

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Effects of a School-Based Prevention Program on Smoking in early Adolescence: Six-Month Follow-up of the 'Eigenständig werden' Cluster Randomized Trial
AUTHORS	Isensee, Barbara; Hansen, Julia; Maruska, Karin; Hanewinkel, Reiner

VERSION 1 - REVIEW

REVIEWER	Roger E. Thomas Department of Family Medicine, University of Calgary, Calgary, Canada.
REVIEW RETURNED	16-Nov-2013

GENERAL COMMENTS	<p>This is an excellent trial, well designed and well analysed.</p> <p>Intervention: The authors used a social competence + social influences/skills intervention, and the recent Cochrane review (Thomas RE, McLellan J, Perera R. School-based programmes for preventing smoking. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD001293. DOI: 10.1002/14651858.CD001293.pub3.) found social competence and social competence + social skills interventions to be the most effective interventions to prevent starting smoking.</p> <p>The Thomas et al. review found 135 C-RCTs. Researchers have attempted to obtain better results by modifying and combining the interventions of previous researchers, and adding booster sessions and sessions taught by peers. It would be very helpful to future researchers to know how the authors built on previous research to arrive at the comprehensive set of interventions listed in Table 1 of their 2012 article.</p> <p>The content of the "usual curriculum" in the control groups is not described.</p> <p>Design: The power computation required 3160 students and 158 classes, and 2513 provided data at the 6 month follow-up.</p> <p>Risk of bias. The risk of bias from randomisation is low (coin toss). There is no comment on concealment. Attrition rates of those assessed at baseline were high (27%) with selective attrition of males, students not attending Gymnasia, those with a migration background, current smokers, older students and those of lower SES, but there were no systematic differences between intervention and control groups.</p> <p>The authors in the 2012 article describe the measures to assess delivery fidelity but there is no report for this 6 month follow-up.</p>
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	<p>Results: Among baseline never-smokers, the difference in the percentage starting smoking was 3.4%, the OR = 0.66 ([0.43 to 1.00]. p = 0.047. In the Discussion section they also present results as Cohen's d, which many readers find difficult to compare to other outcome measures. The Number Needed to Treat to prevent one baseline non-smoker becoming a smoker after 6 months is 29.</p> <p>Altogether a meritorious study. More assessment of the content of the interventions in relationship to ongoing attempts to improve interventions over the past 40 years would be very helpful to the field in providing insights about the next needed improvements.</p> <p>There are several sentences where the definite article is missing. There are also several instances of data described by a singular verb. Data are plural, datum is singular.</p>
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REVIEWER	<p>Anthony Zehetner Service of Addiction Medicine in Youth Dept of Adolescent Medicine The Children's Hospital at Westmead Sydney, NSW, Australia</p>
REVIEW RETURNED	18-Nov-2013

GENERAL COMMENTS	<p>This is an important paper as the authors state. Most articles published in this field are from USA and not Germany.</p> <p>This is an important paper as the authors' state. Most articles published in this field are from USA and not Germany.</p> <p>For background I would like to see some statistics on the current rate of juvenile smoking and gender differences in Germany. So was their sample representative of the general population? When can teens purchase cigarettes legally (18 years?) The authors state that 47.9% were girls and mostly boys dropped out of the study. Would this make the intervention appear less effective? Also there is a natural uptake of smoking as seen by their intervention-control group graphs. From these, there is a 4.2% ARR for lifetime smoking in mid-grade 7. Current smoking is not statistically significant, while smoking incidence (3.4% lower in the intervention group) is less robust as the CI crosses 1.0. This makes me question what happens to the outcomes at further points in time, eg one or two years after completing the program. Is the effect maintained (higher abstainers or less smoking if already a smoker) or is there a delay in age of smoking onset? Follow-up of this data set and patient cohort should occur at a later time point. There is literature that Brief Intervention and Motivational Interviewing have cumulative and sustained effects; though these are personal, rather than group, programs.</p> <p>The authors attempt to describe reasons and attributes, such as skills training, to explain why education does not fully translate to smoking abstinence or cessation. For existing smokers, the paper proposes that the education program did not change existing smoking practice. Neither did 'perceived norms of smoking' and 'self-efficacy to refuse cigarette offers'. Did the authors expect the magnitude of outcome of the results they found? Was this better or worse than expected? Was a pilot study conducted to see if "Eigenständig warden 5+6" works and for what populations? For</p>
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	<p>example, would it be better to target Grade 6+7 or 7+8 students (as Grade 5+6 has low numbers of smokers)? Or is it 'too late' for education purposes of students in those grades?</p> <p>Possibly the "Eigenständig warden 5+6" intervention program may operate better as a primary prevention program in schools? Does such an existing health education program exist in Year 5 & 6 curricula? Is "Eigenständig warden 5+6" a replacement candidate or a supplemental one? If it is a replacement, is it easier to implement, more effective or cheaper to operate?</p> <p>The two drawbacks I see with the paper are (i) the high attrition rate and (ii) small effect seen for the sample size.</p> <p>Regarding attrition rate, from the 2437 students allocated to the intervention group, only 1179 were analysed (48%). The control group had 2335 students allocated and 1334 analysed (57%). Why did some schools agree then decline to participate? Were the included schools catering to a different socio-economic status? Under 'Results': 'Attrition Analysis', 27% of students had no data available. Why was this the case? No hints for selective attrition were found even though migration and socio-economic status were recorded.</p> <p>180 students with 'data set inconsistencies' (76 intervention, 104 control) were excluded. Would this have significantly altered the final results? Sometimes a best/worse case scenario using included numbers and running the statistical analysis again will determine if results remain robust.</p> <p>For (ii) small effect for sample size, the small rates of intervention and control students smoking at baseline (1%) and follow-up (5%) mean that the impact of the "Eigenständig warden 5+6" program is harder to quantify: for a small effect, smaller confidence intervals require a larger sample size. The intervention is diluted by the 'natural history' of smoking uptake (regression away from the mean).</p> <p>In the discussion, the authors acknowledge that "Finding no effect on current smoking might also be explained to some extent by the young age of the sample with only very few students smoking already on a regular basis". Again this proposes larger student numbers. Also the cognitive state of the pre-adolescent should be considered. The mean age is 10.37 years which is late-childhood to early adolescence in understanding. It may be that the students are yet to experience the direct pressures and influences of peers that usually comes with early-to-middle adolescence (12-15 years) when smoking experimentation and uptake occurs, so there may be less effect because the subject (and outcome) of interest is of low prevalence or incidence anyway.</p> <p>The authors should be applauded for recognising and discussing the potential for study bias. Good aspects include teachers not being involved in data assessment and the use of sealed envelopes. Response bias for drug use is acknowledged and reduced by using anonymous surveys and private lodgement system. Could there be objective measures of cigarette use to reduce response bias, eg exhaled air in a cotinine breathalyser, urinary cotinine levels? The authors acknowledge that the "Eigenständig warden 5+6" intervention program is delivered in a subjective manner. It is also time consuming. I would like a cost-effectiveness statement to help</p>
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	<p>determine if the program has good external validity (generalisation) and ability to be implemented to other populations, eg USA. Maybe there might be some electronic applications, eg online program?</p> <p>A statement regarding confounders may also be of benefit. For example, do cigarette packets in Germany have warning statements or graphic images of smoking related diseases? Are they expensive? With baseline randomisation, it is hoped that students have similar characteristics, eg rate of mental illness, smoking parents or siblings, etc. Would a reduction in smoking lead to an increase in cannabis or alcohol? The authors should explicitly state that only tobacco smoking and not including cannabis smoking was recorded.</p> <p>If this paper is not published in BMJ, then it should be resubmitted to a Paediatric Medicine, Adolescent Medicine or Addiction Medicine journal.</p>
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REVIEWER	Professor Robert M West University of Leeds UK
REVIEW RETURNED	25-Nov-2013

GENERAL COMMENTS	<p>The subject matter is of considerable interest and I am keen to see these trial results published. There are some minor omissions that the authors can respond to easily and I have some further comments that might be of some help to the authors.</p> <p>There are some major difficulties encountered, described and dealt with in this trial report. Specifically there are issues regarding selection of schools, selection of teachers, selection of parents (through consent), high drop out, and potential for self-completion biases.</p> <p>The authors have chosen to dichotomize their lifetime and current smoking outcomes. This loses power for their analyses. They might mention results using more detailed outcomes and perhaps ordinal regression.</p> <p>On Page 10 Line 21 was control meant rather than intervention?</p> <p>There are no power calculations provided. The sample size is determined by the recruitment process. The authors however should indicate what power their analyses have.</p> <p>The authors have contributed an analysis of attrition which is to be encouraged with such a high rate. This is however restricted to some chi-sq tests and would be much improved with logistic regressions accounting for clustering.</p> <p>Inconsistencies in data are treated as missing observations and are dropped. That is only a complete case analysis is offered. Even though there are only 180 such cases. Some sensitivity analysis might be offered - or if appropriate multiple imputation, although I would prefer to see sensitivity analyses.</p> <p>Those lost to follow up are excluded. Since the rate of attrition is so large, it does not appear to me that alternative analyses are</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer #1

Roger E. Thomas

Department of Family Medicine, University of Calgary, Calgary, Canada.

This is an excellent trial, well designed and well analysed.

Intervention: The authors used a social competence + social influences/skills intervention, and the recent Cochrane review (Thomas RE, McLellan J, Perera R. School-based programmes for preventing smoking. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD001293. DOI: 10.1002/14651858.CD001293.pub3.) found social competence and social competence + social skills interventions to be the most effective interventions to prevent starting smoking.

The Thomas et al. review found 135 C-RCTs. Researchers have attempted to obtain better results by modifying and combining the interventions of previous researchers, and adding booster sessions and sessions taught by peers. It would be very helpful to future researchers to know how the authors built on previous research to arrive at the comprehensive set of interventions listed in Table 1 of their 2012 article.

The content of the "usual curriculum" in the control groups is not described.

Response: cf. Response to Editor's comment no. 3

Design: The power computation required 3160 students and 158 classes, and 2513 provided data at the 6 month follow-up.

Risk of bias. The risk of bias from randomisation is low (coin toss). There is no comment on concealment. Attrition rates of those assessed at baseline were high (27%) with selective attrition of males, students not attending Gymnasias, those with a migration background, current smokers, older students and those of lower SES, but there were no systematic differences between intervention and control groups.

Response: For the discussion of the topic attrition, please cf. response to the last Editor's comment.

The authors in the 2012 article describe the measures to assess delivery fidelity but there is no report for this 6 month follow-up.

Response: As outlined in the study protocol, we assessed delivery fidelity in our study. In the current analysis, we chose to treat all intervention classes as "treated as intended" without differentiation for treatment integrity as indicated by the teachers. Nevertheless, further analyses should examine this topic, e.g. whether efficacy differs between classes which received the entire program and classes which received only parts or whether a specific set of "core elements" of the intervention is necessary to achieve effects etc.

Results: Among baseline never-smokers, the difference in the percentage starting smoking was 3.4%, the OR = 0.66 ([0.43 to 1.00]. $p = 0.047$). In the Discussion section they also present results as Cohen's d , which many readers find difficult to compare to other outcome measures. The Number Needed to Treat to prevent one baseline non-smoker becoming a smoker after 6 months is 29.

Altogether a meritorious study. More assessment of the content of the interventions in relationship to ongoing attempts to improve interventions over the past 40 years would be very helpful to the field in

providing insights about the next needed improvements.

There are several sentences where the definite article is missing. There are also several instances of data described by a singular verb. Data are plural, datum is singular.

Response: We would like to thank this reviewer for his kind and positive evaluation of our work. Concerning the content of the intervention, we added some more information (cf. Response to Editor's comment no. 3). We went carefully through the entire manuscript and hope that we were able to eliminate the grammatical errors (missing of definite article, "data" followed by a singular verb).

Reviewer #2

Anthony Zehetner

Service of Addiction Medicine in Youth

Dept of Adolescent Medicine

The Children's Hospital at Westmead

Sydney, NSW, Australia

This is an important paper as the authors' state. Most articles published in this field are from USA and not Germany.

For background I would like to see some statistics on the current rate of juvenile smoking and gender differences in Germany.

Response: We added information on the current rate of adolescent smoking in Germany in the background section:

Most recent data from Germany reveal smoking rates of about 12% for both female and male adolescents aged 12 to 17 years and 6.6% for young adolescents aged 12 to 15 years.^{2;3}

So was their sample representative of the general population?

Response: In the paragraph on limitations in the Discussion section, we added the restricted generalizability due to including only regular schools.

When can teens purchase cigarettes legally (18 years?)

Response: The information that selling cigarettes to minors (<18 years) is forbidden by law in Germany, is given in the Discussion section (p. 15).

The authors state that 47.9% were girls and mostly boys dropped out of the study. Would this make the intervention appear less effective?

Response: We included a paragraph on sensitivity analyses to clarify this topic in more detail, cf.

Response to the last comment of Reviewer 3.

Also there is a natural uptake of smoking as seen by their intervention-control group graphs. From these, there is a 4.2% ARR for lifetime smoking in mid-grade 7. Current smoking is not statistically significant, while smoking incidence (3.4% lower in the intervention group) is less robust as the CI crosses 1.0. This makes me question what happens to the outcomes at further points in time, eg one or two years after completing the program. Is the effect maintained (higher abstainers or less smoking if already a smoker) or is there a delay in age of smoking onset? Follow-up of this data set and patient cohort should occur at a later time point. There is literature that Brief Intervention and Motivational Interviewing have cumulative and sustained effects; though these are personal, rather than group, programs.

Response: We do fully agree with the reviewer that our results are limited by the time frame of the follow-up period and no conclusions about long term effects can be retrieved. Therefore, another follow-up survey 15 months after the end of the intervention (as indicated in the last paragraph of the discussion) is currently under way to clarify whether effects can be maintained.

The authors attempt to describe reasons and attributes, such as skills training, to explain why education does not fully translate to smoking abstinence or cessation. For existing smokers, the paper proposes that the education program did not change existing smoking practice. Neither did 'perceived norms of smoking' and 'self-efficacy to refuse cigarette offers'. Did the authors expect the magnitude of outcome of the results they found? Was this better or worse than expected? Was a pilot study conducted to see if "Eigenständig werden 5+6" works and for what populations? For example, would it be better to target Grade 6+7 or 7+8 students (as Grade 5+6 has low numbers of smokers)? Or is it 'too late' for education purposes of students in those grades?

Possibly the "Eigenständig werden 5+6" intervention program may operate better as a primary prevention program in schools? Does such an existing health education program exist in Year 5 & 6 curricula? Is "Eigenständig werden 5+6" a replacement candidate or a supplemental one? If it is a replacement, is it easier to implement, more effective or cheaper to operate?

Response: We were indeed unable to show any intervention effects on current smoking rates, but would like to stress that only a very small proportion of students indicated current smoking at baseline (about 1%), i.e. there was almost "no room for improvement". Furthermore, the content of "Eigenständig werden 5+6" does not address topics like smoking cessation but should rather be classified as a primary prevention program, i.e. we do not expect the intervention to primarily affect smoking students but rather to motivate smoke-free students to remain smoke-free. Therefore, the program was conceptualized for grade 5 and 6.

The expected magnitude of outcomes is clarified in the new paragraph on sample size determination (c. Response to Editor's comment no. 4).

We were not able to conduct an explicit pilot study on the entire intervention, but pretested single parts of the intervention and integrated the feedback of teachers which were not involved in the development of the intervention.

In Germany, there are no standard health education programs being implemented on a regular basis in the curricula of schools in general nor specifically in grade 5 and 6. Therefore, it is not aimed to replace any established and well evaluated program by "Eigenständig werden 5+6", but rather to fill a gap and to be able to offer an evaluated program to schools.

The two drawbacks I see with the paper are (i) the high attrition rate and (ii) small effect seen for the sample size.

Regarding attrition rate, from the 2437 students allocated to the intervention group, only 1179 were analysed (48%). The control group had 2335 students allocated and 1334 analysed (57%). Why did some schools agree then decline to participate? Were the included schools catering to a different socio-economic status?

Response: In most of the schools in which the headmasters agreed first and then the agreement was withdrawn, this revised decision was mainly driven by the teachers of the classes who did not comply with the headmaster's decision, especially in the intervention schools where the supplemental work load due to the study was much higher for teachers than in the control schools. All schools invited to participate in the study were public regular schools, i.e. covering a broad range of students with different intellectual capabilities and different socio-economic status. We did not invite specialized schools tailored to particular needs, e.g. severely handicapped students.

Under 'Results': 'Attrition Analysis', 27% of students had no data available. Why was this the case? No hints for selective attrition were found even though migration and socio-economic status were

recorded.

Response: The drop-out of 27% of students during the 26 months from baseline to follow-up (spanning over three school-years resp. involving two changes in grade from 5 to 6 and from 6 to 7) was caused by two reasons: entire classes dropping out of the study (30 classes in intervention group, 10 classes in control group; mostly due to a refusal by the teacher) which led to a substantial proportion of the drop-out and individual students being absent at the day of assessment or having left the class/school during in the meantime (and efforts of contacting them via the teacher on a different day or in their new class failed).

For comment on attrition, also cf. response to Editor's last comment.

180 students with 'data set inconsistencies' (76 intervention, 104 control) were excluded. Would this have significantly altered the final results? Sometimes a best/worse case scenario using included numbers and running the statistical analysis again will determine if results remain robust.

Response: We added a paragraph on sensitivity analyses dealing also with the 180 cases with inconsistent data to the results section (cf. response to last comment of Reviewer #3)

For (ii) small effect for sample size, the small rates of intervention and control students smoking at baseline (1%) and follow-up (5%) mean that the impact of the "Eigenständig warden 5+6" program is harder to quantify: for a small effect, smaller confidence intervals require a larger sample size. The intervention is diluted by the 'natural history' of smoking uptake (regression away from the mean). In the discussion, the authors acknowledge that "Finding no effect on current smoking might also be explained to some extent by the young age of the sample with only very few students smoking already on a regular basis". Again this proposes larger student numbers. Also the cognitive state of the pre-adolescent should be considered. The mean age is 10.37 years which is late-childhood to early adolescence in understanding. It may be that the students are yet to experience the direct pressures and influences of peers that usually comes with early-to-middle adolescence (12-15 years) when smoking experimentation and uptake occurs, so there may be less effect because the subject (and outcome) of interest is of low prevalence or incidence anyway.

Response: As far as the interplay of power, effect size and sample size is concerned, we hope that we could clarify our planning of the study by adding a paragraph on sample size determination (cf. response to Editor's comment no. 4). Furthermore, we hope that we could contribute to a less misleading presentation of the study sample's age in the revised version of the manuscript (cf. response to Editor's comment no. 2).

The authors should be applauded for recognising and discussing the potential for study bias. Good aspects include teachers not being involved in data assessment and the use of sealed envelopes. Response bias for drug use is acknowledged and reduced by using anonymous surveys and private lodgement system. Could there be objective measures of cigarette use to reduce response bias, eg exhaled air in a cotinine breathalyser, urinary cotinine levels?

Response: We would like to thank the reviewer for his kind evaluation of our study. For the discussion of the use of biochemical validation of smoking, please cf. the response to the respective Editor's comment.

The authors acknowledge that the "Eigenständig warden 5+6" intervention program is delivered in a subjective manner. It is also time consuming. I would like a cost-effectiveness statement to help determine if the program has good external validity (generalisation) and ability to be implemented to other populations, eg USA. Maybe there might be some electronic applications, eg online program?

Response: We fully agree with the reviewer that cost-effectiveness and external validity / potential or limitations for cross-cultural implementation are important quality criteria for prevention programs. But at the current time with the first results on efficacy gathered by the presented study, we do not think that we are able to state any valid conclusions on these topics. We added these issues to the "outlook" paragraph at the end of the Discussion section:

On the basis of findings for efficacy, effectiveness in relation to costs as well as generalizability to other populations should be investigated.

A statement regarding confounders may also be of benefit. For example, do cigarette packets in Germany have warning statements or graphic images of smoking related diseases? Are they expensive?

Response: Even though Germany is a federal state, the entire legislation concerning tobacco is regulated on a state-wide level, i.e. tobacco taxes/price for cigarettes, regulations for (currently only) text warnings on cigarette packets, advertising bans, ban of smoking in schools or laws concerning youth protection are the same in all federal states. Therefore, these factors do not vary in our sample and there would be no supplemental variance explanation by including these as confounding variables.

With baseline randomisation, it is hoped that students have similar characteristics, eg rate of mental illness, smoking parents or siblings, etc. Would a reduction in smoking lead to an increase in cannabis or alcohol?

Response: Since the prevalence of current or even regular smoking is low and the intervention is conceptualized mainly as a primary prevention program (cf. response to the respective comment of Reviewer #2 above), we do not have any explicit models concerning "symptom shift". We would rather assume that smoking is a precursor or even "gateway drug" for the use of illegal drugs or alcohol misuse – but these hypotheses could hardly be tested in the current sample with the low rates for smoking.

The authors should explicitly state that only tobacco smoking and not including cannabis smoking was recorded.

Response: Done.

If this paper is not published in BMJ, then it should be resubmitted to a Paediatric Medicine, Adolescent Medicine or Addiction Medicine journal.

Reviewer #3

Professor Robert M West

University of Leeds

UK

The subject matter is of considerable interest and I am keen to see these trial results published. There are some minor omissions that the authors can respond to easily and I have some further comments that might be of some help to the authors.

There are some major difficulties encountered, described and dealt with in this trial report. Specifically there are issues regarding selection of schools, selection of teachers, selection of parents (through consent), high drop out, and potential for self-completion biases.

The authors have chosen to dichotomize their lifetime and current smoking outcomes. This loses power for their analyses. They might mention results using more detailed outcomes and perhaps ordinal regression.

Response: For lifetime and current smoking, we reanalyzed the data using multilevel mixed-effects ordered logistic regression (STATA command meologit) with the origin outcomes (without dichotomization). The results were comparably with a significant intervention effect on lifetime smoking ($p=0.026$) and no effect on current smoking ($p=0.457$) Since these results could be aligned

very well with the results for the dichotomized outcomes and due to shortage of space, we did not add these findings to the Results section.

On Page 10 Line 21 was control meant rather than intervention?

Response: Thank you very much for your careful examination – this is indeed an error and we changed “intervention” to “control”.

There are no power calculations provided. The sample size is determined by the recruitment process. The authors however should indicate what power their analyses have.

Response: We are sorry that the information on power calculation with referring to another publication was obviously not sufficient. We hope that the extensions on how we determined sample size a priori (cf. response to Editor’s comment no. 4) contribute to set the record straight.

The authors have contributed an analysis of attrition which is to be encouraged with such a high rate. This is however restricted to some chi-sq tests and would be much improved with logistic regressions accounting for clustering.

Response: We reran the attrition analysis using multilevel mixed effect logistic regressions, revealing a reduced number of significant associations in the overall analyses (group condition, type of school and SES failed to reach significance now) and comparably to the first results no interaction effects. We changed the paragraphs “Analyses” and “Attrition analysis” accordingly.

Inconsistencies in data are treated as missing observations and are dropped. That is only a complete case analysis is offered. Even though there are only 180 such cases. Some sensitivity analysis might be offered - or if appropriate multiple imputation, although I would prefer to see sensitivity analyses. Those lost to follow up are excluded. Since the rate of attrition is so large, it does not appear to me that alternative analyses are appropriate but again some sensitivity analyses might be suggested.

Response: As suggested by the Reviewer, we conducted some sensitivity analyses to explore whether the results might be biased by exclusion of inconsistent cases or restricting the sample to complete cases.

We added a paragraph “Sensitivity analyses” at the end of the Results section and a comment on them in the Discussion section:

Sensitivity analyses

Since a substantial proportion of cases was excluded from the analysis sample due to inconsistent data (N=180) or as they were lost to follow-up (N=931), we conducted some sensitivity analyses to estimate the risk that the findings might be biased by these exclusions. First, we reran the analyses with inconsistent cases left in the dataset. This re-inclusion of inconsistent cases hardly changed the results for metric outcomes with significant effects for knowledge and attitudes and slightly changed results for smoking behavior with marginally significant associations for lifetime smoking ($p=0.086$) and incidence ($p=0.083$). To address the restriction of sample to complete cases, predictors for higher attrition were used as guide to create subsamples. As the attrition rate was highest in baseline current smokers and therefore this (small) subgroup of students smoking already very early might differ substantially from the majority of non-smoking students, we excluded baseline current smokers (N=25) completely. For this subsample, we found the same significant effects for lifetime smoking ($p=0.030$), knowledge ($p<0.001$) and attitudes ($p=0.002$) and no effects on current smoking, norms and self-efficacy. Further factors being associated with a higher risk of attrition (male gender, higher age, migration background) were explored by analyzing subsamples of male students, students aged ≥ 11 years at baseline and students with migration background. In these subsamples, incidence rates in control students exceeded those of intervention by 4 to 7 percent points (reaching significance for older students, $p=0.026$, marginal significance for students with migration background, $p=0.061$, and failing to reach significance for male students, $p=0.225$).

Furthermore, we did not find any hints for selective attrition which could restrict the validity of findings

and sensitivity analyses revealed very comparable patterns of results in subsamples with higher risk for attrition and smoking.

VERSION 2 – REVIEW

REVIEWER	Anthony Zehetner Department of Adolescent Medicine, The Children's Hospital at Westmead Sydney, New South Wales, Australia
REVIEW RETURNED	16-Dec-2013

GENERAL COMMENTS	Excellent revision
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