Chapter 16
Ethics in Research and Publication

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Abstract Medical research and publication serve to promote the scientific integrity and efficacy of the medical profession. The ethical principles of beneficence and nonmaleficence demand that physicians strive to advance medical knowledge so as to improve patient's lives and avoid harmful or ineffective patient care. The objective of medical research is to seek scientific truths and support these ethical principles. The integrity of clinical investigation involves the just and honest conduct of experimentation, the honest analysis and reporting of data, and then, the fair peer review and publication of these investigations. Research and the publication of research executed dishonestly divert the search for factuality and defile the medical literature. Within the last two decades, several clinical researchers from various specialties whose publications profoundly influenced the practice of anesthesiology were guilty of extensive research fraud and misconduct, and therein, adversely affected the safe practice of anesthesiology.

Keywords Research and Publication Fraud • Research Misconduct • Fabrication and Falsification of Data • Plagiarism • Ghost and Honorary Authorship • Redundant Publication • Ethical Peer Review • Ethical Journal Editorship • Perioperative Beta-Blockade • Quality Performance Measures

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B.G. Jericho (ed.), *Ethical Issues in Anesthesiology and Surgery*,
DOI 10.1007/978-3-319-15949-2_16

Case Presentation
Your hospital is vigorous in ascertaining compliance to the Surgical Care Improvement Project (SCIP). In fact, the anesthesia record, newly constructed in 2013, has a specific area for confirming adherence to SCIP measures, including perioperative continuation of beta-adrenergic blocking drugs for patients on chronic therapy. A 78-year-old patient is scheduled for a same-day outpatient bilateral laparoscopic inguinal hernia repair. Other than hypertension treated with a beta-blocker (and one other antihypertensive taken at night) and some mild memory loss, the patient has an otherwise normal history with no cardiac symptoms. The patient was instructed by the preanesthesia nurse to take her usual evening dose of antihypertensive medications, including metoprolol. However, on the morning of surgery, she admits to having failed to take her nightly medications, attributing this to her forgetfulness and being distracted by concerns over her surgery. Without any anesthetic premedication, she arrives at the operating room alert and moderately apprehensive, with vital signs unchanged from the admission area – pulse 47 and blood pressure 90/68. Your resident judges that she might be overly beta-blocked and does NOT want to administer any beta blockade drugs in the perioperative period unless indicated. Yet, she knows that she then would not be in compliance with the SCIP beta-blockade measure unless a note documenting the reasons for such were placed in the chart. She suggests that it would be easier and prudent to administer 1 mg of esmolol IV in order to satisfy the SCIP requirement. She and most of her department are unaware of the retirement of this SCIP measure by the Centers for Medicare and Medicaid Services and The Joint Commission as of December 31, 2014. You notify the resident that the establishment of the beta-blocking drug quality measure was largely based on two studies [1, 2] from the 1990s that later were found to be insufficient scientifically, and even of greater concern, in one case, likely fraudulent [2].

Introduction

The "social contract" of physicians obliges them to *demonstrate that they deserve social trust, authority and reward. Societies expect that a physician's primary concern is their patient's well being. Three themes – personal character, interpersonal duty and social responsibility – are recurrent topics of ethical reflection, and constitute the threads that bind medicine and morality. This has come to be known as medical ethics* [3].

The ethics of clinical research may best be understood from three disparate perspectives: (1) the process of obtaining new knowledge; (2) the moral use of that knowledge; and (3) the personal ethics of the scientist pursuing this knowledge [4]. This latter element, that of the personal morality of the clinical investigator, deserves

particular attention, as the physician researcher is the ultimate guardian of the design, safety, conduct and analysis of the study, the knowledge gained there from, and its dissemination to the medical profession. The personal ethics of a research scientist is a critical element of the moral quality of human research.

Clinical researchers have potentially conflictive roles as *scientist, physician and private individual*, and each of these roles is commanded by a different ***value*** [4].

For ***science***, the value system is truth – knowledge is good in its own sake – and the discovery of "generalized concepts, theories or laws about human physiognomy or disease" [4]. Scientists must rigorously design studies and examine these experiments for their verifiability and falsifiability. "Observations must be accurate, honestly reported, objectively interpreted, subject to peer review, and shared openly with colleagues and the world at large" [4].

For ***medicine***, the value is *beneficence* toward the patient or patient population – the good of the patient – the helping and healing of human beings. Medicine, therefore, is not purely science, but rather applies science and the truths that science provides for the good of the patient.

For the ***individual***, the primary value likely is self-interest in the form of advancing one's career, economic gain, and the personal satisfactions of patient appreciation/satisfaction, peer approval and societal acknowledgment. Unfettered, this interest can introduce moral obstacles and obfuscate moral sensitivity. The covenants that the physician (clinical investigator) holds with both the patient (experimental subject) and society serve as the foundation for the moral obligation specific to clinical research. These covenants spring from a trust relationship that despite the oversight of governmental regulations and institutional review boards (IRB), ultimately relies on the good character and moral integrity of the physician investigator.

The manner in which physician scientists address these conflicts in value determines the degree to which society will facilitate or restrict the scientific autonomy necessary for fruitful research. Thus the ethical sensitivity and moral integrity of the clinical investigator is paramount in the quest for medical knowledge. A research project, from design to publication, that is void of scientific integrity places knowledge, truth and humans at risk and violates society's expectations of science and scientists.

Institutional hubris is another potentially corrosive element. Competitiveness amongst such institutions can potentially lower an IRB's ethical guardianship, and can, as we shall soon demonstrate, promote overreliance on the supposed moral character of a scientifically prolific or prominent researcher.

Scientific Misconduct [3, 5, 6]

Two prominent ethical principles – beneficence and nonmaleficence – demand that physicians must seek to further medical knowledge with the goal of bettering their patients' lives *while concomitantly* identifying harmful or ineffective treatments.

The integrity of the process of scientific advancement is more than simply the just and honest conduct of scientific investigation. It also includes honest and truthful analysis and synthesis of the experimental results, appropriate attributions for the submitted product, the integrity of the subsequent peer review, and, last but not least, the unbiased and fair publication of the research.

Publication is an important component of academic medicine as it sets scholarly efforts apart from the actual practice of medicine. As an essential factor for achieving a successful academic career, authorship is integral to receiving credit for one's research, creative ideas and other educational forays. Publications influence promotions, enhance job searches, and facilitate future research opportunities, including, importantly, funding for such endeavors.

While investigators and authors of scientific papers have primacy over the ethical conduct, analysis, reporting and submission of their studies, there also are important ethical obligations for those involved with the publication process – that is, the reviewers, editors and publishers.

Medicine and Medical Science as Moral Enterprises

Medicine is a moral enterprise, individually and collectively, and physicians are obligated to exercise moral integrity. This behavior, in turn, builds the public trust and serves as a structurally stabilizing and protective force for the medical profession's interaction with the society it serves. In return, physicians, including researchers, retain considerable authority and privilege to control the critically important aspects of their practice and research. Indeed, medicine's scientific endeavors necessarily are built upon a foundation of trust: "If science is to flourish and attain its appropriate role in aiding human progress, it is incumbent upon … the scientific community to help provide a research environment that, through its adherence to high ethical standards … will attract and retain individuals of outstanding intellect and character" [7].

Researcher-Author Fraudulent Behavior and Misconduct [3, 5, 6]

Fabrication and Falsification

Among the most ethically troublesome categories of research and publication fraud are ***fabrication*** – the invention of false results – and ***falsification*** – the manipulation or omission of key data leading to inaccurate representation of the research.

Research and the publication of research executed dishonestly divert the search for factuality and defile the medical literature, ultimately diminishing the quality of care delivered to patients, or potentially even leading to the endorsement of actually

harmful treatments. Research fraud also *prevents beneficence* by dissuading physicians from utilizing beneficial therapies. Moreover, corrupted information can divert other investigators from pursuing a truthful path of scientific research. Fabrication and falsification, when exposed, damage the image of scientific investigation as a noble undertaking. The social contract that physician investigators hold with the society they serve demands a bedrock of honesty and a spirit of selfless service to the public.

How frequent is such misbehavior? Although likely underreported, evidence points to a significant frequency. One study found about one in 50 researchers admitted to at least one episode of fabrication during their career, but of interest, about 14% claimed to know of colleagues who did such [8]. Another survey reported almost 5% of authors admitted to having been participant to research that involved fabrication or misrepresentation, and, again not surprisingly, a larger number (more than one-sixth) claimed to be aware of such behavior in colleagues [9].

Misbehavior in research has been exposed in all specialties. Historically, perhaps the most potentially harmful to society may be the now discredited false claim published in 1998 linking regressive autism and measles-mumps-rubella (MMR) vaccinations [10]. The subsequent MMR vaccine scare later was determined to be based on a deliberate fraud. Appallingly, the researcher's claims followed his retention by a law firm to assist with lawsuits against manufacturers of the vaccine [11]! The worldwide consequences of this moral and ethical transgression in terms of morbidity and mortality due to arousing scientifically unfounded parental fears of vaccinating their children with MMR vaccine is huge and ongoing 17 years later. Regrettably, the process of reversing such egregious dishonesty, which involves retraction and expunging from the literature, inevitably will be incomplete.

But, we need not wander from anesthesiology to find examples of some of the largest individual research and publication fraud [3, 5, 6]. American anesthesiologist Scott Reuben was found by the medical center in which he conducted his research to have published a number of fraudulent research articles [12]. These studies promoted the routine worldwide clinical administration of "replacement" drugs for postoperative narcotic therapy with theoretically detrimental effects on bone healing in orthopedic patients. The editor-in-chief of the journal *Anesthesia and Analgesia* (A&A) listed 21 journal articles (ten from *A&A* and three from *Anesthesiology*) that had been based on the fraudulent data, and then correctly predicted their retraction [13]. Moreover, research findings from numerous studies that had relied upon Reuben's articles for their design and comparisons were called into question. The culprit was fined and imprisoned.

Not confined to the United States, extensive cases of scientific fraud in anesthesia and surgery research have been identified in Germany and Japan. German anesthesiologist Joachim Boldt misrepresented major aspects of a published study, involving fabricated data on the deployment of hydroxyethyl starch as a priming agent for cardiopulmonary bypass [14]. Moreover, the researcher failed to seek institutional review board (IRB) approval for his investigations as well as to obtain informed consent from the patients. Unprecedented widespread publication of his ubiquitously published work necessitated an international collaboration of the

editors of 16 medical journals to publish a collective letter acknowledging that 88 of his 102 studies had failed to adhere to basic ethical standards for human experimentation [15]. Many of the study files were missing or incomplete, and false data were published in at least 10 of the 91 studies examined, thus further setting the stage for retractions. The researcher had his academic position removed and was subject to both monetary fines as well as imprisonment. In stark contradistinction to the United States, in Germany the state medical association holds jurisdiction over physician misbehavior and misconduct [16].

A Japanese anesthesiologist, Yoshitake Fujii, likely holds a "Guinness-type" world record for the number of fraudulent publications thus far [17]. A retraction of virtually all of his extensive research papers has ensued. Interestingly, an initial question regarding the integrity of his investigations arose a decade earlier [18], but was not pursued in depth [19]. It now has been determined that there was consistent violation of obtaining IRB approval, adhering to ethical standards for human investigation, and veracity of data. Furthermore, for some articles he named co-authors who were unaware of such and whose signatures on submission letters had been forged! Again, there was an international collaboration of editors from prominent anesthesiology journals to prompt investigation of these misdeeds and deception at the host institutions as well as to correct and retract, as much as feasible, the falsified literature. The editors were "*completely engaged with the process of coordinating our efforts to identify and reduce research fraud. … It is a team effort. … Everyone is on board*" [20–22]. The researcher was fired by his university.

Interestingly, to identify falsified data, statistical techniques to identify unusual patterns of categorical and continual variables have been developed. As a result, in addition to earlier methodology to detect plagiarism [23], editors now have substantial technology to detect research and publication dishonesty [24, 25].

Plagiarism

Plagiarism is the "appropriation of someone else's words and/or ideas as one's own" [5]. Because science and scholarship involve new knowledge and creative ideas, the wording utilized might be less important than the ideas that the words convey for the determination of whether a scientific thesis has been plagiarized. Plagiarism is an ethical violation because it harms the true authors by not giving them credit and not recognizing their work. But, plagiarism also damages the reader by deception and obfuscation of the pathway taken in the development of an idea. Furthermore, trust of the body of work of the plagiarist inevitably surfaces. In 1998, it was determined that complaints (likely underreported) involving medical authorship such as the plundering of non-credited work of junior faculty had risen precipitously, and moreover, appeared to disproportionately involve females and non-United States citizens as victims [26]. Perhaps the most infamous example of scientific plagiarism involved the unauthorized acquisition of Rosalind Franklin's unpublished research on DNA – as well as her confidential research progress report – by Watson and Crick. The

latter of these famed biologists later acknowledged that the double helix model was based on her data, by which time Franklin, tragically, was deceased [27, 28].

Plagiarism is antithetical to the principles of nonmaleficence and justice. Nonetheless, identifying plagiarism is difficult. Editors now have within their armamentarium reliable methodology to detect plagiarism. This notwithstanding, words, when compared with ideas, do not in every circumstance hold equal weight in determining originality [29].

"Ghost" Authorship and "Honorary" Authorship

The International Committee on Medical Journal Editors defines an author as someone who has made a substantial contribution to a scientific publication. This would include participating in all of the following arenas of the scientific project: concept, design and acquisition of data, drafting or critical revision of the publication, and final approval of the version that is published.

"Ghost" authorship involves the acceptance of credit for a publication written by another ("ghost") individual. Industry, for example, often provides a professional writer (the "ghost" who is not identified or acknowledged) to compose a substantial portion of a publication to which is attached the name of an "author" who did not actually write the piece. "Honorary" authorship constitutes the assignment of credit to an individual (usually a senior academic or industry leader, or even government regulator or administrator) who did not participate to a meaningful degree in the research, analysis, review and/or synthesis of ideas upon which the publication is based. Both of these behaviors are commonplace, particularly in industry-financed publications [30, 31].

Such dishonest attribution of authorship is deleterious to the publication process in several ways. The attachment of the name of a well-respected researcher or prominent policy-maker to a paper might falsely give more significance and credibility of an investigation. Ghostwriters can conceal conflicts of interest that could influence the credibility of a publication as, for example one extolling the value of a new drug or medical device. Identification of the true author(s)/researcher(s) is key with respect to accountability and the ability to retrospectively investigate data of past publications that may have come into question. Pure and simply: authors who knowingly permit their name to be attributed to a publication in which they did not participate are engaging in fraud.

Redundant Publication

Redundant or duplicative publication is publication of the same results of one research project in more than one journal, or publishing a review of such results nearly at the same time in another journal, or the deliberate division of results from

one study into several publications. This practice spuriously inflates academic "achievements," but unfortunately, is commonplace [32]. Inflating an already oversized medical literature and publication process is disingenuous and misleading. Self-plagiarism is a form of duplicative publication.

Ethical Duties of Peer Reviewers [5, 6]

As a fundamental segment of the process of medical publications, appropriately conducted peer review is, in the end, a major determinant for safe, quality patient care. Peer review determines whether research has been properly and ethically designed and conducted, and also accurate in its analysis, discussion and conclusions. It therefore affirms and confirms research as being a credible origin of new scientific information. Review articles as well as research also fall under the protective canopy of peer review.

Peer review serves to maintain professional autonomy for evaluating professional performance, impacts career development, and determines directions for the generation of new knowledge. Given the aforementioned examples, it becomes evident that there are numerous opportunities for unethical behavior. As such, peer review assuredly is a challenging task and invaluable filtering service to scientific advancement. Indeed, we believe it to be overlooked and not fully valued and appreciated by the medical profession.

Peer reviewers assuredly must have the expertise to serve in such a role. Far too often, incompetent review hampers the process, but this situation is not restricted to the scientific realm as it also occurs in the humanities and social sciences. In fact, over half of polled researchers complained that they had experienced what they believed to be incompetent reviews, which included inadequate familiarity of the subject matter, failure to diligently read the article, or making mistakes of fact and/or reasoning [33].

Peer reviewers are trusted to be fair and balanced in their application of their knowledge and expertise, free of bias and conflicts of interest, guardians of the confidentiality of submitted data, and shields against fraud and misconduct. Breaches of confidentiality, plagiarism and even theft, while infrequent, do occur and abuse the ethical duty of protecting the work and attribution of the author(s). The peer review process also serves to guard against inordinate delays of dissemination of scientific knowledge [33]. Although difficult to believe, there even have been instances of abusive reviews in the form of personal and retributive attacks on authors!

Ethical Duties of Journal Editors [5, 6]

Last, but certainly not least, we visit the gatekeepers of the publication process, journal editors. These powerful and influential individuals carry a huge responsibility, once again underappreciated and overlooked by the scientific community. Their

value and obligation is to ensure, as much as is feasible, that the process of scientific publication is transparent and that the manuscripts published are original, truthful, accurate and ethically achieved. When one considers all the potential for misconduct as described heretofore, we should appreciate that editors carry the herculean burden of a determinedly diligent and courageous stewardship of the advancement of medical science.

External Safeguards [5]

As we have seen, scientific misconduct is a serious international problem – and recognized as such. However, only a dearth of countries have regulatory mechanisms in place to mitigate against such fraud. Even prior to the aforementioned examples, the United States Congress did respond to a then mounting amount of investigative misbehavior with potential for far-reaching adverse consequences to human health by establishing the Office of Scientific Integrity (now the Office of Research Integrity) in 1989. In the United Kingdom, all medically related fraud is referred to the General Medical Council. In the early 1990s Norway, Sweden, Denmark and Finland instituted formal review councils for examining scientific fraud. Encouragingly, there does exist a voluntary "international" agency to review instances of misconduct, the Committee on Publication Ethics (COPE), which has a membership of the editors and publishers of over 300 journals in Europe and Asia. The less enthralling aspect of COPE is that it serves only as an advisory board and has no authority to sanction or punish the detected miscreants. It would seem that federal regulatory agencies are needed to deal with this class of violations of medical ethics. Absent this vehicle, the reporting, investigation, and, when indicated, sanctioning of research and publication miscreants will continue to remain in the perhaps overwhelmed laps of fellow professionals, research institutions, peer reviewers, and journal editors.

Henry K. Beecher and Unethical Human Experimentation

Over a half a century ago, Harvard Professor of Anesthesia, Henry K. Beecher published a landmark paper that forever altered the conduct of human scientific exploration and publication [34]. In that article he described 22 examples of research abuse in human experimentation. With this and other publications, Beecher largely single-handedly initiated a transition from an insulated research community without any meaningful internal or external oversight to a medical community mandating informed consent and public oversight (such as institutional review boards) of both standard and research medical procedures. He was a staunch supporter of researchers having an understanding and adherence to the rules governing morality. Interestingly, in none of the cases he reported did he believe there was fabrication or

falsification of data, but rather that of ethical transgressions in "thoughtlessness and carelessness" (not "willful" acts) in experimental conduct that showed no regard or respect for patient autonomy and rights. Beecher staunchly believed, however, that the integrity of medical knowledge and advances in clinical medicine rely on the truthful pursuit of ethically designed and conducted research, on "the presence of an intelligent, informed, conscientious, compassionate investigator," that is, *on the integrity of individual researchers* [34, 35].

Returning to the Case Presentation

Establishing quality performance measures in anesthesia and surgery has become a high priority item for institutional and system-wide quality improvement programs, regulators and payors (both private and government). We now shall focus on our case involving perioperative beta-blocking drugs.

Largely based on the results of two 1990s investigations (that later would be called in question) [1, 2], in 2001, the US Agency for Healthcare Research and Quality labeled preoperative beta-blockade as a "major advance in perioperative medicine" for which "wider use … should be promoted" [36]. This soon was followed by an enthusiastic recommendation by the American College of Cardiology/American Heart Association (ACC/AHA) that beta-blockers should be used for high-risk patients similar to those of the 1999 Poldermans study [2], and a somewhat lesser level of endorsement for use in moderate to high-risk patients like those in the 1996 Mangano [1] study [37]. The Leapfrog Group, a juggernaut of public and private healthcare purchasers, soon adopted beta-blockade use for high-risk surgical patients.

The ensuing two decades witnessed the waxing prominence of employing beta-blocking drugs for prevention of adverse post-surgical cardiac events *despite* the fact that *from its inception* the evidence supporting such practice had been highly debatable and controversial. Several credible randomized studies in the ensuing decade failed to support the beta-blockade quality measure [38–41]. Indeed, there now is widespread agreement that there is *no* valid scientific evidence-base for the beta-blocker measure as a "best practice."

In retrospect, within only a couple of years of publication of the Mangano study there appeared the first of numerous criticisms for its being poorly designed for demonstrating benefit in the *immediate and/or early* perioperative period. Immediate deaths were excluded from the statistical analysis, and the major benefit was detected only *months* following surgery [42, 43].

More importantly and pertinent to this chapter, the 1999 Poldermans study [2] and a multitude of his other articles contained what still remains as an unquantified but significant amount of fraudulent research and publication (including failure to obtain informed consent, fabricating data and dishonestly manipulating

analyses). Poldermans, a highly regarded, prolific Dutch researcher (over 500 papers in respected peer-reviewed journals) ultimately was dismissed from his academic position at Erasmus University [44]. His "research" had been the basis for worldwide evidence-based guidelines, medical policies, and, ultimately, the care of millions of patients. His data, like that of Fujii mentioned earlier, were considered "too good to be true" [45]. His reputation and belief in his publications were so widespread and ingrained that even when his misconduct was exposed, extensive research efforts by others continued to try to validate his discredited work [41].

While we now know that beta-blockade can diminish the incidence of non-fatal myocardial ischemia and/or infarction, it also *increased* the incidence of clinical stroke and 30-day mortality [46, 47].

Looking back, it now is frightening that the beta-blockade guidelines of both the European Society of Cardiology (ESC) (Poldermans chaired its committee) and the ACC/AHA relied heavily on information dominated by Poldermans' now known to be "non-secure" work [46, 47]. For well over a decade, beta-blockade has been harming an untold (but assuredly huge) number of patients undergoing *noncardiac* surgery.

The ESC guidelines, constructed in 2009, advocated initiation of a course of perioperative beta-blockade in three classes of patients: (1) with known ischemic heart disease or myocardial ischemia according to preoperative stress testing; (2) scheduled for high-risk surgery; and (3) scheduled for intermediate risk surgery. All of these groups' recommendations were classified as Class I. Poldermans' studies dominated the meta-analysis "conclusion that beta-blockers had a neutral effect on mortality and allowed them [cardiologists] to focus on the reduction of non-fatal myocardial infarctions as a surrogate endpoint" [46, 47]. Appallingly, all of these recommendations are taking a long time to modify [48, 49].

The ACC/AHA guidelines, initially written in 2007, endorsed perioperative beta blockade in patients: (1) undergoing vascular surgery and coronary ischemia demonstrated on preoperative testing – Class I evidence base; (2) having vascular surgery and with already documented coronary artery disease – class IIa; (3) scheduled for vascular surgery with more than one risk factor for coronary arterial disease – Class IIa; (4) to undergo intermediate risk surgery with established coronary artery disease and/or more than one risk factor [50].

A 2013 meta-analysis of the secure trials (eliminating those of Poldemans' unsecure data) detailed that initiation of beta-blockers prior to surgery caused a 27% risk *increase* in 30-day all cause mortality [46, 47]. The Poldermans family of studies had heavily out-weighted and mal-influenced the meta-analysis of the *secure* trials with respect to mortality. While the secure trials showed that beta-blockade reduced *nonfatal* myocardial infarction, these drugs concomitantly increased stroke and hypotension – likely contributing to the cause of the high mortality.

Quality Performance Measures: From There to Here and Back to There

The National Quality Forum (NQF) is a nonprofit, nonpartisan, public service organization committed to transforming the US healthcare system to be "safe, equitable, and of the highest value" [51]. The NQF "reviews, endorses, and recommends" use of quality performance measures that are "tools used to evaluate how well healthcare services are being delivered." They supposedly "have undergone a rigorous review by a panel of *providers*, *measurement experts*, and *consumer representatives*." The Centers for Medicare and Medicaid Services (CMS) has chosen to be a "steward" of some of these NQF quality measures, one of them being "surgery patients on beta-blocker therapy prior to arrival who received a beta-blocker during the perioperative period" (NQF, #0284).

Another entity, the Surgical Care Improvement Project (SCIP), is a national quality partnership of organizations whose collective goal is to enhance surgical care by reducing surgical complications. SCIP is an element in the US government-sponsored effort to introduce evidence-based strategies into the clinical care of patients undergoing anesthesia and surgery [52]. The Joint Commission has aligned with the CMS with respect to the so-called core measures for surgical patients. It defines quality measures, adopting some created by the NQF, that then are tracked by institutions where surgery is performed. For over a decade the SCIP quality measure for beta-blocking drug use in noncardiac surgical patients tracked those patients who had, previous to their surgery, been on beta-blocking therapy, and the percentage of "surgery patients on beta-blockade therapy prior to arrival who receive a beta-blocker during the perioperative period." The perioperative period was defined as either the day before or the day of surgery, and also either the first or second postoperative day. Exclusion populations were defined, necessitating documentation of a reason for *not* administering the beta-blocker.

Compliance with SCIP is supported by the American Society of Anesthesiologists (ASA): "*The ASA is firmly committed to high-quality patient care and supports SCIP's goal to reduce the incidence of postoperative complications. Anesthesiologists play a key role in providing the clinical services that are embodied in the SCIP evidence-based recommendations for improving perioperative care.* Furthermore, *The ASA encourages anesthesiologists to consider the SCIP recommendations for all patients and to implement them when appropriate for patients under their care*" [53].

As clinical guidelines are offered as vehicles to improve quality of care and enhance cost effectiveness, the durability of these recommendations over time is critical for informing clinical practice and healthcare policy. Recommendations arrived at prematurely can lead not only to ineffective care, but even to morbidity and/or mortality, a violation of the ethical obligation of physician beneficence and nonmaleficence [54-56]. The ACC/AHA have been held as the gold standard for construction of credible guidelines, yet even the durability of Class 1 ("procedure/treatment should be performed/administered") "varied significantly across individual guidelines and levels of evidence, with recommendations that were based on

multiple clinical trials being the most likely to endure over time" [56]. Of interest, although only 1% of recommendations were reversed, 9% were downgraded and 11% omitted at the time the guidelines were next revised. Performance measures based on single trial observational studies, consensus opinions or a standard of care were threefold less durable than those based on multiple randomized trials.

Another report reviewed the guidelines of "interventional medicine subspecialties" (*non* anesthesia-related or those of the ASA), which tend to have much less rigorous review and oversight by the Federal Drug Administration than do pharmaceuticals. Startling as is may seem, only 11% of these invasive specialties' guidelines deployed evidence that included randomized controlled trials and meta-analysis, and perhaps worse, almost half were based solely on case studies or expert opinion [57]! Possible conflicts of interest were not mentioned in the majority of these guidelines.

An eye-opening, informative and thoughtful analysis of the mistakes that can be made with clinical practice guidelines recants the beta-blockade saga [58]. In fact, the beat-blocker fiasco is only one of several recent examples in which expert, well-intentioned endorsements changed dramatically when newer evidence alerted clinicians of the potential harms that had been overlooked. This "story shows how the prestige that medical researchers and clinicians afford to randomized controlled trials can obscure important uncertainties surrounding new treatments, particularly when placed in political contexts that prioritize the rapid translation of research into practice. … [These] guidelines went wrong not because they overlooked the need for randomized trials but because of experts' very faith in such trials" [58].

In the dust storm of the final days of the beta-blockade quality performance measurements, the Joint Commission has quietly "retired" this SCIP requirement as of the last day of 2014. No fanfare, no acknowledgements, no clinical alerts by any of the involved specialties. At the time of writing this chapter, many if not most anesthesiologists and surgeons are unaware of this retraction and continue to practice according to guidelines that now no longer are supported by any base of scientific evidence, and antithetically, now are considered potentially unsafe and even harmful.

And, finally, with respect to the case, even if beta-blockade were a best practice (which it is not), it is *un*ethical to play the 'guideline adherence and compliance' game by administering small (homeopathic) doses of a short acting beta-blocking drug (esmolol). Even when clinical guidelines are "proven" to be "secure" and "valid" according to *existing* evidence, physicians always should employ their clinical judgment so as to care and treat each patient as a unique individual with a unique physiognomy and needs.

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