IN MEMORIAM: Joan Elaine Althouse Weiler

Our Fight Against Breast Cancer

Respected colleagues

Last year, I was reluctant to write this article. Now that the Genetic Information Nondiscrimination Act: 2007–2008 has been passed, it's easier.

As many of you know, I was the founding Editor-in-Chief of Cancer Informatics. I am truly grateful that the publisher, Tom Hill, and the Editorial Board that we recruited had the confidence in my vision to go forward with CI. It pleases me endlessly to see that the journal is flourishing, and that it has a rigorous peer-review process. This is a testament to Tom Hill's diligence and his role in bringing about high standards for the publication of research and related articles.

Of course, it saddens me that we need journals like this at all.

Mom was a lovely woman, who loved her children, and who loved to laugh. She was loved by her siblings, and her parents, and her children. We were blessed to have her, even if, for us, for only a short time.

Mom passed her BRCA1 variant to my sister, who developed breast cancer at the age of 42. My sister's clinical story was a cliff-hanger; a GP told her that the lump was a clogged milk duct; when she finally told me about it, I told her to schedule the biospy and to schedule the mastectomy even before the pathology results came back. The path report came back on a Friday; I arranged for the protocol for the Precision Therapeutics' ChemFX chemosensitivity assay kit to be sent to her surgeon from Pittsburgh, PA to Rochester over the weekend. Her surgeon agreed it was a good idea; he read the protocol over the weekend, and she went under the knife at 9AM. The kit arrived at 11 AM.

Her cancer was triple-negative. The test convinced my sister to undergo chemotherapy; she did well on the first round. Allergic reaction almost took her on the second round. She ended up with two full courses and two half-courses. She's the brave one. Like our mom. Our mom went to Rochester in the early 1970's for experimental treatment. Knowing what I know now, she gave part of herself so breast cancer patients today have better options.

My sister is now doing extremely well; she had a bout of chemo-induced cardiomyopathy; that was a risk, we knew about it. She had decided for chemo at Block Medical Center; her husband drove her every other week from Rochester to Chicago. They offered chemo with an augmented regime of diet and vitamins. The vitamins plus the CoEnzyme Q10 she started taking combined probably helped to reverse her cardiomyopathy. We are eternally grateful to Laura Esserman, and Adam Brufsky for providing real-time reality checks and advice as we went along.

Familial breast cancer is a long-term emotional torture. My two sisters have six girls and three girls, respectively. The oldest is 20. My mother's brother's daughter developed breast cancer last year, and is undergoing treatment. My mother's sister developed breast cancer in the 1980s, and lost two girls at the age of 25. All of the women who have developed breast cancer in my family have been tested and are also positive for our family's mutation. It's not yet known whether the mutation is 'clinically significant'. It's hard to remain objective when the evidence I have is so personal. Nevertheless, I am fronting the bill for my two >50 year old breast-cancer free aunt's BRCA1 testing, so Myriad can make the case for insurance-billed testing for my mother's nine (maybe 10) granddaughters and their descendents. I have two uncles as well; Uncle J played guitar for us, a habit I took up at a late age and started a second mini-career as a songwriter. He developed prostate cancer and is doing fine after prostatectomy. His daughter developed triple-negative breast cancer last year and is undergoing treatment. Our fingers are crossed.

My personal fight against breast cancer began when I was most unprepared. As a four-year old boy, I had no knowledge of death, let alone cancer. I was prepared for school, though; and when mom died in 1971, I found escape there. My teachers were kind and generous; I found learning helped me feel better. Not to be too dramatic, but mom died on Valentine's Day; it could have come from a very bad made-for-T.V. movie; me with arms full of Valentine's cards, hearing the news, and the rest of the day seemed so quiet. Every year, until last year, I fell into depression coming up to February 14th. Last year I changed things by planning, and performing at a fundraiser concert for the National Aviary in Pittsburgh. My sister and all her children were all there; it was a lovely night, all in all, it was an evening of grace.

I'll take this opportunity to ask my statistician friends to weigh in on the problem of whether BRCA1 and 2 mutations confer increased risk of breast cancer due to mammography. The article I'd recommend for re-consideration is Goldfrank et al.[1] in that study, the authors report association between BRCA status and cancer incidence associated with mammography, specifically that the association is significant with BRCA1+2 and BRCA2 combined are nearly arguably significant ($p = 0.06$). Association with lifetime exposure was significant for BRCA1 carriers. Trouble is, the interpretation by the authors does not seem supported by the reported results. Power to reject is a likely issue; moreover, selection bias might play a role, and the use of the particular test of association (unconditional logistic regression) might also determine the outcome. Re-analysis seems warranted, and articles that re-analyze published data sets and validate or refute the original interpretation should be a regular feature of articles in CI. Meta-analysis might also help, but only if the original data analysis is vetted. Also, the current NCCN Clinical Practice Guidelines in Oncology™ 's *Breast Cancer Screening and Diagnosis Guidelines* remain weakly non-committal in their recommendations on this issue. We need definitive studies that compare the effectiveness and outcome of annual clinical manual breast exams combined with MRI follow-up to current practice. I have weighed in with my family members to be diligent w/self-exams and clinical exams, and to ask for MRIs, but to forego mammography. I would rather not having them risk inducing cancer, given that it appears we cannot rule out the possibility of increased risk due to mammography for BRCA mutation carriers. We also need studies to settle the issue of whether triple-negative breast cancer patients should or should not receive low-dose tamoxifen.

For my family, it's now down to setting up the future of clinical testing for third and fourth-generation family members. We would obviously hope for structural and functional studies of the BRCA1 variant, and for insurance-billable testing for all willing and counseled family members. Whatever the challenges are in life, it's easiest if you take the negative and transform it into something positive. I want my family, friends, and colleagues to know that I consider CI one of a few lasting monuments I've made to my mother, Joan Elaine Althouse Weiler. I consider the creation of the Bioinformatics Analysis Core at the University of Pittsburgh, and the analysis service that we do there are all types of genomics and proteomics studies, to be an homage to her. I am grateful to Igor for stepping up to the task to take over CI as Editor-in-Chief after my short initial tenure. Thank you, Igor, keep up the great job. So far, the articles are really top-notch.

Odds are, mom would have enjoyed the music better.

Acknowledgment

I thank Eleanor Feingold for reminding me of the role of selection bias in the outcome of association studies.

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Reference

1. Goldfrank et al. Effect of mammography on breast cancer risk in women with mutations in BRCA1 or BRCA2. *Cancer Epidemiol Biomarker Prev*. 1996;15:2311–2313.