

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Ongoing university studies and the risk of suicide. A register-based nationwide cohort study of 5 million young and middle-aged individuals in Sweden, 1993-2011
<b>AUTHORS</b>	Takami Lageborn, Christine; Ljung, Rickard; Vaez, Marjan; Dahlin, Marie

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Trine Madsen, PhD Post Doc position Danish Research Institute of Suicide Prevention, Copenhagen Mental Health Center, Denmark
<b>REVIEW RETURNED</b>	06-Oct-2016

<b>GENERAL COMMENTS</b>	<p>The authors address a very important question as we want to identify young people in distress and consequently at risk of suicide. The paper is easy understandable and well written, however I have some concerns about the design of the study.</p> <p>My major concern with the design of the study is mentioned by the authors in the introduction. You write and argue as the reason to examine suicide risk in university students:</p> <p>“The university period carries responsibilities and a pressure to succeed which may increase mental distress, depression or excess alcohol use (4-7). In addition, university students have been found to experience low life satisfaction and to be more depressed than a non-student population of a similar age”.</p> <p>First of all I think that statement is correct – young people under studies are under mental pressure, however I think it is a lack of this study that you only address suicide risk in university students, what about other types of students for instance those studying to achieve an upper secondary educational level? I would suspect that suicide risk may be even higher in this group and if we do this to identify young students at risk then maybe we should not only look at university students? Therefore, perhaps the research question could aim higher if it did not ‘only’ include students at a university?</p> <p>Secondly, which also address the above sentence from the introduction, which states that students are more vulnerable to psychological distress, I think that in the design of the study it is a major concern that the analyses is not adjusted for psychiatric diagnosis/or contacts (which I think you have information on in the Swedish registers). Adjusting for that may take away the risk effect associated with ‘ongoing studies’ versus attained education, ...especially if the student population is more depressed than the ones who attained high educational level?</p>
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	<p>Minor concerns: Some unclear sentences follow here: Methods section: “Person years for attained university studies were distributed as follows: 20-36% of less than 2 years of university studies and 60-77% of over 2 years of university studies. Having attained less than 2 years of university studies was more common between 1993 and 2000 than in later years. 1-3% of person years consisted of postgraduate studies.” This needs to be explained more in details. First of all why is it important to mention this? And secondly I don’t understand why it goes from for instance 20-36% (why is it a range?) – why is it not exactly for instance 20% or 36%? Also where do you allocate the 1-3% of post graduate studies? Are they allocated in the ongoing student group or in the attained university group?</p> <p>“Time at risk of having attained university education was chosen as reference. This sentence is not really clear to me – I assume it means that in the poison regression analysis in the independent variable having attained university education is the reference group – I think I would just state Having attained university education was chosen as reference.</p> <p>Period was divided into three categories (1993-1999, 2000-2005 and 2006-2011). For all subjects, person-time at risk was calculated and allocated to the corresponding exposure category.” Does exposure category in this sentence refer to the three different calendar periods or to the variable about what level of educational level is attained? I think it is the latter, but it follows the sentence on calendar periods, so it could be clearer.</p> <p>Result section: In the explanation of table 2a and 2b: “In the age group of 18-29 year olds a larger proportion of female suicides, 8.6-18%, than male suicides, 7.2-12.5%, were committed during ongoing university studies (Table 2a and 2b).” It took me a while to figure out how to find these percentages in the table to be honest because intuitively I kept looking at the first calendar year period only. That might just be me but maybe you can put a few extra words on this explanation?</p> <p>Last comment: some people react negatively to using the word ‘commit suicide’ – maybe consider using ‘died by suicide’ instead? To commit is often associated with ‘committing a crime’ – like a behavior associated with negativity.</p>
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<b>REVIEWER</b>	<p>Professor Dr Sherina Mohd Sidik 1. Department of Psychiatry, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, UPM Serdang, Selangor, Malaysia 2. Cancer Resource and Education Center (CaRE), Universiti Putra Malaysia, UPM Serdang, Selangor, Malaysia</p>
<b>REVIEW RETURNED</b>	07-Nov-2016

<b>GENERAL COMMENTS</b>	<p>In Table 2b: the age category is missing (25 – 29)</p> <p>In Table 3: “Unnatural death” is stated in the title but not shown in the table</p> <p>In Page 15 line 35: Is the value for suicide rate 10.9/10,000 correct? Or is it 10.9/100,000?</p> <p>In Page 17 lines 3 – 16: The discussion in the first paragraph is not convincing and can be rephrased.</p> <p>Some of the references can be updated.</p> <p>A flow diagram would be helpful to facilitate understanding of the methods and results sections (especially in methods of selection of participants, methods of follow-up and report of the number of participants in each stage of the study).</p>
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<b>REVIEWER</b>	Ashwin Rao University of Washington, Seattle, WA
<b>REVIEW RETURNED</b>	12-Nov-2016

<b>GENERAL COMMENTS</b>	<p>I have a difficult time understanding your definition of attainment, as you have described it. I worry about a number of confounders that could factor in. For example, circumstances that those who have attended part, but not all of university could affect their social circumstance causing confounding stressors. I would like to understand if you took into account any other potential models for classifying individuals based on education level.</p> <p>I had a difficult time reading the prose, due to a number of grammatical errors. I think that this must be addressed in a second draft. For example, page 5, line 45-46, you state the "Time at risk of having attained university education". I am not sure that I would use the word "Risk" for attaining education. The context of this word use is incorrect.</p> <p>I am also confused about how you specifically divided years reviewed, as this could very much affect risk calculations.</p> <p>I presume that Register and Registry are both the same</p> <p>I have a very difficult time understanding your interpretation of the data. Would it not be cleaner to compare the risk of education level per aged matched peer?</p> <p>I do not agree with including death of undertermined intent in your suicide pool, given the risk of biasing the numbers toward suicide, especially given your subgroup analysis. The paper would be strengthened by considering autopsy information for those cases in question, though this may be out of the scope of your research design.</p>
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**VERSION 1 – AUTHOR RESPONSE**

Reviewer 1 Trine Madsen, PhD  
Post Doc position, Danish Research Institute of Suicide Prevention, Copenhagen Mental Health

Center, Denmark

C: My major concern with the design of the study is mentioned by the authors in the introduction. You write and argue as the reason to examine suicide risk in university students:

“The university period carries responsibilities and a pressure to succeed which may increase mental distress, depression or excess alcohol use (4-7). In addition, university students have been found to experience low life satisfaction and to be more depressed than a non-student population of a similar age”.

First of all I think that statement is correct – young people under studies are under mental pressure, however I think it is a lack of this study that you only address suicide risk in university students, what about other types of students for instance those studying to achieve an upper secondary educational level? I would suspect that suicide risk may be even higher in this group and if we do this to identify young students at risk then maybe we should not only look at university students? Therefore, perhaps the research question could aim higher if it did not ‘only’ include students at a university?

R: You raise an interesting question. The group of people you mention, young adults who for different reasons may not have succeeded in gaining a degree from upper secondary school, and who study to achieve it as adults, may well be under significant pressure.

However, the scope of the present study was to investigate, precisely, the risk of suicide while studying at university and our data was collected for that purpose.

There is further, to our knowledge, no data with sufficient validity and coverage in Swedish national registers on ongoing studies at the upper secondary school level for adults, since this level is not as properly regulated as tertiary education.

C: Secondly, which also address the above sentence from the introduction, which states that students are more vulnerable to psychological distress, I think that in the design of the study it is a major concern that the analyses is not adjusted for psychiatric diagnosis/or contacts (which I think you have information on in the Swedish registers). Adjusting for that may take away the risk effect associated with ‘ongoing studies’ versus attained education, ...especially if the student population is more depressed than the ones who attained high educational level?

R: You are correct, of course, and we do address this question in the Discussion. However, for the present study, we did not wish to adjust for the effect of possible mediators, but rather describe the overall risk for those who attend tertiary education from a “naturalistic” perspective.

Different fields of higher education are presumably heterogeneous with regard to evocation of mental distress as well as the propensity to attract vulnerable individuals, and adjustment might lead to a false perception of having control over possible mediators. We think these inquiries require further research, but goes beyond the scope of the present study.

C: Minor concerns: Some unclear sentences follow here:

Methods section:

“Person years for attained university studies were distributed as follows: 20-36% of less than 2 years of university studies and 60-77% of over 2 years of university studies.

Having attained less than 2 years of university studies was more common between 1993 and 2000 than in later years. 1-3% of person years consisted of postgraduate studies.”

This needs to be explained more in details. First of all why is it important to mention this? And secondly I don't understand why it goes from for instance 20-36% (why is it a range?) – why is it not exactly for instance 20% or 36%?

Also where do you allocate the 1-3% of post graduate studies? Are they allocated in the ongoing student group or in the attained university group?

R: The ranges in the mentioned sentence refer to the different time periods. We have deleted the mentioned sentences in the manuscript; we agree that it may be more confusing than informative. The following sentence was included to stress the wide variation within the category Attained university education:

"The level of attained university education ranged from a minimum of one completed semester at university to finalised post-graduate education."

Post-graduate studies were thus allocated to Attained university education, also clarified under by the sentence following the description of the category Ongoing university studies: "Doctoral education was not included in this category."

C: "Time at risk of having attained university education was chosen as reference.

This sentence is not really clear to me – I assume it means that in the poison regression analysis in the independent variable having attained university education is the reference group – I think I would just state Having attained university education was chosen as reference.

R: We wanted to stress that the category is actually person-years, not individuals. We agree that the wording is not optimal and have revised and moved the sentence to Statistical analysis section. "Attained university education was chosen as reference."

C: Period was divided into three categories (1993-1999, 2000-2005 and 2006-2011). For all subjects, person-time at risk was calculated and allocated to the corresponding exposure category." Does exposure category in this sentence refer to the three different calendar periods or to the variable about what level of educational level is attained? I think it is the latter, but it follows the sentence on calendar periods, so it could be clearer.

R: We have rewritten the methods section to improve clarity and chosen to introduce the information about periods in the Statistical analysis section only.

C: Result section:

In the explanation of table 2a and 2b: "In the age group of 18-29 year olds a larger proportion of female suicides, 8.6-18%, than male suicides, 7.2-12.5%, were committed during ongoing university studies (Table 2a and 2b)."

It took me a while to figure out how to find these percentages in the table to be honest because intuitively I kept looking at the first calendar year period only. That might just be me but maybe you can put a few extra words on this explanation?

R: We included the phrase "over the three periods" in the text you quote, in order to guide the reader.

C: Last comment: some people react negatively to using the word 'commit suicide' – maybe consider using 'died by suicide' instead? To commit is often associated with 'committing a crime' – like a behaviour associated with negativity.

R: Thank you. We agree and have revised accordingly.

Reviewer: 2

Reviewer Name: Professor Dr Sherina Mohd Sidik Institution and Country: 1. Department of Psychiatry, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, UPM Serdang, Selangor, Malaysia, 2. Cancer Resource and Education Center (CaRE), Universiti Putra Malaysia, UPM Serdang, Selangor, Malaysia

C: In Table 2b: the age category is missing (25 – 29)

In Table 3: "Unnatural death" is stated in the title but not shown in the table

R: Thank you for pointing out these mistakes. They have been corrected.

C: In Page 15 line 35: Is the value for suicide rate 10.9/10,000 correct? Or is it 10.9/100,000?

R: It should be 10.9/100,000. Thank you again, it has been corrected in the ms.

C: In Page 17 lines 3 – 16: The discussion in the first paragraph is not convincing and can be rephrased

R: We have clarified the argument in the first paragraph.

C: Some of the references can be updated.

R: We have reduced the number of references, by removing two that were not quite up-to-date, and some that were not vital to the argument (listed below) and added two recent publications which are both very recently published and relevant (Farrell S, Kapur et al. *Crisis*. 2016 & Mortier P et al.. *J Affect Disord*. 2017). Reference number 23 (Hawton K et al. *Psychol Med*. 1995) is not of recent date, but we deem it central to the field and judge that it should be kept.

(The following references were removed from the manuscript of the first submission:

Farabaugh A, Bitran S, Nyer M et al. Depression and suicidal ideation in college students. *Psychopathology*. 2012;45(4):228-34.

Balint L, Osvath P, Rihmer Z, Dome P. Associations between marital and educational status and risk of completed suicide in Hungary. *Journal of Affective Disorders*. 2016;190:777-83.

Beautrais AL. Suicide and serious suicide attempts in youth: A multiple-group comparison study. *American Journal of Psychiatry*. 2003;160(6):1093-9.

De Grande H, Vandenheede H, Deboosere P. Educational Inequalities in the Transition to Adulthood in Belgium: The Impact of Intergenerational Mobility on Young-Adult Mortality in 2001-2009. *PLoS One*. 2015;10(12):e0142104.

Kaplan RM, Howard VJ, Safford MM et al. Educational attainment and longevity: results from the REGARDS U.S. national cohort study of blacks and whites. *Ann Epidemiol*. 2015;25(5):323-8.)

C: A flow diagram would be helpful to facilitate understanding of the methods and results sections (especially in methods of selection of participants, methods of follow-up and report of the number of participants in each stage of the study).

R: We realise that the design is complicated and that we have not described it with enough detail and clarity. All participants contribute with exposure time. We have added Figure 1 to the manuscript and also rewritten the methods section, which we hope will be helpful.

Reviewer: 3 Reviewer Name: Ashwin Rao

Institution and Country: University of Washington, Seattle, WA

C: I have a difficult time understanding your definition of attainment, as you have described it. I worry about a number of confounders that could factor in. For example, circumstances that those who have attended part, but not all of university could affect their social circumstance causing confounding stressors. I would like to understand if you took into account any other potential models for classifying individuals based on education level.

R: First of all, we realise that the design was not described clearly enough, and have rewritten the methods section and added Figure 1 to explain the exposure categories better. In the category of

attained university education, those you mention - who have attended part, but not all of university - are actually included.

There are of course many ways to go about and we chose this classification in order to be able to compare time when subjects are university students to time as non-student. For exposure time as non-student, we then wanted to take educational attainment into account, as argued in the introduction. (Please also see our response to your second last comment below)

There are, obviously, a range of possibly confounding or mediating factors, but we think this design has a major strength, as subjects actually may move between exposure categories and contribute with person time for several categories. Thus, the effects of individual-bound confounders are reduced. Please see our response to comment no. 2 of Reviewer 1.

C: I had a difficult time reading the prose, due to a number of grammatical errors. I think that this must be addressed in a second draft. For example, page 5, line 45-46, you state the "Time at risk of having attained university education". I am not sure that I would use the word "Risk" for attaining education. The context of this word use is incorrect.

R: We apologise for epidemiological jargon, which in this case certainly have rendered undesired effects. We have responded to a related comment of Reviewer 1 as follows:

We wanted to stress that the category is actually person years, not individuals. We agree that the wording is not optimal and have revised and moved the sentence to Statistical analysis section. "Attained university education was chosen as reference."

The manuscript has also been proof-read for the English.

C: I am also confused about how you specifically divided years reviewed, as this could very much affect risk calculations.

R: Person years during studies at university were divided with respect to the semesters of Swedish university (spring semester usually from third week of January to second week of June and autumn semester from first week of September to second week of January) and in order to ensure that e.g. the long summer breaks were covered (by spring semester). We think that it is important to identify time during summer breaks as "student time", assuming that someone who attend university should be perceived as a student also during holidays. This procedure does not affect calculations per se, since the time scale was full calendar years all along (5/12 for autumn semester and 7/12 for spring semester).

C: I presume that Register and Registry are both the same

R: Yes it is. Thank you, we have corrected accordingly.

C: I have a very difficult time understanding your interpretation of the data. WOULD it not be cleaner to compare the risk of education level per aged matched peer?

R: We agree the chosen design might seem complicated, but the use of person years instead of individuals ensure that each suicide (or death) has either occurred during university studies or under any of the other exposure conditions. For the design you suggest we would not be able to allocate the outcome to a specific exposure. Please also see our response to your first comment.

C: I do not agree with including death of undertermined intent in your suicide pool, given the risk of biasing the numbers toward suicide, especially given your subgroup analysis. The paper would be strengthened by considering autopsy information for those cases in question, though this may be out of the scope of your research design.

R: As stated in the manuscript, we performed a sensitivity analysis, excluding deaths of undetermined intent, and estimates did not change markedly. All deaths in Sweden due to suicide or undetermined intent are examined by forensic medicine.

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Sherina Mohd Sidik Universiti Putra Malaysia, MALAYSIA
<b>REVIEW RETURNED</b>	22-Dec-2016

<b>GENERAL COMMENTS</b>	All corrections have been done satisfactorily.
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