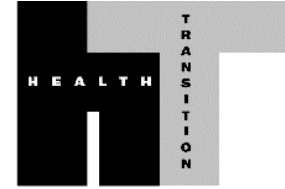


Rationalizing health care in a changing world: the need to know



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Abstract

The World Development Report 1993 announced that global life expectancy was then 65. Experience in the developed world suggests that the World Health Organization's dictum, 'health is a state of complete physical, mental and social well-being', is simply not attainable for the foreseeable future. As physical health has improved, mental problems have become more prominent and a sense of well-being has declined. Furthermore, as the population ages and medical technology improves, the cost of health care grows almost exponentially. Since the population of the developed world is continuing to age and aging is spreading rapidly throughout the developing world, knowledge is the principal way of dealing with this seemingly intractable problem: we must know, quantitatively, the age-specific causes of ill health, and we must know which means of prevention and treatment are effective. Finally, we must apply that knowledge rationally

The first childhood of humankind essentially began when primates descended from the trees millions of years ago; it lasted until about the end of the nineteenth century when life expectancy began to rise in the Western world. It began to accelerate only about 50 years ago and touched the developing world only in the last 30 years. Richard Peto found that half the population was dead before the age of 40 in the pre-agricultural Palaeolithic and agricultural Neolithic periods, in a Roman colony in North Africa, in old rural Britain (pre-industrial revolution) and in tropical Africa only a short time ago (R. Peto, personal communication). A Rockefeller Foundation meeting in 1985 called *Good Health at Low Cost* made us aware that three of the poorest areas in the world, China, Sri Lanka, and India's Kerala State, had verifiable life expectancies of 65 (Halstead, Walsh and Warren 1985). In 1988 at a conference in Bellagio, Caldwell gave this ubiquitous aging process both a name, the 'health transition', and a formula encompassing the demographic transition with its decrease in infectious disease mortality and decline in fertility, and the epidemiological transition with its aging population and increase in chronic non-communicable diseases.

In 1993 the *World Development Report: Investing in Health* trumpeted the startling statistic that global life expectancy had achieved 65: China's had leapt to 69, Sri Lanka's to 71 and the composite figure for all of Latin America and the Caribbean had reached 70. In China the communicable, non-communicable and injury related deaths were respectively 13, 77 and 10 per cent, and in India 35, 57 and 8 per cent. In the last 50 years humankind in the aggregate has undergone a startling transition from a child-based to an aging population rapidly moving towards its second childhood.

These massive transformations, due to a combination of social, political, economic and medical changes, have resulted in a population explosion which, in turn, is having major environmental effects. Moreover, the economies of the developed world of the North are

being threatened by the high cost of health care delivery, while those of the developing world of the South cannot even begin to afford the profligate health care systems and technologies adopted by the governments of the North. Paradoxically, the World Health Organization's famous dictum that 'Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity', is proving to be a more and more tenuous goal. As physical well-being has increased in Europe and North America, mental illness has become more prominent. In fact 'mental illness and handicap' was the most prevalent condition, based on morbidity indicators as well as mortality rates, in Black and Pole's (1975) pioneering study of the relative burden of disease in the United Kingdom. As social well-being has improved, both within and among nations, the disparity between wealth and poverty has become more pronounced. For instance, life expectancy at birth in the poverty-stricken areas of many inner cities in the United States is comparable to that of parts of Africa (McCord and Freeman 1990). Finally, as people live longer and healthier lives they become more disgruntled with medicine and health care, as described

Although the collective health of the nation [USA] has improved dramatically in the past 30 years, surveys reveal declining satisfaction with personal health during the same period. Increasingly, respondents report greater numbers of disturbing somatic symptoms, more disability, and more feelings of general illness (Barsky 1988).

A key necessity in dealing with these complex matters is the gathering of valid data on factors as crucial as the age-specific prevalence of the diseases occurring in the areas of concern, and the relative efficacy of the interventions used to diagnose, treat and prevent them. Strategies for maintaining health and ameliorating disease must be based on knowledge; 'need to know' is an essential part of the process. During this century many conflicting health concepts and strategies have been advocated. These were often based on erroneous scientific, epidemiologic, demographic or economic data. Moreover, many national, regional and even global projects were launched on the basis of these ideas, but, for the most part, their outcomes were disappointing.

Concepts and crusades

From the beginning of the twentieth century there have been conflicting concepts on the diseases responsible for morbidity and mortality, their relative quantity and importance, and how to treat and prevent them. Withal there has been a constantly changing playing field as the disease spectrum has altered with socio-economic development. This began before the turn of the century in Europe and the United States. Only in the last few decades has it spread, at an unprecedentedly rapid rate, throughout the rest of the world. The fundamental change has been from high infant and child mortality rates due largely to infectious agents, to the chronic diseases of aging.

Over this span of more than 100 years there has been enormous controversy about what was going on, and on how to deal with those problems deemed to be of importance. During this age of metamorphosis academicians and bureaucrats were either unaware of it, ignored it, or vied with each other over the causes or the means of coping with it. As is usual in such situations, those involved were virtually all limited by their own professional points of view: biomedical, public health, agricultural, political, demographic, economic, sociological, even religious. The fundamental reality, however, was that almost all of them were right to a certain degree, but, unfortunately, most of them believed that their particular concept was the predominant or only one.

At the beginning of the twentieth century, when the colonial powers were concerned with the high mortality of their soldiers and administrators in the tropics, a major controversy erupted over whether the answer to the high death rate in young and healthy individuals lay in

biomedical research or public health application (Warren 1990). In 1898, Manson, the 'father of tropical medicine', stated:

I now firmly believe in the possibility of tropical colonization by the white races. Heat and moisture are not in themselves the direct causes of any important tropical disease. The direct causes of 99% of these diseases are germs. To kill them is simply a matter of knowledge (Manson 1898).

His student, discoverer of the means of transmission of malaria, and great adversary, Ross believed passionately that the main determinants of health were 'general living conditions, diet and sanitation.' Three decades later Ross conceded the battle:

I must say that I was rather disappointed with Manson's attitude towards the whole subject of prevention. He never seemed very keen on it and was chiefly interested in the parasitological side of the subject while I was interested more in the practical side ... The British Empire has generally followed his example during the last thirty years (Ross 1928).

At that time, the 1920s, the Rockefeller Foundation had begun its crusade to eradicate hookworm by a combination of chemotherapy, sanitation and education in '52 countries, 6 continents and 29 islands of the seas'. This was soon followed by a campaign led by Gorgas to eradicate yellow fever from its reservoirs in Latin America and Africa by mosquito control. But the greatest battle of them all was the World Health Organization's campaign from 1955 to 1970 to end transmission by a campaign in a short space of time that would eliminate the 'reservoir' of infected cases. Unfortunately, none of these magnificent initiatives achieved their ultimate goal, leading to general disillusionment with targeted campaigns driven by science and technology.

Thus, it was not surprising when Professor of Social Medicine, McKeown (1976), proclaimed, on the basis of his studies of changes in mortality in England and Wales from 1838 to 1970 that 'Medical measures of immunization and treatment were relatively ineffective; they were also unnecessary' (McKeown 1976). This point of view was reinforced by a working paper commissioned by the Rockefeller Foundation for a conference on Health and Population in Development (Grosse 1980). Using data gathered in Indonesia, this document reported multiple regression comparisons of life expectancy and infant mortality rates with a multiplicity of health, economic and social indicators. Its primary conclusion was that 'health inputs and sanitation facilities were less able to explain variations in levels of life expectancy than were social factors' (Grosse 1980), one being the availability of transistor radios.

Grosse's use of monolithic figures such as life expectancy in his working paper led to concern that, being composites of numerous diseases and other health-related factors, they do not permit a clear grasp of the issues or enable the development of specific strategies to control them. This concern resulted in another paper that, for the first time, tried to elucidate the specific killers of infants and children in the developing world. It revealed that the major causes of mortality were diarrhoeas (5-10 million per annum), respiratory infections (4-5), malaria (1.2), and measles (0.9) followed by schistosomiasis, whooping cough, tuberculosis, neonatal tetanus, diphtheria and hookworm (Walsh and Warren 1979). This quantitative compendium of the specific medical causes of infant and child mortality immediately suggested that a few low-cost 'technologies' — immunization, oral rehydration therapy, breastfeeding and antimalarial prophylaxis — might rapidly decrease infant and child mortality (Walsh and Warren 1979).

Unfortunately, this targeted approach was perceived to conflict with a major new strategy which had just been adopted by the World Health Organization at a conference in Alma Ata (1978). The meeting reaffirmed WHO's founding statement that 'health is a state of complete physical, mental and social well-being'. It then agreed that the means of achieving this lofty

goal was through primary health care, 'which reflects and evolves from the economic conditions and socio-cultural and political characteristics of the country and its communities' (WHO 1978). This broad approach included at least

education concerning prevailing health problems and the methods of preventing and controlling them; promotion of food supply and proper nutrition; an adequate supply of safe water and basic sanitation; maternal and child health care, including family planning; immunization against the major infectious diseases; prevention and control of locally endemic diseases; appropriate treatment of common diseases and injuries; and provision of essential drugs (WHO 1978).

Several years later, however, UNICEF announced its Children's Revolution which focused largely on four

social and scientific advances [that] now offer vital new opportunities for improving the nutrition and health of the world's children. For all four actions, the cost of the supplies and technology would be no more than a few dollars per child. Yet that could mean that literally hundreds of millions of young lives would be healthier. And within a decade, they could be saving the lives of 20,000 children each day. It is not the possibility of this kind of progress that is now in question. It is its priority (Grant 1983).

These four initiatives were oral rehydration therapy, universal child immunization, the promotion of breastfeeding, and growth charts (Grant 1983). When it appeared that this targeted 'vertical' approach called selective primary health care might be implemented, it was considered to be in conflict with the World Health Organization's 'horizontal,' comprehensive primary health care strategy and was widely and strongly condemned. Banerji (1986) of New Delhi found 'an ominous similarity between the spread of a highly malignant cancerous tumor and the promotion of the technocentric approach by western countries' (p. 1233). Rifkin and Walt (1986) of London criticized an approach 'based on medical and technological interventions'. They believed that

radical health improvement will only come after a long period in which changes must occur on both levels of social, economic and political structures and on the level of individual and community perceptions (Rifkin and Walt 1986).

Over the last decade things have begun to shake out. Most important of all was the realization that no one approach or factor is responsible for the remarkable improvements in health statistics. A great moment came at a major international meeting in Talloires, France in 1988 when the Director General of WHO drew four vertical lines perpendicular to one horizontal line, and averred that the former enhanced the latter by providing 'knowledge and motivation'. In one fell swoop, Mahler resolved the five-year controversy between selective and comprehensive primary health care. This illustrates what a fruitless and negative exercise it is to support one means of improving health at the expense of another. Nevertheless, polarization is still alive and well. A recent editorial in *The Lancet* (1995), 'Fortress WHO: breaching the ramparts for health's sake', again takes a one-sided approach. Attention is called to the preamble to WHO's constitution which

recognizes the morality of global health interdependence, calls for individual, community, and national action, identifies societal factors as the main determinant of health status, and encourages work to ensure the fundamental conditions in which all people can achieve physical, mental, and social well-being.

There is no mention of biomedical research and medical interventions as possible determinants of the health of populations.

In order to rationalize health care and to make it affordable and universal whether in children or the old, whether in poor countries or rich countries, it is essential to know the specific problems we are facing. We need to base our actions on facts not opinions. If the facts are not available then we need to know that, and we must do our very best to find out what is going on. Given the vast variety of options, we need to know which interventions are effective and what they cost.

What is going on ?

'The intellectual free lunch,' a recent article by Kinsley (1995) in the *New Yorker* describes a University of Maryland opinion poll on foreign aid. It found that 75 per cent of Americans believe that the United States spends too much on foreign aid, and 64 per cent want it cut. When asked how big a share of the federal budget goes to foreign aid the average answer was 18 per cent. When asked the appropriate level of spending, the median answer was 5 per cent, and when asked how much would be too little the median answer was 3 per cent. The correct answer is less than 1 per cent. Kinsley noted that

people are forming and expressing passionate views about foreign aid on the basis of no information at all. Or perhaps they think that the amount being spent on foreign aid is a matter of opinion, like everything else (Kinsley 1995).

He makes the reasonable suggestion that

it is not asking too much to expect a citizen to recognize that he or she **needs to know** that number, at least roughly, in order to have a valid opinion about whether it is too large or too small (Kinsley 1995).

It is particularly disheartening that not only the general public, but 'experts' in biomedical research, public health, economics, even politics, are prepared to present their opinions on matters about which they have little or no factual knowledge. Even worse, governmental and international agencies often develop policies based on little or no knowledge. This is compounded by the fact that the data-starved developing world is virtually bereft of up-to-date information.

In order to develop rational and cost-effective strategies for health care it is important to know why people are getting sick, and the best way of doing this is by studying the age-specific causes of mortality. Beginning with infants and children under five years of age, it was believed, since the turn of the century, that protozoan and helminth parasites were the most important causes of disease during childhood in the developing world. Moreover, malnutrition was considered to be the major underlying cause of mortality, supposedly leading to enhanced susceptibility to infectious agents. This opinion was greatly fostered by McKeown's (1976) claim that infectious diseases declined in the United Kingdom before the availability of vaccines and antibiotics. He ascribed this change to better nutrition due to greater food availability, and suggested that this was the principal cause of the observed decrease in mortality and consequent rise in population. Landers (1992) and others have recently discussed both the infectious disease and nutritional aspects of McKeown's theory and found them wanting, thereby refuting McKeown's claim that socio-economic development was virtually the only explanation for the rise of population. It was not until the magnificent studies of Mata (1978) in the village of Santa Maria Cauqu, in Guatemala that the crux of the problem became reversed, that is, repeated respiratory and diarrhoeal infections in very young children were the primary cause of malnutrition.

In the last several years those concerned with health in the developing world have realized that school-age children were particularly neglected. At a UNESCO meeting in 1989

it was suggested that ubiquitous infection by multiple helminth species in the tropics was the most important factor in poor primary school performance (Halloran, Bundy and Pollitt 1989). Fortunately, this realization came at a time when the development of several different types of oral, single-dose, non-toxic anthelmintic drugs made it possible to control virtually all of these infections at very low cost (Warren 1990). Soon thereafter micronutrient deficiency, especially in vitamin A, iron and iodine, was identified as another significant and easily remediable problem in this age group. The United Nations Development Programme, the Rockefeller Foundation, the James S. McDonnell Foundation, the Edna McConnell Clark Foundation and the World Health Organization have now organized a Partnership for Child Development that is exploring the effect of these problems on development and cognition, and inexpensive means of ameliorating them. A Scientific Coordinating Centre, led by Professor D.A.P. Bundy, has been established at Oxford University to provide expertise in the implementation and evaluation of school health programs in many countries in Asia, Africa and Latin America.

Young adults are now particularly prone to violent and accidental deaths. Furthermore, the remarkable spread of the almost invariably fatal Human Immunodeficiency Virus is having a major effect on mortality in this age group, especially in the developing world. There is very little at the moment that technology can do about these problems; they are now being dealt with largely by relatively inefficient social and political approaches.

In 1988 Walsh updated the data on the causes of mortality in the developing world for the United Nations Development Programme, but in this case included all age groups. While respiratory diseases came first, diseases of the circulatory system were second followed by diarrhoeal diseases, measles, injuries and neoplasms. Escovitz (1992) wrote of the health transition in developing countries in the context of a didactic role for specialists of internal medicine from the developed world. He pointed out the importance of gathering data on the prevalence, morbidity and mortality of the chronic diseases of the old, as had been done for the acute diseases of children. Furthermore, he spoke of the development of selective secondary and tertiary care strategies based on both effectiveness and affordability.

Which interventions are effective ?

In his book *Effectiveness and Efficiency* (1989) originally published in 1972, the great British epidemiologist, Cochrane, wrote:

When I was a medical student in London in the 1930s there was to be some rally about the possibility of a National Health Service in some London suburb, and I decided to go alone with my own banner. After considerable thought I wrote out my slogan: ALL EFFECTIVE TREATMENT MUST BE FREE. I had a deep inner feeling that this was absolutely right: although I doubt very much if I would have passed a viva on the meaning of 'effective'! The slogan, I regret to say, was a flop, ... but I still thought it had something (Cochrane 1989).

While this idea was quite remarkable, Cochrane simply could not lose. Thomas (1983) observed in his essay '1937 Internship' that hospitals were 'simply custodial'. 'Whether you survived or not depended on the natural history of the disease itself. Medicine made little or no difference'. Therefore, at the time when Cochrane carried his provocative banner very little effective treatment was available and the costs of health care based on this premise would have been minimal. The catch, however, was that in the 1930s there were no effective methods of determining whether a treatment was effective or not. It was not until the early 1940s that Austin Bradford Hill designed the randomized controlled trial to eliminate bias in the evaluation of interventions (Daniels and Hill 1952). The only other effective method is meta-analysis, which was developed by sociologists several decades ago to pool the results

from series of similar papers on the same subject. This powerful tool only began to be applied to medical interventions in the last ten to 15 years.

The problem with evaluating interventions is eliminating opinion based on personal experience, which almost always involves the observation of too few patients, and bias, which is often based on the laudable desire to achieve good results. At a recent New York Academy of Sciences meeting entitled *Doing More Good than Harm: The Evaluation of Health Care Interventions*, 1993, a variety of methods in addition to randomized controlled trials (RCTs) and meta-analyses (MAs) were evaluated. In 1977 the National Institutes of Health initiated a series of Consensus Conferences (Ferguson 1993) in response to the director Fredrickson's statement that

NIH and the rest of the scientific community must assume greater responsibility for the effect of research on the quality and cost of health care. The need for assuring effective transfer of useful new knowledge across the interface between biomedical research and the health care community and systems is a major issue.

The key to the process is a panel of scientists, clinicians, bibliometricians, and a public representative who are all interested in the general area, but have never done specific research on the problem. Because of its expense, no evaluation of the literature is done beforehand. Another approach, which is quite costly, was developed at the Rand Corporation; it begins with an exhaustive literature review, but then depends on a panel of nine distinguished practising physicians to decide which patients, if any, the procedures would benefit (Brook 1993). Finally, there is an approach with the particularly compelling name of 'outcome analysis'. It seems reasonable that if the outcomes of all interventions could be monitored, their efficacy would become immediately apparent. Unfortunately, this is simply not so, except in the simplest of situations where the results are particularly striking. Without randomized selection of patients and, in many cases the use of appropriate blinding, it is virtually impossible to eliminate opinion and bias. The usual outcome of outcome analysis is to follow-up interesting leads with randomized controlled trials.

Sir Richard Doll (1993) summed up the conference with these words: 'I conclude that we have need for both overviews (MAs) and large-scale simple randomized trials because they provide the only techniques for making small advances in the treatment of common conditions.' He added that if these matters were 'taken to heart by the profession and by those responsible for providing medical care [it] will ensure that the conference marks a turning point in the history of medicine in the developed world' (Wennberg et al. 1993).

A major advance in broadening the use of the best methods for evaluating interventions and the dissemination of the results thereof is the establishment of the Cochrane Centre in Oxford by the UK National Health Service Research and Development Programme. The Centre is led by Dr. Iain Chalmers, the senior editor of the first textbook of medicine, *Effective Care in Pregnancy and Childbirth* (1989), based on evidence largely provided by RCTs and MAs. His group also developed the computer software to prepare meta-analyses and to keep them up-to-date. An international network, the Cochrane Collaboration, has grown from this experience which prepares and maintains systematic reviews of RCTs covering all of the fields of medicine and health (Chalmers 1993). We now have the methods, both statistical and digital, for determining the effectiveness of treatment, and groups such as the Cochrane Collaboration are making a critical mass of such crucial information available, and keeping it current.

This leads to us to one area that is almost studiously avoided: the enormous utilization of alternative medical systems, not only in the developing world but the developed world as well. In China there is the vast, sanctioned world of traditional medicine. India has Ayurvedic medicine, for which 'Western medicine' may be the alternative. In the United Kingdom it is

well known that many members of the royal family, among others, have an interest in alternative medicine. For the United States, a recent study has examined alternative, unconventional, unorthodox forms of medicine, including relaxation techniques, chiropractic, massage, spiritual healing, herbal medicine, megavitamin therapy, energy healing, hypnosis, homoeopathy, acupuncture, and folk remedies. It was found that there were an estimated 425 million visits to unconventional therapists in 1990, exceeding all visits to primary care physicians (388 million). Expenditures on unconventional therapy were approximately \$13.7 billion, of which \$10.3 billion was out-of-pocket. This compares with \$12.8 billion spent out-of-pocket for all hospitalizations in the United States (Eisenberg et al. 1993). Under political pressure by the Congress, the National Institutes of Health has recently set up a program to evaluate alternative treatment, an initiative that should be going on all over the world. Unfortunately, meagre funds and political interference have led to the resignation of the first director of this important program.

The particular importance of such an initiative in the developing world is graphically described in a superbly controlled study of modern and traditional health systems in two Nigerian villages (Orubuloye and Caldwell 1975). These villages, one with good medical facilities (Ido) and the other with no facilities other than the traditional ones (Isinbode), were culturally and geographically as similar as possible and their social and economic indices showed no great difference except in the provision of medical services. Deaths per thousand among under-one-year-olds in Ido (medical facilities) were 99 compared with 288 in Isinbode (traditional); life expectancy at birth was 52 in Ido and 24 in Isinbode.

Application

A recent conference organized by the New York Academy of Sciences, *Doing More Good Than Harm* (Doll 1993), opened with a paper entitled 'All effective treatment could be free' (Warren 1993). This paraphrase of Archie Cochrane's famous statement was done advisedly, in view of the State of Oregon's recent development of a health plan that would not reimburse for ineffective or questionable therapies in order to afford more equitable health care. This pioneering approach, which the *Wall Street Journal* (1993) described as 'an unprecedented way to expand basic medical coverage to all people living in poverty,' was approved for implementation by the Clinton administration of the American government on 19 March 1993.

The basic concept of the Oregon plan is to 'prioritize health services in an era of limits' (Kitzhaber 1993). By eliminating categories covering minor conditions, futile care, and services that have little or no effect on health services, they were able to reduce costs so that 95 per cent of the population under the age of 65 were covered by the state health plan. Only part-time workers with incomes above the poverty level and seasonal workers were not covered. Those over 65 were enrolled in the federal Medicare program.

The process of prioritization was largely a social and political one. A Health Services Commission was created, consisting of five primary-care physicians, a public health nurse, a social worker and four consumers. They were charged with developing a list of services ranked in priority from the most important to the least important, according to the comparative benefits of each service to the entire population being served, and judged by clinical effectiveness and social values. The determination of clinical effectiveness was provided by panels of physicians who were asked to supply information about each condition-treatment pair in their areas of practice. It was recognized that 'this information provides a consensus by physicians rather than hard empirical outcomes data'. It is worthy of note that the prioritization process is dynamic and continuing with a new list generated each budget cycle 'to take into consideration new technologies and new information on outcomes' (Kitzhaber 1993).

Furthermore, the commission set up a broad-based public process to identify and integrate social values into the process, through extensive community meetings and a series of public hearings. The first priority list consisted of 709 condition-treatment pairs. Those ranked highest were for acute, fatal conditions where treatment prevents death and returns individuals to their previous health state. High values were placed on prevention, and maternal, dental and hospice care. The final priority list was given to an independent actuarial firm, which determined the cost of delivering each element through capitated managed care. On the basis of this information the Oregon legislature appropriated new revenue funding all condition-treatment pairs to line 587 on the list of 709. It is important to realize that this benefit system, modified over the years, will become the standard benefit offered by all private policies in the state. The Oregon plan, approved overwhelmingly by both houses of the state legislature, is clearly a social and political triumph. The 'scientific approach' to prioritization, however, while explicit, was unscientific, being essentially a matter of opinion.

This brings us to the enormous opportunity offered by the burgeoning of large-scale randomized evidence, now being gathered together by the global Cochrane Collaboration, and being maintained in continuously updated digital form. The combination of this sophisticated scientific evidence with the remarkable social and political process pioneered by the State of Oregon can truly offer the possibility that all effective treatment can be provided by comprehensive health systems at affordable cost.

Rationalizing health care

Health care systems in many parts of this aging world are grossly deficient. Even in countries where they have functioned well in the past they are breaking down because of high public expectations, inequities, inefficiencies and unsupportable costs. In order to have an efficient health care system it is essential to have quantitative estimates of the age-specific disease burdens in the population and to develop strategies for preventing and treating disease with known effective and, wherever possible, low cost interventions.

References

- Banerji, D. 1986. Technocentric approach to health: Western response to Alma-Ata. *Economic and Political Weekly* 21:1233.
- Barsky, A.J. 1988. The paradox of health. *New England Journal of Medicine* 318:413-418.
- Black, D.A.K. and J.D. Pole. 1975. Priorities in medical research. Indices of burden. *British Journal of Preventive and Social Medicine* 29:222-227.
- Chalmers, I. 1993. The Cochrane Collaboration: preparing, maintaining, and disseminating systematic reviews of the effects of health care. Pp. 156-165 in *Doing More Good Than Harm: The Evaluation of Interventions*, ed. K.S. Warren and F. Mosteller. *Annals of the New York Academy of Sciences* 703.
- Cochrane, A.L. 1989 (reprint). *Effectiveness and Efficiency: Random Reflections on Health Services*. Cambridge: Cambridge University Press.
- Daniels, M. and A.B. Hill. 1952. Chemotherapy of pulmonary tuberculosis in young adults. An analysis of the combined results of three Medical Research Council trials. *British Medical Journal* 1:1162-1168.

- Doll, R. 1993. Summation of the conference. Pp. 310-313 in *Doing More Good than Harm: The Evaluation of Interventions*, ed. K.S. Warren and F. Mosteller. *Annals of the New York Academy of Sciences* 703.
- Eisenberg, D.N., R.C. Kessler, C. Foster, F.E. Norlock, D.R. Calkins and T.L. Delbanco. 1993. Unconventional medicine in the United States: prevalence, costs, and patterns of use. *New England Journal of Medicine* 328:246-252.
- Escovitz, G.H. 1992. The health transition in developing countries: a role for internists in the developed world. *Annals of Internal Medicine* 116:499-504.
- Ferguson, J.H. 1993. NIH conferences: dissemination and impact. Pp. 180-199 in *Doing More Good Than Harm: The Evaluation of Interventions*, ed. K.S. Warren and F. Mosteller. *Annals of the New York Academy of Sciences* 703.
- Grant, J.P. 1983. *The State of the World's Children 1982-83*. New York: Oxford University Press.
- Grosse, R.N. 1980. Interrelation between health and population. Observations derived from field experiences. *Social Science and Medicine* 14C:99-120.
- Halloran, M.E., D.A.P. Bundy and E. Pollitt. 1989. Infectious disease and the UNESCO basic education initiative. *Parasitology Today* 59:359-362.
- Halstead, S. B, J.A. Walsh and K.S. Warren. 1985. *Good Health at Low Cost*. New York: Rockefeller Foundation.
- Kinsley, M. 1995. The intellectual free lunch: everybody's entitled to an opinion, right? Wrong. *New Yorker* 6 February:4-5.
- Kitzhaber, J. A. 1993. Prioritising health services in an era of limits: the Oregon experience. *British Medical Journal* 307:373-377.
- Lancet*. 1995. Fortress WHO: breaching the ramparts for health's sake. 345:203-204.
- Landers, J. 1992. Introduction. Pp. 1-28 in *Historical Epidemiology and the Health Transition*, ed. J. Landers. *Health Transition Review* 2 (Supplement).
- Mata, L. 1978. *The Children of Santa Maria Cauqu:, A Prospective Field Study of Health and Growth*. Cambridge MA: MIT Press.
- McCord, C. and H.P. Freeman. 1990. Excess mortality in Harlem. *New England Journal of Medicine* 322:173-177.
- McKeown, T. 1976. *The Modern Rise of Population*. New York: Academic Press.
- Orubuloye I.O. and Caldwell J.C. 1975 The impact of public health services on mortality: a study of mortality differentials in a rural area of Nigeria. *Population Studies* 29:259-272.
- Rifkin S.B. and G. Walt. 1986. Why health improves: defining the issues concerning 'comprehensive primary health care' and 'selective primary health care'. *Social Science and Medicine* 23:559-566.
- Ross, Ronald. 1928. *Studies on Malaria*. London: John Murray.
- Thomas, L. 1983. *The Youngest Science*. New York: Viking Press.
- Walsh, J.A. 1988. *Establishing Health Priorities in the Developing World*. New York: United Nations Development Programme.
- Walsh, J. A. and K.S. Warren. 1979. Selective primary health care: an interim strategy for disease control in developing countries. *New England Journal of Medicine* 30:967-974.
- Warren, K.S. 1990. An integrated system for the control of the major human helminth parasites. *Acta Leidensia* 59,1 and 2:433-442.
- Warren, K.S. 1993. All effective treatment could be free. Pp. 1-4 in *Doing More Good Than Harm: The Evaluation of Interventions*, ed. K.S. Warren and F. Mosteller. *Annals of the New York Academy of Sciences* 703.

- Wennberg, J.E., M.J. Barry, F.J. Fowler and A. Mulley. 1993. Outcomes research, PORTs, and health care reform. Pp. 52-62 in *Doing More Good Than Harm: The Evaluation of Interventions*, ed. K.S. Warren and F. Mosteller. *Annals of the New York Academy of Sciences* 703.
- World Bank, *World Development Report 1993: Investing in Health*. New York: Oxford University Press.
- World Health Organization (WHO). 1978. *Declaration of Alma Ata (Report on the International Conference on Primary Health Care, Alma Ata, USSR, September 6-12, 1978)*. Geneva.