

ETHICS & MEDICS

A Commentary of The National Catholic Bioethics Center on Health Care and the Life Sciences

THE ABORTION-BREAST CANCER LINK REVISITED

On May 13, 2004, Ellen Goodman, in a column in the *Boston Globe* entitled "Just the Schmacks, Ma'am," stated that the research linking breast cancer to abortion "keeps reappearing no matter how many scientists drive a stake through its heart."¹ She reported that even though the government web site at the National Cancer Institute had "expunged" the abortion-breast cancer (ABC) link, the information continues to appear on pro-life web sites. Goodman's column illustrates the reason there is such widespread misinformation about the ABC link. She claims that the link is merely a pro-life "scare tactic." It is not. It has a proven scientific basis.²

Unfortunately, the popular press does not seem willing to convey accurate information about this issue. The media erroneously reported that one hundred scientists meeting at the National Cancer Institute in February 2003 had "unanimously" arrived at the conclusion that there was so little evidence for the ABC link that it need not be studied further.³ The conclusion was not unanimous. The dissenting opinion by scientist Joel Brind, who was at the February meeting, can be found on the web site www.bcpinstitute.org.⁴ More recently, a study published in the *Lancet's* March 27, 2004, issue⁵ has become the latest "stake" picked up with great fanfare by the press. The *Atlanta Journal Constitution* quoted Valerie Beral, the study's first author, as saying, "Scientifically, this is really a full analysis of the current data."⁶ Nothing could be further from the scientific truth. Instead, it illustrates Dr. Donald DeMarco's recent thoughts regarding the inappropriate influence of wishes and beliefs on the outcomes of "scientific research" and medical information.⁷

Beral's own words, as reported by the Associated Press, were that "The totality of the worldwide epidemiological evidence indicates that pregnancies ended by induced abortion do not have adverse effects on women's subsequent risk of developing breast cancer."⁸ This conclusion is scientifically inaccurate for many reasons. Selection bias in choosing studies for reanalysis, the unproven assumption of recall bias in retrospective studies, and the choice of a scientifically invalid control group all resulted in a very flawed reanalysis.

My article examines and refutes the conclusions of the *Lancet* paper. My hope is that as many women as possible will read this critique so that they will not be deceived by

the media into thinking that there is no link between abortion and breast cancer.

Selection Bias

Studies that take data from many previous studies and "reanalyze" them (or put them into a meta-analysis) need to have sound scientific reasons for excluding some published studies. Without valid exclusion and inclusion criteria, the results can be skewed and inaccurate because they may allow an author's personal bias to consciously or subconsciously enter the selection process, thus corrupting the conclusion. Undoubtedly, this sort of bias is what has led some observers to call epidemiology a pseudoscience. For instance, if many studies were to show a positive association between breast cancer and abortion, but were eliminated so that only those showing no or a negative association remained, then obviously the result would show little or no association of abortion with breast cancer. Therefore, it is essential that studies be eliminated solely for rigorously scientific reasons; for example, if the data were not collected properly, or the study was proven flawed after peer review.

Of the forty-one previously published, peer-reviewed studies that could have been included in her reanalysis, seventeen were excluded: fourteen for invalid, non-scientific reasons. Of these fourteen, four published studies were simply not acknowledged to exist,⁹ even though three of them were coauthored by members of Beral's collaborative group.

Let us look at the reasons some of these studies were excluded:

1. Four studies¹⁰ were excluded because the "principal investigator (PI) could not be found." These four studies were published an average of over twenty years ago (1978–1986). It is not unreasonable to assume the PI might be retired, expired, incapacitated, or unreachable. Those circumstances would not make his study unimportant or scientifically invalid.

2. Three studies were excluded¹¹ because the PI could not find the original data. Certainly that does not make the

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DEBUNKING THE "NO LINK" CLAIM
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NEW EDITORIAL OFFICES

(AND PROCEDURE FOR PERMISSION TO REPRINT)

published data inaccurate. One of those studies¹² had gotten its data from the New York State Department of Health records and a fetal death registry. An additional two studies¹³ were excluded because the PI did not want to participate. This preference would not invalidate their studies.

3. One study¹⁴ was excluded because the PI felt his "information was unreliable." One would want to know why that study went through peer review and had been published.

Looked at from another angle, Beral eliminated ten of sixteen statistically significant published studies showing an association between abortion and breast cancer. If all fourteen of the excluded studies were combined, they would show approximately an 80 percent increase in the risk of breast cancer with abortion.

Other studies which should have been correctly omitted due to scientific flaws, such as the 1997 Melbye¹⁵, 2001 Goldacre¹⁶, and 2003 Erlandsson¹⁷ studies, were included. All three studies have been demonstrated to have major methodological flaws. For example, the 1997 Melbye study misclassified sixty thousand women as not having had abortions when governmental records show that they did.

In addition to the twenty-four published studies Beral used for her reanalysis, she chose to include twenty-eight unpublished and therefore non-peer reviewed studies. This again was a very questionable decision. Published studies undergo scrutiny by other researchers who may uncover serious flaws that invalidate the conclusions, as illustrated by the Melbye study. Unpublished studies have not undergone the same level of scrutiny and therefore may be less reliable.

Assumption of Recall Bias

In the interpretation section of the summary of her paper, Beral states that studies of breast cancer using retrospective recording of induced abortion yielded misleading results. Her study found that there was an 11 percent increased risk of breast cancer when she evaluated the retrospective data from thirty-nine worldwide studies. She decided to exclude this data because of "recall bias." The theory of recall bias holds that, when women are interviewed, those with breast cancer will more accurately recall and report their abortion history than those who have not had breast cancer, thereby skewing the results. However, when recall bias in the case of abortion has been studied (and it has been studied several times), it has not been found to influence the results, or, for that matter, even to exist.

For example, the 1991 Lindefors-Harris study¹⁸ showed only a 16 percent recall bias effect in which women without breast cancer "under reported" their abortions compared to women with breast cancer. This small effect is not enough to change the outcome of a large study, and in fact, in this same study, 27 percent of the women admitted to abortions that were not recorded in an abortion registry, thereby "over-reporting" their abortions. Lindefors and Harris claimed the "over-reporting" women were admitting to abortions they never had because they were

not in the abortion registry used by them. Peer review caused them to retract that obviously flawed opinion. In another study by Ye in 2002,¹⁹ the researchers found the same risk of breast cancer when they used medical records as when they used retrospective interviews of the same patients, proving that recall bias did not exist.

Beral's blanket assumption that the recall bias theory calls into question the results of all retrospective studies that involve the questioning of people about potentially embarrassing behavior such as abortion has never been applied to other studies investigating the number of sexual partners, type of sexual behavior, and the amount of alcohol consumed as it relates to disease. The association of cervical cancer with increased number of sexual partners, HIV infection with sodomy, and heavy drinking patterns with liver disease has not invalidated retrospective studies that show positive associations. Why then does the potential for recall bias invalidate thirty-nine studies that show an association between induced abortion and breast cancer?

Inappropriate Comparison Group

Another error in Beral's study design occurs in the inappropriate choice of control group for the reanalysis. Beral charts the relative risk of breast cancer by comparing the effects of having had a pregnancy that ended in an induced abortion with the effect of "not having had" that pregnancy.

As soon as a woman becomes pregnant, even before implantation occurs, her estrogen levels start to rise. This affects her breast tissue by causing the number of Type 1 and Type 2 lobules in her breast to increase. She is physiologically different from a woman who has never been pregnant because, as a result of her pregnancy, however long, her breast tissue will have changed in a way that affects her breast cancer risk. If she completes that pregnancy to term she will have lower breast cancer risk, as her breast tissue will have matured to predominantly Type 3 lobules, which are resistant to carcinogens. If that pregnancy is interrupted, either through induced abortion, late miscarriage, or premature delivery before thirty-two weeks, she will have increased numbers of Type 1 and 2 lobules due to the hormonal stimulation during her pregnancy. Both Melbye and Hsieh, in two studies published in 1999, showed that premature deliveries before thirty-two weeks more than doubled breast cancer risk.²⁰

The only valid comparison that Beral et al. should have chosen as a proper control group for pregnant women who end their pregnancy with induced abortion is pregnant women who do not end their pregnancy with induced abortion. Including in the comparison group women who are not pregnant or who never have been pregnant skews the results.

By choosing a scientifically invalid control group, Beral invalidated her study's outcome. When the effect of hormone replacement therapy (HRT) on breast cancer risk was studied, postmenopausal woman taking HRT were compared to postmenopausal women not taking HRT. This resulted in the finding that HRT increased breast cancer

risk. If the investigators had chosen to compare *postmenopausal* women taking HRT to *premenopausal* women taking HRT, no increase would have been found. Both groups would have risk elevation and no difference between the groups would have been apparent. Only by comparing physiologically equivalent groups of women can breast cancer risks be discerned.

Epidemiology and Biology

Epidemiological associations are studied to give scientists a place to start when investigating the biologic principles of disease. In fact, even as the National Cancer Institute discounted the ABC link, it did so while also admitting an "epidemiologic gap," as they put it, concerning premature deliveries before thirty-two weeks and an increase in breast cancer risk. This is not a "gap" that is inexplicable if one is aware of breast physiology as described by standard texts. Over 80 percent of all breast cancers are ductal cancers and arise in Type 1 lobules. At puberty, when estrogen levels rise, the breast enlarges partly by increasing the number of Type 1 lobules. When estrogen levels again rise during pregnancy, a woman's breast further enlarges by making increased numbers of Type 1 and 2 lobules. The longer she is pregnant before thirty-two weeks, the more Type 1 and 2 lobules she forms.

After thirty-two weeks her breasts stop enlarging and the Type 1 and 2 lobules develop into Type 3 lobules in preparation for breast-feeding. These Type 3 lobules are resistant to carcinogens. This is the reason that women who have given birth have a lower breast cancer risk than women who have never been pregnant.

The reason that premature delivery before thirty-two weeks more than doubles breast cancer risk is the same reason that induced abortion increases breast cancer risk. The breast has developed more Type 1 and 2 lobules. There are now more places where breast cancers can start.

In reply to Ellen Goodman's mock surprise that the ABC link is alive and well, despite the "stakes" of many scientists and the National Cancer Institute, I would simply state that facts can be very persistent things. I would also add that the sorts of manipulations discussed above reinforce my general concurrence with Disraeli's statement that there are three kinds of lies: lies, damnable lies, and statistics.²¹

Angela Lanfranchi, M.D., F.A.C.S.
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Notes

¹Ellen Goodman, "Just the Schmacks, Ma'am," *Boston Globe*, May 13, 2004.

²Angela Lanfranchi, "The Abortion-Breast Cancer Link: What Today's Evidence Shows," *Ethics & Medics* 28.1 (January 2003): 1-4.

³Joel Brind, "Breast Cancer and Scientific Integrity: The National Cancer Institute Meeting," *Ethics & Medics* 28.5 (May 2003): 1-2; Joel Brind, "Early Reproductive Events and Breast Cancer: A Minority Report, March 10, 2003," *Ethics & Medics* 28.5 (May 2003): 2-4.

⁴Joel Brind, "Early Reproductive Events and Breast Cancer: A Minority Report," March 10, 2003, http://www.bcpinstitute.org/nci_minority_rpt.htm (Breast Cancer Prevention Institute).

⁵Valerie Beral et al., "Breast Cancer and Abortion: Collaborative Reanalysis of Data from 53 Epidemiological Studies, Including 83,000 Women with Breast Cancer from 16 Countries," *Lancet* 363.9414 (March 27, 2004):1007-1016.

⁶David Wahlberg, "Study: Breast Cancer Not Tied to Abortion; Group Backs Up Institute's Earlier Findings," *Atlanta Journal-Constitution*, March 26, 2004, A9.

⁷Donald DeMarco, "Abortion-Breast-Cancer Malpractice: New Legal Developments," *Ethics & Medics* 29.5 (May 2004): 3-4.

⁸Associated Press, "Study: Abortion, Breast Cancer Not Linked," March 26, 2004.

⁹E. Luporsi, study in meta-analysis of N. Andrieu et al., "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* 72.3 (September 1995): 744-751; L. Bu et al., "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); D.G. Zairdze, study in meta-analysis of N. Andrieu et al., "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* 72.3 (September 1995): 744-751; A. Laing et al., "Reproductive and Lifestyle Factors for Breast Cancer in African-American Women," *Genetic Epidemiology* 11 (1994): 300.

¹⁰V.V. Devorin and A.B. Medvedev, "Role of Reproductive History in Breast Cancer Causation" (in Russian) in *Methods and Results of Breast Cancer Epidemiology* (Moscow: Oncology Science Center of the USSR Academy of Sciences, 1978), 53-56; B. Burany, "Gestational Characteristics in Women with Breast Cancer" (in Croatian) *Jugoslavenska Ginekologija i Opstetricija* 19.5-6 (September-December 1979): 237-247; F. Nishiyama, "The Epidemiology of Breast Cancer in Tokushima Prefecture" (in Japanese) *Shikoku Ichi [Shikoku Medical Journal]* 38 (1982): 333-343; V. F. Levshin and A.D. Chepurko, "Reproductive Anamnesis and Breast Cancer" (in Russian) *Sovetskaia Meditsina* 6 (1986): 15-21.

¹¹T. Hirohata et al., "Occurrence of Breast Cancer in Relation to Diet and Reproductive History: a Case-Control Study in Fukuoka, Japan," *National Cancer Institute Monograph* 69 (December 1985): 187-190; B.M. Harris et al., "Risk of Cancer of the Breast after Legal Abortion during the First Trimester: a Swedish Register Study," *British Medical Journal* 299.6713 (December 9, 1989): 1430-1432; H.L. Howe, "Early Abortion and Breast Cancer



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¹²Howe, "Early Abortion."

¹³J. R. Palmer et al., "Induced and Spontaneous Abortion in Relation to Risk of Breast Cancer," *Cancer Causes and Control* 8.6 (November 1997): 841-849; L. Rosenberg et al., "Breast Cancer in Relation to the Occurrence and Time of Induced and Spontaneous Abortion," *American Journal of Epidemiology* 127.5 (May 1988): 981-989.

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¹⁵M. Melbye et al., "Induced Abortion and the Risk of Breast Cancer," *New England Journal of Medicine*; 336.2 (January 9, 1997): 81-85.

¹⁶M. J. Goldacre et al., "Abortion and Breast Cancer: a Case Control Record Linkage Study," *Journal of Epidemiology and Community Health* 55.5 (May 2001): 336-337.

¹⁷G. Erlandsson et al., "Abortions and Breast Cancer: Record-Based Case-Control Study," *International Journal of Cancer* 103.5 (February 20, 2003): 676-679.

¹⁸B. M. Lindefors-Harris et al., "Response Bias in a Case-control Study: Analysis Utilizing Comparative Data Concerning Legal Abortions from Two Independent Swedish Studies," *American Journal of Epidemiology* 134.9 (November 1, 1991): 1003-1008.

¹⁹Z. Ye et al., "Breast Cancer in Relation to Induced Abortions in a Cohort of Chinese Women," *British Journal of Cancer* 87.9 (October 21, 2002): 977-981.

²⁰M. Melbye et al., "Preterm Delivery and Risk of Breast Cancer," *British Journal of Cancer* 80.3-4 (May 1999): 609-613; C. C. Hsieh et al., "Delivery of Premature Newborns and Maternal Breast-Cancer Risk," *Lancet* 353.9160 (April 10, 1999): 1239.

²¹*The Oxford Dictionary of Quotations*, 3rd ed. (New York: Oxford University Press, 1980), 246.

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