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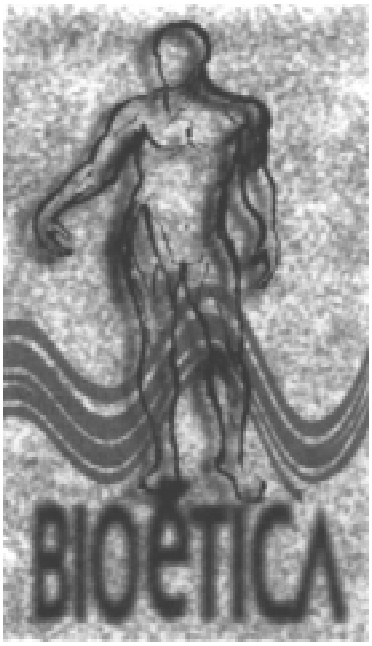
INTERFACES BETWEEN BIOETHICS AND THE EMPIRICAL SOCIAL SCIENCES

Fernando Lolas S. Lorenzo Agar C.

Editors



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N O T E

This technical document series is produced by the Regional Program on Bioethics of the Division of Health and Human Development of the Pan American Health Organization / World Health Organization (PAHO/WHO), with the purpose of disseminating information and stimulating discussion about topics of interest in bioethics.

The opinions expressed in these documents are the sole responsibility of the authors and should not be attributed to the Pan American Health Organization.

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FOREWORD

Welcome message

As Director of the Pan American Health Organization I would like to welcome you as participants in this meeting of the International Advisory Board in Bioethics. I appreciate the effort and enthusiasm with which the members of the academic community have responded to our request for advice and support and I am pleased to say that the substance of the different abstracts submitted make us expect a very useful and profitable meeting. We have insisted that training of personnel in bioethical matters and appropriate scholarly work are fundamental components of those policies aimed at reducing inequities and improving the health of the people of the countries of the Americas. I am confident that the development of the main working lines in bioethics which you are helping us to establish will last throughout time.

With this in mind, I urge you to broaden the local view towards the international scene so as to find a common language in bioethical values, to work actively with governments and to help to mobilize organizational and financial resources for bioethics. The bioethics cause has both a cosmopolitan and a local dimension. The two are important. We have to think globally but act locally, as Rene Dubois would say.

I believe that our activities in this field should focus initially on clinical bioethics as a starting point for a retrospective analysis. We have also to study carefully the new developments in biomedical research thay promise to have a profound influence on health and wellbeing. The conclusions reached after this assessment should then be clearly debated at the global Forum on Bioethics to be held in Brasilia during 2002 at which I hope to see you all.

I wish you a successful meeting.

Dr. George A.O. Alleyne
Director of the Pan American Health Organization

EMPIRICAL SOCIAL SCIENCE STUDIES AND BIOETHICS
An interface for the Regional Program on Bioethics

Fernando Lolas Stepke

The Advisory Board of PAHO Regional Bioethics Program

Since its establishment in 1993, the Regional Program on Bioethics of the Pan American Health Organization has been a tool for addressing controversial issues in healthcare, biomedical research, and technical cooperation among the countries of the Americas and the Caribbean. One of its first commitments was the creation of a network of professionals with a reasonable capacity for deliberation and ethical analysis. This explains why part of its resources has been devoted to training and consultation.

Another concern was, and continues to be, to anticipate those challenges which may constitute dangers and opportunities for the bioethical enterprise in the Region. It soon became apparent that several deeply rooted controversies and problems had to be dealt with if the goal to construct a culturally relevant discipline and sound applications was to be achieved. For instance, the tension between the public and the private, which varies in intensity in different communities, is a rich source of problems and challenges for a "culturally fair" bioethics. In addition, the tendency towards theoretical speculation may sometimes hamper the exam of the very practical problems people face in the context of healthcare and biomedical research. And, last but not least, the misrepresentation of what people actually believe and feel is a serious problem at the time of making decisions in sensitive areas.

In the countries of the Latin American and Caribbean Region, as in other areas of the world, interest in bioethical issues has grown enormously during the past years. Our database lists hundreds of persons and institutions purportedly engaged in bioethics, journals are founded, courses taught, and meetings organized. There are reasons to believe that much of this effort will be worthwhile. Unfortunately, there are also reasons to believe that much of what is produced in this frenzy is short of junk which, if not properly harnessed or accompanied, will result in confusion and wasting of resources, aside from the damage inflicted to the bioethical enterprise in terms of credibility or intellectual quality. Requests for sponsorship on the part of the Regional Program range from asking to use the name to expecting full coverage of costs and logistics. Standardized criteria for judging quality are difficult to establish and may collide with entrenched practices in Latin American academia or with local prestiges which extend their halo effect to bioethics without realizing its critical potential or the possibilities for prudent application.

This state of affairs is certainly not new. In order to prevent major flaws in the development of programs and strategies, PAHO Director, Sir George Alleyne, decided, at our request, to appoint an International Advisory Board whose opinion would be taken into consideration whenever new directions or courses of action were devised. This board is

composed by experts drawn from among those most seriously involved in the field of bioethics, irrespective of their institutional affiliation. The only requisite to be invited is demonstrated capacity for academic contributions. The members of the board are not representatives of their institutions nor are they supposed to represent countries, opinion groups or otherwise. Their contribution is ad honorem.

It has been a principle, since the establishment of the Board, to hold annual meetings. In them, aside from reviewing current activities of the Bioethics Program and discuss PAHO orientations in general, it has been customary to deal with a particular topic and to publish the contributions presented. Thus, the first meeting examined research involving human subjects and lead to a book-length publication *(1)*. The second addressed the topics of equity and rights and its proceedings were also presented as a book *(2)*. The present volume stems from the third meeting of the Board, held in Buenos Aires on October 2, 2001, and has as broad topic the interface between bioethics and empirical research in the social and behavioral sciences.

Bioethics and empirical social science

There are many reasons for the relevance of this interface in the current atmosphere and developmental stage of Latin American bioethics. Some of them have been mentioned above. There are persons and groups allegedly cultivating bioethics in the countries of the Region, albeit with strong and complex differences between them. There are hopes and expectations, both personal and institutional, that bioethics may help solving problems in the delivery of health care and in the establishment of sound scientific research. Practices and theories are heavily influenced by religious beliefs, emotional responses to new developments, and political agendas.

For the people in the countries of the Region, there is the danger that some topics may altogether be omitted from the discussion. Another danger, called “ethical imperialism”, is the acritical adoption of ideas and practices from developed countries. Sometimes, irrational opposition to valuable contributions may hamper development and serve no useful purpose.

Our proposed topic can be clearly reduced to two interrelated concerns. First, we need an empirical analysis of what constitutes the social practice called bioethics. This research uncovers interesting dimensions, for sometimes people believe they are doing something and a more careful analysis reveals that their practice, though resembling others, has nothing to do with them. Superficial resemblance is found, for instance, in the operation of research ethics committees, established in some countries due to pressures for funding from US agencies but with no real rooting in local research culture. Working as a member of an ethics committee is considered by some good-intentioned people to mean voicing one’s own convictions and convincing others of their importance.

There is a second dimension to the interface. Empirical social science research is no less demanding in terms of ethical analysis than biomedical research, and problems uncovered by a bioethical analysis of research protocols are all the more urgent since they have hitherto not received attention from bioethicists. There are institutions where social science research is not ethically regulated in the belief that it does not entail risk, danger, or harm.

Even if these two aspects of the interrelation between bioethics and empirical social science are not explicitly discussed, it is obvious that human behavior and discourse about human behavior are infinite and that the context—social, cultural, or economic—greatly affects what is done and what is not. The two-way relationship is in practice just one and the same preoccupation.

Descriptive and prescriptive dimensions of practices related to health care, biomedical research, and policy formulation find their place in the analysis and development of cultural bioethics. The modulation of norms and the different reception of knowledge in diverse societies require prudent evaluation and careful study. This set of contributions will certainly help both practitioners and scholars and are meant to encourage local researchers to undertake empirical work in the interface between bioethics and social science.

The contributions of this volume

In his chapter, *James F. Drane* describes the origins of bioethics in a very personal account. Drane was one of the experts PAHO consulted during the early stages of the establishment of the Regional Program on Bioethics. His extensive experience and his personal involvement lead to those recommendations which made this pioneer initiative possible.

Ruth Macklin addresses the critical issue of deception in social science research, and how it may affect procedures and results. Her experience as committee member of numerous working and study groups and her profound knowledge of different research environments make this contribution an important reference for those involved in project evaluation. Insight into problems posed by deception may be considered essential for a sound discussion of bioethical issues in research involving human participants.

Ezekiel Emanuel deals with the central issue of the relevance of empirical research for bioethics. His careful conclusion warns the reader about the dangers of "*dataism*" while retaining the usefulness of collecting and analyzing empirical information. He delineates some of the areas in which further research is badly needed.

In the same vein, the paper by *Daniel Wikler* places emphasis on the results of studies using polls and focus groups and takes resource allocation as an example. His balanced presentation will certainly encourage others to undertake this line of reasoning and to produce much needed data.

One of the most debated issues in current research bioethics relates to placebo controls in clinical trials. Discrepancies on this topic arose in connection with the revision of the Declaration of Helsinki and with the drafting of the revised CIOMS Guidelines. It is an issue with profound impact on future research practice, particularly in industry-led investigations, multicenter studies, and research conducted in less developed countries. One of the best known experts in this field, *Robert J. Levine*, provides useful conclusions and recommendations to all those involved in research and teaching, and will certainly constitute a source of debate in the coming years.

Diego Gracia provides an example of the two-way interaction between research agenda and bioethical reasoning in his account of pharmacogen-ethics, a field which will

undoubtedly grow in the future and will confront researchers and administrators with interesting challenges. The economic implications of these developments add to the complexity of the issue.

A well-known writer and researcher in the field of justice and healthcare, *Norman Daniels*, presents a balanced account of how distributive justice impacts health and health care and proposes thoughtful ideas for a bioethics research agenda.

Daniel Callahan's paper can be considered a summary of those challenges and contradictions associated with technological developments in medicine and health care. His questions are not new, but his answers may serve as a trigger for renewed consideration of the final goals of the healing practices in contemporary societies.

The future of bioethics

It may sound undue to associate the activities of a technical program to the future of an intellectual discipline with high practical impact. The challenges uncovered by the deliberations of our Advisory Board, however, clearly link the modest daily work of supporting small initiatives with the expectations people place on their health care systems and on their societies. Latin America presents not only a complex picture in terms of political institutions and economic policies. It is also a battlefield for beliefs on how to devise and implement more fair societies and more equitable access to services. Reform and health are words so closely associated that it is not striking that the ethical dimension has come to the foreground, for all reform involves change and change defies beliefs and entrenched customs.

In order to safeguard the quality of the bioethical enterprise in Latin America and the Caribbean, the Regional Program not only relies on the advice and support of accredited scholars and experts. It also conducts surveys, keeps databases, encourages the production of texts and educational materials, fosters and sponsors meetings and seminars, and, above all, tries to integrate bioethical thinking to the practice of research, to health care, and to technical debate.

This volume may be considered a contribution to these goals and will certainly add permanence to our efforts.

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WHAT IS BIOETHICS? A HISTORY

James F. Drane

No other field of study reflects the contemporary age more faithfully than bioethics, a systematic study of moral conduct in life sciences and medicine. Medicine and the life sciences are to our period in history what religion and salvation were in medieval times.They are the focus of enormous societal resources and the central concerns of most modern people.Bioethics pulls together under a single discipline the ethical dilemmas associated with bioscientific research and its application in medicine. This enormously expanding field began only recently in the developed countries which had to face many new ethical challenges generated by the biosciences. But the same ethical problems now challenge people everywhere.

It's hard to specify with exactness the beginning of an historical period or a cultural development or even an academic discipline. In most cases beginnings are too far in the past and become lost. Even when relatively few years have passed from the start of something new, initiating events may be diverse and distinguishing a first step from preliminary or background influences is always problematic. To talk about the beginning of bioethics is inevitably to speculate.

Did bioethics as a new discipline begin with the founding of *The Hastings Center* and *The Kennedy Institute* in 1969 - 1970? Or was it the formation of an Ethics Committee in Washington State during the sixties trying to set up ethical standards for the distribution of a scarce medical technology to dying patients (Renal Dialysis). Or perhaps a book by Van Rensselaer Potter *(1)* in 1971, called *Bioethics, Bridge to the Future* launched the discipline? Beginnings are rarely discrete, specific and easily identifiable realities.

The beginnings

Developments in life sciences that gave impetus to the field of bioethics in developed countries now are part of contemporary life in developing nations as well. Modern hi-tech medical centers can be found in major cities all over the world. People everywhere face the same ethical problems associated with human experimentation. The press in Europe and Latin America and Japan now gives the same prominence to ethical problems in medicine that we have seen for decades in the U.S. Physicians in other countries are aware of the need to understand the ethical issues generated by modern medical practices and to update their professional codes. Foreign and domestic politicians anticipate direct government involvement in healthcare regulation and this means involvement with ethical values, especially the principle of justice. In just a few decades bioethics has become a major concern worldwide. In the foreseeable future, it will reflect the ethos of 21st century civilizations.

Because of its important place in contemporary society, the field of bioethics has undergone a meteoric development in the last three decades. First bioethics centers, institutes, commissions and boards were established in the U.S. and Canada. European nations and the European Community followed quickly with their own initiatives. Scholars from Japan and Southeast Asian countries who spent time in Canada or the U.S. or Europe, returned to direct the establishment of bioethics institutes in their own countries. A bioethics program has been established in Santiago, Chile, which promotes development of the discipline throughout Latin America and the Caribbean. Bioethics conferences have already been held in Eastern Europe, and work has started on the development of bioethics centers there. Even recently independent countries in the former Soviet Union and Yugoslavia are organizing conferences on bioethical problems and planning bioethics institutes. International bioethics exchanges have begun to take place, and already the field is changing as a result of efforts to agree internationally on ethical rules and policies. An originally dominant North American-style bioethics is now changing under the influence of European, Asian, and Latin American perspectives.

In its initial stages bioethics was concerned with ethical issues generated by developments in medicine. Later the subject matter was broadened to include all the biosciences, but biomedical ethics remains a core part of this now larger field. Difficult as it is to identify precisely its actual beginning, several events can be recognized as important contributors to the rapid development of the now paradigmatic discipline.

Medical experimentation

German medicine in the nineteenth and twentieth centuries served as a paradigm for modern medicine and medical practice. Both were linked to laboratory science which meant that main-line medicine required proven effectiveness based on rigorous experimentation which inevitably involved human subjects. The misuse of human subjects in medical experimentation created the first modern ethical crises and the first calls for a new medical ethics. The Nuremberg Code responded with what came to be one of the foundations of the new ethics, an informed consent requirement. Whenever medical professionals use human subjects for their research, they have to guarantee respect for each research participant.

The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment [1].

[1] Nuremberg Code. Cited by Robert J. Levine, *Ethics and Regulation of Clinical Research, Second Edition*, New Haven: Yale University Press, 1988.

The violation of traditional medical ethical standards by misusing patients created widespread moral outrage. Vulnerable, weak, and needy human beings, instead of being cared for and protected were used and misused. This called for a new set of ethical standards. Quickly the new ethical standards were extended from medical experimentation to medical treatment because vulnerable patients required protection there as well. Benefit balancing against risks, and disclosure of dangers became as much a part of treatment ethics as of research ethics.

News of grossly unethical behavior by some Nazi physicians during World War II was followed in the U.S. by a series of revelations of similar ethical failures involving experimentation on vulnerable patients in American medicine (Willow Brook School, Jewish Hospital in New York, and the Tuskegee Syphilis Study). In 1966 Henry K. Beecher, a Harvard physician, published an article in the *New England Journal of Medicine* in which he exposed patterns of unethical conduct in medical research *(2)*. The misuse of human subjects by U.S. physicians and Beecher's comments on the misuse, were widely publicized and contributed substantially to a growing public interest in a revised ethics of medicine[2]. Ethical failures associated with research had a major influence on this new field of study. Concern about ethics and experimentation is as strong today as it was at the beginning of modern medicine, and bioethical regulation of research now takes place around the world.

The imperative to make scientific progress in medicine is present anywhere contemporary medicine is practiced. Because the authority of physicians tends to be stronger in foreign countries than it is in the U.S., conditions exist for similar ethical failures everywhere. Only a well-developed and widespread bioethics could keep ethical tragedies generated by research from occurring. No society can afford to leave the balancing of individual patient rights with scientific progress solely a matter for medical scientists to decide. Standards for the conduct of human experimentation had to be imposed everywhere modern medicine was practiced. This is true in the great medical centers certainly, but today, even community hospitals and doctors offices have become places where testings of medicines and other medical research occurs.

Bioethics and government involvement

After World War II, developed nations put great emphasis and large amounts of money into the medical field. Consequently, greater attention had to be given to the ethical issues which inevitably accompany medical advances. In the United States the U.S. Public Health Service, an agency of HEW and later HHS, was made responsible for protecting the rights and welfare of human research subjects. In the 1960s it promulgated ethical standards for the conduct of research. In the 1970s a National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was formed. It worked for four years and made 125 recommendations for improving protection for the rights and welfare of human subjects. The commission published the *Belmont Report*, which identified the basic ethical principles (respect for persons, beneficence, justice) and provided philosophical justification for humane treatment of human subjects.

[2] Later, Jay Katz published important books and articles on ethical aspects of the doctor/patient relationship.

Subsequently, the federal government under the auspices of the same Public Health Service continued to update regulations and to require assurances of ethical compliance with them from any group carrying out research on human subjects. Government, through its support of medical projects, became not just a source of bioethics policy and rules, but it established commissions which articulated ethical justifications for a new ethical approach in the conduct of medical practice. Government and its interests played a major role in the development of modern bioethics.

After the National Commission's work, the U.S. government continued its involvement in bioethics in the form of a new *President's Commission for the Study of Ethical Problems in Biomedical Research*. This commission was formed in the 1980s and mandated to provide reports to the President, the Congress, and relevant departments of government in order to guide politicians in developing legislation. In addition, its work provided guidance to health professionals, health educators, and the general public. *The President's Commission* published eleven volumes, nine reports, and the proceedings of a workshop on whistle blowing in research, and a guidebook for local committees that review research with human beings. The work of this one government commission has had an enormous influence on bioethics. A list of the commission's works provides some indication of just how bioethics expanded in the first few decades: "*Compensating for research injuries; deciding to forego life sustaining treatment; defining death; implementing human research regulations; making health care decisions; protecting human subjects; screening and counseling for genetic conditions; securing access to health care; splicing life; whistle blowing in biomedical research"*.

Government has continued to play an important role in bioethics. There are bioethics programs associated with all the major government research efforts in medicine. Part of the funding committed to medical research is usually allocated for bioethics. Sometimes government funding for controversial research is withheld as a way of exercising bioethical regulation. Federal bioethics legislation and regulations are on going.

Bioethics and medical technology

Flowing from government investment in medical science were all sorts of new medical technologies and therapeutic interventions. The linkage of medicine with science which had begun in the late nineteenth century began to pay off handsomely. New medicines, dialysis machines, organ transplant techniques, mechanical organ support systems, medically delivered hydration/feeding technologies, ICU's, life saving surgeries, etc. were developed. Each new development created new ethical problems. In the 1960s, an Ethics Committee was formed in Washington State which tried to make ethically defensible decisions about who would receive dialysis when this scarce technology could not be provided to all. Bioethics was not just concerned with medical experimentation using human subjects. It was concerned with medical treatment and the participation of patients and communities in medical decision making as well as with who has access to the treatments.

Historically the medical profession always accepted moral responsibility for the exercise of physician's power over patients. The medical profession expressed this responsibility in medical codes and association treatises. All socially authorized professional

power requires public accountability, and this is especially true of medical professional power. The right to practice medicine is associated with moral restrictions on that practice imposed either from inside the profession or by the government. As medical practice became more powerful, ethical problems associated with medical practice proliferated. The range of things physicians could do for patients expanded along with the effectiveness and intrusiveness of their interventions. Micro problems arose with each intervention. Macro problems generated by the relationship of technology and human life also had to be addressed. In both developed and developing nations, physicians became concerned with creating and updating their ethical codes.

Scientific and technological medicine moved medical treatment procedures into the public forum. Medical treatment began to take place principally in public hospital settings where ethical responses had to be publicly defensible. Twenty-first century technologies may make earlier therapies look primitive and uncomplicated, but we can see in early technological breakthroughs the driving force behind the new focus on ethics and the emergence of modern bioethics. The importance of health as a value and medicine as a discipline made biomedical ethics an important field of study almost everywhere.

Before the 1950s, "*doctors know best*" captured the attitude most people had toward medicine and summarized a traditional paternalistic ethics. After the Nuremberg trials and the increased influence of experimentation on practice, this older paternalistic ethics gradually gave way to different standards of right and wrong. Other attitudes, different norms, more and different principles coalesced to create the beginnings of the new bioethics. Once bioethics was born, it quickly developed.

Non-governmental influences

Millions of government dollars contributed to the birth and expansion of bioethics. Modern bioethics, however, came from more than government initiatives. Non-governmental institutes and centers also sprang up to respond to the pressing new problems generated by bioscience.

As early as the 1950s, the *Institute of Religion at Texas Medical Center* in Houston, started working on ethical issues in medicine and a Society for Health and Human Values was formed by religious thinkers interested in promoting the humanities in medical education. In the 1960s the first Department of Medical Humanities was started at *Pennsylvania State University Medical Center* in Hershey, PA, with a faculty weighted toward medical ethics. The next decade witnessed the appearance of *The Hastings Center* in Garrison, N.Y. (late 1969, early 1970), and *The Kennedy Institute of Ethics* at Georgetown University (1971). Both these initiatives attempted to bring depth and rigor to the new discipline.

The Kennedy Institute model was university-based. It developed a National Reference Center for Bioethics Literature which in effect became the best library resource in the world for an expanding new literature. Its scholars came from many different disciplines, worked somewhat independently of one another, and served as faculty for a Ph.D. program in bioethics at the university. One of the first scholars, Warren Reich, a Catholic theologian, put together the *Encyclopedia of Bioethics*, which became a major literary resource for the discipline. A Protestant scholar, Leroy Walters, started an annual *Bibliography of Bioethics*

and developed "BioethicsLine," an on-line computer database. Tom Beauchamp and James Childress published the important book, *Principles of Bioethics*. As new areas of the expanding field of bioethics emerged, scholars from the new areas who were interested in ethics came to the Kennedy Institute to study, to write, and to teach.

On the West Coast, bioethics was advanced by the writings and teachings of Albert Jonsen, at the *University of San Francisco and the University of California* in San Francisco. In Southern California, William Winslade, a lawyer, taught and wrote about the issues. In Chicago, Dr. Mark Siegler, a professor of medicine at the University of Chicago started a training program for clinical bioethicists. In Texas, Dr. Tristram Engelhardt promoted humanities in medical education and clinical bioethics. He worked at *Baylor University Medical School* with a Jewish scholar, Baruch Brody. Both published prolificly.

The Hastings Center was started by Daniel Callahan, a Catholic layman with a background both in philosophy and theology. At the Hastings Center scholars were brought together to work both independently and in groups in order to develop sound ethical policies for specific problems. The Hastings Center continues to publish policy recommendations and topical reports and to influence government responses both directly and indirectly. *The Hastings Center Report*, founded in 1971, carried articles on ethical issues in medicine, the life sciences, and the professions. Over the years, it became the most important journal in the new field.

Since the early 1970's and the work of bioethics pioneers, literally hundreds of bioethics centers, programs, journals, and newsletters have sprung up. Every year the books and articles on bioethical subjects number into the tens of thousands. From a small and recent beginning, bioethics became a major field of study. The American Hospital Association in 1987 published a description of 77 bioethics organizations. Since that time, the number of such organizations has tripled.

Government commissions, academic centers and non-governmental institutes combined to contribute to the development of bioethics in the U.S. Increased interests on the part of professionals fed interested personnel into the growing number of bioethics education institutes. Academically based bioethics centers trained professionals for teaching posts in the new field. Hospitals sometimes hired their own bioethicist for education and consultation, thereby creating job opportunities for trained bioethicists. Bioethics committees were organized in health care settings, and committee members needed education in a field now with an extensive literature. Attitudes of skepticism and resistance towards the humanities components in scientific medicine gradually gave way to acceptance on the part of faculties, students, and professionals. The thousands of bioethics articles and books annually testify to what this field has become over the last few decades.

Bioethics and medical culture

In the early days, bioethics was all about medicine. The discipline did not develop within medicine, but early in the 1970's it muscled its way into the medical culture, largely as a result of the effort of one man, Dr. Edmund Pellegrino. Dr. Pellegrino was both a physician and a humanist, a practicing doctor and a bioethicist. His efforts show how

government and non-governmental groups cooperated to launch a new discipline and an important new social enterprise. But for the combined effort of different forces, the field of bioethics would have been a social and a political influence, but would have remained marginal to actual medical practice. The story of how bioethics entered medical culture links Dr. Pellegrino with the *Institute on Human Values in Medicine* (Non-Governmental Institute), *The National Endowment for the Humanities* (a Federal Government Program) and with medical school faculties all over the country. It was Pellegrino who made bioethics part of the medical school curriculum.

More and more doctors became specialists and operated the new technologies which developed after World War II. For the first time in medical history, doctors became strangers to their patients. And the moral assumptions which doctors and patients had shared for centuries (e.g. paternalism, beneficence, non-maleficence, confidentiality, and respect) were increasingly compromised. More and more moral questions arose from the use of the powerful new technologies. Journalists recognized these as issues of interest and conflicts over the uses of these technologies were given prominent coverage in the press. What was the proper use of the new technologies: respirators, artificial nutrition and hydration, dialysis, artificial insemination, birth control devices? Could patients simply trust the doctor to do what was in their best interest or did they have to insist on more personal freedom and a more adult relationship with the medical stranger who was using new technologies on them?

The new moral questions about doctors and patients and technologies were being asked at a time when traditional ethical values rooted in religion were being either revised or rejected. Questions posed by medicine, medical practice, dying patients, defective newborns, etc. had been addressed for centuries in Catholic moral theology because the Catholic Church was engaged in health-care ministries. But in the late 1960's and early 1970's, the moralists and ethicists who stepped in to think about all the new questions came from very diverse backgrounds. There were some moral theologians but many of the early bioethicists were lawyers, doctors, philosophers and social scientists.

A new set of secular ethical theories were proposed to justify recommended ethical directions. In addition to theoretical literature, the new discipline was engaged in the development of practical procedures for conflict resolution. Bioethics in effect was digging into the doctor/patient relationship, the core of the medical profession. Once this turn was taken, there was not way that bioethics could remain outside the strongly walled culture of medicine. Medical students had to be taught the discipline. Medical faculty members had to be trained. The medical curriculum had to be expanded to include this new discipline. The physician who saw this inevitability was the physician bioethicist, Edmund Pellegrino.

Dr. Pellegrino worked with members of the Institute on Human Values in Medicine and the Society for Health and Human Values. Many of the members were Protestant clergymen and chaplains who were in dialogue with physician members of their organizations. These persons recognized the changes which were taking place in the doctor/patient relationship and saw the need to train medical professionals in the new legal and ethical standards for this relationship. The operating background assumptions of this group of professionals were theological. Gradually the members merged with more secular groups like the *Society for Bioethical Consultation and American Association of Bioethics.*

In 1969, the *National Endowment for the Humanities*, a federal government initiative, provided grant money for Dr. Pellegrino. The project was to train medical school faculty in bioethics and then to carry out visits to U.S. medical schools. These visits put the new discipline of bioethics on the ground in the middle of the medical world. The grant money also supported fellowships for the training of medical school students and faculty in bioethics. Physicians were enabled to study ethics, and ethicists were provided opportunities to become familiar with the hands-on culture of medicine. This effort by Dr. Pellegrino and colleagues resulted in a major innovation in medical education. It started what later would become the separate branch of clinical bioethics.

This project brought bioethics teams to most U.S. medical schools. (77 different locations). The team members brought organizational ideas, lectures, teaching techniques, and encouragement to faculty and students to pursue the new discipline. They were able to influence both faculty members and medical school administrators. They held meetings with interested faculties and students. Gradually, the most influenced faculties became advocates for the new discipline within the medical school environment. As bioethics programs got up and running, return visits by team members provided evaluations of the school's efforts and recommendations for improvement. Through this one effort, bioethics was able to move from academic reflection to practical changes in the way doctors handled their patients. Bioethical norms and values were given concrete expression in medical practice so that they became more than just social/legal/political standards.

Bioethics and the law

Bioethics was not just a new field of study. It was a topic the general public read about in newspapers and saw on television. Famous cases in bioethics like the Karen Ann Quinlan case were at one time as well known as movie stars and prominent politicians. The propensity in the U.S. to look for legal solutions to problems led to an immediate involvement of bioethics with the law.

When issues raised by experimentation and treatment could not be resolved at the patient-physician-family level, they were taken to the courts. The first court cases involved tragic situations with dying patients. Families and hospital staffs disagreed about whether to withdraw life-sustaining technologies, and courts were asked to make life-and-death decisions. The disputes attracted the media and created front page stories. People wanted to hear about the tragic cases because they touched concerns and worries in every family. Court decisions in the highly publicized cases contained ethical arguments that themselves stimulated further ethical arguments. Later court decisions either approved or overturned earlier ones, and a whole corpus of legal bioethics literature came to be.

The combination of media attention and public interest made bioethics important to politicians who saw the need for creating statutes to defend patient and family rights in healthcare settings. Every state now has laws covering bioethical concerns. New laws and new cases continue the interrelation between bioethics and law. Other nations are facing the same pressures, and lawmakers as well as judges everywhere look for help from experts in this new field in order to develop sound legislation.

In Europe and North America, the law adopted many of its positions from ethics. For centuries moral theology or theological ethics held that patients have a right to refuse any treatments, even life-sustaining treatments, if these were experienced as burdensome, risky, or costly. Statutory law and court cases upheld this ethical rule. And the influence went both ways. North American bioethics adopted standards for surrogate decision-making which were developed in the law: e.g., *subjective standard* (what the patient actually chose), *substitute judgment* (what the patient would have chosen), and then *best interest* (what is considered medically best for the patient). And the core bioethical requirement of informed consent came directly from case law.

Questions about proper treatment of patients or the proper form of a doctor/patient relationship were taken to court and what gradually accumulated were judicial decisions which set out new legal requirements for medical practice. Despite a platitude to the contrary, morality is legislated in the U.S. and elsewhere in the world. Judges, state and federal legislators established the foundation of a new medical ethics discipline by setting out, as early as 1940's-1950's, ethical standards for medical practice. Law was definitely involved in the beginning of contemporary bioethics.

Ordinarily, successful law codifies custom and this was true to some extent of the new medical ethics legislation. Surgeons had traditionally sought patient consent for their dangerous interventions. The information they provided was aimed at helping patients to endure the agonizing pain of the surgery. What traditionally took place in the exchange between surgeon and patient however would not meet later standards of informed disclosure and voluntary consent. Almost any communication between the surgeon and patient satisfied traditionally understood consent, as long as what the doctor said was not untruthful and the patient gave some form of assent. Without any communication from the surgeon or consent from the patient, courts considered surgery to be unauthorized and a form of assault[3] .

One court case in the middle nineteen fifties actually used the term informed consent[4] to describe a legally imposed ethics for doctors. Later decisions built on the Salgo decision, and gradually spelled out in greater detail the parameters of a physician's duty to make adequate disclosure to a patient. In 1960, Natanson vs. Kline[5] spelled out a standard for reasonable disclosure. The court required that the nature and possible consequences of a treatment be disclosed. Reasonable disclosure after Natanson meant that the required communication between doctor and patient address questions about risks, consequences, and options; i.e. what reasonable persons want to know.

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[3] Corn v. French, 289 P.2d 173 (Nev. 1955).
Wall v. Brim, 138 F.2d 478 (5th Cir. 1943).
Waynick v. Reardon, 72 S.E.2d 4 (N.C. 1952).
Nolan v. Kechijian, 64 A.2d 866 (R.I. 1949).

[4] Salgo v. Leland Stanford Jr. Univ. Bd. of Trustees, 317 P.2d 170 (Cal. Ct. App. 1957).

[5] Natanson v. Kline, 350 P2d 1093 (Kan. 1960).

In the Natanson decisions, the legal system established a new ethical standard for the doctor/patient relationship which in turn became a bioethics cornerstone. Initially, this discipline focused on trying to justify the new legally created practices by using the principle of autonomy, and then by trying to settle questions like; which risks, how much information, how many alternatives? However one defines the beginning of bioethics, court cases in the 1940's, 1950's, and 1960's laid the groundwork for its initial focus and direction. American courts however were not the only background influence. International courts, as far back as 1948 (Nuremberg) had spelled out legal and ethical standards for informed consent in research which gradually were accepted as well as for treatment procedures.

The expansion of bioethics

Bioethics began as a separate field in the 1960s and early 1970s. At the beginning it addressed the ethical problems associated with medical practice but quickly expanded to social issues related to health, animal welfare, and environmental concerns. Every bioscientific advance contributed to the expansion of bioethics.

Bioethics has undergone an incredible development corresponding to the expansion of biosciences. The original focus expanded to value-related problems in all health professions: nursing, allied health, mental health, etc. A broad range of social issues are now included under the term "bioethics": public health, occupational health, international health, population control, women's issues, etc. Bioethics includes animal welfare issues and environmental concerns. The clinical issues have expanded to include issues related to reproductive technologies, transplants, genetics, and molecular biology. The connection between the concerns of bioethics and contemporary society is obvious. With good reason, bioethics is looked upon as a paradigmatic discipline in this era.

The academic efforts of bioethicists to address the dilemmas so characteristic of modern societies provided crucial assistance to societal leaders, both political and professional. But society and societal leaders were not the only ones to benefit. Ethics itself was benefited by bioethics. In 1973 Stephen Toulmin wrote an article about how medical ethics had saved ethics from decline and disinterest *(3)*. The problems with which medical ethics grappled not only created a new interest in ethics but also saved ethics from an irrelevance created by an overly abstract, rationalistic, linguistic approach. Philosophers, theologians, lawyers, social scientists suddenly found the ethical aspects of medicine and biosciences to be areas of fascination and started studying and writing about them. Today newspapers carry daily and weekly columns on ethical questions generated in contemporary life.

The future of bioethics

Will the astounding expansion and central importance of bioethics continue into the twenty-first century? A quick and clear response to this question comes from considering two recent issues: the genome project and AIDS. Now that the human genome is mapped and the information locked into human genes is opened, the ethical problems generated by this new information have exploded. Data banks of individual DNA's are being established.

Government agencies, police, employers, insurance companies, if they gain access to the data, could substantially influence human lives. The information developed by this one biomedical project has ominous as well as hopeful potential. Only with well thought out ethical standards and judiciously developed ethical policies can the worst imaginable results be avoided. The very dignity and freedom of human life swings in the balance between ethical and unethical handling of this one bioscientific project.

The genome project was the life science project of the 1990s and can easily be compared with the physics project to unlock the atom in the 1940s. The potential for good is great, but unless the associated ethical issues are openly discussed and thought through in advance, human life as we know it today in a civilized, free and democratic society may be undermined. The sheer numbers of ethical complexities are hard to imagine, but the ominous consequences of not attending to them are even more ominous. With good reason some portion of the money allocated for the genome project is committed to bioethics. Ethical questions generated by genetic developments are already present in clinical settings but in nowhere near the intensity which will develop when the new knowledge turns into widespread new therapies.

AIDS is another biomedical challenge shot through with ethical dilemmas. Like so many other diseases with which physicians battled over the years, waging an effective and aggressive campaign against AIDS requires attention both to its biological and bioethical dimensions. Sound strategy has from the start considered scientific and ethical dimensions of the disease. Commitments to find vaccines and therapies have been joined with campaigns to protect the human rights and dignity of people with HIV and AIDS. Efforts to stop transmission of the disease are combined with efforts to stop discrimination against disease bearers in employment, travel, housing, access to health care, and in hospital based medical care provided by doctors and nurses.

AIDS, like the genome project, shows the inevitability of bioethics as well as the ever expanding complexity of this field. On the pragmatic, concrete level there are the problems of confidentiality, allocation of resources, use of human subjects for research, public policy for schools, work place, prisons, and society at large, education and public campaigns, privacy, screening, informed consent, and on and on. No single aspect of the AIDS epidemic is devoid of its bioethical dimension.

Bioethics will continue to expand and to remain important throughout this century because biosciences will do both, and the two are inseparable. Institutional policies and codes and laws, both national and international, political and professional, will have to be developed, then continually improved and updated. No end is in sight for the need of clinical professionals who are conversant with clinical bioethics.

The early culture of bioethics

In the early days of the new discipline there was no sense of bioethicists exercising power either within the medical establishment or in the broader culture. The first practitioners came from different disciplines (theology, philosophy, law and medicine) and ordinarily

understood their roles as clarifiers of problem areas or creators of practical procedures for solving specific clinical problems. The early practitioners of the discipline divided along theoretical and practical lines. As far as I can remember, there was little interdisciplinary nastiness. Most of us who worked in academia, taught courses in bioethics for graduate and undergraduate students, delivered papers at conferences on religion, philosophy and medicine, and offered consultation services to hospitals and hospital ethics committees. Complaints about the restrictive power of bioethics and bioethicists on medical practice and scientific freedom came much later.

During the short history of this discipline there have been many instances of political involvement and attempts to manipulate ethical decisions of committees and commissions. Bioethicists who served on government committees or commissions sometimes were chosen in order to guarantee approval of some ethically controversial direction. Something similar happened in the clinical setting. Some hospital administrators and/or local bishops "cleansed" ethics committees so that the committee's decisions would reflect a certain prescribed orthodoxy. Problems like abortion, physician-assisted suicide, reproductive technologies, embryo research, cloning, inevitably invited political involvement and divided bioethicists along ideological lines.

In the beginning different opinions were generally respected. The bioethicist was expected to be able to explain different sides of a debate fairly and then to develop a position without being disrespectful of opposing views. The early bioethicist had to take stands but did not have to advance an ideology. He or she would be expected to be able to state different sides of an issue fairly. Now, more and more bioethicists are advocates for certain positions and often engage in the same style polemics which one sees on TV shows, like *Crossfire*. Older bioethicists felt obliged to know their background convictions, but not to defend ideologies. They did however have to be sensitive to institutional missions and organizational priorities. They were more comfortable in the role of mediator than as a partisan or polemicist.

Bioethics in the beginning was different from other forms of applied ethics and it remains so today. If the issues under consideration were war or exploitation of children or forced abortion, or drug trade, the ethicists had to look carefully at facts and extenuating circumstances but ultimately had to take a strong stand against an evident evil. If the issue under consideration in bioethics is research with human subjects, socio-cultural circumstances have to be considered, and then international standards have to be applied. Final judgements however have to be nuanced. Medical research using human subjects is not intrinsically evil. New knowledge can serve both the research subjects and countless others. Without such research, medicine loses its scientific base. In clinical medicine, aggressive technological interventions on dying patients sometimes can be torture. At other times, with different patients, the same interventions can be life saving. Bioethicists have to be able to simplify complex situations, gather relevant data, develop clarifying concepts and apply appropriate laws and ethical standards. Medical research and clinical treatment were always full of ambiguity.

Human beings are creative but there are limits to human creativity. There are also inevitable limits to be respected in the use of medical technology. Bioethics has to change

in order to address the challenges created by contemporary bio science but also has to preserve what bioethics started out being: a clarifying, mediating, discriminating, and a critical voice in an essentially humane medical enterprise. Bioethicists have to avoid the simple-minded solutions of ideologues and pursue the development of sound, inter-cultural, international bioethical policies. In some controversial areas they have to avoid the worst options.

In the beginning, bioethics tried to be helpful to professionals and mediation was very often its principle role. However, there were times when the clinical bioethicists had to take a stand, had to say no, and possibly even had to anger those who asked for a consult. The discipline of bioethics, at the beginning was not ideological and yet, neither was it ethically neutral. There were mainstream ethical stands dictated by considerations of facts, legal policies, and guiding ethical principles. Early on, the discipline offered broadly agreed upon answers to frequently posed questions especially about the end of life. Bioethicists provided medical and nursing students whom they taught with ethical direction supported by law, philosophy, and theology. Most early bioethicists also wrote newspaper articles defending or disputing or explaining the ethical dimensions of widely publicized legal cases.

A shift toward socio-economic issues

When the discipline which emerged out of U.S. culture spread to other parts of the world, the strong cultural influences at work in American bioethics became more evident. Once persons in Europe, Asia, and Latin America became involved in bioethics, they reacted sometimes strongly to the U.S. emphasis on individual rights and on the principle of autonomy. The new discipline, was imprinted with a U.S. cultural stamp. One of the fruits of a dialogue with bioethicists from other cultures was a move toward a broader bioethics which is still in its formative stages. Now, more than ever, bioethicists are aware of social and cultural influences on ethical reasoning.

During the early years, bioethics was dominated by clinical problems at the beginning and end of life. Those problems are still with us but now it is not the withdrawal of life supports that is being argued (for example, the Karen Ann Quinlan case) but rather the active involvement of a physician in directly taking a patient's life (the Jack Kavorkian campaign). Genetic technologies and their associated dangers now dominate the field. Increasing attention especially is also being given to professional medical ethical standards which can easily be compromised by health care delivery systems which are market dominated. Socioeconomic factors today threaten to turn doctors and nurses into obedient employees rather than independent professionals.

I first started reading *American Medical News*, years ago, to keep up with the culture of the medical profession. Then, the paper was full of stories and articles about clinical issues. Now this weekly AMA newspaper is full of articles about economics: salary concerns of doctors; pressure on doctors coming from HMO administrators; problems associated with the management of a practice; *Medicare* and *Medicaid* policies and how these affect physician working conditions; moves to approve collective bargaining units for physicians;

the increasing dominance of free market capitalism in hospitals and nursing homes. These are the problems which now seem to preoccupy the medical profession. Correspondingly bioethics and bioethicists are increasingly involved with socio-economic issues.

In the early years the principles of beneficence and autonomy were dominant, and bioethics was about balancing the two or choosing one over the other in a clinical dilemma. Now the discipline is more focused on justice and equality and about the structures of the health care delivery system. The dominant issue now is how to bring about fair access to health care. In order to do bioethics seriously when justice and equality principles and economic problems dominate, the bioethicist must know in depth the social science.

In an earlier book *(4)*, I took a strong stand in favor of limiting the issues addressed by an institutional bioethics committee to clinical care problems. Admittedly allocation problems or the socio-economic issues are every day more important. But the older ethics committees were not formed and trained to handle the allocation issues so dominant today. The same is true of most practicing bioethicists. Clinical bioethicists and health-care ethics committee members have to be familiar with clinical contexts, with contemporary medicine, with state statutes, court cases, and government regulations which address clinical matters, as well as with the concepts and theories of bioethics which were designed to handle clinical subtleties. It is unrealistic, I believe, to expect these same persons to master a very different set of ethical concepts and theories, a totally different type of fact or data, and a completely different group of social sciences. To understand the socio-economic or justice issues in sufficient depth to be able to offer realistic ethical guidance to institutions, requires a differently trained bioethicist and a different type of ethics committee.

Human beings cannot be expected to be experts in every field. One of the worse dangers bioethics and its practitioners are exposed to is superficiality, joined to an inflated sense of authority. Once I attended an international meeting and a very inexperienced member of the bioethics community spoke about ethics committee responsibility. She had the committee solving life and death dilemmas in the intensive care unit, in addition to problems of the kitchen staff and maintenance personnel. The talk was plainly ridiculous and pointed up a danger: inexperience and superficial understanding of one's limits can create "ethics experts" ready to solve any and every conceivable problem as long as it is articulated in terms like good and bad, or right or wrong. In order to avoid this pitfall, bioethicists and ethic committee members should be either trained in clinical medicine and ethics or trained in health care organization and social sciences, but not ordinarily both. Rare is the person or group of persons conversant with the complexities of clinical medicine and in addition, the background sciences, relevant data, applicable court decisions, and all the different ways in which justice and equality can be applied in particular institutional or organizational crises.

The core issues for a socio-economic committee are related to what treatments a just health care system should offer its patients, or what limits on treatment may ethically be imposed. No health care system, whether private or public, capitalistic or socialistic, can offer every therapeutic option. Human beings can never be satisfied either in their demands

for enough health or in their demands for enough defense. Military budgets and health-care budgets always have to set limits. Any company indeed any government would quickly go broke trying to satisfy every request or demand. Limits have to be set, and at some point someone has to say no. But what would constitute a basic fair minimum which everyone would have access to, and what could justifiably be denied? Medical help in a humane health care facility is an obvious good which persons want, but it is not the only good.

Other goods, like education and police protection and a judicial system and roads and welfare compete with health care for limited socio-economic resources. But how and where to set the limits without violating a rightful demand for justice and equality? These are crucial questions today but very different type ethical questions from those earlier ones having to do with the removal of technologies at the end of life. The latter remain with us and have become more complicated. New clinical technologies and treatment possibilities raise all sorts of complex new clinical problems (e.g. genetic diagnosis and therapy). There are some gifted bioethicists who have managed to develop the background understanding to address the new and the old issues with expertise, but these are rare. I worry about less talented people who presume to handle all issues without adequate background training.

Bioethicists who presume to help a health care system or a particular health care organization to decide how much to offer, and what limits to impose, are faced with a monumental task. Systems and institutions have to be economically sound or everyone looses. But how do we make decisions about whom to cover or when to treat? Who decides to deny treatment? Do we do what is most just by providing treatments which have statistically the best outcomes or do we provide treatments for those who are the most disadvantaged? How do we determine best outcomes or greatest need?

Bioethicists who focus on such questions have their hands full. They are forced into areas which traditionally were addressed with the help of economics, accounting, and political science. They are forced into areas which once were addressed in the philosophy of medicine. What is medicine? What are the limits of medicine? What are the objectives and goals of medical practice? Doctors cannot do everything their techniques and powers make possible. They cannot ethically amputate an arm to help a man get more social security benefits. But other questions about limits are more difficult and throw open tough economic issues and highly philosophical questions about medicine's reason for being. Can the first clinical bioethicists presume to know enough about social science, economics, and philosophy of medicine to offer defensible responses to socio-economic questions today? Even to devise fair procedures for deciding such questions requires a very specialized expertise.

And yet, if no qualified ethical reflection on these questions is available, then decisions will be made by administrators of health care organizations, or politicians, or stockholders. Without serious bioethical reflection on socio-economic questions, greed and self-interests will permeate and dominate health care decision-making. Patients do not have to be professionally trained economists or accountants to notice when their interests are not being taken seriously. It is already obvious to most people that large amounts of health care monies are being spent on advertisement, salaries for CEO's, and payouts to stockholders. Everyone

who has any contact with today's health care system notices new obstacles to care created by long lines and delays in access to appointments with specialists. Issues of fair access and just limits are critical and yet they demand an ethics expertise which only persons who know economics and accounting and politics and the inner workings of the medical care delivery system can provide. They require a new-type bioethicist with a different type of academic background. Making ethically acceptable socio-economic public policy is not the same as making discrete clinical decisions about individual patients at the end of life.

Both type of questions, however fall under today's broader definition of bioethics. They are ethical questions raised by the practice of medicine. They emerge in health care systems and institutions and involve both patients and health care professionals. And both types of bioethics questions can be generated by particular cases. What to do with this and that patient can be the initiating event for both types of ethical reflection. In socio-economic cases the questions would be whether the patient or the condition can be covered. Responding to cases in a consistent manner gradually creates a direction for an institutional ethics policy. Over time and with added experience, ethics policy can be modified. Setting the limits of medical care is too important an issue to be excluded from the new discipline or from today's bioethics committees.

Helping medical practitioners with clinical problems characterized the first steps of the discipline and helped to define bioethics. Since its beginning, other problems have emerged. The discipline has expanded. And yet, ethical problems associated with the treatment or non-treatment of particular patients in a clinical setting cannot be set aside. Continued effort has to be expended to refine both the norms and the procedures for deciding about clinical cases. Bioethics can become as abstract and theoretical as any other academic discipline but it started out as an applied ethics— and cannot abandon this continually important activity without loosing its soul.

Changes and continuities

The beginning concerns gave early bioethics a casuistic style. Casuistry certainly has its limitations but it also has its advantages. Bioethics has to be more and more international because modern medicine and medical technologies both are. The clinical case can be the common starting point for bioethical reflection in any or every culture. And developing humane solutions to common clinical problems can easily be imagined to coalesce into ever-more widely accepted solutions. International policies can then gradually develop from similar resolutions of common re-occurring problems.

Besides being similar, cases can also be rather easy to solve because widely accepted principles directly apply. The test either for a bioethicist or a bioethics committee is to develop functional procedures and sophisticated patterns of reflection for handling tough cases. These too can and should become international. Relevant facts have to be identified, background conditions and underlying influences have to be made explicit, misconceptions and confusions have to be clarified. Clinical bioethics requires special sensitivities for the existential or lived dimension of an ethical problem. Moving toward defensible solutions starts with a sophisticated analysis of the subtleties of a case. Bioethics started with clinical

problems and bioethicists worldwide have to continue to improve their techniques for finding defensible solutions to complex clinical cases.

As important as it is, clinical bioethics can never be the whole of the discipline. Abstract and theoretical bioethics will always have a place. What is the good, how can justice be understood, which principles prevail in conflict situations? These questions are always posed by clinical cases and should be addressed in the discipline of bioethics. Some bioethicists should be concerned about certain new technologies even before they begin to generate particular problems in the clinic.

If bioethicists specializing in justice and access issues have to understand social sciences and the structures of health care bureaucracies, the clinical bioethicist has to know medicine or nursing and understand the subtleties of the clinical context. Theoretical conceptual models ultimately are linked up with the existential particulars of a case. Procedure for the clinical bioethicist moves from the practical to the theoretical. The test of a good clinical bioethicist is to have conceptual categories adequate to reorganize the data of a complex clinical reality so as to understand it and respond to it in an ethically defensible way. The clinical bioethicist does for confused and complicated cases—what an insightful psychiatrist does for a confused and complicated patient. She figures out what is actually going on behind appearances and provides a number of possible options or explanations. He understands both the important facts and the less obvious background dimensions.

Court cases, legal statutes, government regulations, have driven bioethical developments and given to bioethics a reorganized importance. The fact that JCAHO (*Joint Common of the Accreditation of Health Care Organizations*) which accredits hospitals, nursing homes, hospices and home health care agencies in the U.S., requires a mechanism for addressing ethical problems, continues to make bioethics important in U.S. clinical settings. License requirements put pressure on the discipline to establish programs to train ethics committee members in every type of health care facility. This is true in the U.S., and similar pressures in other countries are leading in the same direction. If bioethics will continue to be an important discipline in the 21st century, the next generations of bioethicists will have to know how the discipline began and its first stages of development. Changes are inevitable and continuity is essential for survival.

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EQUITY, QUALITY, AND PATIENT RIGHTS: CAN THEY BE RECONCILED?

Daniel Callahan

Contemporary medicine and health care is a battleground of a number of ideals. The World Health Organization has declared that every human being has a right to the best available health care. That is a powerful claim for equity. At the same time, many countries are working hard to improve the quality of their health care, not only making health care available to all but aiming for a very fine level of care, as close to the technically best care as possible. There is still another ideal that has taken root: that patients have a right to determine whether and when to accept health care and the right to have that care terminated even if that might take their life.

I call each of those developments "ideals," to indicate that there is still a gap in most places between those ideals and the reality of much health care. Equity is not everywhere honored, quality is often ignored, and patient's rights frequently set aside. Nonetheless, the existence of those ideals has been a great stimulus to modern medicine and health care systems, and much progress has been made in the direction of their achievement.

Yet even as progress has been made, a serious conflict is coming into view: can those three values be made compatible with each other, or is there perhaps an inherent tension among them that will not easily be resolved. My argument is that there is such tension, which becomes visible only when the ideals have been pursued with some vigor and when each is taken with full seriousness. A lukewarm effort to respect patient autonomy, to achieve equity, and to improve quality, will not provoke a struggle between them. But a serious effort will.

It is not hard to understand why that will happen. If each of the values is taken with full seriousness, conflict is inevitable. Few if any health care system can provide everyone with the best possible quality of care; some people will receive better care than others, even in the most equaled health care systems. Hence, full equality of care for the best possible care will not be achievable (at least it has never yet happened anywhere in the world). As for the rights of patients, it is one thing to allow patients to decline various kinds of treatment, and quite another to meet all their demands for treatment, even when those demands are reasonable.

In short, once the reality of limited health care budgets is understood—and there are limits in even the most affluent countries—then it becomes clear that the ideals of health care must themselves be limited. Patients will have to settle for less than the very best care, not everyone will have full access to health care, and their right to care will have to be a restricted right. The ideals must, that is, be lived out in a less than ideal context. If that is so,

then the main question will be which of them should have a priority or, alternatively, to ask if it would be better to pursue all three in a more or less equal way even if none was achieved in a perfect way.

I want to argue that priorities need to be set. To pursue all three more or equally is likely to do more harm then good. But which of the ideals should have the highest priority? I believe it is the ideal of equal access to care that is most important. Everyone during his or her lifetime will need health care. People fear illness and death, but they also fear the economic consequences of poor health: its affect on their families, their jobs, their income, their future life prospects. The only way to relieve such worries is to guarantee that money will not be an obstacle in gaining access to a health care system.

Yet, as suggested above, no health care system can afford to give everyone, in the name of decent access, the best imaginable health care. Part of the reason is a matter of logic: not everyone can go to the best hospital, have the best transplant surgeon, or the best cardiologist—the "best" cannot accommodate everyone, even if there was a desire to try. A more important part of the reason is that the highest quality of care is ordinarily expensive care; "quality" is rarely inexpensive. But health care systems must live with limited budgets. They will have to give patients the best care they can within those budgets—but the best care within a limited budget will almost always be something less than the most ideal quality of care. Even so, I would contend, patients are better off in systems where they are guaranteed good care at an affordable price than a system with the highest quality of care that is not available to all. The great problem with the provision of health care in the United States is that some 40 million people have no health insurance at all, and many millions of others have inadequate insurance—and yet there is available in the United States some of the highest quality medicine in the world, but a medicine out of reach for too many people. A reduction in quality in order to facilitate equitable and full access to care would, for me, represent a sensible trade-off; but it has so far been impossible to persuade most Americans to accept such a bargain.

Where do patient rights fit into the setting of priorities? One point is clear enough: when there are limited resources there must be limits to patient needs and demands. But there may still be some room for choice, that of enabling patients to choose among different levels of health care. People have different values and perspectives on illness and the threat of death, and different worries about the financial implications of their health care system. In that context, it would make sense to enable people to choose among health care plans. Some people would prefer to be insured against catastrophic illness, even at the cost of losing access to treatment of less serious conditions. Others might be willing to take their chances with expensive conditions, choosing instead coverage for a broader range of conditions. Even in systems that cannot provide the very best care, choices of that kind would go a long way toward accommodating patient needs and patient differences.

My greatest concern is that many countries are drifting into a dangerous situation. In the name of constant medical progress and technological innovation, health care costs are everywhere being forced up. That pressure is greatly exacerbated by the increasing

number and proportion of elderly people and by increased public demand. The result is that a country like the United States, which does not have universal health care, is finding it harder than ever to reach that goal. Even those countries that already have it, however, are having trouble hanging on to it. Equitable access to care is threatened, patient rights are limited, and the quality of care suffers. The main villain in this trend is the technological innovation, which is in effect a quest for always better, higher quality care; and it is what people have come to expect. But when the cost of care exceeds politically plausible budgets, then inequitable access is likely to be the result—usually by means of forcing patients to pay more of their own money for care. When that happens those who are less affluent will not come anywhere near the best care, and in fact are likely to get poor care by virtue of the financial pressure they feel to curtail personal expenditures.

Is there a way out of the inevitable tensions I have described? Priority setting is not a way out. It is, instead, a meaning of choosing among the values of equity, quality, and patient rights but at the price of choosing one of the values as the most important and ranking the others lower on the scale. There is another possible solution, which would be to weaken all three values at the same time, but then keeping all three on the same plane. We would simply settle for inequitable access, lower than optimal quality, and a limitation on patient rights. But this could well turn out to be the worst of all possible solutions. And it is in fact the situation now found in the poorest countries in the world. In those countries the affluent receive better care than the poor, almost everyone receives low quality care, and (when the medicine is paternalistic, as is the case in most poor countries) patients are accorded no rights.

Another alternative would be to base access to care on population-health considerations, then to define quality in terms not of individual health but of technologies and health strategies also based on population health outcomes. Access to care based on population health considerations would, for instance, place the greatest emphasis on techniques of health promotion and disease prevention, supplementing them with various means of behavior modification techniques and disease screening modalities. The emphasis, that is, would be away from high technology medicine, most of which is curative or ameliorative in nature and oriented toward the care of individuals. A population-based strategy would work to improve population outcomes, even at the expense of some individual health. Thus not only would access to care be determined by the likelihood of improving population health but the quality of care would be no less focused on those medical means designed to help groups and not individuals. It might be of course that individuals would, in the aggregate, turn out to be better off with that kind of emphasis, but not necessarily. Moreover, those not likely to be reached by population-oriented techniques could well live in a state of anxiety that their conditions would fall outside of the scope of the health care system. The main advantage of this approach would be the controls it would bring to bear on expensive high-technology medicine. It is that kind of medicine—a main source of cost pressures in developed countries—that at present is the principal threat to an equitable medicine. It is also the preeminence of that kind of medicine, aiming always at improved quality, which in effect makes quality the dominant note and patient choice a dominant value—but both of them at the expense of equitable access.

That last reflection suggests, however, another possible escape route. Researchers and equipment makers could in the future work much harder to develop technologies that would be less expensive and more amenable to wide, equitable distribution. At present, medical research proceeds without much consideration of the costs of the drugs and other products developed. They are simply created and then thrown casually into health care systems with no rational distribution plan, much less one oriented toward equitable access. Or perhaps it would be more accurate to say that the products are thrown casually but ordinarily with a major advertising and promotion campaign to make sure they are sold. It is then left to health care administrators, hospital directors, insurance companies, and governments to figure out how to pay for them. Whether it would be possible to orient research toward affordable outcomes is, however, uncertain. For one thing, most research is in the hands of the private sector, and there is little incentive there for the development of inexpensive products. For another, it is difficult in the early stages of research to know what the outcome will be, whether expensive or inexpensive. Even so, with the exception perhaps of vaccine development, very little thought seems to have been given to the development of low-cost drugs and other technologies. That could be changed.

Does not evidence-based medicine offer a way out of the tensions I have outlined? If it were possible to make use only of efficacious diagnostic procedures and therapies, would not that lead to a higher quality of medicine, and perhaps a more affordable medicine? Indeed it might, but not necessarily. What is often forgotten is that evidence-based medicine can lead to a determination that some technologies are effective, but effective and costly. It is by no means the case, that is, that evidence-based medicine will simply eliminate everything expensive that does not work. It can just as well legitimate that which does work and works well. The very worst dilemma for health care systems are those technologies, or other treatment methods, that are both effective and yet unaffordable. Then rationing of the most harsh kind is needed. That is the situation in sub-Saharan Africa where effective drug combinations to treat those with AIDS is simply not available; and, even if the price were significantly lower, would still not be available.

What I have tried to show in this essay is that it is exceedingly difficult to devise a health care plan that would provide the highest quality medicine, maximize patient rights, and at the same time be equitably accessible. We have, in other words, a set of values in the developed world that will not admit any perfect reconciliation, and may in some cases force the setting of priorities or the imposition of unpleasant rationing plans. Yet while this may seem to be an inherently frustrating situation, I believe it need not to be seen in an entirely dark light. As a matter of fact health status is improving throughout the world. Hardly anyone has perfectly equitable access or the highest quality of medicine. Even so, health continues to improve, as much from changes in socioeconomic conditions as from changes in the provision of health care. We may not, in other words, need the highest quality of medicine to improve health, or a full panoply of patient rights, or even equitable access. If educational standards continue to rise, if jobs are available, if basic health promotion strategies are in place, then people will over time become healthier. That is the good news, and news not dependent upon the existence of perfect health care systems.

WHY JUSTICE IS GOOD FOR OUR HEALTH[1]

Norman Daniels

Justice and health inequalities

We have known for over 150 years that an individual's chances of life and death are patterned according to social class: the more affluent and better educated people are, the longer and healthier their lives.[2] These patterns persist even when there is universal access to health care—a fact quite surprising to those who think financial access to medical services is the primary determinant of health status. In fact, recent evidence suggests that the greater the degree of socioeconomic inequality that exists within a society, the steeper the *gradient* of health inequality. As a result, middle income groups in a more unequal society will have worse health than comparable or even poorer groups in a society with greater equality. Of course, we cannot infer *causation* from *correlation*, but there are plausible hypotheses about pathways which link social inequalities to health, and, even if more work remains to be done to clarify the exact mechanisms, it is not unreasonable to talk here about the social "determinants" of health *(1)*.

We must answer a basic question of distributive justice: When is an inequality in health status between different socioeconomic groups unjust?[3]

An account of justice should help us determine which inequalities are unjust and which acceptable. Many who are untroubled by some kinds of inequality are particularly troubled by health inequalities. They believe that a socioeconomic inequality that otherwise seems just becomes unjust if it contributes to health inequalities. Is every health inequality that results from unequally distributed social goods unjust? If there is an irreducible health gradient across socioeconomic groups, does that make the very existence of those inequalities unjust?

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[1] This manuscript is excerpted and revised from a longer paper by the same title that appeared in *Daedalus* 1999;128(4):215-52. I have largely omitted the sections my co-authors were most directly responsible for, which addressed the empirical basis and the policy implications of the findings on the social determinants of health, concentrating here on the philosophical material in that paper.

[2] Villerme LR. *Tableau de l'État Physique et Moral des Ouvriers*, vol. 2 Paris: Renourard; 1840. Cited in Link BG, Northridge ME, Phelan JC, Ganz ML. Social epidemiology and the fundamental cause concept: on the structuring of effective cancer screens by socioeconomic status. *Milbank Quarterly* 1998;76(3):375-402. Throughout, we view disease and disability as departures from (species typical) normal functioning, and we view health and normal functioning as equivalent.

[3] To avoid additional complexity, we concentrate in this paper on class or socioeconomic inequalities, though many of our points generalize to race and gender inequalities in health as well.

Alternatively, are some health inequalities the result of acceptable tradeoffs? Perhaps they are simply an unfortunate byproduct of inequalities that work in other ways to help worse-off groups. For example, it is often claimed that permitting inequality provides incentives to work harder, thereby stimulating growth that will ultimately benefit the poorest groups. To whom must these tradeoffs be acceptable if we are to consider them just? Are they acceptable only if they are part of a strategy aimed at moving the situation toward a more just arrangement? Does it matter in our judgments about justice exactly how social determinants produce inequalities in health status?

These are hard questions. Unfortunately, they have been almost totally ignored within the field of bioethics, as well as within ethics and political philosophy more generally. Bioethics has been quick to focus on exotic new medical technologies and how they might affect our lives. It has paid considerable attention to the doctor-patient relationship and how changes in the health care system affect it. With some significant exceptions, it has not looked "upstream" from the point of delivery of medical services to the role of the health care system in delivering improved population health. It has even more rarely looked further upstream to social arrangements that determine the health achievement of societies *(2-4)*.

This omission is quite striking, since a concern about "health equity" and its social determinants has emerged as an important consideration in the policies of several European countries over the last two decades *(3)*. The World Health Organization (WHO) has devoted growing attention to inequalities in health status and the policies that cause or mitigate them. So have research initiatives, such as the Global Health Equity Initiative, funded by the Swedish International Development Agency and the Rockefeller Foundation.

The failure of bioethics to the look at the social determinants of population health is not primarily a philosophical failing, nor is it simply disciplinary blindness to the social science or public health literature. Rather, for complex sociological, political and ideological reasons that we can only mention here, people in bioethics, like the public more generally, concentrate on medical care rather than on intersectoral public health and the social determinants of health. Encouraged by scientists and the media, the public is fascinated by every new biomedical discovery -perhaps it is a Promethean urge- and have come to believe that most of our "success" in improving population health is the result of exotic science. Vast economic interests benefit from this focus of the public and of bioethics. The economic incentives to people in bioethics come largely from medicine and the scientific and policy institutions that interact with medical delivery.

The idea that scientific medicine is responsible for our health blinds us to socioeconomic inequality as a source of worse population health. Science, we are told, can rescue us all from our shared biological fate, and so we should all unite in supporting a focus on medicine, and, if we care about justice, on the equitable access of all to its benefits. Challenging deeper inequalities in society, however, is divisive, not unifying, and it threatens those with the greatest power and the most to lose. In the absence of well-organized social movements that are capable of challenging that inequality, the complaints of public health

advocates pointing the need for more basic changes, rather than simply joining existing forces asking for more and better medical care, can seem utopian.

In what follows, I shall attempt to fill this bioethical gap by addressing some of these questions about justice and health inequalities. Because of space limitations, I shall omit a review of the empirical literature contained in longer versions of this paper, though I shall briefly sketch several empirical findings presupposed by what follows. After looking briefly at some earlier, intuitive efforts to answer the question, "When are health inequalities inequities?" I shall briefly sketch two promising approaches to answering it that supply some guidance from ethical theory. Sen's work on positive freedom has attracted considerable attention, but it leaves many systematic questions about justice unaddressed. More promising, in my view, is a Rawlsian approach that I shall develop, though I emphasize from the beginning that my view of Rawls makes his account converge considerably with Sen's.

My contention is that, quite unintentionally, Rawls's theory provides a defensible account of how to distribute the social determinants of health fairly. If I am right, this unexpected application to a novel problem demonstrates a fruitful generalizability of the theory, analogous to the extension in scope or power of a non-moral theory, and permits us to think more systematically across the disciplines of public health, medicine, social science, and political philosophy.

Though serendipitous, this surprising result is not just serendipity. Justice as fairness was formulated to specify terms of social cooperation that free and equal citizens can accept as fair. Specifically, it assures people of equal basic liberties, including the value of political participation, guarantees a robust form of equal opportunity, and imposes significant constraints on inequalities. Together, these principles aim at meeting the "needs of free and equal citizens," a form of egalitarianism Rawls calls "democratic equality." *(5)*[4] . A crucial component of democratic equality is providing all with the social bases of self respect and a conviction that prospects in life are fair. As the empirical literature demonstrates, institutions conforming to these principles together focus on several crucial pathways through which many researchers believe inequality works to produce health inequality. Of course, this theory does not answer all of our questions about justice and health inequality, since there are some crucial points on which it is silent, but it does provide considerable guidance on central issues.

Social determinants of health: some basic findings

The argument that follows builds on four central findings in the literature on the social determinants of health. I briefly summarize them here and refer the reader to the longer paper for citations providing the basis for this summary. First, the SES/health gradients we observe are not the result of some fixed or determinate laws of economic development but are influenced by policy choices. Cross national studies show a relationship between

[4] Daniels N. Democratic Equality: Rawls' Complex Egalitarianism. In: Freeman S, (ed.). Companion to Rawls. Blackwells (in press).

per capita GDP and mortality that disappears after a modest level of $6 – 8 000, and even among poorer countries, as well as among wealthier ones, there is great variation in population health outcomes depending on other public policies.

Second, the income/health gradients are not just the result of the deprivation of the poorest groups. Rather, a gradient in health operates across the whole socioeconomic spectrum within societies, such that the slope or steepness of the income/health gradient is affected by the degree of inequality in a society. Third, relative income or socioeconomic status is as important as, and may be more important than, the absolute level of income in determining health status, at least once societies have passed a certain threshold. Though initial support for this relative income thesis was based on cross national studies among some OECD countries, this support has recently been challenged. The income relativity thesis derives other support, however, from studies within the U.S. of state variations in inequality and the correlations of those inequalities with both health outcomes and possible pathways -such as political participation, social cohesion, investment in human capital. Fourth, there are identifiable social and psychosocial pathways through which inequality produces its effects on health (and little support for "health selection," the claim that health status determines economic position). (1,p.6-7)*(6)* These causal pathways are amenable to specific policy choices that should be guided by considerations of justice.

How can these five theses we have highlighted from scientific literature on social determinants be integrated into our views about the moral acceptability of health inequalities? Historically, disciplinary boundaries have stood as an obstacle to an integrated perspective. The social science and public health literature sharpens our understanding of the causes of health inequalities, but it contains no systematic way to evaluate the overall fairness of those inequalities and the socioeconomic inequalities that produce them. The philosophical literature has produced theories aimed at evaluating socioeconomic inequalities, but it has tended to ignore health inequalities and their causes. To produce an integrated view, we shall need the resources of a more general theory of justice. We can better see the need for such a theory if we first examine an analysis of "health inequities" that has been developed within a policy-based public health literature.

Health inequalities and inequities

When is a health inequality between two groups "inequitable"?

This version of our earlier question about health inequalities and justice has been the focus of European and WHO efforts, as noted above. One initially useful answer to it that has been influential in the WHO programs is the *intuitive* claim that health inequalities count as inequities when they are *avoidable*, *unnecessary*, and *unfair (2,7,8)*. If we can agree on what is avoidable, unnecessary, and unfair, and this analysis is correct, then we can agree on which inequalities are inequitable.

The Whitehead/Dahlgren analysis is deliberately broader than our central question about differences in socioeconomic status. Age, gender, race and ethnic differences in health

status exist that are independent of socioeconomic differences, and they raise distinct questions about equity or justice. For example, should we view the lower life expectancy of men compared to women in developed countries as an inequity? If it is rooted in biological differences that we do not know how to overcome, then, according to this analysis, it is not avoidable and therefore not an inequity. This is not an idle controversy: taking average, rather than gender-differentiated life expectancy in developed countries as a benchmark or goal will yield different estimates of the degree of inequity women face in some developing countries. In any case, the analysis of inequity is here only as good as our understanding of what is avoidable or unnecessary.

The same point applies to judgments about fairness. Is the poorer health status of some social class or ethnic groups that engage in heavy and alcohol use unfair? We may be inclined to say it is not unfair provided that participation in the risky behaviors or their avoidance is truly voluntary. But if many people in a cultural group or class behave similarly, there may also be factors at work that reduce how voluntary their behavior is and how much responsibility we should ascribe to them for it *(9,10)*. The analysis thus leaves us with the unresolved complexity of these judgments about responsibility, and, as a result, with disagreements about fairness (or avoidability).

The poor in many countries lack access to clean water, sanitation, adequate shelter, basic education, vaccinations, prenatal and maternal care. As a result of some or all of these factors, there are infant mortality differences between them and richer groups. Since social policies could supply the missing determinants of infant health, then the inequalities are avoidable.

Are these inequalities also unfair? Most of us would immediately think they are, perhaps because we believe that policies that create and sustain poverty are unjust, and we also believe that social policies that compound poverty with lack of access to the determinants of health are doubly unfair. Of course, libertarians would disagree. They would insist that what is merely unfortunate is not unfair; on their view, we have no obligation of justice, as opposed to charity, to provide the poor with what they are missing. Many of us might be inclined to reject the libertarian view as itself unjust because of this dramatic conflict with our beliefs about poverty and our social obligations to meet people's basic needs.

The problem becomes more complicated, however, when we remember one of the basic findings from the literature on social determinants: we cannot eliminate health inequalities simply by eliminating poverty. Health inequalities persist even in societies that provide the poor with access to all of the determinants of health noted above, and they persist as a gradient of health throughout the social hierarchy, not just between the very poorest groups and those above them.

At this point, many of us would have to reexamine what we believe about the justice of the remaining socioeconomic inequalities. Unless we believe that *all* socioeconomic inequalities (or at least all inequalities we did not choose) are unjust — and very few embrace such a radical egalitarian view — then we must consider more carefully the problem created

by the health gradient and the fact that it is made steeper under more unequal social arrangements. Our judgements about fairness, to which we, rightly or wrongly, felt confident in appealing when rejecting the libertarian position, give us less guidance in thinking about the broader issue of the social determinants of health inequalities. Indeed, we may even believe that some degree of socioeconomic inequality is unavoidable or even necessary, and therefore not unjust.

Justice, positive freedom, and capabilities

The philosopher and economist who has written most influentially about the theory underlying our concerns about health distribution internationally is Amartya Sen. In a series of works dating back to 1980, and culminating in his recent *Development as Freedom* (1999), Sen has argued that the concerns about equality must be focused on a particular space or target, namely the distribution of capabilities. Capabilities to do or to be something, he argues, are another way to describe what other philosophers have called "positive freedom," not simply a freedom from the interference of others, but the effective power to do or be what we aim for. In *Development as Freedom*, Sen provides clear support for the first of the empirical theses summarized earlier, criticizing development policies that abandon support for the equitable distribution of capabilities in the pursuit of unconstrained growth. He also argues that political liberties and investment in human capital through education and other measures enhances positive freedom. It is not surprising, then, that Sen's work has deservingly become the focus of much admiration among those who are concerned about population health and the distribution of health outcomes, especially in developing countries.

Seminal and inspiring as Sen's work is, it does not provide a systematic structure that allows us to answer the kinds of questions left unanswered by the intuitive approach described in the last section. When, for example, should we accept inequalities in health—and therefore in the distribution of capabilities—that result from unequal distributions of the socially controllable factors that determine population health? If our goal is more equality in positive freedom, then we must strive for more equality in health, but when have we reached a point where more equality in health comes at a cost—in other fundamental goods—that we find unacceptable, even from the point of view of justice?

One proposal about how to narrow or refine the focus of Sen's perspective considers those capabilities necessary for the functioning of free and equal citizens *(11)*. I agree that focused in this way, there is considerable promise to Sen's approach, but I choose an indirect way of establishing that point, namely by turning to the Rawls's theory of justice as fairness and arguing for the claim that this view, which provides principles protecting the capabilities of free and equal citizens, converges with Sen's approach (though Sen continues to demur on this point).

Justice as fairness and health Inequalities

One reason we develop general ethical theories, including theories of justice, is to provide a framework within which to resolve important disputes about conflicting moral

beliefs or intuitions of the sort we have just raised. For example, in *A Theory of Justice*, Rawls sought to leverage our relatively broad liberal agreement on principles guaranteeing certain equal basic liberties into an agreement on a principle limiting socioeconomic inequalities, a matter on which liberals have considerable disagreement *(12)*. His strategy was to show that a social contract that was designed to be fair to free and equal people ("justice as [procedural] fairness") would not only justify the choice of those equal basic liberties but would also justify the choice of principles guaranteeing equal opportunity and limiting inequalities to those that work to make the worst off groups fare as well as possible.

My contention is that Rawls account, though developed to answer this general question about social justice, turns out to provide principles for the just distribution of the social determinants of health, unexpectedly adding to its scope and power as a theory. The extra power of the theory is a surprise, since Rawls deliberately avoided talking about disease or health in his original account. To simplify the construction of his theory, Rawls assumed his contractors would be fully functional over a normal life span, i.e., no one becomes ill or dies prematurely.

This idealization itself provides a clue about how to extend this theory to the real world of illness and premature death. The goal of public health and medicine is to keep people as close as possible to the idealization of normal functioning, under reasonable resource constraints. (Resources are necessarily limited since maintaining health cannot be our only social good or goal.) Since maintaining normal functioning makes a limited but significant contribution to protecting the range of opportunities open to individuals, it is plausible to see the principle guaranteeing fair equality of opportunity as the appropriate principle to govern the distribution of health care, broadly construed to include primary and secondary preventive health as well as medical services *(13,14)*. This way of extending Rawls theory also suggests that health status should be incorporated through its effects on opportunity into the index of primary goods, which is used to evaluate the well-being of contractors and citizens. (We return to this point shortly.)

What is particularly appealing about examining the social determinants of health inequalities from the perspective of Rawls theory is that the theory is at once egalitarian in orientation and yet justifies certain inequalities that might contribute to health inequalities. In addition, my earlier extension of Rawls links the protection of health to the protection of equality of opportunity, again setting up the potential for internal conflict. To see whether this combination of features simply leads to contradictions in the theory or to insight into the problem, we must examine the issue in more detail.

How does Rawls justify socioeconomic inequalities? Why wouldn't free and equal contractors simply insist on strictly egalitarian distributions of all social goods, just as they insist on equal basic liberties and equal opportunity?

Rawls answer is that it is irrational for contractors to insist on equality if doing so would make them worse off. Specifically, he argues that contractors would choose his

Difference Principle, which permits inequalities provided that they work to make the worst off groups in society as well off as possible *(6,12,15)*.[5] The argument for the Difference Principle appears to suggest that relative inequality is less important than absolute well-being, a suggestion that is in tension with other aspects of Rawls view. Thus he also insists that inequalities allowed by the Difference Principle should not undermine the value of political liberty and the requirements of fair equality of opportunity. The priority given these other principles over the Difference Principle thus limits the inference that Rawls has no concern about relative inequality. Specifically, as we shall see, these principles work together to constrain inequality and to preserve the social bases of self-respect for all.

Two points will help avoid misunderstanding of the Difference Principle and its justification. First, it is not a mere "trickle-down" principle, but one that requires maximal flow in the direction of helping the worst off groups. The worst off, and then the next worst off, and so on (Rawls calls this "chain connectedness") *(5, p.81ff)* must be made as well off as possible, not merely just somewhat better off, as a trickle-down principle implies. The Difference Principle is thus much more demanding than a principle that would permit any degree of inequality provided there was some "trickle" of benefits to the worst off. Indeed, it is more egalitarian than alternative principles that merely assure the worse off a "decent" or "adequate" minimum. Part of the rationale for the more demanding principle is that it would produce less strain of commitment, less sense of being unfairly left out, at least for those who are worst off, than principles that allow more inequality *(12)*. Indeed, from what we have learned about the social determinants of health, the more demanding Difference Principle would also produce less health inequality than any proposed alternative principles that allow inequalities. By flattening the health gradient, it also benefits middle income groups and not simply the poorest. In this regard, its benefits are important beyond the level where we have helped the worst off to achieve "sufficiency." This point provides a reply to those who suggest that the Difference Principle has no appeal once the worst off are sufficiently provided for *(16,p.XXX)*.

Second, when contractors evaluate how well off the principles they choose will make them, they are to judge their well-being by an index of "primary social goods." *(5, p.62)(14,ch.5)*. The primary social goods, which Rawls thinks of as the "needs of citizens," include liberty, powers, opportunities, income and wealth, and the social bases of self-respect. (These objective measures of well-being should be contrasted with measures of happiness or desire satisfaction that are familiar from utilitarian and welfare economic perspectives.) In his exposition of the Difference Principle, Rawls illustrates how it will work by asking us to consider only the simpler case of income inequalities. In doing so, he assumes that the level of income will correlate with the level of other social goods on the index.

[5] A careful discussion of Rawls argument for the Difference Principle and the extensive critical literature it has generated is beyond the scope of this paper. It is important, however, to distinguish Rawls own social contract argument from the many informal and intuitive reformulations of it. See 6,12,15, and Barry B. *Theories of Justice.* London: Harvester Wheatsheaf; 1989:213-34.

This simplification should not mislead us, for, in crucial cases, the correlation may not be obtained. For example, let us suppose that having "democratic" control over one's workplace is crucial to self-realization and the promotion of self-esteem.[6] Suppose further that hierarchical workplaces are more efficient than democratic ones, so that a system with hierarchical workplaces would have resources to redistribute that meant higher incomes for worst off workers than democratic workplaces would permit. Then the Difference Principle does not clearly tell us whether the hierarchical workplace contains allowable inequalities since the worst off are better off in some ways but worse off in others. Without knowing the weighting of items in the index, we cannot use it to say clearly what inequalities are permitted. When we are evaluating which income inequalities are allowable, by asking which ones work to make the worst off groups as well off as possible, we must, in any case, judge how well off groups are by reference to the *whole* index of primary goods and not simply the resulting income.

This point is of particular importance in the current discussion. Daniels extension of Rawls treats health status as a determinant of the opportunity range open to individuals. Since opportunity is included in the index, the effects of health inequalities are thereby included in the index.

Unfortunately, Rawls says very little about how items in the index are to be weighted. This is one of the crucial points on which the theory says less than we might have wished. Therefore we have little guidance about how these primary goods are to be traded off against each other in its construction. This silence pertains not only to the use of the index in the contract situation, but also to its use by a legislature trying to apply the principles of justice in a context where many specific features of a society are known. We return to this point shortly.

We can now say more directly why justice, as described by Rawls principles, is good for our health.

To understand this claim, let us start with the ideal case, a society governed by Rawls principles of justice that seeks to achieve "democratic equality.". Consider what it requires with regard to the distribution of the social determinants of health. In such a society, all are guaranteed equal basic liberties, including the liberty of political participation. In addition, there are institutional safeguards aimed at assuring all, richer and poorer alike, the worth or value of political participation rights. Without such assurance, basic capabilities of citizens cannot develop. The recognition that all citizens have these capabilities protected is critical to preserving self-esteem, on Rawls view. In requiring institutional support for political participation rights, Rawls rejects the claim that freedom of speech of the rich is unfairly restricted by limiting their personal expenditures on their own campaigns, a limitation the Supreme Court ruled unconstitutional in Buckley vs Valeo *(14)*. After all, the limitation does not unduly burden the rich compared to others. Since there is evidence that

[6] Cohen J. The Pareto Argument. (unpublished ms).

political participation is itself a social determinant of health (see above), the Rawlsian ideal assures institutional protections that counter the usual effects of socioeconomic inequalities on participation and thus on health.

The Rawlsian ideal of democratic equality also involves conformity with a principle guaranteeing fair equality of opportunity. Not only are discriminatory barriers prohibited by the principle, but it requires robust measures aimed at mitigating the effects of socioeconomic inequalities and other social contingencies on opportunity. In addition to equitable public education, such measures would include the provision of developmentally appropriate day care and early childhood interventions intended to promote the development of capabilities independently of the advantages of family background. Such measures match or go beyond the best models of such interventions we see in European efforts at day care and early childhood education. We also note that the strategic importance of education for protecting equal opportunity has implications for all levels of education, including access to graduate and professional education.

The equal opportunity principle also requires extensive public health, medical and social support services aimed at promoting normal functioning for all *(13)(17, p.41-44)*. It even provides a rationale for the social costs of reasonable accommodation to incurable disabilities, as required by the Americans with Disabilities Act. *(18)* Because the principle aims at promoting normal functioning for *all* as a way of protecting opportunity for all, it at once aims at improving population health and the reduction of health inequalities. Obviously, this focus requires of provision of universal access to comprehensive health care, including public health, primary health care, and medical and social support services.

To act justly in health policy, we must have knowledge about the causal pathways through which socioeconomic (and other) inequalities work to produce differential health outcomes. Suppose we learn, for example, that structural and organizational features of the workplace that induce stress and a loss of control tend to promote health inequalities. We should then view modifying those features of work place organization in order to mitigate their negative effects on health as a public health requirement of the equal opportunity approach; it is thus on a par with the requirement that we reduce exposures to toxins in the work place *(13)*.

Finally, in the ideal Rawlsian society, the Difference Principle places significant restrictions on allowable inequalities in income and wealth.[7] The inequalities allowed by this principle (in conjunction with the principles assuring equal opportunity and the value of political participation) are probably more constrained than those we observe in even the most industrialized societies. If so, then the inequalities that conform to the Difference Principle would produce a flatter gradient of health inequality than we currently observe in even the more extensive welfare systems of Northern Europe.

[7] G.A. Cohen has argued that a *strict* interpretation of the Difference Principle would allow few incentive-based inequalities; for a more permissive view, see 6.

In short, Rawls principles of justice regulate the distribution of the key social determinants of health, including the social bases of self respect. There is nothing about the theory, or Daniels extension of it, that should make us focus narrowly on medical services. Properly understood, justice as fairness tells us what justice requires in the distribution of all socially controllable determinants of health.

We still face a theoretical issue of some interest. Even if the Rawlsian distribution of the determinants of health flattens health gradients further than what we observe in the most egalitarian, developed countries, we must still expect a residue of health inequalities. In part, this may happen because we may not have adequate knowledge of all the relevant causal pathways or interventions that are effective in modifying them. The theoretical issue is whether the theory requires us to reduce *further* those otherwise justifiable inequalities because of the inequalities in health status they create.

We should not further reduce those socioeconomic inequalities if doing so reduces productivity to the extent that we can no longer support the institutional measures we already employ to promote health and reduce health inequalities. Our commitment to reducing health inequality should not require steps that threaten to make health worse off for those with less-than-equal health status. So the theoretical issue reduces to this: would it ever be reasonable and rational for contractors to accept a tradeoff in which some health inequality is allowed in order to produce some non-health benefits for those with the worst health prospects?

We know that in real life people routinely trade health risks for other benefits. They do so when they commute longer distances for a better job, or take a ski vacation. Some such trades raise questions of fairness. For example, when is hazard pay a benefit workers gain only because their opportunities are unfairly restricted, and when is it an appropriate exercise of their autonomy? *(13)* Many such trades are ones we think it unjustifiably paternalistic to restrict; others we see as unfair.

Rawlsian contractors, however, cannot make such trades on the basis of any specific knowledge of their own values. They cannot decide that their enjoyment of skiing makes it worth the risks to their knees or necks. To make the contract fair to all participants, and to achieve impartiality, Rawls imposes a thick "veil of ignorance" that blinds them to all knowledge about themselves, including their specific views of the good life. Instead, they must judge their well being by reference to an index of primary social goods (noted earlier) that includes a weighted measure of rights, opportunities, powers, income and wealth, and the social bases of self respect. When Kenneth Arrow *(19)* first reviewed Rawls theory, he argued that this index was inadequate because it failed to tell us how to compare the ill rich with the well poor; Sen *(20,21)* argues that the index is insensitive to the way in which disease, disability, or other individual variations would create inequalities in the capabilities of people who had the same primary social goods. By extending Rawls theory to include health care through the equal opportunity account, some of Arrow's (and Sen's) criticism is undercut *(22)*.But our theoretical question about residual health inequalities reminds us that the theory says too little about the construction of the index to provide us with a clear answer to it.

One of Rawls central arguments for singling out a principle protecting equal basic liberties and giving it (lexical) priority over his other principles of justice is his claim that once people achieve some threshold level of material well being, they would not trade away the fundamental importance of liberty for other goods *(5)*. Making such a trade might deny them the liberty to pursue their most cherished ideals, including their religious beliefs, whatever they turn out to be. Can we make the same argument about trading health for other goods.

There is some plausibility to the claim that rational people should refrain from similar trades of health for other goods. Loss of health may preclude us from pursuing what we most value in life. We do, after all, see people willing to trade almost anything to regain health once they lose it.

If we take this argument seriously, we might conclude that Rawls should give opportunity, including the effects of health status, a heavier weighting in the construction of the index than income alone.[8] Such a weighting would mean that absolute increases in income for that might otherwise have justified increasing relative income inequality, according to the Difference Principle, now fail to justify those inequalities because of the negative effects on opportunity. Although income of the worst off would increase, they are not better off according to the whole (weighted) index of primary social goods, and so the greater inequality is not permitted. Rawls simplifying assumption about income correlating with other goods fails in this case (as it did in the hypothetical example about workplace democracy cited earlier).

Nevertheless, there is also strong reason to think the priority given to health and thus opportunity is not as clear-cut as the previous argument implies, especially where the trade is between a *risk* to health and other goods that people highly value. Refusing to allow any (ex ante) trades of health risks for other goods, even when the background conditions on choice are otherwise fair, may seem unjustifiably paternalistic, perhaps in a way that refusals to allow trades of basic liberties is not.

I propose a pragmatic route around this problem, one that has a precedent elsewhere in Rawls. Fair equality opportunity, Rawls admits, is only approximated even in an ideally just system, because we can only mitigate, not eliminate, the effects of family and other social contingencies *(23)*. For example, only if we were willing to violate widely respected parental liberties could we intrude into family life and "rescue" children from parental values that arguably interfere with equal opportunity. Similarly, though we give a general priority to equal opportunity over the Difference Principle, we cannot achieve complete equality in health any more than we can achieve completely equal opportunity. Even ideal theory does not produce perfect justice. Justice is always rough around the edges. Specifically, if we had good reason to think that "democratic equality" had flattened inequalities in accord with the principles of justice, then we might be inclined to think we had done as

[8] Rawls does suggest that, since fair equality of opportunity is given priority over the Difference Principle, that within the index, we can assume opportunity has a heavier weighting. See (5, p.93)

much as was reasonable to make health inequalities fair to all. The residual inequalities that emerge with conformance to the principles are not a "compromise" with what justice ideally requires; they are acceptable as just.

So far, we have been considering whether the theoretical question can be resolved from the perspective of individual contractors. Instead, suppose that the decision about such a tradeoff is to be made through the legislature in a society that conforms to Rawls principles. Because those principles require effective political participation across all socioeconomic groups, we can suppose that groups most directly affected by any tradeoff decision have a voice in the decision. Since there is a residual health *gradient*, groups affected by the tradeoff include not only the worst off, but those in the middle as well. A democratic process that involved deliberation about the tradeoff and its effects might be the best we could do to provide a resolution of the unanswered theoretical question *(24)*.

In contrast, where the fair value of political participation is not adequately assured -and we doubt it is so assured in even our most democratic societies- we have much less confidence in the fairness of a democratic decision about how to trade health against other goods. It is much more likely under actual conditions that those who benefit most from the inequalities, i.e., those who are better off, also wield disproportionate political power and will influence decisions about tradeoffs to serve their interests. It may still be that the use of a democratic process in non-ideal conditions is the fairest resolution we can practically achieve, but it still falls well short of what an ideally just democratic process involves.

I have focused on Rawlsian theory because it provides, however fortuitously, a developed account of how to distribute the social determinants of health. Some other competing theories of justice, including some recent proposals about "equal opportunity for welfare or advantage" *(10,25,26)* offer no similarly developed framework for distributing the key social determinants of health. On the other hand, Sen's *(21)* account of the importance of an egalitarian distribution of "capabilities," like Nussbaum's, which derives in part from it *(27)*, actually resembles the Rawls/Daniels account of equal opportunity and normal functioning more than it seems at first *(22,28)*. Anderson has imaginatively focused the discussion of capabilities on those needed if citizens are to have "democratic equality." The result is a striking convergence with Rawls's view of democratic equality, though Rawls ability to talk about the fair distribution of social determinants of health follows directly from his principles, whereas Anderson must appeal intuitively to an account of the capabilities needed by citizens.

A bioethics research agenda

The theme of this meeting is the relationship between the social sciences and bioethics. I have argued that work on the ethics of population health and its distribution must integrate the basic findings of the social sciences on the determinants of health. If population health and its distribution is the result of many, intersectoral goods and their distribution, then, for example, we must modify rudimentary appeals to a "right to health

care" so that we understand this to include a right to the proper distribution of the socially controllable factors that affect population health and its distribution. Bioethics must draw on political philosophy and the social sciences if it is to clarify even the most basic beliefs people have about the importance of health and their rights with regard to health.

At the risk of being overly succinct and even cryptic, I pose several questions that I think bioethicists must address. Addressing them will require that they broaden their understanding both of social science methods and results and the tools of the trade in political philosophy.

1. How can we resolve conflicting claims on resources between the medical sector and other sectors that impact health and its distribution? My view is that population health and medical care are not an either/or problem. However much social scientists teach us about the importance of intersectoral public health and the social determinants of health, some people will become ill and need medical care. Resources spent on many forms of medical care may do less for population health and its fair distribution than other allocations we might pursue, yet there are good moral reasons for giving some priority to meeting the needs of those who are ill. Some of the importance of medical care may be explained by our agent-relative concerns for those we are connected to who are ill. Here the resource allocation issue connects to deep questions in ethical theory, and policy debates about identified *vs* statistical victims may not be properly addressed without digging more deeply both into the social sciences, including the bases of our psychological attachments, and into recent work in ethical theory. What tools can bioethicists develop for addressing this sort of resource allocation problem, and how will its solution vary depending on a country's wealth and level of development?

2. What are the causal pathways through which social determinants of health act, and how does understanding them bear on the ethical issues raised by policy debates within medicine and between medicine and public health? Some empirical evidence from U.S. studies suggests correlations between inequality in political participation and the distribution of health. Does this mean that bioethicists must become familiar with debates about campaign financing and freedom of expression, as well as with social science findings about obstacles to political participation? Arguably, bioethicists concerned about health disparities may be wrong to focus all their attention on health sector issues, especially if they do so because that is what they know about the most.

3. How can bioethicists infuse a more informed concern about health disparities into their thinking about a broad range of issues, including those in the medical sector and in medical research?

4. How can bioethics in more developed countries draw on both social science literature about population health and its distribution in developing countries and on the growing body of work on global justice to inform bioethics contribution to discussions of international justice regarding health? The specific areas that have already attracted

considerable attention involve international research and pharmaceutical policy, but the range of topics is much broader and should be expanded to include the impact of globalization through trade and other policies on population health and its distribution, the erosion of public health systems in many countries as a result of privatization and other structural reforms, and the relationship between development policy and health outcomes.

I hope our discussion can help refine the elements in this research agenda, for articulating it more carefully would be a service to PAHO and WHO more generally.

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PHARMACOGEN-ETHICS

Diego Gracia G.

Introduction

The goal of Pharmacogenetics is the use of the new genetic knowledge and techniques in order to improve the efficacy, security, efficiency and effectiveness of human drugs. During the last decades, the way followed by it was the identification of single gene codifyers of proteins with high therapeutic value, like insulin, growth hormone, and others. Today a new door has been opened with the project of identification of the single nucleotides polymorphysms (SNPs) in human genome, and the following analysis of the relationship between these polimorphisms and some phenotypical characters, as for instance the specific response to certain drugs *(1-3)*. This is the field in which a new branch of Pharmacogenetics—known as "Pharmacogenomics" *(4,5)* -is working now. Its aim is the search of the complete "specificity" of drugs, identifying the specific drug for the specific patient, looking for "the personalization of Medicine *(6)*."

The tools used by both disciplines are different. Pharmacogenetics has generally worked with genetically manipulated micro-organisms in order to introduce in them human gene codifiers of some proteins of high therapeutic value. Therefore, these genetic manipulations have been made on micro-organisms and not on human beings, something that reduces drastically their moral implications. Pharmacogenomics, on the other hand, does not intend the manipulation of human genes, but only the knowledge of their structure and polymorphisms, in order to improve the quality and specificity of the drugs used with human patients. If in the future we would be capable of knowing the specific protein which should be useful with a specific patient, we will be able— for the first time— to avoid the mayor part of drug side effects, and also of saving a high amount of money, wasted nowadays in unsafe and inefficient treatments.

In this paper I will use the word Pharmacogenetics as the proper name of the whole discipline *(7-11)*, which includes Pharmacogenomics as one of its parts.

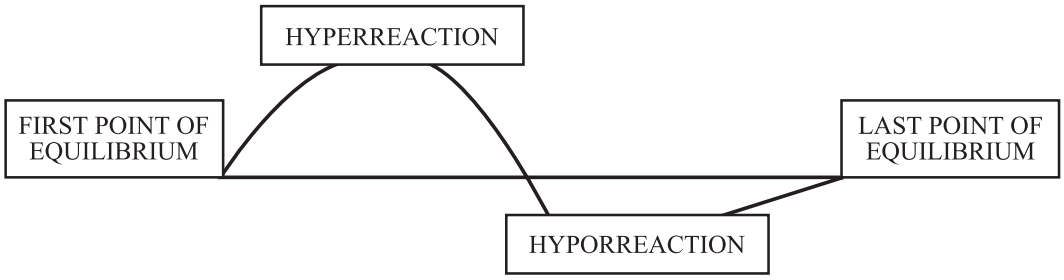
Moral actions, moral reactions

The development of Molecular Biology and Molecular Genetics, and specially the discovery at the beginning of the 70's of Genetic Engineering and the possibility of manipulating the codes of life, triggered the debate about their ethical implications. One of the most common reactions of people to great technical discoveries, in general, is surprise and illusion. They expect that the new procedures will reduce suffering, increasing significantly wellbeing and happiness, and expelling from the earth, perhaps definitively, pain, disease and, at the end, death. But as frequent as this kind of reaction there is another,

completely opposite. Many people react against novelties with fear and anguish, thinking that the new technique will have all the evil consequences one could imagine.

Both reactions are profoundly emotional. Emotions are the first way all living organisms use in reaction to facts. When facts are perceived as distressing or threatening, human beings use to react with fear and anguish, and in general with rejection. On the contrary, when facts are perceived as positive and beneficent, we react with attraction, empathy and love. In both cases, the reaction is at the beginning more emotional than intellectual, and more unconscious than conscious. Only after a longer or shorter period of time, reason can begin to control the situation. Reason works very slowly, compared with emotions. At the same time, the products of reason are less vivid and compelling than emotions. The consequence is that the first reaction is generally emotional, and in many people it is the only one.

What we generally call a "moral action" is in fact a "moral reaction". Morality is always the reaction of human beings towards phenomena and events. Studies have proved that human mind reacts to the great news following a precise process which can be represented as a sinusoid with two points of stability, the first and the last. The first is the state of equilibrium in which was the individual at the moment of the reception of the novelty. This novelty acts always as a stimulus which shoots an hyperreactive answer, represented by the positive part of the curve. After this point, the reaction begins to decrease, until a hypo or arreactivity point. This is not the end, because after this moment of failure, the equilibrium begins to be slowly restored. Only when this last moment is reached, the novelty has been completely assumed by human mind.

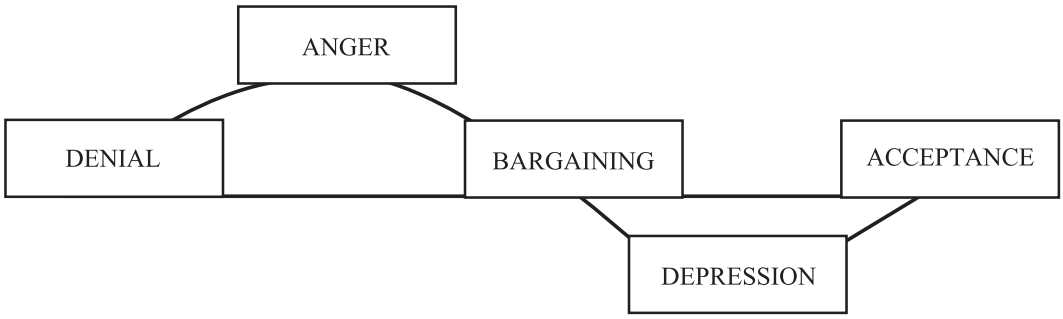


Therefore, the reception of a great novelty always provokes a loss of equilibrium, with two different moments, one of hyper reaction and other of hypo reaction, only after which the novelty can be correctly assumed. The hyper- and hypo reactive moments are basically emotional, and only the last one, the final equilibrium, permits a correct use of reason.

This is the general scheme of reaction against aggressive inputs. These inputs can be perceived by people as positive or as negative. In the first case, when they are considered positive, the first phase is a positive hyper-reaction of hope, love, happiness, etc. These

expectations will be necessarily frustrated by reality, and that is the reason of the second phase of depression, or at least of disenchantment. During this phase emotions are negative, and therefore the novelty is valued as morally bad. Only after that a more nuanced judgement can appear.

When the news are strongly negatives, the scheme is practically the same, but the steps have been analyzed in a more detailed manner. Dr. Elisabeth Kübler-Ross published in 1970 her famous book *On death and dying*, in which she divided into five the stages of dying—after the moment in which the truth of the situation was communicated to the patient—and gave them the following names: Denial, Anger, Bargaining, Depression and Acceptance *(12)*. The denial coincides with the first moment, the anger with the point of highest reaction, the bargaining with the middle point between anger and depression, being this the point with the lowest reactivity, and the last one, the moment of acceptance, in which the equilibrium is reached.



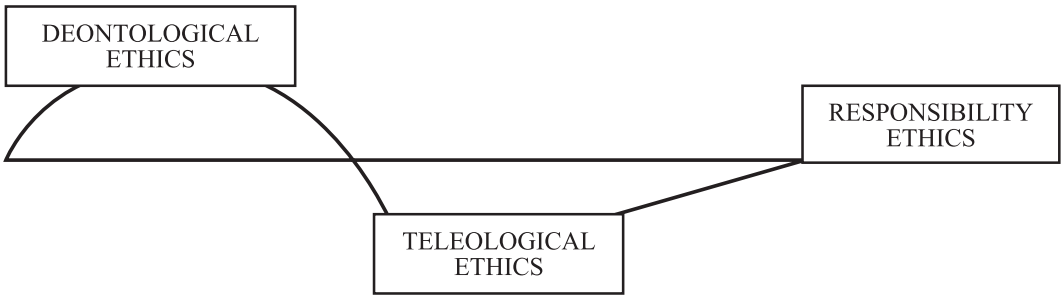
In conclusion, then, people's first reaction to novelties is profoundly emotional, with uncontrolled feelings of acceptance and rejection. Only later, reason begins to control emotions, promoting more prudent attitudes. A big and uncontrolled emotional reaction appears every time that a new important discovery is made in the field of the new Genetics. It appeared when Genetic Engineering began to work in the 70's, it has been present in the discussions of the last years about the Human Genome Project, it is now evident in the debates about Cloning, and it can also appear in the field of Pharmacogenetics. The goal of ethics must be the accurate reflection about these scientific novelties, in order to avoid extreme emotional positions and to promote the responsible and prudent use of these techniques.

Gen-Ethics: from emotional extremes to a reasonable intermediate position

These previous remarks involve an enormous ethical importance. Our first moral reactions, either positive or negative, are highly emotional. During these first moments we all behave as "emotivists." Emotivistic positions are generally extremes, either of love or of hate, either of radical acceptance or of complete rejection. On the contrary, the rational analysis is always more nuanced, balancing pros and cons and looking for an equitable

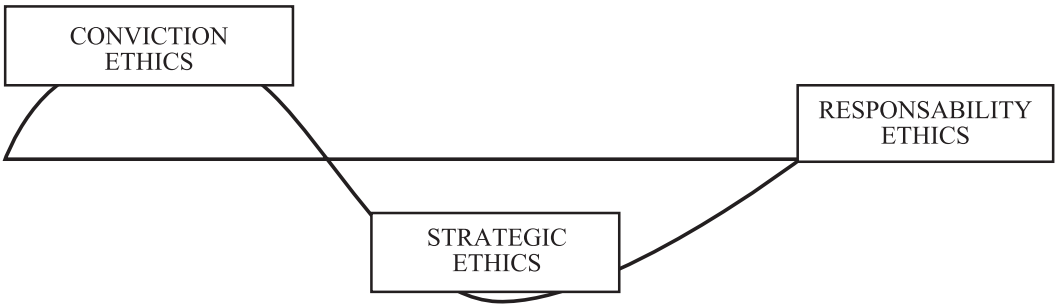
position. As Aristotle said, this equilibrium is placed generally in the middle. The behaviour of taking rational and balanced moral decisions has been "prudence" or "practical wisdom from Aristotle's times till the present *(13)*."

In 1930 C.D. Broad divided the ethical theories in two sets he called "deontological" and "teleological *(14)*". Deontological theories are those that consider human acts to be right when adequate to principles or norms. Therefore, the only criterion to judge the moral correction of an action is its comparison with principles; consequences do not play any role in defining acts as right or wrong. The classical explanation of this point of view is the famous Latin apophthegm, *fiat iustitia, pereat mundus* ("let justice reign even if all the rascals in the world should perish from it"), justice must prevail, even if the consequence would be the disappearance of the whole world *(15)*. This is a typical extreme reaction, generally due to fear, anguish and insecurity. Opposite is the teleological perspective, which defines the correction of an act only by its consequences. It is also an extreme position. Its expression would be: *fiat mundus, pereat iustitia*, "the world should prevail, even unjust or without justice". Both attitudes are extremes and opposites, and when reason begins to take the control of the situation, both are substituted by a third and intermediate position, based in the balance of principles and consequences. This third position is in between of the other two, and now is generally called "ethics of responsibility."



The emotivist approach to the development of new genetics has lead to extreme positions of absolute ban and prohibition, from one hand, and absolute acceptance and liberalization, from the other. Those who perceived new genetics as "good news", reacted with excessive positive emotion. On the contrary, those who considered it as "bad news", hyper-reacted looking for a strict and absolute prohibition of the work with genes. Both attitudes were the most frequent during the first times of Genetic Engineering, and are now active, for instance, in the debates of the last years about the new cloning techniques. These first phases are generally followed by another more mature and more rational, in which some criteria as "reflective equilibrium," "coherentism," and "considered judgements" take precedence to emotions, in order to make prudent judgements *(16,17)*. That is the transition from the "emotivist ethics" to the so-called "ethics of responsibility."

Following Max Weber, the "responsibility ethics" can be seen as the middle point between two extremes, called "conviction ethics" and "strategic ethics *(18)*." The latter is the phase of emotivistic moral hyper-reaction, and the former the phase of moral hypo-reaction. Therefore, these ethical steps can be represented as follows:



These attitudes are always present in society, but their importance is not always the same and they evolve in a certain order. They work dialectically, as "thesis", "antithesis" and "synthesis". The first one to appear is the conviction ethics, which hyper reacts banning generally all dubious novelties. This attitude is the most traditional and conservative. After that appears the contrary, the moral hypo-reaction, the lack of moral tone, which is the most characteristic of the so-called strategic ethics. And only at the end of this dialectic process, the responsible attitude increases its importance. Therefore, the order is the following:

CHRONOLOGY

1. Thesis: The "conviction" ethics
2. Antithesis: The "strategic" ethics
3. Synthesis: The "responsibility" ethics

In the case of Genetic engineering, the responsibility ethics began probably with the agreements of Asilomar, in 1972, distinguishing between the "negative" and the "positive", and also the "somatic" and the "germ line" genetic engineering *(19)*. Genetic engineering made in somatic cells with the intention of correcting or curing diseases (negative genetic engineering) is today considered as responsible and prudent; but there is a great debate about the convenience of changing germ line cells with this same goal, and it is generally rejected as imprudent the manipulation of either somatic or germ line cells in order to enhance the human nature.

Similarly, Pharmacogenetics, a new and promising field, which can improve significantly human wellbeing, must attain in its development some moral rules, developed from the point of view of an "ethics of responsibility", avoiding as extreme and emotional positions both the "ethics of conviction" and the "strategic ethics."

A new pharmacological revolution

Some decades ago, during the 60's, a professor of History of Science, Thomas S. Kuhn, published a very well known book entitled *The Structure of Scientific Revolutions (20)*. The thesis of the book is that there are, in the history of science, wide periods of

normality, in which new knowledge does not transform but only completes and fulfils the core theses and theories of a particular science, without menacing its stability and internal coherence. But in some other moments, very infrequent and rare, the discovery of new data compels to change the nucleus of a theory and consequently of a science. These are the periods called "revolutionary" by Kuhn.

The history of Pharmacology, as the history of every other science, has known some revolutionary moments. One absolutely essential took place exactly one Century ago, when Paul Ehrlich standardized the new system of developing drugs, synthesizing thousands of new chemical substances in the laboratory, and testing their pharmacological activities not only in animals but also in human beings. This was the beginning of the new pharmacological era, which has been developed over all our Century. The traditional empiricism of the old Pharmacy and the first Experimental Pharmacology of R. Buchheim, K. Binz and O. Schmiedeberg in the second half of the 19th Century, was substituted by the new Experimental Therapeutics at the beginning of the 20th Century. Ehrlich thought that the ideal of reaching complete "specific" drugs, capable of destroying definite micro-organisms without injuring other parts of the human body, could be attained in a short period of time. In fact, his discovery of Salvarsan, in 1909, was received as the first success of this new approach, in which the total specificity of drugs was placed as the main goal, synthesizing two other pharmacological properties: efficacy and security. Ehrlich summarized his whole philosophy in the famous expression "magic bullets", which has remained as the permanent goal in Pharmacology all over this Century. First, with the discovery of Sulphonamides by Domagk in 1932, and later with the arrival of Antibiotics, the goal of Ehrlich appeared to be more accessible every day. But the total specificity continued being an ideal instead of a reality. The "magic bullets" did not appear. Every drug had its own side effects, different in every patient, depending of some unknown factors globally described as "idiosyncrasy". Nobody could explain anytime what this idiosyncrasy could mean. In any case, it was frequent that drugs with an important pharmacological activity should be withdrawn of the market due to the important side effects they produced in a more or less reduced amount of people. The complete specificity has been until now only an ideal.

The Ehrlich's ideal is beginning to be a promising reality only now, a Century later, during this change of Century and of Millennium, due to the new ways opened by Genetics and Genomics. Genes are not all in living organisms. As important as genes are the inputs received from the environment, and the interchanges between these two sets of information. Phenotype is always the consequence of the interaction between genes and environment. There is no room in modern molecular biology for a rigid genetic determinism. There are, certainly, cases in which phenotypical traits are determined by genes. This is the case of the traits that Mendel called "dominant". In these cases, the goal of Medicine cannot be other than changing the abnormal or pathological gene if possible (throughout the procedure known as "genetic engineering"), or introducing in a micro-organism the healthy gene, in order to produce the defective protein which is the cause of the disease (what is generally known as "recombinant DNA drugs" production).

But there are many other cases in which the change occurred in a nucleotide of a specific gene does not produce a phenotypical "disease" but only a "predisposition". These are the so called "susceptibility genes", in which the relationship between genotype and phenotype is not governed by the Mendelian law of dominance. In this case, the primary goal of Medicine must be the prevention of the emergence of the disease, and the second its pharmacological treatment, when declared.

This is the new door, opened during the last years. One of the pioneers of this new movement has been Allen Roses, when he discovered some years ago the polymorphism associated with the predisposition of suffering of Alzheimer's disease early in life *(21)*. All of us have specific genetic susceptibilities, which enable us—among other things—to have certain side effects when using some drugs, different from those suffered by others. If in the future we could be able to identify these susceptibilities through genetic tests, one of the historical goals of Pharmacology could be achieved for the first time: the full "specificity" of drugs. This would also be an ethical goal, because only in this way the control of many susceptibilities and side effects would be possible. Pharmacogenetics (including Pharmacogenomics) has its own ethics, and that is why it could be possible to speak about what can be called "Pharmacogen-Ethics".

Pharmacogen-ethics

The main goal of Pharmacogenetics is the search of the right medicine for the right patient, looking for a more strict specificity of drugs, which will increase necessarily their efficacy, their efficiency and their effectiveness. Today this goal is feasible, due to the possibility of identifying "susceptibility genes", that is the polymorphysms associated with the predisposition to suffer some diseases, like Alzhaimer's disease, or to have certain side effects when some drugs are used.

The main question here is defining correctly "susceptibility". Susceptibility is not the same as "disease", or as "genetic disease". A genetic disease is that with a genetic ethiology, discovered throughout the Mendelian laws about the relationship between genotype and phenotype, specially the law of "dominance". On the contrary, we talk about "susceptibility" when the relationship between genotype and phenotype is neither Mendelian nor dominant. In this case, the goal of medicines cannot be the reversion of the state of disease, but the prevention of the appearance of the disease, and its symptomatic treatment, when declared. Therefore, susceptibility is the same than predisposition.

The goal of Pharmacogenetics, the reaching of a total and complete "specificity" of drugs is also an ethical goal because only this way the control of many susceptibilities and side effects will be possible. That is why it is possible and convenient to speak about their ethical implications; therefore, about "Pharmacogen-Ethics." I will examine the content of this discipline ordering some of its main problems and results around the four traditionally invoked bioethical principles, Non-maleficence, Justice, Autonomy and Beneficence.

Non-maleficence

In the next future, the risk/benefit ratio of drugs will change drastically. And the increasing of benefits with a decrease of the associated risks, must be seen as an important moral duty of Non-maleficence. The philosophy of looking for "the right medicine for the right patient" is a fundamental human and bioethical task *(22)*.

Justice

This new pharmacological era can present other important ethical problems, specially related with the principle of Justice. A very important one is the risk of "genetic discrimination." Whether true or not, this risk requires legislation to prevent misuse by Insurers and Employers.

On the other hand, the knowledge of this susceptibility will avoid wasting a lot of money, due to the more restrictive and precise indication of the use of drugs. If in the future we are capable of knowing the specific protein that should be useful to a specific patient, we will be able for the first time to avoid the mayor part of drug side effects, and also to save a great amount of money, nowadays wasted in unsafe and inefficient treatments. Two main bioethical principles, the principle of Non-maleficence and the principle of Justice, will enrich their content with this surprising development of Pharmacogenetics.

Autonomy

Many debates have stressed the risk that the knowledge of genetic susceptibilities would suppose for the people. The rights of privacy, confidentiality, secrecy of genetic data, and also the right of unknowing one's own predispositions, could be damaged. All these rights are related with the ethical principle of Autonomy. Therefore, it can be said that Pharmacogenetics can threaten this moral principle. But this fear seems to be more fantastic than real. As Allen Roses has pointed out:

> "*As long as the SNP Print^{sm} (or SNP "fingerprint") contained no SNP that would provide primary diagnostic information for any disease, the risk of accidental discovery of unwanted medical information would be minimal. Of greater significance, concerns about insurance companies taking advantage of the test for undisclosed diagnostic information would be largely minimized. A separate set of SNPs and other polymorphisms could be used for disease diagnostic purposes, the use of which would remain to be debated publicly with respect to ethics and data privacy. As an aside, the largest variable in that debate is whether the pertinent population of patients has medical coverage guaranteed for all or whether the risk for disease diagnostic capability is only a 'problem' for those who must qualify for medical insurance (23).*"

It is expected that in the next future the SNPs profiles of patients who have the characteristics of being affected by a concrete disease will be quite anonymous, without the possibility of giving collateral information, making the management of this information much easier.

Beneficence

The fourth and last bioethical principle is Beneficence. If the principle of Non maleficence obliges to do no harm, that of Beneficence aims at the achievement of the best. This is also a moral duty, clearly different from that of do no harm. In the case of the knowledge of the susceptibility genes, a major consequence will be the possibility of giving everyone its "DNA health probability forecast", and its "health probability prevention program." This will permit living better, and increasing the personal and the social responsibility over our body, our health and our life.

Conclusion: responsible pharmacogen-ethics

My personal opinion is that new Pharmacogenetics is not only perfectly compatible with the ethical principles of Non maleficence, Autonomy, Justice and Beneficence, but also an important way in order to fulfil their content. What is evident is that a new culture is arising, and that we will be every day more capable of defining the susceptibilities of people, and the diseases they will suffer in the future. This is a necessary consequence of our knowledge' development. Every individual will be more capable of taking care of his future, knowing his susceptibilities, having the possibility of preventing the appearance of his diseases and treating them adequately, when appeared. The developments of science and technology promote the freedom and autonomy of human beings, but at the same time demand of them a higher degree of responsibility. This is, perhaps, the most typical characteristic of our moral situation: codes and norms are everyday less accepted, and at the same time responsibility, individual and social responsibility, is seen as more necessary. The great future of Pharmacogenetics must be controlled with some legal norms and rules, in order to avoid, for instance, discrimination. But over all a great sense of responsibility will be needed. This is the goal of ethics here and now. In other times ethics could have had other goals, but today there is a general agreement that its goal must be the increase of individual and social responsibility. Laws and rules are only consequences of this development. Tell me the sense of responsibility a society has and I could tell you the laws they have. Imitating a famous Kantianian sentence it could be said that laws without responsibility are vain, and responsibility without laws, blind. Pharmacogenetics is opening us to a new and promising panorama. A new way of production of medicines is arising, and therefore a new culture of their use is becoming necessary. And bioethics should join and help each one of us in this way.

Pharmacogen-ethics and research

Pharmacogenetics is now in progress, and therefore many of its main points are

under research. This is the case of the SNP mapping project *(24,25)*. What the SNP Consortium is doing now is research; basic research, which will permit applications and industrial developments in the future. This basic research that now is being done with human beings; better said, with samples taken from human beings, must fulfil some conditions, all of them related to the four bioethical principles of Non-maleficence, Justice, Autonomy and Beneficence. In the following points I would like to describe the main problems concerned with each one of them.

Non maleficence

To conform to the principle of Non-maleficence, research must have a pertinent goal and a right design, the research team must be competent and the risk/benefit ratio adequate for the participants. In the concrete case of the SNP Consortium, it seems evident that all these conditions have been perfectly fulfilled.

The definition of the goal is absolutely essential, because all other moral duties will derive from it. In the concrete case of the SNP Consortium, as Allen D. Roses has pointed out, the goal is not only to get the right drugs for the right patient, but also to make a better linkage in gene discovery than that made with current tools. But the research developed by private drug industries tries only to find the right drug for the right patient. The information is only stored with this purpose, and it cannot be used with other purpose. Therefore, as Roses has written, the abstracted SNP profile would give no information concerning any other genetic characteristic than the medicine response, and thus no collateral information to family members concerning any genetic disease.

In any case, the incorporation of genetics into clinical trials seems very important from an ethical point of view because it will allow targeting therapy more accurately, identifying populations of patients that respond well to pharmacological compounds, and identifying populations of patients that may be susceptible to adverse experiences *(23)*.

Another question related to the principle of Non-maleficence is the right design of the research. The design generally used is clinical trial. But it is not sure that working with genes and SNPs this methodology should not be modified. First of all, because the selection of patients should be done in a way different from the traditional, avoiding all those candidates which in the first phases of the clinical research have been identified as genetically different from the population to which the drug is addressed. In other case, we will doing maleficence.

Justice

Other duties are derived from the principle of Justice. Participation in studies which correlate genetic status with predisposition to diseases always has the risk of genetic discrimination. Another important duty derived from the principle of justice is the control of the research by an independent Ethics Committee. The goal of this Committee must be the defence of human rights for all the participants in the project. Private interests could in some cases injury the basic human rights of research subjects. This Committee must analyse

not only the ethical questions but also the methodological and technical ones, because the latter have always and necessarily ethical consequences.

Autonomy

The third principle is Autonomy. The main procedure in order to fulfil this principle is informed consent. The participation in genotyping must be optional, after an accurate and thorough information. The participant must know the goal of the research, the design used, the way in which samples will be taken, the method of storage and the system of preserving privacy and confidentiality, the time during which their names and identity will be preserved, how the data will be published, etc.

There is a general consensus that for samples to be used for research purposes other than those to which the individual source consented, additional consent from the source must also be obtained or identifiers must be crossed out in the samples, thus making them anonymous. US Federal regulations require that an Institutional Review Board must also approve the research use of non-anonymous or identifiable samples. A number or organizations, including the National Bioethics Advisory Commission appointed by President Clinton in 1996, have developed recommendations on the use of stored samples *(26,27)*.

In the case of the research promoted by pharmaceutical industries, it must be said to participants that the only goal of the research is identifying the possible genetic susceptibilities to some drugs, and no other pathologies or diseases, and that these susceptibilities will perhaps allow in the near future a better use of drugs, also for the own participant.

Beneficence

Finally, there are other duties derived from the principle of Beneficence. The SNP Consortium is a non-profit organisation with no direct or immediate particular interests. Its main interest is general and public. Therefore, no-one should look for private benefits, neither institutions nor participants. All members should take part altruistically, in order to improve our basic knowledge about diseases and drugs. This knowledge will have pharmacological consequences not now but in ulterior phases, when it could be applied to the development to new and more specific drugs.

Conclusion

I would like to stress the ethical importance of this international non-profit collaboration. What the SNP Consortium is doing until now is only basic research, which will permit practical applications and industrial developments in the future. This basic research that now is being done with human beings; better said, with samples taken from human beings, must fulfil some conditions, all of them related to the four bioethical principles of Non-maleficence (pertinent goal, right design, competence of the research team, risk/

benefit ratio), Justice (non discriminatory selection of participants, control by a free and independent Ethics Committee), Autonomy (informed consent, privacy and confidentiality of data) and Beneficence (the need of preserving the public and common benefit in the basic research on human genome).

Some things cannot be matter of commerce and private profit. This is particularly evident in the case of human genome mapping and sequencing. UNESCO tried to protect human genome from private profit declaring it, "in a symbolic sense", "heritage of humanity", as the first article of the Universal Declaration on the Human Genome and Human Rights of 1997 states. This expression "heritage of humanity" is ambiguous and permits all kind of interpretations. But if it has some reasonable meaning, it is that of preserving the basic data related with human genome from commerce. Life is in some way a gift. And a gift should not be object of commerce.

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UNRESOLVED ISSUES IN SOCIAL SCIENCE RESEARCH

Ruth Macklin

Attention to the rights and welfare of human subjects of biomedical research has always eclipsed concerns in bioethics regarding the conduct of research in the social sciences. This is no doubt a consequence of the perception that biomedical research carries risks of serious physical harm, thereby threatening the welfare of human subjects. And because the risks may be serious, great weight is placed on a corresponding right of subjects, the need to obtain voluntary, informed consent from potential volunteers. In contrast, social science research is generally seen as harmless, with the greatest threat to subjects arising from breach of confidentiality, especially in sensitive areas such as research on illegal behavior, sexual behavior, or stigmatizing conditions such as HIV/AIDS and mental illness. Some social scientists have argued that regulations governing research derive from the biomedical model, and should not be applied to social science research. *(1,2)* In some countries, ethical review by an independent, properly constituted committee, even if well established for biomedical research, is not required or carried out for social science research.

Even accepting the need for ethical guidelines for research conducted by social scientists and prospective review of protocols by research ethics committees, a number of unresolved issues deserve special attention. This presentation focuses on three such issues. 1) Ethical controversy continues to surround the use of deception in social and behavioral research, since individuals who are deceived cannot grant properly informed consent. Under what conditions, if any, is deception permissible? 2) Observation or participant/observation research is often conducted without the knowledge or consent of the individuals being studied. When does such research constitute an unacceptable invasion of privacy, and when may it be ethically acceptable? 3) One research methodology involves social scientists obtaining personal or sensitive information about patients through their medical records or directly from physicians, and then approaching the patients in order to gather additional information in surveys or in-depth interviews. Is this methodology an unacceptable breach of medical confidentiality? Are there acceptable ways for social and behavioral researchers to gain access to patients whom they wish to interview?

Deception in social science research

Less than one month ago, an article appeared on the front page of the *New York Times*, entitled "Scholar Sets Off Gastronomic False Alarm."*(3)* The article reported that a Columbia University Business School professor sent 240 letters to leading restaurants in New York city, alleging that he had suffered severe food poisoning after a meal eaten at the restaurant. It was, the professor contended, a celebration of his wedding anniversary and the evening was ruined by the horrible sickness that ensued. The restaurateurs to whom the letters were sent experienced great anxiety, launching investigations into the way food was

being handled in their kitchens and drilling kitchen staffs on proper procedures. Several owners and chefs reported that they spent a great deal of time and effort trying to determine when the professor had eaten the meal at their restaurants, since his letter failed to specify that and other crucial information. They also reviewed menus and product deliveries for possibly spoiled food, and questioned the kitchen staff about their procedures. As it turned out, everything in the letter was a lie. The professor was conducting a study to determine how restaurants responded to complaints. About 60 restaurants replied to the original letter, with some offering the professor a refund and a free meal. At least one letter alleged fraud, which prompted an investigation by the university. When the truth came to light, the Dean of Columbia's business school wrote a formal letter of apology to all the restaurants. The Dean's letter said that it was "*an egregious error in judgment*" that was "*part of an ill-conceived research project*." The Dean added that the professor had designed and carried out the research project on his own, and pointed to his failure "to think through the toll this study would take on its recipients." The professor who conducted the research wrote a follow-up letter, apologizing and explaining that his original letter was fabricated to help collect data for research on "vendor response to consumer complaints."

At least two things are worth noting in the newspaper report of this episode. One is the focus on the consequences of this ill-chosen piece of research. The Dean referred to *"the toll this study would take on its recipients*." The Dean also told the *New York Times* reporter that the matter had taken up almost all of his time, "*in a flurry of meetings and memorandums*." So the adverse consequences of this research began with the time and effort expended by the restaurateurs and their staffs, and continued with the Dean of a business school and his faculty devoting time to investigate and make decisions about what to do. Of course, this was a newspaper account, not an article in an academic journal. Nevertheless, there is no mention of the deception as constituting wrongful behavior. The only reference to the act of lying was the allegation one restaurant made that the professor had committed fraud. Another restaurateur said he suspected a ploy to get a free meal. Whereas 'fraud' is a term commonly employed to refer to deceptive business practices, it does not appear in academic discussions of deception in the conduct of research.

A second thing that stands out in the report is the absence of any mention of the need for ethical review of research such as this. The Dean's letter said the faculty member "*initiated this research project on his own*," and the professor himself said that the study was of his own doing "and not that of the business school or the university." If the professor were on the faculty of the Columbia University College of Physicians and Surgeons, or the School of Public Health, or one of the social science departments in the university, there surely would have been a requirement that research protocols be submitted to a relevant ethics review committee. Apparently, there is no such requirement in the business school at Columbia.

One psychologist with whom I discussed this episode dismissed the business school professor's inquiry as "not real research," but a poorly designed attempt to get answers to a question that could have been investigated by other means. However, the psychologist staunchly defended the need for deception in research conducted by social psychologists

because, she maintained, it is necessary to manipulate variables in order to get the answers to the research questions they pose. The only way to manipulate the variables, she contended, is to give misinformation to subjects.

Discussion of the ethics of deception in social science research surfaces periodically in professional journals and prompts a spate of articles. The first major wave of attention occurred after Stanley Milgram conducted his infamous "obedience" experiments of several decades ago.*(4)* One of the early critics of Milgram's study and others around the same time that involved deception was another social scientist, Diana Baumrind, who in a paper commissioned by the *National Commission for the Protection of Human Subjects*, made a strong case against both the need for deception in research and for its ethical acceptability. *(5)* Another social scientist, Joan Sieber, who contributed to the literature on deception in the early 1980s, revisited the topic in 1995.*(6 - 8)* The most recent wave of attention was prompted by an article in the *American Psychologist* in 1997 that called for outlawing deception in psychological research. *(9 - 12)*

In a nutshell, arguments pro and con make the following contentions. Defenders of deception claim that much significant research in the social sciences could not be done without deception, so to outlaw it would have the unfortunate consequence the valuable knowledge must be forgone. Moreover, some add that the alleged harm that comes from deceiving people has been overstated, and that there is not nearly as much loss of self-esteem on the part of subjects who were deceived and then "debriefed" as critics maintain. *(13)* For their part, critics of deception have adopted either a principled argument against lying (sometimes derived from the philosophy of Immanuel Kant), or they have maintained that other methodologies could be used to arrive at equally valid conclusions, or they point to adverse consequences of various sorts, including loss of self-esteem and distrust of the research enterprise on the part of former subjects and the public. They also question the claim that much research of great significance could not be accomplished without deception. These discussions in the literature are sometimes muddied by imprecision in the meaning of "deception": does withholding some information provided to subjects count as deception? Or must there be an actual misrepresentation for the information to count as misinformation?

The Ethical Principles adopted in 1992 by the *American Psychological Association* permit deception but limit its use. The principle, strangely worded as a declarative statement rather than as a prescriptive judgment, reads: "*Psychologists never deceive research participants about significant aspects that would affect their willingness to participate, such as physical risks, discomfort, or unpleasant emotional experiences." (14)* As a descriptive statement, it is most certainly false. A more detailed and nuanced statement appears in a current draft of the *CIOMS International Ethical Guidelines for Research*. A commentary under the informed consent guidelines includes the following:

> *Some people maintain that active deception is never permissible. Others would permit it in certain circumstances. Deception is not permissible, however, in cases in which the deception itself would disguise the possibility of the subject being exposed to more than minimal risk. When deception is deemed indispensable to the*

> *methods of a study, the researcher must demonstrate to an ethical review committee that no other research method would suffice; that significant advances could result from the research; and that nothing has been withheld that, if divulged, would cause a reasonable person to refuse to participate. The ethical review committee should determine whether and how deceived subjects should be informed of the deception upon completion of the research. Such informing, commonly called "debriefing", ordinarily entails explaining the reasons for the deception. A subject who disapproves of having been deceived is ordinarily offered an opportunity to refuse to allow the researcher to use information obtained from studying the subject. Researchers and ethical review committees should be aware that deceiving research subjects may harm as well as wrong them; subjects may suffer a loss of self-esteem when they learn that they have participated in a study under false pretences. (15)*

How are ethical review committees likely to judge research protocols that involve active deception? I have no statistical information about that and doubt that any exists. However, I can refer to my own experience in this matter. During my twenty years as a member of the IRB at *Albert Einstein College of Medicine*, investigators brought two research protocols that involved active deception of subjects for the committee's review and approval.

The first study was part of a collaborative effort between a biological psychiatrist and a psychologist. The biological psychiatrist was studying PMS, looking at changes in various hormonal levels in women during different phases of their menstrual cycle. The psychological aspect involved correlating the subjects' moods and behavioral responses with the levels of these hormones at the times they were being measured. The hypothesis was that the women's affect would be more volatile during the so-called PMS period (late luteal phase), and the psychologist's intervention aimed to test this hypothesis. The psychiatrist or his medical assistant would draw the required bloods for the hormonal essays. The psychologist, with the aid of a confederate, would invite the volunteers into a classroom to take several tests at the appointed times in the month when the women were assembled for this purpose. The psychologist would then seek to provoke the women to anger on these different occasions, making notes and tape recording the sessions to see whether the subjects were more easily provoked to anger during the PMS period. On one occasion, the psychiatrist and her confederate planned to pore over the answers of women who had completed part of the test, and publicly laugh and ridicule the answers on the test papers. On the next occasion, they planned to spill fake blood on several of the women and record their reactions to this staged accident. After considerable discussion, the committee voted to disapprove the protocol on grounds of absence of requisite informed consent and poor benefit-risk ratio. The psychologist was quite dismayed, and contended that the ethical guidelines of her professional association, the APA, permitted deception of this sort.

The second study was brought to the IRB by an investigator who was both a dentist and a sociologist. His study was designed to determine how dentists in New York state would respond to prospective patients whom they were told or led to believe were gay men. The research hypothesis was that fear of acquiring HIV/AIDS would lead a significant proportion of dentists to deny care to the men requesting appointments. In the first study

design the researcher proposed, actors hired for the purpose (there are many unemployed actors in New York City) would call to make an appointment with dentists who were chosen from a list of members of the state dental society. Some of the actors would say they were HIV positive, others would simply indicate that they were homosexual. The researcher would have no information about whether the actors were, in fact, homosexual or whether they were HIV positive. The IRB rejected the study design because of the outright deception of the dentists and the impossibility of fulfilling the informed consent requirement. The researcher was highly annoyed, claiming that this was a significant study that could prove discrimination on the part of dentists toward prospective patients they knew were HIV-positive or at risk for being HIV-positive. The IRB told him to go back and redesign the study.

The investigator returned with a different study design. This time, the subjects would be actual gay men, recruited for the study from the Gay Men's Health Crisis (GMHC), an HIV/AIDS activist group in New York City. Some of the gay men would, in fact, be HIV positive. The IRB again deliberated, and this time determined that the study design would place the dentists at legal risk. Although this new design did not involve deception, the involvement of gay men from an activist organization could very likely result in reports of discrimination on the part of specific dentists, which would be in violation of a New York state AIDS law. In obtaining informed consent from the dentists, the researchers could not promise that confidentiality would be protected; if the investigator had to mention that dentists who refused appointments would be at legal risk of discriminatory behavior, it would bias the study. The IRB judged that the legal risk to the subjects was unacceptably high. The investigator, this time even more annoyed, went back and redesigned a study that met the committee's approval. However, he maintained that he probably would not get accurate results with the study in which there was no deception or significant withholding of information. In addition, he informed the IRB that he had consulted an IRB chair at another institution, and the chair assured him that his study would have been approved at that institution. For my part, in reviewing the then-current literature on deception in research, I was surprised to discover that dentists are among the most frequently deceived groups in social science studies.

I have long been a critic of deception in social science research. In my early, very naïve days in bioethics (in the early 1970s), I served on a social science review committee at *Case Western Reserve University*. When I saw all the deception in the protocols we reviewed, I posed an innocent question about the ethics of deception in research. I was invited to make a presentation on the topic to the committee, and foolishly chose to invoke the writings of Immanuel Kant. In short, I was laughed out of the place. Some years later, I was a participant in a small project that examined ethical issues in social science research. In an article I contributed to the book that was the outcome of the project, I wrote: "*Although social science research differs in a number of respects from biomedical research, these differences do not warrant adopting another standard for adequate disclosure. This conclusion is supported by an adherence to the respect-for-persons standard—a standard that rules out lying to subjects as well as other forms of deceptive covert research….[D]eceiving subjects prevents their being able to choose rationally whether or*

not to participate in research….[T]here is no compelling reason why the standard of disclosure in social science research should not be the same as that governing biomedical research."*(16)* I still believe those words, written more than twenty years ago.

Observation research in public places

Although the need to obtain informed consent for subjects of social science research is a general ethical requirement, various exceptions can be justified and a research ethics committee may grant a waiver. One of the circumstances in which it is presumed that individual consent is not needed is that of observation research conducted in public places. On a visit I made several years ago to a country in South America, individuals who had designed and were carrying out the following study, described and defended it.[1] The study was as follows.

The subjects to be observed were homosexual men who had sexual encounters with one another at night, in a location known for these encounters in a public park.

The researchers, who were themselves homosexual men, were acquainted with the places in the park known for these encounters. The researchers remained hidden before, during, and after their observations, which consisted of watching the men perform sexual acts. The purpose of the study was to determine the nature and frequency of proposals by gay men to their sexual partners to engage in safe sexual practices, for the most part, willingness to use a condom, and the responses by the partner. The researchers sought to justify this covert observational research by offering the following three reasons: 1) the importance of the information to be learned; 2) the impossibility of obtaining this information using any other methodology; 3) the fact that the researchers were themselves gay men (they maintained that this same research would not be ethical if the researchers were not homosexuals themselves). In support of the first reason, the researchers said that in an era of AIDS, the information that could be learned from this observational study would be of enormous importance; it could save lives. They pointed to other attempts to learn the same information, using other study designs, and said those attempts had failed. In fact, this same group of researchers had tried to carry out such a study but the data they gathered was imprecise. So, they argued, there did not exist another methodology that would yield this important information.

Are the three reasons adequate and appropriate to provide an ethical justification of this study? Since the requirement to obtain individual informed consent for observational studies can often be waived, what are the conditions when a waiver is acceptable? I propose the following three. First, the research must consist solely in observations of behavior, without the possibility of identifying individual subjects; second, the observations must be made in a public place (not behavior observed through a telescope in people's bedrooms);

[1] The visit was conducted under a grant from the Ford Foundation for a project on ethical issues in social science research on reproductive health and sexuality. I do not identify the country in order to protect the confidentiality of the research team.

and third, the information to be learned must be of sufficient importance to science or public health, and there is no other methodology that could be used to gain that information.

Does the observational study of homosexual encounters in the park conform to these conditions? Some would say "yes," others "no." It is true that the study consists only of observations; and in one obvious sense, the location of the study is a public place. However, since the researchers are gay men who live in the same city as the subjects to be observed, and all are homosexual men, the likelihood that the investigators will know some of the individuals whose sexual behavior they observe is reasonably high. In that case, what is important is to maintain strict confidentiality of the subjects. According to one viewpoint, it is adequate protection of the rights of research subjects if their identities cannot be discovered outside the research context; that is, reports of the study will not contain any potentially identifying information. A somewhat different view questions whether it is acceptable even for the researchers to be able to observe intimate behavior of individuals known to them, in the absence of informed consent.

Next we have to consider the location. While it is true that a park is a public place, the type of behavior being observed is certainly private. What people normally do in public places is to engage only in behavior that they suppose other persons might be observing. In this situation, the place is public but the behavior is intimate. If the researchers were simply observing families strolling in the park on Sunday afternoon, that would pose no problem. In contrast, if the researchers were to use telescopes to observe the sexual acts of persons through their bedroom windows, it would be a clear violation of privacy. In both cases, it is clear what is public and what is private. However, the situation regarding the sexual encounters in the park remains ambiguous.

Is the information to be learned of sufficient importance to science or public health? The investigators claimed that obtaining the information about negotiations of safe sex could save the lives of many gay men in the time of AIDS. It is surely true that success in preventing acquisition of AIDS and thereby saving lives is an important goal. However, many steps have to be taken between the data gathered in this observational study and succeeding in the eventual goal of implementing educational programs about the use of condoms, changing sexual practices, and thereby saving lives. Moreover, the question remains whether data from studies such as this are needed in order to implement an educational campaign with information about preventing transmission of HIV. The hardest part of all is to instill a motivation to change unsafe sexual practices, and the observational study is not directed at that achievement. Although it may be important to obtain precise data about the nature and frequency of unsafe sexual practices among gay men, the ethical problem lies in the use of a methodology that violates the privacy or the dignity of subjects in covert observations.

A possible defense of the study could point out that if the gay men never know that they are being or have been observed, how can they be harmed? Those who believe that harm to subjects is the only ethical concern could argue that the remedy lies in ensuring protection of the confidentiality of the subjects. This defense fails to take account of the fact that people can be wronged even if they are not harmed. If being wronged without

being harmed (even psychologically or emotionally) is a genuine concern in research ethics, then it matters not if the individuals who are observed ever come to feel degraded or as if their privacy has been violated. One interpretation of the "respect for persons" principle acknowledges that wronging is a legitimate ethical category, even if social scientists do not normally apply the principle to their own research under this interpretation.

Finally, there is the question whether it matters in a study such as this if the researchers are homosexuals themselves. According to the researchers who conducted this study, it is of great importance. But they failed to provide a convincing rationale for their claim. After all, the importance of the knowledge to be gained would remain the same, no matter who the investigators may be. The motivation of the researchers would be the same: to gain information in the hope of promoting safer sex and reducing the incidence of HIV infections among gay men. The same confidentiality protections could be put in place. Indeed, it would seem that if the researchers were women or straight men, that would afford greater protection of the research subjects because there would be less likelihood they would be known personally to the researchers. Although the investigators did not say so explicitly, perhaps they believed that if non-homosexuals were to observe sex acts among gay men—even as researchers—they would be engaged in a form of voyeurism. But this is precisely the objection of those who claim that this type of research is unethical. Regardless of who the researchers are, as observers they are no different from voyeurs of behavior that the participants expect to be unseen by others. If a type of social science research is the equivalent of an act of voyeurism, should it be considered ethically acceptable or unacceptable?

Review of medical records and follow-up contact with patients

There appears to be widespread uncertainty, if not disagreement, on the ethics of social scientists and epidemiologists gaining access to medical records without the knowledge or consent of patients. When researchers are not part of the treatment team, and therefore would not otherwise have legitimate access to patients' records, should they be given access by a physician or head of a unit where the records are kept?

This question is sufficiently problematic, and opposing judgments have been forthcoming from participants in conferences and workshops. But I want to take the example one step farther. Let us consider the same situation and include an additional circumstance: after reviewing patients' records and identifying the individuals, social scientists then make direct contact with the patients either in an unannounced home visit or a telephone call. Projects like these are carried out in public hospitals, since in that setting physicians routinely give researchers access to patients' records, which physicians would most likely not do with records of their private patients. The following example, presented at a workshop in a Latin American country, is illustrative.[2]

[2] I attended this workshop as part of the same project described above. Here again, I do not identify the researcher or the country in order to protect confidentiality.

The subjects of the study were women with a presumption of uterine cancer who do not return to the hospital following a pap test to learn the results of the test. Uterine cancer is a big public health problem for women in that country. The test results are placed in a registry in the hospital, but the women who have undergone the test are unaware of that. The aim of the social science research is to find out how to improve services to these women, in particular, how to motivate them to return to the hospital following the diagnostic pap tests. The chiefs of service in the hospital grant permission to social scientists to have access to the patients' medical records.

The central ethical problem is that the researchers obtain the names and addresses of the women without the patients' knowledge or permission. The researchers then make a home visit to the women. Once the researchers appear at the door and identify themselves, if the women then grant permission to enter the home the researchers conduct an interview and provide information about the results of the pap test. This step gives rise to a second ethical problem: the researchers have information about a personal, medical diagnosis that the women themselves did not know. The researchers inform the women that they should return to the hospital for follow-up care. The researchers actually facilitate that process by giving the women the names of physicians to go to, thus enabling them to avoid the usual bureaucracy in public hospitals. As a result, the researchers contend, the benefits to the women could be considerable. Yet the ethical questions remain: do those potential benefits justify the breach of confidentiality by the physicians in granting social scientists access to the medical records of patients without their prior consent? Is it an invasion of privacy for researchers to show up at the homes of patients, armed with the confidential medical information, in order to carry out the interview that comprises the research?

Although it is well-established in some countries that patients have the right to see their medical records and obtain copies of them, this is not the case in other countries. However, this type of research does not address the issue of access by patients to their own medical records but rather, the question is who is authorized to make use of that information and to give it to others. There appears to have been a shift from the previous presumption that patients' medical records are confidential and may not be revealed without their consent to the reverse presumption that researchers, as well as insurers, billing clerks in hospitals, and administrative personnel who conduct quality assurance audits should be granted access to records with identifying information. Federal regulations governing research in the United States permit a waiver of informed consent for research that poses no more than minimal risk to subjects, when the research could not practicably be carried out without the waiver, and when a waiver of consent will not threaten the rights or welfare of the subjects. This last condition is the one most open to question when patients' right of confidentiality is ignored. Yet epidemiologists and social scientists contend that the information gained from studying patients' records is of great value for public health, and the research could not be carried out at all or else would result in a very biased sample if individual patients had to be approached for consent to review their medical records. They also argue that if researchers take proper steps to protect confidentiality of the information obtained, then the patients are not harmed in any way. Indeed, it is argued, the patients will never know that researchers studied their records, so where is the harm? The only response to this argument is that

people can be wronged without being harmed, and the wrong lies in breaching confidentiality when patients have the expectation that their medical information is being treated as confidential.

A recent U.S. regulation that went into effect in 2001 is essentially designed to protect the confidentiality of patients' information.*(17)* However, the act permits disclosure in the following circumstances, among others emergency circumstances; identification of the body of a deceased person, or the cause of death; public health needs; research, generally limited to when a waiver of authorization is independently approved by a privacy board or Institutional Review Board; oversight of the health care system. The recently issued regulation is silent on the question of whether social science researchers who are granted access to patients' records may then proceed to contact those patients by telephone or visit them in their homes.

The research ethics committee at my own institution has debated this issue, as well as the broader question of whether social science researchers should be granted access to patients' records without the latter's consent. While the committee did accede to the position championed by epidemiologists to be given access to the records, the committee did not permit the researchers to contact the patients directly. The patients' personal physician, or the physician of record in charge of a hospital unit where patients see many different physicians, must be the one to make the first direct contact with the patients. However, committee members disagreed over whether patients who received this notice must then grant their consent to be contacted, or whether it would be sufficient simply to receive the notice that a researcher would be contacting them. These topics are still under debate. My own view is that having lost the battle to protect the confidentiality of patients' records, we should at least refrain from allowing invasions of their privacy on the part of well-meaning researchers who have already gained a wealth of personal medical information about the persons they seek to interview.

Conclusion

These are only three ethical issues among a more numerous array that deserve attention in social science research. One other concern in observation research pertains to the obligation of researchers when they witness behavior that has an imminent potential for causing harm to human beings, be they research subjects or bystanders. May the social scientist just stand by and observe, under the guise of neutrality of the research enterprise? Or is there a moral obligation to intervene in some way? A quite different concern, one rarely raised until recently, is the involvement of the community where research is carried out. What are the obligations of researchers to the community before, during, and after the research is concluded? These questions have been raised largely in the context of both biomedical and social science research on HIV/AIDS. There is every good reason to extend that concern to other areas of research, an effort that will pose new challenges for researchers in the social sciences.

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PLACEBO CONTROLS IN CLINICAL TRIALS WHEN THERE ARE KNOWN EFFECTIVE TREATMENTS

Robert J. Levine

The use of placebos as controls in research designed to assess the efficacy of therapeutic or preventive agents is highly controversial. This paper is concerned with only one part of this debate: the ethical justification of placebo controls in the evaluation of therapies for diseases or conditions for which there exists a therapy known to be at least partially effective. This analysis of this justification will entail a consideration of the anti-placebo stance of the *Declaration of Helsinki* as well as the closely related position held by some commentators that use of placebo as controls rather than known effective therapy is a violation of the physician's ethical duty to provide only the best known therapy for the patient.

The *Declaration of Helsinki* has recently been revised extensively. This revision was accomplished in response to two major criticisms *(1)*: First, that the document was logically flawed as are all documents that rely on the spurious distinction between therapeutic and nontherapeutic research. Secondly, it was alleged that its position on the ethical justification of placebos was both ambiguous and out of touch with the main stream of contemporary ethical thinking.

Let us begin with a consideration of Helsinki's position on placebo controls as reflected in the fifth edition of the *Declaration of Helsinki* (1996). Then we shall consider the revisions in this position embodied in the most recent sixth edition (2000); these will be called *Helsinki V* and *VI* respectively. *(2)* This appraisal will yield the conclusions that the position on placebo was not ambiguous in the 1996 edition and that it changed very little, if at all, in the 2000 version.

Helsinki V on placebo

In *Helsinki V*, Article II.3 established the 'best proven therapeutic method' as the standard requirement for all patients who serve as research subjects:

> II.3 In any medical study, every patient - including those of a control group, if any - should be assured of the best proven diagnostic and therapeutic method. This does not exclude the use of inert placebo in studies where no proven diagnostic or therapeutic method exists.

The implications of this article extend far beyond the use of placebo controls in clinical trials. This article, if strictly applied, would rule out the development of all new

therapies for conditions for which there are already existing 'proven' therapies. One cannot evaluate a new therapy unless you withhold those that have already been demonstrated safe and effective for the same indication. Strict application of this standard would have prevented the evaluation of the effectiveness of cimetidine and other H2 receptor antagonists for the treatment of peptic ulcer because the withholding of belladonna and its derivatives would have been considered an unethical withholding of the 'best proven therapeutic method'. Similarly, the development of new and improved antihypertensive drugs would have ceased with the establishment of the ganglionic blockers.

Article II.3 also forbids placebo controls in clinical trials in which there is virtually no risk from withholding proven therapy. Consider research in the field of analgesics and anti-histamines. No experienced person would ever recommend that you are required to have an active control in the evaluation of a new analgesic. Article II.3 also rules out the use of placebo controls in clinical trials in which there is a very remote possibility of a serious adverse consequence of withholding the active drug, such as trials of new antihypertensives and of new oral hypoglycemic agents. Insisting on active controls in these areas would introduce major inefficiencies with virtually no compensating benefit; the amount of injury to research subjects that would be prevented by requiring active controls is so small that it can be and generally is considered negligible.

Placebo controlled trials of analgesics, antihypertensives and oral hypoglycemics are conducted commonly and the results are published in reputable, peer-reviewed medical journals. Parenthetically, it is worth noticing that such publication is a violation of Helsinki; Article I.8 (*Helsinki V*) and Article 27 (*Helsinki VI*) hold that: "Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication."

The most controversial interpretation of Article II.3 is that it requires the provision of the best proven therapeutic method that is available in the industrialized countries even when conducting research in countries in which such therapy is not available. This interpretation provoked the most acrimonious debate in the field of research ethics since the 1970's. The debate was begun with the publication in *The New England Journal of Medicine* of an article that denounced as unethical the clinical trials that were being carried out in certain several countries to evaluate the effectiveness of the short duration regimen of AZT in preventing perinatal transmission of HIV infection. *(3)* The editor of the *New England Journal* opined that these trials were, in certain respects, reminiscent of the notorious Tuskegee Syphilis Studies *(4)*; this is, in contemporary American culture, the most powerful metaphor for symbolizing evil in the field of research ethics. The other side of the controversy is exemplified by a statement of a physician-researcher from Uganda, one of the countries in which the trials were conducted. He accused the editor of a form of "ethical imperialism" which asserts that the American vision of research ethics must dominate the conduct of research everywhere in the world.

Let us consider this clinical trial in some detail as a case study. It seems appropriate to do so since it was this controversy which served as the immediate stimulus to undertake

the most recent revision of *Helsinki*. At the time the trial began, and indeed to this day, the standard in industrialized countries such as the United States for prevention of perinatal transmission of HIV is the so-called 076 regimen. The name comes from ACTG protocol number 076, the AIDS Clinical Trial Group protocol that established its safety and efficacy. The 076 regimen reduces perinatal transmission of HIV infection by about 67%; the cost of the chemicals alone for treating each infected pregnant woman was in 1997 about $800. Why can't we just provide the 076 regimen to women infected with HIV in the developing countries? First and foremost is the cost. Eight hundred dollars per woman is approximately 80 times the annual per capita health expenditure in the sub-Saharan African countries in which these trials were carried out. The cost of the chemicals is not the only problem; there are several other obstacles most of which are also related to finances. I shall name some of the others; for a more complete discussion of these problems, see reference *(5)*.

Provision of the 076 regimen would also have required a revision of the host countries' customs for seeking perinatal care. In most of these countries, women simply do not consult a health care professional early enough in pregnancy to begin the regular 076 regimen. It would also have required the establishment of a capability to provide intravenous administration of AZT during delivery; in most regions of the host countries there are no facilities for the intravenous administration of anything. And finally, in the host countries for these trials, with the exception of Thailand, women breast-feed their newborn babies even when they know they are infected with HIV. The risk to the babies of providing them with any available alternatives to breast-feeding may be even greater than the risk of exposing them to infection with HIV through breast-feeding. The transmission rate of HIV infection by way of breast- feeding is about 14%. In the regions in which the 'short-duration' regimen of AZT was evaluated, particularly in sub-Saharan Africa, the death rate from infant diarrheal syndromes is about 4 million per year. In these countries, there is no infant formula. We could make the infant formula available in these countries, but that would not help. One cannot mix the formula with the local water supply because it is contaminated with, among other things, the pathogens that cause the deadly infant diarrheal syndrome.

To sum up: It is clear that the 076 regimen of AZT cannot be made available to most HIV-infected pregnant women in the resource poor countries now or in the foreseeable future. This is the main reason that it is essential to find methods to reduce the rate of perinatal transmission of HIV that are within the financial reach of the resource poor countries. That was the primary justification for conducting the clinical trials of the short duration regimen of AZT. The cost of the AZT in the short duration regimen was about ten percent of that of the 076 regimen. Moreover, there was no need for intravenous therapy or administration of the drug to the babies. At the time the trials began, it seemed likely that two of the countries could afford to provide the short duration regimen if it proved effective; there was also a commitment from international agencies to assist the other resource poor countries in securing and providing the drug.

Should the best proven therapeutic method standard for a clinical trial be construed to mean the best therapy available anywhere in the world or the standard that prevails in the host country? Guidance on this point can be found in another document—the *International*

Ethical Guidelines for Biomedical Research Involving Human Subjects— a document prepared by the Council of International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO) *(6)*. This document, which unlike *Helsinki*, explicitly addresses the problems of multinational research, offers some guidelines which I believe are far superior to informed consent and other traditional protections in preventing the exploitation of people in developing countries. First, for any research that is sponsored by an agency in an industrialized country and carried out in a developing country, the research goals must be responsive to the health needs and the priorities of the host country or community. Secondly, it requires that any product developed in the course of such research be made reasonably available to the inhabitants of the host country. This then focuses multinational research on the needs of the country in which the research is carried out. No more conducting phase I drug studies in Africa simply because it's less expensive and less vigorously regulated.

In my analysis, the initiation of a research program cannot be considered the same as the establishment of an entitlement to the best therapy that is available anywhere in the world *(5)*. Secondly, the relevant standard is the one that prevails in the host country *(5)*. I think it would be improper to withhold anything that is generally available in the host country in order to do research designed to evaluate something else if such withholding presented a non-trivial risk of a serious adverse consequence.

A new ethical standard is now emerging on the international research ethics scene. This standard is called the "highest attainable and sustainable therapeutic method" standard. This ungainly name requires some explanation: 'Highest attainable' means that under the circumstances of the clinical trial, the level of therapy one should provide should be the best one can do. The level of therapy that is generally available in the host country should not necessarily be considered sufficient; rather, it should be considered a minimum — the least that might be considered ethically acceptable.

'Sustainable' means a level of treatment that one can reasonably expect to be continued in the host country after the research program has been completed. It is a level of treatment that the host country can reasonably be expected to maintain when the extra resources provided by sponsors from industrialized countries are no longer available.

'Sustainability', then, serves as a constraint on 'highest attainable'. One should provide the highest level of therapy that one can under the circumstances of the clinical trial; however, one should keep in mind that if the level of therapy is not sustainable, the results of the trial may not be responsive to the needs and priorities of the host country and the therapeutic product developed in the research program may not be reasonably available to inhabitants of the host country.

Those who insist that *Helsinki* must be interpreted as requiring the provision of the best proven therapeutic method that is available in industrialized countries even when research is carried out to address the needs of resource poor countries must understand the implications of this position. To consider once again our case study—the trials of the 'short-

duration AZT regimen' in preventing perinatal transmission of HIV—most resource poor countries cannot even afford to purchase sufficient AZT to implement the best proven therapeutic method (the 076 regimen). In order to truly provide the 'best' it is also necessary to provide all of the other advantages that exist in industrialized countries that enable the 076 regimen to be effective. These include, among other things, infant formula as an alternative to breastfeeding, a water supply that is safe for infants and the facilities for intravenous administration of drugs. All of these 'advantages', taken together would cost far more than the AZT. Clearly the cost of the 076 regimen is beyond the reach of most of the resource poor countries. Insistence on this standard would accomplish nothing other than to deny to resource poor countries the possibility of developing therapies and preventions that they can afford. Moreover, it would preclude the participation of sponsors and investigators from industrialized countries in research and development programs designed to assist the resource poor countries in developing affordable treatments and preventions. (For further discussion of the 'highest attainable and sustainable' standard, see) *(7)*

Application of the 'highest attainable and sustainable therapeutic method' standard is in all relevant respects a more suitable ethical standard. One of its chief advantages is that it tends to facilitate the efforts of resource poor countries to develop needed therapies and preventions that are within their financial reach. Until the imbalances in the distribution of wealth among the nations of the World are corrected, this appears to be the best we can do.

Helsinki VI **on placebo**

As mentioned earlier, one of the major reasons for the most recent revision of *Helsinki* was to clarify its position on the ethical justification of placebo controls. I find no reason to believe that *Helsinki V* was either equivocal or susceptible to differing interpretations. Now let us consider whether *Helsinki VI* changes any aspect of its position on placebo controls. The relevant new passage is Article 29, the replacement for Article II.3:

> 29. *The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists*.

The only improvement over Article II.3 is the removal of the proscription of the development of all new therapies for conditions for which there are already existing 'proven' therapies (*supra*). And even this salutary effect is not entirely clear; it depends completely on the interpretation of the new Article 28:

> 28. *The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects*.

Helsinki's absolute proscription remains intact for placebo controls in clinical trials designed to evaluate therapies for diseases or conditions for which there already exists a therapy known to be at least partially effective.

The duty to care

Historical evidence suggests strongly that the writers of *Helsinki* intended the 'best proven therapeutic method' as a standard of medical practice and that its construction reflected their assigning primacy to the physician's duty to care.[1] As the *Council for International Organizations of Medical Sciences* (CIOMS) noted in 1993 in its *International Ethical Guidelines for Biomedical Research Involving Human Subjects*:

> *"The Declaration [of Helsinki] does not provide for controlled clinical trials. Rather, it assures the freedom of the physician "to use a new diagnostic or therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health or alleviating suffering*." (*6*)

Several commentators on the ethics of clinical trials have argued that the choice of a control group should be dictated by the physician's ethical obligation to provide for each patient only the best known therapeutic method. This obligation is variously known as the 'duty to care' (*8,9*), the duty to provide 'the good of personal care' (*10-12*) and the fiduciary obligation of undivided loyalty to the interests of the patient. (*9,10*).

The physician-ethicist, Weijer, has written an excellent and comprehensive review of the major ethical considerations in the justification of placebo controls in clinical trials (*9*). For Weijer, the central consideration in the ethical justification of clinical trials is the concept introduced in 1987 by Benjamin Freedman, 'clinical equipoise' *(8)* 'Clinical equipoise' is a term used to describe a state of knowledge in the expert clinical community with regard to the relative merits of two (or more) therapies for a given condition. If the expert clinical community is genuinely uncertain as to whether therapy A is superior or inferior to therapy B for the treatment of a given condition, considering both risks and benefits, then a state of clinical equipoise exists. Clinical equipoise exists even though some members of the expert clinical community earnestly believe that one of the therapies is superior to the other. Justification of a particular clinical trial necessarily requires that there can be no third therapy C that is known to be superior to A and B that is being withheld from trial subjects.

The underlying grounding for the concept of clinical equipoise is the 'duty to care' or the fiduciary responsibility of the physician to the patient. As Weijer and Freedman each envision 'clinical equipoise', it serves to enforce adherence to the duty to care in the design and conduct of clinical trials. Using this analytic tool Weijer reaches conclusions about the

[1] Levine RJ. Placebo controls in clinical trials of new therapies for conditions for which there are known effective treatments. In: Guess HA, Kleinman A, Kusek JW and Engel, LW (eds). *The Science of the Placebo: Toward an Interdisciplinary Research Agenda.* British Medical Journal Publications (In press).

conditions in which placebo controls can be justified that are nearly identical with mine (*infra*). In particular, he agrees that placebo controls are justified in certain circumstances in which "effective treatment exists but is not available due to cost or short supply."

The major difference between Weijer's conclusions and mine is that I find placebo controls ethically permissible in circumstances in which the withholding of known effective therapy would be extremely unlikely to result in an increased probability of death or of non-trivial disability. My position relies on an acceptance of my argument that there should be a threshold standard for invoking the requirement for the clinical equipoise justification. Below a certain level of risk the probability of doing any lasting damage to the patient-subject is so small that special justifications such as 'clinical equipoise' are unnecessary. This proposition is closely related to the law's *de minimis* doctrine; *de minimis non curat lex* or, the law does not concern itself about trifles or insignificant matters.

Weijer and some others ask: Can it be said that the fiduciary duty to the well-being of the patient exists only when the physician is doing things that increase the patient's likelihood of sustaining a non-trivial injury? And I reply, of course not. However, we already recognize the authority of the physician to conduct research involving patients when there is no possibility of benefit to the individual patient. This recognition is explicit in US federal regulations for the protection of human research subjects even when the subjects are incapable of informed consent if the permission of a responsible relative or the legal guardian is granted. The conduct of such research is clearly not justified by the duty to care. We find it ethically acceptable to allow the physician to perform non-therapeutic procedures or interventions to serve the interests of research when the goals are of sufficient importance and the risks are reasonable in relation to the expected benefits. To be consistent, we must equally find it ethically acceptable to allow the use of placebo controls even when there is a therapy other than the one being evaluated that is known to be effective when the goals are of sufficient importance and the risks are reasonable in relation to the expected benefits.

The concept of fiduciary requires undivided loyalty to the health interests of the patient. If the physician has or even appears to have any conflicting interests these must be disclosed. The patient, then, is enabled to make a choice of whether or not to become a subject with full awareness of the potential for divided loyalty. I do not mean to claim that informed consent is the answer to all such problems. It has long been known that many patients tend to think that anything proposed by a physician either is or could be intended by the physician to benefit the patient. (*13*). This is the phenomenon to which Appelbaum et al. gave the name 'therapeutic misconception' (*14,15)*. This does not mean that informed consent is not possible; rather it means that one should be especially careful when negotiating informed consent to complex activities such as controlled clinical trials in which there are both therapeutic and non-therapeutic components.

Many commentators have recommended that the inherent conflict between the aspirations of the medical practitioner and those of the medical researcher might best be managed by separating these two roles. One individual could serve in the role of treating physician while another could be the researcher. Most such recommendations have centered

on the problem of informed consent. I have generally resisted such proposals for reasons elaborated elsewhere (*16*). There are some cases, however, in which the potential for confusion might be sufficient to make such separation worthwhile. In most cases, formal clinical trials are not conducted by the patients' primary care physicians. Rather, patients are referred to specialists who are conducting clinical trials. This is almost invariably the case in developing countries where the research setting is obviously very different from the typical health care setting, particularly when the clinical trial is being conducted with sponsorship from a developed country.

In technologically developed countries, there is a common scenario, which is particularly problematic. Patients with certain chronic diseases (e.g. cancer, depression) are referred to a medical center with an expectation that there they will receive expert medical advice and, perhaps, treatment. Once there, they are invited by the specialists to become subjects in controlled clinical trials. This unexpected encounter may easily lead either to the therapeutic misconception or to a feeling of intimidation; either of these can tend to invalidate the process of informed consent (*16*).

I propose that certain clinical trials should be conducted in settings that are physically removed from the patient-care setting by investigators who have not previously had a therapeutic relationship with any of the patient-subjects. The investigators should make it very clear to the subjects that their principal occupation is to conduct clinical research. Such arrangements should be considered for all placebo-controlled trials designed to evaluate new therapies for diseases or conditions for which there are other therapies known to be at least partially effective. When withholding of the known effective therapy could result in a nontrivial adverse consequence, there should be a *prima facie* obligation to establish such a distinct clinical research setting. A *prima facie* obligation means that persons must act accordingly unless there are important ethical reasons to do otherwise.

Impact of the *Helsinki* revision

The *Declaration of Helsinki* has been violated routinely by medical researchers ever since it was first promulgated in 1964. Researchers who think about the requirements of *Helsinki* have noticed that their colleagues do research, for example, in the field of pathogenesis (forbidden by *Helsinki* V, Article III.2; *Helsinki* VI, Article 28) and use placebo controls in studies of new oral hypoglycemics. They have further noticed that these colleagues are not criticized as unethical. Rather, their research is rewarded by the traditional coins of the academic realm. The rewards include publication in respectable medical and scientific journals by editors who have proclaimed publicly their commitment to honor the *Declaration*. This includes its enjoinment against publication of reports of research conducted "not in accordance with [*Helsinki's*] principles." (*Helsinki* V, Article I.8; *Helsinki* VI, Article 27) Recognition that some articles of Helsinki are both routinely violated and widely believed to be erroneous tends to undermine the credibility and authority of the entire document. Researchers who notice that virtually everyone violates Article III.2 with impunity feel free to pick and choose among the other articles to see whether they wish to behave in accord with them.

The WMA deserves congratulations on the accomplishments reflected in *Helsinki* VI. Much language that was either faulty or archaic or both was replaced by more apposite wording. However, the two major flaws that provided the stimulus for this revision remain uncorrected: the distinction between therapeutic and non-therapeutic research and the excessively rigid proscription of placebo controls. I see no reason to suspect that the current iteration of these flawed articles in *Helsinki* VI will command any more respect than did their predecessors.

Conclusions: Recommendations

The use of placebo controls in clinical trials of new therapies should be permitted in the following circumstances and given the following conditions:

I. When the new therapy is being evaluated for the treatment of a disease or condition for which there is no existing therapy known to be at least partially effective. This should be understood as including clinical trials having as an inclusion criterion patients who have tried known existing therapies without success. It should further be understood to include patients who are aware of existing therapies and have rejected them for reasons other than a wish to enroll in a clinical trial. (For example, Jehovah's Witnesses have been enrolled in clinical trials of artificial blood substitutes after having rejected transfusions on religious grounds.)
II. When the new therapy is being evaluated for relief of symptoms and there are provisions in the protocol for allowing patient-subjects to withdraw from the study at any time. In such studies, the prospective subjects should be informed that if their reason for withdrawal is a desire to receive known effective symptomatic relief, this will be provided promptly.

III. When the new therapy is designed to treat a manifestation of disease that, if untreated, could eventually lead to death or nontrivial disability, and there are existing therapies that are at least partially effective in arresting or delaying the progression to death or disability, the use of placebo controls should be limited. There must be a demonstration that under the conditions of the trial withholding of the known effective therapy would be very unlikely to result in a serious adverse consequence. For example, studies of new antihypertensive agents employ reliable surrogate endpoints, recruit subjects with 'mild' hypertension who are very unlikely to have any serious adverse consequences even if untreated and unsupervised, are closely monitored and of relatively short duration. Under such conditions the probability of a serious adverse consequence is extremely small.

IV. When the new therapy is intended to be an inexpensive alternative to expensive therapies that are considered 'the best proven therapeutic method' in technologically developed countries and the research is to be carried out in a developing (resource poor) country with the assistance of sponsors or investigators from one or more of the wealthy countries, the clinical trial should be responsive to the health needs and priorities of the host country and the product being evaluated should meet the 'reasonable availability' and 'highest attainable and sustainable' standards. (In multinational research there are other

standards that must be met by the investigators and sponsors; these are beyond the scope of this discussion.)

V. In categories III and IV there should be good reasons to believe that the new therapy to be evaluated could be superior to existing and available therapies for at least some members of the patient population from which the subjects are to be recruited. When withholding of the known effective therapies could result in a nontrivial adverse consequence, there should be a *prima facie* obligation to establish the clinical trial in a distinct clinical research setting. Such a setting should be physically removed from the patient-care setting and the investigators should include no health care professionals who have previously had a therapeutic relationship with any of the patient-subjects. The investigators should make it very clear to the subjects that their principal occupation is to conduct clinical research.

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POLLS AND FOCUS GROUPS IN BIOETHICS: THE CASE OF RESOURCE ALLOCATION

Daniel Wikler

Introduction

Whose values should guide a society in allocating its health resources? One view, widely held, is that the values of the people in that society are what matter. In that case, part of the bioethicist's job will consist in trying to determine what these values are, using polls and focus groups, among other methods. This "democratic" understanding of the point of rationing contrasts with an "expert" view that would allocate resources according to a well worked-out, maximally consistent theory of justice supported by the balance of reasons. It is an "expert" view insofar as those who would be qualified to offer knowledgeable judgments on this would need to be experts, perhaps philosophers or economists.

My modest goal in this paper is to pose some problems for the "democratic" approach to rationing, if indeed that is the proper label for the view that directs us to base moral judgments on issues in bioethics such as health resource allocation and rationing. Those who recommend that we rely on polls, surveys, and focus groups are well-aware of the problem posed by the fact that most members of the public have not thought these issues through and may respond to polls in an unreflective manner. As such, their answers may change depending on how the questions are asked, what images, comparisons, and frames of reference happen to occupy their minds at the moment they are asked, and what other questions are asked in the same poll. Sophisticated advocates of the "democratic" view offer correctives to these flaws, such as giving respondents the opportunity to discuss their views with others and to alter their initial responses after deliberation. My argument will be that the problem goes deeper still, and that in the end the most qualified responses to polls and the like will be those of…the experts.

A "Framing Problem"?

Peter Ubel *(1)* and his associates, in a paper published recently in the *New England Journal of Medicine*, asked three sets of respondents to choose between two colon cancer screening programs. One program used a cheap, but insensitive test. The budget for the program would permit this test to be given to everyone in the target population, saving 1000 lives. The second program used a test which was twice as costly but more than twice as sensitive. The available budget would permit the test to be administered to only half the population, to be chosen at random, saving 1100 lives thereby. Majorities in two of the groups questioned - members of the public (selected from voter registration records), and members of the American Association of Bioethics-favored the first program. Members of

the Society for Medical Decision Making were largely in favor of the second plan. Ubel et al. reported *that "most of the study participants justified this recommendation on the basis of equity*." They conclude that "*People place greater importance on equity than is reflected by cost-effectiveness analysis. Basing health care priorities on cost-effectiveness may not be possible without incorporating explicit considerations of equity into cost-effectiveness analyses or the process used to develop health care policies on the basis of such analyses*."

This is an interesting result (and a very good teaching example), but the authors have drawn the wrong conclusion from their data. Though the majority of respondents in the first two groups claimed to prefer the first program over the second because it was more equitable, they were wrong in believing that it was (I will supply the argument shortly). Indeed, I will argue that the second plan was no less equitable than the first *in the sense of "equitable" understood and endorsed by these same respondents*. Their preference for the first plan on equity grounds, I claim, was a misperception and misjudgment. And it follows, I believe, that the investigators misrepresent the values of those polled in their admonitions to priority-setters.

My dogmatic claim that the first plan is not more equitable than the second can be secured by the following argument, which will be familiar to readers of this essay. Each member of the target population had an equal chance of being among the lucky 50% to be given the sensitive colon cancer test to be administered in the second plan. Similarly, each member of the target population had the same chance to be one of the unlucky ones destined to die of colon cancer whose disease would be missed by the insensitive screening test to be offered by the first plan. Both plans offered a gamble; each person had a better chance of being among the winners if the second plan was chosen.

Thus, in considering which of the two plans they might hope the public authorities would choose, each member of the target population had reason to hope that the second plan was chosen. And the same deliberation would have been in order if the target population had consisted of two people or (with the relevant modification of the scenario) only one. Each person would do better with a 1-in-2 chance for a test which was more than twice as sensitive than with an assurance of receiving the less sensitive test.

What does all this have to do with setting priorities according to the values of the public? I believe that Ubel's study, and the problem of its interpretation, point to a difficulty for those who would seek to follow the values of the public rather than those of "experts", as might be derived from a given theory of justice. This point follows, I believe, if we accept the following postulate (various qualifications are left unspecified for clarity's sake):

> *"Conflict Postulate"*: if an intervention is in the best interest of each person in a target population, and there is no conflict of interests between members of this population, then the issue of fairness cannot arise.

Since the choice of the second screening program is in the interests of every member of the target population, then if the "Conflict Postulate" is correct, it is not unfair. Thus the

first plan cannot be more fair. Thus any consistent respondent who prefers the first plan over the second plan on the grounds of greater fairness or equity must not accept the Conflict Postulate.

If this is correct, then we should conclude that the majority of people polled by Ubel et al. reject the Conflict Postulate, or else that their beliefs are inconsistent. My guess is that none of their respondents do in fact reject the Conflict Postulate; or, rather, none would reject it if it was carefully explained to them. That Postulate follows almost analytically from the general concept of fairness, which is concerned with the just resolution of conflicts of interest. Surely the respondents in the study done by Ubel et al. simply failed to understand that the Conflict Postulate entails that the second screening program is no less fair than the first. They are inconsistent, in the sense that they maintain that the first plan is fairer, yet endorse the Conflict Postulate, which entails that it is not.

These remarks are offered by way of justification of my dogmatic assertion that the first screening program is not fairer than the second. I would be loath to give up the Conflict Postulate, just as I am imagining that the participants in the polling done by Ubel et al. would be. (I would personally support the second program, since it saves more lives and is no less fair. I would assume that these same participants would reason similarly, but this is not part of my present argument).

If we were determined to set priorities according to the values of the public in this case, which values should we respect? We could, of course, simply point out the inconsistency to the respondents and ask them to resolve it. I have done that informally in lectures many times. In my experience, everyone accepts that the plans are equally fair, if browbeaten long enough. Perhaps the same would happen in an exercise in deliberative democracy, in which participants were given time to hash out differences of opinion and to refine their responses after consulting experts.

Whether these resolutions of the apparent inconsistency amount to creating preferences where they did not exist before, or (alternatively) better articulating preferences (on different choices) which had been present in their minds all the while, or both, will be answered differently depending on our views on what we think we are doing, and what we are getting, when we try to elicit values.*(2)* I have no expertise on this matter and profess no views. But I believe that we can address the moral question—how we should ration fairly, where we mean to follow the public's view of what is fair— without having to settle these kinds of questions.

May we assume that people generally will refuse to accept a view of what is fair that is riddled with contradictions and inconsistencies which are evident to them? This is a minimal "principle of charity" in interpretation. If so, the next step is to assume that people will generally refuse to accept a view of what is fair which is inconsistent, once these inconsistencies are pointed out to them. Again, this assumption of interpretation is so weak that we would be tempted to discount any respondent's account of justice if the assumption seemed unwarranted, i.e., if the individual seemed to be at ease with inconsistencies, since

it would be more likely that either the respondent or the questioner had failed to understand the other.

Consider, then, the responses of those in the first two groups studied by Ubel et al. The majority of people in both groups apparently found nothing inconsistent about preferring the first, universal program. But this, I would posit, is because they did not realize that this view of what is fair contradicts the Conflict Postulate, and once they did realize this, they would change their view. Since I think that no one who understands the Conflict Postulate will deny it, I would expect that they would abandon their support of the first program (as those who have had to submit to my browbeating all have done).

Now suppose that other responses to questions about person trade-offs and other attitudes about justice, fairness, and equity turn out to contradict other principles we all tend to hold to very firmly, as we do the Conflict Postulate. In that case, we would expect our respondents to strive to remove the inconsistencies. At each step, our moral understanding of what is fair would become still more coherent, and more consistent with principles we hold dear, where previously we had not seen that our "surface" judgments about fairness contradicted these "deep" principles.

At certain points, we may lose our way. Ubel's group, for example, in research not yet published[1], has found that members of the public seem ready to trade off efficiency (in terms of total numbers of lives saved) for what they perceive to be equity (giving everyone a chance to be saved), as long as "everyone" would be saved. They were less willing to tolerate the loss of efficiency otherwise, e.g., if "most people" (rather than "everyone") would be included, even if the number of people offered a chance to be saved were great. But Ubel et al. point out that whether or not a program offers a choice to "everyone" depends on how the relevant population is described. Arbitrary and equivalent redescriptions of the same interventions which seem not to offer a chance to "everyone" changed the respondents' answers to questions about trade-offs involving equity and efficacy.

These respondents seem confused, but even very sophisticated thinkers get confused about issues that bear a family resemblance. Brian Barry *(3)*, for example, points out that the fine principle of majority rule cannot resolve a crucial question that must be resolved before the vote: Which population is to be counted? Spain, as Barry points out, claims that the majority of Spaniards (including those who live on Gibraltar) want Gibraltar to be part of Spain, while the UK insists that the majority of those who live on Gibraltar want to remain part of the UK.

Or, to take a quite different example, Derek Parfit's *(4)* "Mere Addition Paradox" arises when we consider some imaginary worlds that differ in terms of the number of their inhabitants and also their relative well-being. First we think of a world in which, say, a billion people enjoy a high and equal level of well-being. Now consider a world like that, to which a million people are added who live lives barely worth living. If we can leave out side-effects, concentrating on the mere addition of a million people whose lives, though

[1] Ubel P, Baron J, Asch D. Preference for equity as a framing effect. 1999 Unpublished ms.

impoverished, are still preferable to death, how could the second world be in any way inferior to the first?

Ubel et al. deemed his respondents' manipulability on what counts as equity to be a framing effect, cautioning that "*we should be cautious about accepting people's preferences for equity at face value, because their preferences could be abandoned if the situation is described differently*." But

I think we can go further than this. If we are to ration according to what the public thinks is fair, our fidelity to the public's view of fairness should extend beyond the responses of people in polls, or in deliberative democracy exercises. We should also respect their deeply held principles (which they may not be able to articulate spontaneously) and also what we might call their "meta-principles", the rules governing the resolution of internal contradictions and conflicts in one's own moral views. That our views be consistent is the weakest of these.

As everyone who has thought hard about ethics knows (and those who have taught ethics know particularly well), hardly anyone has his or her house in order when it comes to moral concepts. Objections abound, no matter which moral view one espouses, and cannot be lightly dismissed. As we instill order among our moral beliefs, altering some and discarding others to make them fit, we may stray far from our initial positions on particular choices and trade-offs. The goal of this activity is to arrive at what we think is right, or fair, or just, all things considered. A lifetime is too short for most of us to engage in this pursuit with complete success, even if we make our living doing it.

In trying to determine what the public thinks is fair, we ask questions about trade-offs. Some of the answers are inconsistent, or shift when the questions are differently framed; these answers we distrust, since they do not represent a coherent moral point of view. But for the same reason, I believe, we should view a respondent's answers to questions about fairness as satisfactory only to the extent that they cohere with deep principles, meta-principles, and judgments on topics we have not yet asked about, not to mention a clear understanding of the empirical facts which may be relevant to the trade-off. This is because each of us will reject particular moral judgments which do not thus cohere, if we can be made to appreciate that they do not. If we do endorse this standard, then a particular moral judgement (e.g. in response to a PTO question) ought not to be ascribed to us as "ours", without qualification, since "our" view is that view at which we would arrive upon ironing out the inconsistencies and other contaminants within the jumble of particular moral view and opinions which we carry around unreflectively. The particular trade-off we endorse in answer to a poller's query should count as "our" moral view only if it survives once this process of ironing-out has occurred.

But this is to describe a path which terminates not in a poll but in a moral theory (in the present instance, a theory of justice), i.e., the maximally comprehensive and consistent ordering of a moral outlook. If this is right, then what we should be after when we vow to ration according to what the public thinks is just the moral theory which the public would

arrive at if given all the time, smarts, and energy needed to do this job. That is, to be very able moral philosophers, economists, or others who do this kind of thing for a living.

We could graph the progress which a given respondent might make in achieving internal consistency, coherence and comprehensiveness in his moral view: the initial effort, a grab-bag of contradictory and ill-considered values, prejudices, and preferences, yielding to a better-ordered set of priorities in which blatant contradictions are absent, giving way in turn to a more comprehensive set of values which accord with deeply-held postulates and axioms. In contemporary work on public beliefs about fairness in health care allocation, not just any responses will do. Obvious contradictions are not accepted as indicators of values the respondents actually hold, and, as in the new work by Ubel et al., there is an effort to detect framing effects. In my view, there is no reason to stop there; if we have reason to believe that the respondents would endorse a deep postulate, such as the "Conflict Postulate", or a particular meta-principle, then those of their responses which contradict these propositions should be ignored as well. The progress chart will show an asymptotic curve upward toward theoretical sophistication; the higher reaches of this graph are populated by the professional theorists.

The problem, if we are trying to ration according to what the public thinks is fair, is that few members of the public have ever done such an examination and rectification of their beliefs about justice, and they certainly do not have the time nor the means to do so in the course of a poll. Deliberative democracy, involving hours or even days of education and mutual criticism, may help, but there is no particular reason to think that the products of those exercises are immune to intellectual criticism. If they were, then we would engage in these exercises to do moral philosophy. So far, philosophers' and economists' jobs are safe. If, in trying to decide what counts as fair or equitable rationing, we are asked to choose between an elegant theoretical account and the results of a poll, PTO result, or deliberative democracy exercise, these considerations score one for the former.

A Different Role for Democracy in Rationing?

Why, when we must ration health care resources, should we be interested in what the public thinks is just? There might be any number of reasons. We might think it is our job to fulfil these preferences, on a par with any other preferences. We might wish to avoid the frustration which could be felt if these preferences are ignored. We might worry about the need to build popular support for the rationing which must be done.

Or we might believe that rationing should be democratic in some appropriate sense. Democratic priority-setting is the opposite pole from "expert" priority-setting, in which the work is done by paid thinkers. But I have argued that the same reasoning that lead us to reject public input when it is blatantly inconsistent, or reflective of framing effects, lends support to the kind of intellectual work these questions about priorities that only philosophers, economists, and other paid thinkers have the means to do.

Does this suggest that priority setting should be turned over to the experts? One very important reason to reject that idea is that, for all their hard work and even with the

luxury of time and a modicum of intellectual ability, these experts do not agree among themselves. Their views, if they have done their work well, may be free from obvious internal contradiction. But still they differ. They may start out from different premises and axioms, or there may be radically different ways of working out the implications of axioms we think we share, or perhaps morality has room for multiple, internally-consistent, mutually-inconsistent theories.

This is hardly an ideal situation for anyone who wants to ration in accordance with what the public values. I've argued that what the public values should be understood as the moral theory that the public would come to if it did the intellectual labor that theory building entails. But I have to concede that theory building is not enough, if only because those who do this kind of work for a living do not end up with the same theories.

So is there nothing that can be certified as "what the public values," even if we make the simplifying (and of course wrong) assumption that people have the same values? I do think that my argument suggests this. How do we ration in accord with what the public values, then? The only answer I can offer is that we should, first, begin with axioms and premises which are arguably those of the public, and beyond this that we try to come up with the best theory we can, from these premises. Unfortunately, thinkers will differ over whether their premises are in fact ones shared by the public, and not all will accept this picture of theory-building that begins with a set of premises. In any case, what this amounts to is paid thinkers who deal in arguments - challenges to their views which prod them into greater consistency and comprehensiveness. That is to say, the work of experts, which earlier seemed to be the view *opposed* to the democratic approach.

But this is not to enthrone experts. What counts is not who they are, but how good their arguments are. Rationing to achieve a just allocation of resources, in this view, should be guided by the best arguments. In criticizing the idea of basing rationing decisions on the results of polls, focus groups, and democratic deliberations, I might seem to be arguing for an elitist solution. If what counts are the arguments, however, the status of the rationer is of no particular importance. We are kept accountable by our acceptance of the authority of reason. Perhaps this salvages something of the democratic appeal of the polls and focus groups.

I would like to close with three concessions and a suggestion for a different way to ration democratically.

The first concession (and this may be a very big one) is that PTO exercises, deliberative democracy, and other kinds of polling may yet detect wide areas of common agreement on priorities for the allocation of health care resources, shared values which are not demonstrably inconsistent with deep principles, meta-principles, or empirical facts. The example I have taken from Ubel et al. might be anomalous. In this case, my remarks have limited application.

The second concession is that even if my argument about the limits of democratic approaches to priority-setting is valid, it would show only that we should be modest in any

claims about rationing according to what the public thinks is fair. There still may be very good reasons to go through democratic priority-setting exercises, even if the result is not priority-setting according to what the public thinks is fair. Democratic approaches have other virtues and benefits. I have mentioned these earlier in the paper.

The third concession is that a democratic approach may be the best way of setting priorities if we cannot make progress through intellectual work and argument. If our best theories are indeterminate or mutually contradictory, there may not be a way of resolving uncertainties by further argument. In that case, a democratic approach can determine the outcome and may be better, for reasons alluded to above, than other available mechanisms.

My final suggestion and last point is that there are ways of aspiring to democratic modes of rationing which do not necessarily involve polling or focus groups. A different (and quite familiar) approach would employ representative government and institutions of the civil society. The basic mechanism is for members of the public to support officials, parties, and organizations that they have good reason to believe have their interests and values at heart. A steelworker, for example, might trust his union; a nun, her church. These institutions and other representatives then take it upon themselves to learn, through data gathering and intellectual work, which kinds of policies, including health care priorities, best protect the interests and values of those whom they serve. The represented can expect that in some instances the representatives will press for policies which do not seem to accord with the opinions of the represented; the latter may not even understand them. But if the trust is present, a division of labor which assigns the role of the priority-setting to the representatives may protect and advance the interests of the represented far better than a process of priority setting via focus groups involving the represented. This approach requires that there exist institutions which have this kind of trust, and which merit it.

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THE RELEVANCE OF EMPIRICAL RESEARCH FOR BIOETHICS

Ezekiel J. Emanuel

To many especially those outside of bioethics, bioethics focuses on analyzing cases, delineating ethical principles that apply to the cases, and determining what is right—or more often just laying out the arguments on each side and not actually rendering a judgment. Indeed, the two most common criticisms of bioethics is that it is divorced from reality and the actual issues that arise in medical practice, research, and health policy debates and secondly that bioethicists are willing to layout arguments but skittish about actually deciding anything. One symbol of this divorce from reality, it is said, is the lack of engagement with empirical data.

This is an out-dated view of bioethics. First, it is important to recognize that articulating principles and good conceptual analysis are critical to good empiric research. Carefully delineating the essential aspects of concepts, defining the key questions, are essential to reliable empiric data. Thus, the conventional view of bioethics is integral to advancing empiric data. The issue is not whether bioethics should focus on conceptual analysis or empiric research but that it must focus on both.

Second, this claim about the role of empiric research in bioethics is empirically inaccurate. Over the last 15 years or so, there has been a substantial amount of empiric research in bioethics focusing on two main areas. The bulk of the early bioethical empiric research focused on end of life care, especially the use of DNR orders, advance directives, and informed consent. *(1 – 9)* Over the last few years not only has there been an expansion in the amount of empiric research but also an expansion in the range of bioethical issues researched, from confidentiality to genetics to health policy issues.

I believe empiric bioethics research serves three essential functions and that it enriches bioethics. The three functions are: 1) debunking widely held but erroneous views; 2) assessing the importance of ethical concerns; and 3) facilitating the realization of certain ethical values. Let us consider examples which illuminate how empiric bioethical research fulfills each of these functions.

Debunk erroneous views

One of the bioethical issues in which empiric research has had its biggest impact is regarding euthanasia and physician-assisted suicide. Over the last decade, the public and legal debate of this issue has included many assertions that can be evaluated empirically. Some of these assertions include that a slippery slope will inevitably result from permitting euthanasia or PAS, that safeguards can prevent abuse, and that these interventions can

relieve extreme pain and suffering. Fortunately this topic has had a substantial amount of excellent empiric research from groups in the U.S., Canada, Australia, and several European countries, especially the Netherlands and Belgium.[1] *(10 – 19)* Indeed it might be said to be a model of empiric bioethical research that should be emulated in other areas.

One of the more important roles of empiric data in this debate has been on the role of euthanasia and PAS in relieving pain and suffering. In the debate, it is widely claimed that pain is the key motivating factor for requests of euthanasia and/or PAS. For instance, a U.S. federal court of appeals argued that:

> Certainly, few decisions are more personal, intimate, or important than the decision to end one's life, especially when the reason for doing so is to avoid excessive and protracted pain. *(20)*

> In this the court was not expressing an isolated, idiosyncratic view, but the common perception of reasons dying patients would have to request euthanasia or PAS.

Empiric data has been critical in showing that this view is simply wrong and unrelated to reality. Pain is not the main or even a predominant reason patients desire or request euthanasia or PAS, depression is. Almost all of the studies that have interviewed patients who might use euthanasia or PAS—patients with HIV/AIDS, cancer and amyotrophic lateral sclerosis—as well as the interviews with physicians who have administered euthanasia and PAS have shown that pain is not a predictor of patients' interest in euthanasia or PAS. For instance, among the patients receiving PAS in Oregon only 1 of 15 had uncontrolled pain.*(21,22)* Breitbart et al. reported that pain, pain intensity and pain related functional impairment were not statistically associated with interest in PAS among HIV/AIDS patients.*(23)* Emanuel et al. reported that for oncology patients pain was not associated with personal interest in euthanasia or PAS.*(24)* However, they did find that for terminally ill patients pain was among the factors associated with personally considering euthanasia or PAS. Similar data exists for the Netherlands. In their 1990 study, the data demonstrate that for fewer than half the patients who received euthanasia was pain a factor in the decision and for less than 10% was pain the sole factor motivating the request for euthanasia or PAS.

Rather than pain, the empiric data demonstrate that depression, hopelessness, and general psychological distress are consistently associated with interest in PAS and euthanasia . Breitbart et al. reported that depression and hopelessness were strongly related to interest in PAS for HIV/AIDS patients.*(3)* Emanuel et al. reported that both for oncology patients

[1] Emanuel EJ. Euthanasia and Physician-assisted Suicide: A Review of Empiric Data from the United States. *Archives of Internal Medicine* 2002; (in press).

and terminally ill patients more generally depressive symptoms were factors most strongly associated with personal interest in euthanasia or PAS such as discussing these interventions and hoarding drugs for the purpose of PAS.*(4,25)* Ganzini et al. reported that hopelessness, but not depression, was associated with "*considering taking a prescription for a medicine whose sole purpose was to end my life."(26)*

These data strongly suggest that the prevailing conventional wisdom about the reasons that motivate patients to desire or request euthanasia or PAS are wrong. Furthermore, they suggest that two of the theoretical justifications for euthanasia are not support by the prevailing practices. That is, they suggest that the autonomy of terminally ill patients who express interest in or request euthanasia or PAS may be undermined by depression, and that using euthanasia or PAS to relieve pain is also not what motivates patients. That these data derive from a number of researchers with different patient populations, using slightly different measures, asking slightly different questions, and in different countries strengthens the likelihood that they are not an artifact but correctly reflect reality. What these data strongly suggest is that there are widely held views that are simply wrong. Further they suggest that anyone using the relief of pain as a justification for permitting or legalizing euthanasia or PAS should be treated with skepticism.

A second way in which empiric data on euthanasia or PAS debunk prevailing wisdom is the view that these interventions are quick, painless, and flawless. Since the 1870s, euthanasia and PAS have been portrayed and endorsed as quick, flawless, and painless ways to end terrible pain and suffering. *(27)* One of the survey questions used since the 1950s puts it*: "When a person has a disease that cannot be cured, do you think doctors should be allowed by law to end a patient's life by some painless means if a patient and his family request it?*"(emphasis added). The problem is that this may not be true at all—it may be more an illusory hope than well considered reality. All medical interventions have complications and problems and can be painful. Even relatively simple ones like drawing venous bloods or placing a naso-gastric tube, can cause pain and have complications. Why should anyone who considers the matter for a minute expect that administering interventions to intentionally end a patient's life will be quick, painless, and flawless?

Empiric data from the United States and the Netherlands suggests that in this respect euthanasia and PAS are similar to all other medical interventions. Emanuel et al. reported that in 15% of cases of PAS failed; that is, patients were given a prescription, attempted suicide but did not die. *(28)* Ganzini et al. recently reported that there were no failed PAS attempts in Oregon since legalization. *(29)* And the reports from the first two year's experience by the Oregon Health Division also report no "failed" PAS attempts. *(30)* As Nuland notes, the lack of problems with PAS in these reports from Oregon contrasts with the recently reported Dutch experience. *(31,17)* In nearly 13% of euthanasia cases there were technical problems, complications, or problems with death. Ironically, PAS, which is more palatable in the US, had problems in significantly more cases. The Dutch data show

that in 7% of PAS cases had complications and in 16% it was taking "longer than expected." In 18.4% of PAS cases in the Netherlands, physicians intervened to administer lethal medications, converting PAS cases into euthanasia. Sometimes the patients cannot actually swallow all the medications necessary to end their lives; sometimes they vomit the medications up; sometimes even after taking the proper medications, the patients do not become comatose, or awake from coma. Other times patients simply do not die requiring that PAS be converted into euthanasia.

These data indicate that like all complex medical interventions, euthanasia and PAS are not foolproof. They are not the guarantee of a quick, painless death portrayed. This is another example of how empiric data debunk widely held but erroneous views.

Assessing the importance of ethical concerns

In addition to debunking erroneous views, empiric bioethical research can help determine what concerns are significant and which concerns are minor. This is more important than most people acknowledge. Usually in debates about any particular bioethical issue there is not just one value at stake. More commonly there are competing values that must be balanced or weighed or specified and this balancing must then be operationalized in practice. For instance, in human subjects research there is a complex balancing of the values of informed consent, fair subject selection, minimizing risk, and the claims of scientific progress. Similarly, in the issue of allocating scarce resources there is the common dilemma of balancing the health needs and choices of one person with the needs of the larger community paying for the health care services. Even in the area of informed consent there is the conflict between comprehensiveness and comprehension of information disclosed. Whether acknowledged or not, selecting a particular approach to bioethical issues inevitably entails emphasizing one set of values while minimizing others when there are good arguments for each set of the values.

One issue in which empiric research can be helpful, but has not yet widely occurred, is regarding the issue of the use of stored biological specimens. Over the last 5 years or so, there has been increasing discussion and proposals about restricting the use of stored biological specimens for research purposes. In the U.S. at least, there are hundreds of millions of samples.*(32)* For decades they have been widely used for path-breaking research. For instance, the landmark study of the importance of angiogenesis in predicting cancer spread and survival was conducted on just over 100 breast cancer tissue blocks originally collected as part of diagnostic and therapeutic procedures.*(33)* Historically, in the US such research was exempt from regulations, especially from the need to obtain informed consent from the patients or research subjects whose samples were being used as long as the sources of the sample cannot be "identified directly or through identifiers linked to the samples." Beginning with the 1995 report by Clayton and colleagues, this policy and the practices it has generated have been strongly criticized.*(34)* Some argue that informed consent for the use of stored

biological samples is necessary in order to respect the patients' right to control the use of their samples, the right to decide whether their samples will be used, for what types of research, and by which researchers. There is also the issue of providing the results from the research on the stored sample to patients. Some argue patients are entitled to the information, others argue that the need to inform patients usually "does not apply to research using human biological materials."

The use of stored biological specimens is clearly one issue that balances many values—respect for individual's views and wishes, efficiency of research, perceptions about the importance of violations of confidentiality and other risks. More importantly, I want to argue that empiric data is a key to determining the appropriate policy on this matter. Why? Much of the debate centers on what people think it means to respect patients' wishes and interests. Is obtaining consent for each use of stored sample key to respect? Is providing research results key to respect? This will depend to a large degree on what people think is critical to respecting them. It is not a theoretical question. More importantly, deciding what information to provide in an informed consent and what choices or options to present to patients depends upon what a reasonable person would want to know before making such a choice. As much as bioethicists might believe, their intuitions are hardly those of the prototypical "reasonable person."

Interestingly, despite more than 5 years of debate about these points, there has been not one published study assessing empirically what people who have stored biological samples think. The extent of the empiric research has been "mini hearing" by the National Bioethics Advisory Commission in seven U.S. cities. The speakers were not randomly selected, or otherwise thought to be representative, and their views were not generalizable to any group.

David Wendler at the NIH has sought to remedy this deficiency with a survey of 504 individuals—246 individuals who are participating in research studies related to being at risk for Alzheimer's disease at four geographically distributed institutions and 258 Medicare beneficiaries.[2] The people enrolled in the research study had all provided samples that would be stored and used for future research. The data are quite revealing. First, they show that there are no differences in views between the two different groups. Participating in research and having stored biological specimens does not seem to influence people's views. Second, two-thirds of people thought their consent was necessary for research using samples with identifiers when the sample was obtained from clinical care, such as a pathology specimen from an operation or saved blood sample. Conversely, only 12% thought consent should be required for anonymized samples that were originally obtained as part of research.

[2] Wendler D, Emanuel EJ. The Debate Over Research on Stored Biological Samples: What do Sources Think? *Archives of Internal Medicine* 2002 (in press).

Interestingly, only 27% thought consent should be obtained for anonymized samples obtained as part of clinical care and a similar 29% thought consent should be obtained for research samples that contained identifiers.

Third, few people thought it made a difference whether consent should be required if the disease was different from that in which it was originally collected. For instance, only 8% of those people in the research studies who thought consent was not necessary to use anonymized research samples thought consent necessary if the research was on diabetes rather than Alzheimer's disease. Fourth, nearly 90% of respondents wanted to be informed of the results even if the results were of uncertain clinical significance.

What do these data mean? Let's highlight four implications. First, consent is research-dependent, not dependent upon whether there are identifiers linked to the biological specimen or not and not dependent upon the absolute risks involved since people seem to permit research-derived identified samples at the same rate as clinically-derived anonymized samples. The distinctions people make are more subtle than identifiers or not, it seems to trace to whether they ever gave consent to use the samples for clinical research. Second, once consent is given for participation in research additional consents for each use of the sample in each different type of study seems unnecessary. Thus asking—as recommended by the U.S. National Action Plan on Breast Cancer—whether a person wants a sample used for different types of research, by different investigators, etc., seems irrelevant to people. This means that the complex forms now being propagated unnecessarily complicated the consent process without adding options that seem to be ethically meaningful to patients. Third, the data suggest that to address the concerns of the large minority of patients who desire consent for use of anonymized clinical samples or identified research samples an opt-out option should be utilized such that investigators make a good faith effort to contact people and provide them an option to decline to have their sample used. But if there is no response, the stored biological specimen can be used for clinical research. Interestingly this is not an option widely considered in the current debate.

Finally, people want the results of research on their samples. This seems to conflict with a number of recommendations that clinically ambiguous data should not be given to people.

I think this example indicates how empiric bioethical research can help determine what ethical values are important and which are not in formulating policy options. It suggests that many of the claims made on the basis of theory may not agree with the values of people who are subjected to policies and practices recommended by bioethicists without data.

Realizing ethical values

These examples of the use of stored biological samples also suggest that empiric data may be important in realizing ethical values such as respect. To know whether providing information about research results back to people is part of respect is not really a theoretic

question but one that depends upon how people view the withholding of data derived from their own samples.

Another case of how empiric data might be critical to realizing ethical values comes from the area of health policy and the allocation of scarce resources. What health care services should be provided to citizens as part of a just health care system has been quite controversial. One theory is that justice requires providing each person a voucher with which they could purchase health insurance. Assuming the amount provided in the voucher is determined fairly, the health care services they would then purchase would constitute a just package of health care services to be socially guaranteed, i.e. the services citizens would be entitled to as a matter of social justice. Philosophers, such as Ronald Dworkin, as well as health policy experts, such as David Eddy, have been drawn to this model. *(35 – 37)* Each commentator provides various refinements and permutations on this basic scheme, including refining how much the voucher is worth, whether the people know their health status, what other information is withheld from the people, etc. Cosmetic surgery and care in a persistent vegetative state are easily excluded while vaccines and therapeutic interventions that are always curative and/or life savings without residual deficits or disabilities, such as antibiotics for otitis media or appendectomies, are also almost always absolutely included. Beyond these simple answers, however, almost nothing more substantive is able to be derived about what services should be covered and which should not. The fact is that sitting in our chair in that proverbial ivory tower—having been relatively healthy and not having confronted substantial illness—makes it hard for us to work out what services prudent people would purchase and which services they would forego. And yet this is critical for the theory to have any practical importance, especially to be a guide for determining whether certain packages—say the group of Medicare benefits or Medicaid benefits or Oregon's proposed list—are just.

My colleague at the NIH, Marion Danis along with Susan Dorr Goold from the University of Michigan have decided to remedy this data deficit. They developed a game called CHAT—Choosing Health Care All Together—in which people are given 50 pegs and must select from among 15 different types of services that range from primary care, hospitalization, and specialist care to infertility services, mental health services, last chance therapies, experimental therapies, eye care, and pharmaceutical coverage.[3] To model the scarcity of resources people have more options of services than pegs. Indeed the 50 pegs cover only about 60% of available options. They have made sure the pegs and choices are actuarially correct—that is, they reflect the real cost of providing each type of service. In addition, once choices are made, people literally "roll the dice" to see how they might be afflicted by a health problem and learn how the service package they selected would cover them. This provides people with some sense of the consequences of their choices.

[3] Danis M, Biddle AK, Goold SD. Insurance Benefit Preferences of the Low-income Uninsured. *JGIM* 2002; 17: (in press).

In an interesting permutation, Danis and Goold run the game allowing each individual to choose the services he or she would want, they then run it with groups of 3 people making the choice of services together, and they then run it with groups of 12-15 people making the choice of services together. Several important results have emerged from preliminary runs of the game in North Carolina and in Minnesota. First, the game provides people with an experience of real tradeoffs but also an experience of deliberating about health care coverage with others. It can show how much importance people place on access to specialists, or pharmacy benefits or desire for last chance therapies. In many cases these choices may not reflect what the experts think. But the CHAT game can provide data on what services those who are to be covered want covered—and this is an important breakthrough on the abstract model.

Second, people in groups make different choices than people individually. People trade off and are comfortable trading off things they prefer with what the group thinks best. Third, choices do vary by some predictors, but probably the most interesting variation has been on willingness to cover the uninsured—an unending and embarrassing problem in the USA. It turns out that people in Minnesota are very willing to provide some of their pegs to ensure that the uninsured receive health care services too. Conversely the people in North Carolina are much less willing to do so. Finally, it does appear that this kind of game can be used to help develop basic health care coverage plans and might be used in some Medicaid experiments.

A Caveat

While emphasizing the importance of empiric data to address certain bioethical questions, I want to clarify certain points. First, I am not saying, to hijack a phrase, "data makes right." But in certain—and I might say many—issues and dilemmas there are claims about what people want or think or what their practices are or what respect or beneficence means. In these cases, data are necessary to determine the shape and structure of the normatively correct positions. Further in many cases data are necessary to know how to apply very abstract and vague philosophical claims—like what services people should receive as a matter of justice.

Second, I do not want to be seen as endorsing all data. Much empiric bioethical research is nothing short of junk. Like all types of research, empiric bioethics research can be done poorly making the results worthless. Emphasizing the importance of empiric research does not mean endorsing everything that is empiric bioethics research. I want to emphasize only quality. Fortunately there is sufficient quality—among the junk—to justify the importance of empiric bioethics research.

Finally, let me say a few words about areas that I think could use additional empiric bioethics research. Multi-national clinical research has been severely criticized recently for

its ethical lapses. For instance it is commonly said that informed consent in developing countries is worthless because subjects are not informed and are coerced to enroll in research by their desperate situation. This may be true but there is woefully little data on this claim. There are just a handful of studies—none very good—assessing the quality of informed consent in research projects conducted in developing countries. *(38, 39)* There is data on literally one question published that deals with the issue of whether people in developing countries are coerced into participating in research. *(40)* Obviously, we need substantially more research on these issues.

Another area in need of substantial research is allocation decisions by physicians and families. We know that there are a myriad of micro-allocation decisions made all the time. Yet we know almost nothing about how these decisions are made, what values are utilized, and whether they are even perceived to be ethical in nature.

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