more formal evaluation of compliance with the protocols, and prespecified secondary analyses that accounted for intersite variation in compliance, may have provided insight into the failure to detect a difference in mortality. Information on steps taken to ensure compliance would also be helpful should there be attempts to disseminate higher PEEP strategies to clinical practice.

In summary, despite the relatively straightforward physiologic basis for the individualized titration of the "best" PEEP, generation of robust clinical evidence in its favor is bedeviled by a number of complicated study design choices and implications. Issues largely solved for placebo-controlled drug trials resurface when testing these complex interventions. Nevertheless, both the Lung Open Ventilation Study and the Express Study demonstrated that it was possible to convert the physiologic principles on which experts base their care into a set of reproducible instructions and then test these instructions in a broad multicenter environment. Although neither study demonstrated a significant improvement in mortality, their findings appear to have implications for future practice.[8] Finally, these studies made important steps toward increasingly rigorous assessment of increasingly sophisticated protocols for the best care of critically ill patients.

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Academic Medical Centers and Financial Conflicts of Interest

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Over the past decade, concern about the consequences of financial conflict of interest has escalated dramatically. Although the principle that the integrity of decision making should not be undermined by self-interest may seem self-evident, not until the 1960s was this concept applied to government office holders and attorneys,[1-3] and then sporadically in the 1980s and 1990s to physicians and clinical researchers.[4] Indeed, it is only now that academic medical centers (AMCs) and professional medical societies are more systematically addressing many of the critical issues involved in institutional conflicts of interest (ICOI). Many leaders and administrators at AMCs are asking how scientific objectivity can be maintained considering the potentially compromising relationships that can ensue from gifts, grants, royalties, equity holdings, and business ownership—not only to individual investigators and clinicians, but also to academic institutions.

As is often the case, it takes a scandal to set off alarms and medical practice has recently generated many alarms and concerns. The easiest cases to draw attention are individual conflicts of interest, as evidenced by extensive media coverage about clinicians who use devices manufactured by companies they own, clinicians who prescribe and overprescribe drugs manufactured by companies that pay them hefty consulting and speaker fees, and researchers who have a financial stake in the outcome of the drug or device they are testing.

Exposure does not necessarily prompt antidotes but notable progress is being made in managing and reducing individual conflicts of interest. Although some can still claim that "modest gifts are harmless," or that "research integrity cannot be undermined by the lure of profits," federal regulations and AMC procedures are becoming far more rigorous. The guidelines on pharmaceutical company–clinician relationships issued by the American Medical Association[5] and also by the Pharmaceutical Research and Manufacturers of America[6] have been superseded by stricter, if not entirely satisfactory, guidance from the Office of Inspector General, US Department of Health and Human Services.[7,8] More

See also p 665.

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impressive are the policies being implemented at an increasing number of AMCs, guided in part by a *JAMA* publication[9] that included a series of recommendations by the American Board of Internal Medicine Foundation/Institute on Medicine as a Profession task force for better managing health industry practices that create conflicts of interest.

Almost all new AMC policies are the result of initiatives undertaken by an individual medical school dean. Change usually has been inspired by a personal distaste for drug company gift giving, a keen sense of professionalism, a commitment to training medical students and residents to do the right thing, and an understandable desire not to be the subject of the next media scandal. Among AMC policies that may serve as successful models for others are those of Boston University,[10] the University of Massachusetts in Worcester,[11] the University of Pennsylvania,[12] the University of Pittsburgh,[13] the University of Wisconsin (G. Mejicano, Assistant Dean for Continuing Medical Education, e-mail communication, September 2006), the University of Michigan (J. Stevenson, Pharmacy Director, e-mail communication, July 2006), Stanford University,[14] Kaiser Permanente of Northern California, and UC Davis.[15] This list includes both public and private institutions, centers that emphasize research, and centers focused on clinical care.

However, as Ehringhaus et al[16] report in this issue of *JAMA*, progress in managing ICOI has been more limited. The problem of ICOI in AMCs was stimulated or at least abetted by the 1980 Bayh-Dole Act, which encouraged universities to patent and license discoveries and enter partnerships with for-profit companies.[17] Even though the goal of the act was to expedite the transfer of technology from bench to bedside, its unintended consequences have been to blur the distinctions between academic and commercial entities and to make ICOI much more pervasive.

The incident that highlighted the negative consequences of ICOI was the 1999 death of 18-year-old Jesse Gelsinger, who was participating in an experimental gene therapy protocol conducted at the University of Pennsylvania. In addition to flaws in recruitment of research participants, incomplete consent form information and disclosure of risks, the research was tainted by both personal and institutional conflicts of interest.[18] The director of the institute conducting the research had also founded a biotech company, and that company gave $3 million in grant support to the institute and in turn had the rights to any discovery made in the laboratory. The University of Pennsylvania was also a shareholder in that same company and would have received royalties from any therapies licensed to the biotech company.[19] There is no way to establish whether the researchers or university officials had made certain clinical decisions based on their personal or institutional financial interest. However, the university was deeply embarrassed, the US Food and Drug Administration halted all genetic research at the institute, and the incident became a cautionary tale that prodded many organizations to scrutinize ICOI practices (personal communications with AMC deans conducted through sponsorship by the Pew Charitable Trusts and the Prescription Project).

Following the Gelsinger case, the US General Accounting Office,[20] the Association of American Universities,[21] and the Association of American Medical Colleges[22] each addressed the relevant elements in ICOI. The underlying principle of the reports is clear: an ICOI arises when the institution or a department, school, or subunit or an affiliated foundation or organization has a "financial interest in a company that itself has a financial interest in a faculty research project."[19] In such instances, which are commonplace, the groups maintain that it is always vital to (1) disclose the conflicts; (2) manage the conflicts; and (3) prohibit the activity when necessary, to protect the interest of the public and the interest of the university.

The US General Accounting Office, the Association of American Universities, and the Association of American Medical Colleges further urge universities to enact disclosure requirements, erect "firewalls" separating financial and research personnel, and establish standing committees to oversee ICOI prevention, with the authority to take remedial action, including halting an inappropriate activity. The groups also emphasized the need to better protect research participants from the implications of ICOI.

Despite the noteworthy calls to action, neither the Association of American Universities nor the Association of American Medical Colleges has issued a model policy. The design of an appropriate and effective system has been left to the individual institutions. However, according to Ehringhaus et al,[16] AMCs have not responded well.

Adoption of ICOI policies is "far from complete."[16] Of the 125 medical schools surveyed, 86 responded and of those, only 30 had issued an ICOI policy. Where such policies do exist, they appear to address the salient issues (equity income, royalties, etc) and create barriers between investment and research officials and investment and IRB officials. However, given the limits of the survey, whether the policies are being effectively monitored and enforced, and what differences they are making is not known. Another 30 schools have reported that they are working to create policy on ICOI, but their methods for policy development, dates of completion, and final policy summaries are also unknown. Given both the seriousness and extent of the ICOI issue, the overall record is disappointing.

It is fair to ask whether it is naive to trust institutions to monitor and discipline their own financial activities, particularly when the financial returns can be substantial. Licensing agreements on patents generate close to $2 billion per year for academic research centers[23]; at Columbia University, for example, 1 patent generated a total of $300 million.[24] At a time when federal research funding is declining and competition for philanthropic gifts is intensifying, universities may not be eager to promulgate policies that would restrict their freedom to maneuver.

Will government regulation step in to fill the vacuum? Current federal and state interests in industry-academy relationships provide reason to believe so. Congressional hearings are addressing the implications of industry support for continuing medical education, gifts to clinicians, the sale of physician-prescribing data, and pharmaceutical company efforts to intimidate researchers critical of their product(s). Currently, 8 states and the District of Columbia have laws or resolutions affecting marketing of pharmaceuticals.[25] Thus, it may not require another Gelsinger-type incident to bring about significant regulation and legislation. If the trend to government regulation continues, a follow-up survey by Ehringhaus et al is likely to report markedly different results.

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