Perspectives

Avoiding Exploitation in Clinical Research

SOLOMON R. BENATAR

Clinical research has become a burgeoning activity in recent years, largely stimulated by the pharmaceutical industry's interest in new drugs with high marketing profiles. Several other forces fuel this thrust: the increasing dependence of academic medical institutions on research funding from industry; the need for large, efficient multicenter trials to obtain reliable and statistically significant results in the shortest possible time for drug registration purposes; and access to research subjects in "developing" countries. The intense interest in HIV/AIDS research and recent controversies about revisions to the Helsinki Declaration, which have been seen by some to be motivated by the desire to facilitate exploitative research in "developing" countries, have stimulated renewed interest in the ethics of clinical research.[1]

It is against this background that avoidance of conflicts of interest and avoidance of exploitation in clinical research have become critically important issues. Although much attention has been directed at conflicts of interest,[2] the problem of exploitation needs more specific attention. It is my contention that understanding and avoiding exploitation will be contingent on: (i) greater awareness of, and knowledge about, the economics and sociology of drug development and the clinical research endeavor; (ii) more open acknowledgment that research may be, and often is, associated with exploitation at many levels; (iii) the will to act on this knowledge; and (iv) the development of policies and practices that could promote healthy lives globally through the achievement of greater social justice.

Although the diseases popularly researched afflict people all over the world, and multicenter trials are thus the vogue, drug research is predominantly directed at the needs of the most affluent quintile of the world's population. Over 90% of annual global expenditure on health research and development ($56 billion) is directed toward disorders responsible for only 10% of the global burden of disease.[3]

Drugs account for a significant and growing proportion of health expenditure in all countries, ranging from 6.9% in the United Kingdom to 10.5% in Germany, and up to 14% in the United States.[4] Expenditure on drugs is the fastest growing component of health expenditure in the U.S. market-dominated practice of medicine.[5] The U.S. drug market accounts for 40% of the industry's sales and 60% of its profits.[6] The size and distribution of the major pharmaceutical houses provide insights into the power structure of the drug industry. Nine U.S. pharmaceutical houses dominate in the top division by market capitalization, with market values ranging from $198 to $59.3 billion. Three companies based in Europe feature in the first division

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and have market values of between $123 and $115 billion. Companies in Europe dominate the second division with market values of just over $30 billion each. It has been estimated that by 2002 only three of the world's 25 top-selling drugs will be made in Europe, whereas U.S. companies will account for 20.[7] In 1992 approximately 44% of global expenditure on health research and development was provided by the pharmaceutical industry.[8]

Without detracting from the major benefits that have flowed from intensive drug development activities, or from some of the recent renewed attention to tropical diseases, it is necessary to point out that

> the multinational pharmaceutical industry operates like any other industry. It makes investment decisions to maximize the present value of future returns from the money invested. As such, it responds to economic demands rather than to statements on social or human needs.[9]

It is also necessary to reflect on criticisms of the role of the pharmaceutical industry in world health and in particular its business in the "third world,"[10] where up to 50% of people do not have access to even the most basic drugs. The lack of pharmaceutical interest in diseases such as malaria and tuberculosis as well as other diseases that cause considerable mortality and morbidity is a reflection of the attitudes expressed in the regrettable statement that two-thirds of the world's population are "superfluous from the perspective of the market. By and large we do not need what they have; they can't buy what we sell."[11]

In industrialized countries, where the "medical industrial complex" is increasingly a reality, the major interest in large profitable markets for drugs has led to the proliferation of research on "me too" drugs (with only marginal potential advantages) that may allow market niches to be captured. There is also a drive to develop "lifestyle drugs" for improving the quality of life and alleviating the symptoms of old age. The desire to make vast sums of money from medicinal drugs can be viewed as a modern version of the gold rush. Why make drugs for sick people who cannot afford them when one can make drugs for people with resources who seek marginal improvements or those who are well and will pay for the possibility of a healthier old age? Proliferation of clinical research, much of it promotional and of dubious scientific value, follows.

Most large clinical studies are multicenter endeavors involving thousands of research subjects. Recruitment of subjects into clinical research studies has become a competitive and lucrative business for investigators and there is considerable potential for exploitation—of both investigators and research subjects. As all protocols require ethical evaluation, the spurt of drug development has resulted in rapid expansion in the number of research ethics committees, many in the private sector. The growing volume of work and pressure to provide rapid reviews, by committees whose members may have had little or no training in research ethics, results in the relatively easy passage of protocols through ethics committees. Remuneration for research subjects and for ethics committee members is also becoming more widespread, indicating the extent to which clinical research is becoming commodified.[12] A recently identified and troubling problem is that some committees may not be aware of the need for data monitoring and safety committees, as illustrated by the British Biotech affair.[13] The fact that there is minimal subsequent audit to evaluate the ethics of conduct of research (as distinct from evaluating the ethical intentions expressed in the protocols)

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aggravates the potential for exploitation even in well-resourced countries.

The Virodene affair in South Africa (in which researchers proceeded with their project despite denial of approval by an ethics committee)[14] and the recent exposure of unethical oncology research at the Witswatersrand University in South Africa (the protocol not having even been submitted to an ethics committee)[15] reveal the even greater potential for exploitative research in less well resourced societies. As has been pointed out in several reports, research partnerships and practices in "North/South" collaborative research can have many insidious, subversive ill effects, particularly for the developing country partner.[16]

The need to protect particular communities on whom research is undertaken poses yet more complex problems.[17] Although workable guidelines have been developed for protecting aboriginal communities, greater difficulties are encountered in extending these guidelines to less clearly definable groups.[18] Such considerations are becoming increasingly important in collaborative international research.

It is patently clear that the drive for clinical research is deeply linked to market forces. In a globalizing world, the sweatshops of developing countries are not only used to manufacture commodities such as shoes and clothes but also to test new drugs. In 1990 it was suggested that there were almost 600 HIV/AIDS–related studies being conducted in Africa.[19] There must be many more today. It should also be clear from the range of drugs being tested that it is the potential market for drugs rather than the extent to which they could be used to reduce human suffering that is the main goal.

These research problems are compounded at the level of practice where the interaction between the medical profession and the pharmaceutical industry has long been a contentious issue. In the United States, more than $11 billion is spent each year by pharmaceutical companies in promoting and marketing drugs (between $8,000 and $13,000 on each physician)—a process that has been shown to affect prescribing and professional behavior.[20] Furthermore, 89% of annual global expenditure on health is on the 16% of the world's population that bears 7% of the global burden of disease.[21]

Avoidance of exploitation in clinical research is a major challenge in a globalizing world in which disparities in wealth, health, and disease have reached grotesque proportions. The challenges for healthcare professionals concerned about health at a global level are greater than ever before. The recent Fogarty International Global Forum on Bioethics in Research reflects an understanding of the depth of the problem and the need to address this as a global collaborative endeavor. The complexity of the problem requires the development of international strategic alliances between people from diverse groups, a wide range of varied expertise and multiple spheres of influence, in public and private sectors across the globe.

Notes

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