FROM OTHER JOURNALS

A global fund for research on neglected diseases

Certain communicable and parasitic infections – in addition to malaria, tuberculosis and HIV – are pervasive in developing countries and responsible for worsening existing inequalities in global health. However, these conditions do not have effective and affordable treatments. It is expensive to develop public health interventions and pharmaceutical companies are not interested in developing drugs for these diseases as there is no money in this market. Between 1975 and 1999, only 16 new drugs were developed for neglected diseases – out of a total of 1,393 drugs developed during that 25-year period.

The authors of this essay blame the current patent regime for this current state of affairs; it supports commercial interests rather than global and national health and economic needs. The most profitable drugs are those which do not demand large research investments, provide small health improvements for a large population, and respond to health conditions in industrialised countries where many people can and are willing to pay the price for the drug.

The authors propose replacing the patent system with a global fund to reward pharmaceutical research conducted for the community's health. The value of this research would be measured in terms of its impact on morbidity and mortality. The authors claim that this system would shift the focus from the profit margins of drug companies (and the economic interests of rich countries) to global health. This shift is critically important for resource-poor settings.

Oprea L, Braunack-Mayer A,Gericke CA. Ethical issues in funding research and development of drugs for neglected tropical diseases. *J Med Ethics.* 2009;35;310-4

An epidemic of injuries in developing countries

The authors of this article note that a neglected public health issue in developing countries is the epidemic of injuries, especially traffic related injuries.There are few prevention programmes, and healthcare systems are ill-prepared to treat them. In the absence of an effective public health response, injuries have far reaching economic and social impacts on individuals, communities and societies.

However, there is little research on injuries as a public health concern in developing countries. This explains why problems like infectious diseases are perceived as more urgent. The authors suggest that the death toll for injuries may be more than for HIV, malaria and tuberculosis combined. The paucity of data has made advocacy on this subject difficult. Data on evidence-based interventions and treatments for road traffic injuries are mostly from developed countries which are not always transferable to developing countries.

The authors argue that there is an urgent need to conduct research on injury, prevention efforts and evidence-based treatments specific to developing countries.

Gosselin RA, Spiegel DA, Richard C, Zirkled LG. Injuries: the neglected burden in developing countries. *Bull World Health Organ*. 2009;87:246

Compensation for injury in Indian clinical trials

The authors report the findings of a study on research related injuries in India, the compensation policies of companies, and the awareness of investigators, ethics committee members and trial sponsors. The study had three parts: first, a questionnaire sent out to 140 investigators, 96 EC members and 37 trial sponsors in 12 cities. (The response rate was 21, 24 and 73% respectively.) Second, in-depth interviews were conducted with three investigators, six EC members and 5 sponsors selected from those who responded. The third part consisted of a study of 119 informed consent and insurance documents of projects submitted to three ethics committees.

The results revealed that almost half (47%) of investigators were either unaware of, or had not understood, the legal requirements for research related injuries and depended on sponsors to manage these issues. The majority (74%) of ethics committee members were aware of the requirements. 40% of investigators, 30% of ethics committee members and all the sponsors in this study had policies to manage compensation issues. However, these policies were mainly to provide short-term medical care or reimburse expenses incurred for the acute management of an "adverse event". The policies did not cover compensation for loss of time/wages, death, physical disability or long term incapacitation.

The review of informed consent and insurance documents submitted to ethics committees showed that these documents did not adequately cover compensation issues. Ethics committees were usually given copies only of the insurance certificates (not the complete insurance documents).

The authors conclude that there is a lack of uniformity in policies on research related compensation, and investigators have low levels of awareness of their responsibilities in this area. They call for the development of national guidelines on compensation for injuries of research participants. These guidelines should categorise injuries based on their risk, severity and seriousness,arbitration committees will be needed to determine compensation, and, finally, workshops should be conducted to increase the awareness of both researchers and trial participants.

Thatte UM, Kulkarni-Munshi R, Kalekar SA. Review of policies for injuries to research participants in India. *J Med Ethics.* 2009;35:133-9

Clinical trials: what are the community's concerns?

The authors report on a study on ethical challenges in the South African context. The research consisted of semi-structured interviews with various stakeholders – community advisory boards, site staff, media personnel, civil society representatives, government representatives, ethics committee members and sponsors. Respondents in this study were asked to identify ethical priorities in the South African context. The priorities identified were: informed consent, social harms, collaborative relationships between research stakeholders, the participation of children and adolescents, access to treatment for participants who become HIV positive, physical harms, fair participant and community selection, confidentiality, benefits and payments. The researchers conclude that stakeholders in this developing country context did not identify any concerns other than those already documented in international ethical guidelines and literature. However, these were interpreted within the distinct socio-historical and cultural context of the country.

The authors make a number of recommendations for future research conducted in developing countries. Researchers should communicate more explicitly their reasons for selecting a particular community for research. They should also make efforts to increase diversity in participant selection. Sponsors should recognise the need to provide concrete benefits to the community, including investment in capacity building. They should clearly state what benefits will be provided to participating communities. In the context of HIV vaccine trials, researchers should monitor the capacity of referral networks to provide treatment to participants who become HIV infected in the course of a trial. Researchers and sponsors should conduct a country-level assessment of the standard of care and treatment offered to participants in HIV vaccine trials. And lastly, researchers, civil society groups and ethics committees should advocate for changes to the policy of payment for trial participants. They should also advocate for an improved framework for child and adolescent involvement in trials.

Essack Z, Koen J, Barsdorf N, Slack C, Quayle M, Milford C, et al. Stakeholder perspectives on ethical challenges in HIV vaccine trials in South Africa. *Dev World Bioeth.* 2009 Apr 30. [Epub ahead of print]

Travelling clinical trials and international law

The author of this essay observes that a decade ago, research in developing countries was conducted without concern for the Nuremberg Code and the Declaration of Helsinki. Medical research in developing countries continues to raise the same concerns. However, a new precedent may have been set when a US court relied on international guidelines and covenants to accept a case filed by Nigerian families accusing a US drug company of conducting medical experiments on their children without their informed consent.

These families filed a case in the US against Pfizer for testing an antibiotic on children with meningitis without their informed consent. They held that the company withheld effective treatment even when it found that the experimental drug wasn't working. Eleven children are reported to have died because of the trial, and many more left severely disabled. Pfizer reportedly failed to secure informed consent of either the children or their guardians; to disclose the experimental nature of the study and the serious risks involved, or to inform them that alternative, effective treatment was immediately from Médecins sans Frontières at the same facility.

When the case was filed in a US court, it was initially dismissed but then admitted on the grounds that informed consent has attained the status of customary international law. On this point, the court relied on the Nuremberg Code, the International Covenant on Civil and Political Rights, the Declaration of Helsinki and the International Ethical Guidelines for Biomedical Research Involving Human Subjects. The author concludes: "The Second Circuit's persuasive opinion that the doctrine of informed consent has attained the status of an international human rights norm that can be enforced in the world's courts should help persuade international corporations and researchers alike to take informed consent – and perhaps the other principles of the Nuremberg Code – much more seriously."

Annas GJ. Globalized clinical trials and informed consent. *N Engl J Med.* 2009 May 14; 360 (20): 2050-3

Ethical issues in xenotransplantation

Xenotransplantation or the transplant of organs from a non-human species into humans carries the risk "xenozoonosis" – of transmitting disease from one species to the other. The new virus or other pathogen may move in pandemic form through the human species. The author suggests that some form of "community consent" is required before whole organ animal to-human xenotransplantation should take place. However, the relevant community is global and there are no institutions with the democratic credentials to establish this global consent.

Given the global inequalities in access to healthcare, the benefits of xenotransplantation will go to the wealthy in developed countries. This means that proceeding with research in xenotransplantation involves risking the lives of the poor without their consent and with little prospect of their benefiting.

The only ethical way for trials of xenotransplantation to proceed is to do away with the global inequalities in health care access that prevent the poor from the benefits of research. So rich countries must ensure global access to basic healthcare before xenotransplantation trials or therapy proceed. The developed world can ensure this without a "politically prohibitive drop in living standards" but there is a lack of political will.

Sparrow R. Xenotransplantation, consent and international justice. *Dev World Bioeth.* 2009 Mar 11. published online

Conflicts of interest and the US Institute of Medicine

This perspective paper discusses a report by the Institute

of Medicine (IOM) on conflicts of interest. It defines conflict of interest as "a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest." The primary interests include "promoting and protecting the integrity of research, the welfare of patients, and the quality of medical education." Secondary interests include "not only financial gain but also the desire for professional advancement, recognition for personal achievement and favors to friends and family or to students and colleagues."

The IOM report focuses on recommendations to regulate financial conflicts of interest. It states that financial conflict of interest is "not necessarily more corrupting" than other secondary interests, but is more quantifiable and effectively regulated.

The IOM's recommendations discussed here include a ban on promotional activities in which medical professionals "present content directly controlled by industry" and a ban on all gifts from medical companies. The IOM also recommends standardising the content and format of disclosures of financial relationships, developing a new, independent system of funding continuing medical education, developing clinical practice guidelines and restricting industry funding. It recommends that the US Congress enact legislation requiring companies and their foundations to report all payments to physicians, various entities and groups.

The author concludes that the IOM's recommendations are comprehensive would have a major impact on the practices of both individual physicians and medical organisations.

Steinbrook R. Controlling conflict of interest--proposals from the Institute of Medicine. *N Engl J Med.* 2009 May 21;360(21):2160-3

Human rights and a nation's health

The authors report on a study of the association between the ratification of human rights treaties and improved health and social indicators. They looked at 170 countries and six human rights treaties. The health indicators included HIV prevalence, maternal, infant and child mortality, and life expectancy. The social indicators included child labour, human development index score, gender gap, corruption index, civil and political rights scores.

The authors found no consistent association between ratification of human rights treaties and health or social outcomes. Health improvements in countries with established market economies were not associated with the number of human rights treaties that the country had ratified. The authors note that treaty ratification must be followed up with monitoring mechanisms to ensure that countries comply with treaty obligations. They conclude: "The fact that economic status was the greatest predictor of good health, but was not associated with likelihood of treaty ratification, emphasises the central role of financing in the realisation of the right to health."

Palmer A, Tomkinson J, Phung C, Ford N, Joffres M, Fernandes KA, et al. Does ratification of human-rights treaties have effects on population health? *Lancet.* 2009 Jun 6; 373 (9679): 1987-92

Allocating resources in a public health emergency

The authors describe the use of ethical principles to decide .on who gets life-saving treatment that is in short supply. A public health emergency, such as an influenza pandemic, will lead to shortages of ventilators and other equipment, drugs and medical services, and someone will have to decide who will receive these resources – and who will not. At present such recommendations are based on a utilitarian perspective: the patients' chances of survival and discharge from the hospital. The authors propose what they describe as a "multiprinciple allocation strategy". Principles guiding resource allocation should include maximising survival to discharge, maximising the number of life-years saved, and maximising patients' chances to live through each of life's stages. The public should be involved early in choosing ethically acceptable allocation strategies.

White Douglas B, Katz Mitchell H, Luce John M, Lo Bernard. Who should receive life support during a public health emergency? Using ethical principles to improve allocation decisions. *Ann Intern Med* .2009;150:132-8.

The "complete lives" system for allocating scarce medical interventions

Another evaluation of arguments on how to allocate very scarce medical interventions also uses a multiprinciple strategy. The authors of this paper categorise eight basic principles as each representing one of four core ethical values – "treating people equally, favouring the worst-off, maximising total benefits, and promoting and rewarding social usefulness". They evaluate three systems for allocating an organ for transplant: the United Network for Organ Sharing points systems, quality-adjusted life-years, and disability-adjusted life-years. They recommend, instead, the complete lives system which "prioritises younger people who have not yet lived a complete life, and also incorporates prognosis, save the most lives, lottery, and instrumental value principles."

Persad Govind, Wertheimer Alan, Emanuel Ezekiel J. Principles for allocation of scarce medical interventions. *Lancet.* 2009; Jan 31. 373 (9661): 423-31.

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