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MODELING INDIVIDUAL BEHAVIORAL CHANGES: THE CASE OF TOBACCO UPTAKE IN A COHORT OF SCHOOL CHILDREN

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Dedicated in memory of Sir Richard Doll, whose outstanding contribution to the epidemiology of smoking-related diseases will continue to inspire future generations of scholars.

ABSTRACT

The aim of this thesis was to elucidate preventable determinants of smoking and smokeless tobacco use in adolescence in the frame of a longitudinal study (BROMS cohort). The study population encompasses 3019 children recruited from 5th grade classes in 96 schools in Stockholm, Sweden during the academic year 1997-1998.

A study of developmental trajectories of tobacco use between the ages of 11 and 17 revealed that *snus* use, once initiated, is best described through three patterns, mainly differing in the speed of progression. The best description of cigarette smoking is provided by four patterns, distinguished by age at onset and speed of progression. Several traditional risk factors for tobacco use measured at baseline, such as gender, parents' and friends' tobacco use, and prevalence of tobacco use among classmates influenced individual probabilities of belonging to a particular trajectory.

Characteristics of the class, rather than of the school were associated with smoking initiation between 5th and 6th grade. A decreased risk of smoking uptake was associated with exposure to short anti-tobacco education before the 5th grade, compared to no education. Problematic interpersonal relations in the class were associated with an increased risk of smoking initiation, compared to positive interpersonal relations. Parents' tobacco use was associated with adolescents' current use of either cigarettes or *snus*. Prevalence of current smoking was lower among children whose fathers used *snus* than among those whose fathers smoked. Maternal influences on youths' tobacco use were stronger than paternal influences.

Sixth grade students' knowledge of tobacco properties and effects was not associated with future use. Despite this lack of association, a clear link was found between access to information sources and knowledge about tobacco.

Nearly two thirds of tobacco users in the middle-high levels of the compulsory school used cigarettes as first tobacco product, while one out of five took up *snus* first. After initial use, experimentation with the other product occurred to greater extent for "cigarette starters" than for "*snus* starters". Whereas the existence of the so called "gateway effect" of *snus* use, i.e. induction of cigarette smoking, could not be excluded, the effect in this cohort was likely modest, accounting at the most for 6% of the final smoking prevalence.

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IV. Rosendahl KI, Galanti MR, Gilljam H, Ahlbom A. Knowledge about tobacco and subsequent use of cigarettes and smokeless tobacco among Swedish adolescents, J Adolesc Health September 2005 (in press)

V. Galanti MR, Rosendahl KI, Wickholm S. Smokeless tobacco as gateway to smoking in early adolescence: an analysis of the Swedish 'BROMS' cohort, Nicotine Tob Res 2005 (accepted for publication)

CONTENTS

LIST OF ABBREVIATIONS

ANOVA	Analysis of variance
BIC	Bayesian information criterion
BROMS	Children's Smoking and Environment in the Stockholm County
CAN	The Swedish Council for Information on Alcohol and Other Drugs
CI	Confidence interval
IARC	International Agency for Research on Cancer
INREGIA Ltd	The Institute for Region Analysis
NYTS	National Youth Tobacco Survey
OR	Odds ratio
PNR	The national registration number, a unique personal identifier
RR	Relative risk
SCB	Statistics Sweden
SD	Standard deviation
ST	Smokeless tobacco
TSNA	Tobacco specific nitrosamines
ZIP	Zero inflated Poisson distribution

INTRODUCTION

The major health consequences of tobacco smoking are hardly unknown for anyone today. Although much has been learned since the days when Doll and Hill in 1950 published their results about smoking and carcinoma of the lung, smoking still is a major cause of poor health and death. In Sweden, where the prevalence of daily smoking is 16% among men and 19% among women[1] there are at least 1.2 million people at risk.

On the other hand, the knowledge of health consequences of smokeless tobacco use is not as deep and widespread as that of cigarette smoking. This represents almost a paradox in Sweden, where the Swedish variety of oral snuff "*snus*" is consumed daily by one out of five men.[1] Nicotine dependence from *snus* use is believed to be as strong as from cigarettes, since the nicotine uptake[2, 3] and plasma concentration[4] are comparable. This may lead to a long lasting use with health consequences such as periodontal diseases[5] and possibly cardiovascular diseases.[6] Recent research has also indicated increased risk for pancreatic cancer[7] and diabetes type 2[8] among users of *snus*.

Although a considerable body of research exists on determinants of tobacco use, there are still many unclear features of this behavior, especially during adolescence, the age span when most of the initiation of use occurs. One reason for this lack of knowledge is the rarity of longitudinal studies with long follow-up among adolescents.

AIMS OF THE THESIS

The general purpose of this thesis was to investigate possible preventable determinants of smoking and smokeless tobacco use in adolescents.

Specific aims were:

- To describe the development of cigarette smoking and *snus* use in a cohort of adolescents between 11 and 17 years of age.
- To quantify the short term effects of factors at the school and class level.
- To investigate the effect of parental use of tobacco on the adolescents' use.
- To test the hypothesis that knowledge on tobacco properties and health consequences would differentially modify smoking and *snus* use.
- To test the hypothesis that *snus* use in adolescence is a gateway to smoking.

BACKGROUND

The growing interest for tobacco use and its determinants among young people[9-11] is motivated by the fact that earlier initiation of smoking has been observed over years,[12] and only a minority of youths will nowadays start using tobacco after the age of 18 years.[13] An inverse correlation has been found between age at first use and lifetime duration of use.[14] Therefore, there is a concern that this early start will increase long-term tobacco use and its devastating health effects at the population level.

TRENDS OF TOBACCO USE AMONG YOUNG PEOPLE

Worldwide, there are few systematic surveys of young people's tobacco use. Moreover, it is often difficult to compare prevalence of tobacco use between surveys, because of differences in age groups or/and behavioral measures. In Europe, the ESPAD project started in 1993 with a main purpose to collect comparable data on alcohol, tobacco and drug use among 15-16 year old students in European countries. The prevalence of past 30 days smoking presents wide variations across countries. In the 2003 survey among 35 European Countries the highest figures were observed in Greenland (60 percent) and the lowest in Iceland (20 percent), with Sweden in second lowest position (23 percent).[15] In addition, smoking prevalence has been constantly higher among girls than among boys in the Scandinavian countries, Great Britain, Greece and Italy. The general trend for the surveyed European countries presents with an increase during the first four years followed by a decrease in the last four-year period. Data from the USA survey: *Monitoring the Future* shows a decrease in smoking prevalence in both genders, also confirmed by data from The National Youth Tobacco Survey NYTS.[16]

In Sweden, annual surveys of smoking and *snus* use among students in the 9th grade of compulsory school (15-16 years of age) have been conducted by The Swedish Council for Information on Alcohol and Other Drugs (CAN) since 1971. The prevalence of current smoking between 1971 and 2004 is shown in figure 1 (the curves are not comparable for the whole period due to changes in the questions on use of tobacco).

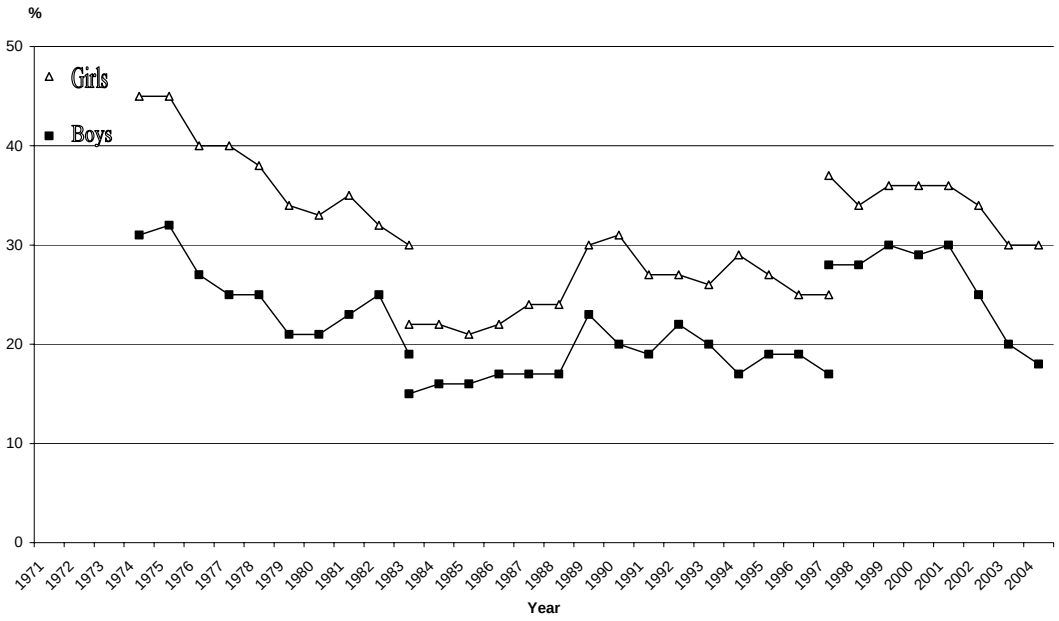

Figure 1. Proportion of smokers by sex in the 9th grade. Reproduced from "Skolelevers drogvanor 2004", CAN.

The proportion of daily and occasional smokers has clearly been higher for girls than for boys during the whole period, but both genders experienced a substantial decrease during the 1970s. The downward trend has leveled off during the 1980s and the smoking prevalence remained stable until recently. In the last three years, however, a further decrease seems to have taken place. The picture of tobacco use in Sweden is made more complex by the use of *snus*. Figure 2 shows the prevalence trend for current daily and occasional use of *snus* by gender.

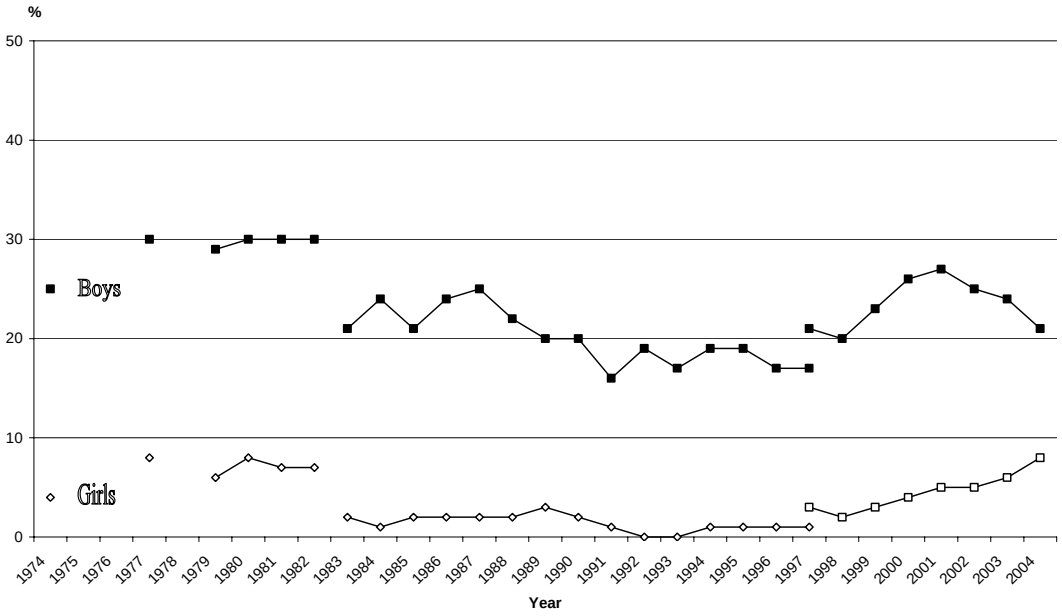

Figure 2. Proportion of *snus* users by sex in the 9th grade, source: "Skolelevers drogvanor 2004", CAN.

The prevalence increased among both boys and girls during the early 1970s and remained stable during the 1980s. From 1998 the prevalence started to increase again among both genders, but during the last four years a decrease among boys and a further increase among girls has been noticed.

Comparing the use of smokeless tobacco between studies and countries is even more difficult than comparing cigarette smoking. In fact, smokeless tobacco is not a single product, since its manufacturing and modality of use largely differ between countries. For instance, in India a huge variety of smokeless tobacco products are consumed (creamy snuff, gul, gutkha, khaini, mawa, mishri, qiwam, red tooth powder, *snus* or snuff).[17] In USA, smokeless tobacco is used both as chewing tobacco and as dry and moist snuff, whereas in Sweden the only product of practical significance is "*snus*", the Swedish variety of snuff. A common feature in Sweden and USA is the much higher prevalence of smokeless tobacco use among boys compared to girls.[16, 18]

TRAJECTORIES OF TOBACCO USE AMONG YOUNG PEOPLE

Trends of tobacco use are important to monitor in order to understand behavioral changes over time at the group or population level. If the focus is rather on behavioral changes at the individual level the study of developmental trajectories is a more appropriate strategy, provided that longitudinal data is available. While there are plenty of longitudinal studies on adolescent smoking this is not true for smokeless tobacco use. Therefore, a description of how this behavior develops over time at young ages is lacking. A few studies have defined behavioral development of adolescent smoking at the group level,[19-23] but results are not easily comparable, since there was a wide variation both in the number of trajectories and in their definition. In general, two patterns of behavioral development were described in all five published studies from cohorts of adolescents: either stability or escalation of different intensity. Decreasing intensity and cessation, on the other hand, were only described in two of them.[19, 22] This is not surprising, since adolescence seems to be a time when most experimentation and escalation of use takes place. Therefore, follow-up beyond adolescence into young adulthood is necessary in order to detect decreasing trajectories. A number of risk factors have been associated with developmental trajectories of smoking escalation, such as gender,[21] poor academic performance,[21-23] friends' smoking,[19, 21-23] intention to smoke,[23] behavior problems,[23] anxiety,[23] parental support,[19] positive health beliefs,[19] parents' low education,[22] single-parent family,[22] parents' approval,[22] and beliefs.[19, 22] Also, smoking seems to co-vary with the use of other substances.[22, 23] As a whole, these findings are confirmatory of analytical studies of risk factors for smoking among adolescents.

DETERMINANTS OF TOBACCO USE AMONG YOUNG PEOPLE

The Surgeon General's report "Preventing Tobacco Use among Young People" in 1994 gave a first systematic overview of tobacco use among young people.[9] The report provided a classification of determinants of tobacco use into four groups: sociodemographic, environmental, behavioral, and personal factors. However, many of the factors empirically associated to youths' smoking may belong to several domains and no classification provides insights about causal processes. For instance, peers-related influences may be conceptualized as social pressure to adopt the behavior as

well as the result of self-selection based on personal affinity.[24] The existing knowledge on smokeless tobacco use is modest, compared with that on cigarette smoking. With a few exceptions, findings concerning determinants of smokeless tobacco use are consistent with those concerning cigarette smoking, suggesting that both tobacco products share at least some pathways, functions and meanings for young people.[25, 26]

Age and gender

Age is an important determinant of tobacco use. Data from a number of surveys and longitudinal studies suggest that increasing age is associated with an increased likelihood of smoking experimentation.[11] The same is true concerning smokeless tobacco use.[27, 28] Gender differences in the uptake and use of tobacco have been described with an earlier initiation among boys for both cigarettes and smokeless tobacco but with a more rapid escalation to regular smoking among girls.[29] The use of smokeless tobacco is constantly higher among boys.[30]

Parental influences

Parents' lifestyles are believed to be of importance in influencing offspring's health behavior,[31] and smoking is no exception. Parental cigarette smoking is associated with increased likelihood that the child also smokes.[10, 11] A similar association has been found for smokeless tobacco.[30] It is not clear whether these associations reflect behavioral modeling, accessibility of tobacco, and/or other pathways.[32] Whether parental influences on their children's behavior are gender- and product specific has not been systematically investigated.

Peers' influences

The influences of peers' smoking on the risk of own uptake of cigarette use has been extensively investigated in cross-sectional as well as in longitudinal studies, with very consistent findings. Having smokers among friends and school-mates increases the risk of own smoking by 2 to 10 times.[10, 11] It has also been posited that this is the single most important factor in determining when and how cigarettes are first tried.[33] However, it is not clear how these social influences work. Since direct pressure effects are not recalled,[34] it has been postulated that the group pressure would rather work in an indirect way, via inclusion and selection rules also affecting other behaviors (e.g. risk-taking behavior).[35] The association with peers' use has been described also for smokeless tobacco, but most studies were based on a cross-sectional design. However, in one longitudinal study peers' use was associated both to onset of use and to continued use.[36]

School prevention and policy

School policy measures and interventions aiming to reduce smoking showed only small and short-lived effects in both experimental and observational studies.[37-40] However, setting and contextual factors at the school level have been proposed as important modifiers of the effectiveness of school-based interventions.[41] For instance, school climate was found to affect smoking behavior both directly and indirectly.[42, 43] Only a few observational studies have explored this dimension in real-life conditions, and they did not present a systematic analysis of factors relevant to tobacco prevention.[44, 45]

Attitudes, knowledge and behavioral correlates

Attitudes towards smoking and knowledge of its health consequences were not strong predictors of smoking uptake among adolescent.[10] Knowledge of the consequences has rather been regarded as a possible mediator of decisions on future cigarette smoking.[10] In cross-sectional studies, differences in knowledge have also been found between users and nonusers of smokeless tobacco[46] but the association appears to be weak.[47] It has been postulated that the importance of knowledge for future behavior might be stronger for smokeless tobacco use.[9] In fact, it is possible that the knowledge of the health consequences of smokeless tobacco is not as widespread as for cigarette smoking. In Sweden, where *snus* is regarded by many as a healthier alternative to smoking,[48] knowledge on effects of tobacco on health may differently predict subsequent use of cigarettes or of *snus*. Due to these beliefs concern has been expressed that smokeless tobacco use may even work as a possible "gateway" to cigarette smoking for some youths.[49] Undoubtedly, the use of these two types of tobacco was strongly associated in several studies.[46, 50] Also, cigarette smoking and smokeless tobacco use co-varied with other substance use[26] as well as with other risk-taking behaviors.[50]

Psycho-biological risk factors for tobacco use and nicotine dependence

A number of personal and psychological characteristics has been associated to adolescent smoking: low self esteem,[51] low self-efficacy,[52] and depressive symptoms[53, 54] In recent studies has an increasing importance been given to psycho-biological factors, such as pre-natal exposure to tobacco components[55, 56] and hormonal events occurring at puberty.[57]

SUBJECTS AND METHODS

STUDY POPULATION

The study population on which the studies included in this thesis are based is known as the "BROMS"* cohort and consists of a sample of 3019 school-children attending the 5th grade in the academic year 1997-1998 in 96 schools of the Stockholm region, Sweden. The cohort was recruited through a cluster sampling, involving the selection of a random weighted sample of all schools in the region with the compulsory intermediate block. Weights proportional to the school size (number of students in the previous academic year) were assigned to avoid overrepresentation of small-size schools.[58] The initial sample size of 118 schools was calculated to obtain an estimated number of 5000 children. Ninety-six schools (81%) agreed to co-operate. All families of the 4671 students listed in the 5th grade classes of the consenting schools were then contacted to provide formal consent to the participation in the study, which was eventually granted for 3050 children (65%). Analyses of non-participation at the school and at the family level have been published elsewhere.[59] Thirty-one children whose parents consented to the study subsequently failed to complete the baseline form because of the following reasons: refusal (n = 20), not in the school during the four weeks when data collection took place (n = 1), moved from the initial school and not further located (n = 1), return of an empty or unreadable form (n = 9). The living status, the place of residence and the school attended by each student at the time of the data collection were obtained by means of the national registration number (PNR), a unique identifier assigned to each resident in Sweden at birth or at the time of immigration. Students who emigrated out of Sweden were not further traced at a particular wave of data collection, but efforts were made to resume the follow-up if they re-entered the country. Different study bases were employed in the studies included in this thesis, as follows.

Paper I: Trajectories of smoking and smokeless tobacco use

The study base consisted of 3010 subjects (1534 boys and 1476 girls) who participated in at least one follow-up assessment up to the second year of the senior high school (i.e. had at least two data points between the age of 11 and 17 years).

Paper II: School and class environments as predictors of future smoking

The analysis was based on 2883 students (1467 boys and 1416 girls) who provided information both at baseline (grade 5) and in the following academic year (grade 6).

Paper III: Influences of parental tobacco use on adolescent tobacco use

The study base consisted of 2232 adolescents (1066 boys and 1166 girls) with follow-up to the 8th grade, who at baseline had never tried tobacco, and lived with at least one parent at that time.

* Swedish acronym for Children's Smoking and Environment in the Stockholm County

Paper IV: Knowledge about tobacco and subsequent use of cigarettes and *snus*

The study in paper IV was based on 2581 adolescents (1285 boys and 1296 girls) who participated both in the 6th grade and in the 9th grade follow-up assessment.

Paper V: *Snus* as a gateway to smoking

The study base in paper V consisted of 2436 adolescents (1209 boys and 1127 girls) with complete follow-up from baseline to grade 9.

DATA COLLECTION

Information on tobacco use and on potential explanatory factors was collected at different levels.

Information from the students

At the student level, a self-completed questionnaire was administered at baseline and at each follow-up year at the beginning of the second school semester (between January and February). At each wave, repeated attempts were made to reach the students during a four-week period. If not traceable at school, a written reminder including a new questionnaire was mailed to the student's home address. In case of non-response, three efforts were made to reach the student by telephone in order to arrange a personal interview. Students who did not participate in a given annual survey were still eligible for coming waves. On the contrary, those who, at any given wave, communicated their intention interrupting their participation were considered lost to follow-up for the remaining study time. Table 1 reports the number of eligible subjects and the proportion of respondents during each year of the study.

Table 1. Annual number and rate of completed student form

School year	Grade	Eligible base	Respondents (%)
1997–1998 (baseline)	5	3050	3019 (99.0)
1998–1999	6	3019	2883 (95.5)
1999–2000	7	3010	2875 (95.5)
2000–2001	8	2975	2809 (94.4)
2001–2002	9	2951	2689 (91.1)
2003–2004	2nd year senior high	2909	2622 (90.1)
2004–2005	3rd year senior high	2851	2485 (87.2)

The students' form encompassed between 50 and 80 questions, most of which aimed to assess patterns of tobacco use at each wave and during the interval between waves. As the scope of the study was to document the progression between stages of all tobacco use, both smoking and use of *snus* were assessed at the same level of detail. The core questions assessing tobacco use were kept almost identical at each wave. A filter

question asked whether the student ever tested a cigarette (even if just puffed it) or *snus*, respectively. Those who answered affirmatively to this question were asked to complete a lifetime history of tobacco use, including information about age at initiation, symptoms experienced at the first use, progression to regular use, intensity of use, attempts to quit, desire to quit, symptoms of nicotine dependence, circumstances of tobacco use and preferred cigarette brand. The remaining questions in the students' form investigated the occurrence of smoking in the social network (family and friends), life events predisposing to tobacco use, knowledge of tobacco related risks, attitudes towards tobacco use, exposure to information about tobacco via media, school, perceived social norms and parental support, other life style and health indicators. This part of the form encompassed different questions each year. The proportion of valid answers was more than acceptable in almost all cases, and for single questions ranged from 93.6% to 99.7% at baseline and from 68.6% to 99.7% at the sixth wave (2nd year senior high school). Questions which did not perform at any wave were subsequently excluded or modified.

Information from the parents

A form was sent to the home address of the parents (or guardian) of the eligible students at baseline and two years later, when the students attended 7th grade. The form encompassed questions concerning the parents' occupation, job title, education (baseline only), current and past use of tobacco (cigarettes and oral snuff), mother's and father's tobacco use during each trimester of the index pregnancy, parental perception of frequency and importance of youth tobacco use (second wave). At baseline the form was returned by 2997 (98.3%) of the consenting parents. At the second wave the form was returned by 2768 (92%) of the parents of the retained students.

Information at the school level

At baseline and in the 7th grade information was requested from the principal of the school attended by each child. The information concerned the school structure and size (number of grades, students, teachers and other personnel) and the school tobacco policy. This latter was investigated as to the implementation of specific anti-tobacco programs, written rules to deter tobacco use during the school time, registration of the students' tobacco use in the nurses' records. The principal was also asked about typology and amount of resources employed in pedagogic activities aiming at tobacco prevention among students. At baseline all of the schools completed the form and at the second wave (grade 7) 186 out of 192 schools (96.9%) returned the questionnaire form. In addition to the information requested from the principals information was also collected at baseline on the prevalence of recipients of social benefits in the health care district where the schools were located. The schools' catchment's area was determined via geo-coding by INREGIA Ltd, The Institute for Region Analysis. The coding was thereafter linked to the registry of the Total Population Survey in 1990 (Statistics Sweden, SCB).

Information at the class level

At each wave from grade 5 to 7 a questionnaire was sent to the teacher of the class where each cohort member was enlisted. The form encompassed questions on the class

structure (number of pupils, gender and country of origin, major compositional changes during the year) together with quantitative and qualitative aspects of pedagogic programs intended to promote health, or specifically concerning tobacco use. The response rate among teachers decreased for each follow-up wave from 100% (at baseline) to 76.9% in grade 7. Due to students' migration the number of classes increased during follow-up from 217 at baseline to 582 in 7th grade.

Data managing

In order to preserve confidentiality, information on individual identifiers was stored at the research center under protection of a password only shared between the project manager and the administrative staff responsible for the tracing of the students. A study-specific identification code provided the link between the study information and the personal data. All study forms carrying individual information (i.e. the student's form, the parent's form and the nurse form) were computerized by means of optical scanning at the Statistics Sweden (SCB). The remaining information was entered manually at the Tobacco Preventions' research center. All information was submitted to validity and consistency check in several instances. Abnormal values were either corrected on the basis of the original data in the forms or discarded. Whenever possible, inconsistent reports were re-interpreted on the basis of the overall likelihood of a particular event of interest. For instance, a negative answer to question whether the student tried any smoking, followed by positive reports of smoking, age at first smoking, etc. implied a reclassification of the smoking status as positive to any smoking. This re-classification was independently done by at least two investigators. If no agreement was reached, or the inconsistency extended through several reports, the corresponding information was discarded.

Validation of reports

A cross sectional analysis of the concordance between self reported tobacco use and saliva cotinine were made on a sub-sample of 520 adolescents from the cohort when they were in the final grade of junior high school (grade 9).[60] Five months before the yearly survey the selected adolescents and their parents received a letter explaining the purpose, but not the time of the test. The free choice of participating and the confidentiality of the results were underlined. Consent was assumed in all cases of no explicit refusal. A team consisting of dental hygienists assisted by the school nurse collected the saliva specimens, either immediately after the questionnaire survey or, with few exceptions, in the next few days. Using a cut point of 5 ng/ml saliva cotinine to discriminate active tobacco use, there was an overall concordance of 93% between self reported tobacco use and saliva cotinine.

OUTCOMES

The papers included in this thesis focused on different outcomes related to tobacco use.

Paper I: Developmental trajectories of tobacco use were modeled using the estimated number of *snus* dips and cigarettes consumed annually, categorized into five categories: <1; 1-9.5; 10-35.5; 36-363.5; >363.5.

Paper II: This study took up two different outcomes (a) proportion of smoking initiation in the 6th grade, among students who had not reported any previous smoking in the 5th grade; (b) rate of smoking progression between 5th and 6th grade among all students.

Paper III: The individual probability of being ever and current user of cigarettes and/or *snus* in the 8th grade was the outcome of interest in this study. Current use was defined as adolescents reporting at least monthly use of the product. Use of tobacco was analyzed as use of cigarettes, *snus* or both tobacco products, and categorized into four mutually exclusive categories: no tobacco use; *snus* only; cigarette smoking only; combined use of *snus* and cigarettes.

Paper IV: This study analyzed the individual probability of having been regular user, current user, or former user between 6th and 9th grade. Regular use and current use were analyzed both in relation to any tobacco product and in four mutually exclusive groups described in paper III. Adolescents' knowledge about tobacco was also an outcome in this study, represented as score obtained in specific questions.

Paper V: This study also analyzed several outcomes: (a) current use of tobacco in the 9th grade, defined as current use of cigarettes and/or *snus* at least once a month; (b) persistent use, defined as report of current use of cigarettes and/or *snus* at all surveys after initiation; (c) recurrent use, defined as report of current use of tobacco on any surveys after initiation; (d) intensity of use, computed as number of cigarettes and *snus* dips per week, categorized into four groups: <7; 7-20; 21-40; >40.

OUTCOME PREDICTORS

Paper I: Parents' tobacco use, friends' tobacco use, socio-economic status, prevalence of tobacco use in class and school at baseline, age and gender were used as time-independent covariates which could affect the trajectories of tobacco use between 11 and 17 years of age. Number of cigarettes smoked and amount *snus* used in the previous year were used as time-dependent covariates that could mutually modify the respective trajectories.

Paper II: Eleven factors were investigated as predictors of tobacco use, related to the school and class attended in the 5th grade. These ranged from class structure (e.g. number of students) to school policy, pedagogic programs and class social climate.

Paper III: Parental use of cigarettes and *snus* was used as predictors of the children's behavior. In addition, a cumulative indicator of exposure was analyzed, as follows: neither parent smokes/uses tobacco; one parent smokes/uses tobacco; both parents smokes/uses tobacco. By combining the information on each parent's current and past tobacco use a dichotomous index of adolescent's lifetime exposure was derived as never (parents never used tobacco or stopped before the child's birth) or ever (parents used tobacco sometime during the child's life).

Paper IV: The outcome predictor in this study was constructed upon the children's responses to questions aiming to explore their knowledge of tobacco properties and

health consequences. The proportion of correct answers to each single item was first analyzed separately. Correct answers were then added to form three scores, one including all items, one including items related only to cigarettes, and one including items related only to *snus*. The full item score was analyzed both as a continuous score and according to the following categories: low, intermediate, or high. Further analyses used children's reports of access to specific sources of information on tobacco (e.g. television, books, school programs, etc.) to predict knowledge score.

Paper V: The order of product use (e.g. cigarette first, *snus* first, or both during the same one-year interval) was used as predictors of future, current, persistent or intensive use. Product order was identified at any wave by the reports of cigarette and/or *snus* use among adolescents who were lifetime non-users at the preceding wave. Ever use at baseline defined as children reporting having at least puffed from a cigarette and/or having tried *snus*.

STATISTICAL ANALYSIS

The developmental trajectories in paper I were identified by means of a semi parametric group-based approach,[61] such as that employed in the SAS procedure TRAJ.[62] In these models, all longitudinal information is used to estimate the number of groups that best fits the data, as well as the shape of the trajectory for each group.

The selection of the best model for the data was primary based on the Bayesian information criterion (*BIC*):

$$BIC = \log(L) - 0.5 * \log(n) * (k),$$

where the maximum *BIC* corresponds to the least negative value. *L* is the value of the model's maximized likelihood, *n* is the sample size, and *k* is the number of parameters in the model. As the quality of the model's fit declines, the first term of the equation declines. The second term extracts a penalty proportional to the log of the sample size for each added parameter. Therefore, based on the *BIC* criterion, an expansion of the model is desirable only if the resulting improvement in the log likelihood exceeds the penalty for more parameters. *BIC* was used in the model selection in order to: (a) determine the optimal number of groups describing the developmental history, (b) identify the covariates to be included in the model and (c) determine the appropriate order of the polynomial used to model each group's trajectory.

An approximation of the Bayes factor, $2\log_e(B_{10}) \approx 2(\Delta BIC)$, was used to test whether the model was essentially improved by adding more parameters. The log form of the Bayes factor is interpreted as the evidence favoring the alternative model, with values 0 to 2 "not worth mentioning", 2 to 6 "positive", 6 to 10 "strong", and > 10 "very strong".

The model also estimates the proportion of the whole population whose behavioral changes over time most closely conform to each trajectory group. Finally, the model computes the individual probability to belong to each of the identified trajectories as follows:

$$\hat{P}(j|Y_i) = \frac{\hat{P}(Y_i|j)\hat{\pi}_j}{\sum_j \hat{P}(Y_i|j)\hat{\pi}_j},$$

where $\hat{P}(Y_i|j)$ is the estimated probability of observing *i*'s actual behavioral trajectory, Y_i, given membership in *j*, and $\hat{\pi}_j$ is the estimated proportion of the population in group *j*. The quantity $\hat{P}(Y_i|j)$ can be calculated post-estimation based on the maximum likelihood estimates of the trajectory parameters.

Time-independent covariates added to the model can affect posterior group membership probabilities while the addition of time-dependent covariates can modify the observed behavior. An extension of TRAJ was also used to jointly estimate developmental trajectories of two distinct, but theoretically related, measurement series.[63]

Since the outcomes of interest were the estimated number of *snus* dips and cigarettes, consumed during the previous year, both ordinary Poisson and zero inflated Poisson (ZIP) distributions were used in the models. The ZIP distribution is useful for modeling the conditional distribution of count data, given group membership when there are more zeros than under the Poisson assumption i.e. overdispersion.[64]

In the analysis of the categorical outcome in paper II, relative risks (RR) were estimated based on a model with a log-link and a Poisson distribution of the error. Particularly consideration of the hierarchical structure of the data was taken by multilevel modeling. In many situations, individuals are grouped into broader contexts termed hierarchies, i.e. units at one level are grouped within units at a higher level. These higher hierarchies are expected to impact on the variability of characteristics measured at the lower level.[65] In our case, students from a class tend to be more similar one another than they are to students from another class. In other terms, this clustering imposes a correlation structure on the data, reflecting the shared experiences within the same school or classroom. The correlation between pupils invalidates classical assumptions of independence that are assumed to exist when applying common regression or ANOVA techniques. Ordinary techniques are therefore inappropriate and will lead to underestimates of standard errors.

From an ordinary regression equation:

$$y_i = \alpha + \beta_p x_{ip} + e_i,$$

where y_i may be a link function for a discrete outcome, α is the 'intercept', x_{ip} represents the set of P explanatory variables and β_p their associated slope coefficients and e_i is a random term, commonly known as the residual. The equation is extended in its simplest form "the basic multilevel model" with only one element which is particular to each unit of the higher level in the hierarchy, for instance schools. If the subscript j refers to the school and i refer to the student, then the notation for the model is given by:

$$y_{ij} = \alpha + \beta_p x_{ijp} + (u_j + e_{ij}),$$

where u_j indicates the effect of school j on the outcome over and above those described by the set of explanatory variables. In this latter model it is assumed that u_j is a random

variable with zero mean and constant variance σ^2_u. Interest lies in the distribution of the u_j, and primary focus is the estimation of the variance σ^2_u across all schools. If the variance is large, then the outcome is dependent on school attended, if it is small, then variations in the outcome may be explained by the measured characteristics alone.

Logistic regression was the method of analysis used in paper III-IV-V. This method can be used when the outcome variable is dichotomous, as it is required that the regression equation will estimate the proportion of individuals with, or the individual probability of the proposed outcome. The logistic model is set up to ensure that whatever estimate of risk we get, it will always be some number between 0 and 1, which is the range for a probability. This is not always true for other models like, for instance an ordinary linear regression equation, which is why the logistic model is often the first choice when a probability is to be estimated. One further advantage of the logistic regression output is that the exponentiated regression coefficients are directly readable as odds ratios of the outcome of interest associated with a determined level of the predictor variable. The odds ratio is derived and computed from the logistic model via the logit transformation denoted as logit (p):

$$\log it(p) = \log_e\left(\frac{p}{(1-p)}\right)$$

This is the most commonly used transformation for dichotomous outcomes while some others are available. The logit can take any value from minus infinity, when $p = 0$, to plus infinity, when $p = 1$. Regression models can be fitted to the logit which are very similar to the ordinary multiple regression and analysis of variance applied to data with a normal distribution. The relationships are assumed to be linear on the logistic scale.

In paper III and IV we used an extension of the logistic regression modeling, namely the multinomial logistic regression.[66] This extension allows the analysis of categorical outcomes with more than two categories (as in the case of tobacco use separated into different products). In the case of ordinal categories, the multinomial model estimates the probability for a subject with given values of the predictor variable of being in any of the most extreme categories vs. being in the lowest one (e.g. being a user of both *snus* and cigarettes vs. being a non user).

MAIN RESULTS

PAPER I

A model with three developmental trajectories among ever users was found to provide the best fit for *snus* use (figure 3), while four trajectories gave the best fit for cigarette use (figure 4).

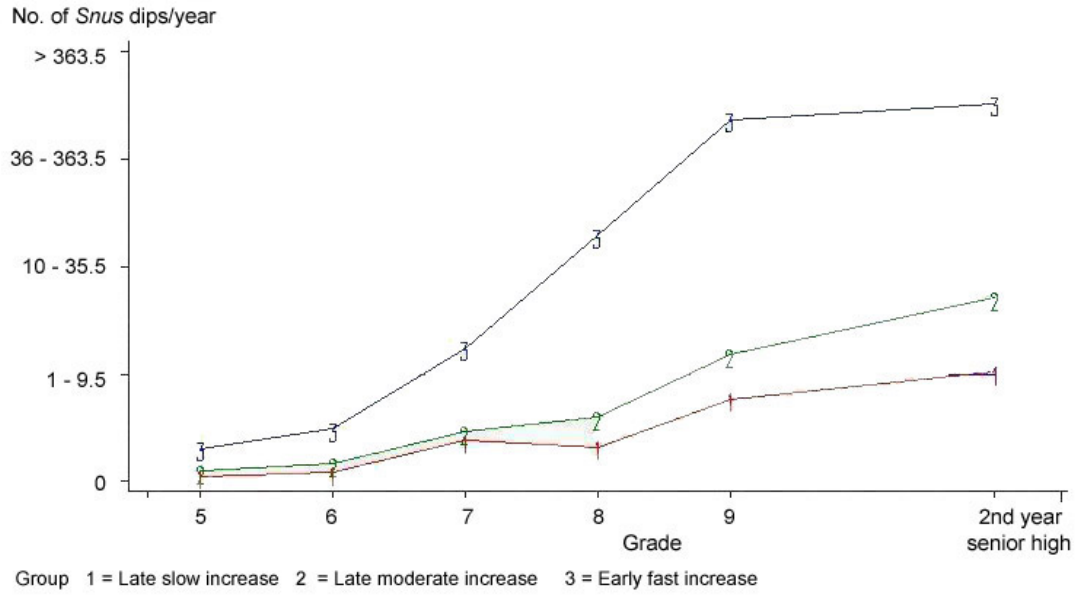

Figure 3 Trajectories of *Snus* use

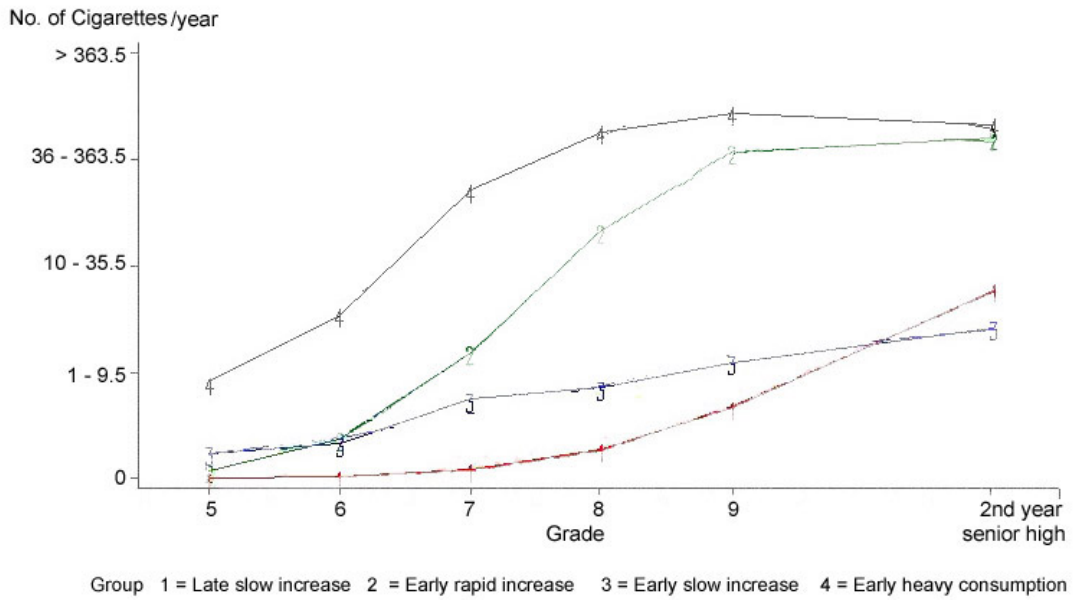

Figure 4 Trajectories of Cigarette Smoking

The three trajectories for *snus* described a late slow increase, a late moderate increase, and an early fast increase. The trajectories of cigarette smoking identified late slow

increase, early fast increase, early slow increase, and early heavy consumption with moderate increase over time. Several risk factors for tobacco use measured at baseline, like parents' tobacco use, friends' tobacco use, gender and tobacco prevalence among students of the same class influenced individual probabilities of belonging to a particular trajectory. The time-dependent annual consumption of cigarettes and *snus* were mutual modifiers of the respective trajectories.

PAPER II

The variance between schools in smoking prevalence and smoking progression in 6th grade was small (0.030; standard error 0.057), while it was larger between classes (0.331; standard error 0.086). Accordingly, school policy and other school characteristics were not significantly associated with preadolescents' smoking while some characteristics on the class level were (table 2). A decreased risk of smoking uptake (relative risk 0.72, confidence interval 0.54 to 0.97) was associated with exposure to short anti-tobacco education prior to 5th grade compared to no education. Problematic interpersonal relations in the class were associated with a relative risk of smoking initiation (relative risk 1.42, confidence interval 1.05 to 1.93) compared to positive interpersonal relations.

Table 2 Class characteristics as risk factors for ever smoking in the 6th grade among never smokers in the 5th grade (n = 2351)

Characteristics	RR	95% CI
Prevalence of ever smoking in 5th grade		
0 – 16	Ref	
17 – 71	1.34	1.05 – 1.70
Number of students		
5 - 19	Ref	
20 – 24	0.84	0.55 – 1.29
25 – 29	0.80	0.52 – 1.23
30 - 84	0.64	0.40 – 1.04
Major changes in composition since previous year		
No	Ref	
Yes	0.87	0.52 – 1.43
Interpersonal relations in the class		
Positive	Ref	
Problematic	1.42	1.05 – 1.93
Anti-tobacco curricula during the previous year		
< 1 h	Ref	
1 – 2 h	0.72	0.54 – 0.97
> 2 h	1.16	0.85 – 1.59
Other health education		
No	Ref	
Yes	1.05	0.78 – 1.41
Students smoking discussed with parents		
No	Ref	
Yes	1.04	0.74 – 1.48

PAPER III

Parents' tobacco use was associated with adolescents' current use of cigarettes and *snus* (odds ratio 2.7, confidence interval 1.8 to 3.9 if both parents used tobacco versus neither parent). Mother's cigarette smoking was associated with adolescents' current exclusive smoking (odds ratio 2.4, confidence interval 1.6 to 3.6). Father's use of *snus* was associated with current exclusive use of *snus* among boys (odds ratio 3.0, confidence interval 1.4 to 6.4), but not with current cigarette use (table 3). The overall prevalence of current smoking was lower among children whose fathers used *snus* than among those whose fathers smoked.

TABLE 3 Parental current tobacco use at baseline as risk factor for adolescents' current use of tobacco in the 8th grade

	Only *snus* (boys)		**Only cigarettes (both sexes)**		**Both cigarettes and *snus* (boys)**	
Exposure to:	**OR**	**95 % CI**	**OR**	**95 % CI**	**OR**	**95 % CI**
Mother's tobacco use*						
No tobacco use	1.0		1.0		1.0	
Only *snus*	4.2	0.8, 21.4	0.7	0.1, 5.7	-	-
Only cigarettes	1.8	0.8, 4.0	2.4	1.6, 3.6	1.7	0.7, 3.8
Both cigarettes and *snus*	4.5	0.5, 43.7	1.9	0.2, 16.1	-	-
Father's tobacco use*						
No tobacco use	1.0		1.0		1.0	
Only *snus*	3.0	1.4, 6.4	1.1	0.6, 1.8	1.4	0.5, 3.8
Only cigarettes	1.2	0.4, 3.6	1.3	0.8, 2.1	2.0	0.8, 5.2
Both cigarettes and *snus*	1.9	0.5, 6.9	1.1	0.5, 2.3	2.9	0.9, 9.3
Parents' use of tobacco						
Neither parent	1.0		1.0		1.0	
One parent	1.3	0.6, 3.0	2.4	1.6, 3.5	1.3	0.6, 3.0
Both parents	4.6	2.1, 10.2	2.2	1.3, 3.6	3.1	1.3, 7.5

∗ Adjusted for the other parent's use of tobacco (any vs. none)

PAPER IV

Sixth grade students' knowledge of tobacco properties and effects was not associated with future use (table 4). Items dealing with addictive properties of nicotine were prospectively associated with *snus* use only. On the other hand, a strong association between access to information sources and knowledge about tobacco facts was found, despite the lack of association between knowledge and use of tobacco. For each source, subjects who reported not being informed were consistently less likely to have a high knowledge score than those reported being informed.

Table 4. Odds ratios* (ORs) and 95% confidence intervals (CIs) of current tobacco use for a correct answer to knowledge items in the 6th grade

Knowledge items	***Snus* only**		**Cigarettes only**		**Cig and *snus***	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Nicotine in cigarettes causes lung cancer (no vs. yes)	1.1	0.6–2.0	0.8	0.5–1.2	1.7	1.0–2.9
Nicotine dependence develops only after smoking several cigarettes per day for many years (no vs. yes)	0.5	0.3–0.9	0.8	0.6–1.0	1.1	0.7–1.7
Nicotine dependence does not occur if one only uses *snus* (no vs. yes)	1.6	1.1–2.3	1.0	0.8–1.3	1.7	1.1–2.6
Quitting smoking causes weight gain (yes vs. no)	1.2	0.8–1.7	1.1	0.9–1.5	1.2	0.8–1.8
Smoking decreases the risk of acne (no vs. yes)	0.8	0.5–1.2	1.1	0.8–1.4	0.8	0.5–1.1
Heart pulse is slower in smokers (no vs. yes)	0.9	0.5–1.7	0.8	0.5–1.3	0.7	0.3–1.5
It is not established that *snus* can cause cancer (yes vs. no)	1.4	0.9–2.0	0.9	0.7–1.2	1.1	0.7–1.6
In Sweden tobacco ads are allowed in weekly magazines (no vs. yes)	1.1	0.8–1.6	0.9	0.7–1.2	1.3	0.9–1.9

* = Adjusted for gender

PAPER V

Lifetime, current, and regular use of tobacco increased with time in both sexes, the largest increase taking place between grades 6 and 8, i.e. 12-14 years of age. The majority of tobacco users (63%) started use with cigarettes, while 20% took up *snus* first. After initial use, experimentation with the other product occurred for 38% of the "*snus* starters" and for 51% of the "cigarette starters". In the analysis of product order using information from all waves, 7.7% of the *snus* starters were currently smoking in grade 9, while the corresponding proportions among cigarette starters and mixed starters were 30.1% and 34.2% respectively. Consequently, the probability of being a smoker or a tobacco user was higher for "cigarette starters" and "mixed starters" than for "*snus* starters" (table 5).

Table 5. Odds ratios* (ORs) and 95% confidence intervals (CIs) of current smoking or any tobacco use in grade 9.

	Current smoking in grade 9			Current tobacco use in grade 9		
	N* (Yes/No)	OR†	CI	N* (Yes/No)	OR†	Ci
Product order						
Snus first	26/313	Ref		52/185	Ref	
Cigarettes first	302/700	3.97	2.63-6.23	366/609	1.76	1.25-2.51
Cigarettes and *snus* at the time	93/179	6.14	3.83-10.15	135/112	3.79	2.52-5.74

* = Numbers do not sum up to the total because of missing information
† = Adjusted for gender, at end of follow-up, and time from initiation

DISCUSSION

METHODOLOGICAL ISSUES

At the time of the Surgeon General's report in 1994 it was remarked that longitudinal studies of tobacco use in youth were comparatively few, most of the knowledge coming from cross-sectional studies. In cross-sectional studies information on outcome and exposure is often referred to the same point in time. Therefore these studies, although useful in order to generate new hypotheses, do not always fulfill the basic requirements for analyzing causal relationships.[67] In the last decade, however, the bulk of knowledge accrued through longitudinal studies of tobacco use among young people has increased steadily. These have not only provided general confirmation of putative risk factors identified in previous studies, but also provided new insights on the natural history of tobacco use and nicotine dependence in the life course.[68, 69] However, with few exception, these studies were conducted in North America. Epidemiological studies focusing on behavioral outcomes may not be as generlizable across cultural and social contexts as epidemilogical studies of diseases. In Europe, particularly in Sweden, there were no longitudinal studies of youth tobacco use at the time the BROMS cohort study was initiated. The BROMS cohort is a unique prospective study in Sweden, designed to study the development of tobacco use and dependence over the entire span of adolescence. Notable characteristics of this cohort are also the very high participation rate and the extensive set of questions on history of cigarette smoking and smokeless tobacco use.

Reliability of reports

How do we know that the answers to self administered questionnaires reflect true behaviors? There are two potential threats to the reliability of unassisted self reports. First, there may be a poor design or a poor comprehension of the question itself.[70] Second, socially undesirable behaviors may be intentionally concealed, among other things because of fear for consequences within the family or the school, a very relevant issue in adolescence.[71] This concern may even be stronger in Sweden, where smoking does not rate very high in public opinion.[72] Nonetheless, the influence of these factors in the BROMS cohort is likely to be minimal, as indicated by the following pieces of evidence. First of all, the prevalence of smoking and *snus* use in the BROMS cohort are in line with those observed in cross-sectional studies in Sweden.[18] Secondly, the results from biochemical validation of the students' answers, performed when the students were in the final grade of the junior high school, indicate that the overall concordance between self reported tobacco use and the saliva cotinine test was very satisfactory, around 93%.[60] Other authors[73-75] have also concluded that children and adolescents tend to give reliable answers in epidemiological studies, especially when anonymity is assured, which is not the case in the BROMS cohort. The identity of cohort members in the BROMS study is potentially disclosed to a few authorized members of the study team, but no document related to the study carries personal identifiers.

Outcome definition

Most surveys of adolescents' tobacco use tackle the process of initiation, since virtually all uptake of tobacco use occurs during this period of life. The "initiation" concept,

however, is not a straightforward one, and needs to be analyzed in detail. Smoking uptake in adolescence has been described as progressing through a sequence of five developmental stages: preparatory, trying, experimental, regular use, and addiction/dependence.[76] However, the behavioral characteristics of, and the borders between these stages are not clearly defined.[68] Furthermore, the stage model has been challenged by the evidence that indicators of nicotine dependence may be present at very early stages of tobacco use.[69]

The estimated annual consumption of tobacco, used to model the trajectories for cigarette smoking and *snus* use in paper I, is an alternative way to describe fluctuations between these stages throughout a long follow-up time, a way that has the advantage of being independent from the subjects' self-appraisal. However, the estimated consumption itself is not a precise measure, as it ignores behavioral changes during the time interval chosen for its computation. The cumulative (lifetime) experience of tobacco use is the measure most often used to capture very early behavior, as for youths in the "trying stage" (paper II). However, since a given explanatory factor (e.g. school policy, family influences) may play different roles at different stages of tobacco use, in these studies we chose to analyze a wider range of outcomes. For instance, in paper II we analyzed a measure of smoking progression by assigning the students in both 5th and 6th grade to one of the following groups: never smoked, smoked only a few puffs, experimented but not smoking now, and current smoking. Any move to a more advanced stage was treated as a case of progression.

Current use was explored as outcome in all analyses from the 8th grade (e.g. paper III, paper V) since more adolescents had by then become frequent users of both cigarettes and *snus*. While there is a general consensus that "monthly use" represents a sort of threshold for current use, the questions used to tackle this minimal frequency vary between studies. Studies conducted in USA rely heavily on the "recency" concept, i.e. use during the 30 days preceding the survey.[16] On the other hand, Swedish and other European surveys rely on self reported "average frequency".[18, 77] Both approaches have advantages and drawbacks. In a validation study of self-reported behavior in a sub-sample of the BROMS cohort,[60] the "recency" concept conveyed a helpful definition of current use. On the other hand, the "average" concept may be more appropriate in capturing the real behavior, since intensity of smoking fluctuates heavily over time in adolescence. Although we measured both recency and average frequency of tobacco use from the 8th grade survey onwards, in our reports of current use we chose the latter approach, which provides a better comparison across time points and different surveys.

There is no consensus on which level of use characterizes regular use, but most studies identify this stage as to weekly use,[78-80] an approach we also followed (paper IV). Finally, in both paper IV and paper V we used measures of stability of tobacco use over several years (i.e. discontinued use, recurrent use, persistent use) as outcomes measures. While these profiles are retrospectively identified with respect to the study time, they rely on prospective or concurrent reports at the child's level, therefore avoiding the risk of biased or imperfect recall.

Internal validity

Internal validity conveys the assurance that the measurements in a given study are accurate apart from random errors (i.e. there is lack of systematic error). Various types of biases can detract from internal validity and distort the estimations in an epidemiologic study. The distinction among these biases is not always straightforward, but three general types has been identified: selection bias, information bias, and confounding although even these categories are not always clearly demarcated.[81]

Selection bias is a distortion of the measured effect in the way that the estimate among subjects included in the study is different from the estimate obtainable from the entire population theoretically targeted for study. In the BROMS cohort, some selection of the study subjects occurred, for instance because of the sampling strategy (weights proportional to the size of the school), or because of the schools' and parents' compliance to the study. While this selection surely contributed to a restriction of the study base (e.g. with respect to the families' socio-economic status), thus affecting the degree with which the results may be generalized, the question is: could selection occurring at each of these steps have biased the results in our studies? It is a difficult argument, since the presence of selection bias must be inferred, rather than observed. First, it should be considered that some selection processes may affect the study base from opposite directions.[59] Selection as a source of bias would therefore also affect the results in opposite directions, but because neither one is easily quantified, the overall amount of bias would remain unknown. Second, if selection is to produce spurious results the selection factors should differentially affect the probability of the outcome under study according to levels of the exposure. An example of potential selection bias is the inverse association found in paper II between size of the class and the relative risk of ever smoking. A possible interpretation was indeed that the small size participating in the study probably carried a high rate of problematic behaviors among students, affecting the likelihood of future smoking. A help on the way is to look at similarities with other studies, since selection bias is unlikely if there is consistency of results across studies. For those studies where comparable counterparts exist, our results are generally in agreement. We have therefore no reason to believe that selection of the study base did bias the presented results away from the null.

Information bias can occur from errors in obtaining the needed information on exposure and/or outcome. The consequences of this bias are different depending on whether the classification errors are independent from each other. Classification errors that are not independent are referred to as differential misclassification, whereas the classification errors for either exposure or outcome that are independent of each other are considered as non-differential misclassification. Non-differential misclassification, which affects every epidemiologic study to some extent, has generally been considered a lesser threat to validity than differential misclassification. The bias introduced by non-differential misclassification is always in a predictable direction: toward the null condition. All measures of tobacco use have most certainly suffered of some degree of misclassification, because of failure in reporting or processing the data. For instance, some students may underreport their experience of tobacco because of perceived disapproval from their parents. If this underreport is likely to vary across categories of exposure, then bias may arise. This may be the case in paper III, where parental tobacco

use was used to predict future use among children. In fact, children of non-smoking parents may tend to conceal own tobacco use more frequently than children whose parents smoke. However, information bias is unlikely to occur when the source of information on exposure/predictors (e.g. school teachers, parents) is different from the source of information on the outcome (the children themselves). Differential underreport of own tobacco use is also unlikely in this cohort, according to the results of the validation study.[60]

The third type of bias comes from confounding, an important issue that has to be considered in all epidemiological studies. A confounding factor must be associated with both the exposure and the outcome under study. A further requirement is that the confounder must not lie in the causal pathway between exposure and outcome. The identification of actual confounders is a much more complicate task in behavioral epidemiology than it is in medical epidemiology, since causal pathways are often uncertainly and equivocally defined. In our studies, we used a two-steps approach for identification of confounders. First, only factors logically or empirically linked to the proposed outcome and exposure were explored. One example is the association between interpersonal relations in the class in 5th grade and ever smoking in 6th grade (paper II) where the association was controlled for class prevalence of ever smoking in 5th grade as a most likely confounding factor. Second, potential confounders were retained for adjustment in further analyses only if they were statistically associated to the outcome and their inclusion in regression models modified the association between main predictor and proposed outcome.

Generalization and abstraction

It has been stated that the essence of knowledge is generalization and that the art of discovery is the art of correct generalization.[82] The scientific merit of a given study is very limited if one can't generalize the results outside its specific study base. Thus, the question arises of the level at which the generalization is warranted. First of all, a distinction ought to be made between scientific generalization/abstraction[83] and generalization of results from the study sample to the underlying population. The first process is a much debated one in social and behavioral epidemiological studies, which often lack a clear causal model.[84] Moreover, it is assumed that results in behavioral and social studies more often depend on specific contextual circumstances; therefore replication of results is always required before abstraction is possible. In the biological domains this problems are often thought of as unimportant.

Concerning the generalization from a given study base to the underlying population it is necessary to observe that a study base is always the product of a complex selection process. However, we ought also to distinguish between "restrictions",[83] i.e. the researcher's conscious manipulation of the entry into the study because of efficiency reasons, and "selection", i.e. uneven representation of the candidate subjects because of processes extraneous to the research design. An example of the former process is the age restriction at the cohort recruitment, which prevents the generalization of the results to younger or older ages (i.e. children and young adults). This limit is mostly evident in paper I (trajectories of use), where the low occurrence of quitting tobacco in such a young cohort could not translate in a detectable "quitting trajectory". However, this

cohort also suffered of selection processes that made it not completely comparable to the underlying population. For instance, the weighted sample of schools resulted in a higher proportion of cohort students attending large units than in the general population in the region. The differences in participation rates among families of different socio-economic status may also impact on the generalizations of certain results. For instance, families with low socio-economic status were underrepresented in our sample, and this demands cautiousness in generalizing to this group results relative to family influences. Since most results in the BROMS study are expressed as associations between a predictor or exposure factor and a behavioral outcome, any obstacle to the generalization of the results implies the hypothesis that the reported association would be different in populations with different levels of the selection characteristic (e.g. education level, geographic area, etc.).

GENERAL SUMMARY AND CONCLUSIONS

Development and determinants of cigarette smoking and the use of the Swedish smokeless tobacco "*snus*" among adolescents is the central theme of this thesis. How cigarette smoking initiates and progresses during adolescence has been reported in quite a few studies,[19-23] while corresponding studies of smokeless tobacco use are lacking. The analysis presented in paper I allows us to conclude that trajectories of *snus* use are essentially no different from those of cigarette smoking. In other terms, the development of tobacco use does not seem to depend on the tobacco product. However, since many youths seem to believe that smokeless tobacco is much safer than cigarettes,[9] one could expect decreasing trajectories for cigarette smoking to appear earlier than for smokeless tobacco use. This difference was not evident in our study, probably because of the insufficient length of follow-up.

Anti-tobacco policy and other school characteristics do not seem to play any decisive role in shaping the tobacco experience of early adolescents. In this respect, the results of paper II only confirm previous findings of both observational[37, 38] and intervention studies.[39, 40] However, factors determining the quality of the social relations between members of a class may be of importance for tobacco use. For instance, Ennett et al. showed that early adolescents in schools situated in less crowded neighborhoods with higher levels of attachment experiment with alcohol and cigarettes more often than their counterparts in less advantaged circumstances.[42] At odds with some intervention studies[41] we could not find evidence of school influences on adolescents' tobacco use even at very short follow-up interval. However, we have to take into account that our measures of exposure to school pedagogy and environment were rather crude, compared to complexity of the educational and preventive efforts. The choice of the outcomes may also have affected the results. Having tried smoking is such a common occurrence in adolescence' life that important individual variations connected to school rules and pedagogy cannot be expected. The multilevel model (three levels) that were used in the analyses showed a small variance between schools and a somewhat larger variance between the classes resulting in wider confidence intervals for the class factors analyzed. The finding of a larger variance at the class level than at the school level is not surprising, since the clustering effect is naturally larger for levels closer to the individual.

The results in the fourth study someway corroborate those in paper II. A good knowledge of tobacco properties and of the health consequences of its use seems actually to be a function of information gathered from several sources, school among others. However, achieved knowledge did not predict the decision to use tobacco among adolescents in this cohort. Furthermore, there was no difference in the association between knowledge and subsequent use of either cigarettes or *snus*. This comparison has never been reported before. Again, one would expect knowledge to affect future smoking differently from *snus* use, due to more convincing information on health hazards from cigarette smoking than from smokeless tobacco. As in paper I, the reason why this difference was not found may be explained by the young age of the cohort.

Quite a few studies found that parental tobacco use is strongly associated to adolescents' tobacco use.[11] If not due to biased reports, this association support the notion of parental modeling of offspring's behavior, through several possible pathways including availability of tobacco, appraisal of risks, attitude shaping, perceived approval.[32] We extend this analysis to encompass a comparison between cigarette smoking and *snus* use. In short, our findings suggest that the parental influences are also product-specific, i.e. that the adolescents seem to do what their parents do, especially what their mothers do. A stronger association of adolescents' smoking with maternal rather than paternal was also found in previous studies,[85] while others showed no evidence of such a gender-specific association.[86] A stronger maternal influence may depend, among other things, on family composition and/or caregiver role within the family (many children spend more time with their mother than with their father, especially in single-parent families). Concerning *snus*, paternal influences are obvious, as *snus* use is an almost exclusive male behavior in Sweden.[1] Interestingly, sons to fathers using *snus* do not run a higher risk of becoming smokers, although they have a much higher probability of becoming *snus* users themselves.

The fifth study included in this thesis is indeed entirely centered on this concern, namely whether the use of *snus* is conducive to smoking (gateway theory). In line with other longitudinal studies,[87] we found that early experimentation with cigarettes, *snus*, or both predicts subsequent smoking or tobacco use. However, a majority of adolescents initiated their "career" with cigarettes or both products in a short interval. Over a four-years period, these adolescents run a higher risk of progressing in smoking and/or *snus* use than those initiating with *snus*. Taken together, these results indicate that *snus* is not an important gateway to smoking in early adolescence. This doesn't exclude the possibility that, once regular use of *snus* is established, under particular life circumstances the transition to smoking will eventually take place, as an American study seems to indicate.[88] In addition, the sizeable group of young people experimenting with both products very close in time had a very unfavorable profile of tobacco use, with protracted and intensive use over time. This pattern may indicate the existence of particularly vulnerable subgroups, with propensity to tobacco escalation and perhaps nicotine dependence, which may be identified by their early transition between or combination of cigarettes and oral tobacco.

PUBLIC HEALTH IMPLICATIONS

What can be learned from these studies in a public health perspective? We can point out the following:

- Adolescence is a time of initiation and intense experimentation with tobacco, unapt to show decreasing trends. This observation indirectly supports the evidence that smoking cessation programs with adolescents show very low success rates.
- The effects of school policies, anti-tobacco programs and achieved knowledge of tobacco risks on children's tobacco use are limited. School education should probably target social skills, interpersonal relations, and personal risks of tobacco use.
- Parental tobacco use influences the use of tobacco among their offspring's. Children do what their parents do, even in the choice of tobacco products.
- *Snus* does not seem to be an important gateway to smoking in early adolescence, but combined use of both cigarettes and *snus* should be tackled as an indicator of susceptibility to protracted and intensive use of tobacco.
- The similarity of trajectories and determinants of use of cigarettes and *snus* among adolescents indicates that there are no reasons to build up product-specific programs targeting this age group.

FUTURE DIRECTIONS

- Developmental trajectories of cigarettes and *snus* use into adulthood are still to be explored, in order to tackle later processes of cessation and/or dependence. The addictive potential of *snus* use is also a debated question, as it is the temporal relation of tobacco, alcohol and other substance use.
- Parental influences also deserve more refined analyses, in order to disentangle the role of different factors, such as product availability, parenting style, and role modeling.
- The long-term health consequences of *snus* use initiated at very young age, as it was the case in quite a few adolescents in this cohort, is also a very important unexplored issue. As late as 16 November 2004 an IARC review concluded, where Swedish epidemiological data were included, that smokeless tobacco is carcinogenic to humans. Previous inconclusive studies may therefore depend on insufficient follow-up of large cohorts of users.

Some of these questions can receive an answer within the frame of the BROMS cohort study, the informative potential of which extends far beyond the studies published in this thesis.

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