PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	From never to daily smoking in 30 months: The predictive value of tobacco and non-tobacco advertising exposure
AUTHORS	Morgenstern, Matthis (contact); Sargent, James; Isensee, Barbara; Hanewinkel, Reiner

VERSION 1 - REVIEW

REVIEWER	Victor C. Strasburger, M.D. Distinguished Professor of Pediatrics University of New Mexico School of Medicine Albuquerque, New Mexico USA No competing interests to report.
REVIEW RETURNED	

GENERAL COMMENTS	This is the newest in a series of studies by a very distinguished cross-national group of researchers. Having identified images of smoking in movies as one key factor in the onset of adolescent smoking, they now examine the possible impact of exposure to tobacco advertising in 1320 6th - 8th grade German students. It is admirable that they took a criticism of their previous research to heart and extended their period of longitudinal observation to 30 months. This research confirms the findings of many, many cross-sectional studies that tobacco advertising contributes significantly to the onset of smoking during adolescence. Different countries vary greatly in what restrictions they place on tobacco advertising. Readers may not be aware of the fact that in the U.S., tobacco is still the leading advertised drug -- as much as $13 billion a year has been spent on tobacco advertising in recent years, compared with $5 billion a year on alcohol and $4 billion a year on prescription drugs (Strasburger & Council on Communications and Media 2010; Pediatrics, 126, 791-799). One of the great untold public health stories of the last millennium was that the only reason cigarette advertising was banned from American TV was because the tobacco industry agreed to the ban and instead used the money to advertise and market in other venues (see Strasburger, Wilson, & Jordan, Children, Adolescents, and the Media, 3rd ed. Los Angeles, CA: SAGE, 2014). The authors correctly point out that they experienced a very large drop-out rate -- nearly 50%. However, as the authors point out, the characteristics of their drop-outs (younger, male, lower SES, poorer school performance, higher sensation-seeking, having 1 parent who smoked) would probably have made their findings even stronger had the drop-outs stayed in the study.

	The authors controlled for every known factor associated with adolescent smoking and yet still found a significant impact of exposure to tobacco advertising. Although it is probably impossible to sort out, I still wonder if the impact could not be motivational in nature -- new-onset smokers either respond to advertising more, notice it more, like it more, or remember it better. At any rate, this is fine research that contributes signficantly to the literature; and the authors deserve a lot of credit.

REVIEWER	Dr. Gera E. Nagelhout, researcher at Maastricht University (CAPHRI) and STIVORO, the Netherlands. Competing interests: none.
REVIEW RETURNED	09-Apr-2013

GENERAL COMMENTS	This study examines the impact of tobacco advertising on youth smoking initiation. It also tests the alternative hypothesis that the impact of exposure to tobacco advertising is simply a marker for adolescents who are more receptive or attentive towards marketing. A recent review mentioned a short follow-up and a broad outcome measure as limitations of earlier studies. This study has both a long follow-up period and a more specific outcome measure. I think this is a very interesting study with a strong design. It is an important paper that is very clearly and nicely written. I have only a few minor comments/suggestions: – Page 6, line 33 “Reasons for study... – ..after sixth grade”: I don't understand this sentence. I'm not sure whether that is due to my understanding of the English language or due to an unclear description. – Page 6, line 42: Is it problematic for the analyses that there are schools with only 3 respondents or classes with only 1 respondent? – Page 11, Table 1: Add information about the categorization of tobacco advertising exposure in three levels. – Page 12, line 35: 98% should be 96% (Table 2)? – Page 12, line 38-41: The lower range of the sum of contacts over all depicted tobacco advertisements than over all depicted non-tobacco advertisements is to be expected because of a lower number of tobacco advertisements than non-tobacco advertisements. Perhaps this could be mentioned. – Page 15, line 53: “Theses” should be “These”? – Page 17, line 18: “memorize” should be “remember”? – Page 17, line 33: add “the” before “WHO”?

REVIEWER	Dr. Ute Mons, M.A. Research Associate Division of Clinical Epidemiology and Aging Research German Cancer Research Center (DKFZ) Heidelberg, Germany I have no conflicts of interest.
REVIEW RETURNED	11-Apr-2013

THE STUDY	The authors should provide more detail with regards to what they mean with using „masked“ images of advertisements (p. 7/l. 37). According to the previous study, “masked” means that all brand-identifying content was digitally removed from the advertisements. This should be more clearly explained. The authors should also think about (and discuss, if necessary) whether the use of such “masked” advertisements instead of the original advertisements has any implications for the measure of advertising exposure used in the study.
RESULTS & CONCLUSIONS	The study encountered severe sample attrition. Although the attrition rate is about the usual size when compared to other longitudinal school-based studies with pupils of this age-group and a observation period of similar length, the loss of whole schools and classes to follow-up causes some concern, and the drop-out analysis clearly shows that lower risk-adolescents were more likely to remain in the study. Although the authors generally mention this as a source of bias, I would like to see a more concrete discussion of how this could have affected the results of the study. In general, I would prefer to see a more critical and precise discussion of the study findings with regards to limitations and potential bias rather than the mere and partly quite abstract listing of limitations (p. 16/l. 45 – p. 17/l. 26). For example, which unmeasured confounders might have distorted the findings? Likewise, what unmeasured memory effects might have played a role? In addition, I would also like to see the research findings critically discussed in the light of previous evidence, including the previous study of the authors. An alternative explanation for the associations found in this study merits attention and should thus be critically discussed: Since the exposure variable measures perceived exposure to advertisements rather than actual exposure, it might actually reflect increased general susceptibility to tobacco smoking which might precede smoking initiation. In other words, adolescents with low susceptibility to smoking might pay less attention to tobacco advertising than adolescents who are highly susceptible to smoking. This could lead to significant differences in perceived exposure to tobacco marketing, even if the actual exposure is the same. (In a country like Germany, where tobacco advertising is ubiquitous, large differences in actual exposure might actually be quite unlikely.) Although the authors account for several risk factors for smoking uptake (parental smoking, peer smoking, sensation seeking…) that might also be associated with susceptibility to smoking uptake, they cannot entirely reject this alternative explanation. It might be helpful to adjust for perceived susceptibility to smoking in sensitivity analyses (if such a variable is available in the study), but even then perceived susceptibility might not fully reflect true susceptibility since subconscious components would remain unmeasured. Although I generally support the authors’ call for stricter tobacco marketing policies, the authors should be more careful with the phrasing of some of their conclusions given the limitations of the study and the potential alternative explanation for the study findings. Statements implying causality like “advertising allowed under partial bans continues to drive adolescents to smoke” might be too far-reaching. Likewise, it would be more appropriate to state that “the study confirms a content-specific association of tobacco advertising with smoking uptake” instead of claiming a “content-specific effect of tobacco advertising”.

GENERAL COMMENTS	The study tests the specificity of the association of tobacco advertising with youth smoking initiation using a longitudinal observational study design in a school setting in Northern Germany. Given the inappropriateness of a randomized controlled trial-design, the observational design used in the study reflects the optimal choice. This present study extends a previous study of the same authors that used different outcomes and a shorter observation period. The paper is overall well-written, and specific strengths of the study include its long observational period, the adjustment for important potential confounders and the validity of the smoking outcomes. The study is of high relevance especially for countries with weak tobacco advertising policies such as Germany, where tobacco billboard advertising is ubiquitous. However, there are some critical limitations to the study as well as a potential alternative explanation for the findings, which I would like to see more specifically addressed and discussed.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1

Reviewer: Victor C. Strasburger, M.D.
Distinguished Professor of Pediatrics
University of New Mexico School of Medicine
Albuquerque, New Mexico USA

No competing interests to report.

This is the newest in a series of studies by a very distinguished cross-national group of researchers. Having identified images of smoking in movies as one key factor in the onset of adolescent smoking, they now examine the possible impact of exposure to tobacco advertising in 1320 6th - 8th grade German students.

It is admirable that they took a criticism of their previous research to heart and extended their period of longitudinal observation to 30 months.

This research confirms the findings of many, many cross-sectional studies that tobacco advertising contributes significantly to the onset of smoking during adolescence. Different countries vary greatly in what restrictions they place on tobacco advertising. Readers may not be aware of the fact that in the U.S., tobacco is still the leading advertised drug -- as much as $13 billion a year has been spent on tobacco advertising in recent years, compared with $5 billion a year on alcohol and $4 billion a year on prescription drugs (Strasburger & Council on Communications and Media 2010; Pediatrics, 126, 791-799). One of the great untold public health stories of the last millennium was that the only reason cigarette advertising was banned from American TV was because the tobacco industry agreed to the ban and instead used the money to advertise and market in other venues (see Strasburger, Wilson, & Jordan, Children, Adolescents, and the Media, 3rd ed. Los Angeles, CA: SAGE, 2014).

The authors correctly point out that they experienced a very large drop-out rate -- nearly 50%. However, as the authors point out, the characteristics of their drop-outs (younger, male, lower SES, poorer school performance, higher sensation-seeking, having 1 parent who smoked) would probably have made their findings even stronger had the drop-outs stayed in the study.

The authors controlled for every known factor associated with adolescent smoking and yet still found a significant impact of exposure to tobacco advertising. Although it is probably impossible to sort out, I

still wonder if the impact could not be motivational in nature -- new-onset smokers either respond to advertising more, notice it more, like it more, or remember it better.

Response: We thank this reviewer for his kind and positive evaluation of our work. We fully agree that these kinds of observational studies will never be able to completely rule out the possibility that there is some unmeasured difference in those being specifically attentive towards tobacco advertisings or motivated to process them. The most likely explanation for being attentive towards tobacco ads is own smoking or at least not being completely reluctant to smoke. This explanation could be ruled out at least with the present findings (see also comments to reviewer #3).

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Reviewer #2

Reviewer: Dr. Gera E. Nagelhout, researcher at Maastricht University (CAPHRI) and STIVORO, the Netherlands.
Competing interests: none.

This study examines the impact of tobacco advertising on youth smoking initiation. It also tests the alternative hypothesis that the impact of exposure to tobacco advertising is simply a marker for adolescents who are more receptive or attentive towards marketing. A recent review mentioned a short follow-up and a broad outcome measure as limitations of earlier studies. This study has both a long follow-up period and a more specific outcome measure. I think this is a very interesting study with a strong design. It is an important paper that is very clearly and nicely written.

I have only a few minor comments/suggestions:
– Page 6, line 33 “Reasons for study... – ..after sixth grade”: I don't understand this sentence. I'm not sure whether that is due to my understanding of the English language or due to an unclear description.

Response: Wording changed into “Reasons for study drop-out were loss of primary schools that end after sixth grade”

– Page 6, line 42: Is it problematic for the analyses that there are schools with only 3 respondents or classes with only 1 respondent?

Response: We repeated the analysis after exclusion of the school with n=3 and found the same results.

– Page 11, Table 1: Add information about the categorization of tobacco advertising exposure in three levels.

Response: We added range information for low, medium, and high tobacco and non-tobacco advertising exposure in Table 1.

– Page 12, line 35: 98% should be 96% (Table 2)?

Response: Text changed from 98% to 96%.

– Page 12, line 38-41: The lower range of the sum of contacts over all depicted tobacco advertisements than over all depicted non-tobacco advertisements is to be expected because of a lower number of tobacco advertisements than non-tobacco advertisements. Perhaps this could be mentioned.

Response: We added the phrase “also reflecting the lower number of tobacco ads (6 vs. 8)”.

– Page 15, line 53: “Theses” should be “These”?

Response: Changed.

– Page 17, line 18: “memorize” should be “remember”?

Response: Changed.

– Page 17, line 33: add “the” before “WHO”?

Response: Added.

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Reviewer #3

Reviewer: Dr. Ute Mons, M.A.
Research Associate

Division of Clinical Epidemiology and Aging Research
German Cancer Research Center (DKFZ)
Heidelberg, Germany

I have no conflicts of interest.

The authors should provide more detail with regards to what they mean with using „masked“ images of advertisements (p. 7/l. 37). According to the previous study, “masked” means that all brand-identifying content was digitally removed from the advertisements. This should be more clearly explained.

Response: Done.

The authors should also think about (and discuss, if necessary) whether the use of such “masked” advertisements instead of the original advertisements has any implications for the measure of advertising exposure used in the study.

Response: The masking might indeed lead to lower recognition rates. We do not consider this a severe bias, as we were mainly interested in inter-individual differences in exposure and not in the “true” individual level of exposure. But we have added this point in the limitations section.

The study encountered severe sample attrition. Although the attrition rate is about the usual size when compared to other longitudinal school-based studies with pupils of this age-group and a observation period of similar length, the loss of whole schools and classes to follow-up causes some concern, and the drop-out analysis clearly shows that lower risk-adolescents were more likely to remain in the study. Although the authors generally mention this as a source of bias, I would like to see a more concrete discussion of how this could have affected the results of the study.

Response: We further elaborate on potential attrition bias in the limitations section. The additional text reads: “Generally, one would assume that the associations get more conservative if higher risk adolescents are excluded, because this group has a higher likelihood of starting to smoke. However, in the context of media effects on smoking initiation there is also evidence that lower risk adolescents have a higher responsiveness towards media effects20;21, indicating that the present results might not be generalised to the whole population of adolescents.”

In general, I would prefer to see a more critical and precise discussion of the study findings with regards to limitations and potential bias rather than the mere and partly quite abstract listing of limitations (p. 16/l. 45 – p. 17/l. 26). For example, which unmeasured confounders might have distorted the findings? Likewise, what unmeasured memory effects might have played a role?

Response: We agree. However, we are not sure if we can really solve this issue, as it is in the nature of unmeasured confounding to be a bit vague and unknown. If we knew the unmeasured differences between individuals that could account for the different initiation rates, we would have assessed them. But we now further elaborate on unmeasured memory effects in the additional sensitivity analysis (see also comment below).

In addition, I would also like to see the research findings critically discussed in the light of previous evidence, including the previous study of the authors.

Response: Done.

An alternative explanation for the associations found in this study merits attention and should thus be critically discussed: Since the exposure variable measures perceived exposure to advertisements rather than actual exposure, it might actually reflect increased general susceptibility to tobacco smoking which might precede smoking initiation. In other words, adolescents with low susceptibility to smoking might pay less attention to tobacco advertising than adolescents who are highly susceptible to smoking. This could lead to significant differences in perceived exposure to tobacco marketing, even if the actual exposure is the same. (In a country like Germany, where tobacco advertising is ubiquitous, large differences in actual exposure might actually be quite unlikely.) Although the authors account for several risk factors for smoking uptake (parental smoking, peer smoking, sensation seeking…) that might also be associated with susceptibility to smoking uptake, they cannot entirely reject this alternative explanation. It might be helpful to adjust for perceived susceptibility to smoking in sensitivity analyses (if such a variable is available in the study), but even then perceived susceptibility might not fully reflect true susceptibility since subconscious components would remain unmeasured.

Response: We generally agree with this comment. There is an inherent hen-egg problem in this observational study. Even though there is this longitudinal design with never-smokers, excluding the explanation that smokers or experimenters pay more attention towards tobacco ads and are more

motivated or able to remember them, the issue remains that there might still be differences in the never-smokers with regard to their "smoking affinity". As the reviewer mentions we are not able to handle implicit/subconscious affinity, which might indeed exist. But we have assessed explicit smoking affinity in this study in terms of self-reported susceptibility. Therefore, we followed the reviewer's advice and now present an additional sensitivity analysis with an even more restricted sub-sample: Never smokers that reported at baseline that they will definitely never smoke in the future and will definitely not try cigarettes if one of their friends offered them one. We think that the result that the adjusted association is still significant in this sub-sample makes a good case against differential attention effects of susceptible never-smokers.

Although I generally support the authors' call for stricter tobacco marketing policies, the authors should be more careful with the phrasing of some of their conclusions given the limitations of the study and the potential alternative explanation for the study findings. Statements implying causality like "advertising allowed under partial bans continues to drive adolescents to smoke" might be too far-reaching. Likewise, it would be more appropriate to state that "the study confirms a content-specific association of tobacco advertising with smoking uptake" instead of claiming a "content-specific effect of tobacco advertising".

Response: We have toned these statements down and also changed the term "effect" into "association".

VERSION 2 – REVIEW

REVIEWER	Dr. Ute Mons Research Associate Division of Clinical Epidemiology and Aging Research, German Cancer Research Center (DKFZ) Heidelberg, Germany I have no conflicts of interest.
REVIEW RETURNED	29-Apr-2013

GENERAL COMMENTS	I appreciate how the authors have attentively responded to the concerns and comments of the reviewers. I feel that their revision has strengthened and clarified the paper. I only have a few further comments. In my previous review I had recommended to adjust for susceptibility towards smoking in sensitivity analyses. The authors however decided to present an analysis restricted to the sub-sample of never smokers with low susceptibility. If the authors confirm that adjusting for susceptibility towards smoking in their analysis of the full sample would not considerably change the results of their study, I'm fine with the sensitivity analyses that the authors conducted. However, since the findings of the sensitivity analyses make a good case against the potential alternative hypothesis of differential attention towards tobacco advertising and are thus of great importance for the paper, I would recommend that the authors also discuss the implications in the discussion section. I'd suggest changing the last sentence of the second paragraph on page 16 to "[…] one might expect a significant further decrease in youth smoking uptake in these countries after a total elimination of tobacco advertising."

	I'd suggest changing the second sentence of the third paragraph on page 15 to "These students reported at baseline that they would definitely never smoke in the future and would definitely not try cigarettes if a friend offered one (n = 803)."

VERSION 2 – AUTHOR RESPONSE

However, since the findings of the sensitivity analyses make a good case against the potential alternative hypothesis of differential attention towards tobacco advertising and are thus of great importance for the paper, I would recommend that the authors also discuss the implications in the discussion section.

Response: We agree and have added the following paragraph in the discussion section: "In addition, a sub-sample sensitivity analysis revealed that the association between tobacco advertising exposure and smoking uptake was also found in the group of unsusceptible never smokers. This is important as one could argue that never smokers with higher exposure were already more susceptible towards smoking at baseline and therefore more attentive towards the tobacco ads."

I'd suggest changing the last sentence of the second paragraph on page 16 to "[…] one might expect a significant further decrease in youth smoking uptake in these countries after a total elimination of tobacco advertising."

Response: Changed.

I'd suggest changing the second sentence of the third paragraph on page 15 to "These students reported at baseline that they would definitely never smoke in the future and would definitely not try cigarettes if a friend offered one (n = 803)."

Response: Changed.

'If the authors confirm that adjusting for susceptibility towards smoking in their analysis of the full sample would not considerably change the results of their study, I'm fine with the sensitivity analyses that the authors conducted. '

Response: We conducted the adjusted analysis as recommended by the reviewer and can confirm that the inclusion of susceptibility does not considerably change the results. In fact, our sensitivity analysis as presented in the manuscript is already the stricter test of this hypothesis.