Invited Commentary: Reporting Bias in Case-Control Studies on Induced Abortion and Breast Cancer

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Despite the widely held concern that reporting bias may distort the relation between a history of induced abortion and risk of breast cancer in interview-based case-control studies, direct evidence is scarce (1–3). More insight into this matter is essential for weighing the results of the many case-control studies (n = 26 (4–7)), all based on interviews or questionnaires, and the few follow-up studies (n = 3 (8–10)) that examined breast cancer risk following induced abortion. Thus, the present attempt of Tang et al. (11) to quantify reporting bias in a sample of participants of two such case-control studies is of great interest.

It is known that induced abortions are markedly underreported in the general population, most probably because of the sensitive nature of the procedure (12, 13). The question now is whether women with breast cancer might be more willing to report an abortion history than controls, for instance, because they are more motivated for a study directed at understanding their illness. Less underreporting by cases than by controls would spuriously increase the odds ratios in interview-based case-control studies.

So far, most information on reporting bias has been based on indirect evidence. Newcombe et al. (14) found a more strongly increased risk of breast cancer for abortions that took place before the date of legalization rather than after that date. Palmer et al. (7) reported a higher odds ratio for women who were interviewed during an earlier time period and thus were more likely to have had their abortions before or shortly after abortion became legal. However, Daling et al. (5) did not find effect modification by legalization date. Furthermore, the legalization date might be associated with true effect modifiers of the association between induced abortion and breast cancer risk, such as age at the induced abortion, length of gestation, or recency of the abortion. Religion has been suggested to affect the magnitude of reporting bias in one study (15) but not in two other studies (5, 7). In two case-control studies, one on invasive cervical cancer and the other on ovarian cancer, no associations with pregnancy termination were found (odds ratio (OR) = 1.0 and OR = 1.2, respectively (5)). These findings are an appealing argument against reporting bias, but they still are not conclusive. Risk factors for breast, ovarian, and cervical cancer are not the same, and thus the various case groups reflect various subgroups in the population that—without a cancer diagnosis—might not be equally prone to underreport an abortion history. In conclusion, the indirect evidence for or against reporting bias has only been suggestive.

Tang et al. (11) now present one of the first methodological studies in this field. They investigated the magnitude of reporting bias by comparing the history of induced abortions provided during an interview with the information in birth records. The results appear reassuring. Among women with a prior induced abortion according to the records, 14 percent of the cases and 15 percent of the controls did not report the abortion to the interviewer. Thus, the authors conclude that their findings do not support the hypothesis that a history of induced abortion is reported more completely by cases than by controls.

However, the “gold standard” of this validity study, the information in the birth records, may not be as valid as it seems. The information had not been recorded at the time of the pregnancy termination. Rather, the birth records reflect the woman’s report of the procedure to the physician who aided in the birth of her last child. By this design, the study basically estimates underreporting to the interviewer within the group of women that has already been willing to report the abortion to the physician. The implicit, rather far-reaching assumption is that, among women who reported their induced abortion to the physician, reporting bias will be the same as it is among women who falsely reported no abortion. Table 1 in the paper

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Abbreviations: CI, confidence interval; OR, odds ratio.

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by Tang et al. shows that, among women who reported their abortion history to the interviewer, at least 49 percent of both cases and controls had not informed the physician. Within the group of women who had no abortion according to the birth records, 36/181 = 20 percent of the cases and 39/253 = 15 percent of the controls still reported an abortion during the interview. This might suggest the presence of bias. The issue becomes even more complicated if we realize that a group of women might have denied their induced abortion on both occasions.

Nevertheless, it is possible to investigate reporting bias taking the actual number of women with an induced abortion into account. It is sufficient to assume that underreporting to the physician is independent of the subsequent occurrence of breast cancer. The point is that it is not necessary to know the absolute number of women who actually underwent an induced abortion, as long as the number of cases in proportion to the number of controls is known. This ratio can be calculated from the presented data (see Appendix), as well as from the ratio of the proportions for cases and controls that reported their pregnancy termination to the interviewer. The ratio of these proportions for cases and controls proves to be very close to unity in Tang's data set, which means that indeed these data are not supportive for reporting bias.

To date, only one other validity study on this issue has been published (16). The authors compared the report of induced abortions in an interview-based case-control study with registered information on induced abortions archived by Swedish authorities. They calculated separate odds ratios based on interview and register information. The ratio of these odds ratios was 1.5, which suggests reporting bias. The study has been criticized, however, because of incompleteness of the registry (17). A calculation similar to that presented above shows that the ratio of the proportion of reported abortions for cases and controls is 1.45 (see Appendix), implying that in these data reporting bias is indeed present.

The inconsistent results of Tang et al. (11) and Lindefors-Harris et al. (16) do not necessarily imply a contradiction. The presence and magnitude of the bias may depend on the attitude toward the procedure in the study sample and on the specific study methods. Thus, annoying as it is, the absence or presence of reporting bias is a study-specific characteristic and, thus, the possibility of bias cannot be dismissed on the basis of findings in other studies. Other differences in the design of the two studies may also have affected the results. Tang et al. restricted their study to abortions prior to the birth of the last child, while the Swedish study covers all abortions, including abortions in nulliparous women and abortions after the birth of the last child. The report of induced abortions by women who decided not to have children, although they obviously can achieve pregnancy, may differ from the report by parous women. Further, the assumption that the information in the "gold standard" is independent of breast cancer risk factors may have been violated more easily when validated against the birth records (based on information from the women) than against the mandatory abortion registry (based on the report of physicians). Lastly, chance may have played a role, since the power of both studies is limited.

The conclusion of Tang et al. (11) that no reporting bias was present in parous women lends credibility to the results of the two case-control studies that were conducted in the same population. However, among parous women a 50 percent increased risk of breast cancer (95 percent confidence interval (CI): 1.2, 1.9) was found following an induced abortion in the first study (17), whereas no association was found (OR = 1.0, 95 percent CI: 0.8, 1.2) in the second study (5). The second study was conducted in the same counties as involved in the report by Tang et al. (11), in addition to two other geographic areas. Geographic heterogeneity was not reported for parous women, although it was present for the total group of parous and nulliparous women. Thus, from these data it is hard to draw conclusions. There is no other case-control study in which reporting bias was directly examined. Furthermore, none of the case-control studies made use of abortion information from other sources than the women themselves.

Apparently, for the interpretation of the association between pregnancy termination and risk of breast cancer, more weight should be given to the results of follow-up studies (8–10), which at least cannot be distorted by reporting bias. Lindefors-Harris et al. (8) used the mandatory Swedish abortion registry and found a relative risk (RR) of breast cancer of 0.8 (95 percent CI: 0.6, 1.0) for women with an abortion history before age 30. However, the result was estimated from four subcohorts (comprising 0.8 percent of the cohort) rather than actually observed, and adjustment could not be made for possible confounders, such as nulliparity.

Recently, the Iowa Women's Health Study (10) showed a relative risk of breast cancer among premenopausal women with a self-reported induced abortion of 1.1 (95 percent CI: 0.8, 1.6). Though the procedure was clearly underreported, the authors calculated that, if the real relative risk were 1.5, this would require that more than one third of the women who reported no induced abortion were misclassified. This is an unlikely high proportion. However, the power of the study was rather limited.
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REFERENCES


APPENDIX

Let the true number of women with an induced abortion for cases (number = \( N_c \)) and controls (number = \( N_c \)) be \( a_1N_{ca} \) and \( a_2N_{co} \), respectively, and let \( p \) be the proportion of women with an induced abortion that inform their physician, assuming independence of subsequent case-control status. Then, the number of women with a positive abortion history in the birth records is \( pa_1N_{ca} \) for cases and \( pa_2N_{co} \) for controls. From the data presented in table I by Tang et al. (11), it follows that \( 43 = 224 pa_1 \) and
From solving these equations for \( p \), it follows that \( a_1 = 1.225 a_2 \), and thus the true number of abortions is \( 224 \times 1.225 a_2 = 274 a_2 \) for cases and \( 300 a_2 \) for controls. The proportion of women who inform the interviewer is \( 73 / (274 a_2) \) among cases and \( 79 / (300 a_2) \) among controls. The ratio of these proportions is 1.01, implying no evidence of reporting bias.

From table 2 of the study by Lindefors-Harris et al. (16), it follows that \( 24 = 317 p a_1 \) and \( 59 = 512 p a_2 \). Solving these equations for \( p \) shows that \( a_1 = 0.66 a_2 \), and thus the true number of abortions is \( 208 a_2 \) for cases and \( 512 a_2 \) for controls. The proportion of women who inform the interviewer is \( 26 / (208 a_2) \) among cases and \( 44 / (512 a_2) \) among controls. The ratio of these proportions is 1.45, suggesting that reporting bias is present.