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Economic evaluation of a brief counselling for tobacco cessation in dentistry – the FRITT study

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ABSTRACT

Objectives: This study aimed to evaluate the cost-effectiveness of brief interventions for tobacco cessation in dentistry, as this has not been established previously.

Design and outcome measures: Intervention effectiveness was estimated in a cluster randomised controlled trial. Number of quitters was estimated based on 7-day abstinence and on smoking reduction at follow-up. Health economic evaluation was performed using two models: 1) A population-based model employing potential impact fractions, and 2) a Markov model estimating the cost-effectiveness of the intervention for the actual participants. The evaluation was performed from health care and societal perspectives and health gains were expressed in quality adjusted life years (QALYs).

Setting: Dental clinics in Sweden.

Participants: 205 Swedish smokers aged 20-75 years.

Interventions: A brief, structured behavioural intervention was compared with "usual care" and "do-nothing" alternatives.

Results: The cost per quitter was 552 USD in the intervention and 522 USD in the "usual care" condition. Compared with "do-nothing" the net saving estimated with the population-based model was 17.3 million USD for intervention and 49.9 million USD for "usual care", with health gains of 1428 QALYs and 2369 QALYs, respectively, and "usual care" was preferable to the intervention. The reverse was true when using the Markov model, showing net societal savings of 71,000 USD for the intervention and 57,000 USD for "usual care", with gains of 5.42 QALYs and 4.74 QALYs, respectively.

Conclusion: Both intervention and "usual care" seemed to be cost-effective compared with "do-nothing" alternative. The comparison of intervention and "usual care" derived from small-scale studies may be highly sensitive to the choice of the model used to calculate cost-effectiveness.

Trial registration: The cluster randomised trial is registered in the ISRCTN Register of controlled trials with identification number ISRCTN50627997.

Strengths and limitations of this study:

- The cost-effectiveness of a brief counselling for tobacco cessation in dentistry was assessed using two different models: an individual level Markov model and a population-based model.
- The comparison of the two models' estimates, due to different modelling assumptions, illustrates the importance of model choice.
- The non-significant differences in the effectiveness of the novel intervention compared with the control condition imply uncertainty of the subsequent economic evaluation.
- The uncertainty of the estimates is further increased by the assumptions made on long-term quit rates.

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INTRODUCTION

Despite continuously declining prevalence, cigarette smoking contributes to 7.5% of the burden of disease in Sweden,[1] and was estimated to stand for 6.7% of the national costs for health care and loss of production in 2001.[2] Quitting smoking substantially decreases the risk for its negative health consequences [3] through a notable reduction in the risks for cancer, cardiovascular disease, and diabetes.[1]

Health care providers in Sweden are encouraged to offer their patients support for tobacco cessation.[5] Optimally, such interventions should be of low-intensity in order to be delivered as a part of the routine care. Due to the high proportion of the general population visiting dental care regularly, and for the oral health consequences of smoking, dental clinics are a particularly suitable setting for the delivery of brief smoking cessation counselling.[6, 7] However, counselling in dentistry is currently underutilized and will remain so unless training of professionals and changes in the health system are introduced.[8, 9] Health economic evaluations offer the possibility to compare interventions in terms of their costs and health effects, thus facilitating decision-making.

Evaluations have so far confirmed the effectiveness and cost-effectiveness of tobacco cessation interventions.[10] Brief advice for smoking cessation has also been found cost-effective,[11, 12] but economic evaluations of such interventions in dental care are lacking. Cost-effectiveness estimates obtained from other health-care settings may not apply to dentistry. In fact, among smoking patients seen in dental care there is an over-representation of healthy individuals and light smokers not very motivated to quit. Also, dental care professionals and dental clinics' organization may have lower capacity to address lifestyle factors compared to other health care settings, thus impacting on the delivery of preventive advice. One Swedish study conducted an economic evaluation of high and low intensity smoking cessation interventions in dental care,[13] but because of their intensity, neither of these formats could be considered as brief advice. In summary, the knowledge about cost-effectiveness of smoking cessation interventions in dental care is incomplete.[14]

The majority of cost-effectiveness studies of smoking-cessation treatments used mathematical modelling based on simulation techniques.[15] Different models have been developed to reflect the influence of smoking and smoking cessation on future health risks. According to Bolin,[15] the two most common modelling approaches are the Markov-type and the population-based simulation. Markov models are typically used to evaluate the cost-effectiveness of an intervention in a specific setting for the intervention's target group. Population-based models aim instead to estimate the population benefits given the dissemination of the intervention to the whole population. The estimates obtained with these two approaches may differ, as may the implications for decision-making.

In this study, we present an estimation of the cost-effectiveness of a brief structured counselling for tobacco cessation delivered in the context of dental care in Sweden, the effectiveness of which was assessed in a randomized controlled trial (FRITT Study).[16] The study was guided by two research questions:

1) Is the brief counselling for tobacco cessation in dentistry a cost-effective public health intervention compared with: a) "usual care"; b) "do-nothing" (null) strategy?

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2) Does the cost-effectiveness of the intervention differ if it is estimated with a population-based model compared with a Markov model?

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METHODS

The study was approved by the Ethical Review Board of Stockholm Region, March 15, 2012 (nr. 2012/237-31/5). The participants were included in the study only after they had given written informed consent.

The intervention

The economic evaluation was conducted based on data from a cluster randomized controlled trial that compared brief counselling for tobacco cessation with usual care provided to Swedish tobacco users in dental clinics.[16] The study is registered in the ISRCTN Register of controlled trials with identification number ISRCTN50627997. The English translation of the original study protocol is available as supplemental file.

Briefly, 27 dental care clinics were randomized to either alternative intervention or control condition and recruited thereafter patients aged 18-75 years who were daily tobacco users (Fig 1). Follow-up was conducted six months after enrolment (97% retention). All information was self-reported by the patients.

The study participants (n=467) consisted of current daily smokers (n=218), current snus users (n=200), and dual users of cigarettes and snus (n=41). Only data from smokers aged 20 years or older was used in the current economic evaluation. The analytical sample comprised 99 smokers in intervention condition and 106 smokers in control condition ("usual care"). For the economic evaluation a theoretical simulated "do-nothing" alternative was added to represent a hypothetical scenario with neither costs nor the effects related to tobacco cessation activities.

The intervention consisted of a structured brief advice based on the 5A's model delivered once during a dental visit performed by a dentist or a dental hygienist. The control condition implied delivering care as usual according to the clinic's routines, if any. Approximately half of the clinics in the control condition had personnel trained in tobacco cessation and routines concerning patients' tobacco use. All patients at intervention clinics and approximately 72% of patients at control clinics received some level of advice on tobacco use. However, counselling at intervention clinics was on average more extensive, including for instance information on available support and pharmacological treatment almost ten times as often as on control clinics. While tobacco cessation advice, if received, lasted on average 3.5 minutes at the control clinics, the duration was 5 minutes longer (i.e. 8.5 minutes) at intervention clinics.

When the analysis was limited to smokers, no statistically significant differences between the intervention and control groups were seen in any of the studied outcomes. The primary outcome, 7-day point prevalence of abstinence, was achieved by 8% of participants both in the intervention and in the comparison condition. Substantial tobacco reduction (≥50 % reduction in amount cigarettes smoked compared to baseline) at six-month follow-up was achieved by 27% of participants in the intervention and by 17% in the comparison condition.

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Economic evaluation

We present an incremental cost-effectiveness analysis with long-term health effects. The alternative intervention was compared with "usual care" and hypothetical "do-nothing" alternatives, this latter assumed to imply zero costs and no health effects. The cost-effectiveness analysis was designed to follow the Swedish recommendations [17] on economic evaluations of health care interventions. Therefore, costs were calculated from healthcare and societal perspectives, while health effects are expressed in QALYs (quality-adjusted life-years). Both costs and QALYs were discounted 3 percent annually. Long-term costs and health effects were simulated using two models:

1) A population-based model employing potential impact fractions, where the intervention effect is assumed to change the incidence in tobacco related diseases, including diabetes mellitus type 2, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD) and seven cancer diagnoses, including lung cancer
2) A Markov model incorporating lung cancer, COPD, and CVD

Intervention costs

Only the costs connected with the delivery of the interventions were included in the analysis. The quantity of resources consumed was obtained from the study's accounting records. The unit costs were obtained from national public databases, from suppliers' websites and from the organizers of the training. Total intervention costs were obtained by multiplying the volume of each cost category by its respective unit cost. Intervention costs were divided into training and operating costs.

Training costs for the brief advice included costs for salary and travel costs for the trainer, venue, and materials, as well as allowance for training time for trainees (4 hours per dental professional). Only 20% of the total costs were considered, in order to accommodate for the spread over a five-year period before refresher training may be needed. Costs were expressed per smoker. The number of patients who smoke, per dental care professional, was estimated based on the prevalence of smoking,[18] and the average number of patients the practitioners in the trial reported having each year.

Operating costs represented the costs of delivering tobacco cessation counselling in intervention and "usual care" conditions and were estimated based on the duration of the counselling and on average salaries including social charges.

Other costs connected with the interventions included patients' time in attending counselling, based on the mean duration of the counselling, and use of nicotine replacement therapy (NRT) or other medications for tobacco cessation. Costing of patients' time was estimated based on the opportunity cost of foregone leisure time and calculated at 25% of the Swedish average gross wage rate.[19] The cost of medications was estimated based on the retail price of the most commonly used drugs and on the recommended duration of use.

Intervention costs were estimated in Swedish crowns (SEK), inflated to reflect 2014 costs according to the Swedish consumer price index [20] and then converted to 2014 US dollars (USD) using the purchasing power parity (PPP) estimates with CCEMG – EPPI-Centre Cost Converter (http://eppi.ioe.ac.uk/costconversion/default.aspx).

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To estimate the cost of the interventions if they were applied to the entire Swedish population we estimated the number of daily smokers who visit dental clinics during a year. The number of smokers was obtained from national surveys,[18] as was the number of adults visiting dental care each year.[6] Each year, 449 000 smokers were estimated to visit dental care.

Estimate of intervention effectiveness

The effectiveness of the novel intervention was estimated from the trial's outcomes, 7-days abstinence and smoking reduction. We assumed that reducing cigarette consumption by half would lead to sustained abstinence for 15% of the reducers,[21-24] while all quitters were assumed to maintain abstinence. On the population level, the change in smoking prevalence was calculated by multiplying the proportion of quitters due to the intervention by the number of smokers seeking dental care each year.

Population-based model

We simulated the impact of changes in incidence of and related societal costs for several chronic diseases during ten years, following the assumed changes in smoking prevalence because of the interventions in the Swedish population 20-84 years old in 2014. A model denominated *Risk factors, Health and Societal Costs* [25] was adapted for this study. The model simulates effects on health outcomes associated with smoking, including diabetes mellitus type 2, ischaemic heart disease, ischaemic and haemorrhagic stroke, COPD, and cancer of the lung, oesophagus, liver, larynx, stomach, pancreatic, colon and rectum.

In this model we used a modified version of the potential impact fraction,[26, 27] where the intervention effect changed the relative risk (RR) of disease of the exposed category (smokers), while keeping the prevalence of exposed category constant. In our case, the RR changes for smokers when some of them quit.

$$PIF = \frac{P_s * RR_s - P_s * RR_s^{'}}{P_s * RR_s} \text{ [1],}$$

where:

P_s is the prevalence of smoking,

RR_s is the relative risk of disease associated with smoking,

$RR_s^{'}$ is the changed relative risk of disease after the intervention when a part of smokers have quit.

The incidence rate of the disease after this change in the related risk factor (I*) becomes:

$$I^* = I \times (1 - PIF) \text{ [2],}$$

where I is the original incidence rate.

The relative risks for smokers compared to non-smokers were estimated from epidemiological studies, as presented in the technical report,[25] and additionally: ischaemic heart disease, ischaemic and haemorrhagic stroke,[28-31] COPD,[32, 33] and different cancers.[34, 35] The changing RRs

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($RR_s^{'}$) were calculated for every year and every disease, based on the decrease in risks for ex-smokers over time. For ischaemic heart disease, stroke, COPD, and lung cancer we used the estimations presented in Hurley and Matthews.[36] We assumed that risks for ex-smokers for diabetes mellitus follows the pattern of CVD decrease while the risks for other cancer diagnoses decrease linearly during 20 years. The health gains were calculated as decreased incidence of the diseases during ten years and increased health-related quality of life (QALYs).

The societal costs include medical treatment costs and municipal costs for care, hence the model adopted a limited societal perspective as patient and productivity costs are not included. Swedish national registers were used to retrieve disease incidence and disease-specific medical care costs, while municipal care costs were estimated via a Swedish study. The model was developed in Excel (Microsoft Office, 2010); details of the model are published in a technical report.[25]

Markov model

A Markov model was used to estimate health consequences and societal costs of smoking cessation.[37] The model has been used in similar studies in Sweden [13, 38] and was updated for the purpose of the current analysis. The model simulates the societal effects of quitting smoking on three diseases: lung cancer, COPD, and CVD, including CHD and stroke. The model incorporates the smoking-related disease risks, time-dependent remaining excess disease risks after quitting, the death risks for the specific and for unrelated diseases, as well as the societal effects of the three diseases. All disease risks are annual age- and gender-specific excess incidence until death or the age of 95 years. The societal effects include costs associated to: medical treatment, municipal costs for care, drugs, informal care and other expenditures for patients and relatives, loss of productivity, and QALYs.

Most of the societal costs were derived from Swedish studies published during the 2010s and were reported as distributions, i.e. with the Gamma parameters or bootstrapped 95 percent confidence interval, in order to enable stochastic estimation.

The Markov stages are one year long, with no half-cycle correction. The probabilistic model is run as a microsimulation with 10,000 repetitions. The Markov-cycle tree was created in Treeage Pro (Treeage Inc., 2015). Details on the model are available from a technical report.[37]

Sensitivity analyses

Several one-way sensitivity analyses were conducted to test the robustness of the results. First, we examined the effect of changing the assumptions about the proportion of smokers assumed to achieve permanent abstinence after reducing consumption by half to: a) 5% and b) 25%. Secondly, we examined the effect of changing the assumption of intervention coverage of dental care patients to 70%.

To illustrate the correspondence between the two models a detailed calculation restricted to one gender and age group was performed with the same time frame (10 years), using only the health care perspective.

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RESULTS

Intervention costs

Table 1 shows the costs of the interventions. Most of the interventions' costs could be attributed to the use of NRT and other medications.

Table 1. Intervention costs, per patient, in 2014 USD

		Intervention		"Usual care"		"Do-nothing"	
	Unit price	Units *	Cost	Units*	Cost	Units*	Cost
Training cost							
Course fee							
Salary for trainer, delivery [a]	26.0	4	103.9				
Salary for trainer, preparation [a]	26.0	1	26.0				
Salary for trainer, travel time [a]	26.0	2	51.9				
Travels for trainer [b]	23.0	1	23.0				
Material [c]	2.30	25	57.5				
Venue and refreshments [c]	777.8	1	777.8				
Total course fee for 25 participants			**1040.0**				
Total course fee per participant (practitioner)			**41.6**				
Compensation for training time for practitioners							
Compensation for training time: dentists [c d]	264.3	4	1057.2				
Compensation for training time: dental hygienists [c d]	103.4	4	413.7				
Average allowance for practitioners (80% dental hygienists)	135.6	4	542.4				
Total training cost per practitioner			584.0				
20% of total training cost per practitioner			116.8				
Estimated yearly training cost per smoker [e]			**2.3**		**0**		**0**
Operating costs							
Salary for dentist [a]	38.7						
Salary for dental hygienist [a]	25.0						
Average salary for practitioners (80% dental hygienists) [a]	27.7	0.14	**3.9**	0.04	**1.1**	0	**0**
Patient's time cost [a]	5.2	0.14	**0.7**	0.04	**0.2**	0	**0**
NRT/other drugs [b f]	172.4	0.28	**48.8**	0.28	**47.9**	0	**0**
Total cost per patient			**55.7**		**49.2**		**0**

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[*] Hours or number
[a] Information on average salaries from Statistics Sweden: www.scb.se
[b] Based on information from suppliers' websites
[c] Based on the study records or information from training organizers
[d] Includes loss of revenue
[e] Estimated yearly number of smokers visiting a dental practitioner: 50
[f] Proportion (units) based on information from the trial

Total cost for the brief advice was estimated at 56 USD per patient and the difference in costs between the intervention and "usual care" was 6.5 USD. The cost per quitter was 552 USD in the intervention and 522 USD in the "usual care" condition. If delivered to all Swedish smokers visiting dental care, the total costs would be 25.0 million USD per year for the alternative intervention and 22.1 million for "usual care".

Intervention effectiveness

Ten smokers (four men and six women) could be expected to quit in "usual care" condition, compared with ten smokers (only women) in the intervention condition.

When the effects were applied to the entire population, the prevalence of smoking among men was projected to decrease from 8.9% to 8.8% for the novel intervention and to 8.3% for "usual care". The prevalence of smoking among women would decrease from 11.6% to 10.5% for intervention and to 10.8% for "usual care". The estimations of effectiveness are presented in Table 2.

Table 2. Effectiveness estimations

	"Do-nothing"			**Intervention**			**"Usual care"**		
Age	20-44	45-64	65-84	20-44	45-64	65-84	20-44	45-64	65-84
Prevalence of smokers in the population (%)									
Men	7.00	12.00	8.00	6.90	11.88	8.00	6.55	11.10	7.42
Women	8.00	16.00	12.00	7.42	14.39	10.51	7.74	15.55	9.87
Quitters (n)									
Men	0	0	0	0	0	0	1	2	1
Women	0	0	0	3	6	1	1	2	3

Cost-effectiveness analyses

Model outputs are presented in Table 3, with a detailed example given for women aged 45-64 years in Table 4.

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Table 3. Model outputs- Markov and population-based models. Costs in thousand USD 2014.

	Intervention							"Usual care"						
	Females			Males			**Total**	Females			Males			**Total**
Age	20-44	45-64	65+	20-44	45-64	65+		20-44	45-64	65+	20-44	45-64	65+	
Study participants (n)	19	31	6	11	20	2	**99**	20	37	11	9	20	9	**106**
Markov model														
Change in cost	-36	- 39	-2	0	0	0	**-77**	-12	-13	-6	-15	- 14	-3	**-60**
Change in QALY	1.99	3.22	0.21	0.00	0.00	0.00	**5.42**	0.66	1.07	0.64	0.93	1.15	0.28	**4.74**
Population-based model														
Change in cost	-2, 427	-16, 797	-20, 338	-502	-2, 254	0	**-42, 318**	-1, 088	-4, 695	-29, 071	- 2, 257	-16, 907	-17, 961	**- 71, 979**
Population: change in QALY	87.0	604.9	635.9	19.1	81.3	0	**1428.2**	39.0	169.1	909.0	85.9	610.1	556.2	**2369.3**

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Table 4. Model outputs in the subgroup of women 45-64 years. Markov and population-based models, 10 years' time horizon, health care perspective. Costs in 2014 USD

	Intervention effect	Health care cost	QALYs
Markov model			
Per quitter:	Quitters: 1	-547	0.02
Population-based model			
Intervention	Change in prevalence: 1.61% Quitters (n): 19 422	-11607004 Per quitter: - 598	604.94 Per quitter: 0.03

Population-based model

The brief intervention applied to smokers showed a total societal saving of 42.3 million USD, of which 27.6 million USD were savings in health care costs, and a gain of 1428 QALYs, compared with "do-nothing" alternative. The corresponding estimates for "usual care" demonstrated a total societal saving of 72.0 million USD, out of which 46.9 million USD were savings in health care costs, and a gain of 2369 QALYs. When both intervention costs and estimated societal savings are considered, the net societal saving was 17.3 million USD for the brief advice and 49.9 million USD for "usual care", with health gains as above. Thus, the brief novel counselling was not cost-effective compared to the control alternative according to the population-based model.

Markov model

The gains associated to the novel intervention compared with "do-nothing" alternative were societal savings of 77,000 USD, including savings of 32,000 USD in health care, and 5.42 QALYs. For "usual care", the gains were societal savings of 60,000 USD, including savings of 26,000 USD in health care, and 4.74 QALYs. The model showed net societal savings of 71,000 USD for the intervention and 57,000 USD for the "usual care" group, with associated gains in QALYs, compared with "do-nothing" alternative. According to this model, the brief intervention was net cost saving compared with "usual care" and resulted in gain of 0.68 QALYs.

Sensitivity analyses

When the proportion assumed to achieve abstinence after reducing by half were set to 5% or to 25% the magnitude of the difference between the conditions changed, but both intervention and "usual care" were still preferable to "do-nothing" alternative, with gains in QALYs and societal savings. As with the main analysis, the population-based model favoured "usual care" over the novel intervention, while the Markov model favoured this latter over "usual care". Likewise, when the coverage of the brief advice or of "usual care" was assumed to be 70% the gains decreased but the patterns of difference were similar to the main analysis.

In order to illustrate the correspondence between the population-based and Markov model, separate calculations were done restricted to women in age group 45-64 years, using 10 years' time horizon and only the health care perspective. The estimation from the population-based model for

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this group shows cost savings for health care sector of 598 USD per quitter. The health care savings estimated with the Markov-model for the same group during 10 years were 547 USD per quitter. In essence, for this group both models show the same level of cost saving for a quitter as well as the same level of health gains (0.02 versus 0.03 QALYs).

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DISCUSSION

In this economic evaluation, the cost-effectiveness of a brief manualized counselling for smoking cessation in dentistry was assessed using two different models: a population-based model comparing different scenarios of tobacco use prevalence, and a Markov model estimating the outcomes for the quitters. A similar population-based model was presented in Magnus et al. [39] while a similar Markov model was presented in Hurley and Matthews.[36]

The original trial did not show any significant effect on smoking cessation of the novel intervention compared to usual treatment in a sample of smokers not selected according to their motivation to quit. The alternative intervention's costs were low, under 60 USD per patient, and the incremental cost compared with "usual care" was less than 7 USD per patient. In the intervention condition, the cost per quitter was only slightly higher than in the control condition and it compares favourably to the estimated cost per quitter in other smoking cessation studies.[10]

Nevertheless, the comparison of the economic effects between the intervention and "usual care" favoured the latter when modelling the population impact. In contrast, using the outcomes for the quitters in a Markov model showed that the intervention was preferable to "usual care", resulting in net societal cost savings and some gain in QALYs. Both approaches showed a net cost saving of both the intervention and "usual care" compared to the "do-nothing" alternative.

The difference in results with the two modelling strategies could be expected, because they differ in several aspects. The population-based model only considers health care costs and municipal costs for care, while the Markov model also considers cost for medications, costs for patients and relatives and morbidity productivity costs. The time frame is also different; 10 years for the population-based model and lifetime for the Markov model, and there were differences in the number of diseases included. However, as the comparison by cost category in Table 4 shows, the magnitude of costs is similar for both models

The opposite conclusions from the two models are probably best explained by the difference in the population to which the simulation is applied. In fact, the population-based model estimates the effect of the intervention brought to the entire population of smokers in Sweden, while the Markov model simulates individual effects for the quitters in the study cohort. Quitters in the intervention group were in average younger than in the "usual care" group and all of them were women, while the gender distribution of quitters was more balanced in the "usual care" group. Thus, the Markov model shows greater gains in QALYs and societal savings for the alternative intervention due to longer time horizon for younger age groups. In contrast, the population-based model converts the trial outcomes to age- and gender-specific population prevalence.

The modelling strategies inherent in the two models explain why the cost-effectiveness results differ between the models. Population-based models simulate how changes in prevalence of risk factors affect the disease incidence over age- and gender-specific groups. The individual-based Markov models simulate the changes in disease incidence because of changes in risk factors in a specific, albeit hypothetical, individual of a certain age and gender. In population-based models, groups with a high disease incidence affect the estimates more than groups where the incidence is lower at the start of the simulation. In this study, the four male quitters in the control group affected the result

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disproportionally, in particular as there were no male quitters in the alternative intervention group. Small trials with few participants, and more importantly, few successful participants, are not likely to represent the population to which the interventions are to be applied, thus skewing the estimates in population-based models.

Economic evaluations are sometimes based on effectiveness estimates from studies that do not have an actual control group, but use a hypothetical comparison group that is assumed to have zero effects and costs.[40] This is a strong assumption, as most of the quit attempts are unassisted.[41] One of the strengths of this study is that the trial included a "usual care" comparison condition, which provided data on behavioural endpoints and on use of resources in absence of the intervention under study. In comparison with the "do-nothing" alternative, both intervention and "usual care" showed net societal savings and gain in QALYs.

The weaknesses of this study include non-significant differences in the effectiveness of the novel intervention compared with the control condition. Further, some assumptions such as the proportion of reducers eventually quitting, or all quitters achieving sustained abstinence, may not be tenable and thus increase the uncertainty of the estimates.

However, to our knowledge this is the first study to evaluate the cost-effectiveness of a brief advice for smoking cessation in dental clinics in Sweden. The combination and comparison of two different approaches for the estimation of cost-effectiveness is an additional original contribution providing insights on factors to be considered in decision making about large-scale dissemination of an intervention. In this regard, we offer the general recommendation to avoid the estimation of cost-effectiveness with population-based models from small-scale trials with skewed effectiveness across participant groups.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the paper. Specifically, SEV analysed data, drafted and revised the paper.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: SV reports grants from The National Board of Health and Welfare, during the conduct of the study and personal fees from The National Board of Health and Welfare, outside the submitted work, PJ reports grants from The National Board of Health and Welfare, during the conduct of the study, MG reports grants from The National Board of Health and Welfare, personal fees from The Stockholm County Council, during the conduct of the study; personal fees from The Stockholm County Council, grants from Public Health Agency of Sweden, grants from FORMAS, outside the submitted work, IF has nothing to disclose.

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DATA SHARING

No additional data available.

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FIGURE LEGENDS

Fig 1. CONSORT flowchart. Enrolment, allocation, and retention of participants.

SUPPLEMENTARY FILES

English version of study protocol for the cluster randomized controlled trial (FRITT)

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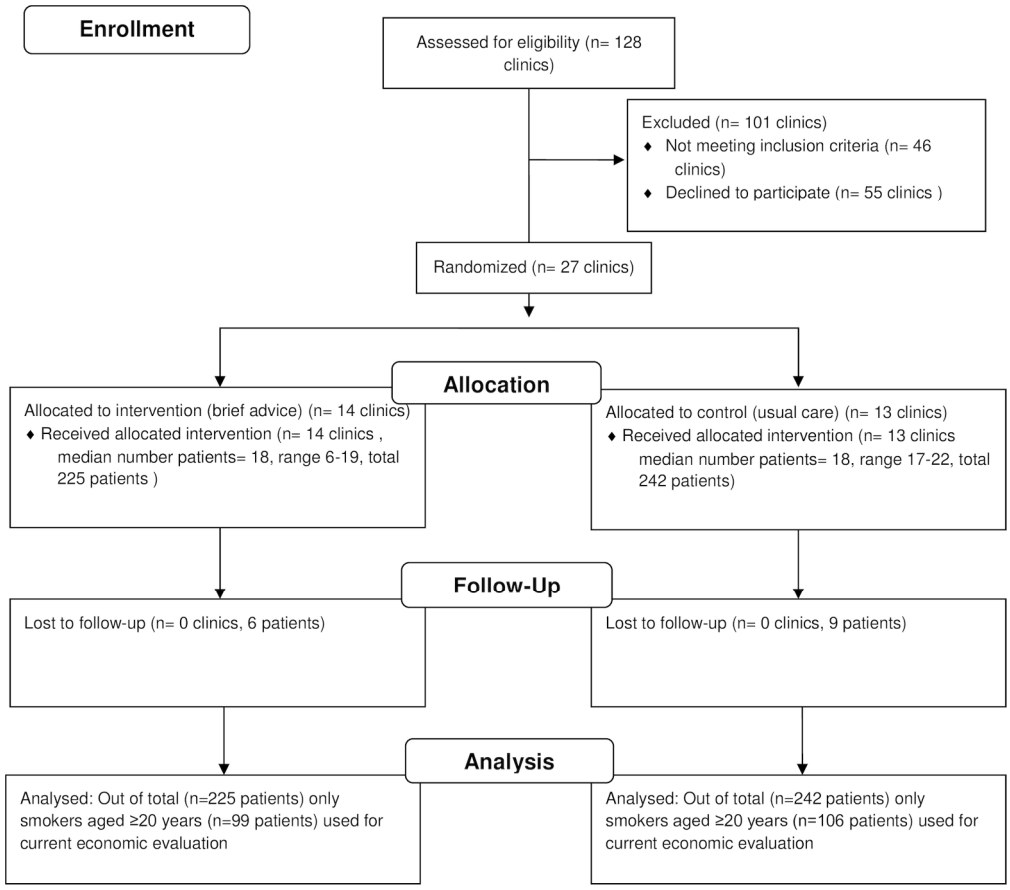

Fig 1. CONSORT flowchart. Enrolment, allocation, and retention of participants

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APPENDIX 2 Research Plan

Project ”Free from Tobacco in Dentistry” (Fri från Tobak i Tandvården - FRITT)

Title: Effectiveness of a brief counselling for tobacco cessation among smokers and snus users in dental care.

Aim and research questions

In accordance with the Ministry of Social Affair's assignment to the National Board of Health and Welfare (Government’s decision 11:18, 2011-06-16) this evaluation plan is primarily aimed to answer the question *whether a brief patient-centred intervention delivered as part of the routine care in a dentistry is effective for promoting behavioural change in tobacco use, on individual level*. If the intervention proved effective, a further aim is to deem the applicability of the intervention in the frame of routine dental care. Additional secondary research questions that the evaluation plan aims to answer are: whether counselling affects intermediary behavioural factors, for instance support seeking at different care givers; costing of diverse intervention components (e.g. training of the personnel, information materials, etc.).

2. Method

2.1 Intervention

The counselling model to be evaluated is developed by the National Institute of Public Health. The main characteristics of the model are:

1. Increasing motivation, if it is taken that high level of motivation, associated with information on available support, is the most important factor for achieving permanent abstinence. The patient can thereafter decide which support is needed and follow the active advice given by the dental care professionals.
2. Includes referral to primary care or other professional counselling as described above
3. Brief counselling (duration of conversation approximately 5 minutes), which is a requirement to be able to carry out the

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intervention without impact the effectivity of the prevailing clinical care.
4. Brief training for the counsellors, which has a positive impact on resource use in the eventual later implementation stage.

2.2 Population

The target group for evaluation of the intervention are patients with established tobacco use (smoking and/or snus) seeking care during the study period at the selected dental care clinics in the counties of Södermanland and Örebro. The choice of the counties was based on:

a. Geographic location in central Sweden, to assure logistical viability
b. Possibility to adopt referral system between dental care and primary care centres
c. The proportion of dental professionals in private sector, where one county with high (Södermanland) and one with low (Örebro) proportion will be included in the evaluation.

2.3 Design

The evaluation will be conducted as a randomized controlled study, in which the dental care clinics will be the entities randomly chosen to either apply the novel counselling model (intervention condition) or to follow the usual counselling according the clinic's practice (control condition). Dentists and/or dental hygienists in the intervention condition will be trained in and to deliver the new counselling to smoking or snus using patients during the project period. The affected dental care professionals in both the intervention and the control conditions will document treatment of their patients tobacco use. The procedure for data collection and follow-up will be identical in both groups. The follow-up period for each patient is six months.

2.4 Study protocol

We aim to include approximately 30 dental care clinics, 30 dental care professionals and at least 460 patients in the evaluation.

2.4.1 Selection and randomization of the dental care clinics

Step 1. A county's stratified sample of approximately 70 dental care clinics - no specialized clinics – is drawn from the most updated registry from The Dental and

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Pharmaceutical Benefits Agency, accessible through each county council.

Step 2. The manager/responsible for each clinic is invited to a meeting held on regional level, where the evaluation team will explain the background and setup of the project. For each clinic information of structural character is collected (Appendix 1).

Step 3. Preliminary consent for cooperation and randomization is given by the operations manager.

Step 4: The dental professionals (dentists or dental hygienists, depending on who meets the patients at first hand) in the affected clinics are contacted by the managers and asked for cooperation, including following obligatory components: participation in a training on counselling skills, implementing of the counselling with the intended number of smoking or snus using patients, registration of information about the intervention and its evaluation (Appendix 2). For each clinic two staff members are selected (one regular and one deputy) to recruit patients for the project, but other staff can choose to participate in the training. Clinics where no personnel are willing to cooperate are considered dropouts, irrespective of earlier position of the manager. Apart from what is needed for implementing the intervention, the clinics are advised against changing their organizational routines in order to enable participation in the study.

Step 5: The cooperating clinics are assigned a minimum number of patients to be recruited for the study, based on an estimation of the patient turnover (average: 15 patients). For the purpose of the study, a unique code will identify each clinic. Thereafter, based on a computer-generated random sequence, the clinics are randomized to intervention or control conditions, with as many clinics in each condition. The key for the group identity is kept at the study secretariat,

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separated from the database in which other relevant data for the study will be registered eventually. This is done to avoid that knowledge about the group identity could influence the interpretation or registering of data.

Step 6: The managers and other cooperating staff at the clinics are informed about the outcome of the randomization and are invited to participate respective training days.

Step 7: Training of the dental care professionals in the intervention condition is provided by the National Institute of Public Health with methods described in the chapter on the intervention. The training day for the control condition is held by Karolinska Institute, and will include general information about the project and its evaluation. During the training, a detailed demonstration on the procedures in the evaluation protocol are given to both groups. The training is obligatory in order to participate in the study. Two opportunities to participate in the training are offered for each clinic, thereafter absence is considered dropout in the study.

Declined participation at steps 1-4 represents pre-randomization dropout, at steps 6-7 post-randomization. We expect a total dropout rate at approximately 50 % on the clinic level.

2.4.2 Recruitment of patients

Patients seeking care at the chosen dental care clinics during the study recruitment period (see section 2.6) can be included in the evaluation if they fulfil the following criteria:

a. Adequate understanding of Swedish, both oral and written or access to interpret
b. Age between 18 and 75 years

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c. Uses tobacco daily (each of the previous 30 days) as cigarettes, other smoked tobacco and/or snus, since at least one year back

Patients are excluded if:

a. Seeking acute care
b. Current use of medicines for tobacco cessation (nicotine replacement therapy, bupropion, vareniklin, etc.)
c. Abuse of drugs or other mental illness which can affect the voluntariness of participation in the study or the reliability of the reported information

The choice to recruit to the study also patients with chronical oral harm is made for two reasons: partly because these patients are interesting as they represent the target group for indicated prevention [2]; party to hasten the recruitment of the desired number of patients.

The recruitment will be done according the following schedule.

Step 1: The patients who have booked visit to the clinic is asked to fill out a form (Appendix 3) where background information is asked about, prerequisites for recruitment is assessed, and short information about the study is given.

Step 2: A dental hygienist or a secretariat controls the information and refers patients not fulfilling the criteria to their appointment. The remaining patients are asked to read detailed information about the study (Appendix 4), to sign an informed consent (Appendix 5), and to provide additional baseline information (Appendix 6). The signed consent is given directly to the dental care personnel at the appointment, and thus they can deliver the intervention (in the intervention condition) or the customary information (in the control condition).

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Step 3: Before the patient leaves the clinic, a new appointment is booked for oral health control after 6 months. The appointment is voluntary and free of charge for the patient. The aim of the visit is to promote adherence to the follow-up questionnaire. Patients who have not been booked for a follow-up visit will be mailed the questionnaire according to the procedure described under 2.4.5

Step 4: A note on the patients included in the evaluation is made in their medical record, while other information from the form are transferred to the study secretariat for central registration in a specifically designed database, in which the patients are identified with the clinic's code and the id number of their record.

Step 5: Basic information (gender, age, tobacco use habits) on the patients excluded from or declining to participate in the study are registered anonymously and without a code key in a separate database.

The procedure is repeated for each consecutive patient until the clinic has achieved the quota of number of patients to be recruited. The duration of the recruitment is estimated to be approximately three months. We expect a dropout rate of approximately 30 % among eligible patients.

2.4.3 *Implementation of the intervention*

The affected dental care staff in the respective groups implements the intended counselling during the appointment following recruitment, at an appropriate time. Information on the counselling (especially duration) is registered locally in an electronic document (template shown in Appendix 7).

2.4.4 *Monitoring of the control group*

In an intervention with a control condition, it is particularly important to document any treatment or

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other actions provided to the control group. The reason for this is to be able to draw correct conclusions on the effectiveness of the novel intervention, especially if only a moderate or no effect is reported. In a naturalistic experiment, the control group's exposure is not manipulated, and therefore it can be assumed that more or less intensive actions with previously unknown effects reach also these individuals. Besides, the use of motivational interviewing, MI, is rather prevalent in the Swedish healthcare, according to recommendations issued by, among others, the National Institute for Public Health (http://www.fhi.se/Metoder/Halsoframjande-och-forebyggande-metoder/Motiverande-samtal/).

The dentists or dental hygienists at the control clinics commit to document the same information as the intervention group on any tobacco counselling with recruited patients, according to the protocol (Appendix 7).

2.4.5 Follow-up and measuring of the outcome

A measurement on the patient level is intended six months after the first visit (recruitment).
The primary outcome will be the so called point prevalence of abstinent patients (have not used tobacco during the past seven days)
The following will be considered as *secondary outcomes*:

a. Continuous abstinence during the past three months
b. Reduction with at least 50 % of the daily tobacco use in the last month (number of cigarettes/day and/or snusboxes/week) compared with the baseline

Information on the outcome is collected by a questionnaire (Appendix 8), in connection with the revisit, which is booked at the time of recruitment (see section 2.4.2) or sent home to the affected patients.

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At follow-up, the following reminder is sent to the absent or non-responding patients:
Reminder 1: text message and a printed or electronic version of the questionnaire are sent at latest one week after the missed appointment or two weeks after the mailed questionnaire. Patients are given opportunity to book a new free visit at latest one week after the reminder.
Reminder 2: text message urging to fill out the questionnaire - without an offer to book visit – is sent at latest two weeks after the first reminder if previous answer to the questionnaire is not received.
Reminder 3: this last reminder is done by telephone, with offer to answer the questionnaire directly via phone interview, at latest one month after the first reminder.

We expect a dropout rate of 10-12% at 6-month follow-up.

In the Appendix 9, there is a summary of the steps and time plan for the follow-up of the patients.

2.4.6 Data management and privacy

The data collected during the project is registered in electronic databases according to following:

1. Data on patients asked to participate and information on consent is manually entered at each clinic. The resulting databases, with no identification information, are transferred in a safe way to the study secretariat.
2. Data from the baseline questionnaire is registered centrally with optical scanning
3. Data on the counselling and patient data from the follow-up in paper format (identified only with the patient's record number) is sent monthly by the dental clinics to the study secretariat (see below), for optic scanning. Only one contact person is appointed between each dental clinic and the study secretariat

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The computerized registry, which is thereby set up, will have KI as principal and will thereafter be reported to KI's Personal Data Act ombudsman. The set up registry will not be based on identification information(such as personal identity number, name, address, etc.).

Patient related documentation related to the study that is found in supporting documents in paper form (e.g. the signed informed consent), is handled in accordance with record keeping at the original clinic.

2.5 Statistical considerations and data analysis methods

2.5.1 Sample size and statistical power

With a recruited sample of a total of 460 patients (230 in each group), distributed on approximately 30 clinics, the study has 80 % power to find as statistically significant on a 5 % level (double sided test) a relative risk of 6-months point estimated abstinence of 2.0 assuming that the prevalence of the outcome in the control condition is approximately 10 %. This statistical power is calculated considering the study design, which is based on cluster selection, and attrition.

The advantage in recruiting more clinics, each with fewer patients rather than fewer clinics with more patients is that the cluster size has a big impact on how big the final sample size needs to be for achieving the same statistical power [3]. For instance, if the aim was to recruit in average 30 patients per clinic, 520 patients distributed on 17 clinics would be needed. The study on the applicability of the intervention is of descriptive character and is not included in the power calculation.

2.5.2 Data analysis

The results will be analysed according to "intention to treat" principle, i.e. each patient is treated according to the initial randomization irrespective of the counselling actually received [4]. The reporting will be based primarily on the primary outcome.

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In the secondary analysis several outcomes can be considered (see section 1) as well as ”per protocol” analyses, in which the patients’ outcomes are analysed according to the actual exposure to counselling, with regard to underlying factors (see section 2.4.4).
Because the primary outcome is dichotomy, multilevel logistic regression will be mainly used as analytical method [5], considering the cluster based design.

2.5.3 Validity of self-reported data
For the outcome measure, self-reported data on tobacco use at baseline and follow-up will be used. For financial reasons a biochemical validation is not feasible for this evaluation. In randomized controlled trials on tobacco cessation which have validated the self-reported behaviour against a biological marker, an underreporting of daily smoking has been noted among 15 % of study participants in average [6].

2.6 Time plan

During the first six months from the project initiation (120101) the necessary administration for the study will be set up (management team, secretariat, logistics) and preparatory work for recruitment of dental clinics and dental personnel will be done. We intend to begin recruiting patients starting in October 2012.
The recruitment period is estimated to be approximately three months. Accordingly, the follow-up period for the last recruited patients will extend to early autumn 2013.

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The following table shows the outline of the time schedule for the evaluation

2012			2013			2014		
Jan-Apr	**May-Aug**	**Sept-Dec**	**Jan - Feb**	**March-Oct**	**Nov-Dec**	**Jan-Apr**	**May-Aug**	**Sept-Dec**
Recruitment of personnel, set up of secretariat and managerial team	Recruitment of the clinics	Training of dentists						
Protocol review and approval	Data collection at clinic level	Recruitment of patients Delivery of intervention Data collection at patient level		Follow-up of patients				
Selection of dental clinics					Preliminary report on implementation	Scientific article on implementation		Report writing and review
					Preliminary data analysis	Outcome analysis begins	Continuation	Complementary analysis

In house and organization
Intervention and data collection
Analysis and summarizing

2.7 Organization and coordination

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The protocol for a randomized controlled trial is complex, and requires a strict monitoring of the different stages to avoid sources of error and thus incorrect conclusions. For this purpose, three organizational bodies are considered necessary:

a. *A study secretariat* with following tasks:
   i. Archiving of administrative data
   ii. Randomization procedures and keeping of code keys
   iii. Contacts with the public and patient requests
   iv. Contacts with the clinics (e.g. reminder)
   v. Focal point for data collection
   vi. Assistance for vid reporting, etc.
   vii. Economic issues

The study secretariat consists of a fulltime research officer/research assistant during first and second years of the project.

b. *A steering group* with following tasks:
   i. Monitoring of the protocol integrity
   ii. Affiliating necessary additional expertise
   iii. Contacts with authorities and orderers
   iv. Assessment of critical incidents of value for the validity of the study results
   v. Disposition of resources
   vi. Contacts with media

   The steering group consists of: a project manager and secretariat; a representative from the National Board of Health and Welfare; an expert in tobacco cessation (not the same who developed the intervention); one/two representatives of dental care; a statistician; a researcher from the same or another institution with expertise in randomized controlled trials. The project manager is the president of the steering group.

c. *An operative group* with following functions*:*
   i. Monitoring of data collection and quality
   ii. Proposals to agenda and supporting information for the steering group
   iii. Execution of the steering group's decisions

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iv. Preliminary analysis of the material

The operative group consists of: the project manager; study secretariat; statistician/data manager (part-time).

3 Ethical questions

The evaluation study will be ethically reviewed before the initiation. The project implies however no physical infringement of risk for the participants. Besides the usual issues with privacy and handling of sensitive personal information, the only ethical consideration is about the usefulness of the novel counselling in contrast with other proven tobacco cessation methods. It is evidently shown in literature reviews, conducted among others by Cochrane Collaboration, that individual qualified counselling is more effective than brief counselling for quitting smoking [7]. The guidelines for disease prevention in health care by the National Board for Health and Welfare [8] recommends that daily smokers and pregnant snus users should be offered qualified individual couselling or proactive telephone courselling, which are much more comprehensive interventions than the brief counselling that will be evaluated in this study.

Intensive tobacco cessation methods are however not applicable in a context, such as dental care clinics, where the time with individual patients is limited, which is why trying a novel approach is warranted. Besides, the proposed intervention is not intended to substitute more intensive tobacco cessation, but rather to increase patients' motivation and hasten the transition to action (e.g. referral to primary care).

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Economic evaluation of a brief counselling for smoking cessation in dentistry – the FRITT study

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Economic evaluation of a brief counselling for smoking cessation in dentistry – the FRITT study

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ABSTRACT

Objectives: This study aimed to assess the cost-effectiveness of a brief counselling of smoking cessation in dentistry comparing two different health economic models.

Design and outcome measures: Intervention effectiveness was estimated in a cluster randomised controlled trial. Number of quitters was estimated based on 7-day abstinence and on smoking reduction at follow-up. Health economic evaluation was performed using two models: 1) A population-based model employing potential impact fractions, and 2) a Markov model estimating the cost-effectiveness of the intervention for the actual participants. The evaluation was performed from health care and societal perspectives and health gains were expressed in quality adjusted life years (QALYs).

Setting: Dental clinics in Sweden.

Participants: 205 Swedish smokers aged 20-75 years.

Interventions: A brief, structured behavioural intervention was compared with "usual care".

Results: The cost per quitter was 552 USD in the intervention and 522 USD in the "usual care" condition. The net saving estimated with the population-based model was 17.3 million USD for intervention and 49.9 million USD for "usual care", with health gains of 1428 QALYs and 2369 QALYs, respectively, for the whole Swedish population during 10 years. The intervention was thus dominated by "usual care". The reverse was true when using the Markov model, showing net societal savings of 71,000 USD for the intervention and 57,000 USD for "usual care", with gains of 5.42 QALYs and 4.74 QALYs, respectively, for lifelong quitters.

Conclusion. The comparison of intervention and "usual care" derived from small-scale studies may be highly sensitive to the choice of the model used to calculate cost-effectiveness.

Trial registration: The cluster randomised trial is registered in the ISRCTN Register of controlled trials with identification number ISRCTN50627997.

Strengths and limitations of this study:

- The cost-effectiveness of a brief counselling for smoking cessation in dentistry was assessed using two different models: an individual level Markov model and a population-based model.
- The comparison of the two models' estimates, due to different modelling assumptions, illustrates the importance of model choice.
- The non-significant differences in the effectiveness of the novel intervention compared with the control condition imply uncertainty of the subsequent economic evaluation.
- The uncertainty of the estimates is further increased by the assumptions made on long-term quit rates.

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INTRODUCTION

Despite continuously declining prevalence, cigarette smoking contributes to 7.5% of the burden of disease in Sweden,[1] and was estimated to stand for 6.7% of the national costs for health care and loss of production in 2001.[2] Quitting smoking substantially decreases the risk for its negative health consequences [3] through a notable reduction in the risks for cancer, cardiovascular disease, and diabetes. [3-5]

Health care providers in Sweden are encouraged to offer their patients support for smoking cessation.[6] Optimally, such interventions should be of low-intensity in order to be delivered as a part of the routine care. Due to the high proportion of the general population visiting dental care regularly, and for the oral health consequences of smoking, dental clinics are a particularly suitable setting for the delivery of brief smoking cessation counselling.[7 8] However, counselling in dentistry is currently underutilized and will remain so unless training of professionals and changes in the health system are introduced.[9 10]Health economic evaluations offer the possibility to compare interventions in terms of their costs and health effects, thus facilitating decision-making.

Evaluations have so far confirmed the effectiveness and cost-effectiveness of smoking cessation interventions.[11] Brief advice for smoking cessation has also been found cost-effective,[12 13] but economic evaluations of such interventions in dental care are lacking. Cost-effectiveness estimates obtained from other health-care settings may not apply to dentistry. In fact, among smoking patients seen in dental care there is an over-representation of healthy individuals and light smokers not very motivated to quit. Also, dental care professionals and dental clinics' organization may have lower capacity to address lifestyle factors compared to other health care settings, thus impacting on the delivery of preventive advice. One Swedish study conducted an economic evaluation of high and low intensity smoking cessation interventions in dental care,[14] but because of their intensity, neither of these formats could be considered as brief advice. In summary, the knowledge about cost-effectiveness of smoking cessation interventions in dental care is incomplete.[15]

The majority of cost-effectiveness studies of smoking-cessation treatments used mathematical modelling based on simulation techniques.[16] Different models have been developed to reflect the influence of smoking and smoking cessation on future health risks. Bolin [16] emphasized two type of models: the more common Markov-type models [17 18] and the dynamic population-based simulation models that allows for the user to specify epidemiological details of the studied population[19 20]. .Markov models are typically used to evaluate the cost-effectiveness of an intervention in a specific setting for the intervention's target group while dynamic population based models are often used to estimate policy impact on public health. The estimates obtained with these two approaches may differ, as may the implications for decision-making.

In this study, we present an estimation of the cost-effectiveness of a brief structured counselling for smoking cessation delivered in the context of dental care in Sweden, the effectiveness of which was assessed in a randomized controlled trial (FRITT Study).[21] The study was guided by two research questions:

1) Is the brief counselling for smoking cessation in dentistry a cost-effective public health intervention compared with "usual care"?

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2) Does the cost-effectiveness of the intervention differ if it is estimated with a population-based model compared with an individual based Markov model?

METHODS

The study was approved by the Ethical Review Board of Stockholm Region, March 15, 2012 (nr. 2012/237-31/5). The participants were included in the study only after they had given written informed consent.

The intervention

The economic evaluation was conducted based on data from a cluster randomized controlled trial that compared brief counselling for tobacco cessation with usual care provided to Swedish tobacco users in dental clinics.[21] The study is registered in the ISRCTN Register of controlled trials with identification number ISRCTN50627997. The English translation of the original study protocol is available as supplemental file.

Briefly, 27 dental care clinics were randomized to either alternative intervention or control condition and recruited thereafter patients aged 18-75 years who were daily tobacco users (Fig 1). Follow-up was conducted six months after enrolment (97% retention). All information was self-reported by the patients. Dental clinics were approached between May and August 2012. The training of personnel was delivered during September 2012. Patients were recruited between October 2012 and January 2013 and the 6-month follow-up was completed in November 2013. The intervention consisted of a structured brief advice based on the 5A's model delivered once during a dental visit performed by a dentist or a dental hygienist. The control condition implied delivering care as usual according to the clinic's routines, if any. Approximately half of the clinics in the control condition had personnel trained in tobacco cessation and routines concerning patients' tobacco use. All patients at intervention clinics and approximately 72% of patients at control clinics received some level of advice on tobacco use. However, counselling at intervention clinics was on average more extensive, including for instance information on available support and pharmacological treatment almost ten times as often as on control clinics. While tobacco cessation advice, if received, lasted on average 3.5 minutes at the control clinics, the duration was 5 minutes longer (i.e. 8.5 minutes) at intervention clinics.

(figure 1 here)

The study sample

In the main study [21] participants (n=467) consisted of current daily smokers (n=218), current snus users (n=200), and dual users of cigarettes and snus (n=41). Due to the much less established burden of disease caused by the Swedish type of smokeless tobacco (snus)[22] only data from smokers was used in the current economic evaluation. In addition, we restricted the analysis to individuals aged 20 years or older because the population based model was limited to adult population 20-84 year old. There were 13 participants younger the 20 years and none of these individuals changed smoking

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habits. Thus, the analytical sample from the effectiveness study on which the present economic analysis is based comprised 99 smokers in the intervention condition and 106 smokers in the control condition ("usual care").

With the analysis was limited to smokers, no statistically significant differences between intervention and control group were seen in any of the studied outcomes. The primary outcome, 7-day point prevalence of abstinence was defined as "not having smoked from a cigarette, not even a single puff in the 7 days preceding the survey". This condition was self-reported by 8% of participants both in the intervention and in the usual care condition. A secondary outcome entailing substantial tobacco reduction was calculated as reporting at follow-up an amount of cigarettes per day equal to or less than 50 % of that reported at baseline. This reduction was achieved by 27% of participants in the intervention condition and by 17% in the comparison condition.

Economic evaluation

We present an incremental cost-effectiveness analysis with long-term health effects. The alternative intervention was compared with "usual care". The cost-effectiveness analysis was designed to follow the Swedish recommendations [23] on economic evaluations of health care interventions. Therefore, costs were calculated from healthcare and societal perspectives, while health effects are expressed in QALYs (quality-adjusted life-years). The intervention under study was conducted in 2012, thus the intervention costs as well as societal costs in the models were estimated in Swedish crowns (SEK) per 2012. Further, the costs were inflated to reflect 2014 costs according to the Swedish consumer price index [24] and converted to 2014 US dollars (USD) using the purchasing power parity (PPP) estimates with CCEMG – EPPI-Centre Cost Converter(http://eppi.ioe.ac.uk/costconversion/default.aspx).

Both costs and QALYs were discounted 3 percent annually. Long-term costs and health effects were simulated using two models:

1) A population-based simulation model employing potential impact fractions, where the intervention effect is assumed to change the incidence in tobacco related diseases, including diabetes mellitus type 2, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD) and seven cancer diagnoses, including lung cancer
2) An individual-level Markov model incorporating the decreased smoking-related risks for lung cancer, COPD, and CVD

Intervention costs

Only the costs connected with the delivery of the interventions were included in the analysis. The quantity of resources consumed was obtained from the study's accounting records. The unit costs were obtained from national public databases, from suppliers' websites and from the organizers of the training. Total intervention costs were obtained by multiplying the volume of each cost category by its respective unit cost. Intervention costs were divided into training and operating costs. The costs were not discounted because the interventions was delivered during four months

Training costs for the brief advice included costs for salary and travel costs for the trainer, venue, and materials, as well as allowance for training time for trainees (4 hours per dental professional). Only 20% of the total costs were considered, in order to accommodate for the spread over a five-year

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period before refresher training may be needed, as it was previously done in similar studies[25 26] . The number of patients who smoke, per dental care professional, was estimated based on the prevalence of smoking in Sweden, [27] and the average number of patients the practitioners in the trial reported seeing each year.

Operating costs represented the costs of delivering tobacco cessation counselling in intervention and "usual care" conditions and were estimated based on the duration of the counselling and on average salaries including social charges.

Other costs connected with the interventions included patients' time in attending counselling, based on the mean duration of the counselling, and use of nicotine replacement therapy (NRT) or other medications for tobacco cessation. Costing of patients' time was estimated based on the opportunity cost of foregone leisure time and calculated at 25% of the Swedish average gross wage rate. [28] The cost of medications was estimated based on the retail price of the most commonly used drugs and on the recommended duration of use.

To estimate the cost of the interventions if they were applied to the entire Swedish population we estimated the number of daily smokers who visit dental clinics during a year. The number of smokers was obtained from national surveys[27], as was the number of adults visiting dental care each year.[6] Each year, 449 000 smokers were estimated to visit dental care.

Estimate of intervention effectiveness

The effectiveness of the novel intervention was estimated from the trial's outcomes, 7-days abstinence and smoking reduction by half. We assumed that reducing cigarette consumption by half would lead to sustained abstinence for 15% of the reducers, [29-32] while all quitters were assumed to maintain abstinence. On the population level, the change in smoking prevalence was calculated by multiplying the proportion of quitters due to the intervention by the number of smokers seeking dental care each year. In the health economic evaluation we assume that the estimated quitters will be continuously abstinent after the study's end (6-month follow-up)

Population-based simulation model

We simulated the impact of changes in incidence of and related societal costs for several chronic diseases during ten years, following the assumed changes in smoking prevalence because of the interventions in the Swedish population 20-84 years old in 2014. A model denominated *Risk factors, Health and Societal Costs* [33] was adapted for this study. The model simulates effects on health outcomes associated with smoking, including diabetes mellitus type 2, ischaemic heart disease, ischaemic and haemorrhagic stroke, COPD, and cancer of the lung, oesophagus, liver, larynx, stomach, pancreatic, colon and rectum.

In this model we used a modified version of the potential impact fraction,[34 35] where the intervention effect changed the relative risk (RR) of disease of the exposed category (smokers), while keeping the prevalence of exposed category constant. In our case, the RR changes for smokers when some of them quit.

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$$PIF = \frac{\mathrm{Ps}*\mathrm{RRs} - \mathrm{Ps}*\mathrm{RRs}'}{\mathrm{Ps}*\mathrm{RRs}} \quad [1]$$

where:

Ps is the prevalence of smoking,

RRs is the relative risk of disease associated with smoking,

RRs' is the changed relative risk of disease after the intervention when a part of smokers have quit.

The incidence rate of the disease after this change in the related risk factor (I') becomes:

$$\mathrm{I}' = \mathrm{I} * (1 - \mathrm{PIF}) \quad [2]$$

where I is the original incidence rate.

The relative risks for smokers compared to non-smokers were estimated from epidemiological studies, as presented in the technical report,[33] and additionally: ischaemic heart disease, ischaemic and haemorrhagic stroke,[36-39] COPD,[40 41] and different cancers.[42 43] The changing RRs (RRs') were calculated for every year and every disease, based on the decrease in risks for ex-smokers over time. For ischaemic heart disease, stroke, COPD, and lung cancer we used the estimations presented in Hurley and Matthews.[44] We assumed that risks for ex-smokers for diabetes mellitus follows the pattern of CVD decrease while the risks for other cancer diagnoses decrease linearly during 20 years. The QALY weights were used to describe the losses in health-related quality of life due to the models diseases. The weights are community-based, derived via the EQ-5D classification system with the UK time-trade-off valuations[45]. The time horizon is 10 years and the economic and health gains were calculated based on decreased incidence of the diseases during ten years and increased health-related quality of life (QALYs).

The societal costs include medical treatment costs and municipal costs for care, hence the model adopted a limited societal perspective as patient and productivity costs are not included. Swedish national registers were used to retrieve disease incidence and disease-specific medical care costs, while municipal care costs were estimated via a Swedish study. The model was developed in Excel (Microsoft Office, 2010); details of the model are published in a technical report.[33]

Markov model

A Markov model was used to estimate health consequences and societal costs of smoking cessation.[46] The model has been used in similar studies in Sweden[14 47] and was updated for the purpose of the current analysis. The model simulates the societal effects of quitting smoking on three diseases: lung cancer, COPD, and CVD, including CHD and stroke. The model incorporates the smoking-related disease risks, time-dependent remaining excess disease risks after quitting, the death risks for the specific and for unrelated diseases, as well as the societal effects of the three diseases. All disease risks are annual age- and gender-specific excess incidence until death or the age of 95 years. The societal costs include costs associated to: medical treatment, municipal costs for care, drugs, informal care and other expenditures for patients and relatives as well as morbidity

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productivity costs. Health outcomes are expressed in QALYs. The number of quality-adjusted life years (QALYs) were calculated during healthy years and years spent diseased, until death or the age of 95 years. Swedish average age- and gender specific QoL weights were used, for healthy years. [48] For years with disease, disease-specific QoL decrements taken from international studies were deducted from the average QoL.
Most of the societal costs were derived from Swedish studies published during the 2010s and were reported as distributions, i.e. with the Gamma parameters or bootstrapped 95 percent confidence interval, in order to enable stochastic estimation.

The Markov stages are one year long, with no half-cycle correction. The probabilistic model is run as a microsimulation with 10,000 repetitions. The Markov-cycle tree was created in Treeage Pro (Treeage Inc., 2015). Details on the model are available from a technical report.[46]

Sensitivity analyses

Several one-way sensitivity analyses were conducted to test the robustness of the results. First, we examined the effect of changing the assumptions about the proportion of smokers assumed to achieve permanent abstinence after reducing consumption by half to: a) 5% and b) 25%. Secondly, we examined the effect of changing the assumption of intervention coverage of dental care patients to 70%. Thirdly, we included the full training costs into the intervention costs.

To illustrate the correspondence between the two models a detailed calculation restricted to one gender and age group was performed with the same time frame (10 years), using only the health care perspective.

RESULTS

Intervention costs

Table 1 shows the costs of the interventions. Most of the interventions' costs could be attributed to the use of NRT and other medications.

Table 1. Intervention costs, in 2014 USD

		Intervention		"Usual care"	
	Unit price	Units *	Cost	Units*	Cost
Training cost					
Course fee					
Salary for trainer, delivery [a]	26.0	4	103.9		
Salary for trainer, preparation [a]	26.0	1	26.0		
Salary for trainer, travel time [a]	26.0	2	51.9		
Travels for trainer [b]	23.0	1	23.0		
Material [c]	2.30	25	57.5		
Venue and refreshments [c]	777.8	1	777.8		
Total course fee for 25 participants			**1040.0**		

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Total course fee per participant (practitioner)			**41.6**		
Compensation for training time for practitioners					
Compensation for training time: dentists [c d]	264.3	4	1057.2		
Compensation for training time: dental hygienists [c d]	103.4	4	413.7		
Average allowance for practitioners (80% dental hygienists)	135.6	4	542.4		
Total training cost per practitioner			584.0		
Estimated yearly training cost per smoker [e]			**2.3**		**0**
Operating costs					
Salary for dentist [a]	38.7				
Salary for dental hygienist [a]	25.0				
Average salary for practitioners (80% dental hygienists) [a]	27.7	0.14	**3.9**	0.04	**1.1**
Patient's time cost [a]	5.2	0.14	**0.7**	0.04	**0.2**
NRT/other drugs [b f]	172.4	0.28	**48.8**	0.28	**47.9**
Total costs					
Per smoker			**55.7**		**49.2**
All smoker visiting dental care/year[+]			**25,000,000**		**22,100,000**

[*] Hours or number

[a] Information on average salaries from Statistics Sweden: www.scb.se

[b] Based on information from suppliers' websites

[c] Based on the study records or information from training organizers

[d] Includes loss of revenue

[e] Estimated yearly number of smokers visiting a dental practitioner: 50

[f] Proportion (units) based on information from the trial

[g] Estimated by costs/smoker * number of adults visiting dental care each year (=449 000)

Total cost for the brief advice was estimated at 56 USD per smoker and the difference in costs between the intervention and "usual care" was 6.5 USD. The cost per quitter was 552 USD in the intervention and 522 USD in the "usual care" condition. If delivered to all Swedish smokers visiting dental care every year, the total costs would be 25.0 million USD per year for the alternative intervention and 22.1 million for "usual care".

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Intervention effectiveness

Ten smokers (four men and six women) could be expected to quit in "usual care" condition, compared with ten smokers (only women) in the intervention condition.

When the effects were applied to the entire population, the prevalence of smoking among men was projected to decrease from 8.9% to 8.8% for the novel intervention and to 8.3% for "usual care". The prevalence of smoking among women would decrease from 11.6% to 10.5% for intervention and to 10.8% for "usual care". The estimations of effectiveness are presented in Table 2.

Table 2. Effectiveness estimation

	Intervention			**"Usual care"**		
Age	20-44	45-64	65-84	20-44	45-64	65-84
Participants in the FRITT study (n)						
Men	11	20	2	9	20	9
Women	19	41	6	20	37	11
Reduced cigarette consumption by half (n)[a]						
Men	2	2	0	1	2	0
Women	5	9	1	2	4	0
Quitters (n)						
Men	0	0	0	1	2	1
Women	2	5	1	1	1	3
Effectiveness data, estimated quitters (n) – used in Markov model [b]						
Men	**0**	**0**	**0**	**1**	**2**	**1**
Women	**3**	**6**	**1**	**1**	**2**	**3**
Proportion of estimated quitters (%)						
Men	3	2	0	13	12	11
Women	14	15	19	7	4	27
Swedish population (n)						
Men	1629855	1228289	788907	1629855	1228289	788907
Women	1561289	1205769	867493	1561289	1205769	867493
Number of smokers in Sweden(n)						
Men	114090	147395	63113	114090	147395	63113
Women	124903	192923	104099	124903	192923	104099

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Number of smokers who visit dental care each year (n)						
Men	57045	95807	41023	57045	95807	41023
Women	62452	125400	67664	62452	125400	67664
Effectiveness data, prevalence of smokers in the population (%) – used in population-based simulation model [c]						
Men	**6.90**	**11.88**	**8.00**	**6.55**	**11.10**	**7.42**
Women	**7.42**	**14.39**	**10.51**	**7.74**	**15.55**	**9.87**

[a] Results from FRITT study

[b] Calculated as 15% of the "Reduced cigarette consumption by half" plus "Quitters"

[c] Calculated as "(number of smokers in Sweden - (proportion of estimated quitters * smokers who visit dental care each year))/ Swedish population in the age and sex group"

Cost-effectiveness analyses

Model outputs and cost-effectiveness analyses are presented in Table 3, with a detailed example given for women aged 45-64 years in Table 4.

Table 3. Model outputs- Markov and population-based models. Costs in thousand USD 2014.

	Intervention			"Usual care"			ICER (Intervention vs "Usual care")		Conclusion
	Female	Male	Total	Female	Male	Total	Diff QALY	Diff costs	
Markov model									
Intervention cost			**4.9**			**5.2**			
Cost savings	-77	0	**-77**	-31	-32	**-63**			
Net costs			**-72.1**			**-57.8**			
QALYs	5.42	0	**5.42**	2,37	2,36	**4,74**			
							0,68	**-14,3**	***Dominant***
Population model									
Intervention cost			**25,000**			**22,100**	Diff QALY	Diff costs	
Cost savings	-39,562	-2,756	**-43,318**	-34,854	-37,125	**-71,979**			

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Net costs			**-18,318**			**-49,879**			
QALYs	1327.8	100.4	**1428.2**	1117.1	1252,2	**2369.3**			
							-941.1	**31,561**	***Dominated***

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Table 4. Model outputs in the subgroup of women 45-64 years. Markov and population-based models, 10 years' time horizon, health care perspective. Costs in 2014 USD

	Intervention effect	Health care cost	QALYs
Markov model			
Per quitter:	Quitters: 1	-547	0.02
Population-based model			
Intervention	Change in prevalence: 1.61% Quitters (n): 19 422	-11607004 Per quitter: - 598	604.94 Per quitter: 0.03

Markov model

The gains associated to the novel intervention resulted in societal savings of 77,000 USD, including savings of 32,000 USD in health care, and 5.42 QALYs. For "usual care", the gains were societal savings of 60,000 USD, including savings of 26,000 USD in health care, and 4.74 QALYs. The model showed the net societal savings of 72,100 USD for the intervention and 57,800 USD for the "usual care" group, with associated gains in QALYs, 5.42 for the intervention and 4.74 for "usual care" during the lifetime. According to this model, the brief intervention was ***dominant***; entailing cost saving and additional health gain of 0.68 QALYs.

Population-based model

The brief intervention applied to smokers showed a total societal saving of 42.3 million USD, of which 27.6 million USD were savings in health care costs, and a gain of 1428 QALYs for the full Swedish population 20-84 years old during 10 years. The corresponding estimates for "usual care" demonstrated a total societal savings of 72.0 million USD, out of which 46.9 million USD were savings in health care costs, and a gain of 2369 QALYs for the full Swedish population 20-84 years old during 10 years. When both intervention costs and estimated societal savings are considered, the net societal saving was 17.3 million USD for the brief advice and 49.9 million USD for "usual care", with health gains as above. Thus, the brief novel counselling was more expensive and less effective, so called ***dominated*** by the "usual care" alternative, according to the population-based model.

Sensitivity analyses

When the proportions assumed to achieve abstinence after reducing by half were set to 5% or to 25% the magnitude of the difference between two models remained. As with the main analysis, the population-based model favoured "usual care" over the novel intervention, while the Markov model favoured this latter over "usual care". Likewise, when the coverage of the brief advice or of "usual care" was assumed to be 70 % the gains decreased but the patterns of difference were similar to the main analysis. When including all training costs into the intervention costs the results were almost similar to the main analysis.

In order to illustrate the correspondence between the population-based and Markov model, separate calculations were done restricted to women in age group 45-64 years, using 10 years' time

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horizon and only the health care perspective. The estimation from the population-based model for this group shows cost savings for health care sector of 598 USD per quitter. The health care savings estimated with the Markov-model for the same group during 10 years were 547 USD per quitter. In essence, for this group both models show the same level of cost saving for a quitter as well as the same level of health gains (0.02 versus 0.03 QALYs).

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DISCUSSION

In this economic evaluation, the cost-effectiveness of a brief manualized counselling for smoking cessation in dentistry was assessed using two different models: a population-based model comparing different scenarios of smoking prevalence, and a Markov model estimating the outcomes for the quitters. A similar population-based model was presented in Magnus et al. [49] while a similar Markov model was presented in Hurley and Matthews.[44]

The original trial did not show any significant effect on smoking cessation of the novel intervention compared to usual treatment in a sample of smokers not selected according to their motivation to quit. The alternative intervention's costs were low, under 60 USD per patient, and the incremental cost compared with "usual care" was less than 7 USD per patient. In the intervention condition, the cost per quitter was only slightly higher than in the control condition and it compares favourably to the estimated cost per quitter in other smoking cessation studies.[11]

Nevertheless, the comparison of the economic effects between the intervention and "usual care" favoured the latter when modelling the population impact. In contrast, using the outcomes for the quitters in a Markov model showed that the intervention was preferable to "usual care", resulting in net societal cost savings and some gain in QALYs.

The difference in results with the two modelling strategies could be expected, in the first place because they differ in several aspects of model specification. The population-based model only considers health care costs and municipal costs for care, while the Markov model also considers cost for medications, costs for patients and relatives and morbidity productivity costs. The time frame was also different, i.e.10 years for the population-based model and lifetime for the Markov model. Finally, there were differences in the number of diseases included. However, as the comparison by cost category in Table 4 shows, the magnitude of costs is similar for both models.

The opposite conclusions from the two models are probably best explained by the difference in the population to which the simulation is applied. In fact, the population-based model estimates the effect of the intervention brought to the entire population of smokers in Sweden, while the Markov model simulates individual effects for the quitters in the study cohort. Quitters in the intervention group were in average younger than in the "usual care" group and all of them were women, while the gender distribution of quitters was more balanced in the "usual care" group. Thus, the Markov model shows greater gains in QALYs and societal savings for the alternative intervention due to longer time horizon for younger age groups. In contrast, the population-based model converts the trial outcomes to age- and gender-specific population prevalence.

The modelling strategies inherent in the two models explain why the cost-effectiveness results differ between the models. Population-based models simulate how changes in prevalence of risk factors affect the disease incidence over age- and gender-specific groups. The individual-based Markov models simulate the changes in disease incidence because of changes in risk factors in a specific, albeit hypothetical, individual of a certain age and gender. In population-based models, groups with a high disease incidence affect the estimates more than groups where the incidence is lower at the start of the simulation. In this study, the four male quitters in the control group affected the result disproportionally, in particular as there were no male quitters in the alternative intervention group.

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Small trials with few participants, and more importantly, few successful participants, are not likely to represent the population to which the interventions are to be applied, thus skewing the estimates in population-based models.

The weaknesses of this study include non-significant differences in the effectiveness of the novel intervention compared with the control condition. Further, some assumptions as about the proportion of reducers eventually quitting, or about all quitters achieving sustained abstinence may not be tenable and thus contribute to increase the uncertainty of the estimates.

To our knowledge this is the first study to evaluate the cost-effectiveness of a brief advice for smoking cessation in dental clinics in Sweden. The combination and comparison of two different approaches for the estimation of cost-effectiveness is an additional original contribution providing insights on factors to be considered in decision making about large-scale dissemination of an intervention. In this regard, we offer the general recommendation to avoid the estimation of cost-effectiveness with population-based models from small-scale trials with skewed effectiveness across participant groups.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the paper. SeV contributed to acquisition of data, analyzed the data and drafted paper IF and PmJ made substantial contributions to design of cost-effectiveness analyses and interpretation of the results, MrG was a principal investigator in the FRITT study and made substantial contribution to estimation of the effectiveness of the intervention. All the authors critically revised the manuscript and approved the final version for publication

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: SV reports grants from The National Board of Health and Welfare, during the conduct of the study and personal fees from The National Board of Health and Welfare, outside the submitted work, PJ reports grants from The National Board of Health and Welfare, during the conduct of the study, MG reports grants from The National Board of Health and Welfare, personal fees from The Stockholm County Council, during the conduct of the study; personal fees from The Stockholm County Council, grants from Public Health Agency of Sweden, grants from FORMAS, outside the submitted work, IF has nothing to disclose.

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DATA SHARING

No additional data available.

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FIGURE LEGENDS

Fig 1. CONSORT flowchart. Enrolment, allocation, and retention of participants.

SUPPLEMENTARY FILES

English version of study protocol for the cluster randomized controlled trial (FRITT)

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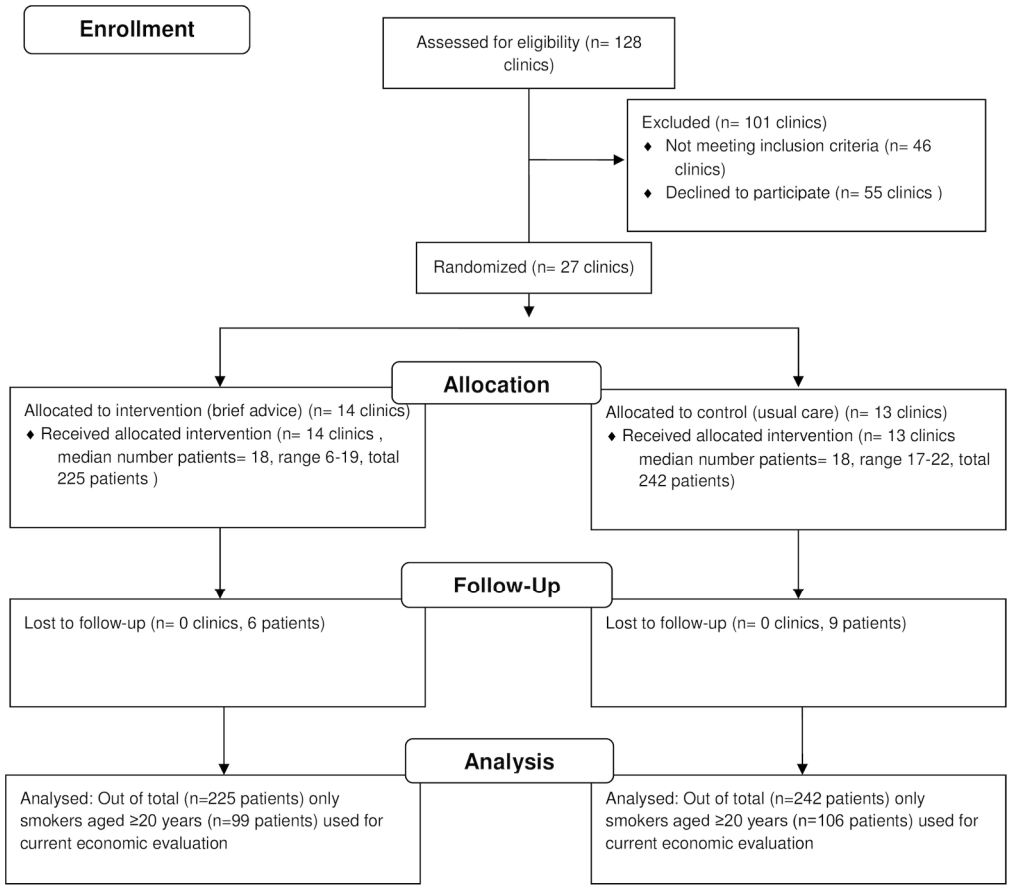

Fig 1. CONSORT flowchart. Enrolment, allocation, and retention of participants

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APPENDIX 2 Research Plan

Project "Free from Tobacco in Dentistry" (Fri från Tobak i Tandvården - FRITT)

Title: Effectiveness of a brief counselling for tobacco cessation among smokers and snus users in dental care.

Aim and research questions

In accordance with the Ministry of Social Affair's assignment to the National Board of Health and Welfare (Government's decision 11:18, 2011-06-16) this evaluation plan is primarily aimed to answer the question *whether a brief patient-centred intervention delivered as part of the routine care in a dentistry is effective for promoting behavioural change in tobacco use, on individual level*. If the intervention proved effective, a further aim is to deem the applicability of the intervention in the frame of routine dental care. Additional secondary research questions that the evaluation plan aims to answer are: whether counselling affects intermediary behavioural factors, for instance support seeking at different care givers; costing of diverse intervention components (e.g. training of the personnel, information materials, etc.).

2. Method

2.1 Intervention

The counselling model to be evaluated is developed by the National Institute of Public Health. The main characteristics of the model are:

1. Increasing motivation, if it is taken that high level of motivation, associated with information on available support, is the most important factor for achieving permanent abstinence. The patient can thereafter decide which support is needed and follow the active advice given by the dental care professionals.
2. Includes referral to primary care or other professional counselling as described above
3. Brief counselling (duration of conversation approximately 5 minutes), which is a requirement to be able to carry out the

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intervention without impact the effectivity of the prevailing clinical care.

4. Brief training for the counsellors, which has a positive impact on resource use in the eventual later implementation stage.

2.2 Population

The target group for evaluation of the intervention are patients with established tobacco use (smoking and/or snus) seeking care during the study period at the selected dental care clinics in the counties of Södermanland and Örebro. The choice of the counties was based on:

a. Geographic location in central Sweden, to assure logistical viability
b. Possibility to adopt referral system between dental care and primary care centres
c. The proportion of dental professionals in private sector, where one county with high (Södermanland) and one with low (Örebro) proportion will be included in the evaluation.

2.3 Design

The evaluation will be conducted as a randomized controlled study, in which the dental care clinics will be the entities randomly chosen to either apply the novel counselling model (intervention condition) or to follow the usual counselling according the clinic's practice (control condition). Dentists and/or dental hygienists in the intervention condition will be trained in and to deliver the new counselling to smoking or snus using patients during the project period. The affected dental care professionals in both the intervention and the control conditions will document treatment of their patients tobacco use. The procedure for data collection and follow-up will be identical in both groups. The follow-up period for each patient is six months.

2.4 Study protocol

We aim to include approximately 30 dental care clinics, 30 dental care professionals and at least 460 patients in the evaluation.

2.4.1 Selection and randomization of the dental care clinics

Step 1. A county's stratified sample of approximately 70 dental care clinics - no specialized clinics – is drawn from the most updated registry from The Dental and

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Pharmaceutical Benefits Agency, accessible through each county council.

Step 2. The manager/responsible for each clinic is invited to a meeting held on regional level, where the evaluation team will explain the background and setup of the project. For each clinic information of structural character is collected (Appendix 1).

Step 3. Preliminary consent for cooperation and randomization is given by the operations manager.

Step 4: The dental professionals (dentists or dental hygienists, depending on who meets the patients at first hand) in the affected clinics are contacted by the managers and asked for cooperation, including following obligatory components: participation in a training on counselling skills, implementing of the counselling with the intended number of smoking or snus using patients, registration of information about the intervention and its evaluation (Appendix 2). For each clinic two staff members are selected (one regular and one deputy) to recruit patients for the project, but other staff can choose to participate in the training. Clinics where no personnel are willing to cooperate are considered dropouts, irrespective of earlier position of the manager. Apart from what is needed for implementing the intervention, the clinics are advised against changing their organizational routines in order to enable participation in the study.

Step 5: The cooperating clinics are assigned a minimum number of patients to be recruited for the study, based on an estimation of the patient turnover (average: 15 patients). For the purpose of the study, a unique code will identify each clinic. Thereafter, based on a computer-generated random sequence, the clinics are randomized to intervention or control conditions, with as many clinics in each condition. The key for the group identity is kept at the study secretariat,

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separated from the database in which other relevant data for the study will be registered eventually. This is done to avoid that knowledge about the group identity could influence the interpretation or registering of data.

Step 6: The managers and other cooperating staff at the clinics are informed about the outcome of the randomization and are invited to participate respective training days.

Step 7: Training of the dental care professionals in the intervention condition is provided by the National Institute of Public Health with methods described in the chapter on the intervention. The training day for the control condition is held by Karolinska Institute, and will include general information about the project and its evaluation. During the training, a detailed demonstration on the procedures in the evaluation protocol are given to both groups. The training is obligatory in order to participate in the study. Two opportunities to participate in the training are offered for each clinic, thereafter absence is considered dropout in the study.

Declined participation at steps 1-4 represents pre-randomization dropout, at steps 6-7 post-randomization. We expect a total dropout rate at approximately 50 % on the clinic level.

2.4.2 Recruitment of patients

Patients seeking care at the chosen dental care clinics during the study recruitment period (see section 2.6) can be included in the evaluation if they fulfil the following criteria:

a. Adequate understanding of Swedish, both oral and written or access to interpret
b. Age between 18 and 75 years

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c. Uses tobacco daily (each of the previous 30 days) as cigarettes, other smoked tobacco and/or snus, since at least one year back

Patients are excluded if:

a. Seeking acute care
b. Current use of medicines for tobacco cessation (nicotine replacement therapy, bupropion, vareniklin, etc.)
c. Abuse of drugs or other mental illness which can affect the voluntariness of participation in the study or the reliability of the reported information

The choice to recruit to the study also patients with chronical oral harm is made for two reasons: partly because these patients are interesting as they represent the target group for indicated prevention [2]; party to hasten the recruitment of the desired number of patients.

The recruitment will be done according the following schedule.

Step 1: The patients who have booked visit to the clinic is asked to fill out a form (Appendix 3) where background information is asked about, prerequisites for recruitment is assessed, and short information about the study is given.

Step 2: A dental hygienist or a secretariat controls the information and refers patients not fulfilling the criteria to their appointment. The remaining patients are asked to read detailed information about the study (Appendix 4), to sign an informed consent (Appendix 5), and to provide additional baseline information (Appendix 6). The signed consent is given directly to the dental care personnel at the appointment, and thus they can deliver the intervention (in the intervention condition) or the customary information (in the control condition).

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Step 3: Before the patient leaves the clinic, a new appointment is booked for oral health control after 6 months. The appointment is voluntary and free of charge for the patient. The aim of the visit is to promote adherence to the follow-up questionnaire. Patients who have not been booked for a follow-up visit will be mailed the questionnaire according to the procedure described under 2.4.5

Step 4: A note on the patients included in the evaluation is made in their medical record, while other information from the form are transferred to the study secretariat for central registration in a specifically designed database, in which the patients are identified with the clinic's code and the id number of their record.

Step 5: Basic information (gender, age, tobacco use habits) on the patients excluded from or declining to participate in the study are registered anonymously and without a code key in a separate database.

The procedure is repeated for each consecutive patient until the clinic has achieved the quota of number of patients to be recruited. The duration of the recruitment is estimated to be approximately three months. We expect a dropout rate of approximately 30 % among eligible patients.

2.4.3 Implementation of the intervention

The affected dental care staff in the respective groups implements the intended counselling during the appointment following recruitment, at an appropriate time. Information on the counselling (especially duration) is registered locally in an electronic document (template shown in Appendix 7).

2.4.4 Monitoring of the control group

In an intervention with a control condition, it is particularly important to document any treatment or

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other actions provided to the control group. The reason for this is to be able to draw correct conclusions on the effectiveness of the novel intervention, especially if only a moderate or no effect is reported. In a naturalistic experiment, the control group's exposure is not manipulated, and therefore it can be assumed that more or less intensive actions with previously unknown effects reach also these individuals. Besides, the use of motivational interviewing, MI, is rather prevalent in the Swedish healthcare, according to recommendations issued by, among others, the National Institute for Public Health (http://www.fhi.se/Metoder/Halsoframjande-och-forebyggande-metoder/Motiverande-samtal/).

The dentists or dental hygienists at the control clinics commit to document the same information as the intervention group on any tobacco counselling with recruited patients, according to the protocol (Appendix 7).

2.4.5 Follow-up and measuring of the outcome

A measurement on the patient level is intended six months after the first visit (recruitment).
The primary outcome will be the so called point prevalence of abstinent patients (have not used tobacco during the past seven days)
The following will be considered as *secondary outcomes*:

a. Continuous abstinence during the past three months
b. Reduction with at least 50 % of the daily tobacco use in the last month (number of cigarettes/day and/or snusboxes/week) compared with the baseline

Information on the outcome is collected by a questionnaire (Appendix 8), in connection with the revisit, which is booked at the time of recruitment (see section 2.4.2) or sent home to the affected patients.

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At follow-up, the following reminder is sent to the absent or non-responding patients:
Reminder 1: text message and a printed or electronic version of the questionnaire are sent at latest one week after the missed appointment or two weeks after the mailed questionnaire. Patients are given opportunity to book a new free visit at latest one week after the reminder.
Reminder 2: text message urging to fill out the questionnaire - without an offer to book visit – is sent at latest two weeks after the first reminder if previous answer to the questionnaire is not received.
Reminder 3: this last reminder is done by telephone, with offer to answer the questionnaire directly via phone interview, at latest one month after the first reminder.

We expect a dropout rate of 10-12% at 6-month follow-up.

In the Appendix 9, there is a summary of the steps and time plan for the follow-up of the patients.

2.4.6 Data management and privacy

The data collected during the project is registered in electronic databases according to following:

1. Data on patients asked to participate and information on consent is manually entered at each clinic. The resulting databases, with no identification information, are transferred in a safe way to the study secretariat.
2. Data from the baseline questionnaire is registered centrally with optical scanning
3. Data on the counselling and patient data from the follow-up in paper format (identified only with the patient's record number) is sent monthly by the dental clinics to the study secretariat (see below), for optic scanning. Only one contact person is appointed between each dental clinic and the study secretariat

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The computerized registry, which is thereby set up, will have KI as principal and will thereafter be reported to KI's Personal Data Act ombudsman. The set up registry will not be based on identification information(such as personal identity number, name, address, etc.).

Patient related documentation related to the study that is found in supporting documents in paper form (e.g. the signed informed consent), is handled in accordance with record keeping at the original clinic.

2.5 Statistical considerations and data analysis methods

2.5.1 Sample size and statistical power

With a recruited sample of a total of 460 patients (230 in each group), distributed on approximately 30 clinics, the study has 80 % power to find as statistically significant on a 5 % level (double sided test) a relative risk of 6-months point estimated abstinence of 2.0 assuming that the prevalence of the outcome in the control condition is approximately 10 %. This statistical power is calculated considering the study design, which is based on cluster selection, and attrition.

The advantage in recruiting more clinics, each with fewer patients rather than fewer clinics with more patients is that the cluster size has a big impact on how big the final sample size needs to be for achieving the same statistical power [3]. For instance, if the aim was to recruit in average 30 patients per clinic, 520 patients distributed on 17 clinics would be needed. The study on the applicability of the intervention is of descriptive character and is not included in the power calculation.

2.5.2 Data analysis

The results will be analysed according to "intention to treat" principle, i.e. each patient is treated according to the initial randomization irrespective of the counselling actually received [4]. The reporting will be based primarily on the primary outcome.

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In the secondary analysis several outcomes can be considered (see section 1) as well as ”per protocol” analyses, in which the patients’ outcomes are analysed according to the actual exposure to counselling, with regard to underlying factors (see section 2.4.4).
Because the primary outcome is dichotomy, multilevel logistic regression will be mainly used as analytical method [5], considering the cluster based design.

2.5.3 Validity of self-reported data
For the outcome measure, self-reported data on tobacco use at baseline and follow-up will be used. For financial reasons a biochemical validation is not feasible for this evaluation. In randomized controlled trials on tobacco cessation which have validated the self-reported behaviour against a biological marker, an underreporting of daily smoking has been noted among 15 % of study participants in average [6].

2.6 Time plan

During the first six months from the project initiation (120101) the necessary administration for the study will be set up (management team, secretariat, logistics) and preparatory work for recruitment of dental clinics and dental personnel will be done. We intend to begin recruiting patients starting in October 2012.
The recruitment period is estimated to be approximately three months. Accordingly, the follow-up period for the last recruited patients will extend to early autumn 2013.

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The following table shows the outline of the time schedule for the evaluation

2012			2013			2014		
Jan-Apr	**May-Aug**	**Sept-Dec**	**Jan - Feb**	**March-Oct**	**Nov-Dec**	**Jan-Apr**	**May-Aug**	**Sept-Dec**
Recruitment of personnel, set up of secretariat and managerial team	Recruitment of the clinics	Training of dentists						
Protocol review and approval	Data collection at clinic level	Recruitment of patients Delivery of intervention Data collection at patient level		Follow-up of patients				
Selection of dental clinics					Preliminary report on implementation	Scientific article on implementation		Report writing and review
					Preliminary data analysis	Outcome analysis begins	Continuation	Complementary analysis

In house and organization
Intervention and data collection
Analysis and summarizing

2.7 Organization and coordination

The protocol for a randomized controlled trial is complex, and requires a strict monitoring of the different stages to avoid sources of error and thus incorrect conclusions. For this purpose, three organizational bodies are considered necessary:

a. *A study secretariat* with following tasks:
   i. Archiving of administrative data
   ii. Randomization procedures and keeping of code keys
   iii. Contacts with the public and patient requests
   iv. Contacts with the clinics (e.g. reminder)
   v. Focal point for data collection
   vi. Assistance for vid reporting, etc.
   vii. Economic issues

The study secretariat consists of a fulltime research officer/research assistant during first and second years of the project.

b. *A steering group* with following tasks:
   i. Monitoring of the protocol integrity
   ii. Affiliating necessary additional expertise
   iii. Contacts with authorities and orderers
   iv. Assessment of critical incidents of value for the validity of the study results
   v. Disposition of resources
   vi. Contacts with media

   The steering group consists of: a project manager and secretariat; a representative from the National Board of Health and Welfare; an expert in tobacco cessation (not the same who developed the intervention); one/two representatives of dental care; a statistician; a researcher from the same or another institution with expertise in randomized controlled trials. The project manager is the president of the steering group.

c. *An operative group* with following functions*:*
   i. Monitoring of data collection and quality
   ii. Proposals to agenda and supporting information for the steering group
   iii. Execution of the steering group's decisions

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iv. Preliminary analysis of the material

The operative group consists of: the project manager; study secretariat; statistician/data manager (part-time).

3 Ethical questions

The evaluation study will be ethically reviewed before the initiation. The project implies however no physical infringement of risk for the participants. Besides the usual issues with privacy and handling of sensitive personal information, the only ethical consideration is about the usefulness of the novel counselling in contrast with other proven tobacco cessation methods. It is evidently shown in literature reviews, conducted among others by Cochrane Collaboration, that individual qualified counselling is more effective than brief counselling for quitting smoking [7]. The guidelines for disease prevention in health care by the National Board for Health and Welfare [8] recommends that daily smokers and pregnant snus users should be offered qualified individual couselling or proactive telephone courselling, which are much more comprehensive interventions than the brief counselling that will be evaluated in this study.

Intensive tobacco cessation methods are however not applicable in a context, such as dental care clinics, where the time with individual patients is limited, which is why trying a novel approach is warranted. Besides, the proposed intervention is not intended to substitute more intensive tobacco cessation, but rather to increase patients' motivation and hasten the transition to action (e.g. referral to primary care).

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Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Title, page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract, page 2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions	Page 3, lines 36-41 Page 4, line 1-2
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 4, lines 15-38 Page 5, lines 1-11
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Not applicable
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 4, lines 13-21
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Page 4, lines 15-20
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 7, line 16-20 Page 8, lines 1-2
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 5, line 22-23 Page 5, lines 35-36
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 6, lines 18-25
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Page 6, lines 18-25 Appendix

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Section/item	Item No	Recommendation	Reported on page No/ line No
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Not applicable
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 7, line 21-25, ref. 33 Page 8, line5-7 ref.46
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 5, line 17-21
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Page 3, line 26-39
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Ref 33, ref 46
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 8, line 11-19
Results			

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Section/item	Item No	Recommendation	Reported on page No/ line No
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Page 10, table 2
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Page 11, Table 3
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Not applicable
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Page 13, line 23-32 Page 14, line 1-5
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Page 13, Table 4
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Pages 19-16
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 17 “Funding”
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 17“Competing interests”

The CHEERS statement checklist format is based on the format of the CONSORT statement checklist

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Economic evaluation of a brief counselling for smoking cessation in dentistry – a case study comparing two health economic models

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Economic evaluation of a brief counselling for smoking cessation in dentistry – a case study comparing two health economic models

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ABSTRACT

Objectives: This study aimed to compare the cost-effectiveness estimates of a brief counselling of smoking cessation in dentistry by using two different health economic models.

Design and outcome measures: Intervention effectiveness was estimated in a cluster randomised controlled trial. Number of quitters was estimated based on 7-day abstinence and on smoking reduction at follow-up. Health economic evaluation was performed using two models: 1) A population-based model employing potential impact fractions, and 2) a Markov model estimating the cost-effectiveness of the intervention for the actual participants. The evaluation was performed from health care and societal perspectives and health gains were expressed in quality adjusted life years (QALYs).

Setting: Dental clinics in Sweden.

Participants: 205 Swedish smokers aged 20-75 years.

Interventions: A brief, structured behavioural intervention was compared with "usual care".

Results: The cost per quitter was 552 USD in the intervention and 522 USD in the "usual care" condition. The net saving estimated with the population-based model was 17.3 million USD for intervention and 49.9 million USD for "usual care", with health gains of 1428 QALYs and 2369 QALYs, respectively, for the whole Swedish population during 10 years. The intervention was thus dominated by "usual care". The reverse was true when using the Markov model, showing net societal savings of 71,000 USD for the intervention and 57,000 USD for "usual care", with gains of 5.42 QALYs and 4.74 QALYs, respectively, for lifelong quitters.

Conclusion. The comparison of intervention and "usual care" derived from small-scale studies may be highly sensitive to the choice of the model used to calculate cost-effectiveness.

Trial registration: The cluster randomised trial is registered in the ISRCTN Register of controlled trials with identification number ISRCTN50627997.

Strengths and limitations of this study:

- The cost-effectiveness of a brief counselling for smoking cessation in dentistry was assessed using two different models: an individual level Markov model and a population-based model.
- The comparison of the two models' estimates, due to different modelling assumptions, illustrates the importance of model choice.
- The non-significant differences in the effectiveness of the novel intervention compared with the control condition imply uncertainty of the subsequent economic evaluation.
- The uncertainty of the estimates is further increased by the assumptions made on long-term quit rates.

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INTRODUCTION

Despite continuously declining prevalence, cigarette smoking contributes to 7.5% of the burden of disease in Sweden,[1] and was estimated to stand for 6.7% of the national costs for health care and loss of production in 2001.[2] Quitting smoking substantially decreases the risk for its negative health consequences [3] through a notable reduction in the risks for cancer, cardiovascular disease, and diabetes. [3-5]

Health care providers in Sweden are encouraged to offer their patients support for smoking cessation.[6] Optimally, such interventions should be of low-intensity in order to be delivered as a part of the routine care. Due to the high proportion of the general population visiting dental care regularly, and for the oral health consequences of smoking, dental clinics are a particularly suitable setting for the delivery of brief smoking cessation counselling.[7 8] However, counselling in dentistry is currently underutilized and will remain so unless training of professionals and changes in the health system are introduced.[9 10]Health economic evaluations offer the possibility to compare interventions in terms of their costs and health effects, thus facilitating decision-making.

Evaluations have so far confirmed the effectiveness and cost-effectiveness of smoking cessation interventions.[11] Brief advice for smoking cessation has also been found cost-effective,[12 13] but economic evaluations of such interventions in dental care are sparse. Cost-effectiveness estimates obtained from other health-care settings may not apply to dentistry. In fact, among smoking patients seen in dental care there is an over-representation of healthy individuals and light smokers not very motivated to quit. Also, dental care professionals and dental clinics' organization may have lower capacity to address lifestyle factors compared to other health care settings, thus impacting on the delivery of preventive advice. One Swedish study conducted an economic evaluation of high and low intensity smoking cessation interventions in dental care,[14] but because of their intensity, neither of these formats could be considered as brief advice. In summary, the knowledge about cost-effectiveness of smoking cessation interventions in dental care is incomplete.[15]

The majority of cost-effectiveness studies of smoking-cessation treatments use mathematical modelling based on simulation techniques.[16] Different models have been developed to reflect the influence of smoking and smoking cessation on future health risks. Bolin [16] emphasized two types of models: the more common individual-level Markov models [17 18] and the dynamic population-based simulation models that allows for the user to specify epidemiological details of the studied population[19 20]. Markov models are typically used to evaluate the cost-effectiveness of an intervention in a specific setting for the intervention's target group while dynamic population based models are often used to estimate policy impact on public health. The estimates obtained with these two approaches may differ, as may the implications for decision-making.

In this study, we present a comparison of two cost-effectiveness estimates of a brief structured counselling for smoking cessation delivered in the context of dental care in Sweden, the effectiveness of which was assessed in a randomized controlled trial (FRITT Study).[21] The study was guided by the following research question: Does the estimates of cost-effectiveness of a brief counselling for smoking cessation in dentistry differ when estimated with a population-based model compared with an individual based Markov model?

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METHODS

The study was approved by the Ethical Review Board of Stockholm Region, March 15, 2012 (nr. 2012/237-31/5). The participants were included in the study only after they had given written informed consent.

The intervention

The economic evaluation was conducted based on data from a cluster randomized controlled trial that compared brief counselling for tobacco cessation with usual care provided to Swedish tobacco users in dental clinics.[21] The study is registered in the ISRCTN Register of controlled trials with identification number ISRCTN50627997. The English translation of the original study protocol is available as supplemental file.

Briefly, 27 dental care clinics were randomized to either alternative intervention or control condition and recruited thereafter patients aged 18-75 years who were daily tobacco users (Fig 1). Follow-up was conducted six months after enrolment (97% retention). All information was self-reported by the patients. Dental clinics were approached between May and August 2012. The training of personnel was delivered during September 2012. Patients were recruited between October 2012 and January 2013 and the 6-month follow-up was completed in November 2013. The intervention consisted of a structured brief advice based on the 5A's model delivered once during a dental visit performed by a dentist or a dental hygienist. The control condition implied delivering care as usual according to the clinic's routines, if any. Approximately half of the clinics in the control condition had personnel trained in tobacco cessation and routines concerning patients' tobacco use. All patients at intervention clinics and approximately 72% of patients at control clinics received some level of advice on tobacco use. However, counselling at intervention clinics was on average more extensive, including for instance information on available support and pharmacological treatment almost ten times as often as on control clinics. While tobacco cessation advice, if received, lasted on average 3.5 minutes at the control clinics, the duration was 5 minutes longer (i.e. 8.5 minutes) at intervention clinics.

(figure 1 here)

The study sample

In the main study [21] participants (n=467) consisted of current daily smokers (n=218), current snus users (n=200), and dual users of cigarettes and snus (n=41). Due to the much less established burden of disease caused by the Swedish type of smokeless tobacco (snus)[22] only data from smokers was used in the current economic evaluation. In addition, we restricted the analysis to individuals aged 20 years or older because the population based model was limited to adult population 20-84 years old. There were 13 participants younger than 20 years and none of these individuals changed smoking habits. Thus, the analytical sample from the effectiveness study on which the present economic analysis is based comprised 99 smokers in the intervention condition and 106 smokers in the control condition ("usual care").

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When the analysis was limited to smokers, no statistically significant differences between intervention and control group were seen in any of the studied outcomes.

The primary outcome, 7-day point prevalence of abstinence was defined as “having smoked 0 cigarettes in the 7 days preceding the survey".This condition was self-reported by 8% of participants both in the intervention and in the usual care condition. A secondary outcome entailing substantial tobacco reduction was calculated as reporting at follow-up an amount of cigarettes per day equal to or less than 50 % of that reported at baseline. This reduction was achieved by 27% of participants in the intervention condition and by 17% in the comparison condition.

Economic evaluation

We aimed to conduct an incremental cost-effectiveness analysis with long-term health effects. The alternative intervention was compared with “usual care”. The costs and health effects were estimated according to the Swedish recommendations [23] on economic evaluations of health care interventions. Therefore, costs were calculated from healthcare and societal perspectives, while health effects are expressed in QALYs (quality-adjusted life-years). The intervention under study was conducted in 2012, thus the intervention costs as well as societal costs in the models were estimated in Swedish crowns (SEK) per 2012. Further, the costs were inflated to reflect 2014 costs according to the Swedish consumer price index [24] and converted to 2014 US dollars (USD) using the purchasing power parity (PPP) estimates with CCEMG – EPPI-Centre Cost Converter(http://eppi.ioe.ac.uk/costconversion/default.aspx).

Both costs and QALYs were discounted 3 percent annually. Long-term costs and health effects were simulated using the two models to be compared:

1) A population-based simulation model employing potential impact fractions, where the intervention effect is assumed to change the incidence in tobacco related diseases, including diabetes mellitus type 2, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD) and seven cancer diagnoses, above all lung cancer
2) An individual-level Markov model incorporating the decreased smoking-related risks for lung cancer, COPD, and CVD

Intervention costs

Only the costs connected with the delivery of the interventions were included in the analysis. The quantity of resources consumed was obtained from the study’s accounting records. The unit costs were obtained from national public databases, from suppliers’ websites and from the organizers of the training. Total intervention costs were obtained by multiplying the volume of each cost category by its respective unit cost. Intervention costs were divided into training and operating costs. The costs were not discounted because the interventions was delivered during four months

Training costs for the brief advice included costs for salary and travel costs for the trainer, venue, and materials, as well as allowance for training time for trainees (4 hours per dental professional). Only 20% of the total costs were considered, in order to accommodate for the spread over a five-year period before refresher training may be needed, as it was previously done in similar studies[25 26] . The number of patients who smoke, per dental care professional, was estimated based on the prevalence

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of smoking in Sweden, [27] and the average number of patients the practitioners in the trial reported seeing each year.

Operating costs represented the costs of delivering tobacco cessation counselling in intervention and "usual care" conditions and were estimated based on the duration of the counselling and on average salaries including social charges.

Other costs connected with the interventions included patients' time in attending counselling, based on the mean duration of the counselling, and use of nicotine replacement therapy (NRT) or other medications for tobacco cessation. Costing of patients' time was estimated based on the opportunity cost of foregone leisure time and calculated at 25% of the Swedish average gross wage rate. [28] The cost of medications was estimated based on the retail price of the most commonly used drugs and on the recommended duration of use.

To estimate the cost of the interventions if they were applied to the entire Swedish population we estimated the number of daily smokers who visit dental clinics during a year. The number of smokers was obtained from national surveys[27], as was the number of adults visiting dental care each year.[6] Each year, 449 000 smokers were estimated to visit dental care.

Estimate of intervention effectiveness

The effectiveness of the novel intervention was estimated from the trial's outcomes, 7-days abstinence and smoking reduction by half. We assumed that reducing cigarette consumption by half would lead to sustained abstinence for 15% of the reducers, [29-32] while all quitters were assumed to maintain abstinence. On the population level, the change in smoking prevalence was calculated by multiplying the proportion of quitters due to the intervention by the number of smokers seeking dental care each year. In the health economic evaluation we assume that the estimated quitters will be continuously abstinent after the study's end (6-month follow-up).

Population-based simulation model

We simulated the impact of changes in incidence of and related societal costs for several chronic diseases during ten years, following the assumed changes in smoking prevalence because of the interventions in the Swedish population 20-84 years old in 2014. A model that incorporates four lifestyles factors, denominated *Risk factors, Health and Societal Costs* [33] was used, with only the smoking domain estimates employed for this study.. The model simulates effects on health outcomes associated with smoking, including diabetes mellitus type 2, ischaemic heart disease, ischaemic and haemorrhagic stroke, COPD, and cancer of the lung, oesophagus, liver, larynx, stomach, pancreatic, colon and rectum.

The model uses a modified version of the potential impact fraction,[34 35] where the intervention effect changed the relative risk (RR) of disease of the exposed category (smokers), while keeping the prevalence of exposed category constant. In our case, the RR changes for smokers when some of them quit.

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$$PIF = \frac{\mathrm{Ps}*\mathrm{RRs}-\mathrm{Ps}*\mathrm{RRs}'}{\mathrm{Ps}*\mathrm{RRs}} \quad [1]$$

where:

Ps is the prevalence of smoking,

RRs is the relative risk of disease associated with smoking,

RRs' is the changed relative risk of disease after the intervention when a part of smokers have quit.

The incidence rate of the disease after this change in the related risk factor (I') becomes:

$$\mathrm{I}' = \mathrm{I} * (1 - \mathrm{PIF}) \quad [2],$$

where I is the original incidence rate.

The relative risks for smokers compared to non-smokers were estimated from epidemiological studies, as presented in the technical report,[33] and additionally: ischaemic heart disease, ischaemic and haemorrhagic stroke,[36-39] COPD,[40 41] and different cancers.[42 43] The changing RRs (RRs') were calculated for every year and every disease, based on the decrease in risks for ex-smokers over time. For ischaemic heart disease, stroke, COPD, and lung cancer we used the estimations presented in Hurley and Matthews.[44] We assumed that risks for ex-smokers for diabetes mellitus follows the pattern of CVD decrease while the risks for other cancer diagnoses decrease linearly during 20 years. The QALY weights were used to describe the losses in health-related quality of life due to the diseases. The weights are community-based, derived via the EQ-5D classification system with the UK time-trade-off valuations[45]. The time horizon is 10 years so the economic and health gains were calculated based on decreased incidence of the diseases during ten years. The societal costs include medical treatment costs and municipal costs for care, hence the model adopted a limited societal perspective as patient and productivity costs are not included. Swedish national registers were used to retrieve disease incidence and disease-specific medical care costs, while municipal care costs were estimated via a Swedish study. The model was developed in Excel (Microsoft Office, 2010); details of the model are published in a technical report.[33]

Markov model

A Markov model was used to estimate health consequences and societal costs of smoking cessation.[46] The model has been used in similar studies in Sweden[14 47] and was updated for the purpose of the current analysis. The model simulates the societal effects of quitting smoking on three diseases: lung cancer, COPD, and CVD, including CHD and stroke. The model incorporates the smoking-related disease risks, time-dependent remaining excess disease risks after quitting, the death risks for the specific and for unrelated diseases, as well as the societal effects of the three diseases. All disease risks are annual age- and gender-specific excess incidence until death or the age of 95 years. The societal costs include costs associated to: medical treatment, municipal costs for care, drugs, informal care and other expenditures for patients and relatives as well as morbidity productivity costs. Health outcomes are expressed in QALYs. The number of quality-adjusted life years (QALYs) were calculated during healthy years and years spent diseased, until death or the age

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of 95 years. Swedish average age- and gender specific QoL weights were used for healthy years. [48] For years with disease, disease-specific QoL decrements taken from international studies were deducted from the average QoL.

Most of the societal costs were derived from Swedish studies published during the 2010s and were reported as distributions, i.e. with the Gamma parameters or bootstrapped 95 percent confidence interval, in order to enable stochastic estimation.

The Markov stages are one year long, with no half-cycle correction. The probabilistic model is run as a microsimulation with 10,000 repetitions. The Markov-cycle tree was created in Treeage Pro (Treeage Inc., 2015). Details on the model are available from a technical report.[46]

Sensitivity analyses

Several one-way sensitivity analyses were conducted to test the robustness of the results. First, we examined the effect of changing the assumptions about the proportion of smokers assumed to achieve permanent abstinence after reducing consumption by half to: a) 5% and b) 25%. Secondly, we examined the effect of changing the assumption of intervention coverage of dental care patients to 70%. Thirdly, we included the full training costs into the intervention costs.

To illustrate the correspondence between the two models and to increase understanding of the comparisons, a detailed calculation restricted to one gender and age group was performed with the same time frame (10 years), using only the health care perspective.

RESULTS

Intervention costs

Table 1 shows the costs of the interventions. Most of the interventions' costs could be attributed to the use of NRT and other medications.

Table 1. Intervention costs, in 2014 USD

		Intervention		"Usual care"	
	Unit price	Units *	Cost	Units*	Cost
Training cost					
Course fee					
Salary for trainer, delivery [a]	26.0	4	103.9		
Salary for trainer, preparation [a]	26.0	1	26.0		
Salary for trainer, travel time [a]	26.0	2	51.9		
Travels for trainer [b]	23.0	1	23.0		
Material [c]	2.30	25	57.5		
Venue and refreshments [c]	777.8	1	777.8		
Total course fee for 25 participants			**1040.0**		
Total course fee per participant			**41.6**		

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(practitioner)					
Compensation for training time for practitioners					
Compensation for training time: dentists [c d]	264.3	4	1057.2		
Compensation for training time: dental hygienists [c d]	103.4	4	413.7		
Average allowance for practitioners (80% dental hygienists)	135.6	4	542.4		
Total training cost per practitioner			584.0		
Estimated yearly training cost per smoker [e]			**2.3**		**0**
Operating costs					
Salary for dentist [a]	38.7				
Salary for dental hygienist [a]	25.0				
Average salary for practitioners (80% dental hygienists) [a]	27.7	0.14	**3.9**	0.04	**1.1**
Patient's time cost [a]	5.2	0.14	**0.7**	0.04	**0.2**
NRT/other drugs [b f]	172.4	0.28	**48.8**	0.28	**47.9**
Total costs					
Per smoker			**55.7**		**49.2**
All smoker visiting dental care/year[g]			**25,000,000**		**22,100,000**

[*] Hours or number

[a] Information on average salaries from Statistics Sweden: www.scb.se

[b] Based on information from suppliers' websites

[c] Based on the study records or information from training organizers

[d] Includes loss of revenue

[e] Estimated yearly number of smokers visiting a dental practitioner: 50

[f] Proportion (units) based on information from the trial

[g] Estimated by costs/smoker * number of adults visiting dental care each year (n=449 000)

Total cost for the brief advice was estimated at 56 USD per smoker and the difference in costs between the intervention and "usual care" was 6.5 USD. The cost per quitter was 552 USD in the intervention and 522 USD in the "usual care" condition. If delivered to all Swedish smokers visiting dental care every year, the total costs would be 25.0 million USD per year for the alternative intervention and 22.1 million for "usual care".

Intervention effectiveness

Ten smokers (four men and six women) could be expected to quit in "usual care" condition, compared with ten smokers (only women) in the intervention condition.

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When the effects were applied to the entire population, the prevalence of smoking among men was projected to decrease from 8.9% to 8.8% for the novel intervention and to 8.3% for "usual care". The prevalence of smoking among women would decrease from 11.6% to 10.5% for intervention and to 10.8% for "usual care". The estimations of effectiveness are presented in Table 2.

Table 2. Effectiveness estimation

	Intervention			**"Usual care"**		
Age	20-44	45-64	65-84	20-44	45-64	65-84
Participants in the FRITT study (n)						
Men	11	20	2	9	20	9
Women	19	41	6	20	37	11
Reduced cigarette consumption by half (n)[a]						
Men	2	2	0	1	2	0
Women	5	9	1	2	4	0
Quitters (n)						
Men	0	0	0	1	2	1
Women	2	5	1	1	1	3
Effectiveness data, estimated quitters (n) – used in Markov model [b]						
Men	**0**	**0**	**0**	**1**	**2**	**1**
Women	**3**	**6**	**1**	**1**	**2**	**3**
Proportion of estimated quitters (%)						
Men	3	2	0	13	12	11
Women	14	15	19	7	4	27
Swedish population (n)						
Men	1629855	1228289	788907	1629855	1228289	788907
Women	1561289	1205769	867493	1561289	1205769	867493
Number of smokers in Sweden(n)						
Men	114090	147395	63113	114090	147395	63113
Women	124903	192923	104099	124903	192923	104099
Number of smokers who visit dental care each year (n)						
Men	57045	95807	41023	57045	95807	41023

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Women	62452	125400	67664	62452	125400	67664
Effectiveness data, prevalence of smokers in the population (%) – used in population-based simulation model [c]						
Men	**6.90**	**11.88**	**8.00**	**6.55**	**11.10**	**7.42**
Women	**7.42**	**14.39**	**10.51**	**7.74**	**15.55**	**9.87**

[a] Results from FRITT study
[b] Calculated as 15% of the "Reduced cigarette consumption by half" plus "Quitters"
[c] Calculated as "(number of smokers in Sweden - (proportion of estimated quitters * smokers who visit dental care each year))/ Swedish population in the age and sex group"

Cost-effectiveness analyses

Model outputs and cost-effectiveness analyses are presented in Table 3, with a detailed example given for women aged 45-64 years in Table 4.

Table 3. Model outputs- Markov and population-based models. Costs in thousand USD 2014.

	Intervention			"Usual care"			ICER (Intervention vs "Usual care")		Conclusion
	Female	Male	Total	Female	Male	Total	Diff QALY	Diff costs	
Markov model									
Intervention cost			**4.9**			**5.2**			
Cost savings	-77	0	**-77**	-31	-32	**-63**			
Net costs			**-72.1**			**-57.8**			
QALYs	5.42	0	**5.42**	2,37	2,36	**4,74**			
							0,68	**-14,3**	***Dominant***
Population model									
Intervention cost			**25,000**			**22,100**	Diff QALY	Diff costs	
Cost savings	-39,562	-2,756	**-43,318**	-34,854	-37,125	**-71,979**			
Net costs			**-18,318**			**-49,879**			
QALYs	1327.8	100.4	**1428.2**	1117.1	1252,2	**2369.3**			

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							-941.1	31,561	*Dominated*

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Table 4. Model outputs in the subgroup of women 45-64 years. Markov and population-based models, 10 years' time horizon, health care perspective. Costs in 2014 USD

	Intervention effect	Health care cost	QALYs
Markov model			
Per quitter:	Quitters: 1	-547	0.02
Population-based model			
Intervention	Change in prevalence: 1.61% Quitters (n): 19 422	-11607004 Per quitter: - 598	604.94 Per quitter: 0.03

Markov model

The gains associated with the novel intervention resulted in societal savings of 77,000 USD, including savings of 32,000 USD in health care, and 5.42 QALYs. For "usual care", the gains were societal savings of 60,000 USD, including savings of 26,000 USD in health care, and 4.74 QALYs. Also including the intervention costs, the net societal savings were 72,100 USD for the intervention and 57,800 USD for the "usual care" group, with associated gains in QALYs, 5.42 for the intervention and 4.74 for "usual care" during the lifetime. According to this model, the brief intervention was ***dominant***; entailing cost saving and additional health gain of 0.68 QALYs.

Population-based model

The brief intervention applied to smokers showed a total societal saving of 42.3 million USD, of which 27.6 million USD were savings in health care costs, and a gain of 1428 QALYs for the full Swedish population 20-84 years old during 10 years. The corresponding estimates for "usual care" demonstrated a total societal savings of 72.0 million USD, out of which 46.9 million USD were savings in health care costs, and a gain of 2369 QALYs for the full Swedish population 20-84 years old during 10 years. When both intervention costs and estimated societal savings are considered, the net societal saving was 17.3 million USD for the brief advice and 49.9 million USD for "usual care", with health gains as above. Thus, the brief novel counselling was more expensive and less effective, so called ***dominated*** by the "usual care" alternative, according to the population-based model.

Sensitivity analyses

When the proportions assumed to achieve abstinence after reducing by half were set to 5% or to 25% the magnitude of the difference between two models remained. As with the main analysis, the population-based model favoured "usual care" over the novel intervention, while the Markov model favoured this latter over "usual care". Likewise, when the coverage of the brief advice or of "usual care" was assumed to be 70 % the gains decreased but the patterns of difference were similar to the main analysis. When including all training costs into the intervention costs the results were almost similar to the main analysis.

In order to illustrate the correspondence between the population-based and Markov model, separate calculations were restricted to women in age group 45-64 years, using 10 years' time

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horizon and only the health care perspective. The estimates from the population-based model for this group show cost savings for health care sector of 598 USD per quitter. The health care savings estimated with the Markov-model for the same group during 10 years were 547 USD per quitter. In essence, for this group both models show the same level of cost saving for a quitter as well as the same level of health gains (0.02 versus 0.03 QALYs).

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DISCUSSION

In this case study, the cost-effectiveness of a brief manualized counselling for smoking cessation in dentistry was assessed using two different models: a population-based model comparing different scenarios of smoking prevalence, and a Markov model estimating the outcomes for the quitters. A similar population-based model was presented in Magnus et al. [49] while a similar Markov model was presented in Hurley and Matthews.[44]

The original trial did not show any significant effect on smoking cessation of the novel intervention compared to usual treatment in a sample of smokers not selected according to their motivation to quit. The alternative intervention's costs were low, under 60 USD per patient, and the incremental cost compared with "usual care" was less than 7 USD per patient. In the intervention condition, the cost per quitter was only slightly higher than in the control condition and it compares favourably to the estimated cost per quitter in other smoking cessation studies.[11]

Nevertheless, the comparison of the economic effects between the intervention and "usual care" favoured the latter when modelling the population impact. In contrast, using the outcomes for the quitters in a Markov model showed that the intervention was preferable to "usual care", resulting in net societal cost savings and some gain in QALYs.

The difference in results with the two modelling strategies could be expected, in the first place because they differ in several aspects of model specification. The population-based model only considers health care costs and municipal costs for care, while the Markov model also considers cost for medications, costs for patients and relatives and morbidity productivity costs. The time frame was also different, i.e.10 years for the population-based model and lifetime for the Markov model. Finally, there were differences in the number of diseases included. However, as the comparison by cost category in Table 4 shows, the magnitude of costs is similar for both models.

The opposite conclusions from the two models are probably best explained by the difference in the population to which the simulation is applied. In fact, the population-based model estimates the effect of the intervention brought to the entire population of smokers in Sweden, while the Markov model simulates individual effects for the quitters in the study cohort. Quitters in the intervention group were in average younger than in the "usual care" group and all of them were women, while the gender distribution of quitters was more balanced in the "usual care" group. Thus, the Markov model shows greater gains in QALYs and societal savings for the alternative intervention due to longer time horizon for younger age groups. In contrast, the population-based model converts the trial outcomes to age- and gender-specific population prevalence.

The modelling strategies inherent in the two models explain why the cost-effectiveness results differ between the models. Population-based models simulate how changes in prevalence of risk factors affect the disease incidence over age- and gender-specific groups. The individual-based Markov models simulate the changes in disease incidence because of changes in risk factors in a specific, albeit hypothetical, individual of a certain age and gender. In population-based models, groups with a high disease incidence affect the estimates more than groups where the incidence is lower at the start of the simulation. In this study, the four male quitters in the control group affected the result disproportionally, in particular as there were no male quitters in the alternative intervention group.

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Small trials with few participants, and more importantly, few successful participants, are not likely to represent the population to which the interventions are to be applied, thus skewing the estimates in population-based models.

The weaknesses in both strategies of economic evaluations include non-significant differences in the effectiveness of the novel intervention compared with the control condition. Further, some assumptions as about the proportion of reducers eventually quitting, or about all quitters achieving sustained abstinence may not be tenable and thus contribute to increase the uncertainty of the estimates.

To our knowledge, this is the first study to compare different health economic strategies to estimate the cost-effectiveness of a brief advice for smoking cessation in dental clinics in Sweden. The combination and comparison of two different approaches for the estimation of cost-effectiveness is an original contribution providing insights on factors to be considered in decision making about large-scale dissemination of an intervention. In this regard, we offer the general recommendation to avoid the estimation of cost-effectiveness with population-based models from small-scale trials with skewed effectiveness across participant groups.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the paper. SeV contributed to acquisition of data, analyzed the data and drafted paper. IF and PmJ made substantial contributions to design of cost-effectiveness analyses and interpretation of the results. MrG was a principal investigator in the FRITT study and made substantial contribution to estimation of the effectiveness of the intervention. All the authors critically revised the manuscript and approved the final version for publication

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: SV reports grants from The National Board of Health and Welfare, during the conduct of the study and personal fees from The National Board of Health and Welfare, outside the submitted work, PJ reports grants from The National Board of Health and Welfare, during the conduct of the study, MG reports grants from The National Board of Health and Welfare, personal fees from The Stockholm County Council, during the conduct of the study; personal fees from The Stockholm County Council, grants from Public Health Agency of Sweden, grants from FORMAS, outside the submitted work, IF has nothing to disclose.

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DATA SHARING

No additional data available.

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FIGURE LEGENDS

Fig 1. CONSORT flowchart. Enrolment, allocation, and retention of participants.

SUPPLEMENTARY FILES

English version of study protocol for the cluster randomized controlled trial (FRITT)

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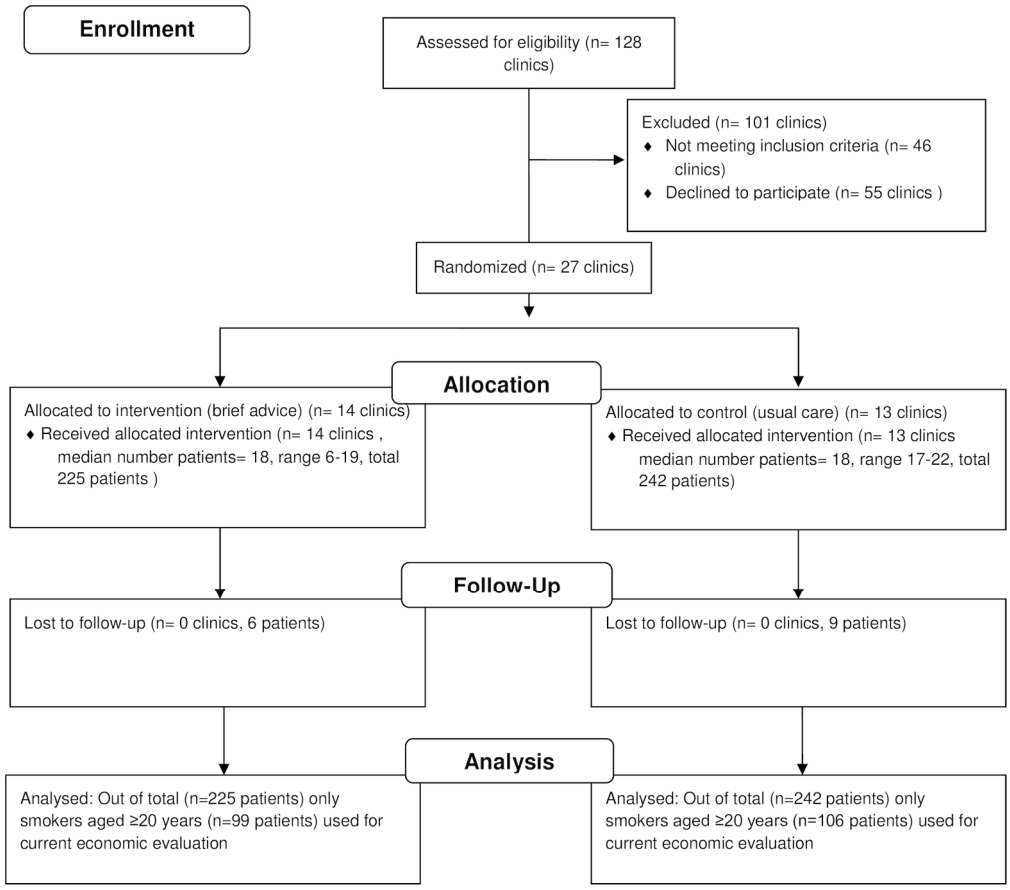

Fig 1. CONSORT flowchart. Enrolment, allocation, and retention of participants

190x167mm (300 x 300 DPI)

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APPENDIX 2 Research Plan

Project "Free from Tobacco in Dentistry" (Fri från Tobak i Tandvården - FRITT)

Title: Effectiveness of a brief counselling for tobacco cessation among smokers and snus users in dental care.

Aim and research questions

In accordance with the Ministry of Social Affair's assignment to the National Board of Health and Welfare (Government's decision 11:18, 2011-06-16) this evaluation plan is primarily aimed to answer the question *whether a brief patient-centred intervention delivered as part of the routine care in a dentistry is effective for promoting behavioural change in tobacco use, on individual level*. If the intervention proved effective, a further aim is to deem the applicability of the intervention in the frame of routine dental care. Additional secondary research questions that the evaluation plan aims to answer are: whether counselling affects intermediary behavioural factors, for instance support seeking at different care givers; costing of diverse intervention components (e.g. training of the personnel, information materials, etc.).

2. Method

2.1 Intervention

The counselling model to be evaluated is developed by the National Institute of Public Health. The main characteristics of the model are:

1. Increasing motivation, if it is taken that high level of motivation, associated with information on available support, is the most important factor for achieving permanent abstinence. The patient can thereafter decide which support is needed and follow the active advice given by the dental care professionals.
2. Includes referral to primary care or other professional counselling as described above
3. Brief counselling (duration of conversation approximately 5 minutes), which is a requirement to be able to carry out the

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intervention without impact the effectivity of the prevailing clinical care.

4. Brief training for the counsellors, which has a positive impact on resource use in the eventual later implementation stage.

2.2 Population

The target group for evaluation of the intervention are patients with established tobacco use (smoking and/or snus) seeking care during the study period at the selected dental care clinics in the counties of Södermanland and Örebro. The choice of the counties was based on:

a. Geographic location in central Sweden, to assure logistical viability
b. Possibility to adopt referral system between dental care and primary care centres
c. The proportion of dental professionals in private sector, where one county with high (Södermanland) and one with low (Örebro) proportion will be included in the evaluation.

2.3 Design

The evaluation will be conducted as a randomized controlled study, in which the dental care clinics will be the entities randomly chosen to either apply the novel counselling model (intervention condition) or to follow the usual counselling according the clinic's practice (control condition). Dentists and/or dental hygienists in the intervention condition will be trained in and to deliver the new counselling to smoking or snus using patients during the project period. The affected dental care professionals in both the intervention and the control conditions will document treatment of their patients tobacco use. The procedure for data collection and follow-up will be identical in both groups. The follow-up period for each patient is six months.

2.4 Study protocol

We aim to include approximately 30 dental care clinics, 30 dental care professionals and at least 460 patients in the evaluation.

2.4.1 Selection and randomization of the dental care clinics

Step 1. A county's stratified sample of approximately 70 dental care clinics - no specialized clinics – is drawn from the most updated registry from The Dental and

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Pharmaceutical Benefits Agency, accessible through each county council.

Step 2. The manager/responsible for each clinic is invited to a meeting held on regional level, where the evaluation team will explain the background and setup of the project. For each clinic information of structural character is collected (Appendix 1).

Step 3. Preliminary consent for cooperation and randomization is given by the operations manager.

Step 4: The dental professionals (dentists or dental hygienists, depending on who meets the patients at first hand) in the affected clinics are contacted by the managers and asked for cooperation, including following obligatory components: participation in a training on counselling skills, implementing of the counselling with the intended number of smoking or snus using patients, registration of information about the intervention and its evaluation (Appendix 2). For each clinic two staff members are selected (one regular and one deputy) to recruit patients for the project, but other staff can choose to participate in the training. Clinics where no personnel are willing to cooperate are considered dropouts, irrespective of earlier position of the manager. Apart from what is needed for implementing the intervention, the clinics are advised against changing their organizational routines in order to enable participation in the study.

Step 5: The cooperating clinics are assigned a minimum number of patients to be recruited for the study, based on an estimation of the patient turnover (average: 15 patients). For the purpose of the study, a unique code will identify each clinic. Thereafter, based on a computer-generated random sequence, the clinics are randomized to intervention or control conditions, with as many clinics in each condition. The key for the group identity is kept at the study secretariat,

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separated from the database in which other relevant data for the study will be registered eventually. This is done to avoid that knowledge about the group identity could influence the interpretation or registering of data.

Step 6: The managers and other cooperating staff at the clinics are informed about the outcome of the randomization and are invited to participate respective training days.

Step 7: Training of the dental care professionals in the intervention condition is provided by the National Institute of Public Health with methods described in the chapter on the intervention. The training day for the control condition is held by Karolinska Institute, and will include general information about the project and its evaluation. During the training, a detailed demonstration on the procedures in the evaluation protocol are given to both groups. The training is obligatory in order to participate in the study. Two opportunities to participate in the training are offered for each clinic, thereafter absence is considered dropout in the study.

Declined participation at steps 1-4 represents pre-randomization dropout, at steps 6-7 post-randomization. We expect a total dropout rate at approximately 50 % on the clinic level.

2.4.2 Recruitment of patients

Patients seeking care at the chosen dental care clinics during the study recruitment period (see section 2.6) can be included in the evaluation if they fulfil the following criteria:

a. Adequate understanding of Swedish, both oral and written or access to interpret
b. Age between 18 and 75 years

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c. Uses tobacco daily (each of the previous 30 days) as cigarettes, other smoked tobacco and/or snus, since at least one year back

Patients are excluded if:

a. Seeking acute care
b. Current use of medicines for tobacco cessation (nicotine replacement therapy, bupropion, vareniklin, etc.)
c. Abuse of drugs or other mental illness which can affect the voluntariness of participation in the study or the reliability of the reported information

The choice to recruit to the study also patients with chronical oral harm is made for two reasons: partly because these patients are interesting as they represent the target group for indicated prevention [2]; party to hasten the recruitment of the desired number of patients.

The recruitment will be done according the following schedule.

Step 1: The patients who have booked visit to the clinic is asked to fill out a form (Appendix 3) where background information is asked about, prerequisites for recruitment is assessed, and short information about the study is given.

Step 2: A dental hygienist or a secretariat controls the information and refers patients not fulfilling the criteria to their appointment. The remaining patients are asked to read detailed information about the study (Appendix 4), to sign an informed consent (Appendix 5), and to provide additional baseline information (Appendix 6). The signed consent is given directly to the dental care personnel at the appointment, and thus they can deliver the intervention (in the intervention condition) or the customary information (in the control condition).

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Step 3: Before the patient leaves the clinic, a new appointment is booked for oral health control after 6 months. The appointment is voluntary and free of charge for the patient. The aim of the visit is to promote adherence to the follow-up questionnaire. Patients who have not been booked for a follow-up visit will be mailed the questionnaire according to the procedure described under 2.4.5

Step 4: A note on the patients included in the evaluation is made in their medical record, while other information from the form are transferred to the study secretariat for central registration in a specifically designed database, in which the patients are identified with the clinic's code and the id number of their record.

Step 5: Basic information (gender, age, tobacco use habits) on the patients excluded from or declining to participate in the study are registered anonymously and without a code key in a separate database.

The procedure is repeated for each consecutive patient until the clinic has achieved the quota of number of patients to be recruited. The duration of the recruitment is estimated to be approximately three months. We expect a dropout rate of approximately 30 % among eligible patients.

2.4.3 Implementation of the intervention

The affected dental care staff in the respective groups implements the intended counselling during the appointment following recruitment, at an appropriate time. Information on the counselling (especially duration) is registered locally in an electronic document (template shown in Appendix 7).

2.4.4 Monitoring of the control group

In an intervention with a control condition, it is particularly important to document any treatment or

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other actions provided to the control group. The reason for this is to be able to draw correct conclusions on the effectiveness of the novel intervention, especially if only a moderate or no effect is reported. In a naturalistic experiment, the control group's exposure is not manipulated, and therefore it can be assumed that more or less intensive actions with previously unknown effects reach also these individuals. Besides, the use of motivational interviewing, MI, is rather prevalent in the Swedish healthcare, according to recommendations issued by, among others, the National Institute for Public Health (http://www.fhi.se/Metoder/Halsoframjande-och-forebyggande-metoder/Motiverande-samtal/).

The dentists or dental hygienists at the control clinics commit to document the same information as the intervention group on any tobacco counselling with recruited patients, according to the protocol (Appendix 7).

2.4.5 Follow-up and measuring of the outcome

A measurement on the patient level is intended six months after the first visit (recruitment).
The primary outcome will be the so called point prevalence of abstinent patients (have not used tobacco during the past seven days)
The following will be considered as *secondary outcomes*:

a. Continuous abstinence during the past three months
b. Reduction with at least 50 % of the daily tobacco use in the last month (number of cigarettes/day and/or snusboxes/week) compared with the baseline

Information on the outcome is collected by a questionnaire (Appendix 8), in connection with the revisit, which is booked at the time of recruitment (see section 2.4.2) or sent home to the affected patients.

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At follow-up, the following reminder is sent to the absent or non-responding patients:
Reminder 1: text message and a printed or electronic version of the questionnaire are sent at latest one week after the missed appointment or two weeks after the mailed questionnaire. Patients are given opportunity to book a new free visit at latest one week after the reminder.
Reminder 2: text message urging to fill out the questionnaire - without an offer to book visit – is sent at latest two weeks after the first reminder if previous answer to the questionnaire is not received.
Reminder 3: this last reminder is done by telephone, with offer to answer the questionnaire directly via phone interview, at latest one month after the first reminder.

We expect a dropout rate of 10-12% at 6-month follow-up.

In the Appendix 9, there is a summary of the steps and time plan for the follow-up of the patients.

2.4.6 Data management and privacy

The data collected during the project is registered in electronic databases according to following:

1. Data on patients asked to participate and information on consent is manually entered at each clinic. The resulting databases, with no identification information, are transferred in a safe way to the study secretariat.
2. Data from the baseline questionnaire is registered centrally with optical scanning
3. Data on the counselling and patient data from the follow-up in paper format (identified only with the patient's record number) is sent monthly by the dental clinics to the study secretariat (see below), for optic scanning. Only one contact person is appointed between each dental clinic and the study secretariat

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The computerized registry, which is thereby set up, will have KI as principal and will thereafter be reported to KI's Personal Data Act ombudsman. The set up registry will not be based on identification information(such as personal identity number, name, address, etc.).

Patient related documentation related to the study that is found in supporting documents in paper form (e.g. the signed informed consent), is handled in accordance with record keeping at the original clinic.

2.5 Statistical considerations and data analysis methods

2.5.1 Sample size and statistical power

With a recruited sample of a total of 460 patients (230 in each group), distributed on approximately 30 clinics, the study has 80 % power to find as statistically significant on a 5 % level (double sided test) a relative risk of 6-months point estimated abstinence of 2.0 assuming that the prevalence of the outcome in the control condition is approximately 10 %. This statistical power is calculated considering the study design, which is based on cluster selection, and attrition.

The advantage in recruiting more clinics, each with fewer patients rather than fewer clinics with more patients is that the cluster size has a big impact on how big the final sample size needs to be for achieving the same statistical power [3]. For instance, if the aim was to recruit in average 30 patients per clinic, 520 patients distributed on 17 clinics would be needed. The study on the applicability of the intervention is of descriptive character and is not included in the power calculation.

2.5.2 Data analysis

The results will be analysed according to "intention to treat" principle, i.e. each patient is treated according to the initial randomization irrespective of the counselling actually received [4]. The reporting will be based primarily on the primary outcome.

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In the secondary analysis several outcomes can be considered (see section 1) as well as ”per protocol” analyses, in which the patients’ outcomes are analysed according to the actual exposure to counselling, with regard to underlying factors (see section 2.4.4).
Because the primary outcome is dichotomy, multilevel logistic regression will be mainly used as analytical method [5], considering the cluster based design.

2.5.3 Validity of self-reported data
For the outcome measure, self-reported data on tobacco use at baseline and follow-up will be used. For financial reasons a biochemical validation is not feasible for this evaluation. In randomized controlled trials on tobacco cessation which have validated the self-reported behaviour against a biological marker, an underreporting of daily smoking has been noted among 15 % of study participants in average [6].

2.6 Time plan

During the first six months from the project initiation (120101) the necessary administration for the study will be set up (management team, secretariat, logistics) and preparatory work for recruitment of dental clinics and dental personnel will be done. We intend to begin recruiting patients starting in October 2012.
The recruitment period is estimated to be approximately three months. Accordingly, the follow-up period for the last recruited patients will extend to early autumn 2013.

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The following table shows the outline of the time schedule for the evaluation

2012			2013			2014		
Jan-Apr	**May-Aug**	**Sept-Dec**	**Jan - Feb**	**March-Oct**	**Nov-Dec**	**Jan-Apr**	**May-Aug**	**Sept-Dec**
Recruitment of personnel, set up of secretariat and managerial team	Recruitment of the clinics	Training of dentists						
Protocol review and approval	Data collection at clinic level	Recruitment of patients Delivery of intervention Data collection at patient level		Follow-up of patients				
Selection of dental clinics					Preliminary report on implementation	Scientific article on implementation		Report writing and review
					Preliminary data analysis	Outcome analysis begins	Continuation	Complementary analysis

In house and organization
Intervention and data collection
Analysis and summarizing

2.7 Organization and coordination

The protocol for a randomized controlled trial is complex, and requires a strict monitoring of the different stages to avoid sources of error and thus incorrect conclusions. For this purpose, three organizational bodies are considered necessary:

a. *A study secretariat* with following tasks:
   i. Archiving of administrative data
   ii. Randomization procedures and keeping of code keys
   iii. Contacts with the public and patient requests
   iv. Contacts with the clinics (e.g. reminder)
   v. Focal point for data collection
   vi. Assistance for vid reporting, etc.
   vii. Economic issues

The study secretariat consists of a fulltime research officer/research assistant during first and second years of the project.

b. *A steering group* with following tasks:
   i. Monitoring of the protocol integrity
   ii. Affiliating necessary additional expertise
   iii. Contacts with authorities and orderers
   iv. Assessment of critical incidents of value for the validity of the study results
   v. Disposition of resources
   vi. Contacts with media

   The steering group consists of: a project manager and secretariat; a representative from the National Board of Health and Welfare; an expert in tobacco cessation (not the same who developed the intervention); one/two representatives of dental care; a statistician; a researcher from the same or another institution with expertise in randomized controlled trials. The project manager is the president of the steering group.

c. *An operative group* with following functions*:*
   i. Monitoring of data collection and quality
   ii. Proposals to agenda and supporting information for the steering group
   iii. Execution of the steering group's decisions

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iv. Preliminary analysis of the material

The operative group consists of: the project manager; study secretariat; statistician/data manager (part-time).

3 Ethical questions

The evaluation study will be ethically reviewed before the initiation. The project implies however no physical infringement of risk for the participants. Besides the usual issues with privacy and handling of sensitive personal information, the only ethical consideration is about the usefulness of the novel counselling in contrast with other proven tobacco cessation methods. It is evidently shown in literature reviews, conducted among others by Cochrane Collaboration, that individual qualified counselling is more effective than brief counselling for quitting smoking [7]. The guidelines for disease prevention in health care by the National Board for Health and Welfare [8] recommends that daily smokers and pregnant snus users should be offered qualified individual couselling or proactive telephone courselling, which are much more comprehensive interventions than the brief counselling that will be evaluated in this study.

Intensive tobacco cessation methods are however not applicable in a context, such as dental care clinics, where the time with individual patients is limited, which is why trying a novel approach is warranted. Besides, the proposed intervention is not intended to substitute more intensive tobacco cessation, but rather to increase patients' motivation and hasten the transition to action (e.g. referral to primary care).

4 Bibliography

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Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Title, page 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract, page 2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions	Page 3, lines 36-41 Page 4, line 1-2
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Page 4, lines 15-38 Page 5, lines 1-11
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Not applicable
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Page 4, lines 13-21
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Page 4, lines 15-20
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Page 7, line 16-20 Page 8, lines 1-2
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	Page 5, line 22-23 Page 5, lines 35-36
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Page 6, lines 18-25
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	Page 6, lines 18-25 Appendix

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Section/item	Item No	Recommendation	Reported on page No/ line No
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	Not applicable
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	Not applicable
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Not applicable
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Page 7, line 21-25, ref. 33 Page 8, line5-7 ref.46
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Page 5, line 17-21
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Page 3, line 26-39
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Ref 33, ref 46
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Page 8, line 11-19
Results			

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Section/item	Item No	Recommendation	Reported on page No/ line No
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Page 10, table 2
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Page 11, Table 3
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Not applicable
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Page 13, line 23-32 Page 14, line 1-5
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Page 13, Table 4
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Pages 19-16
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 17 “Funding”
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 17“Competing interests”

The CHEERS statement checklist format is based on the format of the CONSORT statement checklist

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