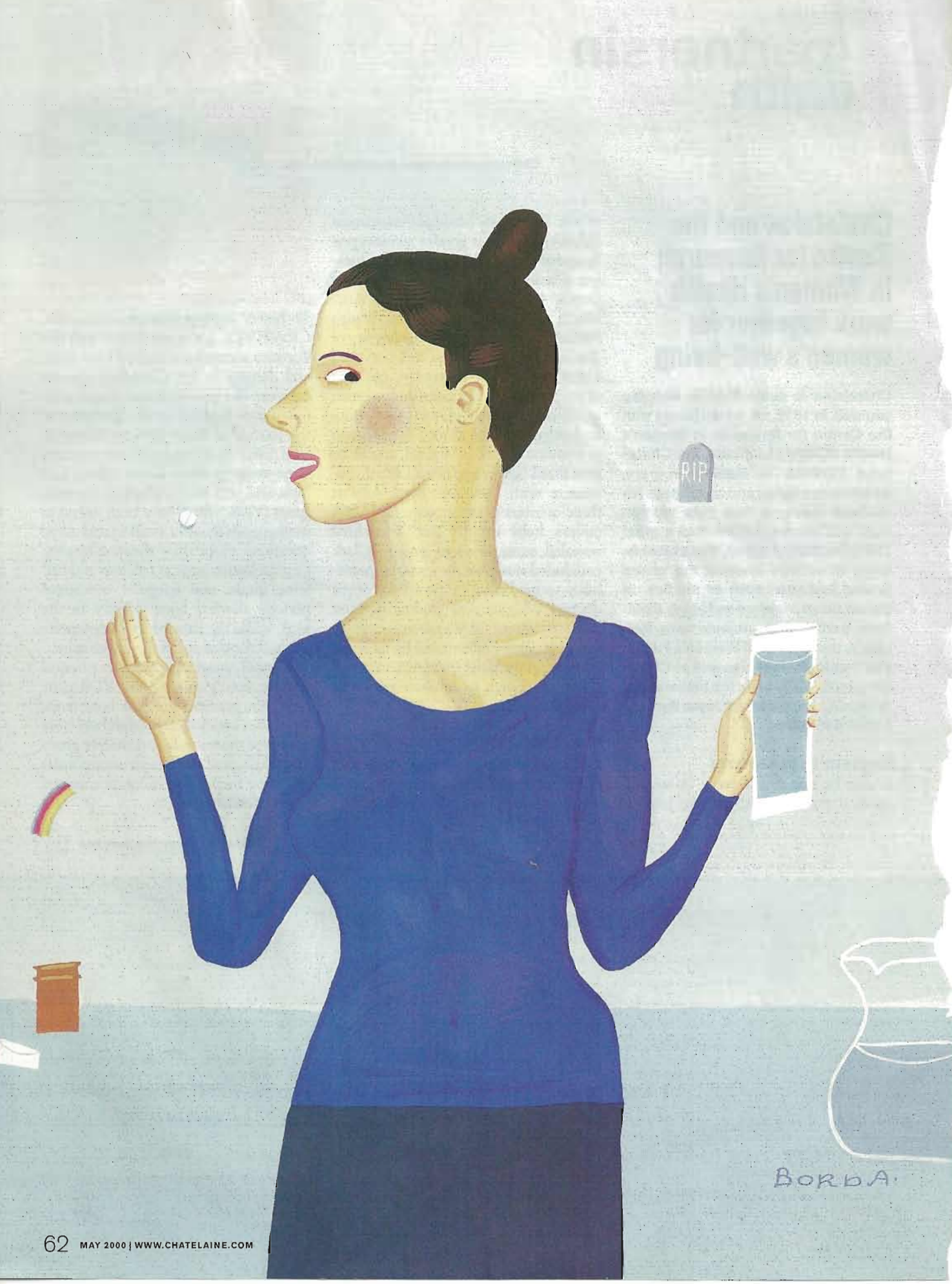
RIP
BORDA

Millions of healthy women with only a slight risk of breast cancer are the target market for pills that could do them no good. Sarah Scott reports

Can this drug prevent breast cancer?

They are sisters, born only 22 months apart. All their lives – through summer holidays, frequent moves, marriages and kids – they've been as close as sisters can be. "We always had each other," says Gwen Luther-Lashley, a music therapist and mother of daughter Quincy, 13. "Whenever anything would happen, we'd pick up the phone, no matter where we were in the world."

So, it was Easter Sunday 1993, when Gwen's younger sister, Emmie Luther-Hiltz, picked up the phone to call Gwen in Toronto. Emmie was in Hubbards, N.S., where she was raising two boys and working as an administrative manager in a provincial cabinet minister's office. That day, she was frightened. Over her morning coffee, she noticed a lump in her right breast. It being Easter, Emmie had to wait for a biopsy that would confirm the worst. She had breast cancer. First, she called her mother, then her sister, Gwen. "I was initially stunned," says Gwen. "Our maternal grandmother was diagnosed with breast cancer in her late 50s. Our father had cancer too. But I couldn't believe it was happening to someone 33 years old."

But then, Gwen visited her doctor in Toronto that summer after noticing a suspicious lump. There she saw a sign calling for sisters of breast cancer patients to participate in a study of a drug called tamoxifen, which blocks the estrogen receptors of normal and cancerous cells. It had been used successfully for more than 20 years in women with breast cancer to prevent recurrences and reduce the risk of getting cancer in the unaffected breast. The purpose of the new trial, however, was to determine whether tamoxifen could actually prevent the disease.

Gwen knew that her risk of getting breast cancer was higher than average. It is estimated that a woman runs a 10 per cent chance of getting breast cancer sometime in her life. But when a sister has it, the risk doubles. Even though her lump turned out to be nothing serious, Gwen was tempted: why not try a pill a day that could potentially prevent you from getting the dreaded disease in the first place?

Naturally, Gwen called her sister. Emmie, who had lost her right breast, was still on chemotherapy, powerful drugs to kill the cancerous cells. She was tired and nauseous. When she ▷

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trial for osteoporosis, for which raloxifene has been approved in Canada.) Eli Lilly's sales pitch is impressive, to be sure, but there's just one tiny hitch. The company has yet to prove that raloxifene reduces the risk of breast cancer. As a result, no government has approved the drug for that purpose.

All the hype raises a pointed question: are the drug companies overselling their drugs as the so-called prevention pill? Is their sales job so slick that it will induce millions of healthy women with a slight risk of breast cancer to take drugs that could do them more harm than good? Some of the critics in the breast cancer movement certainly think so. "I feel as if women are being duped," says breast cancer activist and author Sharon Batt, who holds the Nancy's Chair in women's studies at Mount Saint Vincent University in Halifax. "We're being sold this idea that you can stop breast cancer by prescribing a pill. It's outrageous." Batt's view is shared by chemist Pierre Blais, who worked at Canada's Health Protection Branch, the agency that regulates drugs, and now is a private consultant. "We're looking at a family of pharmaceuticals that are overextended and overpromoted," he says.

For its part, tamoxifen was tested for 4.2 years on 13,388 women in Canada and the U.S. at high risk for breast cancer. While the study showed that significantly fewer women taking tamoxifen got breast cancer, there was virtually no difference in the number of deaths between women on tamoxifen and those on a placebo. In the group on tamoxifen, 124 got breast cancer and three died. In the placebo group, 244 got breast cancer and six died. But that's not the end of the story. Women in the tamoxifen group were twice as likely to develop cancer of the lining of the uterus – 36 of them suffered this potentially fatal side-effect compared to 15 in the control group. (The uterine cancers occurred in women over 50 and most were successfully treated; the one death from this cancer was in the control group.)

There were other serious side-effects too. Fifty-three women in the tamoxifen group suffered blood clots in their lungs or major veins and three died. In the control group, 28 women developed clots and none died. How does it all add up? In total, six women in the tamoxifen group died compared to seven women in the group taking placebos. In other words, the trial did not prove that you can live longer on tamoxifen: just about as many women died on tamoxifen as those on placebo. "It's a wash," said Larry Sasich, a pharmacist at Public Citizen's Health Research Group in Washington.

Public Citizen and other critics complained loudly that the trial was stopped too early to prove whether tamoxifen could reduce the risk of breast cancer over the long term. Its argument was then fuelled by two smaller studies of tamoxifen in Europe that showed no reduction in the incidence of breast cancer. The British study of 2,500 women with a family history of breast cancer was led by Dr. Trevor Powles. He was so annoyed about the U.S. decision to stop the trial that he travelled to Washington to complain before the FDA committee considering tamoxifen: "I am not satisfied that we have proven at this time that long-term use of tamoxifen in healthy women is likely to be beneficial over the risks."

The trial did not prove that tamoxifen could reduce breast cancer risk over the long term.

The FDA's oncologic drugs advisory committee listened – up to a point. In September 1998, the panel voted against approving tamoxifen as a drug to prevent cancer because the study only lasted 4.2 years with a median followup of 3.6 years. It was a slam-dunk no: 11–0. Prevention means you don't get breast cancer for up to 20 years after taking the drug. But in a second vote, the powerful FDA committee said yes (9–2) to tamoxifen as a more limited remedy – to reduce the risk in the short term for high-risk women. In other words, if you take tamoxifen, you'll have less chance of getting breast cancer, at least over the next few years.

A limited approval, to be sure, but it was a victory for the drug company and the researchers who ran the trial. "It's not an ideal drug," says Dr. Norman Wolmark, the Canadian surgeon who chairs the National Surgical Adjuvant Breast and Bowel Project in Pittsburgh, which ran the tamoxifen trial. "But it's a first step. It indicates that one can reduce the incidence of breast cancer using a pill." Even if tamoxifen only delays breast cancer, as the critics contend, it is still a big advance, says Dr. Lavina Lickley, a surgeon investigating the drug at Sunnybrook & Women's College Health Sciences Centre in Toronto. "What woman," she says, "wouldn't rather have breast cancer at 70 than at 50?" Dr. Lickley has made her own decision: she has been on tamoxifen herself to try to prevent a recurrence of her own case of breast cancer.

The FDA approval did not end the debate over tamoxifen. It just kicked off a new phase – this time about aggressive misleading salesmanship. As soon as FDA approval was secured, Zeneca went all out to sell the drug for risk reduction. It didn't call it prevention. It didn't have to. Everyone else did – the media, the scientists, the marketers, the doctors who doled out the drug. The first ad appeared in MAMM, a magazine for the breast cancer community. It showed a row of healthy happy-looking women. The message simply stated: "There is something you can do."

The FDA, however, was not impressed. It ordered Zeneca to pull the ad because it was "false or misleading" and "lacking in fair balance." For one thing, it failed to mention the side-effects. The FDA also complained about a promotional brochure that repeatedly refers to the Breast Cancer Prevention Trial. "While prevention of breast cancer in women at high risk may have been the hypothesis tested in the trial," the FDA said, "the results in fact did not demonstrate that Nolvadex [tamoxifen] prevents breast cancer." ▷

Since then, Zeneca's ads have been more careful. They're all about assessing your risk of breast cancer and doing something about it – presumably by taking tamoxifen once a day. Although the FDA has not complained about this latest batch of ads, critics such as Cindy Pearson, executive director of the National Women's Health Network in Washington, say they subtly inflate the benefits and play down the drug's side-effects. That's why Public Citizen is petitioning the FDA to put more information in plain language on the drug's label.

So far, Zeneca has been the target of most of the complaints about misleading advertising, but a lot of activists have overlooked the subtle but very smart marketing campaign waged by Zeneca's arch rival, Eli Lilly. The drug company's sales representatives have been visiting doctors to push their "designer estrogen," raloxifene. It was approved in Canada and the U.S. to prevent osteoporosis after a four-year trial, which ended in 1999. The researchers, however, noted that there was a potential side benefit: while studying 7,700 women with osteoporosis, investigators noticed that over three years only 13 women in the raloxifene group developed breast cancer compared to 27 women in the control group. But in the scientific world, this finding does not qualify as proof. Since the study was not designed to test whether raloxifene cuts the risk of breast cancer, the finding might just be a coincidence. That's why the FDA has repeatedly rebuffed Eli Lilly's efforts to get raloxifene approved as a risk-reduction drug for breast cancer without further trials.

This has not deterred Eli Lilly from promoting raloxifene's ability to do so. In late 1998, the company was scolded by the FDA for a press release that hyped raloxifene's unproven properties and has even insisted that the company add to raloxifene's label the following words: "The effectiveness of raloxifene in reducing the risk of breast cancer has not yet been established."

But Eli Lilly's enthusiastic sales force pressed on, even claiming that raloxifene was better than tamoxifen because it did not increase the risk of uterine cancer. Those claims have landed the company in hot water on both sides of the border. In the U.S., Zeneca sued Eli Lilly for making false and misleading claims. In a ruling last July, U.S. District Court Judge John Koeltl rapped the competitor: "It is literally false for Eli Lilly to claim that raloxifene has been proven to reduce the risk of breast cancer or that raloxifene is comparable or superior to tamoxifen for that purpose." He issued a temporary injunction to stop Eli Lilly from making those claims. ▷

In Canada, Eli Lilly has worked just as hard to get its message across to doctors. It ran into trouble again. Last year, Eli Lilly placed an ad in a magazine aimed at health professionals that heralded the advantages of its drug, which read: apart from building bones and reducing fractures, raloxifene "reduces the incidence of breast cancer."

The ad was pulled after the British Columbia Health Department complained to the Pharmaceutical Advertising Advisory Board, an industry and medical group that reviews drug company advertising. Eli Lilly insists it was complying with Canadian law. Here, drug company sales representatives are allowed to provide health professionals with additional safety information. In raloxifene's case, that included the breast cancer risk reduction. "We're allowed to do that here. We're not allowed to do that in the U.S.," says Dr. Loren Grossman, associate vice-president of clinical research, Eli Lilly Canada. But, says Ann Sztuke-Fournier, head of the advertising and promotion unit in the Canadian Health Protection Branch's therapeutic products program, "Drug companies have to get approval to print additional safety information on the monographs, and they have to use it in the appropriate context and not make it mislead."

In the winter of 1998, an Eli Lilly sales rep visited Emmie Luther-Hiltz. The rep was upbeat, according to Emmie's notes from the meeting. "He felt Evista is effective in the prevention of breast cancer," she says. It was a powerful sales pitch to a six-year breast cancer survivor who desperately wants to spare her sister the agony of the disease. Emmie came away from the meeting wondering whether either raloxifene or tamoxifen would prevent breast cancer in her sister. A five-year trial called STAR, which began in 1999 in Canada and the U.S., will determine which of the two is more effective and safe against breast cancer.

In the meantime, Emmie and Gwen will keep talking about their kids, their lives and the pros and cons of the pills that might prevent or delay breast cancer. Neither one has decided yet. "It's confusing; that's the problem," says Emmie. "There's so much misinformation out there and it's a big job to decipher it." In the end, she says, "there are no guarantees," either for herself, her sister or for Gwen's daughter, Quincy – the people we love and want to protect, despite our fears. C

Are you worried about breast cancer? Want to talk about it? Visit Chatelaine's Web site at www.chatelaine.com and click on the "talk" oval, then choose Health.