classes of drugs; Strattera (atomoxetine), a presynaptic norepinephrine-reuptake inhibitor, and antidepressants such as Norpramin (desipramine), Effexor (venlafaxine), and Wellbutrin (bupropion) may be effective, and in patients with concomitant depression or substance abuse, they may be better choices than a stimulant.

College students — and their families — tend to have polarized views about medication: either they embrace these types of drugs as a way of improving their performance or even their lives, or they shun medications as a "crutch" and fear becoming dependent on them. A student's last visit to a primary care physician before departing for college may offer an ideal opportunity to provide education about medication, warning signs of common problems, and the need for a balanced lifestyle.

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1. National College Health Assessment: reference group report. Baltimore: American College Health Association, 2004.
2. Wechsler H, Lee JE, Kuo M, Nelson TF, Lee H. Trends in college binge drinking during a period of increased prevention efforts: findings from four Harvard School of Public Health college alcohol study surveys: 1993–2001. J Am Coll Health 2002;50:203-17.

Wall Street and Clinical Trials

Robert Steinbrook, M.D.

Should physicians sell their expertise and knowledge about clinical research to Wall Street? In recent months, financial relationships between some physicians and the investment industry have come under scrutiny.[1-3] Physicians have been paid to provide investors with general information about therapeutic problems, the mechanism of action of drugs, and the regulatory process. Some of these activities may ultimately have benefit to society. However, some physicians have also allegedly been paid to reveal specific confidential data.

In August 2005, the *Seattle Times* reported that it had found "at least 26 cases in which doctors have leaked confidential and critical details of their ongoing drug research to Wall Street firms."[2] In 24 cases, according to the newspaper, investment firms had used the information to issue detailed reports to select clients, advising them whether to buy or sell a drug-company stock. In some cases, trading stock on the basis of secret information purchased from medical researchers is illegal. The person who provides the information — an act known as "tipping," in legal parlance — may also be breaking the law, even if he or she does not actually buy or sell stock (see box).

One of the reported cases involved a pulmonologist at the University of Pennsylvania who was a member of the data and safety monitoring board for the clinical trial of a drug for pulmonary hypertension. During a conference call in February 2005, before the trial's results had been announced, he discussed the safety data with analysts. The physician has denied revealing nonpublic information. In July 2005, an oncologist from the University of California, Los Angeles, allegedly discussed nonpublic information about two investigational drugs for kidney cancer during a recorded conference call.

The *Seattle Times* report also described how Smith Barney Citigroup acquired information about a study of a macular-degeneration drug this past spring. The financial firm systematically interviewed study investigators in order to predict the results before they were announced. Many of these investigators subsequently acknowledged accepting money to talk to investment companies, although none specifically recalled talking to Smith Barney.

Although unlawful insider trading related to biomedical research is not new,[4] the recent allegations point to novel types of wrongdoing. Senator Charles Grassley (R-Iowa), chairman of the Senate Finance Committee, has expressed his outrage about "selling drug secrets" and has asked the Justice Department and the Securities and Exchange Commission to investigate.

The increasing opportunities for physicians to make money by advising not only drug companies but also Wall Street are a response to the rapid growth of private funding for pharmaceutical research and development (see graph). The billions of dollars that may be at stake dwarf the size of the consulting payments, which are typically in the range of thousands to tens of thousands of dollars. One of the complexities is that some financial relationships between physicians and investors are perfectly legal, even if they are ethically problematic.

If investors know what they are doing, they can make money

Insider Trading and Clinical Research

Some insider trading is legal: people who are considered corporate insiders — officers, directors, and employees — may buy and sell stock in their own companies. They must report their trades to the Securities and Exchange Commission (SEC), which makes the information available to the public. According to the SEC's Web site, illegal insider trading entails "buying or selling a security, in breach of a fiduciary duty or other relationship of trust or confidence, while in possession of material, nonpublic information about the security. Insider trading violations may also include 'tipping' such information, securities trading by the person 'tipped,' and securities trading by those who misappropriate such information."

In certain situations, the results of clinical research can constitute a form of inside information.[4] In an interview, James Ferguson, a Chicago attorney who has written about this matter in the *Journal,* listed some of the relevant questions. Was the information nonpublic? Was the information material to a decision by an investor to buy or sell a stock? Did anyone involved have a duty to protect the confidentiality of the information but trade on it or disclose it to others to help them in making a trading decision? Was anyone induced to breach confidentiality? According to Ferguson, "Payment for information makes it more likely — and easier to prove — that the person who is the source of the information was acting knowingly and deliberately in breaching a duty of confidentiality."

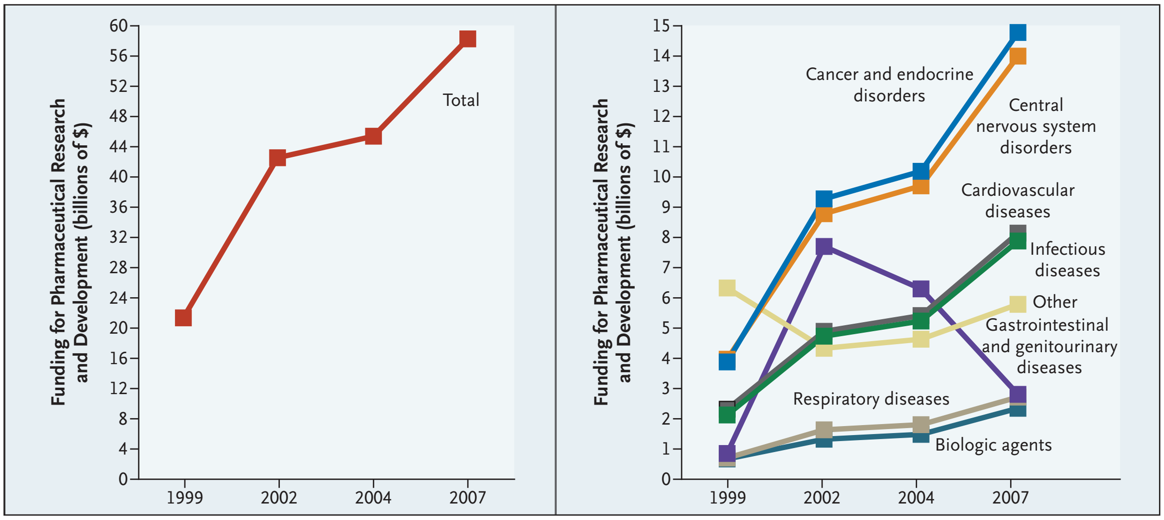
regardless of whether a company's products succeed or fail or whether they fulfill a real medical need. Many investors, however, know little about medicine or clinical research and therefore seek expert advice to help them make decisions. They target prominent researchers and leaders of academic departments — the physicians who are most likely to have key information about unpublished research.

Investment entities that may seek advice from physicians include stockbrokers and analysts, investment bankers, venture capital firms, and hedge funds and other investment firms.[1] Physicians may be asked to participate in telephone calls or private meetings with analysts or to join advisory panels. In addition, in an effort to bring medical knowledge in-house, many investment firms hire physicians as full-time employees. These physicians help their firms to target the right researchers to talk to, craft questions for them, and assess their responses. They also interpret the results of clinical trials, read the medical literature, and attend medical meetings, where they may speak with specialists and researchers informally.

Indeed, more generally, the sums of money at stake are so large that an entire matchmaking industry has developed within the past decade to facilitate consultations between physicians and investment companies. The most commonly cited example is the Gerson Lehrman Group. On its Web site, this New York-based company describes itself as "mining the world's expertise." It advertises a network of more than 100,000 experts in various fields who are available as consultants to investors, including about 48,000 physicians and 12,000 other professionals who are part of its health care and biomedical practice. Physicians can apply online to join the "GLG Healthcare Council." Members set their own consulting fees, which range from $200 to more than $1,000 per hour, and "may accept or decline any project based on their availability or ability to consult on a particular topic." According to the company, however, most of the physicians who have joined have never consulted. Each year, Gerson Lehrman pays about 5000 physicians, typically for one or two hours of telephone calls at fees averaging $230 an hour. Several hundred physicians consult more frequently and are paid more; they are typically "thought leaders" in academic disciplines and make seminar presentations to groups of stock analysts. Another company offering similar services is Boston-based Leerink Swann and Company, whose MEDACorp consulting subsidiary "maintains a network of more than 13,000 biomedical professionals worldwide," according to its Web site.

Gerson Lehrman touts its multiple layers of protection, including explicit written compliance documents, designed to prevent its experts from discussing confidential information or violating other contractual obligations. According to a statement the company issued in August 2005, "scientists participate because they appreciate both the value to science when investors are well educated, and because they understand our particular focus on ethical, contractual, appropriate governance for these types of relationships." But like any business, Gerson Lehrman aims primarily to meet the needs of its clients, and because doctors' consultations with investors are private, it is usually impossible to know what was actually discussed.

The issues raised by such consultations go beyond the potential violations of federal securities laws and secrecy agreements between researchers and drug com-



Funding for Pharmaceutical Research and Development.

Data are from Thomson CenterWatch and represent worldwide spending by companies that are members of the Pharmaceutical Research and Manufacturers of America. "Other" includes dermatology, diagnostics, and nutrients. Data for 2007 are projections.

panies. These confidentiality agreements — which are meant to protect the business interests of drug companies — can also be the gag clauses that may prevent investigators from examining clinical trials data independently or submitting a manuscript for publication without first obtaining the consent of the sponsor. For these reasons, many in academic medicine are seeking to eliminate restrictive confidentiality clauses from trial contracts altogether.[5] Of course, the elimination or scaling back of confidentiality agreements could also facilitate physicians' discussing their work with Wall Street — unless they decline to do so. For example, clinical investigators and members of data and safety monitoring boards have fiduciary duties that in many situations make it wrong to disclose unpublished information about trials regardless of specific contractual obligations.

According to Dr. David Korn, senior vice-president of the Association of American Medical Colleges, "There is a big difference between 'gagging' an investigator who wishes to disseminate scientific findings that fail to support a company's claims for its product and faculty who leak preliminary results of ongoing clinical trials as 'hired guns' of investment firms looking for tips that may well violate federal laws on insider trading."

The broader issues at stake are the integrity of clinical trials and the medical profession. Investigators and members of monitoring boards have a primary obligation to research subjects, rather than to financial markets. The integrity of the trials process and public trust in physicians are threatened if consulting deals and the machinations of investors and the stock market interfere with the dispassionate analysis and publication of study results. When the integrity of a trial is compromised, subjects' exposure to risk is rendered gratuitous.

The attention to the financial relationships between investors and physicians is prompting academic medical centers and medical societies to review their policies regarding consulting and the sharing of confidential information, to remind faculty and members of these policies, or to establish standards if none have existed. Ultimately, however, the admonitions of institutions and medical societies about ethical behavior can accomplish only so much. Physicians will have to make their own decisions about whether to sell their expertise and specific knowledge about clinical research to Wall Street.

Dr. Steinbrook is a national correspondent for the *Journal*.

1. Topol EJ, Blumenthal D. Physicians and the investment industry. JAMA 2005;293:2654-7.
2. Timmerman L, Heath D. Drug researchers leak secrets to Wall St. Seattle Times. August 7, 2005.
3. Saul S, Anderson J. Doctors' links with investors raise concerns. New York Times. August 16, 2005:A1.
4. Ferguson JR. Biomedical research and insider trading. N Engl J Med 1997;337:631-4.
5. Steinbrook R. Gag clauses in clinical-trial agreements. N Engl J Med 2005;352:2160-2.