Author’s response to reviews

Title: The effects of a multi-disciplinary, minimal smoking intervention among pregnant women and their partners: A real-life controlled intervention study

Authors:

Torbjorn Oien (torbjorn.oin@ntnu.no)
Ola Storro (ola.storro@ntnu.no)
Jon A Jenssen (jon-andreas.jenssen@trondheim.kommune.no)
Roar Johnsen (roar.johnsen@ntnu.no)

Version: 2 Date: 4 April 2008

Author's response to reviews: see over
Dear Editor Natalie Pafitis

Thank you for giving us the opportunity to resubmit a revised version of the manuscript.

We highly appreciated the thorough and inspiring review from the four reviewers. Their comments and proposals have led to comprehensive revisions in the manuscript. First, to avoid ambiguities on the included cohorts only longitudinally data are analysed in the revised version, i.e. women who were included six weeks postnatal are omitted. Second, we have analysed the material stratified according to smoking behaviour at start pregnancy, and at inclusion to study changes in behaviour both among smoking and non-smoking women. This has led to replacement of all tables and figures. Third, the abstract has been rewritten, and changes have been made in the background, methods, results and discussion section according to the suggestions from the reviewers. Finally, the conclusions are also reconsidered and rewritten.

Please, find attached a point-by-point response to each of the comments from the reviewers and with reference to the corresponding changes in the manuscript.

Yours sincerely

Torbjørn Øien
Reviewer's report #1

Title: The effects of a multi-disciplinary, minimal smoking intervention among pregnant women and their partners: A real-life controlled intervention study

Version: 1 Date: 19 December 2007
Reviewer: Agneta Hjalmarson

Reviewer's report:

The paper is evaluating intervention to help pregnant women stop smoking. It is an important subject because even small improvements in cessation rates could be of great importance.

However on the whole the paper is difficult to understand and it needs tighter editing.

Major Compulsory Revisions

Abstract

1 In the abstract the data collection is described as if all the women and their partners were followed-up at three points.

*The women are followed-up at two points, and this is stated clearer in the revised abstract.*

2 The aim of the study is described differently in the abstract and the end of the background. It needs to be consistent. Legislation and campaigns are not mentioned in the abstract.

*We have tried in the revised version to describe the aim of the study in the abstract and in the background section in a consistent way.*

3 70% respectively 61% had stopped smoking early in the pregnancy not before pregnancy according to table 4.

*That is correct, in the revised version the result is presented in the results section; subheading “Smoking behaviour during pregnancy” line 1-3 and in the new table 4.*
4. Only report figures from the result section. The odds ratio for smoking during pregnancy had not been reported earlier.

We agree, the odds ratio for smoking during pregnancy is removed from the abstract.

Page 3
5. The background is written as a single paragraph. Split it into sections with the same contents: smoking as a risk factor, prevalence of smoking in Norway, Pact study, effect of minimal smoking cessation interventions, aims of the study.

We agree, and have changed the background section as suggested by the referee.

Page 4
6. It is hard to get a grip on the study design. It would be helpful to have a chart of the study design showing, for control and intervention groups, when the collection of data started and ended, when and what measurements were made, and other relevant information.

We have added a flow chart (figure 1) to the paper which we hope would be helpful to describe the design and the populations.

7. I would suggest that subheadings be used in the method section like study design, subjects, measurements, interventions and statistical analysis.

We agree, and we have used subheadings in the methods section.

8. The objectives of the PACT study belong to the background. Emphasize what in the PACT project is relevant to this study.

The objectives of the PACT study are moved to the second last paragraph in the background section.

Page 5
9. State clearly how many women completed the questionnaires. How many refused or did not provide complete data? Why did only 1023 of the 1788 women respond to the questionnaire six weeks after delivery? A flow chart would be useful.

The flow chart is added (figure 1) and drop-outs are described in more details, result section, subheading "Background characteristics of the intervention and control cohorts", line 4-13.

Page 5 Intervention programme
10. Move the first 2 sentences of this paragraph to the background.

We agree, and the 2 first sentences are moved to the background section, fourth paragraph.
line 1-7.

Page 7
11. Norwegian legislation is not a result.

We agree, and Norwegian legislation is removed from the result section.

Page 8
12. Use statistical test to see if the control and intervention cohort differ. See further suggestion for table 1

Table 1 has been changed to Table 2 in the revised version. Table 2 is revised and now only comprises longitudinal data. Statistical tests have been used to compare the cohorts.

Page 8
13. Change the subtitle "Influence of legislation and public campaigns", as this implies an interpretation of the result, which belongs to the discussion. Use a more neutral subheading like Trends of smoking habits.

The subtitle has been changed to: “Smoking cessation in Trondheim, Bergen and Norway” last paragraph result section.

14. Collection of data should be presented in the method section.

The collection of Medical Birth Registry data are rephrased and moved to line 4-10 under the subheading "National data” in the methods section.

15. The number of participants in PACT was very small compared with the total number of pregnant women in Trondheim. Make a comment on this in the discussion.

A comment on the participation rate is given in the first paragraph under the subheading: “Participation and dropouts” in the discussion section.

Page 9
16. The data as presented is very dense and not easy to follow. It would be preferable to break it up, so that the same information is grouped in the same paragraph?
For example: Comparison of cessation rates in the intervention and control groups/Correlation between background factors and smoking behaviour/Partners smoking behaviour. Present data in a table for quitting and background factors. Give values for intervention and control cohorts separately.

We agree, the results are now grouped into paragraphs with the following subheadings: “Background characteristics of the intervention and control cohorts”
17. Differences between the intervention and control groups are presented as a probability in quitting, but in the abstract as a probability in being a smoker. Please be consistent.

In the revised version we are consistent and present smoking prevalence.

18. What does mean number of cigarettes smoked indoors refer to? Is it the number smoked by the mother or the father, or both together? Suggest that it be divided into two groups, by mother and by father.

“Mean numbers of cigarettes smoked indoors” refers to the total number of cigarettes smoked indoors by either parent. We had no available information that made it possible to divide it into maternal and paternal smoking. In the revised version the question used is cited in the methods section under the subheading "Outcome variables”, “PACT data” line 7.

Page 10 Discussion
19. In the discussion the strength and weaknesses of the study is discussed. However new valuable information about the measurements was also presented. The time aspect is important. Quiting rates at the first antenatal visit should not be labelled as quitting during pregnancy. With a chart showing the study design this confusions could be avoided.

We agree, hopefully Figure 1 clarifies this.

20. Both PACT periods had a much higher quit rate than the rest of the country. Discuss reasons to the differences. Usually only 30-40% of smokers quit during pregnancy, so the PACT figures are surprisingly high.

The quit rate in the PACT study (and in Trondheim) is very high among women, mostly as a consequence of spontaneous quitting at start or early in pregnancy. Reasons for this are discussed in the discussion section under the subheading “Smoking cessation in Trondheim compared to Bergen”

Page 12
21. The moralising sentence about obstinate women should be removed.

We surely agree and the sentence is removed.

22. Table 1. If all of this is PACT data why not call it PACT control cohort and
PACT intervention cohort?

In the new version this is Table 2, new title is “Characteristics of the intervention cohort (N=2051) and the control cohort (N=1788) at inclusion”

The data in the table is not consistent. Percentages have a confidence interval, the mean age has a range, and other variables have just a mean value. Make a table with in which you test control conditions with comparing intervention.

We agree, and statistical tests are used to compare the cohorts at inclusion.

Compare data during pregnancy for control and intervention conditions using statistical test. Do the same for data at 6 weeks after delivery for control and intervention period.

As the cross sectional data at 6 weeks postnatal are removed, a comparison at that time is omitted.

Include a stand.dev. for all mean values. The cigarette consumption data should have a number (n=).

We agree, mean values include a standard deviation in Table 2, and cigarette consumption data have got a number (n)

23. Table 2 describes milestones in Norwegian tobacco legislation. This is of little interest, as the paper does not measure the effect of the legislation. Instead this should be briefly mentioned in the background, with special reference to what happened during the study period.

We reluctantly agree, but the table is removed in the revised version, and the most important events are mentioned under the background section, second paragraph line 7-13.

24. Table 3 This table should be omitted. The same data is presented in table 4, though without data for Trondheim.

We agree, in the revised version results are presented in new tables.

25. Table 4
New title: The prevalence of pregnant smokers in PACT, Trondheim?, Bergen and Norway in 2000-2004
Add data from Trondheim
The percentage of smokers is calculated on the whole cohort, while quitting rates are counted on the number of smokers. This is confusing. Remove the quitters from the table and make another table for smokers called:

Quitting rates among pregnant smokers in PACT, Trondheim?, Bergen and Norway in 2000-2004

In the revised version results from the PACT study and MBR data are separated and we do not compare PACT data and MBR data in tables.

Minor essential revisions

26. Consider changing the title from ##The effect of a multi-disciplinary, minimal smoking intervention among pregnant women and their partners: a real-life controlled intervention study## to:
##The effect of a physician and nurse delivered minimal smoking cessation intervention for pregnant women and their partners: a controlled study.##

We have changed the title to:
”The impact of a minimal smoking cessation intervention for pregnant women and their partners on perinatal smoking behaviour in primary health care: a real-life controlled study “

27. Page 5
Explain NTNU and remove it from the first page

NTNU is explained in background section fourth paragraph line 5-6.

28. Page 6
The intervention program is described in figure 1, but to what extent was it used? Did it reach all smokers?
How many GPs, nurses and midwives attended the education in smoking cessation that they were offered?

Smoking intervention was a part of the new multi behavioural intervention programme in the PACT study. The smoking intervention programme was adapted from the USHPS guideline “Treating Tobacco Use and Dependence. Clinical Practice Guideline”. Under the methods section, subheading “Intervention programme” second paragraph line 1-6 attendance rate among GPs and midwifes are described.

We chose not to make any inquiries as to what extent the health care providers implemented the interventions or followed the guidelines. Neither did we ask the participants to what extent they had received the intervention program. We recognize that this could be very relevant information, and the primary reason for not doing this was that such inquiries could in itself be considered an intervention and therefore not applicable in an ordinary practice setting where the implementation strategies should be in accordance with the real-life demand. Secondly, the value of such inquiries is questionable, as health professional’s
reports on compliance with the study-protocol are prone to be biased. Consequently, possible changes in smoking behaviour due to the interventional program was based on parental reported changes in risk-factor behavior, assuming that the interventional program would be the most reasonable explanation of any significant change in risk-factor behaviour in the intervention cohort. Adherence to all components of the USPHS guideline has been generally low among health care providers as demonstrated in case control studies. This study attempts to test the applicability of these guidelines when implemented as part of the official perinatal program in primary care in a whole community. We have no reason to believe that implementation and fidelity of the intervention were low across clinics.

29. Why was smoking data not available for primary care health workers?

Data were available and this sentence is removed.

30. Page 11

Validation of data might be even more necessary today as it is stated that there is now a stigma attached to being a smoker.

When the study was designed we had reason to believe that Norwegian women reported smoking behaviour correctly (Nafstad, P., Kongerud, J., Botten, G., Urdal, P., Silsand, T., Pedersen, B. S., & Jaakkola, J. J. 1996, "Fetal exposure to tobacco smoke products: a comparison between self-reported maternal smoking and concentrations of cotinine and thiocyanate in cord serum", Acta Obstet.Gynecol.Scand., vol. 75, no. 10, pp. 902-907.) and later studies support these findings (McDonald, S. D., Perkins, S. L., & Walker, M. C. 2005, "Correlation between self-reported smoking status and serum cotinine during pregnancy", Addict.Behav., vol. 30, no. 4, pp. 853-857.) This is way we did not perform any biological validation tests.
Reviewer's report #2

**Title:** The effects of a multi-disciplinary, minimal smoking intervention among pregnant women and their partners: A real-life controlled intervention study

**Version:** 1  **Date:** 31 January 2008

**Reviewer:** Gerard J Van Breukelen

**Reviewer's report:**

Statistical review

Is needed and done by myself, see the list of comments on pages 2-5 of this report

p. 2,

Methods: state clearly whether treatment assignment was by randomization or based on pre-existing groups or cohorts.

*The abstract is rewritten, sequential birth cohorts were established, and in the new abstract assignment to the intervention programme is clarified, abstract, subheading “Methods” line 1-3.*

p. 2, Results:

For the baseline (i.e. at start pregnancy) smoking percentages are reported, whereas only an odds ratio is reported for the 2nd time point (during pregnancy) and no results at all are given for the 3rd time point (after delivery). This is confusing. Give percentages and odds ratio for each time point.

Partner smoking is reported unclearly too: is the OR of intervention relative to control, and if so, at what time point? Or is it at time point 2 or 3 relative to baseline and if so, for which cohort?

*We recognise the indistinctness of the reporting of results in the original abstract. Changing the presentation has hopefully clarified the uncertainties regarding comparisons between cohorts and at which points of time. Abstract,“Results section”.*
This conclusion is weaker than that on page 13. Further, conclusions about the effect of the intervention should be based on a comparison between the treated and control cohorts within this study. It is true that Table 3 suggests a somewhat higher quitting rate during pregnancy in Trondheim (and the PACT cohort) compared with Bergen or Norway. However, the difference in quitting rates between treated and control cohort in Table 4 is small relative to the difference of both with Norway and Bergen in Table 4. This suggests that some common influence in both PACT cohorts, e.g. selection bias, self-report bias, or a placebo effect, explains the higher quitting rates in Trondheim and the study population during pregnancy at least as much as the intervention does.

We agree, and in the revised version we do not compare PACT data with data from the Medical Birth Registry of Norway. These two datasets are treated separately; MBR data are used to illustrate what happened regarding smoking cessation during pregnancy in Trondheim compared to Bergen and Norway 1999-2004.

so there are two control cohorts: one of N=1788 pregnant women and one of N=2116 women after delivery. The relevance of the second cohort to the evaluation of the intervention is unclear to me. Unfortunately, both cohorts are pooled in Table 1, column Control cohort, questionnaire 6 wks after delivery (n=3139). In contrast, table 4 appears to include the first cohort only, which is the correct method.

There is only one control cohort, but smoking behaviour was assessed at different point of time. In the revised version only longitudinally data are presented. The participants who were included at six weeks postnatal (which could be misinterpreted as “the second control cohort”) are omitted in the revised paper and the tables are changed accordingly.

The new flow chart (figure 1) states the dropout rates, and in table 2 smoking prevalence among dropouts are presented. As expected the smoking prevalence among dropouts are higher in both cohorts than among those who completed the questionnaire six weeks postnatal. Other baseline comparisons between the cohorts regarding the dropouts are presented in the results section, subheading “Background characteristics of the intervention and control cohorts” line 4-13.

For the purpose of this study we analysed data in two stratified analysis according to smoking behaviour, firstly at start pregnancy, and then according to smoking behaviour at
inclusion. We compare smoking behaviour between the cohorts from start pregnancy until inclusion, and thereafter smoking behaviour during the intervention period. All tables are revised and replaced with new ones.

p. 6: it is unclear from this page how the primary outcome smoking was exactly defined (e.g. smoking at least one cigarette in the last month versus weekly smoking), and whether it was defined and recorded in exactly the same way in both cohorts and also in Norway, Bergen and Trondheim. If methods differ between cohorts, this may cause differences in smoking prevalences.

In the revised version the smoking variables and the primary outcome variable are described under methods, subheading “Outcome variables”. We hope this clarifies the definitions.

p. 7: Although the two study cohorts are fairly large, a formal sample size calculation is missing. Small effects on binary outcomes require very large samples. Adjustment for confounders, which is indispensable to any nonrandomized study, further increases the total sample size needed (see the Variance Inflation Factor VIF of a treatment indicator after including covariates). Therefore, a proper sample size calculation should be included, if necessary a post-hoc one using the VIF from the data, but using the smallest clinically relevant effect size rather than the present effect size estimate. Note that using the effect size estimate from the sample will give a power of < 50% for non-significant effects and power of > 50% for significant effects, by definition and is therefore useless.

A formal sample size calculation was done for the multiple health behaviour intervention with a 40% reduction in asthma as outcome variable. We then needed to include 3000 pregnant women in the intervention cohort, and this was the basis for this paper. No sample size estimation for each separate intervention has been done. Regarding post-hoc analyses we have consulted local biostatisticians who clearly advice us not to do post-hoc calculations as it is in most circumstances considered improper.

p. 7, l. 7-10:

Apparently, very simple statistical methods were used that ignore both the presence of potential confounders and the nesting of women within general practices, midwife practices or health centres (see p. 4). Ignoring the nesting can lead to underestimation of standard errors with a higher risk of type I errors and too small confidence intervals as a result. Ignoring confounders can seriously bias the effect estimates. Given the difference in smoking rates at the start of pregnancy mentioned on page 2 (l. -6, -7) which, incidentally, differ from those in Table 4, the results during and after pregnancy must be adjusted for smoking at the start of pregnancy and baseline variables on which the two cohorts differ. Inclusion of other baseline variables may further be useful to enhance power if these other variables are predictive of smoking during/after pregnancy. Also include type of centre (gp
versus midwife vs health centre) as covariate using dummy coding or dichotomisation.

During prenatal care in Norway women are free to visit both GPs and midwives. Most women visit both professional groups during pregnancy, and the smoking intervention programme was delivered by both groups of health workers. Due to the fact that nearly all women visit both GPs and midwives during pregnancy we do not find it necessary to control for nesting. We have adjusted for several confounders identified by a priori knowledge and tested possible confounders in several models as described in methods, subheading “Statistics”.

p. 7, l. 11-14:
-Why use UNIANOVA given that the outcome is binary?
-Specify the logistic regression models: what covariates were included in what form (e.g. quantitative or using dummy coding). Was a separate analysis done per time point? If so, why not use mixed logistic regression with the three repeated measures nested within women nested within practices or health centres? This would also solve or at least reduce the problem of bias due to dropout. -Was alfa = 5% one- or two-tailed? Please use two-tailed tests to be consistent with confidence intervals and to be able to detect possible adverse effects of treatment.

We have used ANOVA to adjust smoking prevalence recognising the limitations of the method, especially for small proportions. But for the purpose of this epidemiological study we find it sufficient. For most practical purposes the adjusted prevalence will differ very little from those generated from logistic regression and transformed to prevalence. The logistic regression models are described under the subheading “Statistics” method section.

In the revised paper we wanted to explore what happened from start pregnancy until inclusion, before any intervention was given, and what happened during the intervention period during pregnancy. To study this we chose to perform two analyses stratified according to smoking behaviour, described above, p. 4, l. 1 and l. 9 line 7-11. The results are presented in table 4 and table 5.

We surely agree in using two-tailed tests; alfa was 5% two-tailed.

p. 8, l. 5:
average nr of cigarettes a day: is this including or excluding non-smokers? If included, this measure is a mix-up of two outcomes: smoking yes/no plus amount of smoking among smokers. Further, it will probably be strongly skewed, rendering standard statistical methods dubious. Consider data transformation then (e.g. log or sqrt).

Non-smokers were not included in calculating average number of cigarettes a day. In the revised version this is stated under the method section, subsection “Outcome variables” line
p. 8, l. 9: "... augmented reduction .... in 2003" is not very clear from Table 3. Smoking prevalence appears to drop almost linearly over the years in Norway, Bergen and Trondheim, although a trace of stronger drop from 2003 to 2004 is visible. But is it also significant? Test by e.g. linear trend analysis with an extra dummy indicator for 2004. The latter should be significantly predictive. Given the aggregated nature of these data, with heterogeneity of variance between years (since variance = N*p*(1-p), where p = proportion smokers), use either logistic regression for aggregated data or weighted least squares linear regression (the prevalences are too high for Poisson regression).

*This results which are data from the Medical Birth Registry (MBR) presented in figure 2 as proportion of smoking cessation in Trondheim, Bergen and Norway in the revised version.*

p. 8, l. -9, -8: can you explain this higher smoking prevalence at the start of pregnancy in your PACT cohort compared with Trondheim as a whole? It might indicate selection bias at baseline, with regression to the mean causing an apparent beneficial treatment or PACT cohort effect at follow-ups. Table 3 shows that the baseline difference between PACT and Trondheim has disappeared during pregnancy, but such effect could occur due to regression to the mean (see e.g. Stigler, Statistical Methods in Medical Research, 1997, Van Breukelen, J Clin Epidemiology 2006, Senn, Statistics in Medicine, 2006).

*In this revised version we do not compare PACT data and data from MBR. The observed difference may be due both to report bias and selection of smokers at start pregnancy to the PACT study, as quitters perhaps were more eager to participate. We agree that a selection bias at start pregnancy could cause an apparent effect of the intervention. To study if there was a selection bias we conducted the additional study on 391 women, described under the method section, subheading “Additional study”. The results from the additional study are presented in table 1 and discussed under the subheading “Participation and dropouts” line 3-5.*

p. 9, l. 4: According to Table 4, the 40% must be 14% (i.e. the quitting rate 69.7% is 1.14 times as large as 61.3%, both % being based on the nrs of quitters within the baseline smokers subgroups of n= 475 and 462). Based on the total samples of 1729 and gives a quitting rate of 89.3% for controls and 92.8% for treated according to Table 4, and this is not a difference of 40% either.

*We fully agree, the proportions given were a slip of the pen. To be consistent, results are presented as smoking prevalence in the revised version. In the stratified analysis aORs are given for smoking in the intervention cohort compared to the control cohort.*
p. 9, l. 4: OR = 1.4 must be 1.45 according to Table 4 (i.e. 322/140 divided by 291/184), at least unadjusted for covariates.

We agree.

p. 9, l. 5 till bottom: these nr's are not verifiable without a clear report of the regression modeling procedure used (initial model, model reduction procedure, final model) and the final results (= predictors included, with their unit of measurement or coding, B, SE, p).

The report should also clearly state which N was included into that analysis for each cohort, which time points, and how dropouts were treated in the analysis.

In the revised version we used bivariate logistic regression. Smoking at six weeks was dependent variable, covariates was first tested in a univariate regression analyses, then aOR were computed with maternal age dichotomised comparing lower vs. upper quartile, parity, marital status and number of cigarettes smoked a day with cut off 10 cigarettes. This is described in Statistics, and the results are presented in a table (table 6) as suggested by the first reviewer

p. 10 l. 3-5:
But note that the difference between treated and control PACT cohorts is small relative to the difference between control PACT and Norway or Bergen, see comment on p. 3.

We have reconsidered the comparison between PACT data and MBR data, and we have concluded that a comparison between the two datasets are hampered with several uncertainties and therefore omitted from this paper.

p. 11, l. 1:
Selection bias may have occurred in your study just as well as in an RCT, but it cannot be judged from this report, since you neither say what % of the women invited to participate refused, nor report a baseline comparison between refusers and consenters (which should be done per cohort, i.e. treated and controls apart).

To investigate if there was a selection bias we conducted an additional study where 391 parents who consecutively visited maternal postnatal care were asked to complete a short and anonymous questionnaire on age, education, socioeconomics, allergic disease and smoking behaviour, regardless if they participated in the PACT-study or not. This study showed no selection bias, and this information is now included in the paper in the "methods", "results" (table 1) and "discussion" section. The additional study was anonymous and therefore we were not able to separate the cohorts.

p. 13, conclusion: is too strong, see comments on pages 3, 10, 11.
Due to comprehensive changes in the manuscript the conclusion is rephrased.

Table 1:
-Results of the baseline measurement (at start of pregnancy) are missing
-the two control groups of p 5 lines 1-2 should be kept apart rather than pooling them into one group of 3139 (= 1023 + 2116) women. Perhaps the group of 2116 women having delivered before baseline should be excluded from this Table altogether since their smoking results must have been retrospectively obtained, with potential bias. -nr of cigarettes a day = including or excluding non-smokers? Also, the n's mentioned here are very small and suggest errors of analysis or typing.

Baseline measurements are presented in table 2 in the revised version. Women included at 6 weeks were excluded from this paper and results are not presented. Number cigarettes a day was excluding non-smokers, and only presented in the result section in the new version. As stated also in the revised version very few parents smoked indoors 6 weeks postnatal, results section, subheading “Indoor smoking”. No error of analysis or of typing has been identified.

Table 3:
-How are the sample sizes and smoking rates per year per PACT cohort (control vs treated) related to the nrs on page 4-5 and in Table 4? In answering take care that the results must be consistent with each other.

<table>
<thead>
<tr>
<th>Intervention cohort</th>
<th>N= 2051, participants with smoking data n= 1940</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control cohort</td>
<td>N=1788, participants with smoking data n= 1729</td>
</tr>
</tbody>
</table>

Only participants with complete smoking data were included in the analysis, we agree that this was not clarified. This table is omitted in the revised paper and the MBR results are presented as quitting rates 1999-2004, figure 2.

Table 4:
-Sample sizes for both PACT cohorts at start of pregnancy differ from those stated on pages 4-5 (i.e. 1729 versus 1788 and 1940 versus 2051).
-Why are results from Trondheim missing in this Table? Table 3 includes Trondheim.

Participants with missing smoking data were not included in the analysis and in any table. Data from Trondheim should have been included in the table. This table is also omitted from the revised version.
Reviewer's report # 3
Title: The effects of a multi-disciplinary, minimal smoking intervention among pregnant women and their partners: A real-life controlled intervention study
Version: 1 Date: 4 February 2008
Reviewer: Pamela Pletsch

Reviewer's report:
Title: Suggest revising the title as there were many variables that were not controlled. For example, the information that the non-PACT women received and different measures for cessation for the PACT and comparison groups.

1. The questions are well defined. The researchers wanted to determine the efficacy of the PACT in increasing cessation during pregnancy. The background information is useful. It is helpful to know the legislative history and smoking trends in Norway.

2. The methods are appropriate. Using a baseline control and then introducing the intervention is reasonable given the scope of the study. It would have been stronger if the researchers had measured the degree to which the PACT intervention was implemented. We don’t know if the lack of significant findings for pregnant women was because the intervention was not efficacious or if the intervention was not delivered as planned. The researchers provided training to providers, but we don’t know to what degree the providers actually implemented the intervention. It would be helpful to include the author’s definition of “atopic” on p.4. It would also be helpful to include a brief discussion about how they avoided women being “counted” more than once in the comparisons of PACT women, Trondheim, Bergen, and the whole of Norway.

We chose not to make any inquiries as to what extent the health care providers implemented the interventions or followed the guidelines. Neither did we ask the participants to what extent they had received the intervention program. We recognize that this could be very relevant information, and the primary reason for not doing this was that such inquiries could in itself be considered an intervention and therefore not applicable in an ordinary practice setting where the implementation strategies should be in accordance with the real-life demand. Secondly, the value of such inquiries is questionable, as health professional’s reports on compliance with the study-protocol are prone to be biased. Consequently, possible changes in smoking behaviour due to the interventional program was based on parental reported changes in risk-factor behavior, assuming that the interventional program would be the most reasonable explanation of any significant change in risk-factor behaviour in the intervention cohort. Adherence to all components of the USPHS guideline has been
generally low among health care providers as demonstrated in case control studies. This study attempts to test the applicability of these guidelines when implemented as part of the official perinatal program in primary care in a whole community. We have no reason to believe that implementation and fidelity of the intervention were low across clinics. Some of this is included in the discussion section in the second paragraph.

The use of the terms atopy and allergy has been somewhat confusing. When the study was planned in 1999 the word atopy was used in the title. According to the article by S.G.O Johanson, J. O’B Hourihane2, J. Bousquet et. al; Position paper, A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force Allergy 2001: 56: 813–824, where atopy is defined as “a personal or familial tendency to produce IgE antibodies in response to low doses of allergens, usually proteins, and to develop typical symptoms such as asthma, rhinoconjunctivitis, or eczema/dermatitis.” In accordance with this nomenclature the term “allergy” should be reserved for clinical reactions in which an immunologic mechanism is proven or strongly implicated. Although allergies can be non-atopic, as is seen with helminths, insect sting, and drug reactions we find “allergy” to be the most accurate term to describe the condition we investigate in this study.

Atopic has been replaced with allergic, and the sentence is moved to the background section fourth paragraph.

We had no opportunity to exclude women from the PACT study from the population in Trondheim or Norway. All pregnant women in Trondheim, regardless of participation in the PACT study or not should receive the new smoking intervention programme. In the revised version we do not compare PACT data with data from Trondheim or Norway. But to illustrate what happened in Trondheim compared to Bergen and Norway after the study started, figure 2 is added.

3. Soundness of the data. It would have been stronger for smoking/cessation rates to be collected at the same time during pregnancy and postpartum for all comparison groups, but in this instance that was not possible. The researchers need to include p values when they report changes. For example, are the differences in rates in Table 3 (and pp 8 & 9) statistically significantly different?

We agree, data would have been stronger if they were collected at the same time, but for reasons discussed in the second paragraph in the discussion section this was not possible.

p-values have been added to all statistical comparisons
Reviewer's report #4
Title: The effects of a multi-disciplinary, minimal smoking intervention among pregnant women and their partners: A real-life controlled intervention study
Version: 1 Date: 11 February 2008
Reviewer: Wolfgang Hannöver

Reviewer's report:

Reviewer’s report on manuscript no. 2775 624561711231; Oien, Storro, Jenssen & Johnsen: The effects of a multi-disciplinary, minimal smoking intervention among pregnant women and their partners: A real-life controlled intervention study submitted for publication to BMC Public Health as a research article. The authors report a study from Trondheim, a specially selected region in Norway to lower smoking rates in pregnancy. The manuscript focuses on the effects of a training intervention following the “5 As” guidelines that was administered to three groups of health professionals: midwives, public health nurses, general practitioners (GP) called “health workers”. The intervention consisted of a three hours training and written material supplied four times. The authors investigate the effects of this intervention by comparing two cohorts: the first being assessed between September 2000 and June 2002 (serving as controls) and the second being assessed between June 2002 and December 2004. The investigation addressed all pregnant women who presented with a midwife or a GP for pregnancy care, or with a maternity health centre after delivery in control group. In the intervention group, all women were “invited” to the study without detailed information as to how the women’s data were assessed. The authors found a difference in smoking status between women in the control and intervention group at onset of pregnancy (61% vs. 70%) and different quit rates during pregnancy (OR, 1.4 [1.1 to 1.8]). They also found that smoking rates of partners differed between intervention and control groups at onset of pregnancy, during pregnancy and six weeks post-partum. The also found differing smoking rates compared with other regions in Norway. They conclude that “a minimal intervention delivered repeatedly throughout pregnancy by GPs and midwives [sic!] have [sic!] contributed to a decline in smoking in pregnancy, mostly as a local campaign”. The manuscript provides a deeper insight into the development of smoking habits in Pregnancy in Norway and presents large datasets, gathered under naturalistic circumstances. The second strength of the manuscript lies in the comparison between Trondheim as a specially selected region with regard to smoking cessation in pregnancy approaches and other regions in Norway of similar size and sociodemographic constitution. The manuscript offers vast information on smoking habits in pregnancy and will well contribute to knowledge in the field. However the manuscript in its present form does not speak in favour of it’s publication as a research article in BMC public
health due to conceptual and methodological issues that are addressed in detail hereafter:

1 The question posed by the authors is not well defined. The scope of the paper is to evaluate the effect of the introduction of the 5A into routine health care for pregnant women and new mothers in Trondheim. No clear outcome parameters have been defined, neither in terms of smoking behaviour, habits with regard to indoor-smoking and not with regard to actual counselling behaviour of the trained health workers. For criteria see for example the works of: Hughes et al. 2003 or West et al. 2005 Comparisons with other regions appear in the course of the manuscript.

In the revised version of the manuscript primary outcome variables are defined and placed together in the methods section subheading “Outcome variables”. Both smoking behaviour and indoor-smoking are described.

We chose not to make any inquiries as to what extent the health care providers implemented the interventions or followed the guidelines. Neither did we ask the participants to what extent they had received the intervention program. We recognize that this could be very relevant information, and the primary reason for not doing this was that such inquiries could in itself be considered an intervention and therefore not applicable in an ordinary practice setting where the implementation strategies should be in accordance with the real-life demand. Secondly, the value of such inquiries is questionable, as health professional’s reports on compliance with the study-protocol are prone to be biased. Consequently, possible changes in smoking behaviour due to the interventional program was based on parental reported changes in risk-factor behavior, assuming that the interventional program would be the most reasonable explanation of any significant change in risk-factor behaviour in the intervention cohort. Adherence to all components of the USPHS guideline has been generally low among health care providers as demonstrated in case control studies. This study attempts to test the applicability of these guidelines when implemented as part of the official perinatal program in primary care in a whole community. We have no reason to believe that implementation and fidelity of the intervention were low across clinics.

2 The methods have not been sufficiently described. We do not get a clear flow of participants through the study. No information is given about who addressed the participants in which context. Also we do not know how health workers where trained, and how training was evaluated by the trainees, or how the training was implemented into routine care.

We have added a flow chart (figure 1) to the paper which we hope would be helpful to describe the design and the populations. Hopefully recruitment of both GPs, midwives and participants are better described in the revised version, first paragraph methods section and under the subheading “Cohorts and subjects”.

We have added information of training of GPs and midwives and attendance to the training course in the methods section, subheading “Intervention programme” second paragraph. Regarding implementation of the intervention, see second paragraph response item # 1.
The data are not usable to answer the question of effectiveness of the training of health workers according to 5A. In order to estimate an effect, we would need to compare data against a control group. The group used here to contrast effects against is a natural cohort and differences between groups may as well be attributed to societal changes. Also the groups differ with regard to smoking behaviour before treatment was administered. Attrition rates are high in all groups and we do not receive any information on differential attribution at all.

The use of sequential birth cohorts rather than randomization was a deliberate choice in this study. Our mandate was to develop and implement an intervention in ordinary primary care to evaluate the effectiveness and the feasibility of the intervention as a possible recommended strategy to be adopted nationwide in Norway. To do this we had to develop a type 2 translation from evidence based data to clinical practice. This could for obvious reasons not be done as a randomized trial. Considerations regarding choice of design are discussed in the second and third paragraph in the discussion section.

In the revised version only longitudinally data were used. We performed two stratified analysis according to smoking behaviour, firstly we looked at the time period from start pregnancy until inclusion, and secondly we looked at the intervention period.

We agree that secular trends may have attributed to possible difference in smoking behaviour between the cohorts. Attrition rates are discussed in the discussion section under the subheading “Participation and dropouts” second paragraph. Differential attribution is mentioned in the new flow chart and in the results section, subheading “Background characteristics of the intervention and control cohorts” line 4-13

The manuscript addresses the question of effectiveness and thus should adhere to standards for the reporting of trials. Yet the authors adhere to the STROBE, which essentially reflects the scope and ends of the study much better. In essence the manuscript deals with observational data over time with changes in smoking policy and training of health workers at markedly distinct time points. From my point of view, this is the real strength of this paper that becomes overcast by the effort to report effectiveness data.

We agree, and as a consequence of the comprehensive changes in the revised version the question of effectiveness has been fade down.

The discussion is soundly formulated but for the data at hand lengthy. The conclusions again pertain to the results of an efficacy trial, which the study in essence is not, and thus do not correspond to the data presented.

The conclusions have been moderated according to the results presented.

Judging from the discussion, the authors are well aware of the shortcomings of their approach but do their best to uphold the notion to
report efficacy trial results.

*The discussion section has been rewritten in the revised manuscript and we have avoided describing differences between the cohorts as effects of the intervention.*

7 The research on the cited literature is flawless. The authors take great pains to give a thorough and sound overview over literature. A number of epidemiological studies on smoking in pregnancy are not referred to, e.g. the PRAMS studies, the seminal work by Fingerhut and colleagues or epidemiological data presented by Kahn and colleagues. Also more conceptual papers as e.g. Windsor et al. 1993 or Velicer et al. 1992, or McBride et al 2003 are not cited. Also studies with a similar outlook as from Valanis et al 2001, Tappin et al 2005, Lawrence et al 2003 are not cited. But, as has been said, the authors cover the field from their perspective (which is rooted in allergology as I take it) well.

*We fully agree that the literature cited by the reviewer is relevant regarding smoking in pregnancy. We made our choice from our perspective which is rooted in allergology. In the revised version John R. Hughes MD (2003) Motivating and Helping Smokers to Stop Smoking, Journal of General Internal Medicine 18 (12), 1053–1057 has been added as reference 14.*

8 Title and abstract do not correspond to the contents of the paper since they suggest results from an efficacy trial.

*In the revised version the abstract is rewritten.*

9 Not being of native English tongue it is hard for me to estimate the quality of the writing, but would suggest “as I subject myself to, when submitting manuscripts to international journals” to have the manuscript proof-read by a native speaker.

*The revised version has been proof-red by a native speaker.*

In conclusion I congratulate the authors to their study and would very much like to see their wealth of data published. If guidance is wanted, I’d suggest certain points for improvement:

1. Conceptualization of the manuscript as a “true observational study” as it essentially is.

*In the revised manuscript we have complied with this.*

2. Omit the tempting interpretation of results as effects of an intervention
In the revised version we avoid describing differences between the cohorts as effects of the intervention.

3. Describe clearly how health workers were trained; give insights into the training sessions and ramifications.

We have added information of training of GPs and midwives and attendance to the training course in the methods section, subheading “Intervention programme” second paragraph. Regarding implementation of the intervention, see second paragraph response item # 1.

4. Give an account on how the training was evaluated by the trainees.

We have no formal evaluation of the course. We did not receive any negative response on the training course from GPs or midwives.

5. Describe clearly ways of recruitment for health workers as well as for participants. Who approached them, why did they participate, what happened to those not in the study, clear-cut inclusion and exclusion criteria “if applicable” for both health workers and participants. I wish the authors my best in rewriting their manuscript and for a successful future submission.

Recruitment of both GPs, midwives and participants are described in the revised version, first paragraph methods section and under the subheading “Cohorts and subjects”. The comparison between women in Trondheim and Bergen (figure 2) comprise both participating and non-participating women in the PACT, and the quitting rates in Trondheim 2003 and 2004 give a clue to what happened to non-participants last paragraph results section.

Inclusion and exclusion criteria are described under methods, subheading “Cohorts and subjects” line 12-14. There were no inclusion or exclusion criteria for the health workers, all were invited and only three GPs actively refused to participate, line 3-7 first paragraph methods section.