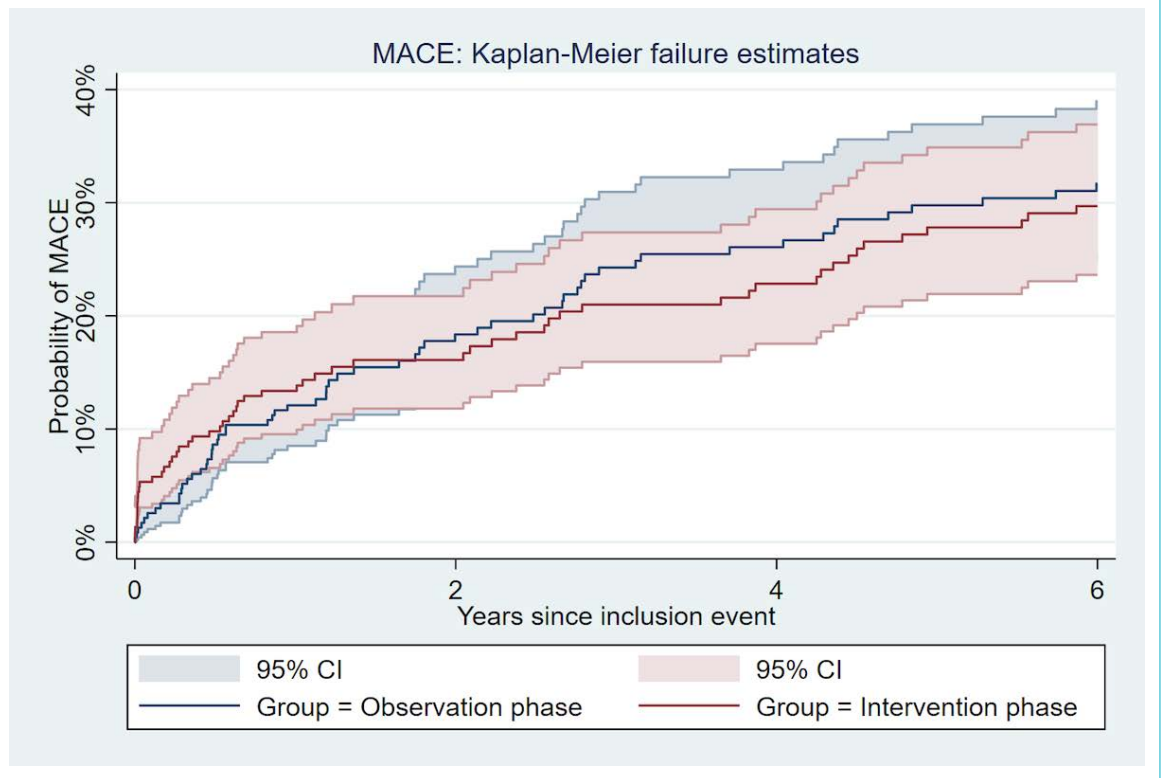
<sup>b</sup> Model 1: adjusted for age, sex, education level, type of acute coronary syndrome (ACS)

<sup>c</sup> Model 2: adjusted for age, sex, education level, ACS type, diabetes, body mass index, hypertension, hypercholesterolaemia, previous cardiovascular disease.

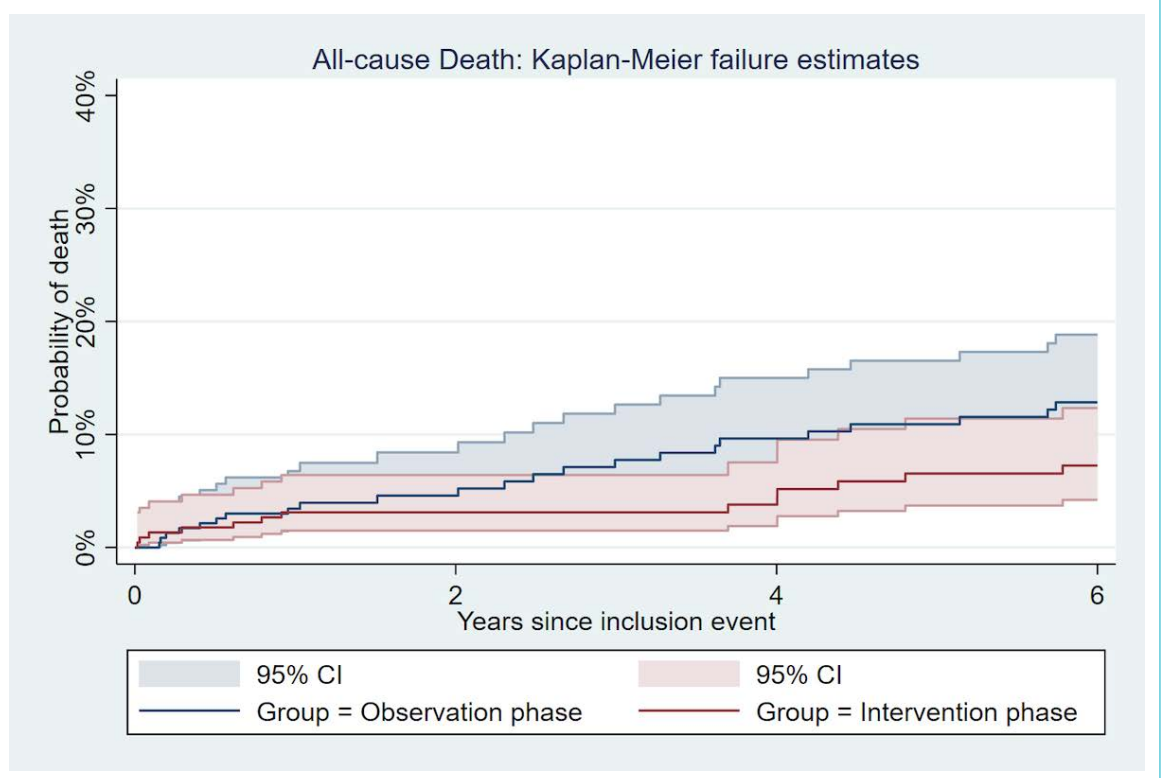
not reach statistical significance. We also found that nearly a third of ACS smokers experience a recurrent cardiovascular event over 5 years. This cardiovascular event rate and all-cause mortality were similar when systematic smoking cessation counselling at hospital was compared with opportunistic counselling.

Our findings differ from results of a previous systematic review indicating that smoking cessation counselling interventions delivered during hospitalisation and lasting at least a month after discharge increased the smoking cessation rate [8]. However, our study assessed a different population because our intervention focused on systematic

**Figure 1:** Incidence of Major adverse cardiovascular event 5 years after an acute coronary syndrome, by study phase.



**Figure 2:** Incidence of all-cause Death 5 years after an acute coronary syndrome, by study phase.



counselling of all ACS smokers, independently of motivation to quit. Therefore, our study addressed a different research question from studies that only included smokers motivated to quit. Among the few other trials that studied the long-term efficacy of smoking cessation counselling over a period of 4 years or more [18–20], most studied patients without previous cardiovascular disease, and none assessed systematic counselling vs opportunistic counselling. Anthonisen et al. offered smoking patients with chronic obstructive pulmonary disease (COPD) an intervention programme of 12 two-hour group sessions during 10 weeks followed by a maintenance programme, and compared this to the usual care. After 5 years, the abstinence rate was higher in the intervention group than the usual care group (21.7% vs 5.4%) [18]. The Nohlert et al. trial compared high versus low-intensity treatment for smoking cessation for 40 minutes counselling during 4 months for healthy patients. After 5–8 years of follow up, the abstinence rate was higher in the high-intensity than in the low-intensity treatment group (31% vs 24%) [19]. In the Lou et al. trial, ambulatory behavioural intervention (home visit 1/week for 1 year then 1/month) was given to COPD patients for 2 years. After 4 years of follow up, smoking abstinence rates were significantly higher in participants receiving behavioural intervention than those receiving usual care (44.3 vs 5.1%) [20]. As reported previously, our systematic smoking cessation intervention led to an increase in prescriptions for nicotine replacement therapy at discharge compared with the observation phase [12]. After 5 years, the use of nicotine replacement therapy to stop smoking remained slightly higher in the intervention phase than in the observation phase. These differences can be related to the higher proportion of prescriptions for nicotine replacement therapy at hospital discharge during the intervention phase. Overall, these results confirm that the more intensive and the longer the counselling, the higher the long-term smoking cessation rates [18–20].

In addition to the smoking cessation rate, our study assessed the 5-year cardiovascular event rate and mortality with systematic smoking cessation counselling at the time of ACS. Although not statistically significant, we found that all-cause mortality was 4% lower in the intervention phase cohort than in the observational phase cohort. The hazard ratio remained shifted towards benefit even after multivariable adjustment such as for diabetes or pre-existing cardiovascular disease. However, as education level was higher in the intervention phase than in the observation phase, the differences of clinical outcomes observed between study phase could be partially explained by education. After multivariable adjustment including education level, the strength of association of the intervention with mortality was reduced.

In most previous trials of smoking cessation counselling interventions after ACS, a shorter follow-up period for cardiovascular event incidence was reported [10]. Mohiuddin et al. studied the 2-year benefit on smoking cessation, hospitalisation and mortality of a smoking cessation intervention among smokers with cardiovascular disease [10]. After a follow-up of 2 years, they found higher pharmacotherapy utilisation, a higher smoking abstinence rate and lower all-cause mortality and hospitalisation rates in

the intervention group. The investigator conducted an intensive smoking cessation counselling intervention with post-discharge counselling sessions. The smoking counselling was approximately 60 min/week for at least 12 weeks and individualised pharmacotherapy was provided at no cost to the intervention group. In comparison with our study, their intervention was not systematically provided to all smokers and their smoking counselling intervention was more intensive than ours. These differences may explain the absence of cardiovascular benefit reported in our study.

Our study has limitations. First, the sample size was not powered to show differences in long-term smoking abstinence nor a significant reduction of the 5-year recurrence of MACE. Therefore, our study results should be interpreted using point estimates instead of confidence intervals. Second, our design was a before-after study. Despite multivariable adjustments, unmeasured differences between participants of the intervention phase cohort and the observation phase cohort may limit comparison of MACE incidence between cohorts. Third, smoking cessation at the 5-year follow-up visit was self-reported. According to a systematic review, smoking abstinence based on self-reports could be overestimated [21]. However, this potential overestimation can be expected to be similar in both the observation phase and intervention phase cohorts and should not affect group comparisons. Fourth, missing information due to death or lost to follow up was very high 5 years after the index ACS. For applying various advanced statistical methods to account for the high lost-to-follow-up rate, we could only rely on our restricted dataset. Observing similar results by including all participants lost to follow-up as smokers or applying multiple imputation strategies for the main outcome and for missing covariables strengthened our confidence in the findings.

## Conclusions

In this controlled long-term interventional study, systematic intensive smoking cessation counselling in all hospitalised smokers with ACS did not significantly increase 5-year smoking cessation rates, nor decrease cardiovascular event recurrence, as compared with opportunistic smoking cessation counselling during hospitalisation. Adequately powered studies for long-term smoking abstinence and recurrence of MACE should be performed.

## Data availability statement

Original data of the SPUM-ACS study are available for secondary analyses upon acceptance of a research protocol by the study steering committee. Original data for this study will be made available upon request based on a signed data transfer agreement. For data access, please first contact the corresponding author.

## Financial disclosure

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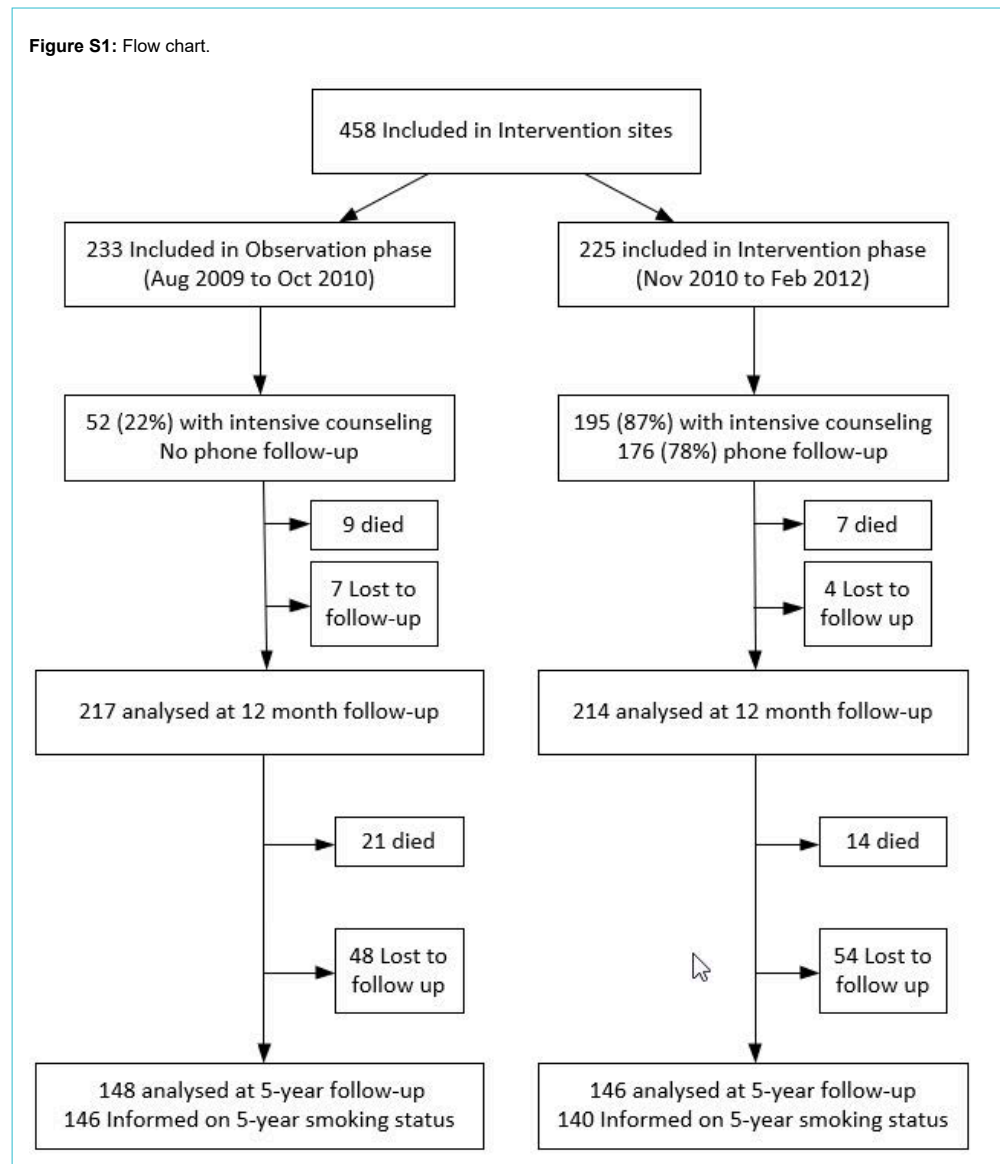
#### Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Prof Lüscher reports receiving research grants to the institution from Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo, Eli Lilly, Novartis, Sanofi, Servier and Vifor and consultant or speaker honoraria from Ablative Solutions USA, Acthera, Switzerland, Amgen Europe, Daiichi Sankyo Switzerland, DalCor, Switzerland, Novo Nordisk Europe, Sanofi Middle East. 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. RA's research on cardiovascular prevention is supported by a grant for prospective researchers from the Swiss National Science Foundation PBLAP3-136774, the Société Académique Vaudoise and the SICPA Foundation. Prof Sudano has received consulting fees, travel grant and honoraria from: Amgen, Astra Zeneca, Daiichi Sankio, Medtronic, MSD, Novartis Recordati, Sanofi und Servier. All unrelated to the topic of the present paper. All other authors report no conflicts of interest.

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## Appendix: Supplementary data





**Table S1:**

Characteristics of patients at baseline, by smoking cessation counselling phase (n = 558).

	Baseline characteristics		
	Intervention phase cohort (n = 225)	Observation phase cohort (n = 233)	p-value
Age, years, (mean ± SD)	55 ± 11	57 ± 11	0.06
Female, n (%)	45 (20%)	46 (20%)	0.9
Education level: less than university, n (%)	185 (83%)	203 (88%)	0.1
Living alone	55 (24%)	68 (29%)	0.3
Working status: employed, n (%)	143 (64%)	136 (59%)	0.3
Previous CHD, n (%)	37 (16%)	46 (20%)	0.3
ACS-type: STEMI, n (%)	116 (52%)	121 (52%)	0.9
Prescription of all recommended drug therapy at discharge n (%) <sup>a</sup>	216 (96%)	222 (95%)	0.6
Attendance to cardiovascular rehabilitation assessed at discharge and 12 months follow-up n (%)	163 (73%)	136 (58%)	<0.01

ACS: acute coronary syndrome; CHD: coronary heart disease; SD: standard deviation; STEMI: ST-segment elevation myocardial infarction

<sup>a</sup> Concomitant prescription at discharge unless contraindicated or not indicated for aspirin, clopidogrel/prasugrel or ticagrelor if percutaneous coronary intervention (PCI) - stent treatment, β-blocker, statin, angiotensin-converting-enzyme inhibitor (ACEI) if left ventricular ejection fraction ≤40%. When participants transferred to peripheral hospital, β-blocker and ACEI / angiotensin receptor II antagonist (ATII) coded as not applicable.

**Table S2:**

Counselling received by the patients, by smoking cessation counselling phase (n = 558).

	Intervention phase cohort (n = 225)	Observation phase cohort (n = 233)	p-Value
Received intensive counselling during hospital stay, (n, %)	193 (87) <sup>a</sup>	52 (22)	<0.001
Duration of in-hospital counselling per participant in minutes, median (Q1,Q3)	40 (35, 60)	45 (45,48)	0.4
Number of in-hospital counselling sessions, median (min, max)	1 (1, 3)	1 (1, 2)	0.3
Prescribed nicotine replacement therapy at discharge (n %)	132 (59)	42 (18)	<0.001

<sup>a</sup> Of the 13% who did not receive an intervention, 24 (11%) were transferred to another facility or discharged home before the counsellor could approach them, 2% (n = 4) completely refused to discuss with counsellor, 1% (n = 2) were in a confused state.

**Table S3:**Smoking cessation prevalence comparing participants in the smoking cessation intervention phase cohort with the observation phase cohort at 1 year (n = 442) and 5 years (n = 407) after the index acute coronary syndrome (ACS), considering lost-to-follow-up patients as current smokers<sup>a</sup>.

		Intervention phase cohort	Observation phase cohort	Risk ratio (95% CI)	Adjusted Risk Ratio <sup>b</sup> (95% CI)
Smoking cessation	1-year rate	110/218 (50%)	94/224 (42%)	1.20 (0.98–1.47, p = 0.07)	1.19 (0.90–1.57, p = 0.2)
	5-years rate	75/204 (37%)	68/203 (33%)	1.10 (0.84–1.43, p = 0.5)	1.12 (0.80–1.56, p = 0.5)

<sup>a</sup> 12 patients (5, 2% in intervention phase cohort, 7, 3% in observation phase cohort) had no smoking status data at 1 year; 114 patients (59, 29% in intervention phase cohort, 55, 27% in observation phase cohort) had no smoking status data at 5 years. Those lost to follow up were considered as still smoking. Dead participants were excluded. Therefore, 442 datapoints were analysed at 1 year, 407 were analysed at 5 years.

<sup>b</sup> Adjusted for sex, age, education level and type of ACS

**Table S4:**

CONSORT Guideline.

Item	Description	Reported on page and line number
Title	Identification of the study as randomized	p.1
Authors *	Contact details for the corresponding author	p. 1–2
Trial design	Description of the trial design (e.g. parallel, cluster, non-inferiority)	p.3, l.2–6
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	p.3, l.9–10
Interventions	Interventions intended for each group	p.3, l.11–15
Objective	Specific objective or hypothesis	p.3, l.16–18
Outcome	Clearly defined primary outcome for this report	p.3, l.9–10
Randomization	How participants were allocated to interventions	p.3, l.11–15
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	p.3, l.15–16
Results		
Numbers randomized	Number of participants randomized to each group	p.4, l.2–3
Recruitment	Trial status	p.3, l.11 and 13
Numbers analysed	Number of participants analysed in each group	p.4, l.3–4
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	p.4, l.4–7
Harms	Important adverse events or side effects	NA
Conclusions	General interpretation of the results	p.4, l.12–16
Trial registration	Registration number and name of trial register	p.3, l.3–4
Funding	Source of funding	p.16 l. 7–19