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The effectiveness of tobacco cessation interventions for different groups of tobacco users in Sweden: a study protocol for a national prospective cohort study

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Abstract

Introduction: Tobacco is still one of the single most important risk factors among the lifestyle habits that cause morbidity and mortality in humans. Furthermore, tobacco has a heavy social gradient, as the consequences are even worse among disadvantaged and vulnerable groups. To reduce tobacco-related inequity in health, those most in need should be offered the most effective tobacco cessation intervention. The aim of this study is to facilitate and improve the evaluation of already implemented national tobacco cessation efforts, focusing on ten disadvantaged and vulnerable groups of tobacco users.

Methods and analysis: This is a prospective cohort study. Data will be collected by established tobacco cessation counsellors in Sweden. The study includes adult tobacco users, including disadvantaged and vulnerable patients, receiving in-person interventions for tobacco cessation (smoking, snus and/or e-cigarettes). Patient inclusion was initiated in April 2020. For data analyses patients will be sorted into vulnerable groups based on risk factors and compared to tobacco users without the risk factor in question.

The primary outcome is successful quitting after 6 months, measured as self-reported continuous abstinence. Secondary outcomes include abstinence at the end of the intervention, 14-days point prevalence after 6 months, and patient satisfaction with the intervention. Effectiveness will be examined using a mixed-effect logistic regression model adjusting for potential prognostic factors and known confounders.

Ethics and dissemination: The project will follow the guidelines from the Swedish Data Protection Authority and have been approved by the Swedish Ethical Review Authority before patient inclusion (Dnr: 2019-02221). Only patients providing written informed consent will be included. Both positive and negative results will be published in scientific peer-reviewed journals and presented at national and international conferences. Information will be provided through media available to the public, politicians, healthcare providers and planners as these are all important stakeholders.

Trial registration: Clinicaltrials.gov identification number: NCT04819152.

Article Summary

Strengths and limitations of this study

- This national project is the first of its kind in Sweden and will provide new knowledge about the effectiveness of tobacco cessation interventions in 'real-life'.
- This study has the potential to identify the most effective interventions to assist different vulnerable and disadvantaged groups of tobacco users to successfully quit.
- If the current cessation interventions show limited effect for specific vulnerable groups, the results of the systematically collected data can be used to tailor programmes to specific groups of tobacco users in the future.
- Limitation: Self-reported outcome measure.

Introduction

Tobacco causes the development of the most common chronic diseases such as cardiovascular disease, cancer and respiratory diseases such as chronic obstructive pulmonary disease (COPD) [1], and smokers have about doubled incidence of surgical complications [2]. This study includes smokers, users of snus, and e-cigarette users.

Overall, smoking is an independent and preventable risk factor responsible for up to 60% of the inequity in health. In Sweden smoking is still one of the most important risk factors [3] causing morbidity and mortality. Every year, 12,000 Swedish citizens die prematurely from smoking [4]. In addition, a Danish study found that the quality of life is significantly reduced in the shorter life course of smokers [5]. In 2002, more than 18 billion SEK was lost in production due to tobacco-related illness [6]. The overall societal costs has been estimated to 75 billion SEK per year [7].

Tobacco cessation interventions are among the most cost-effective treatments within the healthcare system. A smoker who successfully quits at the age of 30 will gain approximately 10 life-years compared with a continuous smoker. The benefits decrease with increased age at smoking cessation; however, an average 50-year-old smoker will still gain 5-6 life-years from quitting. Smoking has a heavy social gradient, as its severe influence on health strikes even harder among disadvantaged and vulnerable groups [8–11].

To reduce the tobacco-related inequity in health, it is pivotal to reach out to those most in need with the most effective cessation interventions, and it is of the highest priority in the guidelines for healthy lifestyle by The National Board of Health and Welfare [12]. In addition policies, strategies and campaigns should be used to prevent new users from initiating tobacco use [13].

Though the smoking prevalence is relatively low in Sweden in an international context, specific groups have a very high prevalence; about 80% in alcohol and drug abusers [14]. Sweden has a unique high prevalence of snus users. The daily smoking prevalence in Sweden in 2016 was 8% and 10% for men and women respectively, when including snus, the daily use of tobacco was 25% for men and 14% for women [15], and in addition, products such as cigarettes, snus, and e-cigarettes are often mixed.

Cessation programmes are increasingly offered to users of snus and e-cigarettes [16]. However, the effectiveness in different groups of users remains unknown.

Effectiveness of tobacco cessation interventions

It is widely accepted that tobacco cessation interventions should build on strong evidence [12], but implementation is difficult [17] and the effect in real life is seldom followed up. In Denmark, data on smoking cessation interventions and follow-up on effect are systematically collected through the national Danish Smoking Cessation Database [18]. With approximately 150,000 participants registered since 2001, the Danish Smoking Cessation Database is one of a kind. A European survey and a comprehensive web search has revealed a few other databases [19], such as the UK NHS stop smoking services [20]. Through collaboration we are familiar with national projects in Ireland and the Czech Republic inspired by the Danish model, implementing a similar data-collection.

Tobacco cessation activities in Sweden

Despite the fact that about a thousand counsellors have been trained in manual-based person-centred tobacco cessation interventions in Sweden [21], it is unknown how effective the interventions are. There is namely no systematic follow-up in Sweden except for the activities performed by the national quitline [9,22]. Therefore, as of today it is not possible, on a national level, to compare the effectiveness of variations of the in-person interventions, providers, or different groups of tobacco users including disadvantaged and vulnerable groups.

During the last decade there has been a common interest among tobacco researchers in Sweden, to document the effectiveness of tobacco cessation interventions across the country. This interest is supported by the independent think tank "Tobaksfakta" [23], and a network of approximately 700 Swedish counsellors declared their support for the project at their autumn-meeting 2016. In addition, tobacco cessation counsellors in Region Skåne and in Region Örebro län have evaluated the effect of smoking cessation interventions based on the Danish model with good results e.g., the follow-up-rate was drastically improved compared to usual routine. The evaluation was done by collecting data on smokers undertaking a smoking cessation intervention, and after informed consent data were collected without any problems or barriers. Based on this it seems both possible and realistic to document the effectiveness of the tobacco cessation interventions in this new national project.

Study aim

This new national project is the first of its kind in Sweden. The purpose is to facilitate and improve the evaluation of the national tobacco cessation efforts, emphasising on which programmes are most effective for different groups throughout Sweden. In this study we will evaluate the effectiveness of already implemented cessation interventions targeting smoking, use of snus and/or e-cigarettes, focusing on disadvantaged and vulnerable groups of tobacco users. Furthermore, we want to identify important factors associated with a successful outcome after controlling for confounders (in relation to programme, patients and setting).

Disadvantaged and vulnerable groups include tobacco users, e.g., without a job, with short or no education, without permanent housing, diagnosed with mental illness, diagnosed with

chronic obstructive pulmonary disease (COPD), undergoing surgery, adolescents, elderly, migrants, pregnant women.

Research questions

1) Among daily smokers what is the effectiveness of in-person tobacco cessation interventions measured as successful quitting after 6 months, among disadvantaged and vulnerable groups compared to other smokers.
2) What are the most important predictors for successful/unsuccessful quitting after controlling for confounders?
3) What is the effectiveness and the most important predictors for successful quitting among users of snus and/or users of e-cigarettes?

Study design

This is a prospective cohort study, based on establishing a systematic collection of individual data to evaluate the effectiveness of already established tobacco cessation interventions organised throughout Sweden.

The data collection is built on the Danish data collection model [18], including relevant adaptions to Swedish conditions.

We aim to recruit a total of 8,000 tobacco users and the patient inclusion was initiated in April 2020, and we have extended the patient recruitment period till the end of 2022.

Setting

This study builds on the involvement of trained tobacco cessation counsellors throughout Sweden. The counsellors will recruit patients and collect data for the project. We hope to collaborate with at least 200 certified counsellors[1] in the initial phase of the project.

All the officially certified counsellors working with person-centered cessation programmes regarding smoking, snus and e-cigarette will be invited to participate in the project. The counsellors can work in primary or secondary care, public or private clinics or other settings.

Counsellors wanting to take part in the study will sign an agreement in accordance with the project. After signing up, information, consent forms and manuals/tutorials for data collection are distributed to the counsellors, and the patient inclusion can begin.

A list of the sites that have collected data to the project will be available at clinicaltrials.gov.

[1] Counsellors can be certified at Örebro, Karolinska and Sahlgrenska University Hospitals, Karolinska Institute, National Tobacco Quit-Line, and Lund University amongst others.

Tobacco cessation interventions

In this study we will include person-centered tobacco cessation interventions aimed at smoking, snus and/or e-cigarettes with face-to-face sessions only. Face-to-face sessions can be conducted as online as well as on-site meetings.

Any in-person tobacco cessation intervention already implementet into the daily clinical routine amongst the tobacco cessation counsellors throughout Sweden can be included, regardless of intensity, supportive medication, and methods used. Information on the intervention given will be recorded through the standard questionnaires used in the study.

Participants

All adult tobacco users (of at least 18 years of age), including disadvantaged and vulnerable patients, receiving an in-person intervention for tobacco cessation (smoking, snus and/or e-cigarettes) are eligible for inclusion in the project after giving informed consent. Both individual and group-based interventions can be included.

Exclusion criteria are withdrawing consent, or reduced ability to give informed consent, due to inadequate language skills, dementia, and other conditions.

Recruitment

The contributing counsellors will inform all eligible patients about the project and ask for their informed consent to collect data on their cessation intervention (Figure 1). If consent is not obtained, the treatment will continue according to the normal daily practice without further ado.

After giving consent to be included in the project, the patient will likewise receive the treatment programme as planned. In addition, the counsellor will collect and document baseline information regarding the cessation activity and patient characteristics. At the end of the programme, the tobacco cessation status will be recorded. A manual-based follow-up call will be conducted after 6 months.

Figure 1: Flowchart for the recruitment and data collection process

Data collection

Baseline date will be collected during the cessation intervention by the counsellors and the patients. Data questionnaires are filled in and mailed to the project data manager, who will enter the data into a REDCap (Research Electronic Data Capture) database, hosted at Lund University [24,25].

All materials and questionnaires used are available on the project website (in Swedish) [26].

Baseline

After giving informed consent patients are included in the study and asked to fill in a questionnaire on baseline characteristics, including:

- Years of smoking/snus and e-cigarettes; tobacco use; previous quit attempts; cohabitating with a smoker/user; persons who has encouraged to quit; housing.
- Social security number; Level of education; employment; pregnancy; planned surgery; place of birth; mother tongue.
- Level of nicotine dependency (measured by Fagerström score (FTND) [27] for smokers; and an adapted test used in the clinical setting for dependency among snus users, based on the Fagerstrøm score (FTND-ST) [28,29]).

The counsellors register details of the cessation intervention and process (both planned and performed), and follow-up at the end of the intervention, including:

- Dates of initiating and ending the cessation intervention; date of quitting; setting.
- Details of intervention method; individual/group format; group size; number of meetings and duration; supplemental contacts; relapse prevention; user fees.
- Compliance with the programme; tobacco status at end of the programme.

Follow-up

Six months (± 1 month) after the initial quit day a manual-based follow-up is conducted by calling each patient. To allow for a more objective evaluation the follow-up call will be conducted by a project team member (or personnel at the National Quit-Line) who had no contact with the patient before the follow-up call. This procedure will eliminate possible impact from the counsellor/patient interaction, as well as insure a unified follow-up procedure for all patients.

Follow-up data includes:

- Continuous successful quitting since planned quit date (or alternatively since the end of the programme) and until the 6 months follow-up; 14 days point prevalence; user satisfaction; use and costs of pharmacologic support; present use of pharmacologic support; interest in new cessation intervention.
- For non-respondents: Reason for un-successful follow-up; e.g., wrong telephone number, deceased, or not available.

If a patient does not want to participate in the follow-up or it is not possible to reach them by phone the reason for loss to follow up is recorded. Before a patient is considered lost to follow up at least 4 attempts to call on different times and days (at least one attempt must be after 5 pm) must be made.

Outcome

The primary outcome is continuous successful quitting after 6 months, measured as self-reported continuous abstinence from the planned quit day to the day of follow-up 6 months later. The planned quit day will be used as a time reference since the toxic effects of tobacco

use should be terminated from that date. Continuous abstinence is defined as smoking no more than 1 cigarette or similar concerning snus and/or e-cigarettes since the quit day.

Secondary outcomes

Several secondary outcomes will be recorded, such as 14 days point prevalence (defined as not smoking/using at all (not even a puff) for the latest 14 days, tobaccofree at the end of the intervention, and satisfaction with the intervention.

Comparators

The objective of this study is to facilitate and improve the evaluation of already implemented national tobacco cessation efforts, focusing on ten disadvantaged and vulnerable groups of tobacco users. For data analyses the patients will be sorted into ten different vulnerable groups based on risk factors and compared to tobacco users without the risk factor in question.

The vulnerable groups will be categorised according to the information collected by the tobacco cessation counsellor, and all patients will be cross-linked with additional data from the Swedish National Patient Register [30].

Analytical strategy

Sample size

The sample size was calculated for the dichotomous main outcome (successful quitting (yes/no) after 6 months) and based on the following assumptions: a two-sided test, a 5% level of significance, a power of 80%, an estimated effect in the control group of 35%, and a minimum relevant difference of 5-10 percentage points.

The online calculator "Inference for Proportions: Comparing Two Independent Samples" (www.stat.ubc.ca/~rollin/stats/ssize/) was used to estimate the necessary sample size of each group. Based on a MiReDif on 10% and 5% each group should include at least 329 and 1377 tobacco users, respectively. As the study groups in this study are not equal-sized, the sample size gives the estimated size of the smallest group (the vulnerable group in question).

We expect to include 8000 patients. Based on the overall existing interest from the tobacco cessation counsellors, at least 200 of them are each expected to collect data from at least 20 patients/year. The large majority of potential patients are expected to accept inclusion and follow-up [31]. To be able to manifest a difference in effect size of 10%, 4% for the included patients would have to belong to each of the given risk factors (vulnerable groups). To show a difference of 5%, this would be the case for 17% of the included patients.

Statistical analyses

Data will be analysed and reported according to the STROBE guidelines [32]. After controlling for confounders, the effectiveness in the different groups of vulnerable patients is compared to the patients without the given risk factor. Differences between counsellors will be taken into consideration by deploying a mixed-effects model adjusted for hierarchical clustering using the different smoking cessation clinics reporting to the project. Each clinic is identified

with its own unique ID-number, and the 1st level cluster will be composed of the group of patients registered in the same smoking cessation clinic.

Relevant univariable and multivariable analyses will be used to analyse differences in continuous abstinence. The final multivariable logistic regression model will be fitted, based on initial univariable tests, and common knowledge, to include relevant variables. Statistically significant predictors of continuous quitting will be identified. Results will be presented as odds ratio (OR) and corresponding 95% confidence intervals (CI), and a two-sided p-value of ≤ 0.05 will be considered as statistically significant.

We expect to encounter both missing data and loss to follow up. Depending on the size and nature of missing data they will be handled accordingly [20,33]. If the proportion of missing data is small (<5%) missingness will be considered negligible and removed from the analysis. If possible multiple imputation will be used to deal with missing data. Otherwise, sensitivity analysis will be performed to explore the possible impact of the missing data.

Regarding the loss to follow up we do not anticipate data to be missing at random but more likely loss to follow up will be missing not at random. Hence a best-worst and worst-best case imputation will be carried out to investigate the theoretical uncertainty of the study results [20,33].

All statistical calculations will be performed using STATA.IC 16 or a later version.

Dissemination

Both positive and negative results of the project will be published in scientific peer-reviewed journals as well as being presented at national and international conferences. All authors must meet the Vancouver criteria.

Information about the project and results will be disseminated throughout the project-time via a public homepage and other media available to the public, politicians, healthcare providers and planners as these are all important stakeholders.

Ethical considerations

Participants are included only after informed consent. The consent can be withdrawn at any time without explanation and without any influence on the treatment programme.

The project will follow the guidelines from the Swedish Data Protection Authority and have been approved by the Swedish Ethical Review Authority before the patient inclusion (Dnr: 2019-02221.)

The project is registered in clinicaltrials.gov with the reference number: NCT04819152.

All research data remains confidential, and it will never be possible to recognize individuals when data is presented and published. Financing of the project, institutional affiliations and potential conflicts of interest will also be published.

Data statement

After publication of study results technical appendix, statistical code, and anonymised datasets will be available upon reasonable request to the corresponding author.

Patient and public involvement

Patient and public have not been involved in the planning of the study, and there are no current plans of involvement.

Discussion

Updates on the global burden of diseases show that tobacco is still a major risk factor for physical illness in Sweden [34]. Though cessation interventions are one of the most cost-effective interventions in the healthcare system, there is no national systematic registration of how many and which groups of tobacco users are treated or about the effect of the interventions in Sweden. However, focusing tobacco cessation services on disadvantaged and vulnerable tobacco users is a key to reduce tobacco related health inequity [11]. The present study will close a major knowledge gap in this field.

Effect of tobacco cessation intervention in disadvantaged and vulnerable groups

The intensity of the cessation programmes seems to be of major importance for successful quitting, [35]. Already, in the year of 2000, the term 'intensive smoking cessation intervention' was defined internationally as a face-to-face program with at least 4 meetings of at least 10 minutes [36,37].

A non-intensive standard program in the UK showed weak effect among low socioeconomic groups in real life setting [38]. In contrast, the Danish standard intensive cessation intervention is effective in real life settings across socioeconomic groups, for heavy smokers, pregnant women, elderly smokers, smokers scheduled for surgery and mentally ill smokers [39–44]. In addition, the Irish results also favour intensive programmes (unpublished data). The current project will add knowledge about the effect of the Swedish cessation interventions.

Snus and e-cigarettes cessation interventions

E-cigarettes are tested as a specific treatment for smoking cessation with contradictory results. A recent study showed that smokers also using e-cigarettes have a lower quit-rate compared to smokers not using e-cigarettes simultaneously [45,46]. A Swedish study has shown that it is possible to quit the use of snus by similar pharmacological support, traditionally used in the smoking cessation programmes [47]. Still, research is lacking on quitting e-cigarettes, themselves.

What this study adds

This project provides new knowledge about the effectiveness of tobacco cessation interventions in 'real-life'.

Our study has potential to contribute to this research area, as it is highly relevant to identify how these specific groups of smokers can get the best possible help to quit smoking. If the

current cessation interventions show limited effect for specific groups of smokers, the obtained results and knowledge can be used to tailor programmes to specific groups of smokers and tobacco users in the future. This will be of great importance for the individual patient, as it will be beneficial to public health and the socio-economy in general, to offer the best programmes in the future. This will further contribute to evening out the inequality in health.

A positive side-effect would be that the systematic monitoring and follow-up on effect raises the awareness of effectiveness and exchange of knowledge between smoking cessation provides across sectors. The project can also stimulate a rise in the interest in research and development of methods among the participating tobacco cessation providers. Furthermore, the systematic data collection can contribute to an administrative relief and be timesaving for the counsellors, time which can be spent treating tobacco addiction instead.

Data sharing statement

Data sharing not applicable as no datasets were generated and/or analysed for this manuscript.

Contributorship statement:

HT, MR, ML, HG, JA, AP and ARH designed the study. SW and TBE made contributions to the conception and design of the project. All authors contributed to the methodology of the study. MR and HT drafted the manuscript. All authors read, revised, and approved the manuscript.

Compering interests:

MR, JA TBE, ARH, HT: Nothing to declare.
HG: Doctors Against Tobacco (unpaid NGO chair).
AP: Nurses against Tobacco (unpaid NGO vice chair); NGO Tobaksfakta – independent think tank (paid general secretary).
SW: Received in total 4 650 £ from Pfizer AB, and 490 £ from Sanofi, for lectures and education about smoking cessation.
ML: Received in total 3 500 £ from Phizer AB, 3 500 £ from ASTRA Zenega AB, 1 500 £ from MSD, and 1 000 £ from Boehringer Ingelheim AB, all for lectures, speech, or education about smoking cessation and/or smoking and covid19.

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FORTE was not involved in the design of the study. They will not be involved in the collection, analysis, or interpretation of data, in writing the manuscript or in any other part of the project.

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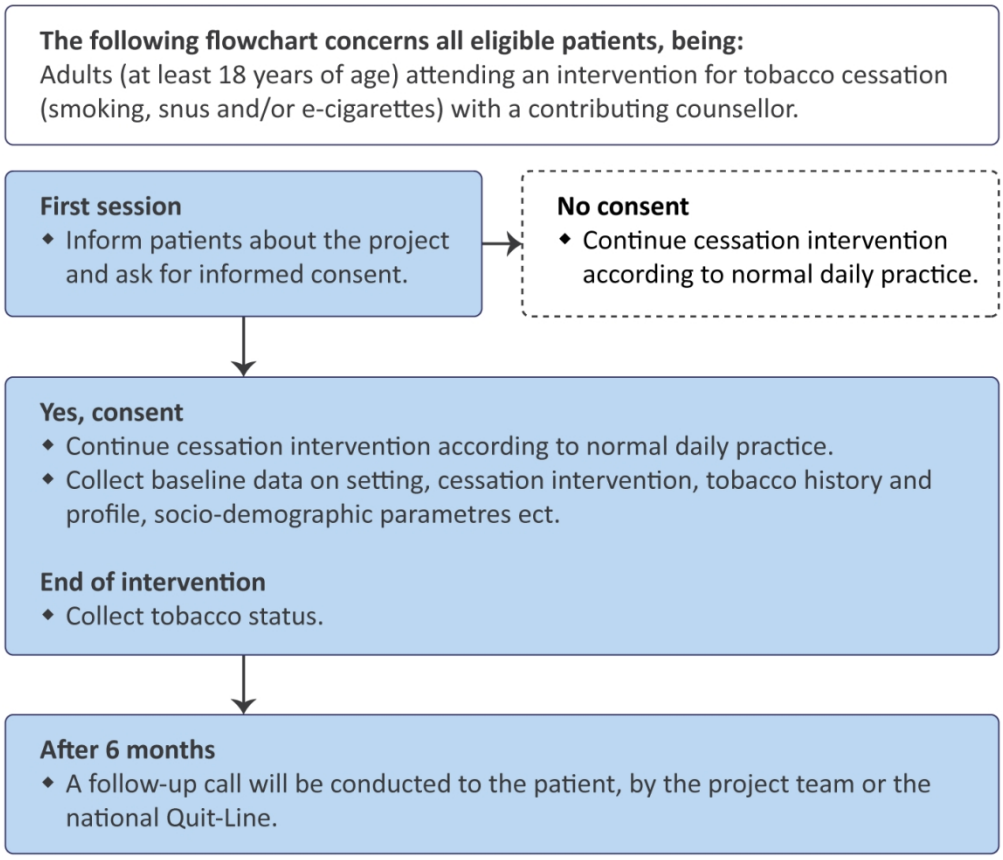

Figure 1: Flowchart for the recruitment and data collection process

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The effectiveness of tobacco cessation interventions for different groups of tobacco users in Sweden: a study protocol for a national prospective cohort study

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The effectiveness of tobacco cessation interventions for different groups of tobacco users in Sweden: a study protocol for a national prospective cohort study

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Abstract

Introduction: Tobacco is still one of the single most important risk factors among the lifestyle habits that cause morbidity and mortality in humans. Furthermore, tobacco has a heavy social gradient, as the consequences are even worse among disadvantaged and vulnerable groups. To reduce tobacco-related inequity in health, those most in need should be offered the most effective tobacco cessation intervention. The aim of this study is to facilitate and improve the evaluation of already implemented national tobacco cessation efforts, focusing on ten disadvantaged and vulnerable groups of tobacco users.

Methods and analysis: This is a prospective cohort study. Data will be collected by established tobacco cessation counsellors in Sweden. The study includes adult tobacco or e-cigarette users, including disadvantaged and vulnerable patients, receiving in-person interventions for tobacco or e-cigarette cessation (smoking, snus and/or e-cigarettes). Patient inclusion was initiated in April 2020. For data analyses patients will be sorted into vulnerable groups based on risk factors and compared to tobacco users without the risk factor in question.

The primary outcome is continuous successful quitting after 6 months, measured by self-reporting. Secondary outcomes include abstinence at the end of the treatment programme, which could be from minutes over days to weeks, 14-days point prevalence after 6 months, and patient satisfaction with the intervention. Effectiveness of successful quitting will be examined by comparing vulnerable with non-vulnerable patients using a mixed-effect logistic regression model adjusting for potential prognostic factors and known confounders.

Ethics and dissemination: The project will follow the guidelines from the Swedish Data Protection Authority and have been approved by the Swedish Ethical Review Authority before patient inclusion (Dnr: 2019-02221). Only patients providing written informed consent will be included. Both positive and negative results will be published in scientific peer-reviewed journals and presented at national and international conferences. Information will be provided through media available to the public, politicians, healthcare providers and planners as these are all important stakeholders.

Trial registration: Clinicaltrials.gov identification number: NCT04819152.

Article Summary

Strengths and limitations of this study

- This national project is the first of its kind in Sweden and will provide new knowledge about the effectiveness of tobacco cessation interventions in 'real-life'.
- This study has the potential to identify the most effective interventions to assist different vulnerable and disadvantaged groups of tobacco users to successfully quit.
- If the current cessation interventions show limited effect for specific vulnerable groups, the results of the systematically collected data can be used to tailor programmes to specific groups of tobacco users in the future.
- Limitation: Self-reported outcome measure.

Introduction

Tobacco causes the development of the most common chronic diseases such as cardiovascular disease, cancer and respiratory diseases e.g. chronic obstructive pulmonary disease (COPD) [1], and smokers have about doubled incidence of surgical complications [2].

Overall, smoking is an independent and preventable risk factor responsible for up to 60% of the inequity in health. In Sweden smoking is still one of the most important risk factors [3] causing morbidity and mortality. Every year, 12,000 Swedish citizens die prematurely from smoking [4]. In addition, a Danish study found that the quality of life is significantly reduced in the shorter life course of smokers [5]. In 2002, more than 18 billion SEK was lost in production due to tobacco-related illness [6]. The overall societal costs has been estimated to 75 billion SEK per year [7].

Tobacco cessation interventions are among the most cost-effective treatments within the healthcare system. A smoker who successfully quits at the age of 30 will gain approximately 10 life-years compared with a continuous smoker. The benefits decrease with increased age at smoking cessation; however, an average 50-year-old smoker will still gain 5-6 life-years from quitting. Smoking has a heavy social gradient, as its severe influence on health strikes even harder among disadvantaged and vulnerable groups [8–11].

To reduce the tobacco-related inequity in health, it is pivotal to reach out to those most in need with the most effective cessation interventions, and it is of the highest priority in the guidelines for healthy lifestyle by The National Board of Health and Welfare [12]. In addition policies, strategies and campaigns should be used to prevent new users from initiating tobacco use [13].

Though the smoking prevalence is relatively low in Sweden in an international context, specific groups have a very high prevalence; about 80% in alcohol and drug abusers [14]. A similar extreme level of daily snus uses was not seen in the group of abusers, where the prevalence was 24-25% [14]. Sweden has a unique high prevalence of snus users, with 18% daily users among men and 4% among women in 2016 [15]. At that time the daily smoking prevalence in Sweden was 8% and 10% for men and women respectively, resulting in a daily tobacco prevalence of 25% for men and 14% for women [15]. Regarding the use of e-cigarettes the prevalence of daily users in 2020 was 0.4% for both men and women [15]. In addition, products such as cigarettes, snus, and e-cigarettes are often mixed, and the negative impact would increase, accordingly.

Cessation programmes are increasingly offered to users of snus and e-cigarettes, as well as heated tobacco products, though the use of the last is still very low in Sweden [16]. However, the effectiveness in different groups of users remains unknown.

Effectiveness of tobacco cessation interventions

It is widely accepted that tobacco cessation interventions should build on strong evidence [12], but implementation is difficult [17] and the effect in real life is seldom followed up. In Denmark, data on smoking cessation interventions and follow-up on effect are systematically collected through the national Danish Smoking Cessation Database [18]. With approximately 150,000 participants registered since 2001, the Danish Smoking Cessation Database is one of a kind. A European survey and a comprehensive web search has revealed a few other databases [19], such as the UK NHS stop smoking services [20]. Through collaboration we are familiar with national projects in Ireland and the Czech Republic inspired by the Danish model, implementing a similar data-collection.

Tobacco cessation activities in Sweden

Despite the fact that about a thousand counsellors have been trained in manual-based person-centred tobacco cessation interventions, following the general Swedish guidelines [12] (i.e. the intervention is tailored to the individual tobacco user, regarding tobacco profile, health profile, needs and preferences according to the clinical guideline, allowing for variations in length as well as in content) in Sweden [21], it is unknown how effective the interventions are. There is namely no systematic follow-up in Sweden except for the activities performed by the national quitline [9,22]. Therefore, as of today it is not possible, on a national level, to compare the effectiveness of variations of the in-person interventions, providers, or different groups of tobacco users including disadvantaged and vulnerable groups.

During the last decade there has been a common interest among tobacco researchers in Sweden, to document the effectiveness of tobacco cessation interventions across the country. This interest is supported by the independent think tank “Tobaksfakta” [23], and a network of approximately 700 Swedish counsellors declared their support for the project at their autumn-meeting 2016. In addition, tobacco cessation counsellors in Region Skåne and in Region Örebro län have evaluated the effect of smoking cessation interventions based on the Danish model with good results e.g., the follow-up-rate was drastically improved compared to usual routine. The evaluation was done by collecting data on smokers undertaking a smoking cessation intervention, and after informed consent data were collected without any problems

or barriers. Based on this it seems both possible and realistic to document the effectiveness of the tobacco cessation interventions in this new national project.

Study aim

The purpose of this study is to facilitate and improve the evaluation of the national tobacco cessation efforts, emphasising on which programmes are most effective for different groups throughout Sweden. This means that we will evaluate the effectiveness of already implemented cessation interventions targeting smoking, use of snus and/or e-cigarettes, focusing on disadvantaged and vulnerable groups of tobacco or e-cigarette users compared with non-vulnerable users. Furthermore, we want to identify important factors associated with a successful outcome after controlling for confounders (in relation to programme, patients and setting). This national project is the first of its kind in Sweden.

Disadvantaged and vulnerable groups include tobacco users, e.g., without a job, with short or no education, without permanent housing, diagnosed with mental illness, diagnosed with chronic obstructive pulmonary disease (COPD), undergoing surgery, adolescents, elderly, migrants, pregnant women.

The groups prioritised were mainly defined by the National Board of Health and Welfare in Sweden and WHO (pregnant women, patients undergoing surgery, persons with severe mental illness, adolescents, migrants, and the elderly) [12]. The remaining groups were chosen by the authors based on needs described in clinical guidelines.

Research questions

1) Among daily smokers what is the effectiveness of in-person tobacco cessation interventions measured as successful quitting after 6 months, among disadvantaged and vulnerable groups compared to other smokers.
2) What are the most important predictors for successful/unsuccessful quitting smoking when using an adjusted model?
3) What are 1) and 2) for daily users of snus and/or users of e-cigarettes?

Study design

This is a prospective cohort study, based on establishing a systematic collection of individual data to evaluate the effectiveness of already established tobacco cessation interventions organised throughout Sweden.

The data collection is built on the Danish data collection model [18], including relevant adaptions to Swedish conditions.

We aim to recruit a total of 8,000 tobacco users and the patient inclusion was initiated in April 2020, and we have extended the patient recruitment period till the end of 2022.

Setting

This study builds on the involvement of trained tobacco cessation counsellors throughout Sweden. The counsellors will recruit patients and collect data for the project. We hope to collaborate with at least 200 certified counsellors[1] in the initial phase of the project.

All the officially certified counsellors working with in-person person-centered cessation programmes regarding smoking, snus and e-cigarette will be invited to participate in the project. The counsellors can work in primary or secondary care, public or private clinics or other settings.

Counsellors wanting to take part in the study will sign an agreement in accordance with the project. After signing up, information, consent forms and manuals/tutorials for data collection are distributed to the counsellors, and the patient inclusion can begin.

A list of the sites that have collected data to the project will be available at clinicaltrials.gov.

Tobacco cessation interventions

In this study we will include person-centered tobacco or e-cigarette cessation interventions aimed at smoking, snus and/or e-cigarettes with face-to-face sessions only. Face-to-face sessions can be conducted as online video calls as well as on-site meetings.

Any in-person tobacco cessation intervention already implementet into the daily clinical routine amongst the tobacco cessation counsellors throughout Sweden can be included, regardless of intensity, supportive medication, and methods used. Information on the intervention given will be recorded through the standard questionnaires used in the study.

Participants

All adult tobacco users (of at least 18 years of age), including disadvantaged and vulnerable patients, receiving an in-person intervention for tobacco or e-cigarette cessation (smoking, snus and/or e-cigarettes) are eligible for inclusion in the project after giving informed consent. Both individual and group-based interventions can be included.

Exclusion criteria are withdrawing consent, or reduced ability to give informed consent, due to inadequate language skills, dementia, and other conditions.

Recruitment

The contributing counsellors will inform all eligible patients about the project and ask for their informed consent to collect data on their cessation intervention (Figure 1). If consent is not obtained, the treatment will continue according to the normal daily practice without further ado.

[1] Counsellors can be certified at Örebro, Karolinska and Sahlgrenska University Hospitals, Karolinska Institute, National Tobacco Quit-Line, and Lund University amongst others.

After giving consent to be included in the project, the patient will likewise receive the treatment programme as planned. In addition, the counsellor will collect and document baseline information regarding the cessation activity and patient characteristics. At the end of the programme, the tobacco cessation status will be recorded. A manual-based follow-up call will be conducted after 6 months.

Figure 1: Flowchart for the recruitment and data collection process

Data collection

Baseline date will be collected during the cessation intervention by the counsellors and the patients. Data questionnaires are filled in and mailed to the project data manager, who will enter the data into a REDCap (Research Electronic Data Capture) database, hosted at Lund University [24,25].

All materials and questionnaires used are available on the project website (in Swedish) [26].

Baseline

After giving informed consent patients are included in the study and asked to fill in a questionnaire. The paper survey is filled in by the patient, with assistance from the counsellor. If necessary, the counsellor is allowed to read the questions to the patient and record the patient's responses. All questions regarding tobacco use or quit attempts etc. are divided into three section a) Smoking, b) Use of snus, and c) Use of e-cigarettes. The baseline characteristics, include:

- Years of smoking/snusing and using e-cigarettes; current daily tobacco use (No/Yes/Not on a daily basis); previous quit attempts (None/1-3/>3/Not using); cohabitating with a smoker (Yes/No); health care personel who has encouraged the quitting (e.g. GP, hospital doctor, midwife, dentist); housing (e.g. own house, rental, without permanent housing).
- Social security number; level of education; employment; pregnancy (Yes/No); planned surgery (Yes/No); place of birth (Sweden, The Nordic countries, Europe, not Europe); mother tongue (Swedish, Nordic, European, not European).
- Level of nicotine dependency (measured by Fagerström score (FTND) [27] for smokers; and an adapted test used in the clinical setting for dependency among snus users, based on the Fagerstrøm score (FTND-ST) [28,29]).

The counsellors register details of the cessation intervention and process (both planned and performed), and follow-up at the end of the intervention, including:

- Dates of initiating and ending the cessation intervention; date of quitting; setting.
- Details of intervention method; individual/group format; group size; intensity of the intervention (number of meetings and duration); supplemental contacts; relapse prevention; user fees.

- Compliance with the programme (treatment attendance); tobacco status at end of the programme.

Follow-up

Six months (± 1 month) after the initial quit day a manual-based follow-up is conducted by calling each patient. To allow for a more objective evaluation the follow-up call will be conducted by a project team member (or personnel at the National Quit-Line) who had no contact with the patient before the follow-up call. This procedure will eliminate possible impact from the counsellor/patient interaction, as well as insure a unified follow-up procedure for all patients.

Follow-up data includes:

- Continuous successful quitting since planned quit date (or alternatively since the end of the programme) and until the 6 months follow-up; 14 days point prevalence; user satisfaction; use and costs of pharmacologic support; present use of pharmacologic support (nicotine replacement therapy (NRT), bupropion, varenicline, or other); interest in new cessation intervention.
- For non-respondents: Reason for un-successful follow-up; e.g., wrong telephone number, deceased, or not available.

If a patient does not want to participate in the follow-up or it is not possible to reach them by phone the reason for loss to follow up is recorded. Before a patient is considered lost to follow up at least 4 attempts to call on different times and days (at least one attempt must be after 5 pm) must be made.

Outcome

The primary outcome is self-reported continuous successful quitting after 6 months, measured from the planned quit day (or last day of the treatment if a specific quit date is not planned during the intervention) to the day of follow-up 6 months later. The planned quit day will be used as a time reference since the toxic effects of tobacco use should be terminated from that date. Continuous successful quitting is defined as smoking no more than 1 cigarette or similar concerning snus and/or e-cigarettes since the quit day.

We will be monitoring smoking, use of snus, and use of e-cigarettes, as successfully quitting one of the above, may lead to an increased use of one or more of the others.

Secondary outcomes

Several secondary outcomes will be recorded, such as 14 days point prevalence (defined as not smoking/using at all (not even a puff) for the latest 14 days, tobacco abstinence at the end of the intervention, and satisfaction with the intervention.

Comparators

The objective of this study is to facilitate and improve the evaluation of already implemented national tobacco cessation efforts, focusing on ten disadvantaged and vulnerable groups of tobacco users. For data analyses the patients will be sorted into ten different vulnerable

groups based on risk factors and compared to tobacco users without the risk factor in question.

The vulnerable groups will be categorised according to the information collected by the tobacco cessation counsellor, and all patients will be cross-linked with additional data from the Swedish National Patient Register to extract relevant diagnoses to uncover e.g. chronic obstructive pulmonary disease (COPD), severe mental illness, or recently giving birth [30].

Analytical strategy

Sample size

The sample size was calculated for the dichotomous main outcome (successful quitting (yes/no) after 6 months) and based on the following assumptions: a two-sided test, a 5% level of significance, a power of 80%, an estimated effect in the control group of 35%, and a minimum relevant difference of 5-10 percentage points.

The online calculator "Inference for Proportions: Comparing Two Independent Samples" (www.stat.ubc.ca/~rollin/stats/ssize/) was used to estimate the necessary sample size of each group. Based on a minimal relevant difference (MiReDif) on 10% and 5% each group should include at least 329 and 1377 tobacco users, respectively. As the study groups in this study are not equal-sized, the sample size gives the estimated size of the smallest group (the vulnerable group in question).

We expect to include 8000 patients. Based on the overall existing interest from the tobacco cessation counsellors, at least 200 of them are each expected to collect data from at least 20 patients/year. The large majority of potential patients are expected to accept inclusion and follow-up [31]. To be able to manifest a difference in effect size of 10%, 4% for the included patients would have to belong to each of the given risk factors (vulnerable groups). To show a difference of 5%, this would be the case for 17% of the included patients.

Statistical analyses

Data will be analysed and reported according to the STROBE guidelines [32]. After controlling for confounders, the effectiveness in the different groups of vulnerable patients is compared to the patients without the given risk factor. Differences between counsellors will be taken into consideration by deploying a mixed-effects model adjusted for hierarchical clustering using the different smoking cessation clinics reporting to the project. Each clinic is identified with its own unique ID-number, and the 1st level cluster will be composed of the group of patients registered in the same smoking cessation clinic.

Relevant univariable and multivariable analyses will be used to analyse differences in continuous successful quitting. The final multivariable logistic regression model will be fitted, based on initial univariable tests, and common knowledge, to include relevant variables. Potential predictors including confounders concerning patients, intervention and tobacco cessation clinic will be included, and as a minimum the following will be examined:

- Patients: Sex, age, compliance with the intervention, tobacco/e-cigarette history, level of nicotine dependency, previous quit attempts, living with a smoker, level of education, job situation, and belonging to more than one vulnerable group.

- Intervention: Intensity, individual or group sessions, and treatment method.
- Clinic: Setting, and geographic location.

Statistically significant predictors of continuous successful quittingwill be identified. Results will be presented as odds ratio (OR) and corresponding 95% confidence intervals (CI), and a two-sided p-value of ≤ 0.05 will be considered as statistically significant.

We expect to encounter both missing data and loss to follow up. Depending on the size and nature of missing data they will be handled accordingly [20,33]. If the proportion of missing data is small (<5%) missingness will be considered negligible and removed from the analysis. If possible multiple imputation will be used to deal with missing data. Otherwise, sensitivity analysis will be performed to explore the possible impact of the missing data.

Regarding the loss to follow up we do not anticipate data to be missing at random but more likely loss to follow up will be missing not at random. Hence a best-worst and worst-best case imputation will be carried out to investigate the theoretical uncertainty of the study results [20,33].

All statistical calculations will be performed using STATA.IC 16 or a later version.

Dissemination

Both positive and negative results of the project will be published in scientific peer-reviewed journals as well as being presented at national and international conferences. All authors must meet the Vancouver criteria.

Information about the project and results will be disseminated throughout the project-time via a public homepage and other media available to the public, politicians, healthcare providers and planners as these are all important stakeholders.

Ethical considerations

Participants are included only after informed consent. The consent can be withdrawn at any time without explanation and without any influence on the treatment programme.

The project will follow the guidelines from the Swedish Data Protection Authority and have been approved by the Swedish Ethical Review Authority before the patient inclusion (Dnr: 2019-02221.)

The project is registered in clinicaltrials.gov with the reference number: NCT04819152.

All research data remains confidential, and it will never be possible to recognize individuals when data is presented and published. Financing of the project, institutional affiliations and potential conflicts of interest will also be published.

Data statement

After publication of study results technical appendix, statistical code, and anonymised datasets will be available upon reasonable request to the corresponding author.

Patient and public involvement

Patient and public have not been involved in the planning of the study, and there are no current plans of involvement.

Discussion

Updates on the global burden of diseases show that tobacco is still a major risk factor for physical illness in Sweden [34]. Though cessation interventions are one of the most cost-effective interventions in the healthcare system, there is no national systematic registration of how many and which groups of tobacco users are treated or about the effect of the interventions in Sweden. However, focusing tobacco cessation services on disadvantaged and vulnerable tobacco users is a key to reduce tobacco related health inequity [11]. The present study will close a major knowledge gap regarding which programmes that work best for different groups of users in different settings, clinics and regions in Sweden.

Effect of tobacco cessation intervention in disadvantaged and vulnerable groups

The intensity of the cessation programmes seems to be of major importance for successful quitting, [35]. Already, in the year of 2000, the term 'intensive smoking cessation intervention' was defined internationally as a face-to-face program with at least 4 meetings of at least 10 minutes [36,37].

A non-intensive standard program in the UK showed weak effect among low socioeconomic groups in real life setting [38]. In contrast, the Danish standard intensive cessation intervention is effective in real life settings across socioeconomic groups, for heavy smokers, pregnant women, elderly smokers, smokers scheduled for surgery and mentally ill smokers [39–44]. In addition, the Irish results also favour intensive programmes (unpublished data). The current project will add knowledge about the effect of the Swedish cessation interventions.

Snus and e-cigarettes cessation interventions

E-cigarettes are tested as a specific treatment for smoking cessation with contradictory results. A recent study showed that smokers also using e-cigarettes have a lower quit-rate compared to smokers not using e-cigarettes simultaneously [45,46]. A Swedish study has shown that it is possible to quit the use of snus by similar pharmacological support, traditionally used in the smoking cessation programmes [47]. Still, research is lacking on quitting e-cigarettes, themselves.

What this study adds

This project provides new knowledge about the effectiveness of tobacco cessation interventions in the 'real-life setting'.

Our study has potential to contribute to this research area, as it is highly relevant to identify how these specific groups of tobacco users can get the best possible help to successful quitting. If the current cessation interventions show limited effect for specific groups of smokers, the obtained results and knowledge can be used to tailor programmes to specific groups of smokers and tobacco users in the future. This will be of great importance for the individual patient, as it will be beneficial to public health and the socio-economy in general, to

offer the best programmes in the future. This will further contribute to evening out the inequality in health.

A positive side-effect would be the possibility to consolidate the culture of systematic monitoring, follow-up and dissemination of effect after the project, which raises the awareness of effectiveness and exchange of knowledge amongcessation provides across sectors. The project can also stimulate a rise in the interest in research and development of methods among the participating tobacco cessation providers. Furthermore, the systematic data collection can contribute to an administrative relief and be timesaving for the counsellors, time which can be spent treating tobacco addiction instead.

Data sharing statement

Data sharing not applicable as no datasets were generated and/or analysed for this manuscript.

Contributorship statement:

HT, MR, ML, HG, JA, AP and ARH designed the study. SW and TBE made contributions to the conception and design of the project. All authors contributed to the methodology of the study. MR and HT drafted the manuscript. All authors read, revised, and approved the manuscript.

Compering interests:

MR, JA TBE, ARH, HT: Nothing to declare.
HG: Doctors Against Tobacco (unpaid NGO chair).
AP: Nurses against Tobacco (unpaid NGO vice chair); NGO Tobaksfakta – independent think tank (paid general secretary).
SW: Received in total 4 650 £ from Pfizer AB, and 490 £ from Sanofi, for lectures and education about smoking cessation.
ML: Received in total 3 500 £ from Phizer AB, 3 500 £ from ASTRA Zenega AB, 1 500 £ from MSD, and 1 000 £ from Boehringer Ingelheim AB, all for lectures, speech, or education about smoking cessation and/or smoking and covid19.

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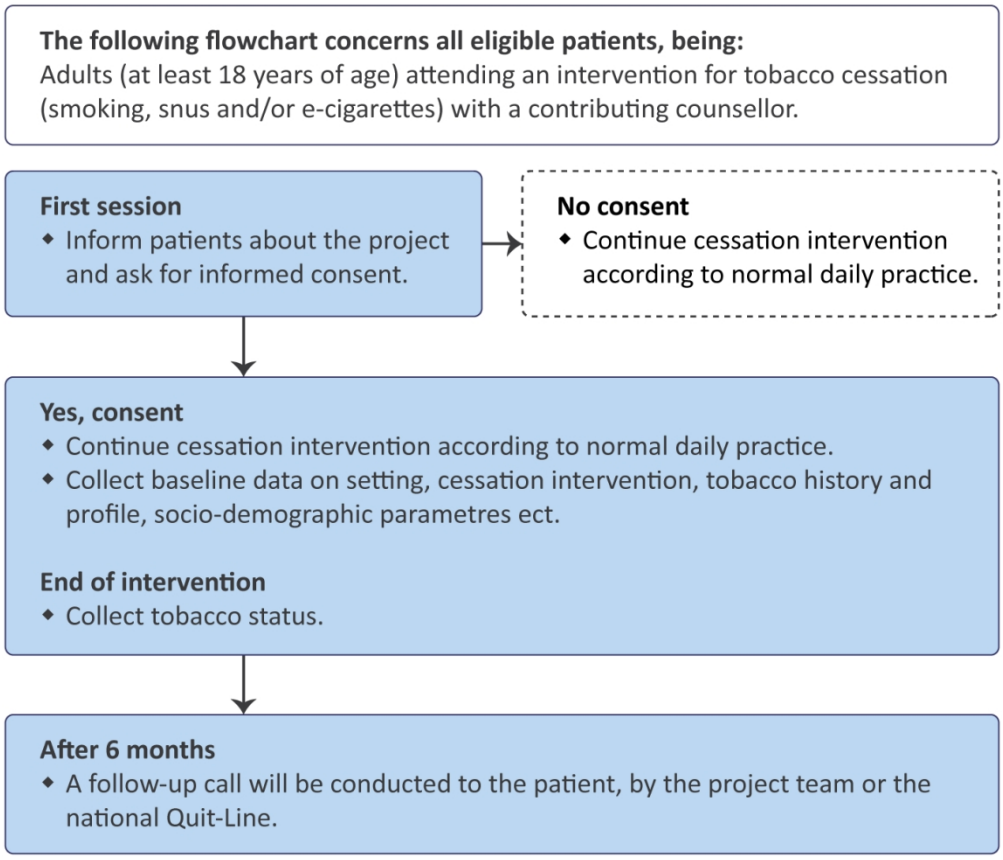

Figure 1: Flowchart for the recruitment and data collection process

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The effectiveness of tobacco cessation interventions for different groups of tobacco users in Sweden: a study protocol for a national prospective cohort study

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The effectiveness of tobacco cessation interventions for different groups of tobacco users in Sweden: a study protocol for a national prospective cohort study

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Abstract

Introduction: Tobacco is still one of the single most important risk factors among the lifestyle habits that cause morbidity and mortality in humans. Furthermore, tobacco has a heavy social gradient, as the consequences are even worse among disadvantaged and vulnerable groups. To reduce tobacco-related inequity in health, those most in need should be offered the most effective tobacco cessation intervention. The aim of this study is to facilitate and improve the evaluation of already implemented national tobacco cessation efforts, focusing on ten disadvantaged and vulnerable groups of tobacco users.

Methods and analysis: This is a prospective cohort study. Data will be collected by established tobacco cessation counsellors in Sweden. The study includes adult tobacco or e-cigarette users, including disadvantaged and vulnerable patients, receiving in-person interventions for tobacco or e-cigarette cessation (smoking, snus and/or e-cigarettes). Patient inclusion was initiated in April 2020. For data analyses patients will be sorted into vulnerable groups based on risk factors and compared to tobacco users without the risk factor in question.

The primary outcome is continuous successful quitting after 6 months, measured by self-reporting. Secondary outcomes include abstinence at the end of the treatment programme, which could be from minutes over days to weeks, 14-days point prevalence after 6 months, and patient satisfaction with the intervention. Effectiveness of successful quitting will be examined by comparing vulnerable with non-vulnerable patients using a mixed-effect logistic regression model adjusting for potential prognostic factors and known confounders.

Ethics and dissemination: The project will follow the guidelines from the Swedish Data Protection Authority and have been approved by the Swedish Ethical Review Authority before patient inclusion (Dnr: 2019-02221). Only patients providing written informed consent will be included. Both positive and negative results will be published in scientific peer-reviewed journals and presented at national and international conferences. Information will be provided through media available to the public, politicians, healthcare providers and planners as these are all important stakeholders.

Trial registration: Clinicaltrials.gov identification number: NCT04819152.

Article Summary

Strengths and limitations of this study

- This national project is the first of its kind in Sweden and will provide new knowledge about the effectiveness of tobacco cessation interventions in 'real-life'.
- This study has the potential to identify the most effective interventions to assist different vulnerable and disadvantaged groups of tobacco users to successfully quit.
- If the current cessation interventions show limited effect for specific vulnerable groups, the results of the systematically collected data can be used to tailor programmes to specific groups of tobacco users in the future.
- Limitation: Self-reported outcome measure.

Introduction

Tobacco causes the development of the most common chronic diseases such as cardiovascular disease, cancer and respiratory diseases e.g. chronic obstructive pulmonary disease (COPD) [1], and smokers have about doubled incidence of surgical complications [2].

Overall, smoking is an independent and preventable risk factor responsible for up to 60% of the inequity in health. In Sweden smoking is still one of the most important risk factors [3] causing morbidity and mortality. Every year, 12,000 Swedish citizens die prematurely from smoking [4]. In addition, a Danish study found that the quality of life is significantly reduced in the shorter life course of smokers [5]. In 2002, more than 18 billion SEK was lost in production due to tobacco-related illness [6]. The overall societal costs has been estimated to 75 billion SEK per year [7].

Tobacco cessation interventions are among the most cost-effective treatments within the healthcare system. A smoker who successfully quits at the age of 30 will gain approximately 10 life-years compared with a continuous smoker. The benefits decrease with increased age at smoking cessation; however, an average 50-year-old smoker will still gain 5-6 life-years from quitting. Smoking has a heavy social gradient, as its severe influence on health strikes even harder among disadvantaged and vulnerable groups [8–11].

To reduce the tobacco-related inequity in health, it is pivotal to reach out to those most in need with the most effective cessation interventions, and it is of the highest priority in the guidelines for healthy lifestyle by The National Board of Health and Welfare [12]. In addition policies, strategies and campaigns should be used to prevent new users from initiating tobacco use [13].

Though the smoking prevalence is relatively low in Sweden in an international context, specific groups have a very high prevalence; about 80% in people who abuse alcohol or drugs [14]. A similar extreme level of daily snus users was not seen in the group of people who abuse alcohol or drugs, where the prevalence was 24-25% [14]. Sweden has a unique high prevalence of snus users, with 18% daily users among men and 4% among women in 2016 [15]. At that time the daily smoking prevalence in Sweden was 8% and 10% for men and women respectively, resulting in a daily tobacco prevalence of 25% for men and 14% for women [15]. Regarding the use of e-cigarettes the prevalence of daily users in 2020 was 0.4%

for both men and women [15]. In addition, products such as cigarettes, snus, and e-cigarettes are often mixed, and the negative impact would increase, accordingly.

Cessation programmes are increasingly offered to users of snus and e-cigarettes, as well as heated tobacco products, though the use of the last is still very low in Sweden [16]. However, the effectiveness in different groups of users remains unknown.

Effectiveness of tobacco cessation interventions

It is widely accepted that tobacco cessation interventions should build on strong evidence [12], but implementation is difficult [17] and the effect in real life is seldom followed up. In Denmark, data on smoking cessation interventions and follow-up on effect are systematically collected through the national Danish Smoking Cessation Database [18]. With approximately 150,000 participants registered since 2001, the Danish Smoking Cessation Database is one of a kind. A European survey and a comprehensive web search has revealed a few other databases [19], such as the UK NHS stop smoking services [20]. Through collaboration we are familiar with national projects in Ireland and the Czech Republic inspired by the Danish model, implementing a similar data-collection.

Tobacco cessation activities in Sweden

Despite the fact that about a thousand counsellors have been trained in manual-based person-centred tobacco cessation interventions, following the general Swedish guidelines [12] (i.e. the intervention is tailored to the individual tobacco user, regarding tobacco profile, health profile, needs and preferences according to the clinical guideline, allowing for variations in length as well as in content) in Sweden [21], it is unknown how effective the interventions are. There is namely no systematic follow-up in Sweden except for the activities performed by the national quitline [9,22]. Therefore, as of today it is not possible, on a national level, to compare the effectiveness of variations of the in-person interventions, providers, or different groups of tobacco users including disadvantaged and vulnerable groups.

During the last decade there has been a common interest among tobacco researchers in Sweden, to document the effectiveness of tobacco cessation interventions across the country. This interest is supported by the independent think tank “Tobaksfakta” [23], and a network of approximately 700 Swedish counsellors declared their support for the project at their autumn-meeting 2016. In addition, tobacco cessation counsellors in Region Skåne and in Region Örebro län have evaluated the effect of smoking cessation interventions based on the Danish model with good results e.g., the follow-up-rate was drastically improved compared to usual routine. The evaluation was done by collecting data on smokers undertaking a smoking cessation intervention, and after informed consent data were collected without any problems or barriers. Based on this it seems both possible and realistic to document the effectiveness of the tobacco cessation interventions in this new national project.

Study aim

The purpose of this study is to facilitate and improve the evaluation of the national tobacco cessation efforts, emphasising on which programmes are most effective for different groups throughout Sweden. This means that we will evaluate the effectiveness of already implemented cessation interventions targeting smoking, use of snus and/or e-cigarettes, focusing on disadvantaged and vulnerable groups of tobacco or e-cigarette users compared

with non-vulnerable users. Furthermore, we want to identify important factors associated with a successful outcome after controlling for confounders (in relation to programme, patients and setting). This national project is the first of its kind in Sweden.

Disadvantaged and vulnerable groups include tobacco users, e.g., without a job, with short or no education, without permanent housing, diagnosed with mental illness, diagnosed with chronic obstructive pulmonary disease (COPD), undergoing surgery, adolescents, elderly, migrants, pregnant women.

The groups prioritised were mainly defined by the National Board of Health and Welfare in Sweden and WHO (pregnant women, patients undergoing surgery, persons with severe mental illness, adolescents, migrants, and the elderly) [12]. The remaining groups were chosen by the authors based on needs described in clinical guidelines.

Research questions

1) Among daily smokers what is the effectiveness of in-person tobacco cessation interventions measured as successful quitting after 6 months, among disadvantaged and vulnerable groups compared to other smokers.
2) What are the most important predictors for successful/unsuccessful quitting smoking when using an adjusted model?
3) What are 1) and 2) for daily users of snus and/or users of e-cigarettes?

Study design

This is a prospective cohort study, based on establishing a systematic collection of individual data to evaluate the effectiveness of already established tobacco cessation interventions organised throughout Sweden.

The data collection is built on the Danish data collection model [18], including relevant adaptions to Swedish conditions.

We aim to recruit a total of 8,000 tobacco users and the patient inclusion was initiated in April 2020, and we have extended the patient recruitment period till the end of 2022.

Setting

This study builds on the involvement of trained tobacco cessation counsellors throughout Sweden. The counsellors will recruit patients and collect data for the project. We hope to collaborate with at least 200 certified counsellors[1] in the initial phase of the project.

All the officially certified counsellors working with in-person person-centered cessation programmes regarding smoking, snus and e-cigarette will be invited to participate in the

[1] Counsellors can be certified at Örebro, Karolinska and Sahlgrenska University Hospitals, Karolinska Institute, National Tobacco Quit-Line, and Lund University amongst others.

project. The counsellors can work in primary or secondary care, public or private clinics or other settings.

Counsellors wanting to take part in the study will sign an agreement in accordance with the project. After signing up, information, consent forms and manuals/tutorials for data collection are distributed to the counsellors, and the patient inclusion can begin.

A list of the sites that have collected data to the project will be available at clinicaltrials.gov.

Tobacco cessation interventions

In this study we will include person-centered tobacco or e-cigarette cessation interventions aimed at smoking, snus and/or e-cigarettes with face-to-face sessions only. Face-to-face sessions can be conducted as online video calls as well as on-site meetings.

Any in-person tobacco cessation intervention already implementet into the daily clinical routine amongst the tobacco cessation counsellors throughout Sweden can be included, regardless of intensity, supportive medication, and methods used. Information on the intervention given will be recorded through the standard questionnaires used in the study.

Participants

All adult tobacco users (of at least 18 years of age), including disadvantaged and vulnerable patients, receiving an in-person intervention for tobacco or e-cigarette cessation (smoking, snus and/or e-cigarettes) are eligible for inclusion in the project after giving informed consent. Both individual and group-based interventions can be included.

Exclusion criteria are withdrawing consent, or reduced ability to give informed consent, due to inadequate language skills, dementia, and other conditions.

Recruitment

The contributing counsellors will inform all eligible patients about the project and ask for their informed consent to collect data on their cessation intervention (Figure 1). If consent is not obtained, the treatment will continue according to the normal daily practice without further ado.

After giving consent to be included in the project, the patient will likewise receive the treatment programme as planned. In addition, the counsellor will collect and document baseline information regarding the cessation activity and patient characteristics. At the end of the programme, the tobacco cessation status will be recorded. A manual-based follow-up call will be conducted after 6 months.

Figure 1: Flowchart for the recruitment and data collection process

Data collection

Baseline date will be collected during the cessation intervention by the counsellors and the patients. Data questionnaires are filled in and mailed to the project data manager, who will enter the data into a REDCap (Research Electronic Data Capture) database, hosted at Lund University [24,25].

All materials and questionnaires used are available on the project website (in Swedish) [26].

Baseline

After giving informed consent patients are included in the study and asked to fill in a questionnaire. The paper survey is filled in by the patient, with assistance from the counsellor. If necessary, the counsellor is allowed to read the questions to the patient and record the patient's responses. All questions regarding tobacco use or quit attempts etc. are divided into three section a) Smoking, b) Use of snus, and c) Use of e-cigarettes. The baseline characteristics, include:

- Years of smoking/snusing and using e-cigarettes; current daily tobacco use (No/Yes/Not on a daily basis); previous quit attempts (None/1-3/>3/Not using); cohabitating with a smoker (Yes/No); health care personel who has encouraged the quitting (e.g. GP, hospital doctor, midwife, dentist); housing (e.g. own house, rental, without permanent housing).
- Social security number; level of education; employment; pregnancy (Yes/No); planned surgery (Yes/No); place of birth (Sweden, The Nordic countries, Europe, not Europe); mother tongue (Swedish, Nordic, European, not European).
- Level of nicotine dependency (measured by Fagerström score (FTND) [27] for smokers; and an adapted test used in the clinical setting for dependency among snus users, based on the Fagerstrøm score (FTND-ST) [28,29]).

The counsellors register details of the cessation intervention and process (both planned and performed), and follow-up at the end of the intervention, including:

- Dates of initiating and ending the cessation intervention; date of quitting; setting.
- Details of intervention method; individual/group format; group size; intensity of the intervention (number of meetings and duration); supplemental contacts; relapse prevention; user fees.
- Compliance with the programme (treatment attendance); tobacco status at end of the programme.

Follow-up

Six months (± 1 month) after the initial quit day a manual-based follow-up is conducted by calling each patient. To allow for a more objective evaluation the follow-up call will be conducted by a project team member (or personnel at the National Quit-Line) who had no contact with the patient before the follow-up call. This procedure will eliminate possible impact from the counsellor/patient interaction, as well as insure a unified follow-up procedure for all patients.

Follow-up data includes:

- Continuous successful quitting since planned quit date (or alternatively since the end of the programme) and until the 6 months follow-up; 14 days point prevalence; user satisfaction; use and costs of pharmacologic support; present use of pharmacologic support (nicotine replacement therapy (NRT), bupropion, varenicline, or other); interest in new cessation intervention.
- For non-respondents: Reason for un-successful follow-up; e.g., wrong telephone number, deceased, or not available.

If a patient does not want to participate in the follow-up or it is not possible to reach them by phone the reason for loss to follow up is recorded. Before a patient is considered lost to follow up at least 4 attempts to call on different times and days (at least one attempt must be after 5 pm) must be made.

Outcome

The primary outcome is self-reported continuous successful quitting after 6 months, measured from the planned quit day (or last day of the treatment if a specific quit date is not planned during the intervention) to the day of follow-up 6 months later. The planned quit day will be used as a time reference since the toxic effects of tobacco use should be terminated from that date. Continuous successful quitting is defined as smoking no more than 1 cigarette or similar concerning snus and/or e-cigarettes since the quit day.

We will be monitoring smoking, use of snus, and use of e-cigarettes, as successfully quitting one of the above, may lead to an increased use of one or more of the others.

Secondary outcomes

Several secondary outcomes will be recorded, such as 14 days point prevalence (defined as not smoking/using at all (not even a puff) for the latest 14 days, tobacco abstinence at the end of the intervention, and satisfaction with the intervention.

Comparators

The objective of this study is to facilitate and improve the evaluation of already implemented national tobacco cessation efforts, focusing on ten disadvantaged and vulnerable groups of tobacco users. For data analyses the patients will be sorted into ten different vulnerable groups based on risk factors and compared to tobacco users without the risk factor in question.

The vulnerable groups will be categorised according to the information collected by the tobacco cessation counsellor, and all patients will be cross-linked with additional data from the Swedish National Patient Register to extract relevant diagnoses to uncover e.g. chronic obstructive pulmonary disease (COPD), severe mental illness, or recently giving birth [30].

Analytical strategy

Sample size

The sample size was calculated for the dichotomous main outcome (successful quitting (yes/no) after 6 months) and based on the following assumptions: a two-sided test, a 5% level of significance, a power of 80%, an estimated effect in the control group of 35%, and a minimum relevant difference of 5-10 percentage points.

The online calculator "Inference for Proportions: Comparing Two Independent Samples" (www.stat.ubc.ca/~rollin/stats/ssize/) was used to estimate the necessary sample size of each group. Based on a minimal relevant difference (MiReDif) on 10% and 5% each group should include at least 329 and 1377 tobacco users, respectively. As the study groups in this study are not equal-sized, the sample size gives the estimated size of the smallest group (the vulnerable group in question).

We expect to include 8000 patients. Based on the overall existing interest from the tobacco cessation counsellors, at least 200 of them are each expected to collect data from at least 20 patients/year. The large majority of potential patients are expected to accept inclusion and follow-up [31]. To be able to manifest a difference in effect size of 10%, 4% for the included patients would have to belong to each of the given risk factors (vulnerable groups). To show a difference of 5%, this would be the case for 17% of the included patients.

Statistical analyses

Data will be analysed and reported according to the STROBE guidelines [32]. After controlling for confounders, the effectiveness in the different groups of vulnerable patients is compared to the patients without the given risk factor. Differences between counsellors will be taken into consideration by deploying a mixed-effects model adjusted for hierarchical clustering using the different smoking cessation clinics reporting to the project. Each clinic is identified with its own unique ID-number, and the 1st level cluster will be composed of the group of patients registered in the same smoking cessation clinic.

Relevant univariable and multivariable analyses will be used to analyse differences in continuous successful quitting. The final multivariable logistic regression model will be fitted, based on initial univariable tests, and common knowledge, to include relevant variables. Potential predictors including confounders concerning patients, intervention and tobacco cessation clinic will be included, and as a minimum the following will be examined:

- Patients: Sex, age, compliance with the intervention, tobacco/e-cigarette history, level of nicotine dependency, previous quit attempts, living with a smoker, level of education, job situation, and belonging to more than one vulnerable group.
- Intervention: Intensity, individual or group sessions, and treatment method.
- Clinic: Setting, and geographic location.

Statistically significant predictors of continuous successful quittingwill be identified. Results will be presented as odds ratio (OR) and corresponding 95% confidence intervals (CI), and a two-sided p-value of ≤ 0.05 will be considered as statistically significant.

We expect to encounter both missing data and loss to follow up. Depending on the size and nature of missing data they will be handled accordingly [20,33]. If the proportion of missing

data is small (<5%) missingness will be considered negligible and removed from the analysis. If possible multiple imputation will be used to deal with missing data. Otherwise, sensitivity analysis will be performed to explore the possible impact of the missing data.

Regarding the loss to follow up we do not anticipate data to be missing at random but more likely loss to follow up will be missing not at random. Hence a best-worst and worst-best case imputation will be carried out to investigate the theoretical uncertainty of the study results [20,33].

All statistical calculations will be performed using STATA.IC 16 or a later version.

Dissemination

Both positive and negative results of the project will be published in scientific peer-reviewed journals as well as being presented at national and international conferences. All authors must meet the Vancouver criteria.

Information about the project and results will be disseminated throughout the project-time via a public homepage and other media available to the public, politicians, healthcare providers and planners as these are all important stakeholders.

Ethical considerations

Participants are included only after informed consent. The consent can be withdrawn at any time without explanation and without any influence on the treatment programme.

The project will follow the guidelines from the Swedish Data Protection Authority and have been approved by the Swedish Ethical Review Authority before the patient inclusion (Dnr: 2019-02221.)

The project is registered in clinicaltrials.gov with the reference number: NCT04819152.

All research data remains confidential, and it will never be possible to recognize individuals when data is presented and published. Financing of the project, institutional affiliations and potential conflicts of interest will also be published.

Data statement

After publication of study results technical appendix, statistical code, and anonymised datasets will be available upon reasonable request to the corresponding author.

Patient and public involvement

Patient and public have not been involved in the planning of the study, and there are no current plans of involvement.

Discussion

Updates on the global burden of diseases show that tobacco is still a major risk factor for physical illness in Sweden [34]. Though cessation interventions are one of the most cost-effective interventions in the healthcare system, there is no national systematic registration of how many and which groups of tobacco users are treated or about the effect of the interventions in Sweden. However, focusing tobacco cessation services on disadvantaged and vulnerable tobacco users is a key to reduce tobacco related health inequity [11]. The present study will close a major knowledge gap regarding which programmes that work best for different groups of users in different settings, clinics and regions in Sweden.

Effect of tobacco cessation intervention in disadvantaged and vulnerable groups

The intensity of the cessation programmes seems to be of major importance for successful quitting, [35]. Already, in the year of 2000, the term 'intensive smoking cessation intervention' was defined internationally as a face-to-face program with at least 4 meetings of at least 10 minutes [36,37].

A non-intensive standard program in the UK showed weak effect among low socioeconomic groups in real life setting [38]. In contrast, the Danish standard intensive cessation intervention is effective in real life settings across socioeconomic groups, for heavy smokers, pregnant women, elderly smokers, smokers scheduled for surgery and mentally ill smokers [39–44]. In addition, the Irish results also favour intensive programmes (unpublished data). The current project will add knowledge about the effect of the Swedish cessation interventions.

Snus and e-cigarettes cessation interventions

E-cigarettes are tested as a specific treatment for smoking cessation with contradictory results. A recent study showed that smokers also using e-cigarettes have a lower quit-rate compared to smokers not using e-cigarettes simultaneously [45,46]. A Swedish study has shown that it is possible to quit the use of snus by similar pharmacological support, traditionally used in the smoking cessation programmes [47]. Still, research is lacking on quitting e-cigarettes, themselves.

What this study adds

This project provides new knowledge about the effectiveness of tobacco cessation interventions in the 'real-life setting'.

Our study has potential to contribute to this research area, as it is highly relevant to identify how these specific groups of tobacco users can get the best possible help to successful quitting. If the current cessation interventions show limited effect for specific groups of smokers, the obtained results and knowledge can be used to tailor programmes to specific groups of smokers and tobacco users in the future. This will be of great importance for the individual patient, as it will be beneficial to public health and the socio-economy in general, to offer the best programmes in the future. This will further contribute to evening out the inequality in health.

A positive side-effect would be the possibility to consolidate the culture of systematic monitoring, follow-up and dissemination of effect after the project, which raises the

awareness of effectiveness and exchange of knowledge among cessation provides across sectors. The project can also stimulate a rise in the interest in research and development of methods among the participating tobacco cessation providers. Furthermore, the systematic data collection can contribute to an administrative relief and be timesaving for the counsellors, time which can be spent treating tobacco addiction instead.

Data sharing statement

Data sharing not applicable as no datasets were generated and/or analysed for this manuscript.

Contributorship statement:

HT, MR, ML, HG, JA, AP and ARH designed the study. SW and TBE made contributions to the conception and design of the project. All authors contributed to the methodology of the study. MR and HT drafted the manuscript. All authors read, revised, and approved the manuscript.

Compering interests:

MR, JA TBE, ARH, HT: Nothing to declare.
HG: Doctors Against Tobacco (unpaid NGO chair).
AP: Nurses against Tobacco (unpaid NGO vice chair); NGO Tobaksfakta – independent think tank (paid general secretary).
SW: Received in total 4 650 £ from Pfizer AB, and 490 £ from Sanofi, for lectures and education about smoking cessation.
ML: Received in total 3 500 £ from Phizer AB, 3 500 £ from ASTRA Zenega AB, 1 500 £ from MSD, and 1 000 £ from Boehringer Ingelheim AB, all for lectures, speech, or education about smoking cessation and/or smoking and covid19.

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FORTE was not involved in the design of the study. They will not be involved in the collection, analysis, or interpretation of data, in writing the manuscript or in any other part of the project.

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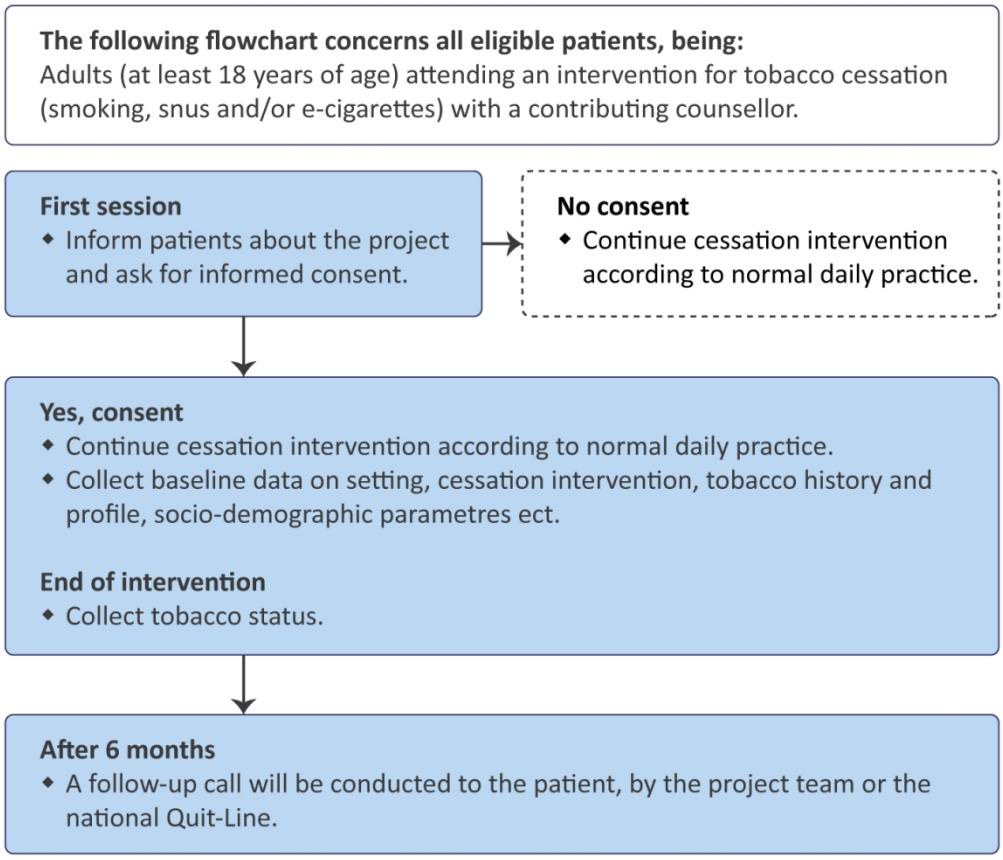

Figure 1: Flowchart for the recruitment and data collection process

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