The association between abortion and breast cancer was first reported in 1981 by Pike.\(^1\) Since that time there have been over 35 publications worldwide that have evaluated this association in an attempt to definitively answer the question of whether abortion is an aetiologic factor in the multicausal web of breast cancer.\(^2\) The results of these studies, both case control and cohort, have been mixed. Despite these contradictory results, the problem of a rising incidence and prevalence of breast cancer remains.

In women, breast cancer is the most common type of cancer in the USA and the second leading cause of cancer mortality. In 1995, it is estimated that there will be 182 000 new cases of breast cancer and 46 000 deaths as a result of breast cancer in America.\(^3\) Among the industrialized countries of the world, the age adjusted death rate from breast cancer is in excess of 20 per 100 000 population.\(^3\) However, perhaps more controversial than the mixed results of the studies evaluating the association between abortion and breast cancer, is the debate over abortion rights. As often happens in politics, good science gets twisted to favour one position over another.\(^4\) The net result of these manipulations can be bad public policy based on poor logic, by individuals not versed in the subtleties of epidemiology or scientific reasoning.

In this Selections, five recent articles addressing the issue of abortion and breast cancer will be reviewed. Following this, a classic paper outlining how causal inferences should be made will be summarized. Then, without considering the politics of abortion, but instead focusing only on the available scientific evidence, a judgement will be made on whether or not abortion has been shown to have a causative role in breast cancer.

Abortion and breast cancer


This case control study was conducted because the epidemiological evidence regarding the relationship between breast cancer and spontaneous or induced abortion is inconsistent. During a 3-year period, from 1989 to 1991, all newly diagnosed women with breast cancer in four major hospitals in Athens were identified.

Eight hundred and twenty of these patients, or 94\% of those with histologically confirmed breast cancer were successfully included as cases in the study. Each case had two controls. There were 795 controls chosen from the orthopaedic wards and 753 healthy controls who were visitors to the same hospital where each case was identified. Cases and controls were matched for age and geographical area. Ninety-six per cent of the orthopaedic controls and 93\% of the visitor controls participated in the study. Each case control triplet was interviewed by the same interviewer using the same questionnaire in the hospital setting.

The questionnaire asked about demographic, socioeconomic, reproductive and biomedical variables. Subjects who had had an abortion were also asked about their age at the time of the abortion, the type of abortion (induced or spontaneous), and timing with respect to first full-term pregnancy. There were 680 complete triplets. Since comparison of the cases with either control series showed similar results, the two control series were combined for most analyses. In order to deal with potential confounding factors, the core model controlled for age, parity, age at first birth, place of birth, Quetelet’s index, age at menarche, menopausal status and alcohol intake.

The authors reported that the risk of breast cancer did not increase with a history of spontaneous abortion, odds ratio (OR) of 0.97 (95\% CI 0.79–1.19). However, the risk appeared to increase significantly with the history of an induced abortion, OR of 1.51 (95\% CI 1.24–1.84). In nulliparous women there was no increased risk of breast cancer with a history of abortion of any type, in both the cases and the controls. However, in parous women a history of induced abortion was associated with an increased risk of breast cancer. In parous women the OR was 2.06 (95\% CI 1.45–2.90) for an induced abortion before the first full-term pregnancy. Also, in parous women the OR was 1.59 (95\% CI 1.24–2.04) for an induced abortion after the first full-term pregnancy. Having a spontaneous...
abortions that occur. They state that this may hinder detecting and reporting the majority of spontaneous abortions that occur. They state that this may hinder the study of these types of abortions, and could contribute to the lack of association that has been found with spontaneous abortions and the risk of breast cancer.


This article reports on a case control study of 845 breast cancer cases and 961 controls performed in three counties in Washington state from 1983 to 1990. It attempts to analyse the association of breast cancer with induced abortion.

A total of 1806 interviews were conducted, representing a response rate of 84% for cases and 78% for controls. Cases were found through a population based tumor registry that serves 13 counties in western Washington state. Controls were found through random digit dialing. There were 210 induced abortions in the case group and 201 in the control group. Also, there were 173 spontaneous abortions in the case group and 211 in the control group. Odds ratios were calculated for risk of breast cancer after induced or spontaneous abortion.

The study was restricted to white women, since 85% of the population in the study area was white and no minority group represented more than 5% of the population. Demographic, life-style and medical history data were obtained. Additionally, data on family history of breast and other cancers, contraceptive methods, menstrual and pregnancy histories were obtained. The analysis focused on the subsequent risk of breast cancer between women who had had an abortion compared to those who had not. The cases and controls were matched on demographic characteristics as well as child bearing histories. The analyses were adjusted for age, family history of breast cancer, religion, age at first pregnancy, and age at first birth. Further adjusting for other variables did not change the odds ratios.

Women who had been pregnant at least once and had a history of an induced abortion had an increased risk of breast cancer, OR of 1.5 (95% CI 1.2–1.9). After adjusting for age at first full-term pregnancy, the OR remained at 1.5. Additionally, the magnitude of the association did not vary according to whether the induced abortion preceded or followed the first birth. The magnitude of increase in the risk of breast cancer was similar between women who had one or more than one induced abortion.

A combined influence of age at first induced abortion and the gestational age at the time of the abortion showed an OR of 9.0 (95% CI 2.0–41.2). However, there were only 15 cases and five controls in this subgroup. Women who have never delivered a child had no increase of breast cancer risk related to history of spontaneous abortion, OR of 1.1 (95% CI 0.4–2.6).
This was another small sub-group, containing only 14 cases and 12 controls. Overall, there was no increased risk of breast cancer following a spontaneous abortion, the OR was 0.9 (95% CI 0.7-1.2).

Since only 84% of cases and 78% of controls were interviewed, the authors do admit that if there was a difference between the participants and non-participants, then their results could be biased. However, if the reasons for being unable to interview those cases were related to breast cancer, then that bias would underestimate the risk of breast cancer that is associated with an induced abortion. Informational bias, that is the accuracy with which induced abortions are being reported, was addressed. The authors state that since they focused on legal induced abortion, this should be a minimal concern since abortion was common and well accepted by US women at that time.

A third bias which they attempted to address was recall bias. They stated that it was reasonable to assume that virtually no woman who truly did not have an abortion would claim to have had one. However, women who are diagnosed with a life threatening disease such as breast cancer might report a history of induced abortion more completely than a healthy control woman contacted at random. Thus, they utilized data from another study to look at this problem. Then, based on their calculations from this other study, they said that recall bias might affect their results by about 16%.

Comment
The authors report that this study was unique as it examines a population that had legal abortion as an option for most of their reproductive years. Yet, the study included women born after 1944 which includes 8 years when subjects were over 18 prior to legal abortion becoming available in Washington state. The risk of recall bias is only partially addressed. Readers are left with the possibility that the results of this study may be off by 16-50%.

The statement that abortions were common and well accepted by US women during this time period may be overstated. The lack of association with spontaneous abortions may be explained by the incomplete reporting of these events, which most often occur early in gestation. Potentially, the difference in gestational age affects the terminal differentiation of the breast tissue as well. The question of whether a full-term pregnancy soon after an abortion, even with breast feeding, causes terminal differentiation of the breast tissue cannot be resolved due to the small sample size of this sub-group in the study. The differential rates of breast feeding and subsequent births between the spontaneous and induced abortion populations is another potential explanation for the difference in OR, but the authors had attempted to control for this.

A major potential bias is the age of controls being younger than the cases. Seventeen per cent of controls were under 30, while only 8% of the cases were under 30. Clearly, the risk of breast cancer rises with age. The comment that the risk was greater in the women who underwent their first abortion before the age of 18 may also be overstated, as the OR was accompanied by a dramatic increase in the width of the confidence intervals. This may be reflective of the fact that this sub-group was very small and small samples give unstable rates.


This case control study attempts to describe the risk of breast cancer related to spontaneous or induced abortions. The cases and controls were drawn from women under age 75 who were admitted to hospitals in Milan, Italy.

Cases were defined as women with histologically confirmed breast cancer diagnosed within a year before the interview. Controls were women admitted for acute conditions to the same network of hospitals as cases with 32% admitted for traumatic condition, 27% for non-traumatic orthopaedic disorders, 17% for acute surgical conditions and 24% for other illnesses. Cases and controls had similar 5-year age group distributions. The potential confounding effects of age, education, marital status, age at first birth, parity, age at menarche, age at menopause, estrogen replacement therapy and body mass index were considered.

The results showed that cases tended to be more educated and reported an earlier age at menarche, later age at menopause and later age at first birth. No consistent associations with abortion were found. The multivariate OR for breast cancer comparing no abortion (either spontaneous or induced) to one abortion was 1.0 (95% CI 0.9-1.2) and compared to two or more abortions was 0.9 (95% CI 0.7-1.0). They found an OR for breast cancer of 1.4 (95% CI 0.9-2.2) for history of a spontaneous abortion among women under age 40. Conversely, they found an OR of 0.7 (95% CI 0.5-1.1) for history of an induced abortion among women under age 40. Women who had at least one abortion before their first full-term pregnancy had an OR of 1.2 (95% CI 0.9-1.7) for breast cancer compared to parous women reporting no abortions. Conversely, an OR of 0.9 (95% CI 0.8-1.0) was seen for first abortion after first full-term pregnancy.

The authors felt that it was unlikely that their results were affected by bias since both cases and control were identified in hospitals covering a comparable catchment area and since their response rate was almost complete. They concluded that neither spontaneous or induced abortions affect a woman’s risk of breast cancer.
A total of 1451 breast cancer cases were reported drawn from New York State excluding New York City. The cases and controls were through utilization of fetal death certificates and breast cancer incidence records. The cases and controls were matched for age, parity, and marital status. The cases were defined as women with breast cancer, independently of parity. In the strictest sense, there may be an interaction between the type of abortion (induced or spontaneous) and reproductive factors such as age at first birth and parity. If such an interaction exists, then combining induced abortions with spontaneous abortions cannot be justified.

While a case control study is an appropriate method for examining the relationship between breast cancer and prior abortion, several issues have not been answered. Biologically induced and spontaneous abortions may have the same hormonal effect on a woman's body and thus on her risk of breast cancer. However, other reproductive factors may confound the relationship between breast cancer and spontaneous abortion differently than induced abortion.

Therefore, a model containing both induced and spontaneous abortions adjusted for confounders as done in this study may not be fully adjusted since the confounding effects may be different for different types of abortion. Similarly, there may be an interaction between the type of abortion (induced or spontaneous) and reproductive factors such as age at first birth and parity. If such an interaction exists, then combining induced abortions with spontaneous abortions cannot be justified.

Controlling for parity and age at first birth is rather difficult, since parity affects the risk of breast cancer but abortion is related to parity. In the strictest sense, the appropriate comparison groups would be nulliparous women versus women with an abortion of their first pregnancy; women with one live birth versus those with one live birth followed by an abortion; to three live births in comparison to abortion of fourth pregnancy after three live births; etc. This controls for parity and may control somewhat for age at first birth and therefore answers the question "given your current reproductive history does abortion in and of itself affect your risk of breast cancer, independently of parity".


This case control study attempts to use record linkage in New York State to study the relationship between breast cancer and prior abortion with limited bias through utilization of fetal death certificates and breast cancer incidence records. The cases and controls were drawn from New York State excluding New York City. A total of 1451 breast cancer cases were reported in New York State between 1976 and 1980 among women younger than age 40 at diagnosis. Controls were selected from the New York State Department of Motor Vehicles' records of drivers newly licensed or renewing their license in 1980.

One control per case was randomly matched by year of birth and residence to each case. In addition to the mandated reporting of cancer cases, the New York State Public Health Law also required the reporting of all induced and spontaneous abortions at any gestational length after induced abortion was legalized in July of 1970. Using a computerized system, all surnames for the cases and controls were linked with fetal death certificates reported from 1971 to 1980. Fetal deaths recorded after the date of diagnosis of breast cancer were not included in the analyses.

The computer system yielded a list of potential matches. A positive match was defined as same first name and same last name or agreement of middle initial with maiden name and one of the following combinations: 1) exact age at time of fetal death and exact address; 2) exact age, same city and same middle initial; 3) exact age and same city or same county; and 4) exact address and same middle initial.

Pregnancy history was only available for cases and controls with a positive fetal death history. A matched-analysis was performed. The authors found that over half of these women under 40 were diagnosed with breast cancer between the ages of 35 and 39. The majority of the cases were white and married. An elevated OR of 1.7 (95% CI 1.2-2.3) was found among all women. When examining induced and spontaneous abortion separately, an OR of 1.9 (95% CI 1.2-3.0) was seen for history of induced abortion and an OR of 1.5 (95% CI 0.7-3.7) for spontaneous abortion. Furthermore, the authors reported an OR of 4.0 (95% CI 1.5-13.6) for history of repeated interrupted pregnancies with no intervening live births. Both cases and controls with a history of a fetal death had a mean age at first live birth of 23 and had a mean of 3.1 total pregnancies, but no information was available for women without a history of fetal death.

Since these analyses were based on mandated state records, the authors argued that the data were not affected by interview refusals, recall bias, death prior to interviews and the social stigma of abortion. However, records did not include abortions before 1971 and only the youngest case control pairs had their peak reproductive years covered during the study period.

While this study seems to have avoided various types of bias, it was not able to control for important confounders. Although they found similar rates of pregnancies and age at first birth between cases and controls, they were only able to examine pregnancy histories among women with a history of fetal death between
1971 and 1980. They were not able to examine whether or not the relationship between abortion and breast cancer was confounded by age at first birth and parity. It is likely that the reproductive histories of women with a history of fetal death are different from those without a history of fetal death. Women without a history of fetal death may have an earlier age at first birth and a higher parity and thus be at a reduced risk of breast cancer. This relationship may also vary between women with an induced abortion and those with history of a spontaneous abortion.

No information was available on abortion before 1971. However, this lack of information is consistent in cases and controls. More importantly, only a short latency period was allowed between the time of an abortion and incidence of breast cancer. It would be interesting to link and compare breast cancer cases through 1990 or 1995 with 1971-1980 "exposed" women from the fetal death tapes. However, such a comparison would still not have the ability to control for potential reproductive confounders.

Finally, while the authors argue that the data which they used is unaffected by several potential biases due to the requirement of mandatory reporting under the law, we all know that the law is sometimes broken. Thus, it would have been important to have checked on the completeness of the data and stated the level of underreporting that existed for both abortions and breast cancer.


This cohort study assessed the risk of developing breast cancer following an induced abortion. The study population were women who had an induced first trimester abortion below the age of 30. The authors used data collected between the years 1966 and 1974 on individual women who had had an induced abortion. The records prior to 1966 were excluded because of incompleteness and after 1974, abortions were no longer registered individually.

There were 166 840 reports between the years 1966 and 1974 that the authors used to construct the study cohort. This cohort included women who had had a legal abortion and met three additional criteria: 1) age below 30 at the time of abortion; 2) abortion performed during the first period of gestation (within 90 days after the last menstrual period); and 3) Swedish citizenship. The number of women in the study cohort was estimated because manual searches of records of the total cohort were too expensive. The study cohort was estimated to consist of approximately 49 000 women.

The authors obtained information on diagnosed cases of breast cancer by linking the 49 000 women's records with the Swedish Cancer Register. The Swedish Cancer Register estimates their completeness of the registration of cases of breast cancer to be 98.2%. In calculating the years the women were at risk for breast cancer, allowance was made for an induction period of five years, the most common period of latency shown in research on breast cancer. To assess the risk of breast cancer immediately after a legal abortion, calculations were made using an induction period of one year.

The ratio between the observed number and the expected number of breast cancer cases constituted the relative risk (RR) of developing breast cancer following an induced abortion. The observed number of breast cancer cases with an induction period of five years was 65 compared to an expected number of 84.5. The RR of developing breast cancer five years after a legal abortion was 0.77 (95% CI 0.58-0.99). Parous women had a RR of 0.58 (95% CI 0.38-0.84) and for nulliparous women the RR was 1.09 (95% CI 0.71-1.56). The observed number of breast cancer cases with an induction period of one year did not show a major change in the risk of breast cancer compared to an induction period of five years.

In conclusion, the authors state that contrary to most earlier reports, their study did not indicate any overall increased risk of breast cancer after an induced abortion in the first trimester of women below the age of 30. They do state that confounding factors about which they had little or no information, such as smoking, family history of cancer, socioeconomic status, contraceptives, education and marital status, could change their results.

They go on to point out that due to the short follow up period of their study, with only 5000 women being followed for more than 11 years, a similar linkage study would be appropriate in 10-20 years. Finally, the authors tried to explain why their results were so contrary to those of earlier studies. They suggest that because they conducted a cohort study which relied on data from two registers, the risk of recall bias was nonexistent, and recall bias may have played a large role in the positive findings of the earlier case control studies.

Comment
An important methodological strength of the study, as a result of using the computerized registries of the National Board of Health and Welfare and the Swedish Cancer Register given their completeness, is that interview refusal, death prior to the interview, and social stigma of abortion did not affect the data in the study. Secondly, since this was a cohort study, recall bias was minimized. As the authors point out, this may be the reason for the contradictory results of their study.

Weaknesses of the study include insufficient follow up of the vast majority of the cohort, a lack of control for possible confounding biases and, perhaps most importantly, the fact that the cohort size was estimated.
Estimating the cohort size instead of manually searching for the accurate number was cheaper, but at a potential cost of the study's validity. This is so because the RR changes with respect to the cohort size.

However, given their results, the authors appropriately conclude that having an induced abortion significantly decreases a woman’s risk for getting breast cancer.

### Assessing causation


This classic paper is the address given by Sir Austin Bradford Hill on 14 January 1965 at the first meeting of the Section of Occupational Medicine of the Royal Society of Medicine.

In his address, he discussed how in some cases it is quite easy to say that "a particular chemical is known to be toxic", based on the available medical knowledge. However, he stated that it is more common to note an association between two events and then have to go back to find out if the association is in fact a causal one. Hill posed the question, "Upon what basis should we proceed to do so? 'establish causation'". He then outlined nine "viewpoints" or suggestions, as opposed to "hard and fast rules", which he felt were not possible in trying to establish causation. These nine "viewpoints" are summarized below.

Strength of association was the first of his viewpoints. He stated that the stronger an association was, the more likely it was to be causative. He also pointed out that because there may only be slight absolute differences in the observed associations, it was very important to look at "the differences revealed by ratios".

Consistency of the observed association was his second viewpoint. In order to ensure that the association was not due to some constant error, he wanted to make sure that the association had "been repeatedly observed by different persons, in different places, circumstances and times".

Specificity was the third requirement called for to establish causation. However, due to the multifactorial web of causation of most diseases, Sir Hill warned against over-emphasizing the importance of specificity. Still, if an association is limited to a specific event, then "that is a strong argument in favour of causation".

Temporality was the fourth characteristic listed in the viewpoints for assessing causation. Essentially, did the behaviour lead to the disease, or did the disease lead to the behaviour? This temporal relationship has a special relevance to diseases that are slow to develop.

Biologic gradient, or having a clear dose-response curve was the fifth viewpoint. Having a dose-response curve can lead to a simple and satisfying explanation of the cause and effect hypothesis.

Biological plausibility was the sixth viewpoint. Here however, Hill warned of the danger of dismissing an observed association too quickly as not being biologically plausible. Observations may be so new to science that the limited biological knowledge of the time may be incapable of properly explaining them immediately.

Coherence was the seventh viewpoint. This is integrally related to biological plausibility, and relates to the fact that the interpretation of the observation "should not seriously conflict with the generally known facts of the natural history and biology of the disease".

Experimental evidence was the eighth characteristic that Hill laid out. In it, he explained that sometimes it is possible to garner supporting evidence from experiments. This evidence can sometimes turn out to be "the strongest support for the causation hypothesis".

Analogies were the ninth and last of Hill's viewpoints. In it, he showed how because of similar evidence in other circumstances, it may be possible to accept a similar conclusion in a similar type of association that you are observing.

Hill reiterates that these nine viewpoints are not hard and fast rules, but guidelines for studying associations before declaring causation. He goes on to point out that formal "tests of significance merely serve as guides to caution before drawing a conclusion", they do not prove a hypothesis. Instead they show the part that chance plays and the magnitude of an effect.

Finally, he discusses the "real life" consequences of declaring an association to be a causal one. While acknowledging that "all scientific knowledge is incomplete" and "liable to be upset or modified by advancing knowledge", Hill declares that "the evidence is there to be judged on its merits and the judgement should be utterly independent of what hangs upon it—or who hangs because of it".

### Comment

These nine brief "viewpoints" for establishing causation, written over 30 years ago are still widely accepted as the standard for assessing causation. They are perhaps even more relevant to the present time than when Hill gave his speech in 1965. Given the multifactorial web of causation of most diseases, the greater prevalence of insidious chronic diseases and the need to explain ever decreasing relative risks and odds ratios that are being reported in the medical literature, the need for objective guidelines in evaluating associations prior to ascribing a causative role is vital.

### Summary

If Hill’s viewpoints are used to review the association between abortion and breast cancer, it is clear that for most of these viewpoints the evidence does not withstand close scrutiny. The strength of association is small, with RR and OR rarely exceeding 2. There is
also no consistency, specificity, nor biologic gradient. However, there is a biologically plausible explanation. It has been postulated that during early pregnancy, oestrogen stimulation of the breast tissue causes it to undergo differentiation that is abruptly halted when there is an abortion. Subsequently, these partially differentiated structures within the breast are more susceptible to carcinogens.

It has been suggested that the studies with positive findings may have suffered from recall bias. Misclassification bias and informational bias have been suggested as other weaknesses of many of these studies. Additionally, a multitude of potential confounding factors need to be addressed in subsequent studies. Among these are age, parity, age at first birth, induced or spontaneous abortion, abortion before or after first birth, length of gestation, and whether or not there was a subsequent pregnancy with or without breast feeding.

Clearly there are mixed results on this issue from the many studies that have been done. While some studies have shown a positive association, others have shown an inverse association, and still others have shown no association. The scientific work on this topic is incomplete and needs further scrutiny. However, perhaps a meta-analysis of the 35 reports that have addressed this topic, in an attempt to quantitatively synthesize these results, would be a useful endeavour. Finally, from this Selections, it should be clear that there is insufficient evidence to claim that the association between abortion and breast cancer is a causal one.

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