REVERSING, RIGHTING, AND REDEFINING MEDICAL PRACTICE

Medical practice and their guidelines, even those based on literature published in high impact journals, are not infallible, as highlighted in recent years by the phenomenon known as “medical reversal.” Medical reversal occurs when a more recent and rigorous study gainsays the validity of a current medical practice and the studies upon which they are based. For example, a seminal study by Prasad et al in Mayo Clinic Proceedings in 2013 evaluated original articles published in the New England Journal of Medicine over a 10-year period and showed that while 38% of articles addressing standards of care supported the appropriateness of current practices (reaffirmation), approximately 40% of articles refuted practices based on prior literature (medical reversal). In the present issue of Mayo Clinic Proceedings, Herrera-Perez et al significantly advance the field by examining medical reversal in studies involving cardiopulmonary resuscitation (CPR). Their analysis was based on a previously published systematic review (Sinha et al. Circ Cardiovasc Qual Outcomes. 2016;9:749-756) of 92 randomized controlled trials of cardiac arrest occurring in- or out-of-hospital in approximately 65,000 patients and published over a 20-year period (1995 to 2014). Of these 92 trials, 16 were excluded by Herrera-Perez et al either because they did not meet the inclusion criteria or were indeterminate. Analyses of the remaining 76 studies demonstrated that the majority evaluated established practices, while the minority involved new practices. Notably, reversal of a current practice was reached in 58% of studies, with the majority of the reversals involving drug therapies or devices. Herrera-Perez et al discuss reasons why the relative high frequency of medical reversals occurs in CPR, including the possibility that the exigency of CPR may more readily incorporate new practices that have not been rigorously evaluated. Broadly considered, the following concepts have emerged from the field of medical reversal. First, while experts may differ in their definitions, medical reversals are not simply low value health care, but rather they reverse practice that was inherently devoid of any value. Medical reversals should also be distinguished from medical replacement as the latter provides a more beneficial practice in place of an existing one of lesser (but still tangible) benefit. In contrast, medical reversals bespeak complete inefficacy or lack of benefit, or worse, the potential for harm, of a given practice, and the attendant compromised and misguided care of patients. A second major consideration is how do reversals arise. Medical reversals are generally driven by prospective, randomized controlled trials that incorporate more rigorous methodology, greater statistical power, improved trial design, and more relevant endpoints and controls than trials supporting the reversed practice; reversals may also reflect weak clinical evidence to begin with, or the premature application of biologically plausible preclinical findings. Finally, another pathway for reversals arises from considerations percipiently delineated by Dr Ioannidis in a previous editorial in Mayo Clinic Proceedings. These considerations center on the fact that the majority of treatments and interventions in medical practice are incremental in nature, with beneficial effects that are hardly striking, and that interventions which substantively and consistently improve such incontrovertible endpoints as mortality are relatively rare. Given this relatively limited amplitude of benefit with most new therapies and interventions, entirely unforeseen vagaries
such as those pertaining to the targeted patient population, real world effects, unexpected adverse effects, and unanticipated costs — in aggregate and in time — may cast a new and now unfavorable light on a once appealing and apparently supported therapy. Medical knowledge generally moves forward with small and, not uncommonly, tentative steps, and what may seem at a given time as beneficial, substantiated, and plausible, may decidedly fall from favor in the light of subsequent analysis and added experience. The present study by Herrera-Perez et al highlights the need to scrutinize the validity of current medical practices and guidelines, to apply the most rigorous and best available evidence in informing such practices, and to be ready for course correction when indicated by subsequent data and knowledge.


SURVEYS AND THE SIGNIFICANCE OF SILVER BLAZE

In Arthur Conan Doyle’s celebrated story on the disappearance of the champion racehorse Silver Blaze, Sherlock Homes homed in on his suspect by reasoning that whoever was involved in the disappearance of Silver Blaze that night must have been very well known at the stable because the stable dog never barked during the night. This key finding in solving the mystery exemplifies the general principle that a lack of response — and not just a response — may reveal its own inimitable truths. This principle is highly relevant to biomedical research, and a remarkable example of it is provided by the timely study by Simsek et al in the current issue of Mayo Clinic Proceedings. These investigators conducted a survey of patients with the first-ever code for heart failure and who resided in southeast Minnesota. They assessed the characteristics and the outcomes of those surveyed through the medical record database of the Rochester Epidemiology Project. In this survey involving approximately 8000 patients, the response rate was 43%, and, on follow-up of some 1.5 years after the survey was conducted, there was a remarkable divergence in outcomes between nonparticipants and participants in the survey: nonparticipants exhibited a two-fold increased risk of death and an increased rate of hospitalization after adjustment for a number of relevant factors. Nonparticipants differed from participants in several ways in that the nonparticipant group comprised a higher percentage of individuals who were female, single, nonwhite, less well educated, resident in rural areas, and with diagnoses of mental and psychiatric disorders; in contrast, nonparticipants were less likely to be diagnosed with cancer and assorted cardiovascular diseases. The findings of Simsek et al have several major and far-ranging implications. First, they speak to the issue of participation bias as a limitation that may weaken the validity of epidemiologic studies; specifically, Simsek et al showed that their survey did not capture information from individuals with significantly different health outcomes. Second, as pointed out by the authors, the current literature describes an association of a lack of participation in surveys with certain characteristics, several of which (lower levels of education, being single, among others) were also observed in their study. A lack of participation in surveys by patients may also reflect their lower sense of connectivity with their health care system or their greater sense of the burden of their disease and treatment. Third, health care delivery increasingly emphasizes patient-centric care, the latter enabled by patient reported outcomes; a lack of response in reporting such outcomes by significant subsets of patients would compromise patient-centric care. Fourth, while the basis for worse outcomes such as mortality and hospitalization rates in nonparticipants remains unknown, it
is notable that almost 50% of nonparticipants refused to respond to the survey, and some 25% did not respond to attempts to contact them by study personnel; this raises the issue whether such denial intimates a much broader denial of their disease, and the extent to which disease denial may be relevant to adverse outcomes. The findings by Simsek et al are especially important because they reach beyond a disease-specific (heart failure) survey to speak to the issue of participation bias in surveys in general. Finally, these findings show how important epidemiologic clues and information can be gleaned from surveys by interrogating outcomes in those who do not respond or do not participate.


INSTITUTIONAL STRATEGIES IN ADDRESSING THE OPIOID CRISIS

Recent articles in Mayo Clinic Proceedings have addressed key aspects of the opioid crisis including, among others, the historical underpinnings and scope of this epidemic, the appropriate use of opioids for specific syndromes, the indications for medication assistance programs, and the need for a reasoned approach in balancing the risks and benefits of the use of opioids. In the present issue of Mayo Clinic Proceedings, Gazelka and colleagues provide an institutional perspective regarding the opioid crisis. This perspective draws upon the experiences, knowledge, and initiatives of the Mayo Clinic Opioid Stewardship Program that evolved shortly after a multidisciplinary work group was convened by Mayo Clinic leadership in 2016. Key findings from initial surveys undertaken by this work group indicated that there was a consensus regarding the need for consistency in the way opioids are prescribed; and that doses and patterns of opioid prescribing ranged widely in the surgical practice, with many prescriptions never utilized or not appropriately discarded. The Mayo Clinic Opioid Stewardship Program targeted four main areas that include short- and long-term prescribing, education, and electronic health record (EHR)-related initiatives. Groundwork to the development of institutional prescribing guidelines included a review of the opioid guidelines formulated by the Centers for Disease Control and Prevention as well as a review of relevant state legislation where Mayo Clinic’s practice is based (Arizona, Florida, Minnesota, and Wisconsin). Short-term opioid guidelines included provider responsibilities (including prescription drug monitoring program), patient selection, and dosing. Three aspects of these guidelines merit emphasis. First, as short-term prescribing by total morphine milligram equivalents (MME) may predispose to chronic opioid use, the guidelines included recommendations on a daily supply in addition to a MME maximum. Second, the guidelines were based on tiers determined by the severity of pain anticipated from the type of intervention or procedure. Third, these guidelines were made available to providers in the intranet database of Mayo Clinic, AskMayoExpert. Long-term prescribing included patient selection, dosing, provider responsibilities and monitoring, and deescalation. Educational strategies drew upon surveys and focus groups that assessed understanding of opioid prescribing and utilized multiple conduits to provide information on opioid prescribing: email, AskMayoExpert, computer-based modules, CME content, and an Opioid Stewardship Intranet website. Special attention was given to messaging for patients that utilized handouts, pamphlets, and videos. Public messaging was also pursued through community engagement and engagement with regional and national media. EHR-related initiatives and features were introduced to harmonize prescribing practices and patient monitoring within the context of institutional policies and to facilitate EHR-based administrative tasks for providers. The article concludes with an overview of difficulties encountered, insights derived, and current initiatives in the Opioid Stewardship Program. Gazelka and colleagues are to be
commended for leading, synthesizing, and effecting these institutional initiatives and policies and for their clear summary of them in this important article.


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