Author's response to reviews

Title: Effect of an antepartum Pap smear on the coverage of a cervical cancer screening programme: a population-based prospective study

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Author’s response to reviews: see over
Dear Dr. Lolu da-Silva,

Thank you for the e-mail, dated August 23rd, 2006. As you have asked, we performed an extensive language revision of the manuscript MS: 3196964911162924 “Effect of an antepartum Pap smear on the coverage of a cervical cancer screening programme: a population-based prospective study” by Anne-Kjersti Daltveit Daltveit, Steinar O Thoresen and Jan F Nygard.

A senior epidemiologist with English as a native tongue has read the draft and given his comments. The manuscript has been changed accordingly. Thank you for suggesting the language revision.

Please, find the point-by-point description of the changes made after the language revision.

Sincerely yours,

Mari Nygård, for the authors

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Less than 30% Almost one-third of the Norwegian women aged 25-69 years of age do not invited to have a Pap smear do not attend during the recommended three years period in spite of invitation, and therefore constituting thus constitute a population of with high-risk for of cervical cancer (CC). Non-attendance to CC screening has been associated with time-consuming or economical barriers.

….same decade of in women life aged 25 to 35 years of age, the antepartum antepartum care presents an opportunity to offer a Pap smear in order to increase thereby increasing the …

…of the antepartum Pap smear toon the …

…estimate the relative probabilities for of having a Pap …

….non-pregnant women, respectively.

… smear, out of with the …

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… compared to 28.7% of Reference cohort (p<0.0001) the non-pregnant women, OR=2.1 (95% CI 1.9 to 2.4). As an indication for of “over-screening”, 5397 pregnant women
(57.8%) with a smear shortly before the start of follow-up also had a new Pap smear, compared to 83 023 (32.3%) in the Reference cohort. The contribution of the intervention to “over-screening” exists but its effect is modest.

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... and it has been reported that both the organised and opportunistic Pap smear taking... have has... Yet, more than 50% of the CC cases are diagnosed however among the 29% remaining group of the female population, who are not participating at the programme, constituting a population of high-risk for cervical cancer. Unfortunately, not all women attend to screening following the invitation and; The peak age of incidence... pregnancies within the same decade of women’s life: age range 25–35 years of age... might not go... routine health check-ups in resulting with increased, and a means to increase coverage of the programme. On the contrary, the screening of all the pregnant women... Screening of this population can however cause so called “over-screening” as given many of pregnant... To learn about Understanding the potential...

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makers to understand the attitude recognise conflicting attitudes towards screening and to evaluate the effect of routine antepartum Pap smear: as a routine activity. The objective of the current study was to... the overall coverage...

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...the pregnancy duration of the pregnancy were excluded (N=39 707). The final size of the study population was consisted of 2 175 762 females, and the personal identification number (PIN), an unique 11 digit code containing the date of birth and in combination of five numbers uniquely identifying every resident in Norway, was identified for each subject the subjects...

Briefly, the heart of the Screening programme in Norway is built around the Cytology... is mandatory....... irrespectively of age of the woman, the nature of the health service (private/public-funded health service)...

...smear in during a period... in three years the period are was identified on a monthly basis and they receive an invitation letter received personal invitations to participate at the screening.

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...than one offspring per birth (1904 twins, 58 triples and 2 women had 4 offspring) we used information about the one who was first born first.
... as the beginning of the antepartum ...

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Women with pregnancy outcomes of <400 gram were excluded from the study. We discriminate three-categorised the following, three mutually ...

\( C_{preg} \): subjects giving birth during the period ±3 month from the date 31.12.1996. \( T_0 \) is the date remarkingdenoting the start ...

\( C_{ref} \): subjects who did not neither gave birth nor were pregnant during this calendar period respective to the follow-up period of the pregnant women i.e. approx. e.g. from 01.01.1996 to 31.12.1997.

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... time since mailing the invitation was mailed in relation to the women in respect \( T_0 \), i.e. 24 to beginning 2 months prior to \( T_0 \), one month prior to 3 months after the \( T_0 \), more than three months after the \( T_0 \). ... the study, i.e. \( T_{ref} \) for Reference \( C_{ref} \) and Pregnant women subcohorts \( C_{preg} \). Odds ratios (OR) with 95% Confidence Interval (95% CI) were ...

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... were classified into assigned to the Pregnant women \( C_{preg} \), 2 060 118 into the Reference \( C_{ref} \) and 91 347 into the Mixed mixed cohort. Altogether 44% of the Reference cohort \( C_{ref} \) ... the Pregnant women cohort \( C_{preg} \), reflecting the much larger wider age span in the Reference cohort \( C_{ref} \) ... Pregnant women cohort \( C_{preg} \) ... compared to than the Reference cohort \( C_{ref} \).

More than 50% of By the end of the Pregnant women had Pap smears within a period follow-up of 5 month since \( T_0 \), compared to approximately 20% among the Reference cohort. By the end of a one year, 31.6% of the Reference cohort \( C_{ref} \) had a smear compared to 67.8% of Pregnant women cohort \( C_{preg} \).

... who were ... Altogether 80% of the Pregnant women \( C_{preg} \) ... 46% of the Reference ... e. Reference cohort women \( C_{ref} \).... ... before and after \( T_0 \), i.e. within 0-1 year and with Pap smear within one year were ... Among pregnant women \( C_{preg} \) ... 32.3% of the Reference cohort. Expressed in the \( C_{ref} \) terms, ... the Pregnant women \( C_{preg} \) and the Reference cohort \( C_{ref} \) ... close to the \( T_0 \), defined as the 4 months time period, from one month prior to \( T_0 \) to three months after \( T_0 \), altogether 74.6% of Pregnant women cohort \( C_{preg} \) had a Pap smear in during one year of follow-up, compared to only 37% of Reference cohort. When letter...
was mailed 24-2 months prior to \( T_0 \), 67% of Pregnant women cohort had a smear compared to 25% of Reference cohort, the \( C_{\text{ref}} \).

... to Reference cohort, the non-pregnant women, crude ...

While limiting the estimate was limited to Pregnant women \( C_{\text{preg}} \), ... estimated for the Reference cohort \( C_{\text{ref}} \) only (not in tables).

... of \( T_0 \), OR=2.1 (95% CI 1.9 to 2.4) compared to Reference cohort, the non-pregnant women.

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... with 69% of the pregnant women having had an a Pap smear during one year of follow-up. Most of the Pap smears from pregnant women were taken during the antepartum period, within 4 months from the start of the pregnancy, and therefore they will be further referred as antepartum Pap smears.

... irrespectively of their age or screening history of... In the Pap smear. For \( C_{\text{ref}} \) the Reference cohort, Pap smear-timing of the Pap smear from start of the follow-up shows linear increase, a smear taking increased linearly, a pattern which is expected for the screening-screened population in Norwegian Norway given there exists a co-ordinated screening programme context, indicating, and one that indicates the appropriate selection of Reference cohort. Most of the Pap smears from pregnant women were taken during antepartum period, within 4 month since start of the pregnancy, therefore will referred further as antepartum Pap smear \( C_{\text{preg}} \).

... the Reference cohort, non-pregnant women

... partially be explained... Reference cohort \( C_{\text{ref}} \) ... be have been ...

... account while by estimating the risk for a smear... comparatively for women without the smear in three years period and for women with last smear \( > 3 \) years and 0-12 months who had smear shortly prior to \( T_0 \), the start of the study.

... realise observe......

have had last Pap smear taken shortly before \( T_0 \) were screened lately, OR=0.76 (95% CI 0.75 to 0.77).

... were more likely to continue this such a pattern, whereas women who have had a smear seldom taken rarely or never, were less likely to have a smear in the near future. One can imagine postulate that in the population there is a dynamical balance between these two groups, and one of the most important duties obligations of a organized CC screening programme is to minimise the proportion of women without a smear: if and as a consequence, this risk estimate should eventually increase. To illustrate this, within the screening programme only women without a smear in \( C_{\text{preg}} \), women who had a last Pap smear more than three years are invited, this estimate (OR) would eventually increase. To illustrate this dynamics, pregnant women who had last Pap smear more than three years prior to the start of the study, were 2.6 times more likely to have a smear in one year compared to women with a smear shortly before start of the study. Comparative The comparative figure for the Reference cohort, non-pregnant women was 0.73. This indicates together with the fact that pregnant women showed a higher probability of a favourable response to smear taking by invitation letter than non-pregnant women OR=2.12 (95% CI 1.89 to 2.38) it implies that Pap smear in pregnancy increasing increases the coverage of the programme.
Yet, 24% of pregnant women without a smear more than 3 years had no smear in follow-up. Only these women belonging to the screening age have received an invitation letter Elucidating as to screening from the Norwegian Cancer Registry. 75% of the Pregnant women had a smear within one year of the letter, compared to the 37% why almost two-thirds of the Reference cohort, when non-pregnant women aged 15–44 years with an invitation letter did not have Pap smear, and why there was mailed close to start of the follow-up. These observed differences indicates that pregnant women have higher probability to respond with smear to invitation letter than non-pregnant women OR=2.12 (95% CI 1.89 to 2.38) and, that antepartum screening improves coverage of the programme.

Why as much as 63% of the non-pregnant women in 15–44 years of age with an invitation letter did not have Pap smear, and why is there more than a three times higher attendance to screening among Pregnant pregnant women compared to non-pregnant women compared to Reference cohort? This might be explained by the is important. Possibly an explanation lies in the relatively ….. take care of tend to, or all carry out a combination of these duties. The need for a regular check up for precursors of cervical cancer could be given less priority due to busy life in such demanding settings.

… the proportion exhibiting … as and some of them this proportion could probably be explained by the presence…. Altogether 32% of the women were pregnant before the start of screening age: i.e. aged <25 years of age and should not be yet screened because of due to young age. Women inaged 15 to 19 years of age had Pap smears more seldom compared to than women in aged 25–29 years, OR=0.53 (95% CI 0.52 to 0.54). However, the probability for Pap of a smear was as high as 66.1% for pregnant women compared to 19.3% in Reference cohort for non-pregnant women indicating that antepartum Pap contributed to increased screening among young women. Expressed in absolute numbers, 1129 pregnant women inaged 15 to 19 years of age had a smear during the one-year period. Even, if all pregnant women in this young age group would have had a smear, the consequent number would have been 1706, which is a considerably lower, compared to. figure relative to the 25 630 Reference cohort women with a smear in the Cref. It is clear that other factors than pregnancy seems to be also relevant while trying to explain Pap smear in explaining the Pap smear-taking activity in among young women. It cannot be forgotten, should be remembered that…

… would not be unnecessary … contribution to so called “over-screening” or screening too often. As much as.. Approximately 58% of the Pregnant womenCpreg had …

… before antepartum period (last Pap smear was taken 0–12 months since pregnancy started) and after the start of the study compared to 32% among in the Reference cohortCref, emphasizing the fact that pregnant women taking a an antepartum Pap cannot be solely responsible the reason for this the frequent screening observed.

…. … as the The 32% among the Reference cohortCref consists of as much as 83 023 women compared to 5397 Pregnant womenCpreg (58%), underlines underlining that the antepartum Pap does not…

… Pap smears taken shortly before the start of the follow-up was were abnormal, and per definition, should have been as defined, that they should be followed up
shortly\textit{soon after} with \textit{a} Pap smear. Nor did we consider that \textit{after normal smear a-the onset of} clinical symptom(s) occurred, leading to \textit{the new} Pap smear.

These are relevant concerns \textit{that ... as, Here} we were interested \textit{to assessin assessing} the effect of pregnancy \textit{to the on} coverage only. However, there \textit{is are no...}

... \textit{Pregnant and Reference cohort-the pregnant and non-pregnant women are even smaller to likely to be only weakly affect the estimates for coverage. YetHowever, in order to recommend Pap smear for all pregnant women unless she has had Pap without a smear shortly i.e. 0-1 one year prior to the visit, the information on the antepartum Pap accuracy of the antepartum Pap to diagnose the underlying pre-invasive...}

The conclusions on \textit{Conclusions regarding the} necessity of routine Pap smear(s) during pregnancy are often missing or, sometimes \textit{contradictive, and contradictory}, reflecting \textit{often that information on availability or history about cervical cancer screening is often missing}. \textit{The current This registry linkage study has been conducted to estimate the effect of Pap smear during pregnancy to on the coverage only, and our study suggests that providing the Pap smear the provision of Pap smears to all pregnant women will increases the coverage of the programme whereas, The contribution to of such an action on over-screening and screening among young women is likely to be modest.}

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