

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	The „Eigenständig werden“ prevention trial: a cluster randomised controlled study on a school-based life prevent substance use onset.
<b>AUTHORS</b>	<a href="#">Hansen, Julia</a> (contact); Hanewinkel, Reiner; Maruska, Karin; Isensee, Barbara

### VERSION 1 - REVIEW

<b>REVIEWER</b>	<b>Anthony Zehetner</b> The Children's Hospital at Westmead, Adolescent Medicine
<b>REVIEW RETURNED</b>	01/09/2011

<b>THE STUDY</b>	The authors have prepared an excellent trial protocol to ensure study integrity and internal validity and collected appropriate baseline data. The statistically significant higher baseline scores for self-efficacy and empathy in the control group will ensure that any gains made in the intervention group will be trustworthy! The population sample is appropriate, though unfortunately less higher achievement (gymnasium) schools were included beyond the authors' control.
<b>RESULTS &amp; CONCLUSIONS</b>	The authors have examined for and commented on sources (and potential) for bias. Any potential confounding factors beyond the education program(intervention) and the influence of peers (who also complete the program) should be commented upon when the results are available. Is there any (foreseen) cross contamination of groups (eg students moving between schools) during the trial? Can the drug experimentation phase of adolescence ever be eliminate? Does part completion of the program deliver part-success?  What is the external validity (generalisability) of this program to other areas/countries?
<b>REPORTING &amp; ETHICS</b>	
<b>GENERAL COMMENTS</b>	

<b>REVIEWER</b>	<b>Roger Thomas</b> University of Calgary
<b>REVIEW RETURNED</b>	08/09/2011

<b>THE STUDY</b>	No Consort statement - because only parts could be completed as final data have not been collected
<b>RESULTS &amp; CONCLUSIONS</b>	This article describes the study design and baseline data, and final data have not yet been collected, so replies to all questions above must be no, except credible for the design and baseline data
<b>REPORTING &amp; ETHICS</b>	Final data not yet collected
<b>GENERAL COMMENTS</b>	It is quite common for authors of a large RCT to have the design accepted as a separate article, so BMJ Open may wish to do this.

You have commendably started on a large and time consuming RCT!

Analysing many RCTs in detail for the Cochrane Collaboration systematic review, and perceiving how design and execution problems made them difficult to interpret, leads me to make the following observations. I would like your final study to be a great study with no (or minimal) design or execution problems, and thus one that is a key study in the field. I hope you accept my comments in this spirit.

1. The key current issue in RCTs to prevent substance use and smoking in adolescents is which interventions to choose. The interventions should build on the past most effective research and improve them by paying attention to which components were most effective and insights that the researchers present in their Discussion sections as to the next design steps. You as authors do not explain why you chose the particular interventions you did, and the combinations you chose. You reference articles but do not analyse how your study will advance the field. Your combination of interventions is standard in many RCTs. The statement: "interactive didactics, working in small groups, relaxation exercises, pantomime, identification figures, and active games are used." is all we are told. Most RCTs in the field describe enough detail that the intervention could be replicated. Also what activities will happen in the parent-teacher conferences according to the Protocol Manual?

2. The recruitment of the sample, and problems in recruitment are clearly described.

3. The method of randomisation was not described. The Cochrane Collaboration uses criteria for deciding whether a strong method was used, and it is not possible to say from this description.

4. Whether allocation was concealed from the researchers was not described. Again, whether this meets the Cochrane Collaboration criteria cannot be said.

5. Pretesting the questionnaire was an excellent step, but the focus group of 7 students is too small.

6. The overview of the variables (Table 1) is exemplary.

7. The table (Table 2) of scale psychometrics is exemplary and unusual in the literature and sets a standard.

8. Process evaluation. This is a key step, especially in any RCT in which psychological interventions are administered by teachers, is an independent process analysis by the researchers to ensure that 100% of the lessons are presented according to the Protocol Manual. If you do not have funds for a process analysis by the researchers, can you consider a random sample process analysis of e.g. 10% of the classes by the researchers?

9. Baseline comparability of the intervention and control groups. You have demonstrated comparability of the groups, but the difference of 36.8% Gymnasium students in the intervention and 43.7% in the control ( $p = .001$ ) needs to be carefully analysed.

	<p>10. Analysis. As this article describes your design, can you specify your multilevel modelling analysis plan in more detail?</p> <p>11. Do you plan an intention to treat analysis? You have carefully listed the withdrawals before and after randomisation, and the students with insufficient identifiers. This is a complex problem, and a real headache, but I would recommend you specify your intention to treat analysis now. Studies which offer both a per protocol and an intention to treat analysis are confusing.</p>
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<b>REVIEWER</b>	
<b>REVIEW RETURNED</b>	

<b>THE STUDY</b>	
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### VERSION 1 – AUTHOR RESPONSE

BMJ Open Manuscript ID 2011-000352

The „Eigenständig werden“ prevention trial: a cluster randomised controlled study on a school-based life skills programme to prevent substance use onset

Dear Mr Sands,  
 dear Dr. Zehetner,  
 dear Dr. Thomas,

thank you for your positive acknowledgments to the „Eigenständig werden“ prevention trial. Also your constructive critical remarks help us a lot and we hope we could ameliorate the submitted manuscript. We excerpted your remarks and commented on each of them (see below).

Review Zehetner

#### Remark 1

“The authors have prepared an excellent trial protocol to ensure study integrity and internal validity and collected appropriate baseline data. The statistically significant higher baseline scores for self-efficacy and empathy in the control group will ensure that any gains made in the intervention group will be trustworthy! The population sample is appropriate, though unfortunately less higher achievement (gymnasium) schools were included beyond the authors' control.”

Answer:

Thank you for this positive acknowledgment. We are indeed not happy about the different distribution concerning school type and condition. We will consider this circumstance in the analyses carefully.

#### Remark 2

“The authors have examined for and commented on sources (and potential) for bias. Any potential confounding factors beyond the education program(intervention) and the influence of peers (who also complete the program) should be commented upon when the results are available. Is there any (foreseen) cross contamination of groups (eg students moving between schools) during the trial? Can

the drug experimentation phase of adolescence ever be eliminated? Does part completion of the program deliver part-success? What is the external validity (generalisability) of this program to other areas/countries?"

Answer:

We have carefully examined for and commented on sources for bias. By planning this study thoroughly, we have integrated broad analyses with special regard to documentation process. So, part-completion will be considered as well in the analyses. Cross contamination (students moving between schools) cannot be completely ruled out, but it is unlikely. Schools that participate in the study are spread over four federal states of Germany and located in 30 different regions. The highest local participation rate can be found for a city with more than 500.000 residents and 78 schools altogether: five schools take part in the study. Three schools were allocated to intervention group, two schools to control condition – therefore it seems very unlikely, though not impossible, that a student from one of these three/two schools moves to one of the other two/three schools of the opposite condition. Because of the different location, cross contamination is not expected.

We assume that the life skills approach can be transferred to other western cultures since alcohol consumption, smoking cigarettes, or common manners resemble each other. Some aspects like laws on underage drinking, measures of tobacco control or substance use culture and climate differ from country to country, so the program is developed for German culture in this respect. Other aspects concerning life skills like communication skills are similar in western cultures. Therefore, we assume that the intervention program can be generalised in major aspects. Whether the intervention program can not be transferred to countries located e.g. in Asia or the Middle-East is rather questionable since e.g. communication skills and substance use differ tremendously from those in Western countries

Review Thomas

Remark 1

"The key current issue in RCTs to prevent substance use and smoking in adolescents is which interventions to choose. The interventions should build on the past most effective research and improve them by paying attention to which components were most effective and insights that the researchers present in their Discussion sections as to the next design steps. You as authors do not explain why you chose the particular interventions you did, and the combinations you chose. You reference articles but do not analyse how your study will advance the field. Your combination of interventions is standard in many RCTs. The statement: "interactive didactics, working in small groups, relaxation exercises, pantomime, identification figures, and active games are used." is all we are told. Most RCTs in the field describe enough detail that the intervention could be replicated. Also what activities will happen in the parent-teacher conferences according to the Protocol Manual?"

Answer:

We agree with the reviewer that we need to describe more details concerning the interventions content. We specified the interventions by adding a table (Table 1) to the manuscript (chapter intervention, page 5). This table gives an overview about each unit, its contents, information about parent leaflets and parent evenings. Parent leaflets were handed out after certain units. They inform the parents of the topic discussed, and give tips how to support their children at home.

The table provides more information that helps to replicate the intervention.

Table 1. Overview of interventions' contents.

Parent evening 1: Overall introduction to the programme

Unit Length/ Contents Parent leaflet (contents)

5.1 Klasse sein - Gemeinschaft werden (Class community) 45 min: introduction, familiarisation, relationships Introduction to the programme and overview

5.2 Klassenregeln

(Class rules) 90 min: development of class rules, incentives and sanctions Explanation for the need of rules

5.3 Miteinander sprechen (Communication) 90 min: communication skills and self-assertion --

5.4 Feedback

(Feedback) 90 min: how to provide and get feedback --

5.5 Klassenrat

(Class board) 45 min: introduction of a class board, social learning Introduction of a family board

5.6 Und was jetzt?

(How to solve problems) 90 min: learning of a useful strategy of solving problems (five-finger-strategy)

Introduction of the five-finger-strategy

5.7 Weniger ist mehr/Liebe Gewohnheiten (Less is more- beloved habits) 135 min: developing awareness of addiction, habits, rituals Explanation for the need of learning about habits, rituals, and addiction

Aktionsparcours Nikotin

(Workshop: Smoking cigarettes) 4-6 hours: nine different tasks with topics concerning smoking (e.g. risks, components, consequences of addiction, self-resistance, peer pressure) Information of rules that help to prevent smoking onset

Parent evening 2: Topic Smoking:

Leading Questions: why does the child learn about smoking and how can it be supported?

6.1 Gemeinsam lernen (Learning together) 90 min: learning to cooperate, working in a team --

6.2 Mit Gefühl

(Sentimentally) 90 min: cognition and expression of comfortable and unpleasant emotions like fear, anger, sadness, happiness Explanation for the need of expressing emotions

6.3 Stärken stärken

(Strengthening my strengths) 90 min: empathy and self-awareness, strengths and weaknesses How to support the child in recognising its strengths and weaknesses

6.4 Anders sein

(Being different) 45 min: learning to accept of being different --

6.5 Konflikte lösen

(Dealing with conflicts) 90 min: learning of a strategy to deal with conflicts in an adequate and peaceful manner How to support the child in dealing with conflicts

6.6. Stress und Entspannung

(Stress and relaxation) 90 min: realising the importance of relaxation, methods to handle stressful situations How to support the child in handling stressful situations

6.7 Mobbing

(Bullying) 90 min: learning of recognising and realising bullying, strategies to prevent it and to help if it occurs Realising bullying, support the child if it is bullied

Aktionsparcours Alkohol (Workshop: Alcohol) 4-6 hours: nine different tasks with topics concerning alcohol consumption (e.g. risks, consequences of addiction, self-resistance, peer pressure)

Information about rules and support

Parent evening 3: Topic Alcohol:

Leading Questions: why does the child learn about alcohol consumption and how can it be supported?

Remark 2:

“The recruitment of the sample, and problems in recruitment are clearly described.”

Answer:

Thank you for this positive remark.

Remark 3:

“The method of randomisation was not described. The Cochrane Collaboration uses criteria for deciding whether a strong method was used, and it is not possible to say from this description.”

Answer:

We are sorry for not having described the method of randomisation yet. We included this information (we used “coin toss” as method of randomisation after stratification).

The text now reads as follows:

Schools were stratified according to the following criteria: (1) study region, (2) type of school, (3) number of fifth grade classes per school. According to these strata, schools were randomly assigned to the two arms of the study with a 50 per cent chance of being allocated to either group by using coin toss method.

Remark 4:

“Whether allocation was concealed from the researchers was not described. Again, whether this meets the Cochrane Collaboration criteria cannot be said.”

Answer:

During randomisation process, the allocation was concealed, so researchers could not foresee assignment.

Remark 5:

Pretesting the questionnaire was an excellent step, but the focus group of 7 students is too small.

Answer:

We agree that a pre-test of a questionnaire in a group of seven students is too small. We would like to point to a potential misunderstanding that could have occurred: Before we started the development of the questionnaire to assess data, we interviewed a focus group of seven students to get information that we used in the process of questionnaire development (e.g. to use items that are easy to understand and examples that are linked to student’s environment).

The actual pre-test of the first version of the questionnaire took place in four classes with 109 students. We are sorry for this misunderstanding and have revised the introduction of this chapter to clarify this point.

The text now reads as follows:

Before starting to develop the questionnaire, a focus group of students (N=7) was interviewed to gain insight into student’s environment to detect, for example, typical situations that might be stressful or that cause problems for this age group. This information helped to develop a questionnaire that is appropriate for students in grades five and six.

Remark 6:

“The overview of the variables (Table 1) is exemplary.”

Answer:

Thank you for this acknowledgment. We included this overview to display all variable constructs with references for reconstruction.

Remark 7:

“The table (Table 2) of scale psychometrics is exemplary and unusual in the literature and sets a standard.”

Answer:

Again, thank you for this acknowledgment.

Remark 8:

“Process evaluation. This is a key step, especially in any RCT in which psychological interventions are administered by teachers, is an independent process analysis by the researchers to ensure that 100% of the lessons are presented according to the Protocol Manual. If you do not have funds for a process analysis by the researchers, can you consider a random sample process analysis of e.g. 10% of the classes by the researchers?”

Answer:

Thank you for this remark. Only the teachers will document the process and programme implementation in school routine. It would definitely be desirable to include individual rating (e.g. video analysis, supervision) for an analysis independent of those who deliver the intervention, but we do not have any funds to include an independent process evaluation in this trial.

Remark 9:

“Baseline comparability of the intervention and control groups. You have demonstrated comparability of the groups, but the difference of 36.8% Gymnasium students in the intervention and 43.7% in the control ( $p = .001$ ) needs to be carefully analysed.”

Answer:

We will carefully consider this different distribution in intervention and control group when analysing.

Remark 10:

“Analysis. As this article describes your design, can you specify your multilevel modelling analysis plan in more detail?”

Answer:

Multilevel modelling is needed since the responses of individuals within a cluster tend to be more similar than those of individuals of different clusters. 4-level models including levels of school, classes, individuals, and waves with random intercepts for school, classes and individuals will be conducted.

The text now reads as follows:

To test efficacy of the programme and to give consideration to cluster effects, i. e. higher similarity of responses within a cluster than between different clusters, multilevel modelling will be carried out. Therefore, 4-level models including levels of school, classes, individuals, and waves with random intercepts for school, classes and individuals will be conducted. Condition and covariates will be considered as fixed effects.

In order to test effective programme components mediation analysis will be performed. In a first step, it can be analysed if the lessons of prevention programme have affected what they

ought to affect: Students of the intervention group should have higher substance-specific competencies and also higher substance-unspecific skills. In a second step, it can be analysed if a given change in substance use (=dependent variable) in the intervention group is mediated by (1) the substance-specific skills, (2) the substance-unspecific skills, (3) by both, or (4) by neither nor. Attrition analyses will be conducted to compare students who remain in intervention with the students lost to follow up and test for differences between conditions.

Remark 11:

“Do you plan an intention to treat analysis? You have carefully listed the withdrawals before and after randomisation, and the students with insufficient identifiers. This is a complex problem, and a real headache, but I would recommend you specify your intention to treat analysis now. Studies which offer both a per protocol and an intention to treat analysis are confusing.”

Answer:

Thank you for this remark. We would like to specify this point as follows:  
Origin source is the baseline data since no data of individuals were gathered prior to this assessment. For schools that dropped out after allocation and prior to the baseline assessment, only universal data like region, and number of fifth grade classes is available. Therefore, this “originally intended to that group” will and can not be analysed.  
Moreover, we pursue two different strategies of analyses: first, we plan an intention-to-treat analysis with all data available at baseline and further waves and second, we will conduct complete case analysis.

We would like to revise the contribution section to clarify that KM qualifies as an author according to the ICMJE criteria:

KM developed and pretested the questionnaire, participated in acquisition of data and statistical analysis, and critically revised the manuscript.  
If her contribution was not conveyed during submitting process, we are sorry for that. For us, it is self-evident that all authors substantially contribute to the manuscript, read and revise it critically for important intellectual content, and of course, approve the final version.