PERSPECTIVE

Evidence, Values, Guidelines and Rational Decision-making

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Medical decision-making involves choices, which can lead to benefits or to harms. Most benefits and harms may or may not occur, and can be minor or major when they do. Medical research, especially randomized controlled trials, provides estimates of chance of occurrence and magnitude of event. Because there is no universally accepted method for weighing harms against benefits, and because the ethical principle of autonomy mandates informed choice by patient, medical decision-making is inherently an individualized process. It follows that the practice of aiming for universal implementation of standardized guidelines is irrational and unethical. Irrational because the possibility of benefits is implicitly valued more than the possibility of comparable harms, and unethical because guidelines remove decision making from the patient and give it instead to a physician, committee or health care system. This essay considers the cases of cancer screening and diabetes management, where guidelines often advocate universal implementation, without regard to informed choice and individual decision-making.

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Medical decision-making involves uncertainty. Even in the most evidence-based circumstances, as when several large well-designed randomized controlled trials (RCTs) provide consistent evidence regarding group outcomes, prudent clinicians understand that individual outcomes are uncertain, and that available data may or may not generalize to their patients. At best, RCT data allow estimation of the probability and magnitude of benefits for people similar to those enrolled in the supporting trial(s).[1]

Familiar patient-oriented benefits include reduced chance of cardiovascular event or disease-specific death, improved function, or reduced symptom load. For most clinical decisions there are also harms to be considered, such as unpleasant side effects, major adverse events, or onerous economic or opportunity costs. Both benefits and harms come in ranges of frequency and magnitude. For example, heart attacks and strokes range from minor to devastating, as do adverse events resulting from medical interventions. Thus, when choosing among available options (including watchful waiting), the clinician and patient should consider the likelihood, magnitude, and importance of all relevant benefits and harms. Following the ethical principle of autonomy,[2] decision-making should be at the individual level, with the patient's values the final arbiter.

To bring this theoretical discussion to a practical level, let us consider two examples: 1) screening for cancer, 2) monitoring and treating diabetes.

Both colonoscopy and mammography are supported by considerable evidence. Numerous studies have demonstrated that these screening tests are sometimes able to detect cancers that might have grown and metastasized without screening. In both cases, there are treatments that may reduce cancer spread and/or extend life. An optimistic interpretation of current evidence suggests that regular colon cancer screening starting at age 50 may reduce lifetime chances of dying from colon cancer from about 3% to about 2.5% (absolute risk reduction=0.5%; relative risk reduction=17%; number needed to screen for benefit=200).[3] The risk of serious harm from colonoscopy, such as intestinal perforation, major bleeding, or induced cardiovascular event, is estimated to be approximately 2.8% (number needed to harm=36).[3] Weighing these estimates of potential benefits and harms, along with near-certain discomfort and some monetary and opportunity costs, an intelligent, rational, health-conscious adult might very well choose not to be screened.[4] As the doctor I may or may not agree with that decision, but it is the patient's values, not mine, that should drive the decision-making process.

Similar reasoning applies to mammography. Without screening, approximately 5.3 of 1000 women aged 50 to 60 will die from breast cancer over a 10 year period.[5] Regular screening could reduce this to 4.6, thus reducing one breast cancer death for every 1,500 women screened over a decade. However, for every 1000 women screened, between 50 and 200 will have a false positive result requiring biopsy, and at least one or two will be diagnosed and treated for a breast cancer that would have spontaneously regressed or otherwise not caused any harm.[5–8] Biopsies rarely cause harm, but unnecessary cancer treatments surely do. Factoring in fear, pain and quality of life, it is not difficult to understand that many intelligent, health-conscious and well-informed women might choose not to screen.

Additional relevant information comes from the prostate, lung, colorectal, and ovarian cancer screening trial, where one paper reported that during a 3-year screening period, 60% of men and 48% of women had false positive tests, and 28% of men and 22% of women in the trial had an invasive biopsy due to false positive screening.[9] A large number of such procedures will lead to a small number of serious adverse consequences, such as serious infection, induced cardiovascular event, or

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even anaphylaxis or death. Considering the imprecise estimates of both benefits and harms, and factoring patient values, it seems reasonable that some well-informed health-conscious rational adults might choose to not screen.

Our second example comes from the linked epidemics of obesity, inactivity, and type 2 diabetes. A robust body of knowledge demonstrates that people with elevated blood glucose levels, reflected in higher HbA1c, tend to have worse outcomes, such as more frequent heart attack, stroke, kidney failure, blindness and amputation. Until recently, it was generally assumed that medications that reduce blood sugar would also improve diabetic outcomes. Perhaps due to this assumption, numerous guidelines have advocated aggressive blood sugar treatment, with frequent HbA1c monitoring and targets of 7% or less. However, data from the flawed UKPDS,[10] combined with the higher quality ACCORD[11]and ADVANCE[12] trials, fail to demonstrate that intensive blood sugar lowering leads to significant reductions in patient-oriented outcomes. The ACCORD trial, which aimed for a HbA1c of≤6%, was stopped prematurely because of excess deaths in the intensive treatment arm.[13] While it is widely claimed that pharmacologic treatment of hyperglycemia improves microvascular outcomes, the degree of benefit, the target population, and the appropriate target HbA1c have not been determined. Thus, it seems reasonable to assume, that given adequate understanding of this evidence, some substantive proportion of intelligent, rational, health-conscious adults with type 2 diabetes might choose to forgoe antihyperglycemic medications and frequent HbA1c testing, and instead focus their efforts on diet, exercise, platelet inhibition, and appropriate blood pressure control. I am not saying that this is the preferred course for everyone or even that doctors should advocate this pathway, only that it would be completely reasonable and rational for a patient to do so.

What is neither reasonable nor rational is a medical system that purports to be both evidence-based and patient-centered, yet persists in the paternalistic practice of making decisions for people, without informing them of the pros and cons of the options available. The number of women undergoing mammography is used as a marker of quality, as is the frequency of HgA1C testing among diabetics. Systems aim for 100% compliance, and rewards or punishments are often attached. Yet evidence showing that HgA1C-monitoring or drug-based HgA1C-lowering is useful to patients is rudimentary at best, as is knowledge of what proportion of women would judge mammography's benefits to outweigh harms. Indeed, our very language is biased. The term "benefit" is often paired with "risk," as if positive outcomes from medical interventions were inevitable and negative outcomes only possible. It would be more rational (and honest) to use terms such as "possible benefits" and "possible harms," and to accompany them with understandable portrayals of the evidence.

A rational approach to medical research would investigate potential harms and benefits equally, and would be targeted at maximizing public health, not pharmaceutical profit.[14] A rational approach to medical decision-making would involve evidence-based assessment of likelihood and magnitude of positively and negatively valued outcomes, with careful targeted communication of that information to patients. I am not saying that this will be easy. However, I am arguing that such an approach is possible, ethically mandated, and long overdue. Because of time limitations and associated economic costs, decision aids such as fact sheets, informational videos, and risk communication tools might be needed.[15,16] Clinicians might need additional training in numeracy,[17] natural frequency presentation,[18] or risk communication.[19] Wider incorporation of health educators may be needed. The paradigm of shared decision-making must be accepted, incorporated and expanded.[20–22]

Archie Cochrane is said to have in his youth marched through the streets of London with a banner proclaiming that "all effective treatment must be free."[23] Since that time, many thousands of RCTs have been reported, and the upstart science of clinical epidemiology has evolved into the robust and mature field known as evidence-based medicine. Medical science has progressed so rapidly that the re-framing of known truth as discarded dogma has become routine. Nevertheless, it remains the individual patient, preferably guided by a knowledgeable physician, who must decide whether the benefits-suggested-by-evidence outweigh the harms-suggested-by-evidence.

Given my own reading of the medical literature, it seems that there are very few circumstances where potential benefits so clearly outweigh potential harms that decisions can be made without consulting the patient's own values. Guidelines often promote universal implementation of evidence-based interventions. This seems wrongheaded, both from scientific and ethical perspectives. Could it be that 99% of type 2 diabetes with HgA1c levels between 7% and 9% would want to take several medications and have their blood tested every 3 months in order to achieve potential benefits that are so far unproven? Could it be that 99% of women aged 50 to 60 would want mammography, if they understood the evidence on both benefit and harm? While developing their guidelines, well-meaning and presumably well-informed scientific review groups and medical societies may have conflated evidence-of-benefit with evidence-that-benefits-outweigh-harms, neglecting the ethical mandate that medical decisions should be shared, informed, and driven by patients' values. If Archie Cochrane were here today, I would gladly march with him, but would carry a banner reading, "Patients should be free and fully informed when making their evidence-based medical decisions."

Conflicts of Interest: *None.*

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