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Complete List of Authors:	Auer, Reto; Universite de Lausanne, Department of Community Health and Ambulatory Care Gencer, Baris; Geneva University Hospital, Division of Cardiology, Faculty of Medicine Tango, Rodrigo; Geneva University Hospitals, Division of Primary Care Medicine and Community Health, Faculty of Medicine Nanchen, David; University of Lausanne, Department of Ambulatory and Community Medicine Matter, Christian; Universitat Zurich Medizinische Fakultat, Department of Cardiology Luescher, Thomas; Universitat Zurich Medizinische Fakultat, Department of Cardiology Windecker, Stephan; University Hospital Bern, Department of Cardiology Mach, François; Universite de Geneve Faculte de Medecine, Division of Cardiology Cornuz, Jacques; Lausanne University Hospital, Policlinique Médicale Universitaire Humair, Jean-Paul; Universite de Geneve Faculte de Medecine, Division of Primary Care Medicine and Community Health Rodondi, Nicolas; Inselspital Universitatsspital Bern, Department of General Internal Medicine
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Uptake and efficacy of a systematic intensive smoking cessation intervention using motivational interviewing for smokers hospitalized for an acute coronary syndrome

Short title: Uptake and efficacy of a systematic smoking cessation intervention

Reto Auer, MD, MAS[1]; Baris Gencer, MD[2];Rodrigo Tango, MD[3]; David Nanchen, MD, MSc[1]; Christian M. Matter, MD[4]; Thomas Felix Lüscher, MD[4]; Stephan Windecker, MD[5]; François Mach, MD[2]; Jacques Cornuz, MD, MPH[1]; Jean-Paul Humair, MD, MPH[3]; Nicolas Rodondi, MD, MAS[6]

[1] Department of Ambulatory and Community Medicine, University of Lausanne, Lausanne, Switzerland; [2] Division of Cardiology, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland; [3] Division of Primary Care Medicine and Community Health, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland; [4] Department of Cardiology, University Hospital Zurich, Zurich, Switzerland; [5] Department of Cardiology, University Hospital Bern, Bern, Switzerland; [6] Department of General Internal Medicine, Inselspital, Bern University Hospital, Bern, Switzerland

Corresponding author: Dr. Reto Auer, MD, MAS.
Department of Ambulatory Care and Community Health, University of Lausanne, Rue du Bugnon 44, 1011 Lausanne, Switzerland.
Phone: + 41 21 314 49 28. Fax: +41 21 314 48 93
Email: Reto.Auer@hospvd.ch

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Key words: Smoking; prevention; acute coronary syndrome; hospitalization; motivational interviewing

Preliminary results have been presented as an oral presentation during the meeting of the Society of Medical Decision Making (SMDM) in Baltimore, MD on October 23rd 2013 and at the meeting of the European and Swiss Conference of Internal Medicine in Geneva (ESCIM) on May 15th, 2014.

Abstract

Objectives: To compare the uptake and efficacy of a proactive approach compared to a reactive approach to offer intensive smoking cessation intervention using motivational interviewing (MI).

Design: Before-after comparison in two academic hospitals with parallel comparison in two control hospitals without intervention.

Setting: Academic hospitals in Switzerland.

Participants: Smokers hospitalized for an ACS.

Intervention: In the intervention phase, a resident physician trained in MI offered counseling to all smokers admitted for ACS, followed by four telephone counseling sessions over two months by a nurse trained in MI. In the observation phase, the in-hospital intervention was offered only to patients whose clinicians requested a smoking cessation intervention.

Primary and secondary outcomes: The primary outcome was 1-week smoking abstinence (point prevalence) at 12 months. Secondary outcomes were the number of smokers who received the in-hospital smoking cessation intervention and the duration of the intervention.

Results: In the intervention phase and in the intervention centers, 87% of smokers (N=193/225) received a smoking cessation intervention compared to 22% in the observational phase (p<0.001). Median duration of counseling was 50 minutes. During the intervention phase, 78% received a phone follow-up for a median total duration of 42 minutes in 4 sessions. Prescription of NRT at discharge increased from 18% to 58% in the intervention phase (Risk ratio: 3.3 (95% CI:2.4 to 4.3;p=<0.001). Smoking cessation at 12-month increased from 43% to 51% comparing the observation and intervention phases (Risk ratio (RR) =1.20, 95% CI:0.98-1.46;p=0.08; 97% with outcome assessment). In the control hospitals without dedicated smoking intervention the RR for quitting was 1.02 (95% CI:0.84-1.25;p=0.8, 92% with outcome assessment).

Conclusion: A proactive strategy offering intensive smoking cessation intervention based on motivational interviewing to all smokers hospitalized for ACS significantly increases the uptake of smoking cessation counseling and might increase smoking abstinence at 12 months.

Strengths and limitations of this study

- The study questions current guidelines who recommend that only motivated smokers should receive intensive smoking cessation counseling intervention.
- Four university centers were involved with two centers serving as a parallel comparison.
- Smoking cessation outcome assessed after 12-months in 97% of participants in the intervention centers.
- The weak before-after design with parallel comparison limits causal inference of the potential effects of the intervention.
- Participants received phone counseling after their hospital stay in the intervention phase, but not in the observation phase, thereby limiting the interpretation of the comparison between a proactive and reactive approach of offering a smoking cessation intervention on smoking cessation rates at 12 months.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in adults in the United States (US) and in Europe and smoking is the leading cause of CVD.[1] Smokers who quit after a myocardial infarction can expect a 36% reduction in CVD mortality over 2 years compared with continuing smokers.[2 3] In a meta-analysis of randomized controlled trials of smokers hospitalized for a CVD diagnosis, smoking cessation interventions started in the hospital and sustained in the ambulatory setting for at least 1 month after discharge, increased smoking cessation rates by more than 40%.[4 5]

While the effectiveness of smoking cessation counseling interventions and their components has been extensively studied, the optimal delivery of smoking cessation interventions has been less studied.[6 7] Current guidelines promote the use of the 5A's for the delivery of smoking cessation interventions where healthcare providers *assist* smokers willing to make a quit attempt after having *assessed* their "readiness to quit".[8 9] However, past negative experiences with healthcare workers, where smokers felt to be negatively judged because of their behavior, may impact their willingness to explore their habit with a counselor.[10-12] The Clinical Practice Guideline for Treating Tobacco Use and Dependence recommends the use of Motivational Interviewing (MI) with smokers who express low motivation to quit.[13] MI is a collaborative, person-centered guidance to elicit and strengthen motivation to change; MI could allow approach all smokers, regardless of their self-reported motivation to quit smoking.[14 15] While a recent study showed promising results on increasing the uptake of smoking cessation interventions when systematically identifying and assisting hospitalized smokers, 30% declined consent to participate in the study and an additional 30% of those offered behavioral support refused it.[16]

We aimed at testing the uptake and efficacy of a proactive approach compared to a reactive approach to offer intensive smoking cessation intervention using motivational interviewing (MI) to smokers hospitalized for an acute coronary syndrome (ACS).

MATERIAL AND METHOD

STUDY POPULATION

The study population comprised smoking participants to the SPUM ACS cohort study; a national cohort of patients with acute coronary syndrome (ACS) conducted in four academic hospitals in Switzerland and registered at clinicaltrials.gov (NTC 01000701 and NCT 01075867).[17-19] Inclusion criteria were patients aged 18 years or older presenting with the principal diagnosis of ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) or unstable angina (UA). Active smoking was defined as smoking one cigarette or more per day during the month preceding the hospital stay. Participants were included from August 2009 to February 2012 in all four sites (Figure 1). The observation phase was from August 2009 to October 2010 and the intervention phase from November 2010 to February 2012. Two study sites (study site A and B) were considered as the intervention sites and 2 sites, the control sites (study site C and D). Detailed documentation of the flow of participants from the arrival to the emergency room for suspicion of ACS to the inclusion in the clinical follow-up study was performed in study site A (Appendix, online).

STUDY PROTOCOL AND INTERVENTIONS

During the observation phase in the intervention sites (study sites A and B), clinicians in charge of patients could request a specialized smoking cessation intervention for hospitalized smokers a simple phone call.[20 21] Patients also systematically received information about the smoking cessation consultation. In the intervention phase, a resident physician trained in MI identified each smoker included in the clinical follow-up study. Residents then systematically approached each smoker and asked permission to discuss with patient about their smoking habit.

In addition to training in tobacco cessation counseling and prescription of nicotine replacement therapy (NRT),[21] residents were trained in MI during 4 sessions of 4 hours each separated by one week over one month before the intervention phase. To allow residents to adapt the interview to the patient's needs, we did not develop a detailed manual for directing the MI.[22] To minimize interference with the

intervention, most data were collected during the inclusion of patients before the residents approached patients. There was no restriction on the duration of the interview and residents ended the discussion once they felt an increase in the resistance of the patients, if they were interrupted by competing care to patients, or if patients specifically asked the interview to end. Multiple MI sessions were allowed during the hospital stay if requested by patients. If not already prescribed by the HCP in the ward, resident offered NRT and brochures on smoking cessation. At the end of the interview, residents offered to smokers 4 ambulatory telephone contacts with a study nurse. Residents provided the HCP in charge of the patient with a brief summary of the intervention and recommendations for NRT and sent a medical report to the patient's primary care provider. Study nurses followed the same training in MI as the residents. Whenever possible, the nurse tried to meet all counseled smokers for a brief face-to-face encounter before discharge. After discharge, study nurses contacted patients at their preferred phone contact 2 days, 1 week, 1 month and 2 months after discharge from the acute care hospital.[4] NRT, which is not reimbursed in Switzerland, was available free of charge during the hospital stay, but were at the patients' charge as an outpatient.

The study protocol was approved by the institutional review board of all participating centers; namely, the Ethics Committee on Clinical Research of the University of Lausanne, the Ethics Committee of the Department for Internal Medicine and Community Medicine of the University Hospital of Geneva, the Cantonal Ethics Committee (KEK) of the Canton of Bern, and the Cantonal Ethics Committee (KEK) of the Canton of Zurich. All patients provided written, informed consent.

COVARIATES

Current smoking status, age of smoking initiation and daily cigarettes consumption were assessed for all patients throughout the study duration in all sites during the inclusion process in the clinical study. In the intervention sites during the intervention phase, patients were given a brochure of questionnaire to be filled during the hospital stay.

Administrative (length of stay, discharge at home or direct transfer to a peripheral hospital or to cardiovascular rehabilitation (CR)), demographic (age, sex, race, education), medical (type of ACS

(NSTEMI/UA and STEMI); previous coronary health disease (CHD)) data and processes of care were collected during the inclusion in the clinical follow-up study and completed after discharge. Attendance rate to CR and type of CR (ambulatory vs. hospital) were assessed from administrative data available at discharge and from self-report during the ambulatory follow-up visit at one year. In Switzerland, health care providers organize CR during the hospital stay or provide patients with information to benefit from CR. Thus patients could be directly addressed to an inpatient CR facility or attend ambulatory CR in the outpatient setting. Quality indicators were based on cardiologic guidelines and included systematic collection of reason for non-prescription for preventive medication.[23]

OUTCOMES

The primary outcome for smoking cessation was 1-week smoking abstinence (point prevalence) at 12 months. Self-reported smoking cessation was biochemically confirmed by exhaled carbon monoxide levels (Micro Smokerlyser; Bedfont Scientific Ltd) at the 1-year follow-up visit in all sites.[24] We classified those with carbon monoxide levels of at least 10 ppm as current smokers. The main process outcome was the number of patients who received smoking cessation counseling. We also collected the duration and number of interventions during the hospitalization and follow-up.

STATISTICAL ANALYSIS

Frequencies, means with standard deviations (SDs), medians with inter-quartile ranges (IQR) were used when appropriate, as were χ^2 tests, Fisher's exact test, Wilcoxon rank sum test and ANOVA for bivariate analyses. The primary analysis examined the point estimate and 95% confidence interval (CI) of the risk ratio for smoking cessation at 12 months between both phases in the intervention sites and using an intention-to-include approach. We conducted stratified analyses by attendance to CR and education status (with or without university degree). We tested the association between the presence and duration of counseling between phases using logistic regression models and Poisson logistic regression models. The sample size calculation was based on an expected 10% absolute increase in smoking abstinence at 12 months in the two intervention centers. The 10% difference was based on a summary estimate of 11

previous RCTs identified in a systematic review and meta-analysis which included smokers hospitalized with CHD and tested the effect of a high intensity intervention with phone follow-up. [5 25-37] The summary quit rate over all these studies in the intervention groups was 45% and 31% in the control groups, thus an absolute risk difference of 14%. Using an α level of 0.05 and a power of 80%, and given the potential increase in abstinence due to the intervention in some smokers in the observation phase, we estimated that 400 patients had to be included in the intervention sites (sites A and B) over the entire study period to detect a 10% absolute difference in quit rates. The study was not powered to detect a significant difference between intervention and control sites over the observation and intervention phases. Statistical significance was set at 0.05. All analyses were performed using STATA version 12 (StataCorp, College Station, Texas).

RESULTS

STUDY POPULATION

Between August 2009 and February 2012, 616 patients admitted for ACS were included in the clinical follow-up study in site A, and 510 in site B. 458 (40%) were current smokers and included in the subsequent analyses (Appendix Figure 1). At 12-month follow-up, smoking status was assessed in 97% while 15 participants had died (Appendix Figure 1). In the control sites, 192 smokers were included in the observation phase and 244 in the intervention phase (Appendix Table 1). At one year follow-up, smoking abstinence was obtained for 92% while 12 participants died.

Mean age of participants included in the intervention sites in the intervention phase was 55 years, 20% were women and 52% had been hospitalized for STEMI (Table 1). There were no significant differences in baseline characteristics between participants in observation and intervention phases, except for the longer stay of patients directly discharged home.

PROCESS OUTCOMES

Twenty-two percent of patients received intensive smoking cessation counseling during the observation phase compared to 87% in the intervention phase (Table 2). Among the 13% who did not receive

counseling in the intervention phase, 10% (n=24) were transferred to another facility or discharged home before the counselor could approach them; 2% (N=4) completely refused to discuss with counselor and 1% (N=2) had a major language barrier. The median duration of the intervention during the hospital stay was 50 minutes and did not significantly vary between both phases. During the intervention phase, 78% received a phone follow-up (90% of those receiving in-hospital counseling) for a median total duration of 42 minutes in 4 sessions. Prescription of NRT at discharge increased significantly from 18% to 58% in the intervention phase (Risk ratio: 3.3 (95% CI: 2.4 to 4.3; p=<0.001).

The proportion reporting having attended cardiac rehabilitation significantly increased during the intervention phase in the intervention sites from 58% to 73% (p<0.01). The proportion attending ambulatory CR compared to hospital-based CR increased from 55% in the observation phase to 67% in the intervention phase.

SMOKING ABSTINENCE AT 12-MONTHS

In the intervention sites, validated 12-months smoking abstinence increased from 43% during the observation phase to 51% in the intervention phase (RR 1.20; 95% CI: 0.98 to 1.46, p=0.08; absolute risk difference (ARD) 8%,Table 3). In the control sites, 47% quit smoking in the observation phase compared to 48% in the intervention phase (RR: 1.02 (95% CI:0.84 to 1.25;p=0.8; ARR 1%).

In exploratory stratified analyses comparing cessation rates in intervention sites between both phases, the apparent benefit was mostly seen in those not attending CR and those without university degree.

DISCUSSION

In this multicenter study involving smokers hospitalized for an ACS, a systematic smoking cessation intervention sharply increased the number of patients exposed to motivational interviewing and nicotine replacement therapy. The median duration of counseling during the hospital stay was 50 minutes and did not vary between phases. Comparing observation to intervention phases, the smoking abstinence at one year increased from 43% to 51% (8% absolute difference in abstinence, p value 0.08). At sites without

dedicated in-hospital smoking cessation intervention during the entire study period, no difference in smoking abstinence was observed. In subgroup analyses, the benefit of the systematic intervention appeared limited to smokers not attending CR and those with lower education level.

Murray et al. recently tested the effectiveness of systematically providing support to all identified smokers in a RCT randomizing medical wards in one medical center in the UK.[16] The systematic identification permitted to increase the offer of behavioral support from 46% to 100% of smokers and the acceptance of behavioral support from 29% to 70% of smokers. However, out of 1072 smokers identified on ward, 30% declined consent to participate in the study and an additional 30% of those offered behavioral support refused it. In our study, detailed analysis of the flow of participants until inclusion in the clinical study showed that 4% refused to enter the clinical follow-up study, followed by 2% who completely refused to open the discussion with the resident approaching them to start a motivational interview. The benefits of counseling all smokers regardless of their motivation to quit using MI had also previously been tested in a rigorously performed RCT in 1996-1997.[30] Out of 164 smokers with acute MI, 8 (5%) refused to participate in the smoking cessation intervention including follow-up at 6 months. The smoking cessation rate at one year was 34% in the observation group and 55% in the intervention group ($p<0.005$). However, the study was performed in a single study site and the rate attending CR was not provided and is expectedly lower than the rate in our population, thus limiting the comparison to our population.

The sharp increase in uptake of the smoking cessation intervention highlights the effect of changes in the choice architecture described in behavioral economic theories. Setting the default option from an *opt-in* to an *opt-out* has been shown to be a powerful driver of uptake in interventions.[38 39] In the context of our study, the systematic offer of a smoking cessation intervention is similar to an *opt-out* policy where patients ask not to have the intervention compared to the *opt-in* policy where patients or their caregivers specifically have to request a smoking cessation intervention.

In our study, the rate discharged to CR in the intervention sites increased from 58 to 73% between the observation and intervention phases. Given that CR includes smoking cessation counseling and

support, it could be considered a follow-up intervention as recommended by guidelines and might be explained by higher attendance rate to CR.[4] However, in stratified analyses by attendance to CR, the benefit of the systematic smoking cessation intervention was mostly apparent among participants not attending CR. The systematic approach might permit to counsel those most at risk of lack of follow-up in the ambulatory care. The high attendance rate to CR overall in our study might explain the negative findings on smoking cessation rates over follow-up [40-43] Overall, attendance rates in the US range from 14% to up to 55%.[40-43] We based our sample size estimation on previous studies on smoking cessation after ACS where attendance rates to CR were expectedly lower. Unfortunately, we are unable to compare the attendance rates in our study to previous smoking cessation studies because previous studies included in the Cochrane systematic review and to the recent study by Murray et al. have not reported on rates of ambulatory CR. [5 16 25-37] Future studies should also better describe the concomitant interventions in the ambulatory care in order to facilitate the interpretation and translation of findings into clinical practice.

Our findings challenge the recommendation of allocating high intensity counseling only to those "willing to make a quit attempt" recommended in smoking cessation guidelines based on the 5A's framework.[9] According to MI, motivation occurs in the interpersonal context, which depends on the style used by counselors with smokers and may influence the acceptance rates of the intervention.[14] A previous rigorously performed RCT only including those willing to make a serious quit attempt was unable to show a benefit on smoking cessation.[28]

Our study has limitations. The weaker before-after design does limit the causal inferences from our results. Participants received phone counseling after their hospital stay in the intervention phase, but not in the observation phase. A systematic review on the benefits of smoking cessation intervention for hospitalized smokers suggested that only interventions including a follow-up intervention in the ambulatory setting have shown an effect on smoking cessation outcomes at 12 months. This strongly limits the comparison of smoking cessation rates between the observation and intervention phase as it is unclear if the study tests the efficacy of a lower intensity intervention in the observational phase to a high intensity intervention in the intervention phase or if the study compares a proactive vs. reactive approach

of offering smoking cessation intervention. Rates of referral to CR were based on information at discharge and self-report at one year follow-up. The reliability of self-reported CR referral has been validated in patients after an ACS in Canada and used recently to report on enrollment rate to CR in the US.[43 44] Exploratory subgroup analyses on the differential effect of education level and attendance to CR should be carefully interpreted, as these analyses were defined *a posteriori.* Patients were included in 4 high quality academic hospitals and results may not apply to different settings. The MI sessions were not recorded and the quality of interactions can therefore not be directly assessed. We did not develop a detailed manual for directing the MI. A prior meta-analysis suggested that clinical trials in which MI was delivered without a manual had showed better treatment outcomes.[22]

CONCLUSIONS

In summary, we found that a systematic smoking cessation intervention using motivational interviewing for smokers hospitalized for an ACS compared to a reactive strategy relying on busy healthcare providers to contact a specialized smoking cessation consultation permitted to sharply increase the number of patients counseled. In exploratory subgroup analyses of data collected in one study center, patients with lower education level and not attending cardiac rehabilitation appeared to be more likely to benefit from the intervention. The comparison of smoking cessation rates at 12 months between the observation and intervention phases are limited by the study design and showed a trend towards an increase in smoking cessation rates. Future studies should further evaluate the benefit of systematically exposing smokers to a smoking cessation intervention based on motivation interviewing.

CONTRIBUTORSHIP STATEMENT

All authors do meet the ICMJE criteria for authorship:

- Conception or design of the work or the acquisition: RA, BG, RT, CMM, TFL, SW, FM, JC, JPH, NR
- Analysis, or interpretation of data for the work: RA, BG, DN, RT, JC, JPH, NR
- Drafted the work: RA, BG, RT, JPH, NR
- Revising it critically for important intellectual content: DN, CMM, TFL, SW, FM, JC
- Final approval of the version to be published: RA, BG, RT, DN, CMM, TFL, SW, FM, JC, JPH, NR
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: RA, BG, RT, DN, CMM, TFL, SW, FM, JC, JPH, NR

COMPETING INTERESTS

The following authors have the following conflicts. Dr Lüscher reports receiving research grants to the institution from Abbott, Biosensors, Biotronik, Boston Scientific, and Medtronic, and consultant payments from AstraZeneca, Boehringer Ingelheim, Bayer, Merck, and Pfizer. Dr Matter reports receiving grants from MSD, Eli Lilly, AstraZeneca, and Bayer; expert testimony from MSD; payment for lectures from MSD, AstraZeneca, and Roche; and having patents from Mabimmune, CH. Dr Windecker reports receiving research contracts to the institution from Abbott, Biotronik, Boston Scientific, Biosensors, Cordis, Medtronic, St. Jude Medical and speaker fees from: Abbott, Biotronik, Boston Scientific, Biosensors, Medtronic, Eli Lilly, Astra Zeneca. All other authors have declared that no competing interests exist.

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DATA SHARING STATEMENT

Primary data on analyses reported in the manuscript are available upon written request.

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Table 1 Baseline characteristics of participants hospitalized for an acute coronary syndrome in 2 academic hospitals (study sites A and B) in Switzerland in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Intervention Sites (A and B)		p-value
	Observation phase N=233	Intervention phase N=225	
Demographic variables			
Age, y (mean ± SD)	57 ± 11	55 ± 11	0.06
Female, N (%)	46 (20)	45 (20)	0.9
Education, less than university degree, N (%)*	203 (88)	185 (83)	0.1
Living alone	68 (29)	55 (24)	0.3
Working status, employed, N (%)	136 (59)	143 (64)	0.3
Previous CHD, N (%)	46 (20)	37 (16)	0.3
Smoking variables			
– Cigarettes per day (median, Q1, Q3)	20 (10, 25)	20 (10, 25)	0.5
– Age at smoking start (mean ± SD)	19 ± 6	18 ± 6	0.6
Clinical variables			
ACS-type:			
– STEMI (vs. NSTEMI/UA), N (%)	121 (52)	116 (52)	0.9
Hospital stay			
Length of stay, median (Q1,Q3), in days			
– For patients directly discharged home	5 (3,6)	5 (4,7)	0.04
– For patients transferred to peripheral hospital	1 (0.5, 1)	1 (0.5, 2)	0.3
Treatment at discharge			
Destination at discharge, N (%)			
– Home	148 (64)	138 (61)	
– Direct transfer to cardiac rehabilitation	47 (20)	39 (17)	0.3
– Transfer to peripheral hospital	36 (16)	47 (21)	
Prescription of all recommended drug therapy at Discharge†	222 (95)	216 (96)	0.6
Attendance to cardiovascular rehabilitation assessed at discharge and 12 months follow-up (N, %)‡	136 (58)	163 (73)	<0.01
– Ambulatory vs. stationary§	74 (56)	109 (67)	0.05

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; STEMI: ST-segment elevation myocardial infarction

* 6 participants with missing information on education status or who refused to disclose their education status.

† Concomitant prescription at discharge unless contra-indicated or not indicated for aspirin, clopidogrel/prasugrel or ticagrelor if PCI-stent treatment, beta-blocker, statin, ACEI if LVEF ≤40%. When participants transferred to peripheral hospital, beta-blocker and ACEI/ATII coded as not applicable.

‡ Both ambulatory and stationary cardiovascular rehabilitation are covered after an ACS in Switzerland. Attendance rate computed using data on direct referral to in-patient CR and on self-reported attendance at one year follow-up in order to capture information on those directly transferred to a stationary CR and those attending CR in the ambulatory setting.

§ 3 participants with missing information on type of CR.

Table 2 Process outcomes in intervention sites (Sites A and B) comparing smokers hospitalized in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Observation phase N=233	Intervention phase N=225	Risk ratio (95% CI) or coefficient*	p-value†
- Received intensive counseling during hospital stay (N,%)	52 (22)	193 (87)‡	3.9 (3.0 to 5.0)	<0.001
- Duration of in-hospital counseling per participant in min (median, Q1, Q3)	45 (45, 48)	50 (35,60)	2.6 (-3.7 to 8.7)	0.4
- Number of in-hospital counseling sessions (median, min, max)	1 (1,2)	1 (1,3)	0.15 (-0.15 to 0.45)	0.3
- Received phone follow-up (N,%)	NA	175 (78)	-	-
- Duration of each phone follow-up in min (median, Q1,Q3)	NA	11 (8,17)	-	-
- Total duration of phone follow-up in min (median, Q1,Q3)	NA	42 (30,61)	-	-
- Number of phone follow-ups (median, Q1,Q3)	NA	4 (3,4)	-	-
- Prescribed nicotine replacement therapy at discharge (N,%)	42 (18)	132 (59)	3.3 (2.4 to 4.3)	<0.001

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; min: minutes; NA: non-applicable; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; STEMI: ST-segment elevation myocardial infarction

* Risk ratio and 95% CI calculated for dichotomous outcomes. Coefficients for duration of counseling obtained by linear regression. For number of counseling sessions, coefficient obtained by Poisson logistic regression model.

†P-value calculated by χ^2 for dichotomous outcomes (e.g. proportion receiving counseling) and linear regression for duration of encounters

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

Table 3 Smoking cessation outcomes at 12 months follow-up comparing participants in observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012) at 4 university sites in Switzerland. 7-day point prevalence abstinence, validated by exhaled carbon monoxide (CO). *

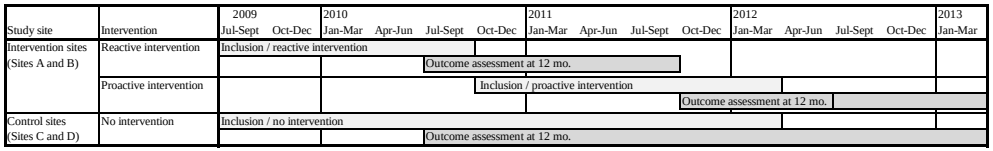
	N total for analysis	% quit in obs. phase / interv. phase	Risk ratio (95% CI)	Absolute risk difference	p-value
Main outcome					
- Intervention sites (sites A and B) (n=454)	443	42.0/50.2	1.20 (0.98 to 1.47)	8.3%	0.08
- Observational sites (sites C and D) (n=436)	428	46.8/47.8	1.02 (0.84 to 1.25)	1.1%	0.8
Secondary analyses for participants in intervention sites (sites A and B) (n=440)					
- Cardiac rehabilitation					
- With cardiac rehabilitation	296	51.5/53.7	1.04 (0.84 to 1.30)	2.2%	0.7
- No cardiac rehabilitation	143	29.5/43.6	1.48 (0.95 to 2.30)	14.1%	0.09
- Education status					
- University degree	64	59.3/51.3	0.87 (0.56 to 1.34)	-7.9%	0.5
- No university degree	371	40.7/50.8	1.24 (1.0 to 1.6)	10.1%	0.05

N, number of participants; CI: confidence interval.

* Participants lost to follow-up or who withdrew consent (n=11, 97% follow-up rate) considered as smokers for these analyses. Participants who died (n=16) during follow-up excluded from these analyses. Validated smoking cessation by CO in 68% of quitters in intervention sites and 40% of quitters in control sites. 2 participants reported having quit during last 7 days despite a CO level of more than 10 ppm considered as smokers.

Figure Legends

Figure 1. Study design. Before-after intervention with parallel temporal comparison: We compared the 7-days point smoking prevalence at 12 months follow-up between participants included in the reactive vs. the proactive intervention phases in intervention sites (site A and B). We also compared the 7-days point smoking prevalence at 12 months follow-up between participants included during the same period in observation sites (sites C and D).



ONLINE DATA SUPPLEMENT

Efficacy of systematic intensive smoking cessation intervention after acute coronary syndromes

Corresponding author: Dr. Reto Auer, MD, MAS.

Department of Ambulatory Care and Community Health,

University of Lausanne, Switzerland.

Phone: + 41 21 314 49 28. Fax: +41 21 314 48 93

Email: Reto.Auer@hospvd.ch

Appendix Table 1 Baseline characteristics of participants hospitalized for an acute coronary syndrome in 2 academic hospitals in Switzerland in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Control sites		p-value
	Observation phase N=192	Intervention phase N=244	
Demographic variables			
Age, y (mean ± SD)	57 ± 11	57 ± 11	0.9
Female, N (%)	36 (19)	31 (13)	0.1
Education, less than university degree, N (%)[a]	151 (89)	196 (93)	0.1
Living alone	41 (22)	50 (21)	0.8
Working status, employed, N (%)	124 (68)	158 (69)	0.7
Previous CHD, N (%)	19 (10)	28 (12)	0.6
Smoking variables			
– Cigarettes per day (median, Q1, Q3)	20 (10, 20)	20 (10, 25)	0.5
– Age at smoking start (mean ± SD)	21 ± 8	21 ± 7	0.7
Clinical variables			
ACS-type:			
– STEMI (vs. NSTEMI/UA), N (%)[b]	156 (81)	195 (80)	0.7
Hospital stay			
Length of stay, median (Q1,Q3), in days			
– For patients directly discharged home	3 (2,4)	2 (1,4)	0.01
– For patients transferred to peripheral hospital	1 (0.5, 1.5)	1 (0.5, 1.5)	07
Treatment at discharge			
Destination at discharge, N (%)			
– Home	38 (20)	62 (25)	
– Direct transfer to cardiac rehabilitation	7 (4)	19 (8)	0.06
– Transfer to peripheral hospital	145 (76)	157 (64)	
Prescription of all recommended drug therapy at discharge[c]	183 (96)	226 (94)	0.4
Attendance to cardiovascular rehabilitation	137 (72)	172 (72)	1.0

assessed at discharge and 12 months follow-up (N, %)[d]			
– Ambulatory vs. stationary[e]	98 (73)	112 (66)	0.2

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; SD: standard deviation; STEMI: ST-segment elevation myocardial infarction

[a]56 participants with missing information on education status or who refused to disclose their education status.

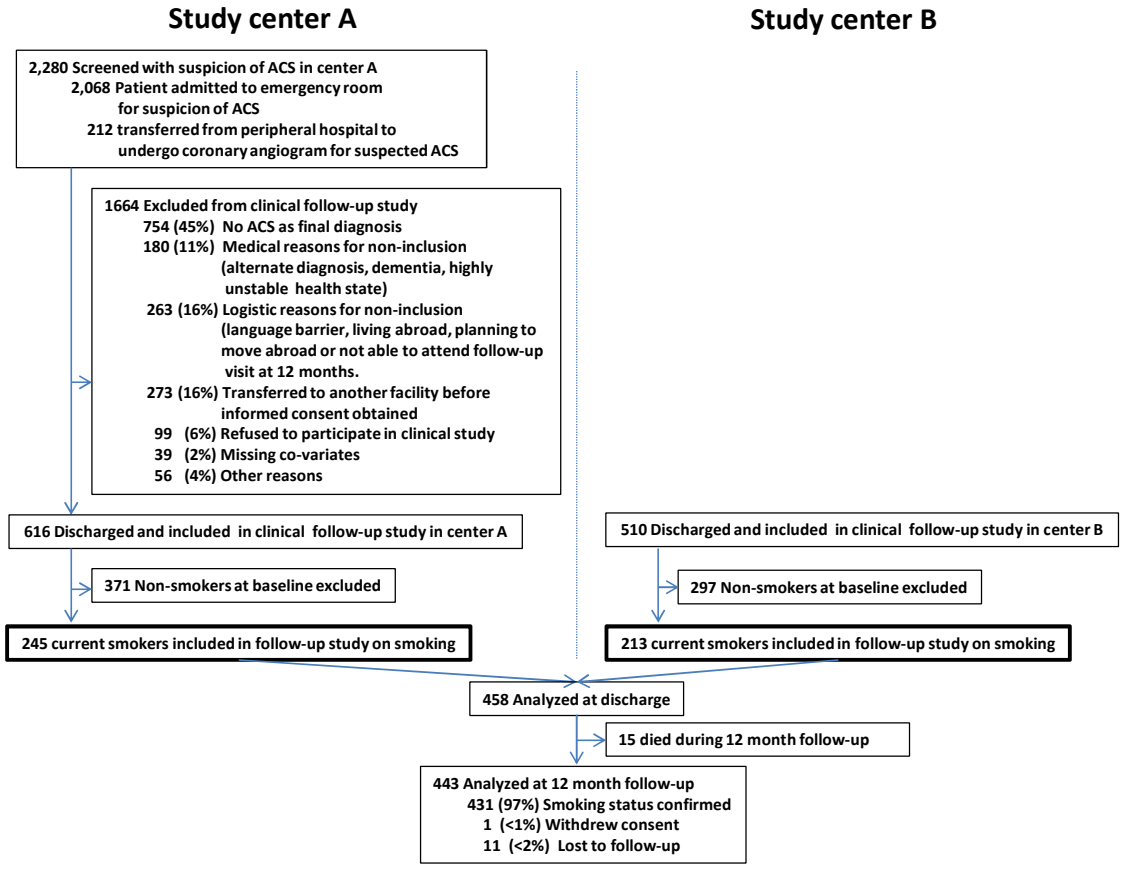
[b] Restriction to STEMI participants in one center, as only STEMI were systematically included in cardiac registry.

[c] Concomitant prescription at discharge unless contra-indicated or not indicated for aspirin, clopidogrel/prasugrel or ticagrelor if PCI-stent treatment, beta-blocker, statin, ACEI if LVEF $\leq$40%. When participants transferred to peripheral hospital, beta-blocker and ACEI/ATII coded as not applicable.

[d] Both ambulatory and stationary cardiovascular rehabilitation are covered after an ACS in Switzerland. Attendance rate computed using data on direct referral to in-patient CR and on self-reported attendance at one year follow-up in order to capture information on those directly transferred to a stationary CR and those attending CR in the ambulatory setting.

[e] 3 missing on type of CR in ambulatory setting

Appendix Figure 1. Flow of study participants in the two intervention sites. Detailed data on selection of participants from arrival to the emergency room to final inclusion was performed in one site.



Abbreviation: ACS: acute coronary syndrome

Appendix References

1. Chouinard MC, Robichaud-Ekstrand S. The effectiveness of a nursing inpatient smoking cessation program in individuals with cardiovascular disease. Nurs Res. 2005;54(4):243-54.
2. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. J Consult Clin Psychol. 1983;51(3):390-5.

Appendix Table 2 STROBE Statement – Filled Checklist

	Item no	Recommendation	Done	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	√	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√,	2
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√	3
Objectives	3	State specific objectives, including any prespecified hypotheses	√, NA	3
Methods				
Study design	4	Present key elements of study design early in the paper	√	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√	5, see also reference listed in the methods
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	√	4, Appendix Table and Figure 1
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√	6, eMethods
Bias	9	Describe any efforts to address potential sources of bias	√	6,7
Study size	10	Explain how the study size was arrived at	√	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√	6,7
Statistical methods	12	(*a*) Describe all statistical methods, including those used	√	6,7

		to control for confounding		
		(*b*) Describe any methods used to examine subgroups and interactions	√	7
		(*c*) Explain how missing data were addressed	√	7
		(*d*) If applicable, explain how loss to follow-up was addressed	√	7
		(*e*) Describe any sensitivity analyses	√	7
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	√	8, eMethods
		(b) Give reasons for non-participation at each stage	√	7,8, Appendix Figure, Appendix Table 1
		(c) Consider use of a flow diagram	√,	Appendix Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	√	8, Table 1 and Appendix Table 1
		(b) Indicate number of participants with missing data for each variable of interest	√	7,9, Table 1
		(c) Summarise follow-up time (eg, average and total amount)	√	8-9
Outcome data	15*	Report numbers of outcome events or summary measures over time	√	8-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	√	9, Table 3
		(*b*) Report category boundaries when continuous variables were categorized	-	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√	9, Table 3

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√	9, Table 3
Discussion				
Key results	18	Summarise key results with reference to study objectives	√	9-10, 12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	√	11-12
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√	13

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Uptake and efficacy of a systematic intensive smoking cessation intervention using motivational interviewing for smokers hospitalized for an acute coronary syndrome: A multicenter before-after study with parallel group comparisons.

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Complete List of Authors:	Auer, Reto; Universite de Lausanne, Department of Community Health and Ambulatory Care Gencer, Baris; Geneva University Hospital, Division of Cardiology, Faculty of Medicine Tango, Rodrigo; Geneva University Hospitals, Division of Primary Care Medicine and Community Health, Faculty of Medicine Nanchen, David; University of Lausanne, Department of Ambulatory and Community Medicine Matter, Christian; Universitat Zurich Medizinische Fakultat, Department of Cardiology Luescher, Thomas; Universitat Zurich Medizinische Fakultat, Department of Cardiology Windecker, Stephan; University Hospital Bern, Department of Cardiology Mach, François; Universite de Geneve Faculte de Medecine, Division of Cardiology Cornuz, Jacques; Lausanne University Hospital, Policlinique Médicale Universitaire Humair, Jean-Paul; Universite de Geneve Faculte de Medecine, Division of Primary Care Medicine and Community Health Rodondi, Nicolas; Inselspital Universitatsspital Bern, Department of General Internal Medicine
Primary Subject Heading:	Smoking and tobacco
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Smoking, PREVENTIVE MEDICINE, acute coronary syndrome, hospitalization, motivational interviewing

Uptake and efficacy of a systematic intensive smoking cessation intervention using motivational interviewing for smokers hospitalized for an acute coronary syndrome: A multicenter before-after study with parallel group comparisons.

Short title: Uptake and efficacy of a systematic smoking cessation intervention

Reto Auer, MD, MAS[1]; Baris Gencer, MD[2];Rodrigo Tango, MD[3]; David Nanchen, MD, MSc[1]; Christian M. Matter, MD[4]; Thomas Felix Lüscher, MD[4]; Stephan Windecker, MD[5]; François Mach, MD[2]; Jacques Cornuz, MD, MPH[1]; Jean-Paul Humair, MD, MPH[3]; Nicolas Rodondi, MD, MAS[6]

[1] Department of Ambulatory and Community Medicine, University of Lausanne, Lausanne, Switzerland; [2] Division of Cardiology, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland; [3] Division of Primary Care Medicine, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland; [4] Department of Cardiology, University Hospital Zurich, Zurich, Switzerland; [5] Department of Cardiology, University Hospital Bern, Bern, Switzerland; [6] Department of General Internal Medicine, Inselspital, Bern University Hospital, Bern, Switzerland

Corresponding author: Dr. Reto Auer, MD, MAS.
Department of Ambulatory Care and Community Health, University of Lausanne, Rue du Bugnon 44, 1011 Lausanne, Switzerland.
Phone: + 41 21 314 49 28. Fax: +41 21 314 48 93
Email: Reto.Auer@hospvd.ch

Word Count: Abstract: 314 words (300 max), Manuscript: 3731 (4000 max); 3 tables, 2 figure; 43 references.
1 Appendix: 2 tables, 1 figure.

Key words: Smoking; prevention; acute coronary syndrome; hospitalization; motivational interviewing

Preliminary results have been presented as an oral presentation during the meeting of the Society of Medical Decision Making (SMDM) in Baltimore, MD on October 23rd 2013 and at the

meeting of the European and Swiss Conference of Internal Medicine in Geneva (ESCIM) on May 15th, 2014.

Abstract

Objectives: To compare the uptake and efficacy of a proactive approach with a reactive approach to offer intensive smoking cessation intervention using motivational interviewing(MI).

Design: Before-after comparison in two academic hospitals with parallel comparisons in two control hospitals.

Setting: Academic hospitals in Switzerland.

Participants: Smokers hospitalized for an acute coronary syndrome(ACS).

Intervention: In the intervention hospitals during the intervention phase, a resident physician trained in MI systematically offered counseling to all smokers admitted for ACS, followed by four telephone counseling sessions over two months by a nurse trained in MI. In the observation phase, the in-hospital intervention was offered only to patients whose clinicians requested a smoking cessation intervention. In the control hospitals, no intensive smoking cessation intervention was offered.

Primary and secondary outcomes: The primary outcome was 1-week smoking abstinence(point prevalence) at 12 months. Secondary outcomes were the number of smokers who received the in-hospital smoking cessation intervention and the duration of the intervention.

Results: In the intervention centers during the intervention phase, 87% of smokers(N=193/225) received a smoking cessation intervention compared to 22% in the observational phase (p<0.001). Median duration of counseling was 50 minutes. During the intervention phase, 78% received a phone follow-up for a median total duration of 42 minutes in 4 sessions. Prescription of NRT at discharge increased from 18% to 58% in the intervention phase (Risk ratio: 3.3 (95%CI:2.4 to 4.3;p=<0.001). Smoking cessation at 12-month increased from 43% to 51% comparing the observation and intervention phases (Risk ratio(RR) =1.20, 95%CI:0.98-1.46;p=0.08; 97% with outcome assessment). In the control hospitals, the RR for quitting was 1.02 (95%CI:0.84-1.25;p=0.8, 92% with outcome assessment).

Conclusion: A proactive strategy offering intensive smoking cessation intervention based on motivational interviewing to all smokers hospitalized for ACS significantly increases the uptake of smoking cessation counseling and might increase smoking abstinence at 12 months.

Strengths and limitations of this study

- The study questions current guidelines who recommend that only motivated smokers should receive intensive smoking cessation counseling intervention.
- Four university centers were involved with two centers serving as a parallel comparison.
- Smoking cessation outcome assessed after 12-months in 97% of participants in the intervention centers.
- The weaker before-after design with parallel comparisons limits causal inference of the potential effects of the intervention.
- There were significant differences in attendance rates to cardiac rehabilitation and length of stay between the observation and intervention phase, limiting the interpretation of the findings.
- Participants received phone counseling after their hospital stay in the intervention phase, but not in the observation phase, thereby limiting the interpretation of the comparison between a proactive and reactive approach of offering a smoking cessation intervention on smoking cessation rates at 12 months.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in adults in the United States (US) and in Europe and smoking is the leading cause of CVD.[1] Smokers who quit after a myocardial infarction can expect a 36% reduction in CVD mortality over 2 years compared with continuing smokers.[2 3] In a meta-analysis of randomized controlled trials of smokers hospitalized for a CVD diagnosis, smoking cessation interventions started in the hospital and sustained in the ambulatory setting for at least 1 month after discharge, increased smoking cessation rates by more than 40%.[4 5]

While the effectiveness of smoking cessation counseling interventions and their components has been extensively studied, the optimal delivery of smoking cessation interventions has been less studied.[6 7] Current guidelines promote the use of the 5A's for the delivery of smoking cessation interventions where healthcare providers *assist* smokers willing to make a quit attempt after having *assessed* their "readiness to quit".[8 9] However, past negative experiences with healthcare workers, where smokers felt to be negatively judged because of their behavior, may impact their willingness to explore their habit with a counselor.[10-12] The Clinical Practice Guideline for Treating Tobacco Use and Dependence recommends the use of Motivational Interviewing (MI) with smokers who express low motivation to quit.[13] MI is a collaborative, person-centered guidance to elicit and strengthen motivation to change; MI could allow approach all smokers, regardless of their self-reported motivation to quit smoking.[14 15] While a recent study showed promising results on increasing the uptake of smoking cessation interventions when systematically identifying and assisting hospitalized smokers, 30% declined consent to participate in the study and an additional 30% of those offered behavioral support refused it.[16]

We aimed at testing the uptake and efficacy of a proactive approach compared to a reactive approach to offer intensive smoking cessation intervention using motivational interviewing (MI) to smokers hospitalized for an acute coronary syndrome (ACS) in two sites in a before-after comparison. We also aimed at making a parallel comparison of the smoking cessation rates of smokers hospitalized in

these intervention sites to the quit rates of smokers hospitalized in two other sites without intensive smoking cessation intervention throughout the study duration.

MATERIAL AND METHOD

STUDY POPULATION

The study population comprised smoking participants to the SPUM ACS cohort study; a national cohort of patients with acute coronary syndrome (ACS) conducted in four academic hospitals in Switzerland and registered at clinicaltrials.gov (NCT 01000701 and NCT 01075867). [17-19] Inclusion criteria were patients aged 18 years or older presenting with the principal diagnosis of ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) or unstable angina (UA), actively smoking at the time of inclusion and willing to participate in a clinical study including a follow-up exam at 12 months follow-up. Active smoking was defined as smoking one cigarette or more per day during the month preceding the hospital stay. Exclusion criteria were index revascularization with coronary artery bypass graft (CAGB), severe physical disability, inability to give consent (dementia), impossibility of returning for a follow-up clinical visit at 12 months and less than 1 year of life expectancy for non-cardiac reasons. Patients were followed at 12 months follow-up for assessment of smoking cessation outcomes (Figure 1). The observation phase was from August 2009 to October 2010 and the intervention phase from November 2010 to February 2012. The study includes 2 intervention sites (A and B) and 2 control sites (C and D). There are five major academic medical centers in Switzerland and four participated in the prospective cohort study of ACS patients.[17-19] The two intervention sites were chosen based on the existence of a team providing smoking cessation interventions to hospitalized smokers before the start of the study on a reactive basis. There was no random allocation of study sites into control and intervention sites. Detailed documentation of the flow of participants from the arrival to the emergency room for suspicion of ACS to the inclusion in the clinical follow-up study was performed in study site A (Appendix, online).

STUDY DESIGN

The study design is a multicenter before-after study with parallel group comparisons. We made two comparisons for smoking cessation outcomes at 12 months follow-up and process outcomes: a before-after comparison between observation and intervention phases in intervention sites A and B; a parallel group comparison between intervention (A and B) and control (C and D) sites in both observation and intervention phases.

STUDY PROTOCOL AND INTERVENTIONS

During the observation phase at the intervention sites (study sites A and B), the standard practice in place was that patients received information about the possibility of a dedicated smoking cessation intervention and clinicians in charge of patients could request a specialized smoking cessation intervention for hospitalized smokers through a simple phone call and after patient's agreement.[20 21] We called this approach a "reactive approach" to delivering smoking cessation interventions. In the intervention phase, a resident physician trained in MI identified all smokers included in the clinical follow-up study and systematically approached them to get permission to discuss their smoking habit. We called this approach a "systematic approach" to delivering smoking cessation interventions. There was no restriction on the duration of the interview and residents ended the discussion once they felt an increase in the resistance of the patients, if they were interrupted by competing care to patients, or if patients specifically asked the interview to end. Multiple MI sessions were allowed during the hospital stay and at the end of each session, resident systematically offered the possibility of additional consultations during the hospital stay provided the logistics were possible. In the intervention phase, residents also systematically asked patients at the end of the session if they accepted to be contacted by a study nurse after their hospital stay for four ambulatory telephone contacts. Study nurses systematically contacted by phone each patient at 2 days, 1 week, 1 month and 2 months after discharge from the acute care hospital.[4] Whenever possible, the nurse tried to meet all counseled smokers for a brief face-to-face encounter before discharge. In addition to training in tobacco cessation counseling and prescription of nicotine replacement therapy (NRT),[21] residents were trained in MI during 4 sessions of 4 hours over one month each separated

by one week before the intervention phase. To allow residents to adapt the interview to the patient's needs, we did not develop a detailed manual for directing the MI.[22] To minimize interference with the intervention, most data were collected during the inclusion of patients before the residents approached patients. If not already prescribed by the hospital care physician (HCP) in the ward, resident offered NRT and brochures on smoking cessation. Residents provided the HCP in charge of the patient with a brief summary of the intervention and recommendations for NRT and sent a medical report to the patient's primary care provider. Study nurses followed the same training in MI as the residents. NRT, which is not reimbursed in Switzerland, was available free of charge during the hospital stay, but were at the patients' charge in ambulatory care. In the control study sites (study site C and D), there was no dedicated smoking cessation intervention throughout the study duration and participants received minimal smoking cessation advice by hospital clinicians in charge of their care.

The study protocol was approved by the institutional review board of all participating centers; namely, the Ethics Committee on Clinical Research of the University of Lausanne, the Ethics Committee of the Department for Internal Medicine and Community Medicine of the University Hospital of Geneva, the Cantonal Ethics Committee (KEK) of the Canton of Bern, and the Cantonal Ethics Committee (KEK) of the Canton of Zurich. All patients provided written, informed consent.

COVARIATES

Current smoking status, age of smoking initiation and daily cigarettes consumption were assessed for all patients throughout the study duration in all sites during the inclusion process in the clinical study. In the intervention sites during the intervention phase, patients were given a brochure of questionnaire to be filled during the hospital stay.

Administrative (length of stay, discharge at home or direct transfer to a peripheral hospital or to cardiovascular rehabilitation (CR)), demographic (age, sex, race, education), medical (type of ACS (NSTEMI/UA and STEMI); previous coronary health disease (CHD)) data and processes of care were collected during the inclusion in the clinical follow-up study and completed after discharge. Attendance rate to CR and type of CR (ambulatory vs. hospital) were assessed from administrative data available at

discharge and from self-report during the ambulatory follow-up visit at one year. In Switzerland, health care providers organize CR during the hospital stay or provide patients with information to benefit from CR. Thus patients could be directly addressed to an inpatient CR facility or attend ambulatory CR in the outpatient setting. Quality indicators were based on cardiologic guidelines and included systematic collection of reason for non-prescription for preventive medication.[17]

OUTCOMES

The primary outcome for smoking cessation was 1-week smoking abstinence (point prevalence) at 12 months. At the time of inclusion, patients were informed that they would be asked about their smoking status during a visit at 12 months. Self-reported smoking cessation was biochemically confirmed by exhaled carbon monoxide levels (Micro Smokerlyser; Bedfont Scientific Ltd) at the 1-year follow-up visit in all sites.[23] Patients who did not come back at 12 months were contacted by phone or mail. We classified those with carbon monoxide levels of at least 10 ppm as current smokers. Secondary process outcomes were: the number of patients who received smoking cessation counseling, NRT at discharge and follow-up as well as the duration and number of interventions during the hospitalization and follow-up.

STATISTICAL ANALYSIS

Frequencies, means with standard deviations (SDs), medians with inter-quartile ranges (IQR) were used when appropriate, as were χ^2 tests, Fisher's exact test, Wilcoxon rank sum test and ANOVA for bivariate analyses. The primary analysis examined the point estimate and 95% confidence interval (CI) of the risk ratio for smoking cessation at 12 months between both phases in the intervention sites and using an intention-to-treat approach. The sample size calculation was based on an expected 10% absolute increase in smoking abstinence at 12 months in the two intervention centers. The 10% difference was based on a summary estimate of 11 previous RCTs identified in a systematic review and meta-analysis which included smokers hospitalized with CHD and tested the effect of a high intensity intervention with phone follow-up. [5 24-36] The summary quit rate over all these studies in the intervention groups was 45% and

31% in the control groups, thus an absolute risk difference of 14%. Using an α level of 0.05 and a power of 80%, and given the potential increase in abstinence due to the intervention in some smokers in the observation phase, we estimated that 400 patients had to be included in the intervention sites (sites A and B) over the entire study period to detect a 10% absolute difference in quit rates. Secondary analyses were a comparison of the smoking cessation rates at 12-months between both phases in the control study sites (study sites C and D) (Figure 2). The study was not powered to detect a significant difference between intervention and control sites over the observation and intervention phases. We also conducted stratified analyses by attendance to CR and education status (with or without university degree). We further tested the association between the presence and duration of counseling between phases using logistic regression models and Poisson logistic regression models. Statistical significance was set at 0.05. All analyses were performed using STATA version 12 (StataCorp, College Station, Texas).

RESULTS

STUDY POPULATION

Between August 2009 and February 2012, 616 patients admitted for ACS were included in the clinical follow-up study in site A, and 510 in site B. 458 (40%) were current smokers and included in the subsequent analyses (Figure 2 and Appendix Figure 1). At 12-month follow-up, smoking status was assessed in 97% while 15 participants had died (Figure 2 and Appendix Figure 1). In the study sites C and D, 192 smokers were included in the observation phase and 244 in the intervention phase (Figure 2 and Appendix Table 1). At one year follow-up, smoking status was obtained for 92% while 12 participants died.

Mean age of participants included in the intervention sites (study sites A and B) in the intervention phase was 55 years, 20% were women and 52% had been hospitalized for STEMI (Table 1). There were no significant differences in baseline characteristics between participants in observation and intervention phases, except for the longer stay of patients directly discharged home.

PROCESS OUTCOMES

In the intervention sites (study sites A and B), 22% percent of patients received intensive smoking cessation counseling during the observation phase compared to 87% in the intervention phase (Figure 2 and Table 2). Among the 13% who did not receive counseling in the intervention phase, 10% (n=24) were transferred to another facility or discharged home before the counselor could approach them; 2% (N=4) completely refused to discuss with counselor and 1% (N=2) had a major language barrier. The median duration of the intervention during the hospital stay was 50 minutes and did not significantly vary between both phases. During the intervention phase, 78% received a phone follow-up (90% of those receiving in-hospital counseling) for a median total duration of 42 minutes in 4 sessions. Prescription of NRT at discharge increased significantly from 18% to 58% in the intervention phase (Risk ratio: 3.3 (95% CI: 2.4 to 4.3; p=<0.001). Of those who received phone follow-ups in the intervention phase, 67% were prescribed NRT at discharge, but only 41% were still taking NRT at the first phone follow-up 2 days after discharge.

In the intervention sites, the proportion reporting having attended cardiac rehabilitation (CR) significantly increased during the intervention phase in the intervention sites from 58% to 73% (p<0.01). The proportion attending ambulatory CR compared to hospital-based CR increased from 55% in the observation phase to 67% in the intervention phase.

SMOKING ABSTINENCE AT 12-MONTHS

In the intervention sites, validated 12-months smoking abstinence increased from 43% during the observation phase to 51% in the intervention phase (RR 1.20; 95% CI: 0.98 to 1.46, p=0.08; absolute risk difference (ARD) 8%, Table 3). In the control sites, 47% quit smoking in the observation phase compared to 48% in the intervention phase (RR: 1.02 (95% CI:0.84 to 1.25;p=0.8; ARR 1%).

In exploratory stratified analyses comparing cessation rates in intervention sites between both phases, the apparent benefit was mostly seen in those not attending CR and those without university degree (Table 3).

DISCUSSION

In this multicenter study involving smokers hospitalized for an ACS, a systematic smoking cessation intervention sharply increased the number of patients exposed to motivational interviewing and nicotine replacement therapy. The median duration of counseling during the hospital stay was 50 minutes and did not vary between phases. Comparing observation to intervention phases, the smoking abstinence at one year increased from 43% to 51% (8% absolute difference in abstinence, p value 0.08). At sites without dedicated in-hospital smoking cessation intervention during the entire study period, no difference in smoking abstinence was observed. In subgroup analyses, the benefit of the systematic intervention appeared limited to smokers not attending CR and those with lower education level.

Murray et al. recently tested the effectiveness of systematically providing support to all identified smokers in a RCT randomizing medical wards in one medical center in the UK.[16] The systematic identification permitted to increase the offer of behavioral support from 46% to 100% of smokers and the acceptance of behavioral support from 29% to 70% of smokers. However, out of 1072 smokers identified on ward, 30% declined consent to participate in the study and an additional 30% of those offered behavioral support refused it. In our study, detailed analysis of the flow of participants until inclusion in the clinical study showed that 4% refused to enter the clinical follow-up study, followed by 2% who completely refused to open the discussion with the resident approaching them to start a motivational interview. The benefits of counseling all smokers regardless of their motivation to quit using MI had also previously been tested in a rigorously performed RCT in 1996-1997.[29] Out of 164 smokers with acute MI, 8 (5%) refused to participate in the smoking cessation intervention including follow-up at 6 months. The smoking cessation rate at one year was 34% in the observation group and 55% in the intervention group ($p<0.005$). However, the study was performed in a single study site and the rate attending CR was not provided and is expectedly lower than the rate in our population, thus limiting the comparison.

The sharp increase in uptake of the smoking cessation intervention highlights the effect of changes in the choice architecture described in behavioral economic theories. Setting the default option from an *opt-in* to an *opt-out* has been shown to be a powerful driver of uptake in interventions.[37 38] In the context of our study, the systematic offer of a smoking cessation intervention is similar to an *opt-out*

policy where patients ask not to have the intervention compared to the *opt-in* policy where patients or their caregivers specifically have to request a smoking cessation intervention.

In our study, the rate discharged to CR in the intervention sites increased from 58 to 73% between the observation and intervention phases. Given that CR includes smoking cessation counseling and support, it could be considered a follow-up intervention as recommended by guidelines and might be explained by higher attendance rate to CR.[4] However, in stratified analyses by attendance to CR, the benefit of the systematic smoking cessation intervention was mostly apparent among participants not attending CR. The systematic approach might permit to counsel those most at risk of lack of follow-up in the ambulatory care. The high attendance rate to CR overall in our study might explain the negative findings on smoking cessation rates over follow-up [39-42] Overall, attendance rates in the US range from 14% to up to 55%.[39-42] We based our sample size estimation on previous studies on smoking cessation after ACS where attendance rates to CR were expectedly lower. Unfortunately, we are unable to compare the attendance rates in our study to previous smoking cessation studies because previous studies included in the Cochrane systematic review and to the recent study by Murray et al. have not reported on rates of ambulatory CR. [5 16 24-36] Future studies should also better describe the concomitant interventions in the ambulatory care in order to facilitate the interpretation and translation of findings into clinical practice.

Our findings challenge the recommendation of allocating high intensity counseling only to those "willing to make a quit attempt" recommended in smoking cessation guidelines based on the 5A's framework.[9] According to MI, motivation occurs in the interpersonal context, which depends on the style used by counselors with smokers and may influence the acceptance rates of the intervention.[14] A previous rigorously performed RCT only including those willing to make a serious quit attempt was unable to show a benefit on smoking cessation.[27]

We found that the systematic smoking cessation intervention led to an increase in NRT prescription at discharge comparing the observation and intervention phase at the intervention study sites. However, the high cost of NRT after discharge, given that NRTs are not covered by health care insurances in the ambulatory setting in Switzerland, might explain the lower rate of participants still

taking NRT at the phone follow-up. Future studies should test the effect of removing potential financial barriers for using NRT after the hospital stay on smoking cessation outcomes.

Our study has limitations. The weaker before-after design with parallel group comparisons does limit the causal inferences from our results. Participants received phone counseling after their hospital stay in the intervention phase, but not in the observation phase. A systematic review on the benefits of smoking cessation intervention for hospitalized smokers suggested that only interventions including a follow-up intervention in the ambulatory setting have shown an effect on smoking cessation outcomes at 12 months. This strongly limits the comparison of smoking cessation rates between the observation and intervention phase as it is unclear if the study tests the efficacy of a lower intensity intervention in the observational phase to a high intensity intervention in the intervention phase or if the study compares a proactive vs. reactive approach of offering smoking cessation intervention. We urge for careful interpretation of the results given differences in covariates between participants included in the observation phase and intervention phase (Table1). In the participants included in the intervention sites, we found a significant increase in length of stay in addition to the previously discussed increase in attendance rates to CR between the observation and intervention phase. Smoking cessation rates at 12 months were based on self-report. We validated the 1-week smoking abstinence by measurement of exhaled carbon monoxide whenever possible.[23] However, misclassification of the smoking cessation outcome is still possible. Rates of referral to CR were based on information at discharge and self-report at one year follow-up. The reliability of self-reported CR referral has been validated in patients after an ACS in Canada and used recently to report on enrollment rate to CR in the US.[42 43] Exploratory subgroup analyses on the differential effect of education level and attendance to CR should be carefully interpreted, as these analyses were defined *a posteriori.* Patients were included in 4 high quality academic hospitals and results may not apply to different settings. The MI sessions were not recorded and the quality of interactions can therefore not be directly assessed. We did not develop a detailed manual for directing the MI. A prior meta-analysis suggested that clinical trials in which MI was delivered without a manual had showed better treatment outcomes.[22]

CONCLUSIONS

In summary, we found that a systematic smoking cessation intervention using motivational interviewing for smokers hospitalized for an ACS compared to a reactive strategy relying on busy healthcare providers to contact a specialized smoking cessation consultation permitted to sharply increase the number of patients counseled. In exploratory subgroup analyses of data collected in one study center, patients with lower education level and not attending cardiac rehabilitation appeared to be more likely to benefit from the intervention. The comparison of smoking cessation rates at 12 months between the observation and intervention phases are limited by the study design and showed a trend towards an increase in smoking cessation rates. Future studies should evaluate the benefit of systematically exposing smokers to a smoking cessation intervention based on motivation interviewing.

CONTRIBUTORSHIP STATEMENT

All authors do meet the ICMJE criteria for authorship:

- Conception or design of the work or the acquisition: RA, BG, RT, CMM, TFL, SW, FM, JC, JPH, NR
- Analysis, or interpretation of data for the work: RA, BG, DN, RT, JC, JPH, NR
- Drafted the work: RA, BG, RT, JPH, NR
- Revising it critically for important intellectual content: DN, CMM, TFL, SW, FM, JC
- Final approval of the version to be published: RA, BG, RT, DN, CMM, TFL, SW, FM, JC, JPH, NR
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: RA, BG, RT, DN, CMM, TFL, SW, FM, JC, JPH, NR

COMPETING INTERESTS

The following authors have the following conflicts. Dr Lüscher reports receiving research grants to the institution from Abbott, Biosensors, Biotronik, Boston Scientific, and Medtronic, and consultant payments from AstraZeneca, Boehringer Ingelheim, Bayer, Merck, and Pfizer. Dr Matter reports receiving grants from MSD, Eli Lilly, AstraZeneca, and Bayer; expert testimony from MSD; payment for lectures from MSD, AstraZeneca, and Roche; and having patents from Mabimmune, CH. Dr Windecker reports receiving research contracts to the institution from Abbott, Biotronik, Boston Scientific, Biosensors, Cordis, Medtronic, St. Jude Medical and speaker fees from: Abbott, Biotronik, Boston Scientific, Biosensors, Medtronic, Eli Lilly, Astra Zeneca. All other authors have declared that no competing interests exist.

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DATA SHARING STATEMENT

Primary data on analyses reported in the manuscript are available upon written request.

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Table 1 Baseline characteristics of participants hospitalized for an acute coronary syndrome in 2 academic hospitals (intervention sites, study sites A and B) in Switzerland in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Intervention sites (A and B)		p-value
	Observation phase N=233	Intervention phase N=225	
Demographic variables			
Age, y (mean ± SD)	57 ± 11	55 ± 11	0.06
Female, N (%)	46 (20)	45 (20)	0.9
Education, less than university degree, N (%)*	203 (88)	185 (83)	0.1
Living alone	68 (29)	55 (24)	0.3
Working status, employed, N (%)	136 (59)	143 (64)	0.3
Previous CHD, N (%)	46 (20)	37 (16)	0.3
Smoking variables			
– Cigarettes per day (median, Q1, Q3)	20 (10, 25)	20 (10, 25)	0.5
– Age at smoking start (mean ± SD)	19 ± 6	18 ± 6	0.6
Clinical variables			
ACS-type:			
– STEMI (vs. NSTEMI/UA), N (%)	121 (52)	116 (52)	0.9
Hospital stay			
Length of stay, median (Q1,Q3), in days			
– For patients directly discharged home	5 (3,6)	5 (4,7)	0.04
– For patients transferred to peripheral hospital	1 (0.5, 1)	1 (0.5, 2)	0.3
Treatment at discharge			
Destination at discharge, N (%)			
– Home	148 (64)	138 (61)	0.3
– Direct transfer to cardiac rehabilitation	47 (20)	39 (17)	
– Transfer to peripheral hospital	36 (16)	47 (21)	
Prescription of all recommended drug therapy at Discharge†	222 (95)	216 (96)	0.6
Attendance to cardiovascular rehabilitation assessed at discharge and 12 months follow-up (N, %)‡	136 (58)	163 (73)	<0.01
– Ambulatory vs. stationary§	74 (56)	109 (67)	0.05

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; STEMI: ST-segment elevation myocardial infarction

* 6 participants with missing information on education status or who refused to disclose their education status.

† Concomitant prescription at discharge unless contra-indicated or not indicated for aspirin, clopidogrel/prasugrel or ticagrelor if PCI-stent treatment, beta-blocker, statin, ACEI if LVEF ≤40%. When participants transferred to peripheral hospital, beta-blocker and ACEI/ATII coded as not applicable.

‡ Both ambulatory and stationary cardiovascular rehabilitation are covered after an ACS in Switzerland. Attendance rate computed using data on direct referral to in-patient CR and on self-reported attendance at one year follow-up in order to capture information on those directly transferred to a stationary CR and those attending CR in the ambulatory setting.

§ 3 participants with missing information on type of CR.

Table 2 Process outcomes in intervention sites (study sites A and B) comparing smokers hospitalized in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Observation phase N=233	Intervention phase N=225	Risk ratio (95% CI) or coefficient*	p-value†
- Received intensive counseling during hospital stay (N,%)	52 (22)	193 (87)‡	3.9 (3.0 to 5.0)	<0.001
- Duration of in-hospital counseling per participant in min (median, Q1, Q3)	45 (45, 48)	50 (35,60)	2.6 (-3.7 to 8.7)	0.4
- Number of in-hospital counseling sessions (median, min, max)	1 (1,2)	1 (1,3)	0.15 (-0.15 to 0.45)	0.3
- Received phone follow-up (N,%)	NA	175 (78)	-	-
- Duration of each phone follow-up in min (median, Q1,Q3)	NA	11 (8,17)	-	-
- Total duration of phone follow-up in min (median, Q1,Q3)	NA	42 (30,61)	-	-
- Number of phone follow-ups (median, Q1,Q3)	NA	4 (3,4)	-	-
- Prescribed nicotine replacement therapy at discharge (N,%)	42 (18)	132 (59)	3.3 (2.4 to 4.3)	<0.001

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; min: minutes; NA: non-applicable; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; STEMI: ST-segment elevation myocardial infarction

* Risk ratio and 95% CI calculated for dichotomous outcomes. Coefficients for duration of counseling obtained by linear regression. For number of counseling sessions, coefficient obtained by Poisson logistic regression model.

†P-value calculated by χ^2 for dichotomous outcomes (e.g. proportion receiving counseling) and linear regression for duration of encounters

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

Table 3 Smoking cessation outcomes at 12 months follow-up comparing participants in observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012) at 4 university sites in Switzerland. 7-day point prevalence abstinence, validated by exhaled carbon monoxide (CO). *

	N total for analysis	% quit in obs. phase / interv. phase	Risk ratio (95% CI)	Absolute risk difference	p-value
Main outcome					
- Intervention sites (study sites A and B) (n=458)	443	42.0/50.2	1.20 (0.98 to 1.47)	8.3%	0.08
- Control sites (study sites C and D) (n=436)	428	46.8/47.8	1.02 (0.84 to 1.25)	1.1%	0.8
Secondary analyses for participants in intervention sites (study sites A and B) (n=440)					
- Cardiac rehabilitation					
- With cardiac rehabilitation	296	51.5/53.7	1.04 (0.84 to 1.30)	2.2%	0.7
- No cardiac rehabilitation	143	29.5/43.6	1.48 (0.95 to 2.30)	14.1%	0.09
- Education status					
- University degree	64	59.3/51.3	0.87 (0.56 to 1.34)	-7.9%	0.5
- No university degree	371	40.7/50.8	1.24 (1.0 to 1.6)	10.1%	0.05

N, number of participants; CI: confidence interval.

* Participants lost to follow-up or who withdrew consent (n=11, 97% follow-up rate) considered as smokers for these analyses. Participants who died (n=15) during follow-up excluded from these analyses. Validated smoking cessation by CO in 68% of quitters in intervention sites and 40% of quitters in control sites. 2 participants reported having quit during last 7 days despite a CO level of more than 10 ppm considered as smokers.

Figure Legends

Figure 1. Study design. Before-after intervention with parallel group comparisons: We compared the 7-days point smoking prevalence at 12 months follow-up between participants included in the reactive vs. the proactive intervention phases in intervention sites (site A and B). We also compared the 7-days point smoking prevalence at 12 months follow-up between participants included during the same period in observation sites (sites C and D).

Figure 2. Flow-chart of participants included in the intervention sites (site A and B) and control sites (sites C and D) during observation phase (Aug. 2009 to Oct. 2010) and intervention phase (Nov. 2010 to Feb. 2012). Intensive smoking cessation counseling was offered during the observation phase in the observation upon request and systematically during the intervention phase. Phone follow-up was only offered in the intervention phase in the intervention sites (see Methods).

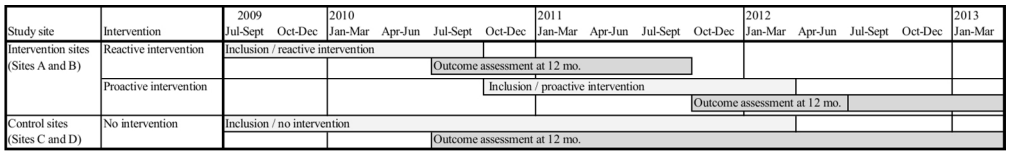


Figure 1. Study design. Before-after intervention with parallel group comparisons: We compared the 7-days point smoking prevalence at 12 months follow-up between participants included in the reactive vs. the proactive intervention phases in intervention sites (site A and B). We also compared the 7-days point smoking prevalence at 12 months follow-up between participants included during the same period in observation sites (sites C and D).
130x18mm (300 x 300 DPI)

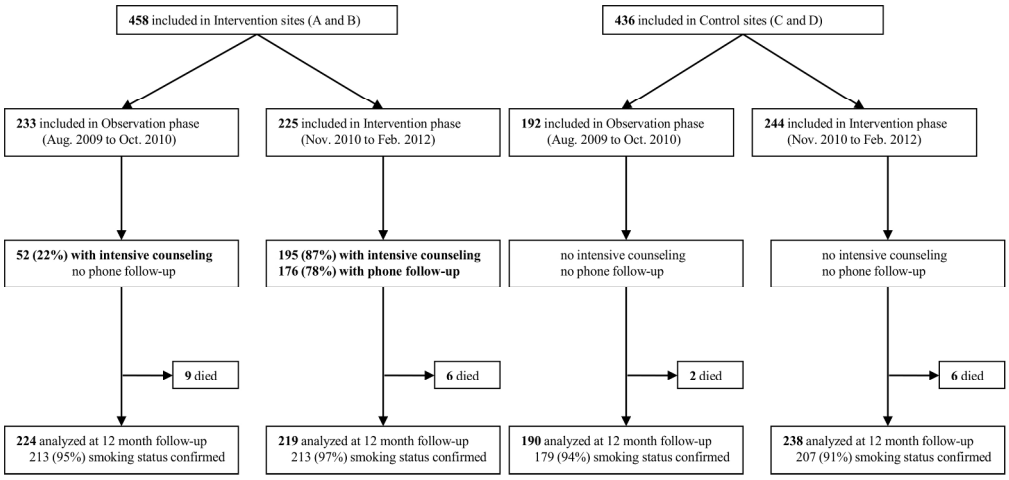


Figure 2. Flow-chart of participants included in the intervention sites (site A and B) and control sites (sites C and D) during observation phase (Aug. 2009 to Oct. 2010) and intervention phase (Nov. 2010 to Feb. 2012). Intensive smoking cessation counseling was offered during the observation phase in the observation upon request and systematically during the intervention phase. Phone follow-up was only offered in the intervention phase in the intervention sites (see Methods).
214x100mm (300 x 300 DPI)

ONLINE DATA SUPPLEMENT

Efficacy of systematic intensive smoking cessation intervention after acute coronary syndromes

Corresponding author: Dr. Reto Auer, MD, MAS.

Department of Ambulatory Care and Community Health,

University of Lausanne, Switzerland.

Phone: + 41 21 314 49 28. Fax: +41 21 314 48 93

Email: Reto.Auer@hospvd.ch

Appendix Table 1 Baseline characteristics of participants hospitalized for an acute coronary syndrome in 2 academic hospitals in Switzerland in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Control sites		p-value
	Observation phase N=192	Intervention phase N=244	
Demographic variables			
Age, y (mean ± SD)	57 ± 11	57 ± 11	0.9
Female, N (%)	36 (19)	31 (13)	0.1
Education, less than university degree, N (%)[a]	151 (89)	196 (93)	0.1
Living alone	41 (22)	50 (21)	0.8
Working status, employed, N (%)	124 (68)	158 (69)	0.7
Previous CHD, N (%)	19 (10)	28 (12)	0.6
Smoking variables			
– Cigarettes per day (median, Q1, Q3)	20 (10, 20)	20 (10, 25)	0.5
– Age at smoking start (mean ± SD)	21 ± 8	21 ± 7	0.7
Clinical variables			
ACS-type:			
– STEMI (vs. NSTEMI/UA), N (%)[b]	156 (81)	195 (80)	0.7
Hospital stay			
Length of stay, median (Q1,Q3), in days			
– For patients directly discharged home	3 (2,4)	2 (1,4)	0.01
– For patients transferred to peripheral hospital	1 (0.5, 1.5)	1 (0.5, 1.5)	07
Treatment at discharge			
Destination at discharge, N (%)			
– Home	38 (20)	62 (25)	
– Direct transfer to cardiac rehabilitation	7 (4)	19 (8)	0.06
– Transfer to peripheral hospital	145 (76)	157 (64)	
Prescription of all recommended drug therapy at discharge[c]	183 (96)	226 (94)	0.4
Attendance to cardiovascular rehabilitation	137 (72)	172 (72)	1.0

assessed at discharge and 12 months follow-up (N, %)[d]			
– Ambulatory vs. stationary[e]	98 (73)	112 (66)	0.2

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; SD: standard deviation; STEMI: ST-segment elevation myocardial infarction

[a]56 participants with missing information on education status or who refused to disclose their education status.

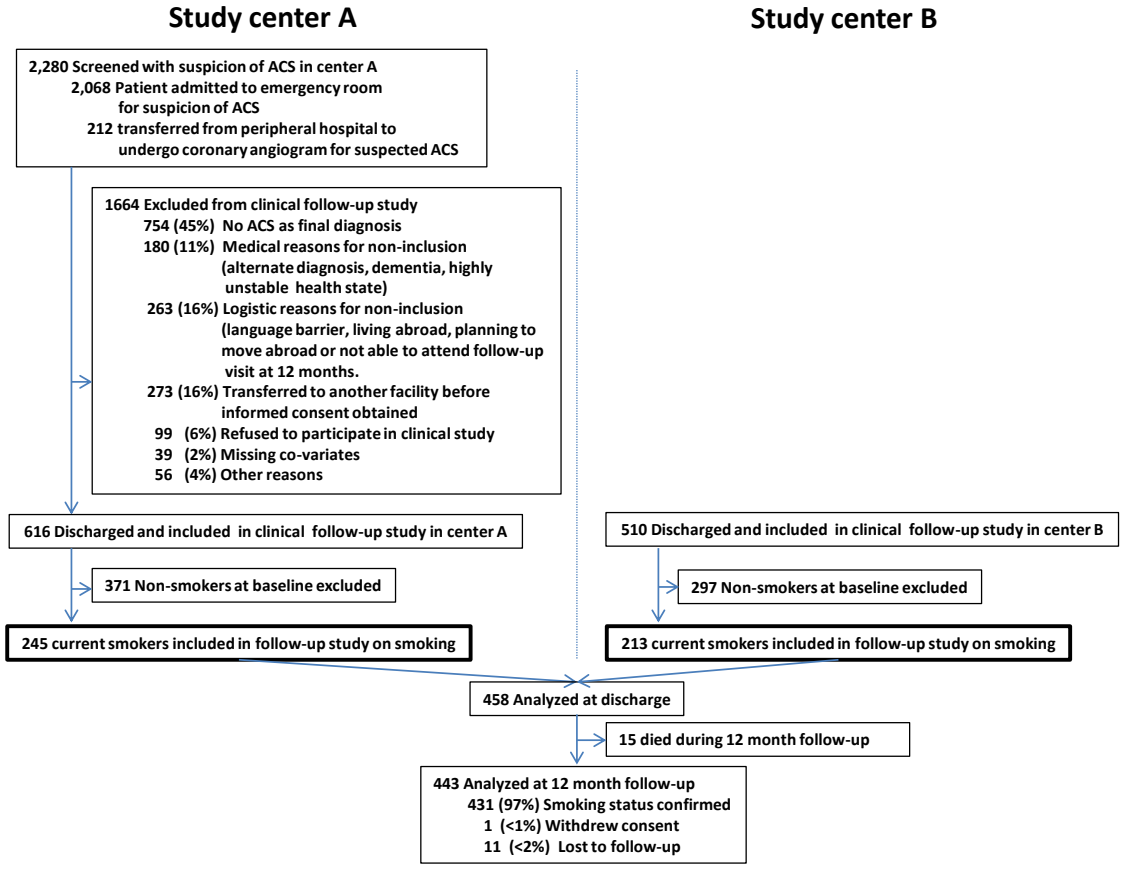
[b] Restriction to STEMI participants in one center, as only STEMI were systematically included in cardiac registry.

[c] Concomitant prescription at discharge unless contra-indicated or not indicated for aspirin, clopidogrel/prasugrel or ticagrelor if PCI-stent treatment, beta-blocker, statin, ACEI if LVEF $\leq$40%. When participants transferred to peripheral hospital, beta-blocker and ACEI/ATII coded as not applicable.

[d] Both ambulatory and stationary cardiovascular rehabilitation are covered after an ACS in Switzerland. Attendance rate computed using data on direct referral to in-patient CR and on self-reported attendance at one year follow-up in order to capture information on those directly transferred to a stationary CR and those attending CR in the ambulatory setting.

[e] 3 missing on type of CR in ambulatory setting

Appendix Figure 1. Flow of study participants in the two intervention sites. Detailed data on selection of participants from arrival to the emergency room to final inclusion was performed in one site.



Abbreviation: ACS: acute coronary syndrome

Appendix References

1. Chouinard MC, Robichaud-Ekstrand S. The effectiveness of a nursing inpatient smoking cessation program in individuals with cardiovascular disease. Nurs Res. 2005;54(4):243-54.
2. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. J Consult Clin Psychol. 1983;51(3):390-5.

Appendix Table 2 STROBE Statement – Filled Checklist

	Item no	Recommendation	Done	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	√	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√,	3
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√	5
Objectives	3	State specific objectives, including any prespecified hypotheses	√, NA	5
Methods				
Study design	4	Present key elements of study design early in the paper	√	7-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√	7, see also references listed in the methods
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	√	7 and 10, Appendix Table and Figure 1 and 2
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√	9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√	9-10
Bias	9	Describe any efforts to address potential sources of bias	√	10-11
Study size	10	Explain how the study size was arrived at	√	10-11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√	10-11

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	√	10-11
		(*b*) Describe any methods used to examine subgroups and interactions	√	10-11
		(*c*) Explain how missing data were addressed	√	11
		(*d*) If applicable, explain how loss to follow-up was addressed	√	10-11
		(*e*) Describe any sensitivity analyses	√	11
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	√	8, eMethods
		(b) Give reasons for non-participation at each stage	√	7,8, Appendix Figure, Appendix Table 1
		(c) Consider use of a flow diagram	√,	Appendix Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	√	11, Table 1 and Appendix Table 1
		(b) Indicate number of participants with missing data for each variable of interest	√	11, 12, Table 1
		(c) Summarise follow-up time (eg, average and total amount)	√	11-12
Outcome data	15*	Report numbers of outcome events or summary measures over time	√	11-12, Figure 2, Table 2 and 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	√	12, Table 3
		(*b*) Report category boundaries when continuous variables were categorized	-	-

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√	12, Table 3
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√	12, Table 3
Discussion				
Key results	18	Summarise key results with reference to study objectives	√	11-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√	13-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√	13-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	√	14-16
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Uptake and efficacy of a systematic intensive smoking cessation intervention using motivational interviewing for smokers hospitalized for an acute coronary syndrome: A multicenter before-after study with parallel group comparisons.

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Article Type:	Research
Date Submitted by the Author:	13-Jun-2016
Complete List of Authors:	Auer, Reto; Universite de Lausanne, Department of Community Health and Ambulatory Care; University of Bern, Institute of Primary Health Care (BIHAM) Gencer, Baris; Geneva University Hospital, Division of Cardiology, Faculty of Medicine Tango, Rodrigo; Geneva University Hospitals, Division of Primary Care Medicine and Community Health, Faculty of Medicine Nanchen, David; University of Lausanne, Department of Ambulatory and Community Medicine Matter, Christian; Universitat Zurich Medizinische Fakultat, Department of Cardiology Luescher, Thomas; Universitat Zurich Medizinische Fakultat, Department of Cardiology Windecker, Stephan; University Hospital Bern, Department of Cardiology Mach, François; Universite de Geneve Faculte de Medecine, Division of Cardiology Cornuz, Jacques; Lausanne University Hospital, Policlinique Médicale Universitaire Humair, Jean-Paul; Universite de Geneve Faculte de Medecine, Division of Primary Care Medicine and Community Health Rodondi, Nicolas; Inselspital Universitatsspital Bern, Department of General Internal Medicine; University of Bern, Institute of Primary Health Care (BIHAM)
Primary Subject Heading:	Smoking and tobacco
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Smoking, PREVENTIVE MEDICINE, acute coronary syndrome, hospitalization, motivational interviewing

Uptake and efficacy of a systematic intensive smoking cessation intervention using motivational interviewing for smokers hospitalized for an acute coronary syndrome: A multicenter before-after study with parallel group comparisons.

Short title: Uptake and efficacy of a systematic smoking cessation intervention

Reto Auer, MD, MAS[1,2]; Baris Gencer, MD[3];Rodrigo Tango, MD[4]; David Nanchen, MD, MSc[1]; Christian M. Matter, MD[5]; Thomas Felix Lüscher, MD[5]; Stephan Windecker, MD[6]; François Mach, MD[3]; Jacques Cornuz, MD, MPH[1]; Jean-Paul Humair, MD, MPH[4]; Nicolas Rodondi, MD, MAS[2,6]

[1] Department of Ambulatory and Community Medicine, University of Lausanne, Lausanne, Switzerland; [2] Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland; [3] Division of Cardiology, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland; [4] Division of Primary Care Medicine, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland; [5] Department of Cardiology, University Hospital Zurich, Zurich, Switzerland; [6] Department of Cardiology, University Hospital Bern, Bern, Switzerland; [7] Department of General Internal Medicine, Inselspital, Bern University Hospital, Bern, Switzerland

Corresponding author: Dr. Reto Auer, MD, MAS.
Department of Ambulatory Care and Community Health, University of Lausanne, Rue du Bugnon 44, 1011 Lausanne, Switzerland and Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland
Phone: + 41 21 314 49 28. Fax: +41 21 314 48 93
Email: Reto.Auer@hospvd.ch

Word Count: Abstract: 314 words (300 max), Manuscript: 3731 (4000 max); 3 tables, 2 figure; 43 references.
1 Appendix: 2 tables, 1 figure.

Key words: Smoking; prevention; acute coronary syndrome; hospitalization; motivational interviewing

Preliminary results have been presented as an oral presentation during the meeting of the Society of Medical Decision Making (SMDM) in Baltimore, MD on October 23rd 2013 and at the meeting of the European and Swiss Conference of Internal Medicine in Geneva (ESCIM) on May 15th, 2014.

Abstract

Objectives: To compare the efficacy of a proactive approach with a reactive approach to offer intensive smoking cessation intervention using motivational interviewing(MI).

Design: Before-after comparison in two academic hospitals with parallel comparisons in two control hospitals.

Setting: Academic hospitals in Switzerland.

Participants: Smokers hospitalized for an acute coronary syndrome(ACS).

Intervention: In the intervention hospitals during the intervention phase, a resident physician trained in MI systematically offered counseling to all smokers admitted for ACS, followed by four telephone counseling sessions over two months by a nurse trained in MI. In the observation phase, the in-hospital intervention was offered only to patients whose clinicians requested a smoking cessation intervention. In the control hospitals, no intensive smoking cessation intervention was offered.

Primary and secondary outcomes: The primary outcome was 1-week smoking abstinence(point prevalence) at 12 months. Secondary outcomes were the number of smokers who received the in-hospital smoking cessation intervention and the duration of the intervention.

Results: In the intervention centers during the intervention phase, 87% of smokers(N=193/225) received a smoking cessation intervention compared to 22% in the observational phase (p<0.001). Median duration of counseling was 50 minutes. During the intervention phase, 78% received a phone follow-up for a median total duration of 42 minutes in 4 sessions. Prescription of NRT at discharge increased from 18% to 58% in the intervention phase (Risk ratio: 3.3 (95%CI:2.4 to 4.3;p=<0.001). Smoking cessation at 12-month increased from 43% to 51% comparing the observation and intervention phases (Risk ratio(RR) =1.20, 95%CI:0.98-1.46;p=0.08; 97% with outcome assessment). In the control hospitals, the RR for quitting was 1.02 (95%CI:0.84-1.25;p=0.8, 92% with outcome assessment).

Conclusion: A proactive strategy offering intensive smoking cessation intervention based on motivational interviewing to all smokers hospitalized for ACS significantly increases the uptake of smoking cessation counseling and might increase smoking abstinence at 12 months.

Strengths and limitations of this study

- The study questions current guidelines who recommend that only motivated smokers should receive intensive smoking cessation counseling intervention.
- Four university centers were involved with two centers serving as a parallel comparison.
- Smoking cessation outcome assessed after 12-months in 97% of participants in the intervention centers.
- The weaker before-after design with parallel comparisons limits causal inference of the potential effects of the intervention.
- There were significant differences in attendance rates to cardiac rehabilitation and length of stay between the observation and intervention phase, limiting the interpretation of the findings.
- Participants received phone counseling after their hospital stay in the intervention phase, but not in the observation phase, thereby inherently limiting the interpretation of the comparison between a proactive and reactive approach of offering a smoking cessation intervention on smoking cessation rates at 12 months.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in adults in the United States (US) and in Europe and smoking is the leading cause of CVD.[1] Smokers who quit after a myocardial infarction can expect a 36% reduction in CVD mortality over 2 years compared with continuing smokers.[2 3] In a meta-analysis of randomized controlled trials of smokers hospitalized for a CVD diagnosis, smoking cessation interventions started in the hospital and sustained in the ambulatory setting for at least 1 month after discharge, increased smoking cessation rates by more than 40%.[4 5]

While the effectiveness of smoking cessation counseling interventions and their components has been extensively studied, the optimal delivery of smoking cessation interventions has been less studied.[6 7] Current guidelines promote the use of the 5A's for the delivery of smoking cessation interventions where healthcare providers *assist* smokers willing to make a quit attempt after having *assessed* their "readiness to quit".[8 9] However, past negative experiences with healthcare workers, where smokers felt to be negatively judged because of their behavior, may impact their willingness to explore their habit with a counselor.[10-12] The Clinical Practice Guideline for Treating Tobacco Use and Dependence recommends the use of Motivational Interviewing (MI) with smokers who express low motivation to quit.[13] MI is a collaborative, person-centered guidance to elicit and strengthen motivation to change; MI could allow approach all smokers, regardless of their self-reported motivation to quit smoking.[14 15] While a recent study showed promising results on increasing the uptake of smoking cessation interventions when systematically identifying and assisting hospitalized smokers, 30% declined consent to participate in the study and an additional 30% of those offered behavioral support refused it.[16]

Our primary aim was to test the the efficacy of a proactive approach compared to a reactive approach to offer intensive smoking cessation intervention using motivational interviewing (MI) to smokers hospitalized for an acute coronary syndrome (ACS) in two sites in a before-after comparison. We also aimed at making a parallel comparison of the smoking cessation rates of smokers hospitalized in

these intervention sites to the quit rates of smokers hospitalized in two other sites without intensive smoking cessation intervention throughout the study duration.

MATERIAL AND METHOD

STUDY POPULATION

The study population comprised smoking participants to the SPUM ACS cohort study; a national cohort of patients with acute coronary syndrome (ACS) conducted in four academic hospitals in Switzerland and registered at clinicaltrials.gov (NCT 01000701 and NCT 01075867). [17-19] Inclusion criteria were patients aged 18 years or older presenting with the principal diagnosis of ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) or unstable angina (UA), actively smoking at the time of inclusion and willing to participate in a clinical study including a follow-up exam at 12 months follow-up. Active smoking was defined as smoking one cigarette or more per day during the month preceding the hospital stay. Exclusion criteria were index revascularization with coronary artery bypass graft (CAGB), severe physical disability, inability to give consent (dementia), impossibility of returning for a follow-up clinical visit at 12 months and less than 1 year of life expectancy for non-cardiac reasons. Patients were followed at 12 months follow-up for assessment of smoking cessation outcomes (Figure 1). The observation phase was from August 2009 to October 2010 and the intervention phase from November 2010 to February 2012. The study includes 2 intervention sites (A and B) and 2 control sites (C and D). There are five major academic medical centers in Switzerland and four participated in the prospective cohort study of ACS patients.[17-19] The two intervention sites were chosen based on the existence of a team providing smoking cessation interventions to hospitalized smokers before the start of the study on a reactive basis. There was no random allocation of study sites into control and intervention sites. Detailed documentation of the flow of participants from the arrival to the emergency room for suspicion of ACS to the inclusion in the clinical follow-up study was performed in study site A (Appendix, online).

STUDY DESIGN

The study design is a multicenter before-after study with parallel group comparisons. We made two comparisons for smoking cessation outcomes at 12 months follow-up and process outcomes: a before-after comparison between observation and intervention phases in intervention sites A and B; a parallel group comparison between intervention (A and B) and control (C and D) sites in both observation and intervention phases.

STUDY PROTOCOL AND INTERVENTIONS

During the observation phase at the intervention sites (study sites A and B), the standard practice in place was that patients received information about the possibility of a dedicated smoking cessation intervention and clinicians in charge of patients could request a specialized smoking cessation intervention for hospitalized smokers through a simple phone call and after patient's agreement.[20 21] We called this approach a "reactive approach" to delivering smoking cessation interventions. In the intervention phase, a resident physician trained in MI identified all smokers included in the clinical follow-up study and systematically approached them to get permission to discuss their smoking habit. We called this approach a "systematic approach" to delivering smoking cessation interventions. There was no restriction on the duration of the interview and residents ended the discussion once they felt an increase in the resistance of the patients, if they were interrupted by competing care to patients, or if patients specifically asked the interview to end. Multiple MI sessions were allowed during the hospital stay and at the end of each session, resident systematically offered the possibility of additional consultations during the hospital stay provided the logistics were possible. While the in-hospital counseling intervention was the same in the observation and in the intervention phase, residents also systematically suggested to patients to be contacted by a study nurse after their hospital stay for four ambulatory telephone contacts during the intervention phase, which was not done in the observation phase. Study nurses systematically contacted by phone each patient at 2 days, 1 week, 1 month and 2 months after discharge from the acute care hospital.[4] Whenever possible, the nurse tried to meet all counseled smokers for a brief face-to-face encounter before discharge. In addition to training in tobacco cessation counseling and prescription of

nicotine replacement therapy (NRT),[21] residents were trained in MI during 4 sessions of 4 hours over one month each separated by one week before the intervention phase. To allow residents to adapt the interview to the patient's needs, we did not develop a detailed manual for directing the MI.[22] To minimize interference with the intervention, most data were collected during the inclusion of patients before the residents approached patients. If not already prescribed by the hospital care physician (HCP) in the ward, resident offered NRT and brochures on smoking cessation. Residents provided the HCP in charge of the patient with a brief summary of the intervention and recommendations for NRT and sent a medical report to the patient's primary care provider. Study nurses followed the same training in MI as the residents. NRT, which is not reimbursed in Switzerland, was available free of charge during the hospital stay, but were at the patients' charge in ambulatory care. In the control study sites (study site C and D), there was no dedicated smoking cessation intervention throughout the study duration and participants received minimal smoking cessation advice by hospital clinicians in charge of their care.

The study protocol was approved by the institutional review board of all participating centers; namely, the Ethics Committee on Clinical Research of the University of Lausanne, the Ethics Committee of the Department for Internal Medicine and Community Medicine of the University Hospital of Geneva, the Cantonal Ethics Committee (KEK) of the Canton of Bern, and the Cantonal Ethics Committee (KEK) of the Canton of Zurich. All patients provided written, informed consent.

COVARIATES

Current smoking status, age of smoking initiation and daily cigarettes consumption were assessed for all patients throughout the study duration in all sites during the inclusion process in the clinical study. In the intervention sites during the intervention phase, patients were given a brochure of questionnaire to be filled during the hospital stay.

Administrative (length of stay, discharge at home or direct transfer to a peripheral hospital or to cardiovascular rehabilitation (CR)), demographic (age, sex, race, education), medical (type of ACS (NSTEMI/UA and STEMI); previous coronary health disease (CHD)) data and processes of care were collected during the inclusion in the clinical follow-up study and completed after discharge. Attendance

rate to CR and type of CR (ambulatory vs. hospital) were assessed from administrative data available at discharge and from self-report during the ambulatory follow-up visit at one year. In Switzerland, health care providers organize CR during the hospital stay or provide patients with information to benefit from CR. Thus patients could be directly addressed to an inpatient CR facility or attend ambulatory CR in the outpatient setting. Quality indicators were based on cardiologic guidelines and included systematic collection of reason for non-prescription for preventive medication.[17]

OUTCOMES

The primary outcome for smoking cessation was 1-week smoking abstinence (point prevalence) at 12 months. At the time of inclusion, patients were informed that they would be asked about their smoking status during a visit at 12 months. Self-reported smoking cessation was biochemically confirmed by exhaled carbon monoxide levels (Micro Smokerlyser; Bedfont Scientific Ltd) at the 1-year follow-up visit in all sites.[23] Patients who did not come back at 12 months were contacted by phone or mail. We classified those with carbon monoxide levels of at least 10 ppm as current smokers. Secondary process outcomes were: the number of patients who received smoking cessation counseling, NRT at discharge and follow-up as well as the duration and number of interventions during the hospitalization and follow-up.

STATISTICAL ANALYSIS

Frequencies, means with standard deviations (SDs), medians with inter-quartile ranges (IQR) were used when appropriate, as were χ^2 tests, Fisher's exact test, Wilcoxon rank sum test and ANOVA for bivariate analyses. The primary analysis examined the point estimate and 95% confidence interval (CI) of the risk ratio for smoking cessation at 12 months between both phases in the intervention sites and using an intention-to-treat approach. The sample size calculation was based on an expected 10% absolute increase in smoking abstinence at 12 months in the two intervention centers. The 10% difference was based on a summary estimate of 11 previous RCTs identified in a systematic review and meta-analysis which included smokers hospitalized with CHD and tested the effect of a high intensity intervention with phone

follow-up. [5 24-36] The summary quit rate over all these studies in the intervention groups was 45% and 31% in the control groups, thus an absolute risk difference of 14%. Using an α level of 0.05 and a power of 80%, and given the potential increase in abstinence due to the intervention in some smokers in the observation phase, we estimated that 400 patients had to be included in the intervention sites (sites A and B) over the entire study period to detect a 10% absolute difference in quit rates. Secondary analyses were a comparison of the smoking cessation rates at 12-months between both phases in the control study sites (study sites C and D) (Figure 2). The study was not powered to detect a significant difference between intervention and control sites over the observation and intervention phases. We also conducted stratified analyses by attendance to CR and education status (with or without university degree). We further tested the association between the presence and duration of counseling between phases using logistic regression models and Poisson logistic regression models. Statistical significance was set at 0.05. All analyses were performed using STATA version 12 (StataCorp, College Station, Texas).

RESULTS

STUDY POPULATION

Between August 2009 and February 2012, 616 patients admitted for ACS were included in the clinical follow-up study in site A, and 510 in site B. 458 (40%) were current smokers and included in the subsequent analyses (Figure 2 and Appendix Figure 1). At 12-month follow-up, smoking status was assessed in 97% while 15 participants had died (Figure 2 and Appendix Figure 1). In the study sites C and D, 192 smokers were included in the observation phase and 244 in the intervention phase (Figure 2 and Appendix Table 1). At one year follow-up, smoking status was obtained for 92% while 12 participants died.

Mean age of participants included in the intervention sites (study sites A and B) in the intervention phase was 55 years, 20% were women and 52% had been hospitalized for STEMI (Table 1). There were no significant differences in baseline characteristics between participants in observation and intervention phases, except for the longer stay of patients directly discharged home.

PROCESS OUTCOMES

In the intervention sites (study sites A and B), 22% percent of patients received intensive smoking cessation counseling during the observation phase compared to 87% in the intervention phase (Figure 2 and Table 2). Among the 13% who did not receive counseling in the intervention phase, 10% (n=24) were transferred to another facility or discharged home before the counselor could approach them; 2% (N=4) completely refused to discuss with counselor and 1% (N=2) had a major language barrier. The median duration of the intervention during the hospital stay was 50 minutes and did not significantly vary between both phases. During the intervention phase, 78% received a phone follow-up (90% of those receiving in-hospital counseling) for a median total duration of 42 minutes in 4 sessions. Prescription of NRT at discharge increased significantly from 18% to 58% in the intervention phase (Risk ratio: 3.3 (95% CI: 2.4 to 4.3; p=<0.001). Of those who received phone follow-ups in the intervention phase, 67% were prescribed NRT at discharge, but only 41% were still taking NRT at the first phone follow-up 2 days after discharge.

In the intervention sites, the proportion reporting having attended cardiac rehabilitation (CR) significantly increased during the intervention phase in the intervention sites from 58% to 73% (p<0.01). The proportion attending ambulatory CR compared to hospital-based CR increased from 55% in the observation phase to 67% in the intervention phase.

SMOKING ABSTINENCE AT 12-MONTHS

In the intervention sites, validated 12-months smoking abstinence increased from 43% during the observation phase to 51% in the intervention phase (RR 1.20; 95% CI: 0.98 to 1.46, p=0.08; absolute risk difference (ARD) 8%, Table 3). In the control sites, 47% quit smoking in the observation phase compared to 48% in the intervention phase (RR: 1.02 (95% CI:0.84 to 1.25;p=0.8; ARR 1%).

In exploratory stratified analyses comparing cessation rates in intervention sites between both phases, the apparent benefit was mostly seen in those not attending CR and those without university degree (Table 3).

DISCUSSION

In this multicenter study involving smokers hospitalized for an ACS, a systematic smoking cessation intervention sharply increased the number of patients exposed to motivational interviewing and nicotine replacement therapy. The median duration of counseling during the hospital stay was 50 minutes and did not vary between phases. Comparing observation to intervention phases, the smoking abstinence at one year increased from 43% to 51% (8% absolute difference in abstinence, p value 0.08). At sites without dedicated in-hospital smoking cessation intervention during the entire study period, no difference in smoking abstinence was observed. In subgroup analyses, the benefit of the systematic intervention appeared limited to smokers not attending CR and those with lower education level.

Murray et al. recently tested the effectiveness of systematically providing support to all identified smokers in a RCT randomizing medical wards in one medical center in the UK.[16] The systematic identification permitted to increase the offer of behavioral support from 46% to 100% of smokers and the acceptance of behavioral support from 29% to 70% of smokers. However, out of 1072 smokers identified on ward, 30% declined consent to participate in the study and an additional 30% of those offered behavioral support refused it. In our study, detailed analysis of the flow of participants until inclusion in the clinical study showed that 4% refused to enter the clinical follow-up study, followed by 2% who completely refused to open the discussion with the resident approaching them to start a motivational interview. The benefits of counseling all smokers regardless of their motivation to quit using MI had also previously been tested in a rigorously performed RCT in 1996-1997.[29] Out of 164 smokers with acute MI, 8 (5%) refused to participate in the smoking cessation intervention including follow-up at 6 months. The smoking cessation rate at one year was 34% in the observation group and 55% in the intervention group ($p<0.005$). However, the study was performed in a single study site and the rate attending CR was not provided and is expectedly lower than the rate in our population, thus limiting the comparison.

The sharp increase in uptake of the smoking cessation intervention highlights the effect of changes in the choice architecture described in behavioral economic theories. Setting the default option from an *opt-in* to an *opt-out* has been shown to be a powerful driver of uptake in interventions.[37 38] In the

context of our study, the systematic offer of a smoking cessation intervention is similar to an *opt-out* policy where patients ask not to have the intervention compared to the *opt-in* policy where patients or their caregivers specifically have to request a smoking cessation intervention.

In our study, the rate discharged to CR in the intervention sites increased from 58 to 73% between the observation and intervention phases. Given that CR includes smoking cessation counseling and support, it could be considered a follow-up intervention as recommended by guidelines and might be explained by higher attendance rate to CR.[4] However, in stratified analyses by attendance to CR, the benefit of the systematic smoking cessation intervention was mostly apparent among participants not attending CR. The systematic approach might permit to counsel those most at risk of lack of follow-up in the ambulatory care. The high attendance rate to CR overall in our study might explain the negative findings on smoking cessation rates over follow-up [39-42] Overall, attendance rates in the US range from 14% to up to 55%.[39-42] We based our sample size estimation on previous studies on smoking cessation after ACS where attendance rates to CR were expectedly lower. Unfortunately, we are unable to compare the attendance rates in our study to previous smoking cessation studies because previous studies included in the Cochrane systematic review and to the recent study by Murray et al. have not reported on rates of ambulatory CR. [5 16 24-36] Future studies should also better describe the concomitant interventions in the ambulatory care in order to facilitate the interpretation and translation of findings into clinical practice.

Our findings challenge the recommendation of allocating high intensity counseling only to those "willing to make a quit attempt" recommended in smoking cessation guidelines based on the 5A's framework.[9] According to MI, motivation occurs in the interpersonal context, which depends on the style used by counselors with smokers and may influence the acceptance rates of the intervention.[14] A previous rigorously performed RCT only including those willing to make a serious quit attempt was unable to show a benefit on smoking cessation.[27]

We found that the systematic smoking cessation intervention led to an increase in NRT prescription at discharge comparing the observation and intervention phase at the intervention study sites. However, the high cost of NRT after discharge, given that NRTs are not covered by health care

insurances in the ambulatory setting in Switzerland, might explain the lower rate of participants still taking NRT at the phone follow-up. Future studies should test the effect of removing potential financial barriers for using NRT after the hospital stay on smoking cessation outcomes.

Our study has limitations. The weaker before-after design with parallel group comparisons does limit the causal inferences from our results. Participants received phone counseling after their hospital stay in the intervention phase, but not in the observation phase. A systematic review on the benefits of smoking cessation intervention for hospitalized smokers suggested that only interventions including a follow-up intervention in the ambulatory setting have shown an effect on smoking cessation outcomes at 12 months. This strongly limits the comparison of smoking cessation rates between the observation and intervention phase as the smoking cessation increase could be due to either phone follow-up or a proactive vs. reactive approach of offering smoking cessation intervention. We urge for careful interpretation of the results given differences in covariates between participants included in the observation phase and intervention phase (Table1). In the participants included in the intervention sites, we found a significant increase in length of stay in addition to the previously discussed increase in attendance rates to CR between the observation and intervention phase. Smoking cessation rates at 12 months were based on self-report. We validated the 1-week smoking abstinence by measurement of exhaled carbon monoxide whenever possible.[23] However, misclassification of the smoking cessation outcome is still possible. Rates of referral to CR were based on information at discharge and self-report at one year follow-up. The reliability of self-reported CR referral has been validated in patients after an ACS in Canada and used recently to report on enrollment rate to CR in the US.[42 43] Exploratory subgroup analyses on the differential effect of education level and attendance to CR should be carefully interpreted, as these analyses were defined *a posteriori.* Patients were included in 4 high quality academic hospitals and results may not apply to different settings. The MI sessions were not recorded and the quality of interactions can therefore not be directly assessed. We did not develop a detailed manual for directing the MI. A prior meta-analysis suggested that clinical trials in which MI was delivered without a manual had showed better treatment outcomes.[22]

CONCLUSIONS

In summary, we found that a systematic smoking cessation intervention using motivational interviewing for smokers hospitalized for an ACS compared to a reactive strategy relying on busy healthcare providers to contact a specialized smoking cessation consultation permitted to sharply increase the number of patients counseled. In exploratory subgroup analyses of data collected in one study center, patients with lower education level and not attending cardiac rehabilitation appeared to be more likely to benefit from the intervention. The comparison of smoking cessation rates at 12 months between the observation and intervention phases are limited by the study design and showed a trend towards an increase in smoking cessation rates. Future studies should evaluate the benefit of systematically exposing smokers to a smoking cessation intervention based on motivation interviewing.

CONTRIBUTORSHIP STATEMENT

All authors do meet the ICMJE criteria for authorship:

- Conception or design of the work or the acquisition: RA, BG, RT, CMM, TFL, SW, FM, JC, JPH, NR
- Analysis, or interpretation of data for the work: RA, BG, DN, RT, JC, JPH, NR
- Drafted the work: RA, BG, RT, JPH, NR
- Revising it critically for important intellectual content: DN, CMM, TFL, SW, FM, JC
- Final approval of the version to be published: RA, BG, RT, DN, CMM, TFL, SW, FM, JC, JPH, NR
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: RA, BG, RT, DN, CMM, TFL, SW, FM, JC, JPH, NR

COMPETING INTERESTS

The following authors have the following conflicts. Dr Lüscher reports receiving research grants to the institution from Abbott, Biosensors, Biotronik, Boston Scientific, and Medtronic, and consultant payments from AstraZeneca, Boehringer Ingelheim, Bayer, Merck, and Pfizer. Dr Matter reports receiving grants from MSD, Eli Lilly, AstraZeneca, and Bayer; expert testimony from MSD; payment for lectures from MSD, AstraZeneca, and Roche; and having patents from Mabimmune, CH. Dr Windecker reports receiving research contracts to the institution from Abbott, Biotronik, Boston Scientific, Biosensors, Cordis, Medtronic, St. Jude Medical and speaker fees from: Abbott, Biotronik, Boston Scientific, Biosensors, Medtronic, Eli Lilly, Astra Zeneca. All other authors have declared that no competing interests exist.

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DATA SHARING STATEMENT

Primary data on analyses reported in the manuscript are available upon written request.

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Table 1 Baseline characteristics of participants hospitalized for an acute coronary syndrome in 2 academic hospitals (intervention sites, study sites A and B) in Switzerland in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Intervention sites (A and B)		p-value
	Observation phase N=233	Intervention phase N=225	
Demographic variables			
Age, y (mean ± SD)	57 ± 11	55 ± 11	0.06
Female, N (%)	46 (20)	45 (20)	0.9
Education, less than university degree, N (%)*	203 (88)	185 (83)	0.1
Living alone	68 (29)	55 (24)	0.3
Working status, employed, N (%)	136 (59)	143 (64)	0.3
Previous CHD, N (%)	46 (20)	37 (16)	0.3
Smoking variables			
– Cigarettes per day (median, Q1, Q3)	20 (10, 25)	20 (10, 25)	0.5
– Age at smoking start (mean ± SD)	19 ± 6	18 ± 6	0.6
Clinical variables			
ACS-type:			
– STEMI (vs. NSTEMI/UA), N (%)	121 (52)	116 (52)	0.9
Hospital stay			
Length of stay, median (Q1,Q3), in days			
– For patients directly discharged home	5 (3,6)	5 (4,7)	0.04
– For patients transferred to peripheral hospital	1 (0.5, 1)	1 (0.5, 2)	0.3
Treatment at discharge			
Destination at discharge, N (%)			
– Home	148 (64)	138 (61)	
– Direct transfer to cardiac rehabilitation	47 (20)	39 (17)	0.3
– Transfer to peripheral hospital	36 (16)	47 (21)	
Prescription of all recommended drug therapy at Discharge†	222 (95)	216 (96)	0.6
Attendance to cardiovascular rehabilitation assessed at discharge and 12 months follow-up (N, %)‡	136 (58)	163 (73)	<0.01
– Ambulatory vs. stationary§	74 (56)	109 (67)	0.05

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; STEMI: ST-segment elevation myocardial infarction

* 6 participants with missing information on education status or who refused to disclose their education status.

† Concomitant prescription at discharge unless contra-indicated or not indicated for aspirin, clopidogrel/prasugrel or ticagrelor if PCI-stent treatment, beta-blocker, statin, ACEI if LVEF ≤40%. When participants transferred to peripheral hospital, beta-blocker and ACEI/ATII coded as not applicable.

‡ Both ambulatory and stationary cardiovascular rehabilitation are covered after an ACS in Switzerland. Attendance rate computed using data on direct referral to in-patient CR and on self-reported attendance at one year follow-up in order to capture information on those directly transferred to a stationary CR and those attending CR in the ambulatory setting.

§ 3 participants with missing information on type of CR.

Table 2 Process outcomes in intervention sites (study sites A and B) comparing smokers hospitalized in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Observation phase N=233	Intervention phase N=225	Risk ratio (95% CI) or coefficient*	p-value†
- Received intensive counseling during hospital stay (N,%)	52 (22)	193 (87)‡	3.9 (3.0 to 5.0)	<0.001
- Duration of in-hospital counseling per participant in min (median, Q1, Q3)	45 (45, 48)	50 (35,60)	2.6 (-3.7 to 8.7)	0.4
- Number of in-hospital counseling sessions (median, min, max)	1 (1,2)	1 (1,3)	0.15 (-0.15 to 0.45)	0.3
- Received phone follow-up (N,%)	NA	175 (78)	-	-
- Duration of each phone follow-up in min (median, Q1,Q3)	NA	11 (8,17)	-	-
- Total duration of phone follow-up in min (median, Q1,Q3)	NA	42 (30,61)	-	-
- Number of phone follow-ups (median, Q1,Q3)	NA	4 (3,4)	-	-
- Prescribed nicotine replacement therapy at discharge (N,%)	42 (18)	132 (59)	3.3 (2.4 to 4.3)	<0.001

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; min: minutes; NA: non-applicable; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; STEMI: ST-segment elevation myocardial infarction

* Risk ratio and 95% CI calculated for dichotomous outcomes. Coefficients for duration of counseling obtained by linear regression. For number of counseling sessions, coefficient obtained by Poisson logistic regression model.

†P-value calculated by χ^2 for dichotomous outcomes (e.g. proportion receiving counseling) and linear regression for duration of encounters

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

Table 3 Smoking cessation outcomes at 12 months follow-up comparing participants in observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012) at 4 university sites in Switzerland. 7-day point prevalence abstinence, validated by exhaled carbon monoxide (CO). *

	N total for analysis	% quit in obs. phase / interv. phase	Risk ratio (95% CI)	Absolute risk difference	p-value
Main outcome					
- Intervention sites (study sites A and B) (n=458)	443	42.0/50.2	1.20 (0.98 to 1.47)	8.3%	0.08
- Control sites (study sites C and D) (n=436)	428	46.8/47.8	1.02 (0.84 to 1.25)	1.1%	0.8
Secondary analyses for participants in intervention sites (study sites A and B) (n=440)					
- Cardiac rehabilitation					
- With cardiac rehabilitation	296	51.5/53.7	1.04 (0.84 to 1.30)	2.2%	0.7
- No cardiac rehabilitation	143	29.5/43.6	1.48 (0.95 to 2.30)	14.1%	0.09
- Education status					
- University degree	64	59.3/51.3	0.87 (0.56 to 1.34)	-7.9%	0.5
- No university degree	371	40.7/50.8	1.24 (1.0 to 1.6)	10.1%	0.05

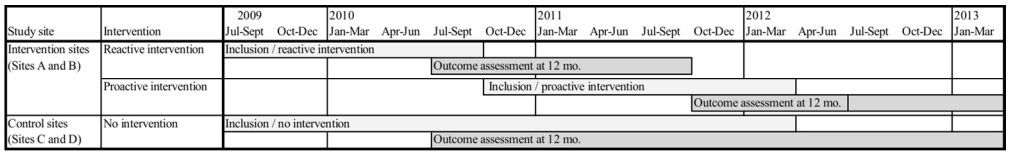
N, number of participants; CI: confidence interval.

* Participants lost to follow-up or who withdrew consent (n=11, 97% follow-up rate) considered as smokers for these analyses. Participants who died (n=15) during follow-up excluded from these analyses. Validated smoking cessation by CO in 68% of quitters in intervention sites and 40% of quitters in control sites. 2 participants reported having quit during last 7 days despite a CO level of more than 10 ppm considered as smokers.

Figure Legends

Figure 1. Study design. Before-after intervention with parallel group comparisons: We compared the 7-days point smoking prevalence at 12 months follow-up between participants included in the reactive vs. the proactive intervention phases in intervention sites (site A and B). We also compared the 7-days point smoking prevalence at 12 months follow-up between participants included during the same period in observation sites (sites C and D).

Figure 2. Flow-chart of participants included in the intervention sites (site A and B) and control sites (sites C and D) during observation phase (Aug. 2009 to Oct. 2010) and intervention phase (Nov. 2010 to Feb. 2012). Intensive smoking cessation counseling was offered during the observation phase in the observation upon request and systematically during the intervention phase. Phone follow-up was only offered in the intervention phase in the intervention sites (see Methods).



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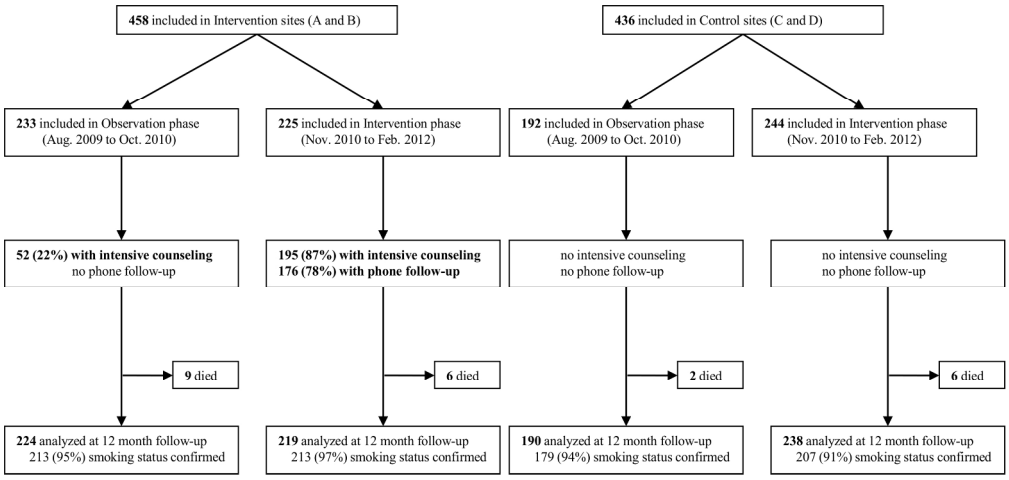


Figure 2. Flow-chart of participants included in the intervention sites (site A and B) and control sites (sites C and D) during observation phase (Aug. 2009 to Oct. 2010) and intervention phase (Nov. 2010 to Feb. 2012). Intensive smoking cessation counseling was offered during the observation phase in the observation upon request and systematically during the intervention phase. Phone follow-up was only offered in the intervention phase in the intervention sites (see Methods).
214x100mm (300 x 300 DPI)

ONLINE DATA SUPPLEMENT

Efficacy of systematic intensive smoking cessation intervention after acute coronary syndromes

Corresponding author: Dr. Reto Auer, MD, MAS.

Department of Ambulatory Care and Community Health,

University of Lausanne, Switzerland.

Phone: + 41 21 314 49 28. Fax: +41 21 314 48 93

Email: Reto.Auer@hospvd.ch

Appendix Table 1 Baseline characteristics of participants hospitalized for an acute coronary syndrome in 2 academic hospitals in Switzerland in the observation phase (August 2009 to October 2010) and intervention phase (November 2010 to February 2012).

	Control sites		p-value
	Observation phase N=192	Intervention phase N=244	
Demographic variables			
Age, y (mean ± SD)	57 ± 11	57 ± 11	0.9
Female, N (%)	36 (19)	31 (13)	0.1
Education, less than university degree, N (%)[a]	151 (89)	196 (93)	0.1
Living alone	41 (22)	50 (21)	0.8
Working status, employed, N (%)	124 (68)	158 (69)	0.7
Previous CHD, N (%)	19 (10)	28 (12)	0.6
Smoking variables			
– Cigarettes per day (median, Q1, Q3)	20 (10, 20)	20 (10, 25)	0.5
– Age at smoking start (mean ± SD)	21 ± 8	21 ± 7	0.7
Clinical variables			
ACS-type:			
– STEMI (vs. NSTEMI/UA), N (%)[b]	156 (81)	195 (80)	0.7
Hospital stay			
Length of stay, median (Q1,Q3), in days			
– For patients directly discharged home	3 (2,4)	2 (1,4)	0.01
– For patients transferred to peripheral hospital	1 (0.5, 1.5)	1 (0.5, 1.5)	07
Treatment at discharge			
Destination at discharge, N (%)			
– Home	38 (20)	62 (25)	
– Direct transfer to cardiac rehabilitation	7 (4)	19 (8)	0.06
– Transfer to peripheral hospital	145 (76)	157 (64)	
Prescription of all recommended drug therapy at discharge[c]	183 (96)	226 (94)	0.4
Attendance to cardiovascular rehabilitation	137 (72)	172 (72)	1.0

assessed at discharge and 12 months follow-up (N, %)[d]			
– Ambulatory vs. stationary[e]	98 (73)	112 (66)	0.2

N, number of participants; BMI, body mass index; CHD, coronary heart disease; CR: cardiac rehabilitation; LVEF: Left ventricular ejection fraction; NSTEMI: Non ST-segment elevation myocardial infarction; Q1: first quartile; Q3; third quartile; SD: standard deviation; STEMI: ST-segment elevation myocardial infarction

[a]56 participants with missing information on education status or who refused to disclose their education status.

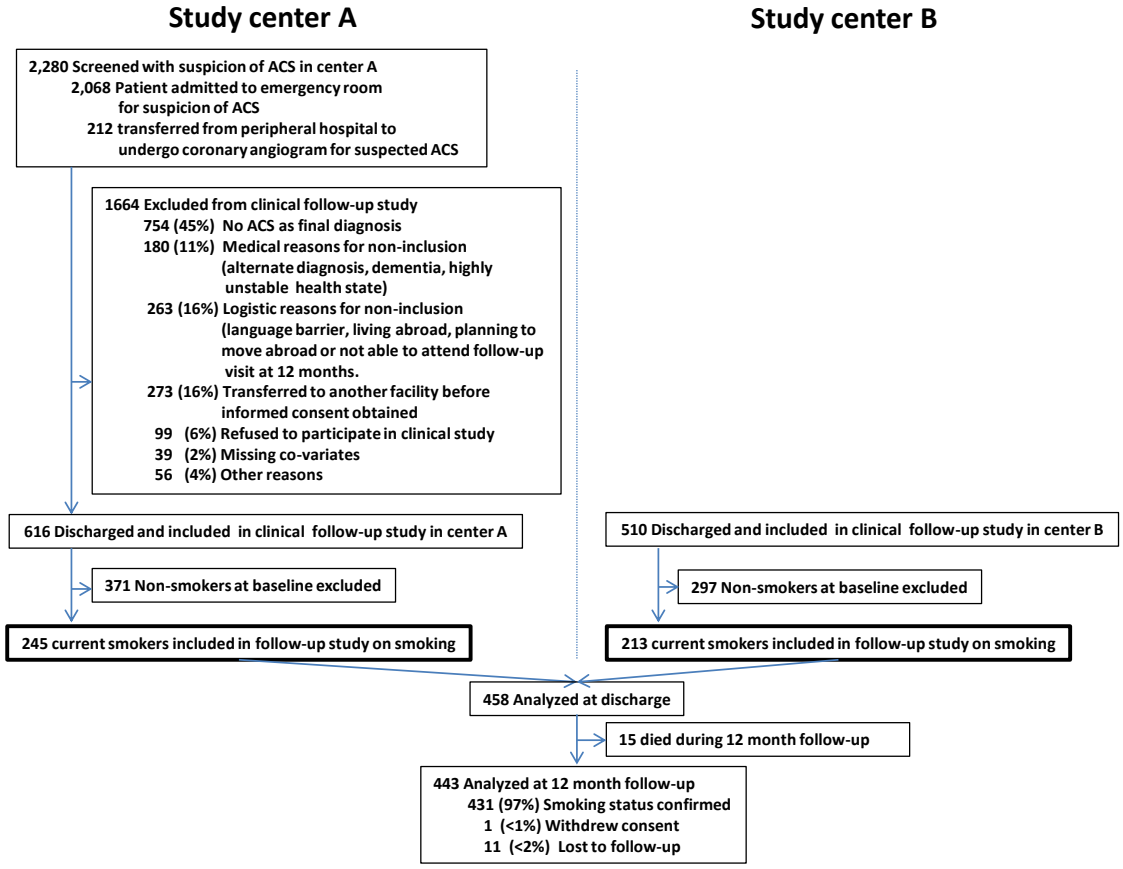
[b] Restriction to STEMI participants in one center, as only STEMI were systematically included in cardiac registry.

[c] Concomitant prescription at discharge unless contra-indicated or not indicated for aspirin, clopidogrel/prasugrel or ticagrelor if PCI-stent treatment, beta-blocker, statin, ACEI if LVEF $\leq$40%. When participants transferred to peripheral hospital, beta-blocker and ACEI/ATII coded as not applicable.

[d] Both ambulatory and stationary cardiovascular rehabilitation are covered after an ACS in Switzerland. Attendance rate computed using data on direct referral to in-patient CR and on self-reported attendance at one year follow-up in order to capture information on those directly transferred to a stationary CR and those attending CR in the ambulatory setting.

[e] 3 missing on type of CR in ambulatory setting

Appendix Figure 1. Flow of study participants in the two intervention sites. Detailed data on selection of participants from arrival to the emergency room to final inclusion was performed in one site.



Abbreviation: ACS: acute coronary syndrome

Appendix References

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Appendix Table 2 STROBE Statement – Filled Checklist

	Item no	Recommendation	Done	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	√	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√,	3
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√	5
Objectives	3	State specific objectives, including any prespecified hypotheses	√, NA	5
Methods				
Study design	4	Present key elements of study design early in the paper	√	7-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√	7, see also references listed in the methods
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	√	7 and 10, Appendix Table and Figure 1 and 2
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√	9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√	9-10
Bias	9	Describe any efforts to address potential sources of bias	√	10-11
Study size	10	Explain how the study size was arrived at	√	10-11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√	10-11

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	√	10-11
		(*b*) Describe any methods used to examine subgroups and interactions	√	10-11
		(*c*) Explain how missing data were addressed	√	11
		(*d*) If applicable, explain how loss to follow-up was addressed	√	10-11
		(*e*) Describe any sensitivity analyses	√	11
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	√	8, eMethods
		(b) Give reasons for non-participation at each stage	√	7,8, Appendix Figure, Appendix Table 1
		(c) Consider use of a flow diagram	√,	Appendix Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	√	11, Table 1 and Appendix Table 1
		(b) Indicate number of participants with missing data for each variable of interest	√	11, 12, Table 1
		(c) Summarise follow-up time (eg, average and total amount)	√	11-12
Outcome data	15*	Report numbers of outcome events or summary measures over time	√	11-12, Figure 2, Table 2 and 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	√	12, Table 3
		(*b*) Report category boundaries when continuous variables were categorized	-	-

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√	12, Table 3
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√	12, Table 3
Discussion				
Key results	18	Summarise key results with reference to study objectives	√	11-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√	13-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√	13-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	√	14-16
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.