Who pays for the pizza? Redefining the relationships between doctors and drug companies. 1: Entanglement

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In this two part article, a journalist based in Washington DC explores the brewing conflicts at one of the world's leading medical campuses as it joins the wider global debate about how to redefine relations with big pharmaceutical companies

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Summary points

- Entanglement between doctors and drug companies is widespread, and evidence shows that interactions with industry influence doctors' behaviour
- Evidence is strong that sponsored research tends to produce favourable results
- Leading academic institutions are currently debating the rules governing relations between researchers and sponsors
- Pharmaceutical expenditures are rising rapidly, and entanglement may undermine rational prescribing strategies
- Critics argue that a culture of industry gift giving creates entitlements and obligations for doctors that conflict with their primary obligation to patients

Twisted together like the snake and the staff, doctors and drug companies have become entangled in a web of interactions as controversial as they are ubiquitous (box). As national drug bills rise at rates that vastly exceed those of inflation (fig 1), this entanglement and the subsequent flows of money and influence are attracting increasing public and academic scrutiny.

Studies from several countries show that 80-95% of doctors regularly see drug company representatives despite evidence that their information is overly positive and prescribing habits are less appropriate as a result.[1 2] Many doctors receive multiple gifts from drug companies every year, and most doctors deny their influence despite considerable evidence to the contrary.[3] Industry interactions correlate with doctors' preferences for new products that hold no demonstrated advantage over existing ones, a decrease in the prescribing of generics, and a rise in both prescription expenditures and irrational and incautious prescribing, according to a recent analysis of the ethics of gift giving.[4] The number of gifts that doctors receive correlates with beliefs that drug representatives have no impact on prescribing behaviour.[3]

Accepting meals and expenses for travel or accommodation for sponsored educational meetings is common despite evidence that this is associated with an increase in formulary requests for and prescribing of the sponsor's drug.[2 3] Most doctors attend company sponsored events providing continuing medical education,[2] yet evidence shows that these preferentially highlight the sponsor's drug.[3] Many professional societies rely heavily on industry sponsorship,[5] just as their medical journals rely on drug company funded trials, company advertisements, company purchased reprints, and company sponsored supplements—despite the consequent conflicts of interest[6] and evidence that sponsored supplements are more promotional than other articles.[7]

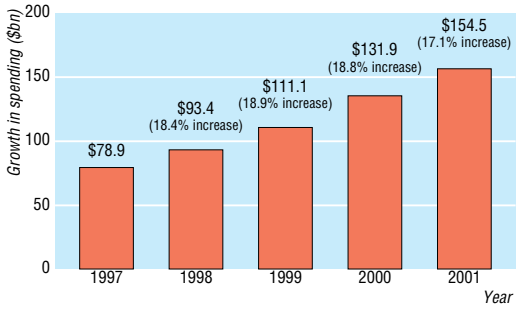

Fig 1 Retail spending on prescription drugs in the United States, 1997-2001.[23]

An estimated 60% of biomedical research and development in the United States is now privately funded, and two thirds of academic institutions have equity ties with outside sponsors.[8] Finding senior medical researchers or clinicians without financial ties to pharmaceutical companies has become exceedingly difficult.[9] Those regarded as "thought leaders" routinely work as paid members of drug companies' advisory boards despite evidence that the practice is part of industry's promotional machinery. According to an article on the "tricks of the trade," published in

Forms of entanglement

- Face to face visits from drug company representatives
- Acceptance of direct gifts of equipment, travel, or accommodation
- Acceptance of indirect gifts, through sponsorship of software or travel
- Attendance at sponsored dinners and social or recreational events
- Attendance at sponsored educational events, continuing medical education, workshops, or seminars
- Attendance at sponsored scientific conferences
- Ownership of stock or equity holdings
- Conducting sponsored research
- Company funding for medical schools, academic chairs, or lecture halls
- Membership of sponsored professional societies and associations
- Advising a sponsored disease foundation or patients' group
- Involvement with or use of sponsored clinical guidelines
- Undertaking paid consultancy work for companies
- Membership of company advisory boards of "thought leaders" or "speakers' bureaux"
- Authoring "ghostwritten" scientific articles
- Medical journals' reliance on drug company advertising, company purchased reprints, and sponsored supplements

Pharmaceutical Marketing, the advisory process is one of the most powerful means of getting close to people and of influencing them.[10]

The familiar becomes strange

Relationships that from the inside feel familiar now look strange to people outside. The routine wining and dining of prescribers is now seen by some legal authorities as bribery, with a major case currently unfolding in Italy[11]; heavy corporate sponsorship of professional societies and their guideline writing panels is regarded in some quarters as suspect, as shown by the case of Genentech's $11m (£7m; €10m) connection with the American Heart Association[12]; accredited events in continuing medical education seem little more than an opportunity for speakers paid by sponsors to speak about their drugs, particularly when even the lecture hall bears the sponsor's name.[13]

Most scrutinised are the relationships that entail corporate funding of academic research: a recent review of the evidence found financial conflicts of interest to be "pervasive and problematic" in biomedical research, with a quarter of university researchers receiving industry funding and a third having personal financial ties to sponsors.[8] The concern is that the evidence base of healthcare is being distorted fundamentally. Strong and consistent evidence shows that industry sponsored research tends to draw conclusions favourable to industry and industry sponsored studies were much more likely to reach conclusions that were favourable to the sponsor than were non-industry studies. Another review, published in this issue, has similar findings and concerns.[14] The explanations for the "systematic bias" in results is not that sponsored science is bad science but rather that the scientific questions being asked reflect the self interest of the sponsor.

"The medical profession is being bought by the pharmaceutical industry, not only in terms of the practice of medicine, but also in terms of teaching and research," says Arnold Relman, a Harvard professor and former editor of the *New England Journal of Medicine*, whose recent critique of the industry's influence in health care, published in the *New Republic*,[15] won him and his co-author one of the top awards for magazine journalism in the United States. "The academic institutions of this country are allowing themselves to be the paid agents of the pharmaceutical industry. I think it's disgraceful."

Major interest groups, including the American Medical Association and the Pharmaceutical Research and Manufacturers of America, have responded to the current concerns about entanglement with revised codes of conduct.[16 17] Although egregious behaviours such as direct cash payments to doctors are discouraged, some of the new codes have generally done little more than endorse the myriad forms of the existing interactions, said a biomedical ethicist at Stanford University, Mildred Cho, a researcher with a strong interest in the entanglement between doctors and drug companies.

Even groups who are genuinely suggesting a greater degree of independence, including the Association of American Medical Colleges, are doing so from within the context of a stable marriage—the association's latest guidelines say: "A principled partnership between industry and academia is essential if we are to preserve medical progress and continue to improve the health of our citizenry."[18] Says Cho: "Conflicts of interest are so pervasive now that many of the existing rules—or their revisions—are working with the assumption that those conflicts are necessary, and somehow even desirable, because the private financial interests of physicians or research institutions actually enhance the interests of the patients, rather than conflict with them. And I don't think that assumption is right."

Inexorably drawn into the debate are institutions like the University of California in San Francisco (UCSF), one of the top recipients in the United States of health research funding from the government and a campus with extensive ties to the pharmaceutical industry and burgeoning biotech sector of nearby Silicon Valley. A special "conflict of interest task force" set up by the academic senate has just produced a draft report canvassing major changes to the rules on relations with private research sponsors. Reflecting profound disagreements within the university and the wider medical establishment, a serious split has occurred in the task force, which is soon to report. Ultimately the academic senate will make a recommendation to the university administration on the topic, and, given the size and prestige of UCSF, the outcomes of this current conflict will resonate far beyond the hills of San Francisco.

Relationships with researchers

UCSF currently has a reputation for one of the strictest policies in the United States on financial ties between

researchers and study sponsors—for two reasons. Firstly, most other institutions don't regard researchers' relations with individual companies that are worth less than $10 000 in any given year as a notable tie and hence don't require their disclosure—whereas at UCSF researchers with any outside tie worth more than $250 must disclose it to the institution. Secondly, a principal investigator conducting sponsored research at UCSF is expressly prohibited from having any other form of financial tie with that sponsor while that research is being conducted.

Despite this perceived restrictiveness a study of two decades of disclosures at UCSF found an intricate web of ties that, although affects only a small minority of the campus population, had steadily increased.[19] Common ties between academics and private drug or biotech companies included:

- Paid speaking arrangements, ranging from $250 to $20 000 a year;
- Paid consultancies, mostly less than $10 000 but up to $120 000 a year;
- Paid positions on advisory boards; and
- Equity holdings, mostly over $10 000 and ranging up to $1m.

The draft report prepared for the academic senate at UCSF has canvassed a fundamental loosening of the university rule—an end to the prohibition on personal ties with a sponsor during the life of a sponsored research project and a change of definition in line with other institutions, so that any tie worth less than $10 000 a year with an individual company would no longer be considered noteworthy. Given that many researchers have financial relations with multiple companies, the new rules could mean that large amounts of the private dealings of public academics would remain undisclosed.

Task force chair Michael Weiner says that, although a consensus recommendation has not yet been reached by the heavily divided committee, his personal view is that the current prohibitions are unnecessarily restrictive—a view that he says is shared by many of his clinical researcher colleagues at UCSF. Meanwhile other task force members are pushing to retain the prohibition on personal financial ties during sponsored research, and an unnamed member told me of potential dangers if UCSF lifts the ban. "Currently the public feels it can trust research from this institution. Loosening the rules could open the door to concerns that researchers may be influenced by corporate funding and their research may be biased towards that sponsor."

Relationships with clinicians

As debate about the ties between academic researchers and their sponsors continues at UCSF, as elsewhere, industry's interactions with prescribing clinicians are also under review. The dean of medicine at UCSF, Haile Debas, has become increasingly concerned about what he sees as industry's uncontrolled access to campus doctors and about data indicating that many young doctors believe that they are immune from promotional influence.[20] "I think this is a very serious problem, and it's one we need to address," he said.

In the United States an estimated 80 000 drug company representatives,[21] backed by more than

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$19bn of industry's combined annual promotional budgets,[22] are visiting doctors every day, including those working on the wards of the hospital at the medical centre of UCSF. The industry magazine *Pharmaceutical Executive* describes them as "industry's favourite marketing tool," because "the reps carry the bulk of the selling expectations" and the relationships they build with doctors are so critical.[21]

Almost every lunchtime a company will sponsor free pizza or pasta at UCSF, and dozens of hungry resident doctors will attend. As Katz observed in her recent analysis of gift giving: "Food, flattery, and friendship are all powerful tools of persuasion, particularly when combined."[4] But the contacts that start with a free lunch are not just one-way sales pitches: many prescribing clinicians are also aspirant academics, and the friendly drug company staff who accompany the food can facilitate the flow of research funding, speaking tours, and precious publications on which successful medical careers are built.

Across the United States drug companies sponsor close to 300 000 events for doctors every year as part of their promotional efforts, many of them far more generous than free pizza. Under the industry's new voluntary code covering relationships with health professionals, if a company flies 300 doctors to a golf resort, reimburses their costs, pays them to attend, and educates them about the company's latest drug, in order to train them to become members of the company's stable of paid speakers, the entire activity would be in compliance.[17]

The senior vice president for scientific and regulatory affairs of Pharmaceutical Research and Manufacturers America, John Kelly, defends the new code as being for the benefit of patients, and in relation to the golf resort event he said that it is "appropriate to train the number of speakers that a company needs to support its communications effort."

The chief of the UCSF hospital's medical services, Robert Wachter, a professor of medicine, does not endorse such company organised junkets but welcomes the free pizzas at lunchtime, arguing they come with no strings attached. "Industry dollars are fine as

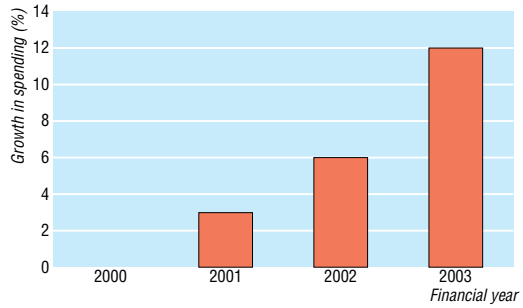

Fig 2 Growth rates of pharmaceutical spending at the University of California, San Francisco (source: UCSF School of Pharmacy)

long as the companies have no role in choosing content or speakers." As a national leader of an emerging specialty of hospital based doctors known as "hospitalists," Wachter sees great value in company funded education, as long as there is a firewall between sponsorship and editorial content. And in his role as "thought leader" he is occasionally paid to meet up with drug industry executives to develop mutual understanding around issues related to this new field—interactions he regards as appropriate as long as they are transparent. For Haile Debas, the free lunches and the sponsored education are part of a much bigger process of companies "buying influence" and building problematic relationships, "creating conflicts of interest for prescribers, which in turn can affect their judgments about the care of patients and inadvertently drive up healthcare costs."

Peaking at around 18% in 1999, UCSF's annual growth in pharmaceutical spending in its hospitals and medical centres was brought under control in 2000, but in 2003 it is already growing again at double digits—for all the familiar reasons: rising drug prices, rising volumes of prescriptions, and rising proportions of prescriptions written for the newer, more expensive drugs (fig 2). In addition, regular shortages of older, cheaper, but effective, medicines are also driving the cost increases at UCSF's medical centre and in hospitals across the United States.

Those in the university who are in charge of achieving more rational use of medicines are convinced that the entanglement between drug companies and doctors is part of the reason for the explosion in costs and part of the reason why attempts to control costs are undermined. The dean of pharmacy at UCSF, Mary Anne Koda-Kimble, has a sympathetic understanding of the mutual benefits that flow from the relationships but says the ties bring undue influence on drug use. Her department, like others at UCSF and elsewhere, is in the process of serious rethinking, with open discussion of plans to wind back the influence of industry fundamentally.

Redefining the relationships

Late last year Haile Debas appointed his own special committee to "redefine the relationships" with industry, and he has just received its final report (see part 2 of this article). "There have to be relationships with industry, but within a framework that respects the independence of the physician and does not unduly effect their judgments about patient care," he said.

Another UCSF researcher advocating a change is Drummond Rennie, a deputy editor with *JAMA* (the journal of the American Medical Association), who argues that the culture of gift giving, which starts with medical students, breeds a long term sense of entitlement. "I don't criticise the marketers for behaving like marketers. What they do is make people feel entitled—so it's not a bribe; it's their due. And you end up with a situation where doctors won't walk fifty yards at a big medical meeting without being transported in a drug company bus."

The flipside of this sense of entitlement is of course indebtedness, which, as Katz points out, is to be repaid by support for the patron's drugs,[4] with a sense of obligation in direct conflict with doctors' primary obligation to their patients.

Numerous requests for an interview with pharmaceutical company Genentech, to discuss the guidelines of the American Heart Association and the broader issues of entanglement, were declined.

Competing interests: None declared.

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