Conflicts of Interest Anesthesia Practice

Relationships with Industry, Responsibility to the Health Care System, and Research Integrity

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- Anesthesia practice • Health care system • Research integrity
- Code of medical ethics

KEY POINTS

- Conflicts of interest (COIs) exist throughout the health care system. Recognizing the sources of conflict and defining management strategies to address them are essential to ensure that patient care is not compromised and credibility of providers questioned.
- Differences in health care financing create challenges and potential risks to patients, providers, and health systems. If not recognized and managed, these conflicts can compromise patient safety and efficiency of care as well as the financial stability of the health care system.
- In addition to the impact of conflicts on clinical care and decision-making, conflicts with research projects, particularly those funded by industry, undermine research integrity and the credibility of investigators.
- It is essential to recognize and confront these potential COIs to develop mitigation strategies, preserve professional ethics, and ensure optimal patient outcomes.

INTRODUCTION

A conflict of interest (COI) is "*a condition that arises when 2 coexisting interests directly conflict with each other … when they are likely to compel contrary and incompatible outcomes*."[1] These may arise from financial, personal, or professional relationships that could influence, or be perceived to influence, the actions of an individual, institution, or industry partner.

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COIs in health care may be overlooked or misunderstood despite being highlighted by various national medical institutions. The American Medical Association Code of Medical Ethics frequently includes consideration of COIs in their discussions of the issues of gifts to physicians from industry, professionalism, and COIs in patient care and research,[2] for example.

Like any other health care professional, anesthesiologists may find themselves in situations where COIs arise. In this article, the authors discuss COIs relevant to anesthesia practice in 3 areas: relationships with industry, responsibility to the health care systems in which we work, and research integrity.

RELATIONSHIPS WITH INDUSTRY

Financial Relationships and Influence

Collaborations with industry by anesthesiologists are widespread across a variety of settings. While many benefits can arise from such associations, including enabling new developments and expediting innovation, COIs can occur. Anesthesiologists may have connections with industries that are relevant to their expertise or roles on advisory committees. Such commercial collaborations may impact their impartiality. In addition, any potential financial benefit to the investigator and clinician, as might arise when having equity or receiving other compensation from a company, can undermine credibility or influence decision-making that is not in the best interest of patients or the health systems in which a clinician works.

Collaboration with medical device manufacturers

Relationships with medical device manufacturers benefit the production of new equipment and support innovation in the field. It has been proposed that this relationship differs significantly from one with developers of pharmaceutical products. The chief operating officer of one biotechnology engineering firm has suggested that devices "*often serve as extensions of the physician's hands*," and therefore, there is "*a more central and essential role for clinicians in development and testing*."[3] Those in such roles also use the products, can evaluate their use, and receive financial compensation for their expertise. However, this essential interaction means clinicians working with medical device companies in development are at increased risk of COI.

The Advanced Medical Technology Association (AdvaMed) has a voluntary code of ethics for interactions between medical technology companies and health care professionals intending to reinforce integrity in medical decision-making and ensure that the use of such devices is in patients' best interests. However, it should be noted that AdvaMed is the American Medical Device trade association and, therefore, also may have significant COIs in collaborating with health care professionals.

Procurement of medical devices

Procuring devices is another area where the relationship between medical device manufacturers and clinicians can result in significant COIs. One example would be an anesthesiologist who has worked with a manufacturer to produce a new video laryngoscope, who then, when it is available on the market, wants to recommend the device be purchased and used in their institution and has influence over procurement practices in their hospital.

Medical device firms develop close relations between clinicians who use their devices and the marketing and sales representatives who often have highly specialized knowledge about the devices and, in some cases, provide formal training and technical assistance in their application. This relationship can be beneficial, allowing innovative products to be put to good use as well as identifying ways to improve the

products. However, this close relationship creates significant conflicts for both the company and health care providers since industry representatives influence clinician decision-making and the clinician can have undue influence on the health care system when purchasing decisions are made, often limiting the ability to consider competing products or negotiate in good faith with the company.

These conflicts are common for decisions related to purchase of new technologies. A 2021 study by the National Bureau of Economic Research found that payments by medical technology firms to clinicians were ubiquitous: 87% of device sales in their sample of hospitals occurred at a hospital where a clinician had received payment from a device firm.[4,5]

Institutions must ensure that they have robust processes to manage such potential conflicts as part of their procurement policies. Decision-making groups, such as procurement panels, should ensure that all disputes, or potential conflicts, are declared and documented. Individuals with a financial interest in a company or other relationship that creates a conflict should not be able to participate in the purchasing decision-making nor negotiating process. At the same time, once the conflict is disclosed, they might be able to discuss their experience with the use of a product so as to minimize discrimination against or in favor of a particular provider. Involving individuals with COIs in such decisions can only take place where the conflicts are disclosed and appropriately managed.

Pharmaceutical companies and drug choices

Anesthesiologists working within the pharmaceutical industry have helped develop a wide range of medicines that have enabled our speciality to markedly improve clinical care, safety, and effectiveness.[6] At the same time, similar to conflicts between clinicians and device manufacturers, COIs exist for clinicians who work closely with the pharmaceutical industry. As one author acknowledged, "*We must recognise that the relationship between drug companies and medical practitioners is a difficult one. We must not only studiously avoid unacceptable influence; we must be seen to do so*."[7]

The impact of these relationships cannot be overestimated. In the United States in 2022 alone, $603 billion was spent on medications.[8] Around $19 billion is spent by the pharmaceutical industry in the United States annually on marketing products to prescribers.[9] Interactions between clinicians and pharmaceutical sales representatives can take various forms. Examples include providing food for physicians and nursing staff as a way to market their products, industry-supported conferences that do not qualify as legitimate continuing education programs, payment for continuing medical education (CME) conference registration fees, informational lunches, invitations for dinners, and provision of free samples. Given the amount of money companies spend, it is not surprising that there is good evidence to show that such strategies influence prescribing practices. For example, physicians attending sponsored lectures prescribed more drugs from the sponsoring companies than ones who do not.[10]

A situation particularly relevant to anesthesiologists—and one that has been called a national crisis—is the opioid epidemic, which evolved directly from physician overprescription of opioids. Advertising to clinicians has been identified as a major contributing factor; an extremely high-profile example is the promotion of OxyContin by Purdue Pharma, which included numerous national, all-expenses-paid pain management symposia, provision of free samples to physicians and distribution of branded promotional items.[11] The actions of Purdue Pharma are just one example of the importance for clinicians to assume a greater role in defining optimal medication management in

general and pain management in particular. Anesthesiologists and pain physicians play a critical role in reducing opioid consumption.[12]

Significant steps are being taken to make potential COIs more transparent to patients, health care systems, and the public at large; the Physician Payments Sunshine Act in the United States was enacted to disclose financial relationships between health care providers and manufacturers of drugs and devices.[13] The Open Payments Web site is available to the public to identify the financial payments to physicians (https://openpaymentsdata.cms.gov).

Guideline production and the influence of industry

Various professional organizations publish a vast number of guidelines and consensus statements to support good practice in anesthesia and support anesthesiologists in making evidence-based decisions. In most cases, the documents drafted by professional organizations reference appropriate evidence to support their recommendations. At the same time, with the large number of sources of "data" posted on Web sites or industry-sponsored publications, it is of the utmost importance that the sources for the recommendations are transparent,[14] based on the available scientific evidence, and are not biased by vested interests. The potential for bias in developing clinical guidelines is a significant concern, with evidence that COIs are often poorly reported and their potential influence not acknowledged.[15]

Potential impacts of industry involvement in anesthesia guideline production
Potential for biased recommendations
Potential for impact on professional integrity
Eroded anesthesiologist trust due to lack of transparency of COIs
Eroded patient trust due to lack of transparency COIs

In 2019, the American College of Physicians, in conjunction with other national bodies in the United States and the United Kingdom, published a management strategy for COI. It states that anyone involved in developing guidelines or undertaking evidence reviews must declare all active and inactive financial and intellectual interests related to health care from the previous 3 years and update this during the production of the guidelines.[16] COIs are then graded:

- High level—any active relationship with an entity with a direct financial stake in the guideline's conclusions.
- Moderate level—intellectual interest that may lead to cognitive bias or relationships with entities that might profit by association with the guidelines.
- Low level—inactive high-level COIs and intellectual interests only tangentially related to the clinical area under review.[16]

For high-level COI, the participants would need to reveal their interest and/or be recused from involvement in the guideline production; for the moderate level, they would be partially restricted in their activities; and for the low level, there are no restrictions on their involvement.[16]

Decisions on patient care must made using the best available evidence to provide the highest quality care and ensure public trust in our care. Transparent and robust management strategies to deal with COIs are vital to ensure this. The Appraisal of Guidelines for Research and Evaluation II is the internationally accepted appraisal tool for clinical guidance documents with 6 domains—including editorial

independence—to ensure funding bodies do not influence the content of the guideline and that competing interests of the guideline development members have been recorded and addressed.[17,18] Several organizations have incorporated this into their guideline programs, including the National Institute for Health and Care Excellence (UK) and the World Health Organisation.[19]

Continuing medical education and industry funding

CME is essential for health care professionals to ensure that their knowledge and skills are up to date and to support reaccreditation or revalidation with medical regulators. Most CME programs are intended to be evidence-based and free from bias.[20] However, CME programs are often, if not always, directly or indirectly financially supported by industry.[21,22] Dr. Fugh-Berman, a Georgetown University Medical Center professor, stated that "industry-funded medical education is always promotion."[23]

Industry funding of CME may compromise the integrity of the education being provided by

a. Biasing content produced
b. Promoting specific products
c. Influencing the choice of speakers and faculty
d. Inhibiting transparency and limiting the ability to assess potential biases

Organizers of conferences and other accredited educational events require disclosure of support from industry or other conflicts. The Accreditation Council for Continuing Medical Education applies standards relating to integrity and independence when accrediting continuing education, including prevention of commercial bias and marketing and identifying, mitigating, and disclosing relevant financial relationships.[24] The risks that such funding opportunities lead to bias by promoting products and practices that increase profits remain, and vigilance is required to ensure that products and practices promoted are best for patients.[25]

RESPONSIBILITY TO THE HEALTH CARE SYSTEM

Cost Containment and Resource Utilization

As a resource, anesthesiologists are a valuable commodity—not only with regard to direct patient care in a vast range of clinical areas but also in driving patient safety, quality improvement, and cost-effective care.

The ethical principle of distributive justice in medicine refers to the fair, equitable, and appropriate distribution of health care resources such that patients in similar positions should be treated similarly.[26] How do we allocate limited health care resources fairly within society when health care systems have competing and sometimes conflicting demands?

The different health care funding models impact patients, clinicians, and institutions differently. In socialized medicine systems (national single-payer systems, eg, the National Health Service (NHS) in the UK and Medicare in Canada), it can be argued that in a publicly funded system, treatment should be decided based on distributive justice.[27] This can be seen to present an inherent COI for clinicians, balancing the need for resource allocation and maximizing efficiency with the aim of treating individuals equally and equitably.[28] Most clinicians in such systems have limited influence on overall resource allocation and feel a professional imperative to maximize the beneficial effects of care for their individual patients. In the NHS, clinicians receive a salary based on a national model rather than being paid for itemized provision of care or capitation models, another factor that can influence attitudes toward the balance between resource allocation and individual treatment.

The American health care system has a very different funding model, including private health insurance systems based on the cost of premiums, co-payments, and deductibles.[29] It has been argued that there are exclusionary health care practices due to comparative costs, health insurance financing/risk reduction, and the relationship between power (insurers providers and clinicians) and rule setting, as in, for example, producing exclusionary criteria for insurance policies.[30] Therefore, it could be argued that the system means care is inherently unequal.[31] This model creates challenges for the anesthesiologists and all other providers when trying to deliver optimal care to each patient, while having to take into account these other challenges that impact clinical decision-making.

Managing Resources

Individual clinicians have a responsibility to manage resources effectively and sustainably. AMA's Physician Charter, which refers to a just distribution of resources, states that "physicians are required to provide health care based on the wise and cost-effective management of limited clinical resources."[32]

During the pandemic, many new potential COIs arose for anesthesiologists. Management was not always as cost-effective as it could have been (albeit with hindsight), and redeployment of staff led to significant changes in working practices, availability of appropriate supplies, equipment, and pharmaceuticals that were often in short supply and required rationing.

Example 1: Resource management during COVID-19

During the COVID-19 pandemic, we experienced stark examples of resource management issues. Anesthesiologists had their role substantially changed, with many staff redirected to expanded airway management roles and greatly enlarged intensive care units, while elective surgery was almost entirely postponed.[33] Anesthesiologists were obliged to use equipment in novel ways, for example, split ventilation systems,[34,35] and were often unable to conduct preoperative assessments traditionally.[35] These could be viewed as a COI between our professional responsibilities to provide the highest standard of care for each patient, our responsibility to health care as a whole, and the constraints of resources imposed by a worldwide pandemic.

One frequent and ingrained habit, drawing up a vast number of "emergency" medications in the operating room "just in case," may seem beneficial but add up to a significant cost and wastage of drugs, with sustainability implications.[36–40]

Example 2: Epidural kit shortages

In 2022 and 2023, there was a shortage of epidural kits due to global supply chain issues.[38] Changes in practice, which by necessity were not evidence-based, were required to enable epidurals to continue to be provided. Strategies included using equipment anesthesiologists were less familiar with (eg, syringes from different manufacturers) and even using equipment not designed for the purpose (eg, using standard syringes instead of loss of resistance syringes), prioritizing usage, and even restricting access.[39,40].

Efficiency and Patient Safety

There is a complex relationship between safety and efficiency in health care—both are included in the list of 6 aims of health care quality established by the Institute of Medicine.[41] Both are important in their own right, and they intersect. All systems aim to improve efficiency and cost-effectiveness by streamlining care and improving the utilization of resources. However, conflicts may arise when efforts to improve efficiency inadvertently compromise patient safety.

Specific conflicts between efficiency and patient safety in anesthetic practice
Time pressures/overbooked lists
Timely turnover (anesthetic time ignored in list design)
Standardization of care versus individualized care
Technology dependency (use of technology including electronic records diverting attention away from the patient)
Resource allocation and staffing

Anesthesiologists frequently experience time pressure to maximize patient throughput in theaters. Staff may feel rushed or anxious when workloads become potentially unachievable, with the risk of making mistakes.[42,43] Time pressure is known to be among the factors that can affect the performance of an anesthesiologist.[44] The recent guidance on implementing human factors in anesthesia published in 2023 recommended that "*operating theatre list planning and scheduling should include time allocated for complex cases and for high turnover lists to enable adequate preparation and reduce time pressures on staff*."[42]

As clinicians, we are responsible for raising concerns when any drive to improve efficiency compromises our commitment to patient safety.

RESEARCH INTEGRITY

The National Institute of Health has announced, "Failure to uphold research integrity undermines confidence and trust."[45] Without either, clinicians cannot practice evidence-based medicine, patients cannot have confidence in their clinicians, and researchers are in a quandary. While the research community is overwhelmingly motivated by honesty, rigor, transparency, and open communication, broader pressures, including financial incentives, can make it challenging to uphold these values.[46] COIs in various forms can reduce the integrity of research.

Industry-Sponsored Research

In the United States, pharmaceutical industry spending on research and development has increased hugely over recent decades; in 2019, the sum was estimated to be $83 billion dollars.[47] More than half of medical research in the United States is funded by pharmaceutical and device manufacturers.[48] This increase in spending is reflected worldwide to a greater or lesser extent.

While the involvement of industry in funding research has obvious benefits, it can lead to COIs, which may affect:

- Study design
- Data analysis
- Production of manuscripts
- Authorship of manuscripts
- Decisions on whether to publish results—leading to publication bias

Internal documents from pharmaceutical companies disclosed during court proceedings in the 1990s showed how extensive their influence and COIs can be. In 2004, the Pfizer subsidiary, Warner–Lambert, admitted that in the 1990s, it broke federal regulations in its promotion of gabapentin for various conditions.[49] The promotion was multifaceted and included the company attempting to publish studies with only positive results and developing financial relationships with physicians publishing review articles.[49–51]

Example: Liposomal Bupivacaine and Pacira

In 2020, Pacira Pharmaceuticals was ordered to pay $3.5 million to "resolve allegations" that it paid physicians research grants and other financial incentives to encourage them to prescribe liposomal bupivacaine (EXPAREL). Research grants were influenced by sales representatives or marketing executives and discussed in relation to internal sales goals, while the grants were contingent on the drug being included on the formulary at an institution before money was awarded.[50]

A review of randomised controlled trials of liposomal bupivacaine found that industry-funded studies were more likely to report outcomes favoring liposomal bupivacaine, with a statistically significant association between total payments by the company and favorable outcomes.[51]

It can be challenging to identify how individual studies have been funded. One study of funding trends of research published in anesthetic journals showed that while 50% of original research articles published were funded, it was difficult to identify the funding source.[52] The authors suggested that a standardized funding reporting template could improve the transparency and integrity of anesthesia research and lead to improved trust in research and publication, with one aspect of such standardization being the origin of the funding in more granular detail.[52]

Studies that produce statistically nonsignificant results or results unfavorable to the experimental intervention are less likely to be published than those that are statistically significant or show the intervention to be beneficial.[53–55] Not only does this lead to a misleading view of an intervention, but the lack of impact of the studies that are not published further increases the uncertainty with which we can evaluate the evidence surrounding an intervention.

Example: Sublingual sufentanil and review articles

A 2018 review article on the pharmacokinetics and pharmacodynamics of sublingual sufentanil tablets for postoperative pain, published in *Anaesthesia*, concluded that they "*allow effective pain relief, and allows patients to control their own pain relief and early postoperative mobility.*"[53] This was accompanied by an editorial that critically examined the data published in the review, aiming to identify any influence of bias or marketing strategy.[54]

The editorial highlighted several areas of concern:

1. Review articles did not routinely document COI statements of the trials included in the review.
2. Eight review articles were based on the same 7 research papers on sublingual sufentanil tablets.
3. Issues involving ethical approval, study design, and the quality of manuscripts included in the review articles.[54]

The editorial authors concluded that this case reflects a much more widespread issue in research, publishing, and transparency.[54]

Systematic reviews are also significantly affected. Systematic reviews with financial COIs come to more favorable conclusions and have poorer methodological ratings than those without.[56] Pharmaceutical-industry-sponsored studies are more often favorable to the sponsor's product compared to studies with other sources of funding.[57,58]

A recent position statement by the editors of *Anaesthesia* on best practices in academic medical publishing outlined the ways in which any COI associated with their submitting authors and their editors should be dealt with. It emphasized the importance

of academic publishing having the highest standards about ethics, research conduct, and manuscript preparation.[59]

Data Fabrication

Several high-profile cases of scientific misconduct specifically involving anesthesiologists have brought this issue to the fore in the speciality. In all of these cases, it was several years and numerous publications before the issue of data fabrication was even suspected.[60–63]

Examples of scientific misconduct by anesthesiologists:

Scott Reuben—the former chief of the Acute Pain Clinic at Bay State Hospital in Springfield, Massachusetts, was found to have falsified data concerning the benefits of Celebrex (celecoxib) and was sentenced to 6 months in prison in 2010 after pleading guilty to one count of research fraud.[60] Reuben had fabricated data to the extent that he had not even conducted the clinical trials he had published in major journals.[61]

Yoshitaka Fujii—the former associate professor of Anesthesiology at the Toho University Faculty of Medicine, had his professorship removed and over 200 papers retracted due to data fabrication in his publications, the main topic of which were medications used to reduce postoperative nausea and vomiting.[62]

Joachim Boldt—the former professor at the University of Giessen, had his professorship removed, and nearly 200 of his research publications retracted after it was found that data had been falsified and manipulated in his publications on colloidal hydroxyethyl starch (HES). Subsequent analysis of the data of HES, excluding his studies, showed mortality increased significantly with the use of HES.[63]

John Carlisle, a British anesthetist and an editor of the journal *Anaesthesia*, with colleagues developed a method of identifying nonrandom sampling in clinical trials, raising the possibility that a trial was not properly conducted or inaccurately reported.[64] In one paper, Carlisle screened 5087 randomized control trials using his method and found a much higher than expected proportion of outliers, suggesting that differences in baseline data were not due to random sampling.[65]

The obvious question is, why fabricate data? There are a multitude of potential reasons for doing so, including

- Desire for publications—positive results are more likely to be published (publication bias).
- Financial interest—publications and increased profile may lead to further research grants.
- Time pressure—the need to build an academic or commercial reputation by publishing as quickly as possible.
- Career advancement—raised profile; invitations to speak at conferences.

False data may directly impact patient care. One review found that 12 studies containing falsified data were cited in 130 reviews and guidelines and that the reviews and guidelines would have been substantially different had the fraudulent results been excluded. Detecting false data can take years, and the retraction of published trials even longer, increasing the number of patients potentially affected.[66] Increased scrutiny should detect more of these cases before publication. Still, Carlisle thinks that "journals should assume all submitted papers are potentially flawed and editors should review individual patient data before publishing randomised controlled trials."[67]

DISCUSSION

Arrangements that create COIs are not inherently wrong. Much research, medical education, and developments in clinical practice would only happen with the support (most often financial) of industry partners. While we accept this, it is essential that we continuously critically examine and address these to ensure the highest standard of evidence-based care, protect our professional integrity, and maintain public trust in the speciality. If we fail to do so, not only will patients suffer, but our regulatory professional bodies will likely intervene. The result for the anesthesiologist can be profound. Probity issues are a common cause for censure by such bodies, including permanent exclusion from clinical practice.

Financial ties between anesthesiologists and industry may have particularly pernicious consequences. They can compromise professional judgment and lead to biased decision-making. The pervasiveness of industry influence, for example, in promoting products, raises obvious concerns regarding the prioritization of commercial interests over clinical best practices. There is a pressing need for heightened awareness with robust safeguards to mitigate the risks associated with these relationships.

Anesthesiologists do not merely provide care for individual patients but play a pivotal role within the system as advocates for patient welfare and stewards of health care resources. Anesthesiologists must navigate responsibilities to patients, institutions, and society with integrity and transparency, prioritizing clinical efficacy and cost-effectiveness over personal interests.

The integrity of scientific research forms the cornerstone of evidence-based medicine. In recent years, some of the worst cases of practice corrupted by COI have been in anesthesiology research. Such cases taint the whole field of research, casting doubt on the credibility and validity of study findings. Anesthesiologists involved in research must disclose all relationships with industry sponsors and other stakeholders to uphold transparency and mitigate potential biases. Furthermore, rigorous peer review processes and adherence to ethical standards are essential to safeguard research integrity and maintain public trust in research findings.

A highly intricate dynamic exists between COIs, industry relationships, health care system responsibilities, and research integrity in anesthesia practice. By acknowledging these complexities and implementing robust measures to identify, disclose, and manage COIs, anesthesiologists can uphold professional ethics, safeguard patient welfare, and preserve research integrity.

CLINICS CARE POINTS

- Potential COIs are ubiquitous in anesthetic practice. Recognition is essential to avoid harmful effects on patient care.
- Keeping the patient's well-being and safety as the anesthesiologist's first priority is the overarching strategy for mitigating COI.
- Funding models for clinical care and research generate challenges that anesthesiologists must remain cognizant of in order to maintain professional integrity.

DISCLOSURE

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