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The Odyssey of Risk Framing in Cardiovascular Medicine: A Patient-Centered Perspective

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"The best interest of the patient is the only interest to be considered."[1]

— William J. Mayo, MD

Patient autonomy and input in clinical decision making has been an area of increasing interest in the past 2 decades. In contemporary practice, patients are frequently asked to take a major part in making complex decisions regarding their health. Indeed, documentation of shared decision making is now required for reimbursement of some major procedures.[2] Optimal implementation of shared decision making requires proper patient understanding of the risks and benefits of the recommended treatment. Unfortunately, the physician's ability to understand and communicate those risks and benefits is hindered by the increasing complexity of data analytics and data presentation methods in modern research, as well as the time constraints imposed by busy practice models. In this viewpoint, we highlight the issue of risk framing in the medical literature and its potential effect on patient and physician perceptions of risks, benefits, and their preparedness to make important decisions regarding their cardiovascular health.

Relative vs Absolute Risk Framing

Discerning the risk of adverse events and the benefit of an intervention to reduce that risk is a fundamental pillar of medical practice. However, the magnitude of risks and benefits can be reported in various forms (relative [RRR] and absolute [ARR] risk reduction, hazard ratio, time-to-event, etc). This variability may have major consequences on the perception of those risks and benefits by both the physician and the patient alike, especially when considering costly medications or interventions. For example, in the field of cardiovascular medicine, the potential benefit from a certain intervention is usually stated to the patient in the form of RRR rather than ARR. Although this may be appropriate from a population health standpoint, it may be misleading and less meaningful to the individual patient, whose main interest remains his or her own health.

Aggregate vs Individualized Risk Framing

The average treatment effects are usually reported for the overall cohort of patients and do not account for individual patients' risk profiles. This practice may obscure important categories of patients who do not benefit and may be harmed by the treatment. However, unfortunately, the ability to devise risk scores that will estimate the risk of benefit or harm for individual patients is often limited by many factors, such as the low number of events, the frequent use of composite end points, the lack of incentives by study sponsors, etc.

Herein we illustrate the challenges associated with risk framing from a patient perspective using the example of 3 cardiovascular interventions (Table).

Dual Antiplatelet Therapy in Patients With Acute Coronary Syndrome Without ST-Segment Elevation

In the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial, patients who received clopidogrel + standard of care had lower rates of the composite primary end point (death [cardiovascular

TABLE. Illustration of the Benefit of Medical Treatment From a Patient Perspective[a]

Clinical statement	Outcome	Event rate (%)	RRR (%)	ARR (%)	NNT	Likelihood of no benefit (%)	Individualized risk/benefit score
ASA + clopidogrel is superior to ASA alone in patients with acute coronary syndrome and no ST-segment elevation	MACE[b]	9.3 vs 11.4	20	2.1	47	97.9	Not available
Apixaban reduces the risk of hemorrhagic strokes by 50% compared with warfarin	Hemorrhagic stroke	0.24 vs 0.47	49	0.23	238	99.8	Not available
Adding canagliflozin to standard of care in diabetic patients with renal insufficiency improves outcomes	MACE[b]	9.9 vs 12.2	20	2.3	40	97.7	Not available

[a]ARR = absolute risk reduction; ASA = aspirin; MACE = major adverse cardiovascular event; NNT = number needed to treat; RRR = relative risk reduction.
[b]Death (cardiovascular causes), nonfatal myocardial infarction, or stroke.

causes], nonfatal myocardial infarction, or stroke) compared with those who received placebo at 1 year (9.3% vs 11.4%; $P < .001$).[3] This represented a remarkable 20% RRR and led to widespread adoption of clopidogrel in the management of acute coronary syndrome. However, for an individual patient, clopidogrel in this setting would reduce his or her chance of the composite end point by only 2.1%, mostly driven by reduction of nonfatal myocardial infarction. Furthermore, despite the routine use of clopidogrel, there are no risk scores that would allow personalized risk/benefit assessment for individual patients.

Apixaban vs Warfarin for Stroke Prevention in Patients With Nonvalvular Atrial Fibrillation

Direct oral anticoagulants are replacing warfarin as the most commonly used anticoagulants for stroke prevention in patients with atrial fibrillation. This shift was driven by the similar efficacy in stroke reduction but the lower rates of intracranial hemorrhage with those agents vs with warfarin. In one landmark trial, the incidence of intracranial hemorrhage per year with apixaban was reported to be approximately 50% lower than that with warfarin (0.24% vs 0.47%; $P < .001$).[4] However, from a single patient perspective, the ARR of intracranial hemorrhage with apixaban was 0.23%, corresponding to a likelihood of not deriving benefit from an incremental reduction in intracranial hemorrhage with apixaban of approximately 99.8%. Such reframing is critically important in understanding the true magnitude of benefit (or risk), particularly when out-of-pocket costs vary markedly between these treatment options (~$18 for warfarin vs $556 for apixaban).[5]

Canagliflozin in Diabetic Patients With Renal Insufficiency

Patients with diabetes mellitus are a disadvantaged group with a high burden of cardiovascular risk factors. Several studies have recently assessed the role of novel agents in reducing the excess cardiovascular morbidity and mortality in diabetic patients. In the Canagliflozin and Renal Events in Diabetes With Established Nephropathy Clinical Evaluation (CREDENCE) trial, patients who received canagliflozin, 100 mg daily, had a lower incidence of the composite primary end point (death [cardiovascular causes], nonfatal myocardial infarction, or stroke) at 2.6 years (9.9% vs 12.2%; $P < .001$), which translates into a 20% RRR.[6] On the other hand, from a patient's perspective, only 2% of patients will derive some benefit from this costly medication (>$500 out-of-pocket monthly copay), whereas the other 98% would see no incremental benefit from the treatment, but all would bear the expense of a costly new therapeutic agent.

Patients live in an absolute world. The focus on RRR and the lack of individualized risk/benefit assessment tools in the literature continues to divert from what is meaningful to

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the main stakeholders in medicine, the individual patient. The time has come to reconsider our data reporting methods and to invest in innovative decision aid tools that will allow patients to be effective partners in making major decisions related to their own health.

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