ANALYZING BENEFITS AND RISKS IN MEDICINE, TO WHOM AND FOR WHOM?

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ABSTRACT

The audience is often not explicitly named as part of a research study, but the framing of the research and the written results tend to be targeted toward particular addressees, without recognition of the impact of the boundaries. As researchers, we often think of this issue as one of "communication." We acknowledge that if our studies are to be understood more broadly, we must learn to write the results in non-scientific terms for a different audience. We do not often consider that research aimed at our traditional audiences may fail to consider the factors that could be the most crucial for the broader objectives our research is trying to achieve. It is within this context that a case study in benefit / risk illustrates the impact of framing and boundaries on the outcomes included in research. A current public debate in the UK and, to a lesser extent, in the US over the use of mammography screening for breast cancer reveals a great deal of well-intended information but not very much clarity. On its surface, defining the outcome of mammography as a benefit or risk would seem to be a straightforward exercise. However, the relative merits as discussed below would suggest otherwise.

Keywords: benefit, risk, health, healthcare, applied research

AN EXAMPLE OF PUBLIC DEBATE OVER BENEFIT AND RISK

The following case study is not meant to sway the reader's opinion about the health issue involved – screening by mammography for breast cancer in women. (*Note: While breast cancer can also occur in men, regular screening by mammography is not recommended for men. Thus, patients in this case study will be referred to as "she."*) The study is neither an exhaustive review of available information nor an accusation toward any particular parties for the ways in which they have addressed the issues. It is instead meant to speak to all of us in research who address our findings in the traditionally accepted manner. The audience is often not explicitly named in our work, but the framing of the research and the written results tend to be targeted toward our usual addressees, without recognition of the impact of that frame. We may think of this issue as one of "communication." We acknowledge that if our studies are to be understood more broadly, we must learn to write the results in non-scientific terms for a different audience. We do not often consider that research aimed at our traditional audiences may fail to consider the factors that could be the most crucial for the broader objectives our research is trying to achieve. It is within this context that I illustrate a current public

debate over mammography, whose benefits and risks are much more difficult to characterize than might be suspected.

The Letter

A March 2009 article in the *New York Times* described a debate in the UK that included a letter from a variety of concerned parties to *The Times of London*. The letter claimed that informational handouts in the UK about mammography overstate the benefits of screening and leave out critical information about the harms. The article stated that, "What women are not told…is that for every woman whose life is saved by breast cancer screening, up to 10 healthy women are given diagnoses — and, often, surgery — for a cancer that is so slow-growing it would never have threatened a woman's life." "The culture is just that mammography is such a very sensible thing to do, so you chug along and have it done," the article quoted one of the letter-signers, Hazel Thornton (Thompson, 2009). The 75-year-old Mrs. Thornton told the reporter that more than 15 years previous, a mammogram had identified that she had a ductal carcinoma in situ, a noninvasive breast cancer that often does not progress. She had a lumpectomy, but said that she was offered a confusing array of treatment options and began to believe that doctors knew little about how aggressively to treat this type of cancer.

The *Times* letter cited statistics from a 2006 analysis by the Nordic Cochrane Center collaborative (Gøtzsche, P.C., and Nielsen, M., 2006), including a finding that for every 2,000 women age 50 to 70 who are screened for 10 years, one woman will be saved from dying of breast cancer, while 10 will have their lives disrupted unnecessarily by overtreatment. Julietta Patnick, the director of cancer screening programs for the British National Health Service, was also interviewed. She claimed that the Cochrane figures were inaccurate and said that British studies showed that the ratio of lives saved to lives unnecessarily disrupted was closer to one-to-one. She elaborated, "We know, from statistics, that there are cancers diagnosed through screening that wouldn't otherwise have been diagnosed — because the woman dies of something else first, because she might get run over by a bus, or she might have a heart attack, or she might live to 90 and it would just sit there, and she wouldn't have died of breast cancer," Ms. Patnick said. But the problem is, "You don't know who that woman is," she continued. "You just know that statistically, she exists."

The article also cites unnamed "experts" who "agree that under a microscope, slow-growing cancers look no different from more aggressive ones, so it is impossible to know which ones can be left untouched." One of the authors of the Cochrane report – Gøtzsche – was reported to have written an alternative version of a patient pamphlet for women considering mammography. It begins by saying, "It may be reasonable to attend breast cancer screening with mammography, but it may also be reasonable not to attend." The open letter claims that the subject of breast cancer screening information "has now come to a head with the publication in the next issue of the British Medical Journal" of Gøtzsche's article on the same topic. In the article, Gøtzsche describes the shortcomings of the UK's revised informational leaflet and then describes the alternative leaflet he and his colleagues have written in Danish and English, already distributed in Denmark, with further translations planned. He concludes the article with the admonition that, "the

responsibility for the screening programmes must be separated from the responsibility for the information material, and information materials should be carefully tested among general practitioners and lay people."

Although not mentioned in the article, this collaboration describes itself on its website as "an international, non-profit, independent organisation" that shares "up-to-date, accurate information about the effects of healthcare interventions" with the intent of facilitating choices made by doctors, patients, policy makers and others. Its central functions are funded by royalties from its publishers, John Wiley and Sons Limited, which come from sales of subscriptions to The Cochrane Library. The individual entities of The Cochrane Collaboration are funded by governmental, institutional and private funding sources, with limited uses of funds from corporate sponsors. The alternative leaflet can be downloaded free of charge.

In this camp as well is letter-signer, Dr. Lisa M. Schwartz, an associate professor at Dartmouth Medical School. She had co-authored the book, *Know Your Chances*" (University of California, 2008), about how to interpret health statistics and risk. She is quoted as saying, "You're not crazy if you don't get screened, and you're not crazy if you do get screened….People can make their own decision, and we don't need to coerce people into doing this….There is a real trade-off of benefits and harms. Women should know that. There's no question on one count: if you get screened, it's more likely you'll have a diagnosis of breast cancer."

Additional Voices

Although not cited in the article, Schwartz had also co-authored an editorial in the British Medical Journal in 2007 after The American College of Physicians had issued new guidelines on screening mammography for women aged 40-49, recommending that US women make an informed decision after learning about the benefits and harms of mammography. She supported this move and included in her editorial a table showing that the relative risk of death from breast cancer for women in their 40s who are screened is 0.85. For those 50 and older, it is 0.78. The figures change slightly if adjusted for noncompliance during the clinical trial, but the message is that in the US, for every 1000 women screened, over the next 10 years less than one life will be "saved" for younger women and about three lives will be saved for older women. To put it another way, they said, screening of women who are 50 or older improves the chance of not dying from breast cancer in the next 10 years from about 991/1000 to 994/1000.

Balanced against that potential for benefit, women must weigh the possibility for false positive results. These results can cause short term anxiety, inconvenience, sometimes unnecessary biopsies, and overdiagnosis, i.e., finding lesions that meet the pathological criteria for cancer, but would not have progressed to cause symptoms or death. We don't know which cancers are overdiagnoses, so everyone is treated, some of whom are overtreated. The interpretation in the editorial is that "women who are overdiagnosed can only be harmed by treatment—they cannot benefit because no treatment was needed." They list the harms as disfiguring surgery, side effects of chemotherapy or hormonal therapy (such as nausea, fatigue, and hair loss), and injury from radiation. They state

that, "once informed about the possibility of overdiagnosis, most women say they would factor it into their decision about screening." They calculated that for both age groups, the risk of having at least one false positive screening examination that resulted in additional testing would be 100-500/1000 (10-50%). The risk of a patient having at least one false positive screening examination that resulted in unnecessary diagnosis and treatment for breast cancer would be 2-5/1000 (0.25-0.5%) for 40-49-year-olds and 3-9/1000 (0.30-0.90%) for ages 50 and above. (Schwartz and Woloshin, 2007).

The *New York Times* article also featured quotes from Dr. Ned Calonge, chairman of the United States Preventive Services Task Force. An expert panel that reviewed the evidence on annual mammography for the task force in 2002 downgraded the recommendation for annual screens to "recommended" from "strongly recommended." That review raised some of the same concerns mentioned by the critics in the UK: the high incidence of false-positive scares that cause anxiety yet turn out to be nothing serious, and the potential overtreatment of ductal carcinoma in situ and other indolent cancers. The panel also expressed concern about the potential for harm from exposure to radiation during the scans. The task force was not further described, but it is an independent panel of experts in primary care and prevention that reviews evidence of effectiveness and makes recommendations for clinical preventive services. The USPSTF is funded by The Agency for Healthcare Research and Quality (AHRQ), one of 12 agencies within the US Department of Health and Human Services. AHRQ says in its website that information from its research helps people make more informed decisions and improve the quality of health care services.

The newspaper article notes that US guidelines recommend annual mammography starting at 40. British guidelines recommend that women start at 50, and get a mammogram once every three years. Although mammography is more effective in older women, even among women 50 and over, the panel concluded, only one death would be prevented after 14 years of observing more than 800 women who had undergone screening. Dr. Calonge is quoted as saying, "That's a hefty number of women" who must be screened to derive a benefit. He was further paraphrased as saying that early detection may not make a difference in survival for many women.

This debate among academics, a nationalized health care system, patient advocates, and public policy providers focuses on evidence from clinical trials specifically looking at the efficacy of mammography for screening. The debate carries over to the effectiveness of mammography, i.e., how well it works in everyday clinical practice for screening for breast cancer. Either endpoint raises further questions, though. "How well it works" at doing what? Identifying abnormalities in breast tissue? Distinguishing precancerous or malignant abnormalities from benign ones? Ultimately prolonging life? The outcomes of interest are key in the framing. The other question of concern, given the very public nature of this discussion, is did it provide any helpful answers from the research to aid women in determining whether or not to have a mammogram, given that this was the stated purpose of bringing the argument to the press. Interestingly, two of the researchers cited above recently were among a group publishing in the Annals of Internal Medicine about the potential biases of press releases from academic medical centers, which "often promote research that has uncertain relevance to human health and do not provide key

facts or acknowledge important limitations." (Woloshin and Schwartz, 2009). The public discussion around breast cancer screening may unwittingly fall into that category.

AN ANALYTICAL PERSPECTIVE

The public discourse described above is an attempt by multiple parties to make sense of research on the benefits and risks of mammography used to screen healthy populations. Recommendations are made on the public's behalf by people charged with protecting the health of a populace. Unlike a public health issue such as prevention/vaccination and treatment of contagious diseases like H1N1 influenza A (the threatened epidemic formerly known as "swine flu"), this particular health measure has more distinctly personal choices. The individual patient and those close to her will see the largest impact of disease or surgery. The implications for society tend to be more in the realm of financial and other resources, given the lack of contagion.

This problem is particularly well-informed by systems thinking. The boundaries of this problem – which outcomes are "in" or "out," – as well as the frame size – at what level we set the perspective – impact the analysis. In addition, there are "time boundaries," if you will. The benefit/risk trade-off at five years could look different from that at 20 years. An analysis aimed at decision making about the value of mammography would have to begin with the question, "value to whom?" The answer to that question guides the analysis and provides clarity on what to do with the output.

Examples of Frame Size and Boundaries

If one is setting disease prevention and treatment guidelines for breast cancer, one is likely focusing on value to "society." Data or uncertainties will probably include

- the levels of risk for developing breast cancer, including types of breast cancer in different subpopulations
- effects and effectiveness of screening options, including scans, clinical examination, and/or self-examination
- costs to an insurance program or nationalized health care system for screening mostly healthy patients versus not screening early, and then treating some patients who may be more advanced in disease by the time the disease is identified without screening
- and consequences of proactive / preventive / aggressive treatment versus watching cancers that are not progressing, but could

Value generally would be placed on keeping the majority of the population healthy and productive, and would weigh heavily toward adding survival time, which might be quality-adjusted based on treatments or procedures that could detract from one's functioning or enjoyment during the days theoretically added to one's life. Cultural

values around extending length of life and what constitutes quality of life come into play. Primary stakeholders would include medical care societies, patient advocacy organizations for breast cancer, regulatory and/or government or public health bodies, and third party payers. These stakeholders would be interested in maximizing the outcomes of prevention and treatment for a population. Their members would have been providing expert advice for the analysis. At the end of the process, they would be expected to endorse the guidelines.

If one were to broaden the boundaries, the same analytical techniques could be used to compare the benefits and costs of mammography breast cancer screening versus other screening for other diseases to determine public policy on recommended screening programs for all citizens. The recommendation could be used to decide which programs would be publicly funded or should be covered in the health promotion offerings of insurance plans. In other words, it is a different analysis with different boundaries and purpose, but many of the same research sources and findings.

Likewise, one can shrink the frame. Decision analysis or other analytical approaches can be used by individuals to make personal decisions. The valuation and quantification of the outcomes can include appropriate weighting for personal preferences. Theoretically, an individual patient could use information from her own family history, her current risk factors for breast cancer, information on radiation exposure from mammography, her preferences around screening procedures and proactive surgery versus clinical- and self-examination only versus waiting for symptoms, potential for surgery and cancer treatment, and out-of-pocket costs to come to her own conclusions about whether to have mammography screening. There are in fact numerous decision tools offered to help individuals. The boundaries for these analyses are quite narrow, of course, with the objective of helping an individual patient maximize the factors she values the most. Conclusions for an individual would not be expected to match those for a population. But the facts on which the analysis is based should be the same. It is the selection and value of the potential outcomes that will differ, with patients potentially focused on outcomes additional to or instead of those of interest at the population level.

THE AVAILABILITY OF INFORMATION

There is some difficulty in trying to find information in research on mammography efficacy that has looked at outcomes helpful for patient decision making. Researchers' work is mainly for audiences making decisions at the population level. But medical decision making is moving toward the patient having more dialogue with the healthcare provider (Veatch, 2009; Painter, 2009). Studies won't predict the outcomes for individual patients, but that of course is the answer they would really like to have – what will happen if I choose this? In the absence of those answers, research needs boundaries that will ultimately inform not only policy makers, but individual caregivers and patients. Without those boundaries in the research, the interpretation of the results leaves loose ends where the data is absent.

The Cochrane Report about breast cancer screening by mammography (Gøtzsche, P.C., and Nielsen, M., 2006), referenced in the newspaper article, is one example of trying to bring research framed for a population to individual patient decision making. Reviews are published electronically by The Cochrane Collaboration. As noted above, their aim is to aid decision making by doctors, patients, policy makers and others. The review on breast cancer screening is a 61-page document with the stated objective, "to study the effect of screening for breast cancer with mammography on mortality and morbidity." The first 14 pages include an abstract, a plain language summary, and the authors' discussion and conclusions. The rest of the report contains references and detailed information from each trial. The plain language summary briefly defines the terms, "screening" and "mammography," then goes on to explain that a review of seven clinical trials collectively including one half million women found that mammography screening for breast cancer is likely to reduce breast cancer mortality, but the magnitude of the effect is uncertain. Screening will also lead to some women getting a cancer diagnosis when their cancer would not have led to death or sickness. Since researchers are unable to distinguish which women these are, the women are therefore likely to have breasts and lumps removed and to receive radiotherapy unnecessarily. The summary then repeats the relative risk and absolute risk statistics from the abstract, with no explanation of these terms. The statistics are followed by the concluding summary statement that, "for every 2000 women invited for screening throughout 10 years, one will have her life prolonged. In addition, 10 healthy women, who would not have been diagnosed if there had not been screening, will be diagnosed as breast cancer patients and will be treated unnecessarily. It is thus not clear whether screening does more good than harm." There is no further information in the plain language summary on the numbers of women who would receive the various treatments for the different types of cancer in the overdiagnosis category. In other words, the comparison information that would have to be balanced against the possibility of a life saved is not addressed in the plain language summary. This omission is not an attempt to hide information from the general reader. The researchers want to make information publicly available. But studies like the ones in their review tend to be geared toward an audience that would make decisions on behalf of groups of patients, which are not very informative for individual decision making.

Randomized clinical trials were chosen by the authors as "the only way to estimate the effectiveness of screening reliably." The seven studies reviewed in the report were identified through PubMed. The authors scanned reference lists and included letters, abstracts, grey literature and unpublished data, including direct communication with investigators to retrieve as much relevant information as they could on the trials. All trials compared screening with mammography versus no screening with mammography in women without previously diagnosed breast cancer. Large, well-designed trials were needed to find small effects such as breast cancer incidence in this population. Outcomes of interest were mortality from breast cancer, mortality from any cancer, all-cause mortality, use of surgical interventions, use of adjuvant therapy, and harms of mammography. Each clinical trial was exhaustively described, including the adequacy of its randomization techniques. Only two trials were deemed to have been randomized appropriately. Four others were judged suboptimal and one was reported separately due

to its poor design not allowing for reliability of the data. Clearly there is not a plethora of information one would deem scientifically valid.

The information that is available can be characterized differently depending upon the interests and preferences of the audience, but unfortunately some of the outcomes that would likely be of interest to patients and health care providers would not normally be included in clinical trials. Trial outcomes included breast cancer mortality as the main focus. The authors of the report explain that this may not translate into improved overall survival, as radiation therapy given to women less likely to have breast cancer recurrence, such as those whose cancer would have been found with screening, may cause other health problems including blood vessel damage from some types of radiotherapy and possible increased risk of lung cancer. References but no statistics are given for these health risks, and it is noted that the risks are likely to be small compared to the decrease in breast cancer mortality. The authors also believe that there is bias in classification of cause of death, even when cause of death is determined blindly, i.e., without knowing whether the patient was in the screened group or the control group. Although the authors describe statistically why they believe this to be the case, they do not explain how the bias is likely to occur with blinded adjudication. With regard to overdiagnosis and overtreatment, which are the authors' main concern with women not being informed of the risks of mammography by information pamphlets, the authors of the report cite a WHO source in saying that, "Overdiagnosis is an inevitable consequence of screening and an obvious source of harm (WHO 2002)." The cancers that will be detected by screening primarily will be slow-growing, or will be biologically benign cell changes. Survival of women with screen-detected cancers is consequently very high. The authors note a source that reports even for cancers within the same stage, survival is higher in cancers detected by screening than for cancers detected clinically (Moody-Ayers 2000). On the surface, that summary would sound like a benefit of having mammography, but no further explanation is given.

In reading the Moody-Ayers et al. article cited above, Moody-Ayers et al.'s conclusion is not that mammography provided an advantage, but that more benign cancers were detected by mammography, thus raising the survival rates associated with mammography, by including lesions that would not have progressed anyway, but would not have been detected and counted in other study groups. The study is a retrospective natural cohort examination of 233 patient records over 5 years. Each woman had a histologically demonstrated, primary carcinoma of the breast, diagnosed while she was alive, and received antineoplastic treatment. The researchers stated that their results should not be used to question the value of mammography screening, whose comparative efficacy is best seen in randomized trials and particularly those with the main outcome of reduction in all-cause mortality. They did note, though, that based on the admittedly small number of 31 cases of carcinoma in situ (CIS), none had recurrences or cancer deaths. Aggressive therapy, meaning treatment beyond lumpectomy alone, was used for 23 (74%) of the patients. Fifteen (48%) had mastectomies, including 3 who underwent bilateral partial mastectomies. None of these patients had cancer death or recurrence, regardless of the extensiveness of treatment, so the authors suggest that the need for aggressive forms of therapy might be reconsidered. The researchers also noted that for patients in earlier progressive stages (TNM stages I and IIA), when the sample was

stratified by method of detection, mammography versus "other-screening" or symptomatic, the mammography screening group had significantly higher survivals, even with multivariable adjustments for age, menopausal status, race, and/or insurance status. They saw these findings as demonstrating again that mammography screening seems to detect more benign tumors than those found by other methods. Other screening, in fact, provided no improvement in outcomes when compared with the symptomatic group. Looking at type of antineoplastic therapy received by these women in stages I and IIA, stratified by method of cancer detection, there were 3 main types of surgical treatment, used alone or accompanied by radiation therapy and/or chemotherapy. All patients had surgery. The rates of the 3 progressively more aggressive forms of therapy were, respectively, 26%, 27%, and 47% in the mammography screened group (N=66), compared with 15%, 25%, and 60% in all others (N=85). Total rates of augmented (added radiation/chemo) therapy were 42% in the mammography group and 41% in all others. The authors state that, "since the MMG [mammography] screened group was not treated more aggressively, treatment cannot be held responsible for the group's better survival." There is no discussion of an alternative explanation such as detection by mammography might have allowed more successful treatment of tumors that would have progressed. Their assumption is that the apparent survival advantage is an artifact of the classification system, with milder tumors having been identified by mammography but put in the same class as more advanced tumors found in the other groups.

For a fuller explanation of tumor types and progression, and their implications for screening, one needs the WHO publication cited above and in the Cochrane Review, *Breast Cancer Screening,* one of the *IARC Handbooks of Cancer Prevention*. This handbook contains a wealth of information and explanation at a technical level. It defines precancerous and possibly precancerous conditions, as well as abnormal findings on mammography and their positive predictive value for malignancy. It also explains some of the difficulties in comparing findings across studies, in part due to differences in classification and inconsistent nomenclature. These explanations can help elucidate the reasons for unresolved debate around screening for breast cancer, but unfortunately can't solve the immediate problem with the current data. The publication also points to research that remains to be done to answer fundamentally important questions about the natural history of different types of cancer. The handbook supports the arguments above that mammograms detect more conditions, including benign abnormalities and potentially precancerous findings than would have been detected without mammography. It also suggests that the characterization of the findings requires skill, and reviews of study findings would be better served if characterization could be done in more consistent ways. It concludes that the currently available evidence supports the efficacy of screening 50-69-year-old women by mammography for reducing mortality from breast cancer. It also confirms that there is limited evidence for the efficacy of screening 40-49-year-old women by mammography. The research under discussion in all of the publications above thus concludes that there is some benefit to screening, but leaves open the question of how to characterize the risk and how to weigh one against the other. In fairness, the point of the entire public debate was to raise the question – to point out that mammography has risks and not just benefits. But what is a patient intended to do with that information in and of itself?

TRANSLATING AGGREGATE FINDINGS TO INFORMATION FOR THE INDIVIDUAL

One venue in which the clinical trials data is translated to the patients, and where the proverbial rubber meets the road, is in publications written specifically to patients, or in this case, healthy women who could become patients. The UK's National Health Service (NHS) published a pamphlet -- the subject of the letter to *The Times of London* – that provides information on breast cancer screening by mammography. The pamphlet explains what mammography is, how and when it is done, and who is eligible. "To help you decide whether or not to come for breast screening," it characterizes the "main benefits and difficulties" as follows:

- Most breast cancers are found at an early stage when there is a good chance of a successful recovery.
- Around half the cancers that are found at screening are still small enough to be removed from the breast. This means that the whole breast does not have to be removed.
- Breast screening saves an estimated 1,400 lives each year in this country.
- Breast screening reduces the risk of the women who attend dying from breast cancer
- We will call back some women for more investigations if we are not sure about their mammogram. After more tests, we will find that many of these women will not have cancer. If you are called back it can cause worry.
- Screening may miss some breast cancers.
- Not all breast cancers that are found at screening can be cured.
- Many women find mammography uncomfortable or painful, but normally just for a brief period of time.

The alternative pamphlet recommended by the authors of the Cochrane Review summarizes the benefits and risks in this way. "If 2000 women are screened regularly for 10 years, one will benefit from the screening, as she will avoid dying from breast cancer. At the same time, 10 healthy women will, as a consequence, become cancer patients and will be treated unnecessarily. These women will have either a part of their breast or the whole breast removed, and they will often receive radiotherapy, and sometimes chemotherapy. Furthermore, about 200 healthy women will experience a false alarm. The psychological strain until one knows whether or not it was cancer, and even afterwards, can be severe." Farther down in the pamphlet, they elaborate on the effects of overdiagnosis and overtreatment. For "false alarm," they explain, "If 2000 women are screened regularly for 10 years, about 200 healthy women will experience a false alarm. The psychological strain until it is known whether or not there is a cancer can be severe.

Many women experience anxiety, worry, despondency, sleeping problems, changes in the relationships with family, friends and acquaintances, and a change in sex drive. This can go on for months, and in the long term some women will feel more vulnerable about disease and will see a doctor more often." They provide summaries of the clinical trial results to back up the impact on mortality, the numbers of women who experience false alarms, and the number of women who report pain associated with the mammogram. There is no further information provided on the anxiety, worry, despondency, sleep problems, changes in relationships, changes in sex drive, or amount or duration of pain felt during the procedure. A line at the bottom of the page below the reference section tells the reader, "Further information can be obtained by contacting the doctor." Given the research reviewed above, it is not clear where the doctor would obtain that information.

MAKING THE DECISION

If an individual candidate for breast cancer screening is trying to decide whether or not to attend her mammogram appointment, it is not obvious that any of the information provided in the newspaper article or the pamphlets answers her questions. Translating the results of research and deciphering the implications for patients seems to have been left to journalists. If current research is not designed to inform an individual patient's choices, consideration needs to be given to the data that will inform the patient and her healthcare provider. While every patient may differ in her priorities and concerns, and certainly there will be many combinations of risk factors to consider, it is reasonable to try to outline the ways in which research can address areas that seem to be of immediate concern, with acknowledgement that more work is needed to gather additional information and to define the most appropriate ways of incorporating multiple points of view in making decisions.

Using an analytic approach, such as decision analysis, to frame research questions, for example, may help to clarify information that would be important for audiences beyond the regulators and payers who are the usual targets for the information. There are efforts in the UK and, to a lesser extent, in the US to use decision analytic approaches to begin making quantitative assessments of benefit and risk in drugs under development. Certainly no analysis will include all variables of interest to all patients, but consideration can be given to important elements that may be missing. For example, it is common as part of a decision analysis to understand not only the probability of an outcome, but the consequences of certain outcomes. If some outcomes are unacceptable, no matter how low the probability, then part of the objective becomes avoiding that outcome. This could color the analysis of mammography outcomes. Health care providers and patients need sufficient information to compare the probabilities of unnecessary surgery versus possible malignancy in the future. To compare unnecessary surgery, more information is needed on what the surgery entails. Do most women have lumpectomies or mastectomies, and under what circumstances? What happens if chemotherapy or

radiation is recommended? How long do side effects generally last? What is the risk of cardiovascular harm from radiation?

Communication skills can help in describing this information so that healthcare providers and patients can weigh the options, but the communicators need the data, preferably in the context of the rest of the studies from which they are deriving information on mortality and morbidity. A report like the Cochrane Review is based on the best scientific studies that could be identified with long-term data to include mortality outcomes, but those studies were never designed for their eventual use in helping patients decide whether or not to have mammograms. Yet there is no better data available, and there is agreement that well designed clinical trials provide the best data to answer these questions.

RESEARCH MOVING FORWARD

Systems theory suggests that research will be more productive and informative when one understands the question to be answered and within what boundaries it is being answered. The stated goals of the efforts to analyze benefits and risks include providing transparency for decision making. The methods for measuring benefit and risk are still exploratory. The published research and commentary surrounding it are generally meant to inform one or more decisions, but as has been seen, it is far from clear whose decision at what level is best informed at present. It seems reasonable to posit that moving forward in this area, clear articulation not only of the benefits and risks we are analyzing, but why we are undertaking the analysis, as well as the intended audience for the results, may provide better insight from benefit/risk research, both in shaping the research and in reporting the results. Techniques for weighing risks and benefits vary widely, but can include simulations, multi-criteria decision analyses, health economic analyses of cost-effectiveness and/or quality of life, and Markov modeling. As with any analysis, the purpose needs to guide the method. The intent here is to encourage explicit articulation of that purpose, and recognition of the broader implications of research into benefits and risks.

Banathy, Ackoff, and Churchman would all be likely to argue for the ethical necessity of the patient's perspective in this research and its use (Banathy, 1996; Midgley, 2000). This was the apparent objective in publishing a letter about mammography in the newspaper. However, the challenge remains in creating a helpful method for dialogue. Making information available is one step of many in creating a healthy and informative public discourse that can benefit a population.

Although the current work admittedly focuses narrowly on Western medicine and a limited number of agents within a few technologically based healthcare systems, it is anticipated that the work may inform other areas of healthcare and applied research.

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