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Hormone therapy and breast cancer: risk communication and the ‘perfect storm’

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ABSTRACT
Many factors are considered when a woman estimates her personal risk of breast cancer. Common to most decisions are four separate influences that have convinced the public and many health-care providers that breast cancer is the greatest concern for menopausal women and that menopausal hormone therapy (MHT) is generally responsible. Historically there have been well-documented situations in which big pharma and doctors have not put patient interests first. Conflicting reports about the safety of MHT and the media imperative to always increase readership by presenting a compelling scary story have created an underlying distrust of science, doctors, and MHT. Numerical and statistical illiteracy in the general population creates a situation where lotteries succeed despite astronomical odds and the risks of medical interventions are exaggerated by their description using relative, rather than absolute, risks. Finally, mammographic overdiagnosis contributing to improved breast cancer survival has contributed to the ‘popularity paradox’ (more screening – more enthusiasm) especially among survivors and advocacy groups. As a result, worry about breast cancer has overshadowed concern about cardiovascular diseases as the major cause of death and disability in the later years. The ongoing challenge for clinicians dealing with menopausal women is to bridge the gap in risk perception with evidence-based common-sense advice.

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Background
Within our population, and even within the medical community, there is widespread suspicion that one of the significant risks of menopausal hormone therapy (MHT) is the development of breast cancer. This fear, which has been fueled by a number of independent factors, has limited the use of MHT among women who would benefit from it and distorted public perception about the risks and impact of breast cancer versus cardiovascular diseases in the lives of women as they age.

The term ‘perfect storm’ was coined in a 2000 cinematic recreation of the confluence of adverse weather events that led to the sinking of the fishing boat Andrea Gail in the North Atlantic in 1991. It seems that a modern-day ‘perfect storm’ may explain the distorted perception and accompanying fear of a link between MHT and breast cancer.

Fear of corporations, big pharma, and synthetic products
In the 1960s, Ralph Nader emerged at the forefront of a movement seeking to alert the public to shortcomings of big business where the value of profit seemed to outweigh concerns about consumer protection and environmentalism. Believing that businesses like the automobile industry were operating largely unchecked, he pushed for greater government regulation. Rachel Carson in her 1962 book Silent Spring drew attention to the impact of indiscriminate use of pesticides on the environment. This created a new awareness of the possibility of contamination of our food and water by man-made chemicals. Irresponsible dumping of by-products of chemical manufacturing, as in the Love Canal disaster near Niagara Falls, New York, brought global attention to the possibility of industry contributing to environmental pollution. As technology has improved over the years, to the extent that chemicals could be measured in parts per billion, there has been a deluge of reports of newly discovered contaminants in our food supply.

Medical disasters such as the thalidomide tragedy heightened public awareness of the adverse effects of a prescribed medication that was said to be safe in pregnancy. In recent years, not a day passes without media reports of adverse effects of currently marketed medications and invitations on television, in papers, and on roadside billboards for medication users to contact lawyers at ‘1-800-BAD DRUG’.

It is hardly surprising that the public has an uneasy sense of distrust for products and medications promoted by companies where investor profits are of paramount importance.

Media hype and publicity
There is a saying in media circles that ‘if it bleeds – it leads’, meaning that bad news sells and will generally make the headlines. Competition for viewers in the media arena is extreme and editors are often chosen for their ability to...
adverse events are generally portrayed as scrutiny. Findings are preliminary and may not hold up to further scientific limitations of research methods to appreciate that the findings are often not well-enough informed about the complexities and financial support for the research and may be useful to self-promotion of early interesting research findings can garner financial support for the research and may be useful to promote an academic career. Unfortunately, reporters are often not well-enough informed about the complexities and limitations of research methods to appreciate that the findings are preliminary and may not hold up to further scientific scrutiny.

When the Women’s Health Initiative (WHI) released its first results in 2002, the media were permeated with alarming warnings about MHT. A decade after the original publication from the WHI, a reanalysis of the data suggested that the benefits of MHT would outweigh the risks for the majority of women entering menopause. Unfortunately, the reassuring evidence about the use of MHT that followed received little media attention. A leading WHI investigator attributed the lopsided reporting to the way that the WHI writing group released the information favoring ‘publicity, fear and sensationalism over science.

Breast cancer, because it can potentially affect half of the population with a devastating disease, is often the focus of media reports. A comprehensive analysis of breast cancer articles in the media in 2008 found that news articles were much more likely to focus narrowly on pharmaceutical products, such as hormones, with little if any coverage of other equally important risk factors or preventive strategies related to lifestyle. Reproductive events (age at first birth, decisions on breast feeding, age of menarche and menopause, etc.) have an important role in defining personal risk for breast cancer. These are factors which cannot be altered when a woman presents with menopausal symptoms. However, estimates suggest that one-third of all breast cancers could be avoided by lifestyle changes introduced at the time of menopause and this, unfortunately, has received minimal publicity.

Innumeracy: mathematical illiteracy

Why are millions of dollars spent on lotteries every day when the odds of winning are so remote? Perhaps when we hear the tag line ‘Someone has to win – it could be you’ it evokes the wishful thinking that leads us to envision how we would spend the winnings. Lotteries are required to state the odds of winning in lay terms on their websites. The Megamillions lottery in 2014 had a payout of $640,000,000. The website stated: ‘If you buy 58 tickets per week you will win in 68,000 years’. The Powerball lottery in 2012 had a $587,000,000 payout and its website stated ‘You have one chance in 175,223,510 of winning’. How many in the lay public realize that they have a greater chance of dying on the way to purchase the ticket?

In both medical and lay literature, relative risks expressed as percentages are often used to lend greater significance to a finding. These percentages are relatively meaningless unless one can determine an attributable risk. Consider this experiment. In a room of lottery enthusiasts, tell them that for a small fee you will tell them how to increase their chance of winning by 100%. You would make a lot of money and all you have to do is to tell them that if they normally buy one ticket they need only buy a second one.

When the WHI reported a 26% increase in breast cancer among women using combined estrogen and progesterin MHT, few readers understood that this relative risk was derived from the data showing 30 breast cancers/10,000 women on placebo and 38/10,000 women on hormones. The absolute difference was eight additional breast cancers per 10,000 women per year. This amounts to an attributable risk of 0.08% per year or less than a 10th of a percentage point increase per year of use. (Indeed, the 74% of the enrolled women who were first-time hormone users showed no increased risk yet this received no media coverage.) Had the findings been conveyed to the media and the public in this way, we would not have seen the widespread panic that followed the 2002 WHI report.

In an article on how to help doctors, patients, journalists, and politicians better understand health statistics, Gigerenzer et al. describe a societal problem called ‘collective statistical illiteracy’. Rather than a course in statistics, he recommends that minimal statistical literacy in health requires, among other things, an understanding of both benefits and risks of screening tests and treatments expressed in absolute terms and individualized to each person’s situation.

Mammographic screening, overdiagnosis, and survivorship

Breast cancer mortality has fallen by 40% over the past 30 years. Some of this can be attributed to earlier detection due to screening programs; however, increased consumer awareness and improved adjuvant treatments have also played an important role. All-cause mortality, however, has shown little improvement, leading some to call for an end to mammographic screening.

The intent of screening is to allow detection of early-stage disease resulting in earlier treatment, thus decreasing late-stage disease. Since the introduction of widespread screening, mammography cases of ductal carcinoma in situ have increased by 300% yet invasive breast cancer cases have fallen only 8%. The lack of a shift from late-stage diagnosis to early-stage disease (stage shift) in population-based mammographic screening programs has led some authors to conclude that improved breast cancer mortality is not the result of mammographic screening.

Significant harms of screening mammography have been identified. A UK independent panel estimated that, if 10,000 women were screened from age 50 for 20 years, 49 breast cancer deaths would be averted at the cost of 129 cases of breast cancer that had been overdiagnosed. Over a 10-year period, between 30 and 50% of women screened every 1–2
years can expect a false-positive result, and between 7 and 20% receive a false-positive biopsy recommendation\textsuperscript{14}. Although screened women should be less likely to present with regional or advanced-stage disease, evidence indicates that screened women were more likely to undergo surgery, chemotherapy, and radiation\textsuperscript{14}. Surveys of physicians have found that most do not appreciate and cannot explain to women the benefits and harms of screening\textsuperscript{15,16}, yet careful explanation of benefits and risks has been shown to influence a woman’s perceptions about the benefits of mammography\textsuperscript{17}.

Treatment when none is needed, in addition to causing unnecessary stress, carries the very real risk of adverse health consequences. Immediate consequences relate to the morbidity of treatment. Later effects include increased rates of coronary artery disease and cardiac mortality in women receiving left-sided chest irradiation and increased rates of lung cancer, pneumonitis, and fibrosis on the irradiated side\textsuperscript{18–20}.

Survivorship numbers are rising due to the improvements in treatment and the fact that women who were overdiagnosed and treated unnecessarily still consider themselves to be survivors. Survivors invariably credit screening and early detection for their successful outcomes; however, this is generally not the case\textsuperscript{21}. This belief resulted in the ‘popularity paradox’ described by Raffle and Gray in 2007: ‘More screening – more enthusiasm’\textsuperscript{22}.

Breast cancer awareness and support organizations play an important role in supporting women and their families as they go through the anxiety of diagnosis and the challenges of treatment. However, most of these organizations aggressively promote mammography (often with celebrity endorsements\textsuperscript{23}) with little mention of possible harms. Pink ribbon logos now appear on packaging of everything from bread and fried chicken to cosmetics and jewelry. A miniscule fraction of the dollars raised is directed to breast cancer research. In a 2006 book entitled \textit{Pink Ribbons, Inc.: Breast Cancer and the Politics of Philanthropy}\textsuperscript{24}, we are warned that this commercialization of the breast cancer movement has, in fact, exploited human generosity, hope, and trust.

The impact of this widespread publicity and commercialization of the breast cancer movement has led to a distorted perspective about the risks of breast cancer compared to cardiovascular disease as women age\textsuperscript{25,26} and has distorted beliefs about the benefits of mammography\textsuperscript{21}. The number of US women who died of heart disease in 2010 is over 7.5 times the number who fell victim to breast cancer\textsuperscript{9}, yet in that same year Susan G. Komen for the Cure Foundation raised $430 million for breast cancer while the American Heart Association’s ‘Go Red for Women’ campaign raised only $30 million.

\textbf{Conclusion}

A confluence of effects over several decades has created a widespread worry about the impact of menopausal hormone therapy on breast cancer and a distorted perception about the role of breast cancer on women’s health (Figure 1). The 2002 WHI report appeared to confirm these apprehensions and the ensuing alarm resulted in a generation of recently graduated health-care providers who have had little or no experience with prescribing hormone therapy for menopausal women. Over the past decade, menopausal women have needlessly suffered from distressing vasomotor symptoms and a multimillion dollar market for unproven complementary and alternative medicines emerged as women sought relief by other means. Several systematic reviews have reached the same conclusion about complementary and alternative medicines: ‘Although individual trials suggest benefits from certain therapies, data are insufficient to support the effectiveness of any complementary and alternative therapy in the management of menopausal symptoms’\textsuperscript{27}.

A review of selective serotonin receptor inhibitor (SSRI) and menopausal hormone therapy prescriptions in Canada after the 2002 WHI report demonstrated a reciprocal relationship between the two, with SSRI prescriptions rising by 25% as prescriptions for hormone replacement therapy (HRT) declined\textsuperscript{28}. The authors concluded that ‘The simultaneous increase in prescriptions of serotonergic antidepressants suggests that antidepressants are being prescribed for symptoms (psychological, physical) previously controlled with the use of HRT’. A recent review suggests that SSRIs afforded minimal if any benefit for control of vasomotor symptoms\textsuperscript{29}. Other well-known ancillary benefits of hormone therapy were lost, as evidenced by reports of increasing urogenital atrophy\textsuperscript{30} and osteoporosis\textsuperscript{31,32}. Although still debated in some circles, there appear to be long-term cardiovascular
benefits when MHT is started early in the menopause and the cohort of women reaching menopause around 2002 lost the opportunity to benefit from this.

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