Studies that Confirm the Abortion-Breast Cancer Link

Ecological epidemiological studies use gross vital-statistic-like data, such as the incidence of breast cancer or abortions in a county, state, or country. Patients are not interviewed, and hospital records are not examined.

Two ecological epidemiological studies, the 1989 Remennick Study and the 2007 Carroll Study, show a strong association between induced abortion and breast cancer. Another 19 epidemiological studies show some relationship between induced abortion and breast cancer. These 19 studies occur across diverse countries and cultures—from Japan and China, to Iran and Armenia, to Germany and the United States. They are organized chronologically and (loosely) in order of increasing statistical and methodological sophistication.

1. 1989 Remennick Study

Larissa Remennick's 1989 study of breast and cervical cancers in the USSR showed a "consistent association between abortion rates…and incidence of both breast and cervical cancers."[1)] The author notes that abortions exceeded live births in the years following abortion's legalization in 1955, due to the procedure's use as the nation's primary means of birth control.

Induced abortion. Remennick found that, overall, the induced abortion rate was the fourth-ranked variable in determining age-adjusted breast cancer incidence (after cumulative fertility rate, early marriage prevalence, and early age at first birth prevalence). This finding is remarkable given the small percentage of women aborting in primigravidas (that is, aborting their first pregnancies) and given that all induced abortions here are aggregated and not parsed out (e.g., by their timing related to first full-term pregnancy). However, the very fact that a small percentage of women aborted in primigravidas provides a clear picture of the potential effects of repeated abortions, even when they take place after full-term pregnancy.

2. 2007 Carroll Study

Induced abortion. In 2007, actuary Patrick Carroll found,[2)] with an empirical model that he built from English and Welsh data, that of the four reproductive risk factors he tested, the greatest predictor of future breast cancer incidence was a nation's abortion rate. Nulliparous abortions, in particular, were significant in determining breast cancer rates.

Carroll also found that falling fertility affected the incidence of breast cancer. Using national abortion, fertility, and breast cancer registries, Carroll made predictions regarding breast cancer rates in nine European countries (England, Wales, Scotland, Northern Ireland, the Irish Republic, Sweden, the Czech Republic, Finland, and Denmark).

3. 1957 Segi Study

The first epidemiologic study examining breast cancer and abortion was published in 1957 in Japan.[3] As the study is written—with data broken down by number of pregnancy outcomes (e.g., induced abortion, miscarriage), rather than by women experiencing these outcomes—the results are not comparable to those of other studies. However, in his 1996 meta-analysis, Joel Brind uses other Japanese studies to approximate the average number of induced abortions to which each woman with induced abortion history was exposed.

As Brind notes, the Segi study only includes parous women, and the control population is "slightly older than the patient population," but by his estimation, the study shows evidence of a statistically significant increase in the risk of breast cancer among women with a history of induced abortion.[4]

4. 1981 Pike Study

The first U.S. study of abortion and breast cancer in 1981,[5] which analyzed the history of a total sample of 435 Los Angeles County women, also suggested an increased (though perhaps not significant) risk of breast cancer with induced abortion.

This study is insufficiently randomized, has a small sample, is based on interviews conducted over the telephone, is marked by sampling bias and survivor or health bias, and may suffer from reporting difficulties surrounding abortion law change. Its cases and controls differ across risk factors other than induced abortion, several possible breast cancer risk factors are left out of its analyses, and its analyses are not multiple regressions. Additionally, its analysis does not distinguish between induced and spontaneous abortion. Many of these are a consequence of its early, exploratory nature; regardless, this study was a very important step in the development of the field of induced abortion and breast cancer.

The case-control study included 163 white breast cancer patients diagnosed, before the age of 33, between July 1972 and December 1978 and identified through the University of Southern California Cancer Surveillance Program. These cases were matched with 153 neighborhood controls and 119 friend controls.

Small sample, limited generalizability, unsuitable data collection means. Pike's sample is quite small. That all participants were white would limit the generalizability of the study's findings. Additionally, the interview's administration over the telephone could diminish any influence of induced abortion through underreporting.

Health or survivor bias. Deceased cases were excluded, and this survivor bias may have weakened the demonstrated effect of induced abortion. Furthermore, "controls had to be malignancy-free," and this health bias may have skewed the demonstrated effect of induced abortion.[6] However, the restriction of the study to women under 33 reduces the likelihood that a very early abortion resulting in breast cancer would eliminate women diagnosed with breast cancer before the start of the study, a problem we discuss in detail above.

Reporting difficulty around abortion law change. Following the signing of the 1967 Therapeutic Abortion Act,[7] the data seem to show that the incidence of induced abortion increased markedly.[8]

Because of the time frame of this study, and because of the eight to 10 years required for the development of detectable breast cancers, it is likely that some fraction of the women with detectable cases of breast cancer in this sample had legally procured abortions and some women had illegally procured abortions. (All women were residing in Los Angeles County at the time of their diagnosis, but it may be that some did not live in California at the time of their abortion or procured their abortion elsewhere.) It would have been interesting to assess the timing of the induced abortions alongside corresponding breast cancer diagnoses.

Lack of multivariate regressions, neglect of potential breast cancer risk factors. It is clear that the case and control groups differ significantly across risk factors other than induced abortion. Also, the authors appear not to have conducted multivariate regressions or applied multiple controls to their analysis of induced abortion (or of other risk factors). Some potential breast cancer risk factors appear to have been left out of their analysis. This is likely a consequence of the study's early date. Lacking multiple controls, this study may attribute the influence of such variables as lower or late parity (or both) or use of oral contraception on breast cancer to induced abortion. Regardless, as we note above, this study—like other such early, developmental, suggestive studies—was a step in the development of the field of induced abortion and breast cancer.

Pregnancy outcomes. The authors found a significant increase in breast cancer risk among women who experience an "early" abortion (i.e., an abortion before 12 weeks' gestation) prior to their first full-term pregnancy. They do not distinguish between induced and spontaneous abortion; 11 of the 24 abortions among cases and eight of 17 abortions among the controls were induced. Those women who subsequently had a full-term pregnancy saw a somewhat reduced risk of breast cancer, though the authors do not specify how precisely this risk reduction is determinable. The authors also note that abortions after first full-term pregnancy or after three months' gestation did not appear to increase one's risk of breast cancer. Pike et al. do not assess the influence of induced abortion history, in general, or the influence of repeated induced abortions or gestational period of or maternal age at induced abortion.

Full-term pregnancy and age at first full-term pregnancy. Ever having a full-term pregnancy and age at first full-term pregnancy (as a trend) were not found to significantly affect the risk of breast cancer.

Various risk factors. History of breast cancer in one's mother or sister, history of benign breast disease, and earlier age at menarche (as a trend—younger than 12 versus at age 12 or at age 13 or older) were all found to significantly increase the risk of breast cancer.

Oral contraceptive use duration, timing, and interaction with other factors. As a trend, increasing the duration of oral contraceptive use was shown to have a positive and statistically significant influence on breast cancer risk. Versus never using oral contraception, using oral contraception for up to four years contributed to a slight increase in risk, and use for more than four years contributed to a larger increase in risk.

As a trend, oral contraceptive use prior to first full-term pregnancy for up to four years contributed to a very slight increase in risk. Using oral contraception prior to first full-term pregnancy for four to eight years, or for eight years or longer, contributed to ever more marked increases in breast cancer risk. No clear trend was detectable in an analysis of duration of oral contraceptive use after first full-term pregnancy (this analysis was conducted among parous women only).

Oral contraceptive use before first full-term pregnancy appeared to have a greater effect on breast cancer risk in concert with benign breast disease, though the number of cases and controls considered is very small and the authors do not show how precisely determinable is the risk.

Induced abortion. In his 1996 meta-analysis, Joel Brind distinguishes between induced and spontaneous abortions in the 1981 Pike study and found, unadjusted for other factors, that the impact of induced abortion prior to first full-term pregnancy had a positive but slightly reduced and statistically insignificant influence on breast cancer risk.[9)]

5. 1982 Nishiyama Study

Brind notes in his 1996 meta-analysis[10)] that the 1982 Nishiyama study,[11)] which was written in Japanese, "compared 767 radical mastectomy patients from a single prefecture in Japan with an equal number of age matched, normal controls identified through a mass breast cancer screening programme." According to Brind's report, the Nishiyama study showed induced abortion to have a positive, significant influence on breast cancer risk.

6. 1988 Ewertz and Duffy Study

In 1988, Ewertz and Duffy[12)] found that having one induced abortion contributed to increased risk of breast cancer among Danish women. This study is marked by health and survivor bias, its analyses neglect some breast cancer risk factors and are not multivariate regressions, it may be marked by difficulties related to reporting and induced abortion law changes, and in some cases it does not distinguish between induced and spontaneous abortion (e.g., when assessing the influence of breast cancer with respect to the timing of one's first full-term pregnancy). Regardless, as in the case of the Pike study, Ewertz and Duffy's study was a step in the development of the field of induced abortion and breast cancer.

The authors conducted a study comprised of 1,486 cases and 1,336 controls residing in Denmark. The cases were women under 70 years of age who had been diagnosed with invasive breast cancer or carcinoma in situ between March 1983 and March 1984, who were identified through the Danish Breast Cancer Co-operative Group and the Danish Cancer Registry. Controls were identified through the Danish Central Population Registry.

Health or survivor bias. The Ewertz and Duffy study is marked by health and survivor bias. Cases and controls with previous history of breast cancer were excluded.[13)] Some cases died, and some were not notified in time to participate in the study, so they were excluded as well. Most women in the Ewertz and Duffy study—around 90 percent of those who responded to the invitation to participate in the questionnaire—were diagnosed after age 40: around one-third were diagnosed in their 40s, around one third were diagnosed in their 50s, and around one-third were diagnosed in their 60s. If breast cancer resulting from an induced abortion is most likely to manifest itself around a decade to 14 years after the abortion's being procured, then the exclusion of women with a previous history of breast cancer likely eliminated all women whose breast cancer was the result of an induced abortion. These survivor or health biases could have skewed the study's results away from induced abortion-breast cancer linkage.

Reporting difficulty around abortion law change. The study also may be marked by difficulties related to abortion law changes. As we note in our analysis of Melbye et al., induced abortion law was liberalized in Denmark in 1973 (around a decade before the breast cancers included in this study were diagnosed). Many women diagnosed with breast cancer in the Ewertz and Duffy study were well

past their reproductive years and, hence, past any "need" for induced abortion at the time of its legalization. These women may have procured illegal abortions and may be reluctant to report them for the purposes of the study. Their classification as non-aborting may have skewed the data away from induced abortion-breast cancer linkage.

Lack of multivariate regressions. The authors analyze and control for differences between age at diagnosis, marital status, and residence between cases and controls, but their analyses are not multivariate regressions. Lacking multiple controls, this study may attribute the influence of other variables on breast cancer to induced abortion. Their various analyses include variables for age at menarche, age at natural menopause, menopausal status, whether one's first pregnancy was incomplete, number of full-term pregnancies, age at first full-term pregnancy, type (e.g., spontaneous or induced) and timing of abortion (relative to first full-term pregnancy), type of cancer contracted, and oral contraceptive use.

Pregnancy outcomes. In their general model, Ewertz and Duffy adjust their risk ratios for age at breast cancer diagnosis and place of residence. Relative to one's first pregnancy being a full-term pregnancy (by which Ewertz et al. mean a pregnancy lasting 28 weeks or longer), "early termination" of one's first pregnancy positively and significantly influenced one's risk of breast cancer. Never experiencing pregnancy also positively and significantly increased one's risk of breast cancer.

Relative to women with no induced or spontaneous abortions (whose first pregnancy was carried to term), among women with no full-term pregnancies, experiencing any type of abortion (spontaneous or induced) was found to increase one's risk of breast cancer.

However, no significant effect was found based on the timing of abortion relative to one's first full-term pregnancy. This may be because, though the authors distinguish abortions as taking place either before or after first full-term pregnancy and based on the trimester in which they take place, they fail to distinguish between spontaneous and induced abortions. We assume they have chosen not to do so because the resulting categories would be too small for any "signal" to be perceptible above fluctuations (in responses) from other sources of error.

Too-simple analysis of abortion. Ewertz and Duffy did not assess the influence of maternal age on either general abortion or abortions broken out by type (induced and spontaneous) on breast cancer risk.

Induced abortion. When stratifying by type of abortion, the authors found that one induced abortion among women with no full-term pregnancies had a positive, significant influence on breast cancer risk, relative to women with no induced or spontaneous abortions (i.e., those women whose first pregnancy was carried to term). That a significant effect was detected is all the more remarkable considering that, compared to 1,142 cases and 1,116 controls with no abortion history, only 13 cases and three controls had induced abortion history.

Spontaneous abortion. No significant effect was found for first-trimester spontaneous abortions or for second-trimester spontaneous abortions. Though the latter contradicts our hypothesis, it may be merely due to the fact that only three cases and two controls had had a second-trimester spontaneous abortion.

Ewertz and Duffy chose the correct comparison group for their aborting cohorts— women with no abortions and at least one full-term pregnancy.

Number of full-term pregnancies. Relative to having only one full-term pregnancy, having four or more full-term pregnancies was significantly protective against breast cancer. (One's first pregnancy

continuing to term, we have already seen, is protective, relative to early termination or never being pregnant. Having four or more full-term pregnancies is not merely protective, relative to nulliparity; it is protective relative to having one full-term pregnancy!) As a trend, increasing the number of full-term pregnancies was negatively correlated with breast cancer risk, and this trend was precisely determinable. The authors would have done well to use nulliparity as the reference category in their analysis of the number of full-term pregnancies. As their regression tables are currently designed, the benefits of increasing numbers of full-term pregnancies are less than clear.

Age at first full-term pregnancy. No particular age at first pregnancy was found to be significantly protective, and as a trend, age at first pregnancy was not found to have any significant association with breast cancer risk.

No significant association was found between age at first full-term pregnancy and type of breast cancer (ductal or lobular) contracted.

Number of full-term pregnancies and age at first full-term pregnancy. Among women with two full-term pregnancies, experiencing first full-term pregnancy between ages 20 and 24, between ages 25 and 29, and at age 30 or older provided increasingly greater protection against breast cancer, relative to experiencing first full-term pregnancy prior to age 20. As a trend, increasing age at first full-term pregnancy among women with two full-term pregnancies was associated with decreased breast cancer risk. No significant associations were found among women with one, three, or four or more full-term pregnancies.

Among women whose first full-term pregnancy was between ages 20 and 24, an increasing number of full-term pregnancies was associated with decreased breast cancer risk, as a trend. No significant effect was found for an increasing number of full-term pregnancies among women whose first full-term pregnancy occurred prior to age 20, between ages 25 and 29, or at or after age 30.

When adjusted for age at first full-term pregnancy, having four or more full-term pregnancies was shown to be even more protective than in the general model, relative to having one full-term pregnancy. As a trend, an increasing number of full-term pregnancies (adjusted for age at first full-term pregnancy) was associated with reduced breast cancer risk, and this trend was precisely determinable.

Number of full-term pregnancies and age at breast cancer diagnosis. When analyzed in concert with age at breast cancer diagnosis, any number of full-term pregnancies was protective against breast cancer, relative to nulliparity. This was especially true among women diagnosed between ages 50 and 59.

Age at first full-term pregnancy and age at breast cancer diagnosis. The risk associated with increasing age at first full-term pregnancy increased among women diagnosed before age 60 but decreased among those diagnosed after age 60.

Number of full-term pregnancies, age at first full-term pregnancy, and diagnosis with breast cancer before or after age 60. The authors tentatively suggest that whereas age at first full-term pregnancy is of more importance than parity among women diagnosed before age 60, parity may be of more importance than age at first full-term pregnancy thereafter. Interpreted: One’s age at first full-term pregnancy is determined at least in part by procured abortions and use of contraception. Any effect of these factors can only persist for a decade to 14 years or so after exposure.[14)] Hence, age at first full-term pregnancy is important in determining breast cancer risk prior to age 60: the effects of abortion and hormonal contraception are unlikely to persist long after

the reproductive years have ended and these factors are no longer active. After age 60, these factors are no longer active. The body is susceptible to other environmental factors, and one's susceptibility is determined by parity (i.e., how much protection has been built up in the body), which is less directly affected by use of oral contraceptives and induced abortion. However, the authors note that "[f]ormal statistical significance was…barely reached in these analyses, so interpretation must be cautious."

Age at menarche. Ewertz and Duffy find menarche at 15 years of age or 16 years of age or older to be significantly protective against (i.e., to be negatively correlated with) breast cancer, relative to menarche prior to age 13. As a trend, increasing age at menarche was negatively associated with breast cancer risk, and this trend was very precisely determinable.

Menopausal status and age at menopause. Being postmenopausal had a significantly negative influence on breast cancer risk. Having commenced menopause between the ages of 50 and 55 also had a significant and positive influence on breast cancer. As a trend, increasing age at menopause was associated with increased risk of breast cancer, and this trend was precisely determinable.

Various risk factors. The general model does not include variables for oral contraceptive use or smoking. This is a weakness and a consequence of the study's early, exploratory nature.

7. 1989 Howe Study

Howe et al.[15] found in 1989 that induced abortions before 20 weeks' gestation had a positive, significant influence on breast cancer risk. The study is flawed by a lack of data on parity for women who did not experience an induced or spontaneous abortion, short time period between abortion and breast cancer diagnosis, possible reporting difficulties surrounding abortion law change, underreporting and inconsistent distinguishing between induced and spontaneous abortions, a lack of distinction between first- and second-trimester spontaneous abortions, an apparent lack of multiple controls, and a small model. However, the authors restrict their analysis to women under 40 at the time of their diagnosis, an effort that would have protected their analysis to some degree from health or survivor bias, and their model is a record linkage model, eliminating any possibility that the "recall bias" or differential "reporting bias" between cases and controls that some assert undermines case-control studies could taint their work.

The authors identified 1,451 women with breast cancer using public records in New York State (excluding women in New York City), which legalized abortion on demand up to 24 weeks in 1970. One control was matched to each case using New York State driver's license records. All women were matched to public health records on incidence of fetal death, whether a fetal death occurred through spontaneous abortion or induced abortion, between 1971 and 1980. (Fetal deaths after breast cancer diagnosis were not included.) These records also included information on previous pregnancies and their outcomes. The study's sample was confined to pregnancies lasting 20 weeks or fewer.

Lack of data on parity. One hundred cases and 63 controls—not a large sample— were found to have had abortions prior to 20 weeks' gestation. Data regarding pregnancies and their outcomes among women who did not have a reported fetal death were not available, and this may have affected the risk of abortion as it is demonstrated in the study.

Insufficient follow-up time. Another shortcoming that affects the study is the lack of time between fetal death and breast cancer diagnosis. As noted earlier, all diagnoses took place between 1976 and 1980, and all fetal deaths were recorded between 1971 and 1980. Though it is unlikely that a spurious

association between abortion and breast cancer would have been created by a lack of follow-up time after fetal death, this dearth of time may have weakened induced abortion's demonstrated influence on breast cancer.

Reporting difficulty around abortion law change. Furthermore, though (as the authors note) abortion was available on demand as of July 1970 in New York State, many of the respondents' reproductive years would have taken place prior to the law's liberalization. This may also have weakened any effect due to induced abortion.

Incomplete distinction between induced and spontaneous abortions. Finally, Howe et al. note "some evidence for underreporting and inconsistent reporting of early pregnancy terminations." For example, some women did not report recorded induced abortions, and some women had reported their abortions were spontaneous when they were recorded as induced. The authors indicate (though they do not demonstrate) that the incidence of this underreporting and inconsistent reporting was approximately even across both cases and controls. However, it is possible that the reporting of induced abortions as spontaneous abortions in case-control studies could skew a study's findings away from induced abortion-breast cancer linkage and show some small positive effect for spontaneous abortions. Additionally, some analyses in the study do not distinguish between induced and spontaneous abortions; these analyses are thus of limited use to the reader.

Record linkage model (no possible "recall bias"). That the study's material proceeds from linked records, however, is a definite strength. Some critics of case-control studies argue that controls may underreport their abortions; the record linkage model (that is, a model that links medical records) employed by Howe et al. eliminates the likelihood that women would underreport abortions based on their status as a case or a control because, at the time the report of fetal death was taken, the cases had not yet been diagnosed with breast cancer.

An attempted reduction of health or survivor bias. All cases were under age 40 at their diagnosis, which took place between 1976 and 1980. This restriction to women still in their reproductive years may have reduced health or survivor bias in their study.

Lack of multivariate regressions. The authors did not build a large model. Howe et al. appear to have assessed the differences between aborting women and the general sample regarding demographic (age at diagnosis, marital status, education, race) and other factors, but not to have thusly adjusted the odds ratios associated with abortion. These factors include age at first pregnancy (between women who did and did not carry their first pregnancy to term), age at first live birth (between cases and controls), age at first "pregnancy interruption" (between cases and controls), average total number of pregnancies (between cases and controls), and average length of gestation (between cases and controls). Their analyses appear not to be multivariate analyses. Lacking multiple controls, this study may attribute the influence of other variables on breast cancer to induced abortion. Howe et al. also neglect to assess the differences between cases and controls on some breast cancer risk factors: Among other factors, their analysis neglects oral contraceptive use, smoking, number of full-term pregnancies, age at menopause, or menopausal status (though, because all women studied were diagnosed prior to age 40, these last two variables are of less concern).

Pregnancy outcomes. In their initial analysis of the effects of abortion before 20 weeks' gestation (spontaneous and induced abortions combined), they find no effect when a first pregnancy ends in abortion. Howe et al. find (combined) abortions after a first pregnancy to have a significant, positive influence on breast cancer risk. When all pregnancies ending in abortion are combined, they are

found, as well, to have a significant, positive influence on breast cancer risk.

When spontaneous and induced abortions are distinguished, no significant effect is found for spontaneous abortions or among women who had both spontaneous and induced abortions. Induced abortions were found to have a positive, significant influence on breast cancer risk.

Too-simple analysis of induced abortion, no distinction between first- and second-trimester spontaneous abortions. Howe et al. do not assess the influence of gestational age or maternal age at the time of induced abortion or spontaneous abortion. They also do not distinguish between first- and second-trimester spontaneous abortions.

Repeated incomplete pregnancies. Howe et al. also note that they find "a history of repeated interrupted pregnancies with no intervening livebirths" to have a positive and significant influence on breast cancer risk. This is stated in the text and not demonstrated in a table, but the odds ratio and confidence interval are stated. This analysis includes both induced and spontaneous abortions.

8. 1993 Laing Study

Laing et al.'s study of breast cancer in African-American women in Washington, D.C., was released in 1993.[16)] The study cited a need for specific research into breast cancer in black women because of an uptick in breast cancer incidence among under-40 black women and an increase in breast cancer mortality among black women younger than 50. The study found induced abortion had a positive, significant influence on breast cancer risk among women diagnosed at age 50 or older and a positive, marginally significant influence among women diagnosed between the ages of 41 and 49. This study is of limited generalizability (because of its exclusion to African-American women), is marked by health bias, excludes important data on various important breast cancer risk factors (and thereby risks introducing omitted variable bias), contains possible reporting difficulties surrounding abortion law changes, fails to distinguish between first- and second-trimester spontaneous abortions, and conducts an unsophisticated analysis of induced abortions.

Limited generalizability, health or survivor bias. The study included 503 African-American cases identified through Howard University Hospital in Washington, D.C., between 1978 and 1987. Five hundred thirty-nine African-American age-matched controls who presented with "nonmalignant conditions" at the same hospital were also included in the study. This restriction of the study to African-American women limits its generalizability, and the exclusion of controls with breast cancer is a health bias that could skew the results of their analysis away from linkage between induced abortion and breast cancer.

Exclusion of some potential breast cancer risk factors. Laing et al. identify the differences between their cases and controls and analyze them in a fairly thorough model. They do not include data on age at first full-term pregnancy, education, smoking, or alcohol use, and therefore risk introducing omitted variable bias, but they do control for number of induced abortions, number of spontaneous abortions, parity, oral contraceptive use, lactation, age at menarche, menopausal status, and marital status.

Induced abortion. Women aged 50 or older at their breast cancer diagnosis who had induced abortion history had a significantly increased risk of breast cancer, relative to women with no history of induced or spontaneous abortion. Women aged 41 to 49 at their breast cancer diagnosis who had induced abortion history had a marginally significantly increased risk of breast cancer. No significant effect was detected with induced abortion among women diagnosed at age 40 or younger.

Laing et al. note evidence of possible underreporting among older controls, which may have shifted the odds ratio associated with breast cancer and abortion upward. The authors state that whereas consistent numbers of cases report induced abortions across age at diagnosis categories, fewer induced abortions are reported by older controls. They find no such shift in spontaneous abortion incidence.

The assertion Laing et al. make is unnecessary for explaining the pattern they see in their data. It is clear that many more cases than controls reported induced abortions in the cohort of women fifty and older at their breast cancer diagnosis. However, these cases were diagnosed five to 14 years after Roe v. Wade, meaning the youngest of the women in this cohort were 36. There would be less demand for abortion in a group so late into their reproductive years. (In 1996, only 10 percent of all abortions in the U.S. were procured by women age 35 or older; this proportion had changed little by 2000 and 2008, in which years about 11 percent of all abortions in the U.S. were procured by women aged 35 or older.[17]) A smaller fraction of women in this cohort took “advantage” of the change legalizing induced abortion. Additionally, women who do choose to procure abortions at this age may be at greater risk of breast cancer than women who procure abortions slightly earlier in their reproductive lives. Thus, there is no need for the hypothesis of reporting bias as it is put forward, but in no way analyzed, by the authors.

Unsophisticated analysis of induced abortion. The authors do not assess the differing effects of induced abortion based on the gestational period at which it was procured, on maternal age at first induced abortion, or on number of induced abortions procured. Though the authors control for parity, they do not assess the effects of induced abortion’s timing relative to first full-term pregnancy, and hence do not examine the effect of parity status at the time of one’s induced abortion on one’s vulnerability.

Spontaneous abortion. Women aged 50 or older at their breast cancer diagnosis with a history of spontaneous abortion had a significantly reduced risk of breast cancer, relative to women with no history of induced or spontaneous abortion. No significant effect was found for women aged 41 to 49 or for women 40 years old or younger at their diagnosis with spontaneous abortion history.

No distinction between first- and second-trimester spontaneous abortions. Laing et al. did not distinguish between first- and second-trimester spontaneous abortions.

Number of full-term pregnancies. Relative to women who gave birth to five or more children (the vast majority of these were live births; very few were stillbirths), those who gave birth to three to four children were at a marginally significantly reduced risk of breast cancer, and those who gave birth to one or two children were at a significantly reduced risk of breast cancer. No significant association was found with breast cancer for nulliparous women. The authors explain that “[o]ur results might be partly explained by the possibility of a pattern of age at first birth in our data. However, age at first birth was not consistently recorded, so our study could not account for it.”

Marital status. Divorce, separation, and widowhood had a negative (i.e., protective) and significant influence on breast cancer risk, relative to marriage, and singlehood was found to have a marginally significantly protective influence on breast cancer risk. Laing et al. state that the gap in the percentage of never-pregnant women between married and single women is much smaller among black women than among white women and that “[i]t seems possible that single black women may be more similar in their reproductive experience to married black women than is the case with whites.”

Age at menarche. Relative to women who were 15 years old or older at menarche, adjusted odds ratios showed those who were 13 to 14 at menarche to be at a significantly increased risk of breast

cancer. No significant associations were found for those who were 11 to 12 or who were 10 years old or younger at menarche.

When women were divided by menopausal status, no significant associations were found regarding age at menarche and breast cancer risk among premenopausal women. Among postmenopausal women, relative to those experiencing menarche at age 15 or older, women who had experienced menarche at 13 to 14 years of age were at a significantly increased risk of breast cancer. Again, no significant associations were found for those who were 11 to 12 or who were 10 years old or younger at menarche.

Menopausal status. No significant associations were found between menopausal status (i.e., being pre- or postmenopausal) and breast cancer risk.

Oral contraceptive use. Analysis of only women born after 1940 showed that ever using oral contraception had a positive and significant influence on breast cancer risk.

Breastfeeding. No significant association was found for lactation history in the multivariate logistic regression, though the authors note that "a large number of cases had missing information on this variable."

Family history of breast cancer. First-degree (mother or sister) family history of breast cancer, mother-only history of breast cancer, and sister-only history of breast cancer were found to have large, positive, significant influences on breast cancer risk. (These odds ratios are unadjusted "because there were so few controls with a positive first-degree family history.")

9. 1994 Daling Study

Public attention was drawn to the induced abortion-breast cancer link in 1994, when TIME magazine covered[18] a U.S. study by Janet Daling commissioned by the National Cancer Institute (NCI).[19] Daling found that having any induced abortion history significantly increased one's breast cancer risk. The study is of limited generalizability and is marked by possible difficulties related to reporting around abortion law changes, as well as health or survivor bias, but it devotes considerable attention to assessing the risk incurred with induced abortion under different circumstances.

The study's cases included white women born after 1944 and residing in King, Pierce, and Snohomish counties, Washington, who were diagnosed with invasive or in situ breast cancer between January 1983 and April 1990. The patients were identified through a SEER cancer registry in Washington State. The authors acquired a total sample of 845 cases and 961 controls. Controls were identified through random-digit dialing in King, Pierce, and Snohomish counties.

Limited generalizability, survivor or health bias. That all participants were white would limit the generalizability of the study's findings. The study was confined to women experiencing a first diagnosis of breast cancer; this health or survivor bias could have reduced the strength of the induced abortion-breast cancer link, as we explain above. The authors note that a health or survivor bias may have affected their data, because women with induced or spontaneous abortions at a young age who have breast cancer may tend to have a "poor prognosis (16), it could be that those women with breast cancer whom we were unable to interview because of serious illness or death may have been more likely to have had an induced abortion that the women we did interview. If this bias were present, we would have underestimated the risk of breast cancer that is associated with induced abortion."[20]

Reporting difficulty around abortion law change. Some of the reproductive years of some fraction of the women studied would have taken place prior to abortion's 1970 legalization in Washington State,[21)] but as the authors note, the study is comprised of "women in whom most or all of their reproductive years occurred after 1970," and most of the abortions included took place following its legalization.

In addition to containing a large sample, the study's strength is that its "primary focus…was on the difference in the subsequent risk of breast cancer between pregnant women who did and did not choose to terminate that pregnancy but who, based on their demographic characteristics and childbearing histories, were otherwise at similar risk." Hence, in analyzing the risk of induced abortion, the authors control for a variety of other factors, such as age, family history of breast cancer, and age at first birth. (Daling et al. even control for religion in their analyses for induced abortion and so attempt to control for any effect of "reporting bias" on the part of devout women.)

Induced abortion. The authors found that induced abortion contributed to breast cancer risk. Having any abortion history contributed to one's risk of breast cancer, relative to having no induced abortion history. Within this category, having one induced abortion had a positive, significant influence on breast cancer risk and having two or more induced abortions had a marginally significant, positive influence on breast cancer risk.

Age at first induced abortion. First induced abortions before age 18 and first induced abortions at or after age 30 were both associated with a marked, significant increase in breast cancer risk. The effects of first induced abortions between ages 18 and 19 and between ages 20 and 29 were marginally significant and positive.

Gestational period at induced abortion. Induced abortions between nine and 12 weeks' gestation had a significant, positive influence on breast cancer risk. Induced abortions at or before eight weeks' gestation had a marginally significant and positive influence on breast cancer risk, and induced abortions at or after 13 weeks' gestation were not found to have any significant influence.

Age at first induced abortion and gestational period at induced abortion. Further analyses showed that first induced abortions among girls younger than 18 between nine and 24 weeks' gestation (though not before eight weeks' gestation) had a large, positive, significant influence on breast cancer risk, relative to completed first pregnancies.

Relative to completed first pregnancies, first induced abortions in women aged 30 or older before eight weeks' gestation and between nine and 24 weeks' gestation had a positive, significant influence on breast cancer risk. It is to be noted that these analyses were conducted with very small subsamples of women.

No significant association was found between week of gestation at induced abortion, age at first induced abortion, and breast cancer risk among women aged 18 to 19 or aged 20 to 29 at their first induced abortion.

Induced abortions relative to timing of first full-term pregnancy. Both induced abortions before and after a first birth were found to have a marginally significant, positive influence on breast cancer risk, relative to women who had been pregnant but had never had induced abortions. However, induced abortions in nulliparous women (i.e., women who never gave birth) were found to have a positive, significant influence on breast cancer risk relative to women who had been pregnant but had never had induced abortions.

Induced abortions relative to timing of first lactation. Induced abortions taking place after a woman first lactated had a positive, significant influence on the risk of breast cancer, relative to parous women who had lactated but never aborted. An induced abortion more than 10 years before lactating had a positive, significant influence on breast cancer risk, relative to parous women who never aborted. The influence of induced abortion five or fewer years, or six to 10 years, before lactating was not found to be significant. No significant differences were found regarding the timing of their induced abortions (i.e., “before first birth,” “not until after first birth”) between parous women who never lactated.

Duration between first induced abortion and diagnosis of breast cancer (and comparable date for controls). The category representing 10 to 14 years between first induced abortion and date at diagnosis was positive and significant. The category representing an interval of zero to nine years was positive and marginally significant, and the category representing 15 or more years was not significant. This is in line with the hypothesis that detectable breast cancer takes eight to 10 years to develop.

Stage of development. Induced abortion was also found to have a positive, significant influence on breast cancer diagnosed at the in situ or local stages and at the regional or distant stages.

Induced abortion and family history of breast cancer. Induced abortion among women with no family history of breast cancer had a marginally significant and positive influence on breast cancer risk. However, among women whose sister, mother, aunt, or grandmother had breast cancer, induced abortion had a positive, significant influence on breast cancer risk. This was particularly true in the case of first abortions before age 18 and at or after age 30.

Spontaneous abortion. No significant association was found between breast cancer risk and history of spontaneous abortion, number of spontaneous abortions, age at first spontaneous abortion, timing of first spontaneous abortion (i.e., before or after first birth), or duration between first spontaneous abortion and diagnosis with breast cancer (and comparable date for controls). However, relative to women who had ever given birth and had never had a spontaneous abortion, a spontaneous abortion at or before eight weeks’ gestation had a marginally protective influence on breast cancer risk.

10. 1995 Lipworth Study

A study of abortion in Greece[22)] found induced abortion to have a positive, significant influence on breast cancer risk. The study is marked by health or survivor bias and failure to distinguish between first- and second-trimester spontaneous abortions, but it has the benefit of being conducted in a clinical environment, which would discourage underreporting.

The Lipworth study contained 820 cases diagnosed with breast cancer between January 1989 and December 1991 in hospitals around Athens. The study also included two matched control groups, comprised of 795 female orthopedic patients and 753 hospital visitors.

Health or survivor bias, differences between cases and controls not demonstrated. Women with a previous history of breast cancer were excluded as controls; this health or survivor bias could have skewed the study’s results away from induced-abortion breast cancer linkage. Additionally, the authors did not identify differences between cases and controls in their study. They should have done so in order to demonstrate that cases and controls were alike across other potential breast cancer risk factors.[23)]

Pregnancy outcomes. Induced abortion was found to have a positive, significant influence on breast cancer risk, as was "spontaneous and/or induced abortion." A general analysis of induced and spontaneous abortion "adjusted for age, parity status, age at first birth, menopausal status, Quetelet's index [i.e., body mass index] and alcohol intake" showed no significant association between spontaneous abortion and breast cancer risk. (Similar controls were applied to odds ratios produced by regressions elsewhere in the study, though some controlled for age at first birth instead of parity status.)

Too-simple analysis of induced abortion. The authors did not assess the effect of the gestational stage at the time of abortion or of repeated abortions.

Pregnancy outcomes and parity status. When broken down by parity, no significant effect was found for any type of abortion in nulliparous women. No significant difference was found between parous aborting women and nulliparous women with no abortion history.

Relative to parous women with no abortion history, parous women with a history of induced abortion were found to be at increased risk of breast cancer. A history of both induced and spontaneous abortion was also found to have a positive, significant influence on breast cancer risk. No significant influence was found for spontaneous abortion. Additional adjustments for the number of full-term pregnancies, total number of pregnancies, "energy intake," and fruit and vegetable consumption did little to shift these odds ratios.

No distinction between first- and second-trimester spontaneous abortions. Lipworth et al. do not distinguish between first- and second-trimester spontaneous abortions.

Pregnancy outcomes relative to timing of first full-term pregnancy. Lipworth et al. further broke down abortions by distinguishing them by their timing relative to first full-term pregnancy. No significant difference was found between parous aborting women and nulliparous women with no abortion history. However, relative to parous women with no abortion history, both induced abortion before first full-term pregnancy and induced abortion after first full-term pregnancy had a positive, significant influence on breast cancer risk. No significant effect was detected for spontaneous abortion. Again, adjustments for "energy intake," fruit and vegetable consumption, and alcohol consumption did little to shift these odds ratios.

The authors also note that when their analysis of abortion relative to first full-term pregnancy was confined to women under 35, the risk of induced abortion was heightened for women aborting before first full-term pregnancy compared to nulliparous women with no abortion history, though "the estimate…is unstable."

The authors caution readers (as other authors do) to regard their findings with some reserve, due to the possibility that "information bias" could be responsible for the connection in their study between induced abortion and breast cancer risk, because "the attribution of more than 50 [percent] of spontaneous abortions to chromosomal abnormalities that are unlikely to affect the associated hormonal status during the pregnancy should have placed spontaneous abortions as a group in an intermediate position between those with no abortion of any type and those with induced abortion." However, if recall bias actually affects studies to the degree that many authors argue it does, the Lipworth study is all the more useful. As the authors also note, "Information bias with respect to induced abortion is certainly possible but not likely to be large in this study, given the permissive social environment with respect to induced abortion in Greece and the fact that the interviews were conducted in the hospital setting by hospital-associated health professionals."

11. 1995 Bu Study (abstract)

A study of women in Harbin, China,[24] found a statistically significantly increased risk of breast cancer among women 45 and younger who had had one induced abortion or two or more induced abortions. This increase in risk was greater when the analysis was confined to women younger than 35. The brief abstract makes no mention of the inclusion of several breast cancer risk factors in its model, its results are generalizable only to parous women, and the mode of its relatively simple analysis of a fairly small sample is unclear, but the study's confinement to young women could diminish the effects of any health or survivor bias introduced by its "rearward-looking" analysis.

Small sample, limited generalizability. The study was confined to parous women younger than 45 at the time of their diagnosis with breast cancer. Its confinement to parous women limits its generalizability. The 232 cases were diagnosed between October 1990 and December 1992. Each case was matched for age and neighborhood with two controls. Their sample is thus relatively small. Information was obtained regarding the reproductive history of cases and controls.

Potential omitted variable bias, unclear means of analysis, an attempted reduction of health or survivor bias. This abstract makes no mention of many other breast cancer risk factors, and its mode of analysis is unclear. Though many studies assessing the histories of breast cancer patients and controls risk introducing health or survivor bias into their analysis, this study reduces that risk by confining itself to women under age 45. These women are still within their reproductive years, and the risk of women being diagnosed with breast cancer "too early" and selecting out of the cohort is therefore reduced.

Induced abortion. Bu et al. found a history of one or two or more induced abortions to have a positive and significant influence on breast cancer risk. The abstract makes no mention of a temporal assessment of induced abortions and live births, or of maternal age or gestational period at induced abortion.

The authors found the influence of induced abortion to be stronger when they restricted their analysis to women under 35 at the time of their diagnosis.

12. 1995 Andrieu Multiple Re-Analysis

Researcher Andrieu and colleagues analyzed studies conducted in France, Australia, and Russia in order to examine potential interaction between family history of breast cancer, abortion history, and risk of breast cancer.[25] The study's analysis found one induced abortion to have a positive, significant influence on breast cancer risk. The design of some studies and the data the re-analysis chose to include or exclude from the studies could have introduced error and bias into their analyses; Andrieu et al. do not distinguish between first- and second-trimester spontaneous abortions; the authors neglect to assess maternal age and gestational stage at induced abortion; and in assessing the effect of abortion timing, they fail to distinguish between induced and spontaneous abortion.

Health or survivor bias, unsuitable data collection means and handling. Individual odds ratios from each study were adjusted for various potential confounding factors, and a combined odds ratio was produced in each analysis from the available data from all studies. However, the design of some of these studies could introduce biases that could skew the effect of induced abortion. The 1988 Rohan study was based on in-home interviews, and its analyses were restricted to cases with first diagnoses of breast cancer. Cases in the 1988 Luporsi study were confined to those with "infiltrating"

(that is, invasive) breast cancer, and women with a history of breast cancer were excluded as controls. Malignant controls included in the 1991 Clavel study were actually excluded from the Andrieu multiple re-analysis.

Incomplete pregnancy. The re-analysis found no significant associations in an analysis of general abortion (a combined category of induced and spontaneous abortions) and breast cancer risk, other than a marginally significant negative influence with two or more abortions in the unpublished Zaridze data.

Induced abortion. When induced and spontaneous abortion were distinguished, data from the 1988 Rohan study and the results of the combined data of five studies both showed one induced abortion to have a significant, positive influence on breast cancer risk. The 1988 Luporsi study showed one induced abortion to have a marginally significant positive influence on breast cancer risk.

The 1984 Lê study found two or more induced abortions to have a marginally significant positive influence on breast cancer risk, and the unpublished Zaridze data showed two or more induced abortions to have a marginally significant *negative* (i.e., protective) influence on breast cancer risk.

Too-simple analysis of induced abortion. Andrieu et al. do not assess induced abortion with regard to maternal age or gestational stage.

Spontaneous abortion. No significant association was found in any study for any number of spontaneous abortions.

No distinction between first and second-trimester spontaneous abortions. Note that Andrieu et al. do not distinguish between first- and second-trimester spontaneous abortions.

Incomplete pregnancy regarding timing of first full-term pregnancy. When general abortions were broken down by timing relative to first full-term pregnancy, no significant effect was distinguished in any of the six studies examined or in the combined analysis of the data.

Inconsistent distinction between induced and spontaneous abortion. Andrieu et al. do not distinguish induced from spontaneous abortion when they perform their analyses of abortions with respect to the timing of first full-term pregnancy.

Family history of breast cancer. In all studies but the 1988 Rohan study (in which a marginally significant positive association was detected), as well as in the analysis of all data combined, a positive, significant association was detected between family history of breast cancer and breast cancer risk.

13. 1999 Fioretti Study

An Italian study[26)] comprised of data from the 1987 and 1995 La Vecchia studies showed a risk of breast cancer among nulliparous women having abortions late in their reproductive lives. The study is of limited generalizability due to its restriction to nulliparous women, is marked by health bias, does not distinguish between first- and second-trimester spontaneous abortions, does not apply multiple controls uniformly across its analyses, and in its more sophisticated analyses (e.g., age at first abortion) fails to distinguish between induced and spontaneous abortions.

Fioretti et al. conducted a study deliberately designed to evaluate breast cancer risk among nulliparous women, whom they acknowledge are at increased risk of breast cancer. The study was comprised of 1,041 nulliparous cases between the ages of 22 and 79 and 1,002 nulliparous controls aged 15 to 79 living in six different geographic areas in Italy.

Limited generalizability. Fioretti et al. write that the study's restriction "to nulliparae avoids the possible modifying effect or confounding from full-term pregnancy, and allows a more precise assessment of the role of other hormonal risk factors for breast cancer." This would limit the study's generalizability to nulliparous women.

Women were "not included [as controls] if they had been admitted for gynaecological, hormonal or neoplastic diseases," and this exclusion could introduce health bias into the analyses.

Lack of (consistently applied) multiple controls. Note that Fioretti et al. do not apply multiple controls uniformly across their analyses. Lacking multiple controls, this study may incorrectly attribute to one variable the influence of other variables on breast cancer.

Pregnancy outcomes. No significant association was detected between breast cancer and spontaneous abortions, induced abortions, or total number of abortions (combined category for spontaneous and induced).

Age at first incomplete pregnancy. Using women experiencing a first abortion (combined category for spontaneous and induced) prior to age 30 as a reference category, experiencing a first abortion at or after age 30 had a positive, significant influence on breast cancer risk within the general sample and among postmenopausal women. No significant association was detected between breast cancer and age at first abortion among premenopausal women.

Inconsistent distinction between induced and spontaneous abortion, too-simple analysis of induced abortion, lack of distinction between first- and second-trimester spontaneous abortions. That this study assesses spontaneous and induced abortions only in a combined category when examining the influence of age at first abortion and number of abortions is a shortcoming. The authors also did not distinguish abortions based on the gestational stage at which they occurred. Note that Fioretti et al. do not distinguish between first- and second-trimester spontaneous abortions.

Age at menarche. Within the general sample and among postmenopausal women, no significant association was detected between age at menarche and breast cancer risk. However, among premenopausal subjects, menarche at age 15 or later had a significant and negative (i.e., protective) influence on breast cancer risk relative to menarche younger than age 12. As a trend, each year's delay of menarche was associated with a significant decrease in breast cancer risk.

Age at menopause. Among postmenopausal women, commencing menopause between the ages of 45 and 49, between the ages of 50 and 52, and commencing menopause at age 53 or later was associated with a significantly increased risk of breast cancer, relative to commencing menopause before age 45. As a trend, increasing age at menopause had a positive, significant influence on breast cancer risk. No significant effect was detected for experiencing artificial menopause.[27)]

Length of menstrual periods. No significant association was detected between breast cancer and duration of menstrual periods.

Oral contraceptive use. Ever using oral contraception, or oral contraceptive use for two years, had a positive, significant influence on breast cancer risk, relative to never using oral contraceptives.

"Hormone replacement therapy" use. Relative to never using hormone replacement therapy, no

significant effect was detected for “hormone replacement therapy” use. No significant effect was detected with two or more years’ use of “hormone replacement therapy.”

Family history of breast cancer. First-degree family history of breast cancer was associated with an increased risk of breast cancer within the general sample and among both the pre- and postmenopausal subgroups.

History of benign breast disease. A personal history of benign breast disease had a positive, significant influence on breast cancer risk within the general sample, among premenopausal women, and among postmenopausal women.

Educational attainment. Relative to having seven or fewer years of education, having seven to 11 years of education and having 12 or more years of education had a positive, significant influence on breast cancer risk within the general sample and among premenopausal women. Among postmenopausal women, having seven to 11 years’ education had a positive, marginally significant influence on breast cancer, and having 12 or more years’ education had no significant influence. Relative to never being married, having ever been married had a positive, significant influence on breast cancer risk within the general sample, but it had no significant effect in either the premenopausal or postmenopausal subgroup.

Various risk factors. No significant association was detected between breast cancer and body mass index, physical activity, or alcohol consumption in the general sample or in either subsample. As a trend, increased consumption of beta carotene (“a nonspecific indicator of fruit and vegetables” intake) was associated with a decreased risk of breast cancer among women in the general sample and women in the postmenopausal subcategory. Among women in the general sample and postmenopausal women, those women who consumed 1,511.3 to 1,953 (kilo)calories daily were at an increased risk of breast cancer, relative to those who consumed fewer than 1,511.3 calories per day. No effect was detected for consuming more than 1,953 calories per day among women in the general sample or postmenopausal women, and no significant association was detected between breast cancer risk and the number of calories consumed daily among premenopausal women.

The authors note that because “[m]ost estimates were consistent with available knowledge of breast cancer epidemiology…it is unlikely that parity is a major modifying factor of breast carcinogenesis.” Nulliparity is one of the most important risk factors in contracting breast cancer. Fioretti et al. are not contradicting this; they are saying parity may act *independent* of the other risk factors. While an interesting hypothesis, the authors would do well to prove this epidemiologically.

14. 2003 National Cancer Institute Workshop

By the year 2000, many studies had shown induced abortion to have a positive, statistically significant influence on breast cancer risk. The NCI website, which reported that the data were “inconclusive” and “inconsistent” from 1994 to 2002, changed its language in 2002: “The current body of scientific evidence suggests that women who have had either induced or spontaneous abortions have the same risk as other women for developing breast cancer.” The new web page also made no mention of the 1994 Daling study.

These alterations drew a reaction from some members of the U.S. Congress, which has budgetary and political oversight of the NCI. That year, 28 congressmen signed a letter asking the NCI to amend its website concerning the link between breast cancer and induced abortion, as a large quantity of the

data demonstrated a risk.

The letter resulted in the removal of this page from the website, pending a February 2003 workshop on “Early Reproductive Events and Breast Cancer Risk” conducted by the NCI. One hundred scientists and breast cancer advocates participated in this three-day workshop; save for one dissenter—Joel Brind—they concluded that induced abortion was not a risk and did not merit further study. The workshop did note, however, that premature delivery was considered an “epidemiologic gap” requiring more study.[28)]

15. 2003 Becher Study

A 2003 study[29)] in Germany designed to assess the importance of reproductive breast cancer risk factors among women genetically susceptible to breast cancer (the authors tested for a “gene-environment interaction”) found an increased risk of breast cancer with induced abortion. The Becher study, while marked (like many studies) by some degree of health or survivor bias, reporting no data on spontaneous abortion, and containing only a simple analysis of induced abortion (it does not, for example, examine the effects of repeated induced abortions), is uniquely beneficial to the field in that it is focused on women genetically predisposed to breast cancer.

The study included 706 cases diagnosed with *in situ* or invasive breast cancer in 40 hospitals in two regions in Baden-Württemberg, Germany. The women were mainly premenopausal and age 50 or younger at the time of their diagnosis between January 1992 and December 1995. The study also included two sets of controls: 252 sisters of cases and 1,381 age- and region-matched population controls identified through German population registries.

All women studied completed a survey requesting information on a variety of potential breast cancer risks: “demographic and anthropomorphic factors, menstrual, reproductive and breast feeding history, use of contraceptives and exogenous hormones, medical and screening history, family history of cancer, selected occupational exposures, diet, smoking history, and alcohol consumption.” Detailed information was also obtained about breast cancer across four generations. The authors delineate some of the differences between their cases and both groups of controls.

To detect genetic susceptibility to breast cancer, the authors relied on family history of ovarian and breast cancer. Using this information, Becher et al. estimated the likelihood that a study participant was at an increased risk of breast cancer due to a genetic susceptibility to the disease.

Health or survivor bias. Selection out of the survey, and the resultant introduction of health bias, is a problem with this study. Women having suffered from breast cancer, found for the “control” population, were excluded. Thus, there are more women in the control group who have experienced abortions but must not have experienced breast cancer. Though a relationship between induced abortion and breast cancer is detected, the study’s very design may have biased the strength of that relationship to be too weak.

Induced abortion. Multivariate regressions showed that ever having an induced abortion had a positive and significant influence on breast cancer risk both within the general sample and among only parous women. No significant association was detected between induced abortion and breast cancer when the analysis was restricted to the cases and their sister controls.

Unsophisticated analysis of induced abortion. No distinction was made based on the timing of abortion relative to first full-term pregnancy (if any); though the effect of induced abortion is

controlled for parity, this does not consider whether or not a woman had the protection of full-term pregnancy at the time of her induced abortion. The analysis also does not assess the influence of the age of the mother at the time of her abortion, the gestational period in which the abortion took place, or the influence of repeated induced abortions.

No reported data on spontaneous abortion. Becher et al. do not note any findings on spontaneous abortion.

Induced abortion and genetic vulnerability to breast cancer. Induced abortion was not found to influence breast cancer rates differently for women with genetic susceptibility to breast cancer and women without that susceptibility.

Number of full-term pregnancies and parity status. Becher et al. found that, within their general sample, no significant effect on breast cancer risk was detected with a number of full-term pregnancies or with parity as a binary variable (relative to nulliparity).

Among only parous women, having three or more full-term pregnancies had a negative (i.e., protective) and significant influence on breast cancer risk, relative to having only one full-term pregnancy. The authors note in the text that "[t]here was a statistically significant decrease in risk with increasing number of full-term pregnancies among parous women." In the analysis of only the cases alongside their sister controls, no significant effect on breast cancer was detected for having one or three or more full-term pregnancies, but having two full-term pregnancies had a positive, significant influence on breast cancer risk, relative to nulliparity. Becher et al. state that this is evidence that the protection that an increased number of full-term pregnancies affords is lessened among women who are genetically susceptible to breast cancer. Indeed, when parity was analyzed in concert with genetic susceptibility to breast cancer, the authors found that parity offered less protection to women genetically susceptible to breast cancer than to those who were not.

Age at first birth. The authors note in the text that they "did not observe an effect of age at first birth on breast cancer risk," though they also note that "age at first life [sic] birth is typically highly correlated with number of life [sic] births." Becher et al. found a significant negative correlation between increasing age at first live birth and number of live births.

Duration of breastfeeding. When the analysis was conducted across all women, across only parous women, and among only cases and their sister controls, multivariate regressions showed an increased duration of breastfeeding had a negative (i.e., protective) and significant influence on breast cancer risk. No significant interaction was found between breastfeeding, genetic susceptibility to breast cancer, and breast cancer risk, though Becher et al. note that "the comparison of results from population controls…and sister controls…suggests a stronger protective effect when comparing with sister controls."

Age at menarche. No significant association was detected within the general sample, among parous women, or among the cases and their sister controls between breast cancer and age at menarche in the multivariate regression.

Family history of and genetic susceptibility to breast cancer. Having a first-degree relative with breast or ovarian cancer had a large, positive, and significant influence on breast cancer risk.

Increasing probability of carrying a genetic susceptibility also had a positive and significant influence on breast cancer risk. This factor was analyzed in various statistical manners: as a trend, by categories representing increased likelihood of being a gene carrier, and as a dichotomous variable

(i.e., “is not likely a gene carrier” versus “is likely a gene carrier”). In all cases, the risk of being a gene carrier was associated with increased breast cancer risk. All these risks were adjusted for induced abortion, number of full-term pregnancies, duration of breastfeeding, and age at menarche. The “gene carrier probability” model employed by Becher et al. is substantiated by these analyses: In all formulations, a higher probability of carrying such a deleterious gene is significantly associated with higher odds of contracting breast cancer.

16. 2006 Tehranian Presentation (abstract)

A 2006 Iranian study found a statistically significant increased risk of breast cancer with induced abortion and with spontaneous abortions after 12 weeks’ gestation.[30)] The brief abstract makes no mention of the inclusion of several breast cancer risk factors in its model, the mode of its relatively simple analysis of a fairly small sample is unclear, and it may be marked by health bias.

The study included 231 cases and 254 population controls and was conducted at a medical university in Mashhad in 2004. Cases and controls were matched “by age, menstruation, family history of breast cancer, breastfeeding, duration of oral contraceptive use, history of [“hormone replacement therapy,”] and body mass index.”

Small sample, neglect of potential breast cancer risk factors, unclear means of analysis. Tehranian et al. do not make plain their mode of analysis and make no mention of controls for parity, number of full-term pregnancies, age at first full-term pregnancy, smoking, or alcohol consumption (though consideration of alcohol may be less crucial, given the fraction of the population that likely abstains from alcohol consumption due to religious beliefs).

Health or survivor bias. It seems that women with breast cancer may have been excluded as controls, who are described as “general healthy population controls,” a health bias which could introduce error into their analyses and skew their results away from induced abortion-breast cancer linkage.

Induced abortion. Tehranian et al. report that women who had induced abortions prior to 12 weeks’ gestation had a significantly larger breast cancer risk than women who had no induced abortion history.[31)]

Too-simple analysis of induced abortion. The authors seem not to have assessed induced abortion relative to the timing of first full-term pregnancy, maternal age at the time of induced abortion, or the number of induced abortions.

Spontaneous abortion. Women who had one spontaneous abortion after 12 weeks’ gestation had a significantly larger breast cancer risk than women with no history of spontaneous abortion. Women who had two or more spontaneous abortions after 12 weeks’ gestation had a further (significant) increased risk of breast cancer, compared to women who had never had a spontaneous abortion. As noted earlier, these later spontaneous abortions (usually those that happen in the second trimester) differ from very early spontaneous abortions, which are usually due to hormone levels insufficient to maintain the pregnancy.

17. 2007 Naieni Study

A 2007 study conducted in the province of Mazandaran in Iran showed a statistically significant increased risk of breast cancer with abortion.[32)] This study may be skewed by health or survivor bias, conducts only an unsophisticated analysis of induced abortion, and does not distinguish between first- and second-trimester spontaneous abortions.

The Naieni study included 250 cases aged 22 to 80 chosen through the cancer registry of Babol Research Station, as well as 500 neighborhood-matched controls aged 19 to 77. The authors demonstrate the differences between their cases and controls. In addition to analyzing the effects of induced and spontaneous abortion, the authors implemented a wide variety of controls, such as first-degree family history of breast cancer, personal history of benign breast disease, oral contraceptive use, age at menarche, and menopausal status, as well as factors such as education and household income.

Health or survivor bias, and an attempted correction. Though the Naieni study's rearward-looking analysis could introduce health or survivor bias, the authors interviewed relatives of deceased participants, a correction that could reduce the effect of this bias.

Induced abortion. Induced abortion had a positive, precisely determinable influence on breast cancer risk.

Unsophisticated analysis of induced abortion. The authors did not distinguish induced abortions based on their timing relative to first full-term pregnancy; though they control for parity, this does not assess the vulnerability status of the mother at the time of her abortion. They also do not distinguish based on age at first induced abortion, or gestational period at the time of the abortion.

Number of full-term pregnancies. Relative to nulliparous women, women who had given birth to three, four, or five or more children had a marked, very precisely determinable reduction in breast cancer risk. With every child delivered, beginning with the third, one's breast cancer risk was significantly diminished. Increased number of full-term pregnancies, in general, was associated with a precisely determined reduction in risk of breast cancer.

Duration of breastfeeding. Each month of breastfeeding was found to slightly (but precisely) reduce one's breast cancer risk.

Menopausal status. Currently experiencing menopause was positively associated with breast cancer risk.

Family history of breast cancer. First-degree family history of breast cancer was positively associated with breast cancer risk.

Educational attainment. The authors found a large, positive, and significant association between college education and breast cancer.

Body mass index. A small but positive and precisely determinable association was also found between body mass index (as a trend) and breast cancer.

Various risk factors. No significant influence on breast cancer risk was found for spontaneous abortion (Naieni et al. do not distinguish between first- and second-trimester spontaneous abortions),

age at first birth, age at menarche, history of benign breast disease, history or duration of oral contraceptive use, history of irregular menstruation, smoking history, or monthly family income.

18. 2009 Dolle Study

A study in the U.S. by Jessica Dolle and colleagues[33] of risk factors for triple-negative breast cancer found evidence of an association between abortion and breast cancer.[34] The study is marked by health or survivor bias, failed to include a variable for spontaneous abortion in their analyses, and conducted only a simple analysis of induced abortion.

The Dolle study included 744 white patients aged 21 to 45 who were diagnosed with invasive breast cancer between January 1983 and April 1990 and identified through the Seattle-Puget Sound SEER cancer registry, as well as 542 patients aged 21 to 44 who were diagnosed with invasive breast cancer between May 1990 and December 1992 and identified through the Seattle site of the Women's Interview Study of Health. To these two sets of cases were matched, respectively, a set of 961 controls and a set of 608 controls. Both sets of controls were identified by random digit dialing.

The authors included controls for age, family history of breast cancer, and lactation history among parous women, as well as controls for oral contraceptive use. For certain models, race, education, income, body mass index, smoking, alcohol consumption, age at menarche, number of live births, and age at first birth were also included as controls.

Health or survivor bias, and an attempted correction. Though the Dolle study's rearward-looking analysis could introduce health or survivor bias into its analysis, the authors' restriction of the study to women yet in their reproductive years is a correction that could reduce the effect of this bias.

The Dolle study included only invasive cases of breast cancer and excluded *in situ* cancer, but it did so to facilitate a focus on invasive triple-negative breast cancer. Their exclusion of *in situ* cancer had a purpose, but it may have introduced survivor bias and weakened any effect of induced abortion on breast cancer risk.

Induced abortion. In regressions analyzing risks for all types of breast cancer combined, ever having had an induced abortion had a positive, significant influence on breast cancer risk. Induced abortion history also had a positive and significant influence on non-triple-negative breast cancer risk (i.e., the category of breast cancers that excluded triple-negative breast cancer), but it had no significant influence on triple-negative breast cancer risk.

Unsophisticated analysis of induced abortion. The authors did not parse out the risks associated with gestational period at induced abortion, maternal age at first induced abortion, or the timing of induced abortion relative to first full-term pregnancy. Dolle et al. also did not assess the effects of repeated induced abortions.

No reported data on spontaneous abortion. The authors did not include a variable for miscarriage.

Age. Being between the ages of 30 and 34, 35 and 39, and 40 and 45 had a positive and significant influence on general breast cancer risk, relative to being younger than 30. Being between the ages of 30 and 34 had a positive and marginally significant influence on non-triple-negative breast cancer risk, and being between 35 and 39 years or 40 and 45 years old had a positive and significant influence. Increasing age, as a trend, was found to be positively associated with general breast cancer

risk and non-triple-negative breast cancer risk. No significant association was detected with any age category or with the trend of increasing age and triple-negative breast cancer risk.

Number of live births. Having four or more live births had a negative (i.e., protective) and marginally significant influence on general breast cancer risk and non-triple-negative breast cancer risk, relative to having no live births. As a trend, an increasing number of live births was associated with reduced breast cancer risk.

Age at first birth. First giving birth prior to age 20 had a negative and marginally significant influence on general breast cancer risk and non-triple-negative breast cancer risk. As a trend, increasing age at first birth was precisely associated with increased general breast cancer risk, triple-negative breast cancer risk, and non-triple-negative breast cancer risk.

Age at menarche. Experiencing menarche between the ages of 13 and 14 had a negative (i.e., protective) and marginally significant influence on general breast cancer risk and non-triple-negative breast cancer risk, relative to experiencing menarche between the ages of eight and 12.

Experiencing menarche at or after age 15 had a negative (i.e., protective) and marginally significant influence on triple-negative breast cancer risk, relative to experiencing menarche between the ages of eight and 12.

As a trend, older age at menarche was negatively associated with general breast cancer risk and triple-negative breast cancer risk.

Family history of breast cancer. First-degree and second-degree family history of breast cancer had a positive and significant influence on general breast cancer risk, triple-negative breast cancer risk, and non-triple-negative breast cancer risk.

Oral contraceptive use. Using oral contraception for at least one year had a positive, marginally significant influence on general breast cancer risk and a positive, significant influence on triple-negative breast cancer risk, relative to having used oral contraception for under one year (or never using oral contraception).

Duration of oral contraceptive use. Using oral contraception for three to fewer than six years, or for six or more years, had a positive and marginally significant influence on general breast cancer risk and a positive and significant influence on triple-negative breast cancer risk, relative to having used oral contraception for under one year (or never using oral contraception).

As a trend, duration of oral contraceptive use in years (among those who had used oral contraception for a year or more) was positively associated with triple-negative breast cancer risk.

Age at first oral contraceptive use. Commencing oral contraceptive use prior to age 18 had a positive and significant influence on general breast cancer risk, triple-negative breast cancer risk, and non-triple-negative breast cancer risk, relative to having used oral contraception for under one year (or never using oral contraception). Commencing use between the ages of 18 and younger than 22 had a positive and significant influence on triple-negative breast cancer risk. Commencing use after age 22 had a positive and marginally significant influence on triple-negative breast cancer risk, relative to having used oral contraception for under one year (or never using oral contraception).

As a trend, earlier age at commencement of oral contraceptive use (among those who had used oral contraception for a year or more) was associated with increased general risk of breast cancer.

Time since first use of oral contraception. A period of 15 to fewer than 20 years or 20 or more years since first use of oral contraception had a positive and marginally significant influence on general breast cancer risk, relative to never having used oral contraception or having used oral contraception for under one year.

However, for all categories representing a period of time since first oral contraceptive use (one to fewer than 15 years, 15 years to fewer than 20 years, and 20 or more years), a positive and significant influence was detected for triple-negative breast cancer risk.

Time since last use of oral contraception. Relative to having used oral contraception for under one year (or never using oral contraception), a period of one to fewer than five years since last use of oral contraception had a positive and significant influence on general breast cancer risk. A period of 10 to fewer than 15 years since last use of oral contraception had a positive and marginally significant influence on general breast cancer risk. However, no significant influence on general breast cancer risk was found for current use of contraception.

A positive and significant influence on non-triple-negative breast cancer was found for a period of one to fewer than five years since last use of oral contraception.

However, for all categories save one representing a period of time since last oral contraceptive use (current oral contraceptive use, one to fewer than five years, five to fewer than 10 years, and 10 to fewer than 15 years, but not 15 or more years), a positive and significant influence was found for triple-negative breast cancer risk.

As a trend, an increasing number of years since last use of oral contraception was significantly associated with reduced risk of triple-negative breast cancer (among those who had used oral contraception for a year or more).

Other oral contraceptive use. The authors conduct further analyses of the effects of oral contraceptive use based on various other factors, but a detailed analysis of the effects of oral contraception is outside the scope of this study.

Educational attainment. Relative to not graduating from college, being a college graduate had a positive and marginally significant influence on general breast cancer risk and non-triple-negative breast cancer risk, but not on triple-negative breast cancer risk.

Various risk factors. No association was found between breast cancer risk and race, income, body mass index, smoking, alcohol consumption, or lactation history.

19. 2009 Xing Study

A study of breast cancer subtypes in China in 2009 found evidence that abortion was associated with an increased risk of breast cancer.[35] (For an explanation of the different subtypes of breast cancer, see Section II, B.) The study is marked by health or survivor bias, conducts only an unsophisticated analysis of induced abortion, and did not distinguish between first- and second-trimester spontaneous abortions.

The Xing study included a total sample of approximately 3,000, which was comprised of 1,417 breast cancer patients diagnosed at a hospital in Shenyang, China, between 2001 and 2009 and 1,587 controls identified in Shenyang City. Xing and colleagues developed a model controlling for many

reproductive factors associated with (or thought to be associated with) different types of breast cancer, including parity status, age at menarche and first live birth, menopausal status, and first-degree family history of breast cancer.

Health or survivor bias. Women with prior breast cancer diagnosis were excluded as controls, a health or survivor bias which could have skewed their results away from induced abortion-breast cancer linkage.

Pregnancy outcomes. Induced abortion was found to positively and significantly influence the risk of luminal A breast cancer. The authors suggest "that the high prevalence of luminal A breast cancer may not vary by race and ethnicity."[36] Interestingly, one or more spontaneous abortions was found to significantly *reduce risk* of luminal A and luminal B breast cancer.

Unsophisticated analysis of induced abortion. However, they did not distinguish the distinct risks associated with differently-timed abortions (gestational period at induced abortion, mother's age at first induced abortion, or induced abortions relative to first full-term pregnancy, if any, though the authors did control for parity). Xing et al. also did not assess the effects of repeated induced abortions.

Lack of distinction between first- and second-trimester spontaneous abortions. Note that Xing et al. do not distinguish between first- and second-trimester spontaneous abortions.

Parity. Having one child significantly reduced the risk of luminal A, luminal B, and HER2-overexpressing breast cancer (the effects of having more than one child were not significant), relative to being nulliparous.

Breastfeeding. Ever having breastfed significantly reduced the risk of luminal A, luminal B, HER2-overexpressing, and triple-negative breast cancer.

Age at menarche. Experiencing menarche before age 13 significantly increased the risk of luminal A breast cancer.

Menopausal status. Being postmenopausal significantly reduced one's risk of luminal A and luminal B breast cancer.

Family history of breast cancer. First-degree family history of breast cancer had a positive, significant influence on the risk of luminal A breast cancer and a positive, marginally significant influence on the risk of luminal B breast cancer.

Hysteromyoma. History of hysteromyoma (a benign tumor in the uterus) had a negative (i.e., protective) and significant influence on the risk of luminal A and HER2-overexpressing breast cancer.

Various risk factors. No significant effects were found for age at first live birth or age at menopause.

20. 2009 Ozmen Study

In 2009, a study in Turkey found induced abortion history contributed to a statistically significant increase in breast cancer risk.[37] The study is marked by health bias, conducts only an unsophisticated

analysis of induced abortion, and does not distinguish between first- and second-trimester spontaneous abortions.

The Ozmen study was comprised of 1,492 breast cancer patients and 2,167 controls aged 18 to 70 visiting Istanbul University Medical Faculty hospital. (Some patients were also selected from the authors' breast cancer database.) The authors built a moderately thorough model and specified the differences between cases and controls. Alcohol consumption was consciously excluded from statistical analysis because of the very limited alcohol intake among Turkish women.

Health or survivor bias. Women with hormonal diseases were excluded from the control group; this exclusion is a health bias that could have diminished the demonstrated effect of induced abortion on breast cancer risk.

Induced abortion. Regressions with multiple controls showed induced abortion to have a positive, significant influence on breast cancer risk.

Unsophisticated analysis of induced abortion. Ozmen et al. did not distinguish induced abortions based on the period of gestation at which they were performed or on their timing relative to first full-term pregnancy (if any), and they did not assess any possible effects of the number of abortions or of maternal age at first abortion.

Lack of distinction between first- and second-trimester spontaneous abortions. Note that Ozmen et al. do not distinguish between first- and second-trimester spontaneous abortions.

Various risk factors. Age at or over 50 years had a significant, positive influence on breast cancer risk. Oral contraceptive use had a significant, negative influence on breast cancer risk. Other controls included body mass index, education, spontaneous abortions, smoking, breastfeeding and nulliparity.

21. 2011 Khachatryan Study

In 2011, an Armenian study of the relationship between breast cancer and diabetes mellitus type two by Khachatryan and colleagues showed an increased risk of breast cancer with induced abortion.[38)] The study is marked by health bias, was conducted over the telephone (which could generate underreporting), and conducts only a simple analysis of induced abortion with its small sample.

The Khachatryan study included 150 cases registered through the National Oncology Center and the Armenian-American Wellness Center between January 2002 and December 2008, as well as 152 controls with no prior history of breast diseases or (non-cosmetic) breast surgeries identified through random digit dialing. The sample was comprised of women aged 35 to 70, residing in Yerevan, Armenia, and participants were interviewed over the telephone.

The authors developed a model that controlled for many factors potentially related to breast cancer, including diabetes mellitus type two, age at menarche and at menopause, number of induced abortions and live births, age at first pregnancy, breastfeeding duration, family history of breast cancer, history of contraception and "hormone replacement therapy," age, and body mass index. The authors noted the distribution of these factors among their cases and controls. Khachatryan et al. did not include a variable for alcohol consumption, and they did little analysis of the effects of "hormone replacement therapy" or oral contraceptives. As they note, alcohol consumption is relatively low in Armenia, and the percentage of Armenian women who have ever used oral contraceptives or "hormone replacement therapy" is in the low single digits.

Small sample, health or survivor bias, unsuitable data collection. The sample assessed in the Khachatryan study is small; the implications of this are discussed above. Both the health bias introduced through the exclusion of controls with previous breast diseases or surgeries and the method of interview chosen (which may generate underreporting) could diminish any influence of induced abortion.

Induced abortion. Multiple logistic regressions showed induced abortion to have a positive and significant influence on breast cancer risk.

Unsophisticated analysis of induced abortion. The authors did not assess the differing effects of abortion based on its timing relative to first full-term pregnancy, if any (though their analysis did include a variable for parity), on gestational stage at the time of the abortion, or on age at first induced abortion.

Various risk factors. Live birth had a negative (i.e., protective), significant influence on breast cancer risk. Increasing age at first pregnancy and diabetes mellitus type two had a positive, significant influence on breast cancer risk.

No significant effect was found in multiple logistic regressions for breastfeeding duration, age at menarche, age at menopause, age, body mass index, or “hormone replacement therapy.”

22. 2012 Jiang Study

A 2012 Chinese study of abortion and breast cancer risk[39] found an increased risk associated with a history of induced abortion. Having two induced abortions or three or more induced abortions contributed to increased breast cancer risk, and an increasing number of induced abortions was associated with increased breast cancer risk. Premenopausal women and postmenopausal women seemed to be affected differently by induced abortion. The authors fail to demonstrate the differences between their cases and controls; their study may be marked by health or survivor bias; they do not assess the effect of induced abortion with regard to timing of first full-term pregnancy, maternal age, or gestational period; they do not show the influence of several breast cancer risk factors; and they fail to distinguish between first- and second-trimester spontaneous abortions.

The Jiang study included 669 cases identified at Jiangsu Province Cancer Hospital from visits between June 2004 and December 2007 and through cancer registries in Huian, Jintan, Wuxi, and Taixing, all in Jiangsu Province, China. Six hundred eighty-two controls were randomly identified in towns near Taixing, Wuxi, Jintan, and Huian.

No demonstration of differences between cases and controls, neglect of some potential breast cancer risk factors. The authors do not demonstrate the differences between their cases and controls, in tables or in text, except for those related to abortions. Jiang et al. show the crude risks associated with induced and spontaneous abortions (the general risks and risk broken down among pre- and postmenopausal women) and the risks adjusted for “age, marital status, educational level, occupations, body mass index, income/month, age at menarche, age at first birth, number of full-term pregnancies and non[-]full-term pregnancies.” They neglected other breast cancer risk factors, such as oral contraceptive use.

Health or survivor bias. The study’s rearward-looking analysis may have introduced health or survivor bias into its analysis, which would weaken any effect of induced abortion.

Induced abortion. The authors found that ever having an induced abortion contributed to breast cancer risk, even after the above-noted adjustments. Relative to having no abortions, the effects of one abortion were not significant after adjusting for the above factors, but having two or three or more induced abortions had a positive and significant influence on breast cancer risk. As a trend, the number of induced abortions was positively and significantly associated with breast cancer risk.

Induced abortion did not seem to affect premenopausal women in this sample as it did postmenopausal women. Among premenopausal women, induced abortion history had no significant effect on breast cancer risk; neither did having one or two abortions (relative to having no abortions). However, having three or more induced abortions was positively and significantly associated with breast cancer risk, even when adjusted for other factors. As a trend, the number of induced abortions among premenopausal women was positively and modestly significantly associated with breast cancer risk.

Among postmenopausal women, ever having an induced abortion had a positive and significant influence on breast cancer risk, even when adjusted for the above-mentioned factors. Having one or two induced abortions had a positive and significant influence on breast cancer risk, but the effect of having three or more abortions was not significant after adjusting for other factors. As a trend, the number of induced abortions among postmenopausal women was positively and very significantly associated with breast cancer risk.

Unsophisticated analysis of induced abortion. Jiang et al. do not assess the influence of induced abortion relative to the timing of a first full-term pregnancy, though they do control for parity. Neither do they assess the effect of age at induced abortion or gestational period at induced abortion.

Spontaneous abortion. The effects of spontaneous abortion in this sample were far less clear. Across the total sample, neither history of spontaneous abortion nor number of spontaneous abortions was found to have any significant effect on breast cancer risk. The same was true among premenopausal women.

Among postmenopausal women, the adjusted risk of ever having a spontaneous abortion was positive and significant, but no significant effect was found when the number of spontaneous abortions was broken out.

Lack of distinction between first- and second-trimester spontaneous abortion. Jiang et al. do not distinguish between first- and second-trimester spontaneous abortions.

23. 2013 Huang Meta-Analysis

A 2013 meta-analysis in China[40)] showed a statistically significant increased risk of breast cancer with abortion. This study references crude odds ratios rather than odds ratios adjusted for confounding breast cancer risk factors; a number of the articles referenced do not distinguish induced from spontaneous abortion; it does not assess abortions and live births temporally; and no significant effect for abortion is detected when the articles it deems of highest quality are assessed together.

This meta-analysis references 36 articles from 14 provinces in China.

Health bias. As we do not have access to the majority of the articles referenced in the meta-analysis, it is impossible for us to determine whether or not health bias affected these studies. However, the authors note that “no significant associations between [induced abortion] and breast

cancer were found in cohort studies ….”[41] As we note above in our explanation of health bias, it may be that health bias is most pernicious in cohort studies, depending on how their populations are selected.

Huang et al. also found, in response to their inquiry as to “whether inadequate choice of referent group” could skew the results of their analysis, that a lower percentage of women with induced abortions in the control group was associated with a higher odds ratio for induced abortion. Clearly, careful randomization of the control population is essential. Additionally, this finding is rather in parallel with the point that if authors introduce health bias into their analyses by eliminating from their case and control population women with a previous history of breast cancer—and who, according to our theory, disproportionately have a history of induced abortion—and thereby shrink the disparity in the number of women with induced abortion history between cases and controls, they skew the odds ratio associated with induced abortion.

This finding—that a higher rate of induced abortion in the control population diminishes the overall study’s odds ratio—is crucial to note, particularly given the very high (over 50 percent) prevalence of induced abortion in the control groups of many studies (both cohort studies, both studies conducted in Shanghai, and a number of the studies ranked as being of highest quality) in the subgroups whose collective analyses detected no significant influence for induced abortion.

Induced abortion. Huang et al. found that having a reproductive history involving at least one induced abortion had a positive, statistically significant influence on women’s breast cancer risk. This was the case in their analysis of studies that isolated induced abortion as well as in their analysis of studies that analyzed both induced and spontaneous abortion and in their analysis of all studies (those that did and those that did not distinguish induced from spontaneous abortion).

Huang et al. did not conduct a temporal analysis of abortions and live births.

Number of induced abortions. Huang et al. also found, when their investigation was further refined, that two or more induced abortions had a slightly larger (than one or more induced abortions) statistically significant influence on women’s breast cancer risk. This was the case in their analysis of studies that isolated induced abortion as well as in their analysis of studies that analyzed both induced and spontaneous abortion and in their analysis of all studies (those that did and those that did not distinguish induced from spontaneous abortion).

Huang et al. found no significant influence on breast cancer risk with three or more induced abortions in studies of only induced abortion. In studies that assessed induced and spontaneous abortions, and in their overall analysis of both types of studies, having three or more induced abortions had a positive and significant influence on women’s breast cancer risk. The authors note that, whereas in the United States “abortion is used predominantly to postpone first childbirth … almost all [induced abortions] in China were performed to limit family size after the first child. Therefore, more [induced abortions] may imply an early age of childbirth. The protective effects of early childbirth will probably dilute the harmful effect of more [induced abortions].”

The authors also noted a possible bias toward underreporting of abortions, particularly among women who have procured more than two. They state that “this underestimation will inevitably create spurious associations between [induced abortion] and breast cancer, especially for more induced abortions.”

Induced abortion and quality of articles reviewed. The authors note that they ranked the articles in their meta-analysis by quality.[42] Eight studies received an “A” ranking (a score of 8 or 9 on

their quality scale), 24 studies received a “B” ranking (a score of 5 to 7), and two received a “C” ranking (a score of 4 or lower). When the “A”-ranked studies were analyzed together, Huang et al. detected no significant influence for induced abortion. A positive, significant influence on breast cancer was detected for induced abortion in the analysis of the “B”-ranked studies and the “C”-ranked studies.

Induced abortion and other characteristics of studies reviewed. No significant influence was found for induced abortion when the cohort studies were analyzed as a group, but the collective analysis of the case-control studies found induced abortion to have a positive, significant influence on breast cancer risk.

Joint analysis of the studies conducted in Shanghai found no significant influence for induced abortion on breast cancer risk. Collective analysis of the studies conducted in Jiangsu and of “other” regions of China found induced abortion to have a positive, significant influence on breast cancer.

Collective analysis of both hospital-conducted and population-conducted studies found induced abortion to have a positive, significant influence on breast cancer risk. The collective analysis of hospital-based studies found a larger effect for induced abortion than did the analysis of population-based studies.

A positive, significant influence was detected for induced abortion on breast cancer risk in collective analyses of both studies with fewer than 800 participants and studies with 800 or more participants.

Likewise, induced abortion was found to have a positive, significant influence on women’s breast cancer risk in collective analyses of both studies conducted before 2007 and studies conducted in or after 2007.

Omitted variable bias. The Huang meta-analysis used crude odds ratios in its analyses rather than odds ratios adjusted for other factors that affect a woman’s breast cancer risk (e.g., age at first birth, parity). They state that they did this because, among other reasons, not all the examined studies released adjusted odds ratios, and where studies did, the factors for which the crude odds ratios were adjusted differed.

Huang et al. add that the collective analysis of the 13 available adjusted odds ratios was close to their overall result based on the 36 crude odds ratios. They state that this “suggest[s] that the primary result was not substantially confounded by the un-adjusted factors.”[43)]

Incomplete reporting and distinguishing between induced and spontaneous abortions. It seems some of the articles included in this meta-analysis do not distinguish between induced and spontaneous abortion. However, Huang et al. perform both joint and separate analyses of studies that do and do not analyze induced abortion alone.

The authors note as justification for including studies that do not distinguish between induced and spontaneous abortion that spontaneous abortion likely occurs in 4.26 to 5.27 percent of Chinese women.[44)] By contrast, in many of the studies in the meta-analysis, (unspecified type) abortion occurred in the control groups at a rate of over “50 [percent], suggesting that abortions tended to be primarily [induced abortion] rather than [spontaneous abortion].[45)]

[1)] Larissa I. Remennick, “Reproductive Patterns and Cancer Incidence in Women: A Population-Based Correlation Study in the USSR,” *International Journal of Epidemiology* 18, no. 3 (September 1989): 498-510.
[2)] Patrick S. Carroll, “The Breast Cancer Epidemic: Modeling and Forecasts Based on Abortion and

Other Risk Factors," *Journal of American Physicians and Surgeons* 12, no. 3 (2007): 72-78.

[3] M. Segi, I. Fukushima, S. Fujisaku, M. Kurihara, S. Saito, K. Asano, and M. Kamoi, "An Epidemiological Study on Cancer in Japan," *Japanese Journal of Cancer Research (GANN)* 48 (Suppl.) (1957): 1-63.

[4] , [9] Joel Brind, Vernon M. Chinchilli, Walter B. Severs, and Joan Summy-Long, "Induced Abortion as an Independent Risk Factor for Breast Cancer: A Comprehensive Review and Meta-Analysis," *Journal of Epidemiology and Community Health* 50, no. 5 (1996): 483-484.

[5] M.C. Pike, B.E. Henderson, J.T. Casagrande, I. Rosario, and G.E. Gray, "Oral Contraceptive Use and Early Abortion as Risk Factors for Breast Cancer in Young Women," *British Journal of Cancer* 43, no. 1 (1981): 72-76.

[6] If the correlation between induced abortion and breast cancer exists, a univariate bias (throwing out malignant people in the control group) throws out aborting people (in the control group). Because the control group has even fewer abortions now (in proportion to the levels cases exhibit), the statistic shows an even stronger correlation (more effect) between induced abortion and breast cancer: Throwing out malignant controls would bias the effect of induced abortion upward.
If there is no correlation between induced abortion and breast cancer, throwing out malignant women would not throw out any extra aborting women (in proportion) in the control group. Aborting women (not being any more likely to be malignant than the other controls) are dropped with the same frequency as the other controls: Throwing out malignant controls would not bias the analysis.

[7] Planned Parenthood Affiliates of California Action Funds, "Issues: History of Abortion Law in California," Planned Parenthood Action Funds in California.
http://www.ppactionca.org/issues/abortion.html (accessed April 18, 2013). The site notes that the 1967 Therapeutic Abortion Act "[m]ade abortion legal if authorized by a hospital committee that finds the pregnancy will gravely impair a woman's physical or mental health, or where a local district attorney or court finds probable cause to believe the pregnancy resulted from rape or incest."

[8] Wm. Robert Johnston, "Historical abortion statistics, California (USA)," Abortion statistics and other data– Johnston`s Archive, November 21, 2012.
http://www.johnstonsarchive.net/policy/abortion/usa/ab-usa-CA.html (accessed April 18, 2013).

[10] Joel Brind, Vernon M. Chinchilli, Walter B. Severs, and Joan Summy-Long, "Induced Abortion as an Independent Risk Factor for Breast Cancer: A Comprehensive Review and Meta-Analysis," *Journal of Epidemiology and Community Health* 50, no. 5 (1996): 484.

[11] F. Nishiyama, "The Epidemiology of Breast Cancer in Tokushima Prefecture," *Shikoku Ichi* 38 (1982): 333-343.

[12] M. Ewertz and S.W. Duffy, "Risk of breast cancer in relation to reproductive factors in Denmark," *British Journal of Cancer* 58, no. 1 (1988): 99-104.

[13] If the correlation between induced abortion and breast cancer exists, a univariate bias (throwing out controls with a previous history of breast cancer) throws out aborting people (in the control group). Because the control group has even fewer abortions now (in proportion to the levels cases exhibit), the statistic shows an even stronger correlation (more effect) between induced abortion and breast cancer: Throwing out controls with a previous history of breast cancer would bias the effect of induced abortion upward.
If there is no correlation between induced abortion and breast cancer, throwing out controls with a previous history of breast cancer would not throw out any extra aborting women (in proportion) in the control group. Aborting women (not being any more likely to have had breast cancer than the other controls) are dropped with the same frequency as the other controls: Throwing out controls with a previous history of breast cancer would not bias the analysis.

[14] Dolle et al. show a positive and significant increase in breast cancer risk in women who used oral contraception one to fewer than five years in the past and 10 to fewer than 15 years in the past. Current oral contraceptive use and use one to fewer than five, five to fewer than 10, and 10 to fewer than 15 years in the past was shown to have a positive and significant influence on triple-negative

breast cancer risk. However, for no breast cancer category assessed was any effect was detected for oral contraceptive use 15 or more years in the past. See Jessica M. Dolle, Janet R. Daling, Emily White, Louise A. Brinton, David R. Doody, Peggy L. Porter, and Kathleen E. Malone, "Risk Factors for Triple-Negative Breast Cancer in Women Under the Age of 45 Years," *Cancer Epidemiology, Biomarkers and Prevention* 18, no. 4 (2009): 1159.
See also Appendix D for further explanation on breast cancer's manifestation.

[15] Holly L. Howe, Ruby T. Senie, Helen Bzduch, and Peter Herzfeld, "Early Abortion and Breast Cancer Risk Among Women Under Age 40," *International Journal of Epidemiology* 18 (1989): 300-304.

[16] A.E. Laing, Florence M. Demenais, Rosemary Williams, Grace Kissling, Vivien W. Chen, and George Bonney," Breast Cancer Risk Factors In African-American Women: The Howard University Tumor Registry Experience," *Journal of the National Medical Association* 85 (1993): 931-939.

[17] Gilda Sedgh, Akinrinola Bankole, Susheela Singh, and Michelle Eilers, "Legal Abortion Levels and Trends By Woman's Age at Termination," International Perspectives on Sexual and Reproductive Health 38, no. 3 (September 2012): 144. http://www.guttmacher.org/pubs/journals/3814312.pdf (accessed July 5, 2013).

[18] Christine Gorman, "Do Abortions Raise the Risk of Breast Cancer?" *TIME*, November 7, 1994, 61.

[19] Janet R. Daling, Kathleen E. Malone, Lynda F. Voigt, Emily White, and Noel S. Weiss, "Risk of Breast Cancer among Young Women: Relationship to Induced Abortions," *Journal of the National Cancer Institute* 86 (1994): 1584-1592.

[20] Janet R. Daling, Kathleen E. Malone, Lynda F. Voigt, Emily White, and Noel S. Weiss, "Risk of Breast Cancer among Young Women: Relationship to Induced Abortions," *Journal of the National Cancer Institute* 86 (1994): 1589.

[21] National Abortion Federation, "History of Abortion." http://www.prochoice.org/about_abortion/history_abortion.html (accessed April 19, 2013).

[22] Loren Lipworth, Klea Katsouyanni, Anders Ekbom, Karin B. Michels, and Dimitrios Trichopoulos, "Abortion and the Risk of Breast Cancer: A Case-Control Study in Greece," *International Journal of Cancer* 61 (1995): 181-184

[23] Other potential breast cancer risk factors could be confounded with factors of interest, such as induced abortion.

[24] 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).

[25] 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.

[26] F. Fioretti, A. Tavani, C. Bosetti, C. La Vecchia, E. Negri, F. Barbone, R. Talamini, and S. Franceschi, "Risk factors for breast cancer in nulliparous women," *British Journal of Cancer* 78, no. 11/12 (1999): 1923-1928.

[27] Artificial menopause involves the surgical removal of the ovaries. Women who undergo this procedure are often offered hormone replacement therapy.

[28] National Institutes of Health, National Cancer Institute, "Summary Report: Early Reproductive Events and Breast Cancer Workshop," National Cancer Institute http://www.cancer.gov/cancertopics/causes/ere/workshop-report/ (accessed January 3, 2013).

[29] H. Becher, S. Schmidt, and J. Chang-Claude, "Reproductive factors and familial predisposition for breast cancer by age 50 years. A case-control-family study for assessing main effects and possible gene-environment interaction," *International Journal of Epidemiology* 32 (2003): 38-50.

[30] Najmeh Tehranian, M. Amelbaraez, R. Salke, and S. Faghihzadeh, "The effect of abortion on the risk of breast cancer" (Iranian study presented at a conference at McMaster University, 2006). http://www.nursinglibrary.org/vhl/handle/10755/163877 (accessed April 29, 2013). Please note that

only the abstract of this study is currently available.

[31] While some authors might attribute the size of the (substantial) effects conferred by induced abortion in the 2006 Tehranian study, by university education in the 2007 Naieni study, and by induced abortion in the 2011 Khachatryan study, to recall bias, we wonder whether the size of the effects is not a consequence of fewer carcinogenic channels in these societies. For example, Khachatryan et al. note that Armenians consume very little alcohol and that very few Armenian women have ever used "hormone replacement therapy" or oral contraception. This reduced exposure to carcinogens would statistically "clarify" any effect of induced abortion (or of any other relevant factor).

[32] Kourosh Holakouie Naieni, Ali Ardalan, Mahmood Mahmoodi, Abbas Motevalian, Yoosef Yahyapoor, and Bahareh Yazdizadeh, "Risk Factors of Breast Cancer in North of Iran: A Case-Control in Mazandaran Province," *Asian Pacific Journal of Cancer Prevention* 8 (2007): 395-398. http://www.apocp.org/cancer_download/Volume8_No3/395-398%20c_Naieni%204.pdf (accessed December 7, 2012).

[33] Jessica M. Dolle, Janet R. Daling, Emily White, Louise A. Brinton, David R. Doody, Peggy L. Porter, and Kathleen E. Malone, "Risk Factors for Triple-Negative Breast Cancer in Women Under the Age of 45 Years," *Cancer Epidemiology, Biomarkers and Prevention* 18, no. 4 (2009): 1157-1166.

[34] Triple-negative breast cancer cases are those in which cells' estrogen receptors, progesterone receptors, and HER2 receptors are "negative." These cases of breast cancer are particularly difficult to treat.

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