Studies that Deny the Abortion-Breast Cancer Link

Often, those who deny the abortion-breast cancer link will cite the findings of a well-publicized study, such as the Melbye study (the Danish study), the Beral re-analysis, the Michels study (the Harvard Nurses' Study), or the Henderson study (the California Teachers Study), as the basis of their argument. However, careful scrutiny shows these studies were all seriously flawed.

1. 1997 Melbye Study (the Danish Study)

In January 1997, the Danish Melbye study was published in the prestigious *New England Journal of Medicine*.[1)] This paper is often used in major textbooks to show there is no link between abortion and breast cancer.[2)] The study was hailed by National Cancer Institute epidemiologist Patricia Hartge[3)] in an editorial accompanying the study: "In short, a woman need not worry about the risk of breast cancer when facing the difficult decision of whether to terminate a pregnancy."[4)] She proclaimed that the study had settled the question and that induced abortion did not increase the risk of breast cancer. Despite Hartge's praise, the Melbye study had several significant flaws.

The Melbye study is insufficient to answer the question of whether induced abortion has any adverse effect on women: It devotes a mere paragraph of text and one unsophisticated comparison to assess the effect of induced abortion (relative to no abortion history), it employs unsuitable comparisons to assess the influence of the number and timing of abortions procured, it possibly eliminates all effect of induced abortion by controlling for the time period at which abortions were procured, excludes women with in situ breast cancer, and fails to consider the pathology of breast cancer in assessing the timeframe in which the disease would manifest itself following an induced abortion.

Unsophisticated analysis of induced abortion. The Melbye study states that "[o]verall, the risk of breast cancer in women with a history of induced abortion was not different from that in women without such a history" after adding controls. However, this in-text statement references the only analysis of the difference between women with and without abortion history. This is a remarkably unsophisticated comparison, particularly in light of the detailed comparisons that could have been performed with a sample of 1.5 million women. Note that three studies published before the Melbye study (the 1994 Daling study, the 1995 Andrieu study, and the 1995 Lipworth study) assessed the influence of induced abortion based on its timing related to first full-term pregnancy. Such a crude, "kitchen sink" approach offers no insight to individual women regarding the potential risk abortion would pose to their future breast health.

The authors reserve sophisticated modeling for a table in which they examine the marginal risks incurred by women based on the circumstances of their procured abortions. All women examined in this analysis have had at least one induced abortion; none of the women considered are without induced abortion history. Hence, this is not an analysis of the effects of induced abortion history relative to having no abortion history, but of the effects of the circumstances of an induced abortion relative to other circumstances.

Unsuitable analyses. To address the effects of repeated induced abortions, Melbye et al. use women who have had only one abortion (76.8 percent of aborting women) as a reference group for women with two abortions (17.1 percent) or three or more abortions (6.1 percent).

The authors' neglect of women without abortion history also results in the lack of a suitable reference group for their analysis of the effects of the ordering of live births and abortions. Women who obtain abortions only after their first live birth are used as a reference group for aborting childless women, women who procure abortions only before their first live birth, and women who procure abortions both before and after their first live birth.

The reference groups used in both the analysis of the effect of number of induced abortions and of timing of the induced abortions are unsuitable. Less than 19 percent of their sample had induced abortion history. The appropriate reference category to assess the effect of number and ordering of abortions is parous women with only full-term pregnancies.

Reporting difficulty around abortion law change and control for abortion's legality. Melbye and colleagues also applied a control that diminished the strength of their findings: Their results are controlled for the time period in which the induced abortion was procured. Abortion became legal in Denmark in 1939,[5] but the law was changed: It was liberalized in October 1973.[6] The number of abortions in Denmark increased markedly after its laws were liberalized.[7] This information is crucial to consider, because the induced abortions included in the Melbye study took place between 1968 and 1992. Melbye and colleagues assigned a set of indicator variables, or dummy variables, to the time in which the abortion took place and controlled for the time the abortion was procured via that set of indicator variables in the study. In short, they controlled out for liberal abortion law. Controlling for—and not reporting—the influence of the time the induced abortion was obtained masks, and likely eliminates, the effect of induced abortion on breast cancer entirely in their regressions. This design error will statistically dominate all other factors involved in the production of cancer through induced abortion. This control for the time in which the abortion took place—a control for liberal abortion law, or free access to induced abortion—may have absorbed all the effect of induced abortion on breast cancer risk. This may be why, in a study of 1.5 million Danish women, just one explanatory variable—abortion at or past 18 weeks—carries any significance.[8] This is a serious error in model interpretation. By ignoring the significance of liberal abortion laws when attempting to compare breast cancer risk within a cohort, they failed to realize what Beral and colleagues grasped when designing their own study: So as "to minimize possible differential reporting of illegal abortion, analyses would be restricted, as far as possible, to populations with access to legal abortion services."[9]

Late induced abortion. As noted above, Melbye [10] addresses the marginal risks incurred based on the circumstances of women who obtain abortions. This finds no effect based on any of the circumstances examined, with the exception of abortion at or after 18 weeks of pregnancy. Melbye's analysis shows doubled odds of breast cancer with abortions at 18 weeks' gestation or later. Again, the additional risk this poses is the only significant explanatory variable for induced abortion's circumstances in the study. Melbye and colleagues attempt to diminish the importance of this, their only significant finding, noting "[t]he fact that such an increase [in risk with second-trimester abortions] did not affect the overall results clearly indicates that it is based on small numbers and, therefore, requires cautious interpretation." To have dismissed their only significant finding, rather than devoting further energy to its investigation, was to disregard the demands of proper statistics.[11]

Health or survivor bias. Melbye et al. risk introducing health bias or survivor bias into their study by excluding women with in situ breast cancer; their study was restricted to women with invasive breast cancer.

Incorrect time frames. Finally, the time frames established in the Melbye study for analysis of cancer development in aborting women are not tailored to the specific pathology of cancer growth.

The authors analyzed the risk of cancer among women for whom under one year had passed since an induced abortion and for whom one to four years had passed. The cohort for whom five or more years had passed since an induced abortion was established as the reference category. Note that breast cancer resulting from an induced abortion would not be detectable until approximately eight to 10 years thereafter. Hence, induced abortion was not found to increase breast cancer risk under one or one to four years thereafter. Furthermore, including women in the reference category whose induced abortions were fewer than eight to 10 years prior and women whose induced abortions were more than 10 to 14 years prior[12)] may have statistically "washed out" any effect. A better classification scheme might, for example, have grouped women who had had abortions seven or fewer years earlier, eight to 14 years earlier, 15 to 21 years earlier, or 22 or more years earlier. Such groupings would be appropriately tailored to the time that breast cancer takes to grow to a detectable size: eight to 10 years.

2. 2001 Goldacre Study

The UK Goldacre study is marked by incomplete reporting and distinguishing of spontaneous and induced abortions; omitted variable bias through the lack of empirical consideration of data on parity, age, and other breast cancer risk factors (and hence no parsing of the effects of differently-ordered abortions); an incompletely specified model; and insufficiently randomized data. Given these flaws, this study is not a significant contribution to the literature.

Incomplete reporting and distinguishing of induced and spontaneous abortions.
Furthermore, the records they reference frequently failed to specify whether an abortion was induced or spontaneous. In response to this ambiguity, they developed a category for "all" abortions that lumped together induced and spontaneous abortions with the unspecified abortions. They analyzed the category for "all" abortions alongside the individual categories for induced and spontaneous abortions. The authors do not state in what fraction of cases there was uncertainty about the nature of the abortion. This lack of specification could potentially lead to serious exclusion bias in the eventual fit of the model on the data that are kept. Exclusion bias would be created if there were a large number of unspecified abortions and if the reason their type was not specified was correlated with abortion type (which would likely explain any differential rate of cancer development). Any risks associated with spontaneous and induced abortion in this population cannot be clarified unless (as is the standard of comprehensive research work) the statistical answers to both of these questions are openly presented. If data (e.g., on parity, gestation, etc.: see below for a further elaboration on these matters) are not available, the onus is on both the researcher and research community to discount the (lack of) finding in any such study.

Incomplete model (lack of parity data). The authors have only incomplete data on abortions and also note that analysis of certain "lifestyle or reproductive variables [was] outside the scope of [their] study." Among these variables is pregnancy. Though the authors assert that they closely matched control groups to cases for data on "these factors" (e.g., "reproductive and lifestyle variables"), they fail to actually demonstrate that the control groups are closely matched. The demographics of their sample are not detailed in tables or text. The authors do not demonstrate similarity between cases and controls regarding the variables of concern or show any differences between the groups in these regards to be insignificant. This produces an obvious problem: Their model does not account for all risks for developing breast cancer. The exclusion of data on other breast cancer risk factors may add bias (an omitted variable bias) to any attempt to distinguish classes of women at risk.

Unsophisticated analysis of induced abortion. Furthermore, without including data on parity status or pregnancy, it is impossible to parse out the timing and ordering of their cohort's

reproductive events and thereby distinguish the risks for breast cancer that abortion poses for various cohorts of women. A study that fails to differentiate between the effects of differently timed and ordered abortions is less effective than one that does differentiate. The authors of the 2001 Goldacre study in the UK[13] do not note (or perhaps their records do not specify) at what stage of gestation the spontaneous or induced abortions took place.

Reporting difficulty around abortion law change, sample age, and expected number of abortions. The women with tabulated breast cancer incidence under investigation include some cohorts without many abortions during their fertile years (older women, who were fertile before abortion was legal in the UK) and those with relatively many during their fertile years (younger women, fertile after abortion was legal). Even though age is stratified (analogous to controlling for age), the recombination of these cohorts' incidence rates will interact age (one being older or younger) with abortion.[14]

Goldacre's "expected" breast cancer incidence comes from the general population's rate (though they do not explain how this number is derived). Their "observed" breast cancer rate is what they measure for those who have had an abortion. But the two quoted rates for the general population and aborting women have very different women in them: These statistics aggregate (recombine) women of very different age types. Those having had an abortion are much younger (because abortion was generally available and legal only after 1967). The aborting women, being younger, will exhibit (what is "observed" in their class) lower breast cancer rates. Younger women get breast cancer much less frequently than older women.

Once (what appears to be) the window has passed for a breast cancer to manifest itself (once 14 years or so have passed), these women (older women) show a decreased risk of breast cancer. The model shows this, albeit imprecisely.

Incomplete and insufficiently randomized data. Finally, the sample suffers from selection bias, as it was confined to women who obtained abortions in hospitals. As Joel Brind notes in a separate review, a mere 300 of the 28,616 cases included in Goldacre (women diagnosed with breast cancer between 1968 and 1998) were classified as having a history of induced abortion—amounting to barely 1 percent of cases over a 30-year period. However, the abortion rate in the UK was over 1 percent per year over that period;[15] Goldacre et al. may have too few women classified as having induced abortion history. Labeling women who have had an induced abortion as women not having had an induced abortion will decrease any measured influence of abortion on breast cancer. The authors admit in their paper that their "data on abortions are substantially incomplete because they only include women admitted to hospital [sic], only include those in the care of the National Health Service, and only in the time and area covered by the study."[16] Hence, their study is insufficiently randomized.

3. 2004 Beral Re-analysis

Valerie Beral's large "re-analysis" of data from 53 epidemiological studies, including 83,000 women with breast cancer from 16 countries, was published in the British journal *The Lancet* in 2004.[17] Beral et al. find, in one analysis, that induced abortion *increases* breast cancer risk and that induced abortion *decreases* breast cancer risk in another analysis. The study was hailed by its researchers as the definitive analysis that put to rest the claim that abortion increases breast cancer risk. Beral stated, "Scientifically, this is really a full analysis of the current data."[18] However, a review of the

study reveals that it is not a “full analysis” and that serious methodological flaws render the study unreliable.

The Beral re-analysis is flawed by two instances of publication bias: The authors unsystematically dismissed the result of their analysis of retrospective data in favor of their analysis of prospective data, and they unsystematically excluded certain peer-reviewed studies from their analysis. Beral and colleagues also chose an unsuitable reference group to assess any influence of induced abortion on breast cancer, excluded studies including women with in situ breast cancer, and failed to distinguish between first- and second-trimester spontaneous abortions.

Induced abortion. Beral and colleagues found induced abortion history contributed to a statistically significant decrease in breast cancer risk in their meta-regression of studies based on prospectively collected data and a statistically significant increase in breast cancer risk in their meta-regression of studies based on retrospectively collected data.

No significant influence was found, in prospectively collected or in retrospectively collected data, for two or more induced abortions relative to one induced abortion, for experiencing a first induced abortion before age 25 relative to after age 25, for an induced abortion being fewer than 10 years in the past versus an induced abortion being 10 or more years in the past, or induced abortion before versus after giving birth.

Spontaneous abortion. The Beral re-analysis found no significant effect for spontaneous abortion in either their analysis of studies based on prospective data or in their analysis of studies based on retrospective data.

Publication bias. As explained above, the Beral study is marked by several flaws, including two types of publication bias. The first type is the dismissal of findings sourced in retrospective data; the second is the unsystematic exclusion of certain datasets from their meta-analysis.

Publication bias: Dismissal of analysis of retrospective data. Beral and her colleagues divided the studies they analyzed into two separate categories: Those that used retrospective methods of data collection (i.e., information from patients after they were diagnosed with breast cancer and control subjects) and those that used prospective methods (i.e., medical records taken before a breast cancer diagnosis). As noted above, the 39 retrospective studies showed evidence of an increase in breast cancer risk with abortion. The 13 prospective studies showed a decreased breast cancer risk with abortion. The study concluded from its prospective data that there was no association between induced abortion and breast cancer, and this conclusion was widely reported in the press. Instead of reporting the results of their study accurately, the authors in their conclusion termed the increase in breast cancer risk based on retrospective data “misleading” and asserted that “recall bias” altered the data.[19)] Despite the theoretical possibility that recall bias exists, the studies most frequently referenced as evidence of recall bias are far from sufficient as a basis for this charge.

The authors’ unsystematic dismissal of their findings based on retrospective data is scientifically unjustifiable because it is arbitrary. Though it is possible that healthy women in retrospective studies underreport their abortions, it is also possible (and the authors admit as much) that underreporting of abortions took place in the prospective studies. They offer no substantiation for their statement that underreporting would not significantly distort prospective studies. Yet the authors do not dismiss the result of their analysis based on prospective data. Rather than dismissing the result of their analysis of retrospective data, they could have built controls for the circumstances under which the data in each study were obtained into their model and thereby controlled for recall bias. They did not. Their dismissal of findings sourced in retrospective data is based on an arbitrarily applied assumption.

The authors state, “In view of the potential for differential retrospective reporting of past induced abortions to distort the results, and given the highly significant differences found here between the overall findings about the studies that had recorded information on induced abortion retrospectively and prospectively, the collective results cannot be trusted. The possibility that, on average, women are more likely to disclose previous induced abortions after they are diagnosed with breast cancer than they would otherwise have been cannot be excluded.” Thus, they simply suppose that recall bias has tainted retrospective studies. They throw out the overall finding of 39 studies because it contradicts the overall finding of 13 studies.

Publication bias: Unscientific exclusion of studies. Beral and colleagues were also unsystematic in choosing which datasets to include and exclude. Beral et al. deliberately excluded a total of 13 peer-reviewed studies from their analysis. They also failed to note the existence at least five published datasets.[20)]

The authors included some unpublished studies and some unpublished abortion data in their analysis: “Only about two-thirds of the eligible studies that had obtained relevant information had published their findings on abortion and breast cancer.” Beral and her colleagues take the perspective that by including unpublished data they have avoided the risks associated with (a particular type of) publication bias[21)] (of course, their study is affected by other forms of publication bias). However, because these data were unpublished, readers of the Beral re-analysis can have only limited confidence in its results. The veracity of the datasets has not been established: there is no way of knowing what means were used to arrive at the conclusions reported. It would have been wise to include indicator (dummy) variables to control for any potential differences in published and unpublished datasets.

For example, among the unpublished datasets Beral referenced is a Scottish study showing a decrease in breast cancer risk with abortion. As the study’s data were unpublished, it had not been assessed independently. However, these data were published the following year as the 2005 Brewster study (with Beral as a co-author), critiqued below. That one of the datasets traced is so flawed casts doubt on the others which cannot be reviewed.

Health or survivor bias. Notably, the authors included only studies of women with invasive breast cancer and excluded in situ breast cancer, the significance of this is addressed above.

Unsuitable comparison. Another major flaw in the Beral study lay in its choice of reference group. The authors compare the risk of a pregnancy ending in induced abortion with the risk of “never having had that pregnancy.” Their language is unclear, but if Beral et al. here refer to nulliparity, then the breast cancer risk contributed by induced abortion would be muted by comparison to the breast cancer risk posed by nulliparity. Regardless, Beral and colleagues have chosen to assess the wrong counterfactual.[22)] Pregnant women who undergo induced abortion ought not to be compared to hypothetical women not experiencing that pregnancy. They ought to be compared to pregnant women who do not undergo induced abortion but continue their pregnancy to term (controlling, of course, for the effect of parity itself). The comparison the authors employ in their analysis of induced abortion is of no benefit to actual pregnant women, for whom “never having had that pregnancy” is not an option. For the sake of actual women’s breast health, the relevant comparison to a cohort with abortion history is a cohort experiencing only full-term pregnancy.

Note also that inappropriate comparisons were set up for Beral et al.’s more sophisticated analyses. For these analyses, when testing the influence of number of induced abortions, age at first induced abortion, number of years since an induced abortion, or the ordering of induced abortions and live births, the preferred reference group is parous women with no induced abortion history.

No distinction between first- and second-trimester spontaneous abortions. Finally, Beral et al. fail to distinguish, in their analysis of spontaneous abortions, between first- and second-trimester spontaneous abortions.

Given these serious methodological flaws and the confusion this study has caused, the best that can be done is to disregard this piece of research. It did not contribute to the steady march of scholarship or to clarity in epidemiological patterns of breast cancer development. Additionally, the study did much to confuse the uninformed, because Beral is a leading breast cancer researcher in a different genotoxin field, the use of estrogen/progesterone (so-called "hormone treatment" or "hormone replacement therapy") during or after menopause. For her Million Women Study, she was made Dame of the British Empire.[23)]

4. 2005 Brewster Study

One prospective study used in the much-quoted Beral re-analysis study is the Brewster Scottish prospective study (of which Beral herself was a co-author).[24)] The Brewster study is negatively affected by a glaring lack of data on parity, which diminishes its ability to distinguish the effect of differently timed induced abortions. The Brewster study introduced health bias into its analyses by including only "new incident breast cancers" and excluding women with a previous history of cancer, as well as excluding controls with cancer and women with a history of in situ breast cancer.

Lack of data on parity. This study included women "with all reproductive events occurring from 1981 onwards[, and] … with some reproductive events occurring before 1981, and number of pregnancies equalled number of births—*that is, no miscarriages or induced abortions before 1981* [italics added]."[25)] This resulted in an unknown age at first birth for nearly two-thirds of cases and controls, though the authors still chose to control for age at delivery of first child in their regressions. The absence of this important information forced the authors to construct the category "unknown sequence" for the purposes of analyzing order of their sample's reproductive events. Combining women whose parity status at the time of their abortion is unknown is of no benefit in identifying the breast cancer risk that abortion poses to different women.

Unsuitable comparisons. Furthermore, the analysis of the ordering and timing of women's reproductive events compares nulliparous aborting women, parous aborting women, and women the sequence of whose abortions and pregnancies are unclear to a reference category of women with "no abortion," without specifying whether these women are parous or nulliparous. Combining non-aborting nulliparous women (who generally have increased breast cancer risk) and non-aborting parous women (who generally have low breast cancer risk) would produce a non-aborting cohort with a breast cancer risk elevated over that of the ideal reference group. This elevated risk would mute the risk associated with abortion, by comparison.

This comparison employs almost 10,000 women with no induced abortion history, over 1,700 women with an unclear sequence of induced abortions and pregnancies, 876 parous (induced) aborting women, and only 155 nulliparous (induced) aborting women. The sequence of approximately two-thirds of the (induced) aborting women's reproductive histories is unknown. Almost all aborting women whose reproductive sequence is known (nearly one third—876 of 2,748) experienced the protection of live birth first. Those with unknown sequence are statistically like those who experienced live birth first: Both categories are statistically protective. The remainder, those who procured abortions while nulliparous, is very small (155 of 2,748). If the sequence of abortions and births matters more than parity—parity is used as a control variable in the rest of the table— or age at abortion, then all statistics in the other regressions are determined numerically by this dominating

effect and by the omitted variable bias of unknown sequence behaving like live birth first. This will decide all other regressions, because the category composed of women aborting while nulliparous (for this purpose, the women at risk) gets tiny weight in the regression: 155 women out of 2,748 is one tenth of the size of the group of women the sequence of whose abortions and births is unknown (1,717 of 2,748). The class adding noise (i.e., unknown sequences of abortion and pregnancy) is 10 times larger than the class whose sensitivity to breast cancer suspected to be most acute (because of their being both nulliparous and aborting).

Additionally, two-thirds of aborting women are shown to have breast cancer risk reduction resembling those who experience live birth first; but that their fertility information is not coded in any way immediately discernible in the other regressions makes it a huge, lurking factor that can bias all statistics. This may be why Brewster sees protective effects associated with abortion. For example: Procuring an abortion at age 30 or later is found to be significantly protective, but the study participants age 30 or older are likely to be the same participants the sequence of whose live births and abortions are unknown (due to the possibility of live births occurring before 1981).

Health or survivor bias. Finally, Brewster et al. excluded women with any history of cancer or of in situ breast cancer prior to their "diagnosis of breast cancer/hospital admission." The exclusion of women with a previous history of cancer is a health bias that could have introduced a large error into their analyses. No reason is given for the exclusion of in situ cancer. Furthermore, controls with cancer were excluded, another bias in their study.

5. 2007 Michels Study (the Harvard Nurses' Study)

The Michels study concluded that there was no increased risk of breast cancer with induced abortion.[26)] Because of the prestigious name of the dataset (the Nurses' Health Study II) and the Harvard University affiliations of some of the authors, the study's conclusions have had massive impact on the induced abortion-breast cancer debate despite its flaws, which are such that the study's conclusion could actually be reversed.

The Michels study suffers from the introduction of massive error through answers supplied by the authors to questions left half-blank, from unsuitable comparisons and the lack of distinction between first- and second-trimester spontaneous abortions, from follow-up time after (some fraction of) induced abortions insufficient to detect cancer, from sampling bias due to the study's focus on educated women, and from health bias or survivor bias from the exclusion of women with a history of previous cancer or of in situ breast cancer. These (and possibly other) flaws are serious enough for this study to be, unhappily, discounted.

The Michels study, which is based on data from the longitudinal Nurses' Health Study II, includes over 100,000 female nurses. These women were initially surveyed in 1989. Ninety-two percent of these were white.

Induced abortion. The Michels study found no significant influence for induced abortion on breast cancer risk, whether assessed generally, by the number of induced abortions, by the age at first induced abortion, or temporally (that is, with respect to the timing of first birth). No effect was distinguished when women were divided by parity status and then re-assessed according to their general induced abortion history and number of induced abortions.

When induced abortions were broken down (among nulliparous and parous women) by potential

relationship with specific types of breast cancer, induced abortion among parous women was found to have a positive, significant influence on the risk of PR-(progesterone receptor negative) breast cancer.

Spontaneous abortion. The Michels study found no significant influence on breast cancer risk for spontaneous abortion or number of spontaneous abortions. It did, however, find a significantly protective effect for spontaneous abortions taking place at or before age 19 (but no other age).

No effect for spontaneous abortions was found when women were distinguished by parity status and their general spontaneous abortion history and number of spontaneous abortions were assessed.

However, when assessed temporally, spontaneous abortions after first birth were found to have a marginally significantly protective (i.e., negative) influence on breast cancer risk. Spontaneous abortions before first birth were not found to have any significant influence on breast cancer risk.

No effect was detected for spontaneous abortions when they were broken down (among parous women) by potential relationship with specific types of breast cancer.

Unsuitable data handling. However, like many studies showing no effect for induced abortion on breast cancer risk, the Michels study contains many flaws. The statistical analysis section shows that the overall sample size includes more than 100,000 women. However, over 50,000 women neglected to complete the most important question on the baseline questionnaire, that on induced and spontaneous abortion. (Some only answered the half of the question addressing induced abortion, and some only answered the half addressing spontaneous abortion.) Interestingly, the authors note that "[w]e assumed that the women who answered only half of the question did not answer the other question because of an oversight or because they felt that the question did not apply to them." This assumption—that nondisclosure is evidence of an actual non-history of abortion—is mutually exclusive of the assumption that women intentionally withhold information about their induced abortion histories unless they feel it is necessary (for example, because of breast cancer) to disclose it. Furthermore, it is far from clear that the terse sensitivity analysis performed[27)] could correct for such a massive introduction of error as the one caused by nearly half the overall sample failing to answer the central questions in the survey.

Table 2 shows that the class of women with two or more induced abortions is fewer than 40 women. Said differently, there is a ratio of 50,000 total women to 40 women in the category of greatest concern (the women with two or more abortions) in a class of women where there is a massive error in response. For this reason, even properly done statistical modeling would hardly be able to conclude anything relevant regarding the effect of repeated abortion on breast cancer risk. This cohort of women is 1,000 times smaller than the group of women through which error has been introduced. The lack of demonstrated effect of repeated induced abortion on breast cancer in this analysis is not a demonstration of non-linkage between the two.

Unsuitable comparisons. Additionally, rather than comparing parous and nulliparous women procuring some number of induced abortions to the key reference group—parous women with only full-term pregnancies—the authors divided their analyses of abortion by parity status and compared nulliparous women who procured induced abortions to nulliparous women who did not procure induced abortions, and parous women who procured induced abortions to parous women who did not procure induced abortions. (Though they elsewhere assess the effect of induced abortion history while controlling for parity, this analysis fails to assess whether or not these women had the protection of full-term pregnancy at the time of their abortion.)

No distinction between first- and second-trimester spontaneous abortions. Notably, the measures, and thus the analysis, do not distinguish between first- and second-trimester spontaneous

abortions.

Insufficient follow-up time. Significantly, subjects who had abortions more than two years after the initial survey, during the study's follow-up time, were classified as having an abortion but were not followed long enough for any resultant cancers to develop to a detectable size. (Eight to 10 years is required for detectable breast cancer to develop after an abortion, based on cell doubling times, and so eight to 10 years is the minimum time required for follow-up.) This increased the number of women in the "abortion class" while decreasing the number of women in the "breast cancer class," a biasing of the outcomes against any abortion-breast cancer link. The authors' proportional hazard models attempt a correction for women followed for a shorter time; however, they do not contain within their formalism the reality posed by cell doubling times—that two or four years is simply not a long enough period to develop detectable breast cancer from an abortion.

Sampling bias (non-randomized sample). Furthermore, the study is marked by sampling bias. The study is 92 percent white and is entirely comprised of female registered nurses, whose IQ (i.e., that of women with at least a Bachelor's degree) is most likely at least one standard deviation higher than that of the general population. No controls are applied for race or for education. In his 2008 essay in Nature, University of Edinburgh professor of differential psychology Ian Deary noted that "[i]ntelligence can predict mortality more strongly than body mass index, total cholesterol, blood pressure or blood glucose, and at a similar level to smoking." Among other things, Deary noted that reduced mortality in high-IQ individuals could be attributed to healthier behaviors. The population studied in the Michels study is not representative of the general population. Hence, though Naieni et al. (and others) have found university education to be correlated with increased breast cancer risk, even results derived from a sound methodology regarding this sample of women would not be generalizable to the population at large.

Health or survivor bias. Finally, women with a previous history of cancer or with a history of in situ breast cancers were excluded from the study. No explanation was given for the exclusion of in situ breast cancer. Though it is highly unlikely that all 4,065 previously-diagnosed and excluded cancers were cancers of the breast, it is likely that some were. Furthermore, only 1,458 invasive breast cancers were found in the study. Thus it is possible that a large fraction of the total number of breast cancers with which respondents were (at any time) diagnosed was excluded, a health bias that could have skewed their data away from non-linkage of induced abortion and breast cancer.

6. 2008 Henderson Study (the California Teachers Study)

The Henderson study104—another study based on a large, "gold standard" dataset (the California Teachers Study)—concluded that there was no increased risk of breast cancer with abortion. The Henderson study has many weaknesses, including unsuitable comparisons that mute the effect of induced abortion, the survivor or health bias produced by the exclusion of women with previous history of breast cancer and women with in situ breast cancer, sampling bias through the confinement of the study to educated women, and failure to distinguish between first- and second-trimester spontaneous abortions.

This study assessed data collected for the California Teachers Study from 1995 to 2004, a nine-year period, on over 100,000 "current, recent, and retired female public school teachers and administrators."

Induced abortion. The Henderson study found no significant influence for induced abortion for

either parous or nulliparous women when assessed generally or when assessed by the number of induced abortions procured, by age at first induced abortion, or by year of first induced abortion.

Spontaneous abortion. The Henderson study found no significant influence for spontaneous abortion for either parous or nulliparous women when assessed generally, by the number of spontaneous abortions, or by age at first spontaneous abortion.

Unsuitable comparisons. However (as is evident by the results described above), rather than comparing all cohorts against women with only complete, full-term pregnancies, the authors of the Henderson study constructed two comparisons: one of nulliparous women and one of parous women. In the first, nulliparous women who had never been pregnant were compared to nulliparous women who had had abortions. This comparison is inappropriate. The breast cancer risk of the nulliparous women who have had abortions is less stark when compared to nulliparous women who have never been pregnant (rather than to the appropriate reference group); hence, the increased risk contributed by abortion is muted.

Unsophisticated analysis of induced abortion. The second comparison was of parous women who had had only full-term pregnancies and parous women who had procured abortions. This a correct comparison, but the critical data on the sequence of births and abortions among the parous and aborting cohort are missing. (It may exist in the raw dataset, but it was not analyzed in the written journal article.) As noted earlier, the sequence of these reproductive events is extremely important in establishing the breast cancer risk abortion contributes.

Health or survivor bias. Though the total number of women sampled who had an induced abortion is reported in the study, the time at which they had an abortion is not. All data regarding pregnancy history were collected by the time of the baseline questionnaire, meaning that all women were followed for at least nine years after an induced or spontaneous abortion. However, the youngest of the women could have obtained abortions 15 years before the time of the baseline questionnaire (and abortions procured by older women could be even further back in their reproductive pasts).105 Note that breast cancers resulting from induced abortions will likely become detectable about a decade to 14 years after the abortion is procured. Furthermore, women with a previous or unknown history of breast cancer were excluded from the studied cohort. Survivor or health bias was thus introduced into the study. This problem is all the greater because whereas a total of 3,325 women were diagnosed with breast cancer during the study, 6,319 women—nearly twice as many—with a previous history of breast cancer or whose breast cancer history was undetermined were excluded. Finally, like the Michels study, this study excluded the development of ductal in situ breast cancers. No explanation was offered for its exclusion. The authors would have done better to select a cohort with no reproductive events before a given date and to examine their cancer development or non-development thereafter, because by including only women with abortion history who were breast cancer-free until the baseline questionnaire, the authors biased their study's results away from abortion-breast cancer linkage.

Data not randomized. Like the Michels study, the Henderson study's population sample is biased. Their sample is mostly white, and (as noted earlier) the IQ of teachers (i.e., of women with at least a Bachelor's degree) is not representative of the general population. Henderson et al. control for race, but they do not control for education; hence, their results are not generalizable. The authors admit as much in their discussion: "The current results, may have limited generalizability. In addition to limited racial/ethnic diversity relative to the general female population of the United States, the CTS is characterized by a higher level of education and associated characteristics such as later age at first full-term pregnancy."

No distinction between first- and second-trimester spontaneous abortions. Finally, the

Henderson study fails to distinguish between first- and second-trimester spontaneous abortions. This is a shortcoming.

The presence of these biases are in line with an attitude expressed by one of the authors, Leslie Bernstein, in an interview in 2003, “I don’t want the issue relating induced abortion to breast cancer risk to be part of the mix of the discussion of induced abortion, its legality, its continued availability.”

As an aside, the Henderson study states in its introduction that no studies that collected prospective data showed a link between abortion and breast cancer. In stating this, it disregarded the Howe study, a record linkage study (that is, a study that links medical records) not subject to the recall bias or reporting bias they suggest taints retrospective studies, that showed a significantly increased risk of breast cancer with induced abortion.

7. 2013 Brauner Study

A 2013 study by Braüner et al. of parous Danish women108 found no association between induced abortion and breast cancer risk. This prospective study included women identified through the Danish Diet, Cancer and Health study and assessed the effect of induced abortion with respect to the timing of one’s first full-term pregnancy. However, the study has several weaknesses that render it insignificant.

Though this study is superior to other prospective studies in its methods and comparisons, it is rendered useless by the massive bias introduced by the 38 percent response rate to the Diet, Cancer and Health study, as well as a possible lack of generalizability. It is also marked by survivor or health bias in concert with the age of its cohort, by failing to assess the effect of repeated induced abortions, by including only parous women, and by failing to include adequate controls for other risk factors for breast cancer.

Induced abortion. The Braüner study found no significant influence for induced abortion, generally or before or after a live birth, on breast cancer risk.

Unsuitable data source. The study relied on data from the Diet, Cancer and Health study, which invited 79,729 women to participate. A mere 29,875 women accepted the invitation. Approximately 63 percent of participants chose to decline the invitation to participate in this study.

Data not randomized. The authors also note that “[t]he rationale behind the study design was to include highly motivated people, and consequently secure a high participation in the follow-up investigation…. Not unlike other follow-up studies, the women who refused to participate had a low socioeconomic status. The participation was greater among women with a high income and a higher education compared to other Danish women (13). The incidence of breast cancer was also higher in the study population.”109 Despite including controls for education, Braüner et al. include no controls for socioeconomic status, and as Patrick Carroll states in his letter to the editor of the journal in which the Braüner study appears, the authors do not note how much higher was the incidence of breast cancer in the study population.110 Hence, as the sample was not representative of the general Danish population, its results may be imperfectly generalizable to the general Danish population.

Health or survivor bias. Second, the study appears to be affected by the same sort of survivor bias or health bias that affects so many other studies. The authors excluded 337 women from their cohort who had previously experienced cancer. Though likely not all 337 cancer incidences were breast

cancer cases, the importance of these cases' exclusion becomes clear when one considers that the Braüner study only assessed 1,215 cases of breast cancer. Hence, up to 22 percent of breast cancers diagnosed within the cohort may have been excluded. This is a serious bias that would skew the results away from linkage of induced abortion and breast cancer.

The error becomes all the more egregious in light of the age of the cohort in the Braüner study. The women included were aged 50 to 65 at the time of their inclusion in the Diet, Cancer and Health study between 1993 and 1997, and they were followed for an average of 12 years thereafter. Given that breast cancer from an induced abortion will most likely show up around a decade to 14 years thereafter, it is likely that only abortions procured about 10 to 14 years before the baseline period, when the women sampled were between the ages of about 36 and 55, would produce breast cancer detectable during the study period. However, females' reproductive years are (approximately) between the ages of 15 and 45, and as demand for induced abortion among women over the age of 40 is relatively low,111 it may be that those breast cancers occurring as a result of earlier induced abortion were excluded. The breast cancers excluded may have been the only breast cancers caused by abortions—and thus precisely the breast cancers of interest to the study.

Too-simple analysis of induced abortion. Third, the study does not assess the effect of repeated induced abortion.

Restriction to parous women. Fourth, though the study utilizes the correct reference group (parous women with no abortion history), it restricts its analysis to parous women. Though the assessment of the effects of induced abortion on parous women is useful, there is also concern with the effect of induced abortion on nulliparous women, who never experience the protective benefit of full-term pregnancy.

Omitted variable bias. Finally, the study neglects to include some important variables in its analysis. Its model is incomplete and does not include family history of breast cancer or age at menarche, for example, in its regressions. The Braüner study also does not include spontaneous abortion in its analyses, let alone distinguish between first- and second-trimester spontaneous abortions.

[1)] Mads Melbye, Jan Wohlfahrt, Jørgen H. Olsen, Morten Frisch, Tine Westergaard, Karin Helweg-Larsen, and Per Kragh Andersen, "Induced Abortion and the Risk of Breast Cancer," *New England Journal of Medicine* 336, no. 2 (1997): 81-85.
[2)] Katherine W. Reeves, Alana G. Hudson, and Victor G. Vogel, "Chapter 19: Epidemiology of Breast Cancer" in eds. Kirby I. Bland and Edward M. Copeland III, 4th ed. *The Breast: Comprehensive Management of Benign and Malignant Disorders*, (Philadelphia: Saunders Elsevier, 2009), 333-348.
[3)] See Hartge's biography on the NCI website: "Dr. Hartge has conducted epidemiologic research at the National Cancer Institute (NCI) since 1977, investigating the etiology of lymphoma, melanoma, and cancers of the bladder, ovary, breast, pancreas, and brain. She developed and adapted a variety of methods widely used in cancer epidemiology. She has served as the Deputy Director of the Epidemiology and Biostatistics Program since 1996, and in that position, she has provided scientific direction and oversight to a large and productive program of research. She has championed the creation of multi-institution consortia in cancer epidemiology, co-founding the lymphoma consortium InterLymph in 2001 and chairing the NCI Cohort Consortium from 2006 through 2010." National Institutes of Health, National Cancer Institute, "Patricia Hartge, Sc.D.," National Cancer Institute. Available at http://dceg.cancer.gov/about/staff-bios/hartge-patricia. Accessed January 3, 2013.
[4)] Patricia Hartge, "Abortion, Breast Cancer, and Epidemiology," *New England Journal of Medicine* 336, no. 2 (1997): 127-128.
[5)] Abortion was legal up to 12 weeks in cases of rape, grave risk to the life or health of the mother, or birth defects. See Katarina Blomqvist, "The Rocky Road to Abortion on Demand," KVINFO, Danish

Centre for Information on Gender, Equality and Diversity.

[6] Induced abortion up to 12 weeks' gestation (and after 12 weeks, in many cases) became legal. See "DENMARK. Law no. 350 of 13 June 1973 on the interruption of pregnancy. (*Lovitidende for Kongeriget Danmark*, Part A, 6 July 1973, No. 32, pp. 993-995)," Berkman Center for Internet and Society at Harvard University. Available at http://cyber.law.harvard.edu/population/abortion/Denmark.abo.htm Accessed March 4, 2013.

[7] In 1968-1972, abortions numbered 6,450 (1968), 7,300 (1969), 9,375 (1970), 11,522 (1971), and 13,667 (1972). In 1973, 16,536 abortions were performed, and in 1974, in the first full year of the law's liberalization, abortions numbered 24,868. Thereafter, the number of abortions fluctuates, but generally stays in the low twenty-thousands. See Wm. Robert Johnston, "Historical Abortion Statistics, Denmark", *Abortion statistics and other data–Johnston`s Archive*, March 11, 2012, http://www.johnstonsarchive.net/policy/abortion/ab-denmark.html, accessed March 4, 2013).

[8] Melbye et al. rather misleadingly note that "neither the calendar period at the time of diagnosis of breast cancer (P=0.17) nor the calendar period at the time of induced abortion (P=0.83) modified the relation between induced abortion and the risk of breast cancer." (See Mads Melbye, Jan Wohlfahrt, Jørgen H. Olsen, Morten Frisch, Tine Westergaard, Karin Helweg-Larsen, and Per Kragh Andersen, "Induced Abortion and the Risk of Breast Cancer," *New England Journal of Medicine* 336, no. 2 (1997): 83.) However, what they show here is merely that the *year in which one procures an induced abortion has no effect on individual risk of developing breast cancer.* Their result is unsurprising. The (lower-order) result that they fail to report is *whether the legalization of abortion affected breast cancer incidence*.

[9] See V. Beral, D. Bull, R. Doll, R. Peto, G. Reeves, Collaborative Group on Hormonal Factors in Breast Cancer, "Breast Cancer and Abortion: Collaborative Reanalysis of Data from 53 Epidemiological Studies, Including 83,000 Women with Breast Cancer from 16 Countries," *The Lancet* 363, (2004): 1008. Though Beral and colleagues list 1938 as the year in which "legal abortion services" became available in Denmark, as noted earlier, abortion before 12 weeks' gestation was available only under certain circumstances from 1939-1973.

[10] Mads Melbye, Jan Wohlfahrt, Jørgen H. Olsen, Morten Frisch, Tine Westergaard, Karin Helweg-Larsen, and Per Kragh Andersen, "Induced Abortion and the Risk of Breast Cancer," *New England Journal of Medicine* 336, no. 2 (1997): 83.

[11] As John Boyd, famed aerospace engineer and military strategist used to say, "The most important data are the data that do not fit. That's where science advances."

[12] See Appendix D in Induced Abortion and Breast Cancer for further explanation

[13] M.J. Goldacre, L.M. Kurina, V. Seagroatt, and D. Yeates, "Abortion and Breast Cancer: A Case-Control Record Linkage Study," *Journal of Epidemiology and Community Health* 55, no. 5 (2001): 336-337.

[14] Here is a putative interaction. Women in their 30s in the 1960s are only in their 60s in the 1990s. All those older (later 60s, or in their 70s or even 80s) will have statistically unmeasurable abortion rates. (In the 1960s, when abortion was legalized, these older women were too late, relative their fertile period, to demand abortions. The diminished number of abortions in their population is evident: As noted below, whereas barely 1 percent of their cases had an abortion over 30 years, the abortion rate in the UK was over one percent per year across those 30 years!) These older women have a plurality of the breast cancer cases. Older women get more breast cancer. In the calculation of "observed" rates of cancer they will not be counted, because they are unmeasurable. Upon re-aggregating the age stratification, the "observed" category (those with abortions) will lack this contributing population (older women) and so not have representative breast cancer rates, as represented in the Goldacre findings.

[15] National Cancer Institute. U.S. National Institutes of Health, *Summary Report: Early Reproductive Events and Breast Cancer Workshop*, (Mar 25, 2003); as cited in Joel Brind, "Induced Abortion as an

Independent Risk Factor for Breast Cancer: A Critical Review of Recent Prospective Studies Based on Prospective Data," *Journal of American Physicians and Surgeons* 10, no. 4 (Winter 2005): 107.

[16] M.J. Goldacre, L.M. Kurina, V. Seagroatt, and D. Yeates, "Abortion and Breast Cancer: A Case-Control Record Linkage Study," *Journal of Epidemiology and Community Health* 55, no. 5 (2001): 337.

[17] V. Beral, D. Bull, R. Doll, R. Peto, G. Reeves, Collaborative Group on Hormonal Factors in Breast Cancer, "Breast Cancer and Abortion: Collaborative Reanalysis of Data from 53 Epidemiological Studies, Including 83,000 Women with Breast Cancer from 16 Countries," *The Lancet* 363, (2004): 1007-1016.

[18] David Wahlberg, "Study: Breast Cancer Not Tied to Abortion; Group Backs Up Institute's Earlier Findings," *Atlanta Journal-Constitution* (March 26, 2004): A9.

[19] V. Beral, D. Bull, R. Doll, R. Peto, G. Reeves, Collaborative Group on Hormonal Factors in Breast Cancer, "Breast Cancer and Abortion: Collaborative Reanalysis of Data from 53 Epidemiological Studies, Including 83,000 Women with Breast Cancer from 16 Countries," *The Lancet* 363 (2004): 1007-1016.

[20] A.E. Laing, G.E. Bonney, L. Adams-Campbell, et al., "Reproductive and Lifestyle Risk Factors for Breast Cancer in African-American Women," *Genetic Epidemiology* 11, (1994): A300;
D.G. Zaridze data (unpublished) in N. Andrieu, S.W. Duffy, T.E. Rohan, M.G. Lê, E. Luporsi, M. Gerber, R. Renaud, D.G. Zaridze, Y. Lifanova, and N.E. Day, "Familial Risk, Abortion and Their Interactive Effect on the Risk of Breast Cancer—A Combined Analysis of Six Case-Control Studies," *British Journal of Cancer* 72, no. 3 (1995): 744-751;
E. Luporsi, "Breast Cancer and Alcohol," (PhD thesis, University of Paris-Sud, 1988), data in N. Andrieu, S.W. Duffy, T.E. Rohan, M.G. Lê, E. Luporsi, M. Gerber, R. Renaud, D.G. Zaridze, Y. Lifanova, and N.E. Day, "Familial Risk, Abortion and Their Interactive Effect on the Risk of Breast Cancer—A Combined Analysis of Six Case-Control Studies," *British Journal of Cancer* 72, no. 3 (1995): 744-751;
L. Bu, L.F. Voigt, Z. Yu, K.E. Malone, and J.R. Daling, "Risk of Breast Cancer Associated with Induced Abortion in a Population at Low Risk of Breast Cancer," *American Journal of Epidemiology* 141, (1995): S85 (abstract 337);
Lynn Rosenberg, Julie R. Palmer, David W. Kaufman, Brian L. Strom, David Schottenfeld, and Samuel Shapiro, "Breast Cancer in Relation to the Occurrence and Time of Induced and Spontaneous Abortion," *American Journal of Epidemiology* 127, no. 5 (1988): 981-989.

[21] The type of publication bias they hope to avoid is the bias in journals against publishing studies with null results (i.e., those that show no effect for a given variable). This bias is a problem in epidemiology, though it does not seem to affect the field of induced abortion research. When a study finds no effect, it is widely discussed and its findings are promoted vigorously; when a study finds induced abortion to have an effect, its findings are often dismissed as the mere result of recall bias.

[22] Beral and colleagues attempt to determine what would have happened had these women not experienced the pregnancy that they aborted. This is a counterfactual. "For a given population, a counterfactual asks, 'What if an identified policy [change] had not happened?'" See Henry Potrykus, *Causal Determination for Social Policy: Counterfactuals, Natural Experiments, Population Shifts*, Marriage and Religion Research Institute, (February 7, 2013). Available at http://marri.us/research/research-papers/causal-determination-for-social-policy/. Accessed July 18, 2013.

[23] The "Million Women Study" applied the *opposite* methodology from Beral's abortion reanalysis. Beral and colleagues did not compare women undergoing "hormone replacement therapy" to women their age who were *not menopausal*; they compared them to other women their age who were *menopausal and not undergoing "hormone replacement therapy"!* They employ the latter comparison and not the former because older women who are not menopausal are a higher-risk group, and the increased risk associated with "hormone replacement therapy" would be muted by comparison. However, the former type of comparison (i.e., the comparison between nulliparous women and women with abortion history) is commonly employed among those who study the link between abortion and breast cancer. Joel Brind deals extensively with this matter in his 2007 published

testimony to the British Parliamentary committee studying the impact of abortion. See Joel Brind, "Scientific Developments Relating to the Effect of Abortion on Risk of Future Breast Cancer," *Memorandum* 14: *Scientific Developments Relating to the Abortion Act 1967*, Twelfth Report of Session 2006-7 (London: The Stationery Office Limited, 2007), 96-97.

[24] David H. Brewster, Diane L. Stockton, Richard Dobbie, Diana Bull, and Valerie Beral, "Risk of Breast Cancer after Miscarriage or Induced Abortion: A Scottish Record Linkage Case-Control Study," *Journal of Epidemiology and Community Health* 59, (2005): 283-287.

[25] David H. Brewster, Diane L. Stockton, Richard Dobbie, Diana Bull, and Valerie Beral, "Risk of Breast Cancer after Miscarriage or Induced Abortion: A Scottish Record Linkage Case-Control Study," *Journal of Epidemiology and Community Health* 59, (2005): 284.

[26] Karin B. Michels, Fei Xue, Graham A. Colditz, and Walter C. Willett, "Induced and Spontaneous Abortion and Incidence of Breast Cancer among Young Women," *Archives of Internal Medicine* 167, no. 8 (2007): 814-820.

[27] Karin B. Michels, Fei Xue, Graham A. Colditz, and Walter C. Willett, "Induced and Spontaneous Abortion and Incidence of Breast Cancer among Young Women," *Archives of Internal Medicine* 167, no. 8 (2007): 816.

This entry draws heavily from Induced Abortion and Breast Cancer.