

Estimating the economic value to societies of the impact of health research: a critical review

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Abstract Estimating the economic value to societies of health research is a complex but essential step in establishing and justifying appropriate levels of investment in research. The practical difficulties encountered include: identifying and valuing the relevant research inputs (when many pieces of research may contribute to a clinical advance); accurately ascribing the impact of the research; and appropriately valuing the attributed economic impact. In this review, relevant studies identified from the literature were grouped into four categories on the basis of the methods used to value the benefits of research. The first category consists of studies that value the direct cost savings that could arise from research leading either to new, less-costly treatments or to developments such as vaccines that reduce the number of patients needing treatment. The second category comprises studies that consider the value to the economy of a healthy workforce. According to this "human capital" approach, indirect cost savings arise when better health leads to the avoidance of lost production. The third category includes studies that examine gains to the economy in terms of product development, consequent employment and sales. The studies placed in the fourth category measure the intrinsic value to society of the health gain, by placing a monetary value on a life. The review did not identify any consistency of methodology, but the fourth approach has most promise as a measure of social value. Many of the studies reviewed come from industrialized nations and a proposal is made by the present reviewers for an international initiative, covering developed and developing countries, to undertake further methodological analysis and testing.

Keywords Health services research/economics; Cost-benefit analysis; Delivery of health care/economics; Cost savings; Longevity; Economic development; Review literature (*source: MeSH, NLM*).

Mots clés Recherche en santé publique/économie; Analyse coût-bénéfice; Délivrance soins/économie; Réduction coût; Longévité; Développement économique; Revue de la littérature (*source: MeSH, INSERM*).

Palabras clave Investigación sobre servicios de salud/economía; Análisis de costo-beneficio; Prestación de atención de salud/economía; Ahorro de costo; Longevidad; Desarrollo económico; Literatura de revisión (*fuentes: DeCS, BIREME*).

Arabic

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Voir page 737 le résumé en français. En la página 738 figura un resumen en español.

Introduction

WHO's planned *World Report on knowledge for better health* aims to demonstrate that health research is an investment (1). A conceptual framework developed for the report highlights the importance of knowledge production leading to health gain (2); a key linkage between the two is often the impact that the results of research have on health-care policy (3). The WHO framework also recognizes the importance of estimating the economic value of health research (2). The proper attribution and valuation of economic benefits can help to justify and identify an appropriate level of expenditure on health research, and indicate ways to increase the yield from future investment in research (4).

This review aims to assess what can be learnt from previous studies that have estimated monetary values for the societal benefits obtained from health research, especially those studies

that have attempted to link (and value) benefits to a specific society from a specified (and costed) body of research. This review thus deals with a specific subset of a broader body of research on the benefits and impacts of health research. The subset is contentious but potentially of particular value in enabling policy-makers to compare returns on investment in health research with returns on other social investments.

The review begins with a methods section describing how we searched for relevant studies and how we addressed three key issues: identifying and valuing the relevant research inputs; accurately ascribing their impact; and appropriately valuing their benefits. In the results section, the studies are arranged according to four categories for valuing the benefits of health research. Finally, the progress made in demonstrating the economic value of research is discussed, and policy recommendations are made for building on this progress, including in developing countries.

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Methods

Literature searches

This review aimed to identify key studies in this field in order to elucidate the main approaches adopted and the principal methodological issues arising. In 2003–04, we undertook a wide search of English language publications by means of Web of Knowledge, MEDLINE, the International Bibliography of the Social Sciences, the Latin American and Caribbean Center on Health Sciences Information (LILACS), POPLINE (population information online), IndMED, KoreaMed, WHOLIS (the WHO library database), MEDCARIB, the library of the Institute of Tropical Medicine in Antwerp, Belgium, and the Health Economics Evaluations Database (HEED) of the Office of Health Economics, England. We looked for papers that combined the following keywords (or nearest equivalents): “research” (or “evaluation” or “research and development” or “assessment”); and health (or “biomedical” or “medical”); and “economic return” (or “economic impact” or “rate of return” or “investment” or “payoff” or “payback” or “impact” or “benefit”). References listed in known and identified studies provided an additional indirect route to “grey literature” (information produced at all levels of government, and by academics, business and industry, in formats not controlled by formal publishing), monographs and books.

Notwithstanding the broad subject area, its cross-disciplinary nature, the lack of agreed terminology and WHO’s previous recognition that, “there are few analyses of the payoff from specific research and development investments” (5), we attempted to present a representative picture of the approaches in use and the issues they raise. Inevitably this review cannot do full justice to the richness and complexity of many of the studies mentioned, and focuses on methods rather than attempting to summarize substantive quantitative results.

To permit a reasonably full review of these topics, important and contiguous areas were not covered. These include: studies of the private returns to companies from their internal research (but see existing reviews (6)); studies addressing less tangible social impacts of research, such as the contribution that an informed society makes to the development of nations (7); studies assessing potential benefits from proposed health research (8); and studies assessing the potential value that would arise from applying existing knowledge, for example, current knowledge of the appropriate and cost-effective use of tuberculosis treatment or oral rehydration therapy (9–11).

Issues

Three main issues are addressed. The first concerns the research inputs in question, an issue that is complicated by the very nature of the research process: typically new findings add to an existing pool of public knowledge (12). Many research projects may lie behind a specific advance in health-care or product development (13–15), and it is often unclear precisely which research has contributed. Furthermore, research is a risky investment; while some research may give high returns, other research may be largely fruitless. In the studies examined, the breadth of the research considered varies considerably; some studies consider specific research projects or programmes, others look at broad topics of research (e.g. Chagas disease), and a few have attempted an overall assessment of medical research. Some studies consider research conducted in a single country, while others consider an international body of research.

The second issue concerns the relationship between research inputs and health and other outcomes. There is uncertainty about how far research, from whatever source, has contributed to advances in health. For example, McKeown (16), in an analysis challenged by Mushkin (17), suggested that during the 20th century much of the observed reduction in mortality was not attributable to medical advances and medical research, but was the result of improvements in general living standards. Such issues raise the problem of the counterfactual — what would have happened had the research not been undertaken? In some cases, however, the history of the research that led to the development of preventive programmes has been traced, and the contribution of those programmes to the control of a disease has been demonstrated (18).

The third issue relates to valuing the outcomes of research. One aspect of this is the scale at which the analysis is to be conducted. The perspective adopted may be subnational, country or international.

There are many ways in which benefits can be measured and valued and we adopt a four-fold categorization as a conceptual, presentational aid. The categories are:

- valuing direct cost savings to the health-care system
- valuing benefits to the economy from a healthy workforce
- valuing benefits to the economy from commercial development
- measuring the intrinsic value to society of the health gain.

Results

Our literature searches indicated that much of the relevant material has not been published in journals but in less-easy-to-access books, monographs and reports. Most material emanates from industrialized countries, particularly the USA. Table 1 lists 31 publications that are either key studies or representative examples, and includes primary studies — both single cases and sets — and some collations and reviews. The table summarizes the features of the studies in terms of the issues addressed above, and states whether costs were presented for the body of research itself.

Direct cost savings to the health-care system

Health research can lead directly to cost savings in the health-care system by means of new therapies that reduce either the number of patients needing treatment or the overall cost of treatment per patient. Some of the clearest examples relate to vaccines or drugs that can reduce or virtually eradicate some diseases. For polio, Fudenberg (19) estimated that the initial cost savings to the health-care system in the USA were lower than the combined costs of the research and the costs of purchasing and applying the vaccines, but that the main benefit was the avoidance of lost production (see section below: benefits to the economy from a healthy workforce). Weisbrod (20, 21) conducted a classic cost–benefit analysis for the development of the polio vaccine and described the benefits in terms of a rate of return. Calculations were also made about tuberculosis in the USA (22–24). At a regional level, research-based moves towards the control of Chagas disease in the Southern Cone countries (Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay) of South America have led to considerable cost savings for health-care systems (25). Some calculations of the benefits to specific countries have been made with no attempt to describe where the

Table 1. Selection of studies showing the economic value to societies of health research

Study	Scope of research	Research input costed	Society of interest	Categories covered
Access Economics (2003) (33)	All biomedical	Yes	National: Australia	Intrinsic value to society
Australian Society for Medical Research (2003) (31)	Set of topics, including ulcers	Partially	National: Australia	Direct cost savings to health-care system
Moncayo (2003) (25)	Review of topic: Chagas disease	No	Multinational: Southern Cone countries	Direct cost savings to health-care system; healthy workforce
Rosenberg (2002) (39)	Review based on all biomedical	Partially	National: USA	Direct cost savings to health-care system; healthy workforce; benefits to the economy; intrinsic value to society
Kettler & Modi (2001) (41)	Review includes public sector contribution	No	National: India	Benefits to the economy: employment, exports, import substitution
United States Senate (2000) (37)	Collation/review related to NIH funding	Partially	National: USA	Direct cost savings to health-care system; healthy workforce; benefits to the economy; intrinsic value to society
Gadelha (2000) (40)	Programme: hepatitis B vaccine	Partially	National: Brazil	Benefits to the economy: import substitution
Funding First (2000) (42–48)	All biomedical	Yes	National: USA	Intrinsic value to society
Pardes et al. (1999) (38)	Review based on various research activities	No	National: USA	Direct cost savings to health-care system; healthy workforce; benefits to the economy
Afseth (1997) (27)	Collation of international research on topics including polio and tuberculosis	No	National: Norway	Direct cost savings to health-care system; healthy workforce; benefits to the economy
Cockburn & Henderson (1997) (13)	Public sector research contributing to drug development	No	National: USA	Benefits to the economy: assisting product development
Jacob & McGregor (1997) (28)	Set of health technology assessment projects	No, but possible	Subnational unit: Quebec, Canada	Direct cost savings to health-care system
Davy (1996) (24)	All biomedical: national and subnational	Partially	Subnational unit: Wisconsin, USA	Direct cost savings to health-care system; healthy workforce; benefits to the economy
Silverstein et al. (1995) (22)	Collation/review of specific topics and programmes	No	National: USA	Direct cost savings to health-care system; healthy workforce; benefits to the economy
Kirschner et al. (1994) (23)	Collation/review of specific topics and programmes	No	National: USA	Direct cost savings to health-care system
National Institutes of Health (1993) (29)	Set of projects and programmes	Yes	National: USA	Direct cost savings to health-care system; healthy workforce
Raiten & Berman (1993) (15)	Topic: methodology for producing monoclonal antibodies	Yes	National: USA	Benefits to the economy: employment
Drummond et al. (1992) (30)	Programme: laser therapy for diabetic retinopathy	Yes	National: USA	Direct cost savings to health-care system; healthy workforce
Mansfield (1991, 1998) (35, 36)	All public basic research	Yes	International	Benefits to the economy: rate of return
Fudenberg (1983) (19)	Programme: polio vaccine	Yes	National: USA	Direct cost savings to health-care system; healthy workforce
Mushkin (1979) (17)	All biomedical	Yes	National: USA	Healthy workforce: rate of return
Weisbrod (1971, 1983) (20, 21)	Programme: polio vaccine	Yes	National: USA	Direct cost savings to health-care system; healthy workforce
Council for Scientific Policy (1967) (26)	Topic: international tuberculosis research	No	National: UK	Direct cost savings to health-care system

research was undertaken. Examples include studies of the control of tuberculosis in the United Kingdom (26) and of tuberculosis and polio in Norway (27).

Jacob & McGregor (28) examined various assessments of health technology that were undertaken in Quebec, Canada, and found that several had directly influenced policy and contributed to health-care cost savings through reduced costs per patient.

A methodologically important set of studies from the National Institutes of Health (NIH) estimated the monetary value of examples of research that they had funded (29). In these studies, estimates were generally made on the basis of expert opinion concerning the likely uptake of the research findings, rather than actual observation of changes in practice, and included, but were not restricted to, estimates of savings for the health-care system. Modelling, undertaken for NIH, of the benefits from a trial of early treatment of diabetic retinopathy emphasized the sensitivity of the results to the assumed impact on clinical practice (30).

Difficult judgements arise with regard to which research was essential to a particular development, and in some cases this is exacerbated by national claims to the key research. For example, NIH suggest (29) that large savings resulted from its research related to the discovery of the role of *Helicobacter pylori* in the development of stomach ulcers. This discovery had a considerable impact on the need for long-term treatment. The Australian Society for Medical Research (31), however, emphasizes that the original work related to this discovery was undertaken in Australia, and in its description of the history of this research and cost savings in Australia, makes no reference to funding from NIH. In the field of mental health, large savings (in terms of hospital costs avoided) have resulted from improvements in treatments, such as the use of lithium to treat manic-depressive illness. This example provides the third-highest savings out of a list of 36 examples of returns in the USA to investment in research by the USA (22). Again, however, others note that basic Australian research made a key contribution to this field (32, 33).

Direct cost savings (or reduction on claims on resources) may accrue more widely than to the health-care system only. Research-based approaches that result in shorter and/or more effective treatments may also result in savings in non-medical direct costs, such as custodial care, transportation, special equipment, and community support programmes run by governments and voluntary agencies (29).

Benefits to the economy from a healthy workforce

Simply focusing on health-care savings is a very narrow viewpoint; many of the studies described above also looked at benefits, or indirect cost savings, in terms of avoidance of lost production. Using the human capital approach, which essentially values health gains in terms of the value of production that is no longer lost due to morbidity and premature mortality, Mushkin (17) attempted to calculate the economic benefits to the USA of all health research. In a series of calculations, Mushkin estimated the economic value of the total reduction in mortality and morbidity in the USA between 1930 and 1975, estimated the value of the share caused by biomedical research, and, after taking away the cost of the research, produced a rate of return of 47%. Similarly, Drummond et al. (30) and others (25, 29), included estimates of savings from avoiding lost production.

As acknowledged by many who use it, there are well-recognized problems with the human capital approach (17, 20, 30). While it tends to exaggerate benefits at a time when labour lost due to morbidity and premature mortality could easily be replaced by unemployed people or through labour migration, it limits benefits from improved health to those of working age. Thus, as a measure of the value of any health-related activity, it has uncomfortable equity implications. Nevertheless, a healthy workforce can make a major contribution to economic development (9).

Benefits to the economy from commercial development

A recent review (34) identifies a range of benefits to an economy from publicly funded basic research. While finding that none of the included studies provided a simple and comprehensive model, it commended the progress made by Mansfield (35, 36) in measuring the benefits resulting from basic research. Mansfield surveyed large corporations covering seven industries in the USA for data concerning the proportion of firms' new products and processes that could not have been developed, without substantial delay, in the absence of recent academic research. Using figures for the value of sales of research-based products, and knowledge of the level of spending on basic research in developed countries, Mansfield estimated a worldwide social rate of return of 28% for research conducted in 1975–78 (35). Of the industries considered, the pharmaceutical industry was the most dependent on basic academic research.

As part of a wider account of the economic value of research in the medical and life sciences, Silverstein et al. (22) listed 10 biomedical discoveries that, it was claimed, had led to industrial applications outside the health sector, which were worth US\$ 92 billion in sales. A report on NIH, from the United States Senate (37), cites several studies that show the importance of publicly funded research in the development of significant new drugs. In one study, 15 of the 21 drugs identified as having had most impact on therapeutic practice were shown to have been developed with input from the public sector, but the complex interaction between public and privately funded research prohibited any attempt to calculate a social rate of return (13).

Many studies identify employment opportunities resulting from research-informed product development, including start-up companies (38), but few link estimates of employment to specific (costed) bodies of research. Rosenberg (39) suggests that the estimated 500 000 jobs in the biopharmaceutical industry in the USA “would not exist if industry wasn't standing on the shoulders of public funding and academic performance”. There have been some attempts to put a monetary value on the creation of employment, including at a subnational level (24). Raiten & Berman (15) traced the developments that led to the discovery of the methodology for producing monoclonal antibodies. They then undertook a cost-benefit analysis to estimate employment created and other benefits induced by the manufacture and use of some of the products resulting from the original research.

Various countries with low and middle incomes use research and development to help support or build a pharmaceutical industry in order to generate a range of economic benefits, including employment, import substitution, and reduced drug costs. Examples include Brazil (40) and India (41).

The intrinsic value to society of the health gain

Several recent studies have attempted to estimate the value of the health gain, without resorting to human capital approaches. The so-called *Funding First* report (42) has attracted considerable attention. The basis for its impressive claims about the huge economic value of health research lies in a series of highly technical papers, which, while broadly compatible in their approach, differ in some aspects of their detailed analysis (43).

The key foundation to the work is use of economic evidence suggesting that an individual's willingness to pay for small reductions in the risk of death is equivalent to a value of around US\$ 3.0 million to prevent a fatality (44). This inputs into calculations of the "economic" value of the increasing longevity of the population of the USA (44, 45). The authors then consider what proportion of these gains can reasonably be attributed to medical research. Lichtenberg looks at spending on pharmaceutical research and estimates that the social rate of return on investment (in terms of the value of additional life years generated) is around 67% (46). Considering the area of cardiovascular disease, it is suggested that one-third of the decline in mortality attributable to cardiovascular disease is due to invasive treatments, one-third to pharmaceuticals and the remaining one-third to behavioural changes (47). The complexity of the link between research findings and practice and behavioural changes is also emphasized (48). The importance of these contributions lies in their common use of a willingness-to-pay value of a statistical life or life year, which enables the intrinsic value of the health gain to be estimated. The robustness of the empirical value they use can be questioned, as can many more detailed assumptions they necessarily make. For example, the studies essentially treat the USA as a research island, which, even if it were a reasonable approximation for the USA, could not easily be generalized to other countries. But in pushing forward this area of analysis, these linked studies make a major contribution to the field.

A "replication" study has used a version of the *Funding First* methodology to estimate the return on Australian biomedical research and development on the basis of overall improvements in Australian lifespan, including reductions in specific mortality rates for a range of illnesses (33). The USA estimate of the value of a life is used, but allowance is also made for the value of reduced morbidity. The base-case assumption is that research and development are responsible for 50% of the improvements in healthy lifespan, and that Australian research and development contribute 2.5% of the total research and development gains, this being the percentage of global research

and development undertaken by Australia. This study leaves several unresolved difficulties. For example, although the approach ingeniously uses disability-adjusted life years (DALYs) to allow for gains in mortality and morbidity, this leads to the suggestion that there has been no return on research on mental health because there are no overall gains in DALYs in this field.

Discussion and issues for further research

Overall, there is a growing evidence base demonstrating that health and biomedical research is an investment: there are tangible benefits and it is quite possible that exceptionally attractive long-term returns may accrue. Substantial efforts are, however, needed to refine existing methodologies and to make them more robust if we are to move from suggestive studies to firm estimates that cannot easily, as now, be challenged and contested.

If the approach based on the societal value of a life year (quality- or disability-adjusted or not) is to be used more widely, then the evidence base for that value also needs to be more robust. That value will, of course, vary empirically between countries, thus implying that the value of equivalent life years saved will be different in different countries. Methodologically, we are still far from being able to calculate realistically the value of the health research produced in each country, or make comparative assessments for basic and applied research, although both types of research have been shown to make a contribution. A fundamental problem is that we cannot observe the counterfactual: what would have happened if the research in question had not been funded?

During the present review, we found that literature on this topic is available from disparate sources and that many publications are difficult to identify and access. As the topic is growing in importance, it may be an opportune time for an international initiative covering developed and developing countries. This would build on the progress to date and develop and test a range of agreed methods by which to assess the economic value of investments in research. Existing studies on the economic benefits and/or costs per life year gained from health programmes, including those in developing countries (49, 50), could contribute to this effort. Such analysis would aim to determine whether the economic value from the use of both the international stock of knowledge and local research could be measured. This could provide strong support for investment in health research globally. ■

Conflicts of interest: none declared.

Résumé

Estimation de la valeur économique des retombées de la recherche en santé pour la société : revue critique

L'estimation de la valeur économique de la recherche en santé pour la société est une étape complexe mais indispensable lorsqu'il s'agit d'établir et de justifier un niveau approprié d'investissement dans la recherche. Il faut faire face à plusieurs difficultés pratiques : identifier et évaluer les résultats pertinents (lorsque de nombreux travaux de recherche peuvent contribuer à une avancée clinique), imputer avec exactitude les retombées de la recherche et faire une estimation correcte de leurs répercussions économiques. Dans le présent article, on a réparti en quatre catégories les études pertinentes relevées dans la littérature en se fondant sur les méthodes utilisées pour estimer les retombées positives de la recherche. La première catégorie comprend les études qui chiffrent

les économies directes réalisées grâce à la recherche, soit par la découverte de nouveaux traitements moins coûteux, soit par des avancées telles que les vaccins qui réduisent le nombre de personnes ayant besoin d'un traitement. La deuxième catégorie comprend les études qui considèrent la valeur économique d'une main-d'œuvre en bonne santé. Selon cette approche du « capital humain », des économies indirectes sont réalisées lorsque l'amélioration de la santé des travailleurs permet d'éviter des pertes de production. Dans la troisième catégorie figurent les études qui examinent les gains économiques en termes de développement de produits, de création d'emplois et de ventes. Les études entrant dans la quatrième catégorie mesurent la valeur intrinsèque des gains

de santé pour la société en chiffrant le prix d'une vie humaine. Cette revue n'a pas fait ressortir de méthodologie commune, mais la quatrième approche semble plus prometteuse en tant que mesure de la valeur sociale des retombées de la recherche.

Nombre des études examinées proviennent de pays industrialisés, et les auteurs proposent une initiative internationale, couvrant les pays développés et les pays en développement, pour poursuivre les analyses et tests méthodologiques.

Resumen

Estimación del valor económico de las investigaciones sanitarias para la sociedad: una revisión crítica

La estimación del valor económico de las investigaciones sanitarias para las sociedades constituye un requisito complejo pero esencial para establecer y justificar unos niveles apropiados de inversión en investigación. Las dificultades prácticas que obstaculizan esas estimaciones guardan relación entre otras cosas con la identificación y valoración de los resultados de investigación pertinentes (cuando la confluencia de muchos elementos de investigación puede facilitar un avance clínico); la determinación precisa del impacto de las investigaciones; y la correcta valoración de la repercusión económica atribuida. En esta revisión, los estudios pertinentes identificados en la literatura se agruparon en cuatro categorías en función de los métodos empleados para evaluar los beneficios reportados por las investigaciones. La primera categoría abarca los estudios que determinan el ahorro directo que puede suponer que la investigación dé lugar a tratamientos ya sea nuevos, ya más baratos, o bien a novedades tales como vacunas que reduzcan el número de pacientes que necesiten tratamiento.

La segunda categoría comprende los estudios que consideran el valor que tiene para la economía una fuerza de trabajo sana; según este criterio del «capital humano», se consiguen ahorros indirectos cuando gracias a esa mejor salud de los trabajadores se evitan pérdidas de horas de trabajo. La tercera categoría incluye los estudios que analizan los beneficios para la economía en términos de desarrollo de productos y del empleo y las ventas consiguientes. Los estudios de la cuarta categoría determinan el valor intrínseco para la sociedad de la mejora de salud asignando un valor monetario a la vida. La revisión no identificó ninguna regularidad metodológica, pero el cuarto enfoque es el que encierra más posibilidades como medida del valor social. Teniendo en cuenta que muchos de los estudios examinados proceden de naciones industrializadas, los autores de esta revisión proponen que se lleve a cabo una iniciativa internacional que abarque los países desarrollados y los países en desarrollo, a fin de emprender nuevos análisis metodológicos y pruebas.

Arabic

References

1. Mexico, 2004: Research for global health and security. *Lancet* 2003;362:2033.
2. Pang T, Sadana R, Hanney S, Bhutta Z, Hyder A, Simon J. Knowledge for better health – a conceptual framework and foundation for health research systems. *Bulletin of the World Health Organization* 2003;81:815-20.
3. Hanney S, Gonzalez-Block M, Buxton M, Kogan M. The utilisation of health research in policy-making: concepts, examples and methods of assessment. *Health Research Policy and Systems* 2003;1:2. Available from <http://www.health-policy-systems.com/content/1/1/2>
4. Buxton M, Hanney S. How can payback from health services research be assessed? *Journal of Health Services Research & Policy* 1996;1:35-43.
5. *Investing in health research for development. Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options.* Geneva: World Health Organization; 1996.
6. Office of Technology Assessment. *Research funding as an investment: can we measure the returns? A technical memorandum.* Washington (DC): Office of Technology Assessment, United States Government Printing Office; 1986.
7. Sen A. *Development as freedom.* New York: Oxford University Press; 1999.
8. Townsend J, Buxton M, Harper G. Prioritisation of health technology assessment. The PATHS model: methods and case studies. *Health Technology Assessment* 2003;7.
9. *Macroeconomics and health: investing in health for economic development. Report of the Commission on Macroeconomics and Health.* Geneva: World Health Organization; 2001.
10. *The world health report 2002 — reducing risks, promoting healthy life.* Geneva: World Health Organization; 2002.
11. Sawert H, Kongsin S, Payanandana V, Akarasewi P, Nunn P, Raviglione M. Costs and benefits of improving tuberculosis control: the case of Thailand. *Social Science and Medicine* 1997;44:1805-16.
12. Cozzens S. The knowledge pool: measurement challenges in evaluating fundamental research programs. *Evaluation and Program Planning* 1997;20:77-89.

13. Cockburn I, Henderson R. *Public–private interaction and the productivity of pharmaceutical research*. NBER Working Paper Series. Cambridge, Massachusetts: National Bureau of Economic Research; 1997 (Report No. 601.)
14. Comroe J, Dripps R. Scientific basis for the support of biomedical science. *Science* 1976;192:105-11.
15. Raiten D, Berman S. *Can the impact of basic biomedical research be measured?: A case study approach*. Bethesda (MD): Life Sciences Research Office, FASEB; 1993.
16. McKeown T. *The role of medicine*. Oxford: Basil Blackwell; 1979.
17. Mushkin S. *Biomedical research: costs and benefits*. Cambridge (MA): Ballinger Publishing Company; 1979.
18. Morel C. Chagas disease, from discovery to control — and beyond: history, myths and lessons to take home. *Memorias do Instituto Oswaldo Cruz* 1999;94:3-16.
19. Fudenberg H, editor. *Biomedical institutions, biomedical funding and public policy*. New York: Plenum Press; 1983.
20. Weisbrod B. *Economics and medical research*. Washington: American Enterprise Institute for Public Policy Research; 1983.
21. Weisbrod B. Costs and benefits of medical research: a case study of poliomyelitis. *Journal of Political Economy* 1971;79:527-44.
22. Silverstein S, Garrison H, Heinig S. A few basic economic facts about research in the medical and related life sciences. *FASEB Journal* 1995;9:833-40.
23. Kirschner M, Marincola E, Teisberg E. The role of biomedical research in health care reform. *Science* 1994;266:49-51.
24. Davy G. *Bioscience research, development and industry: impact on health and economic growth in wisconsin*. Madison/Milwaukee: Wisconsin Association for Biomedical Research & Education; 1996. Available from http://www.wabre.org/report_one/index.html
25. Moncayo A. Chagas disease: current epidemiological trends after the interruption of vectorial and transfusional transmission in the Southern Cone countries. *Memorias do Instituto Oswaldo Cruz* 2003;98:77-591.
26. Council for Scientific Policy. *Second report on science policy*. London: Her Majesty's Stationery Office; 1967.
27. Afseth J. On the value of research in health care. *European Journal of Oral Sciences* 1997;105:454-6.
28. Jacob R, McGregor M. Assessing the impact of health technology assessment. *International Journal of Technology Assessment in Health Care* 1997;13:68-80.
29. National Institutes of Health. *Cost savings resulting from NIH research support*. 2nd ed. Bethesda: United States Department of Health and Human Services, National Institutes of Health; 1993.
30. Drummond M, Davies L, Ferris F. Assessing the costs and benefits of medical research: the diabetic retinopathy study. *Social Science and Medicine* 1992;34:973-81.
31. Australian Society for Medical Research. *Australian case studies*, series I & II. Sydney: Australian Society for Medical Research; 2003. Available from <http://www.asmr.org.au/news/>
32. Mitchell P, Hadzi-Pavlovic D. Lithium treatment for bipolar disorder. *Bulletin of the World Health Organization* 2000;78:515-20.
33. Access Economics. *Exceptional returns: The value of investing in health R&D in Australia*. Canberra: Access Economics; 2003.
34. Salter A, Martin B. The economic benefits of publicly funded basic research: a critical review. *Research Policy* 2001;30:509-32.
35. Mansfield E. Academic research and industrial innovation. *Research Policy* 1991;20:1-12.
36. Mansfield E. Academic research and industrial innovation: an update of empirical findings. *Research Policy* 1998;26:773-6.
37. Joint Economic Committee, United States Senate. *The benefits of medical research and the role of the NIH*. Washington (DC): Government Printing Office; 2000.
38. Pardes H, Manton K, Lander E, Tolley H, Ullian A, Palmer H. Effects of medical research on health care and the economy. *Science* 1999;283:36-7.
39. Rosenberg L. Exceptional economic returns on investments in medical research. *Medical Journal of Australia* 2002;177:368-71.
40. Gadelha C. *Vaccine research, development and production in Brazil. Lessons in research to action and policy*. Geneva: COHRED Working Group on Research to Action and Policy; 2000.
41. Kettler H, Modi R. Building local research capacity for the prevention and cure of neglected diseases: the case of India. *Bulletin of the World Health Organization* 2001;79:742-7.
42. Funding First. *Exceptional returns: The economic value of America's investment in medical research*. New York; 2000.
43. Murphy K, Topel R, editors. *Measuring the gains from medical research. An economic approach*. Chicago: The University of Chicago Press; 2003.
44. Nordhaus W. The health of nations: the contribution of improved health to living standards. In: Murphy K, Topel R, editors. *Measuring the gains from medical research. An economic approach*. Chicago: The University of Chicago Press; 2003. p. 9-40.
45. Murphy K, Topel R. The economic value of medical research. In: Murphy K, Topel R, editors. *Measuring the gains from medical research. An economic approach*. Chicago: The University of Chicago Press; 2003. p. 41-73.
46. Lichtenberg F. Pharmaceutical innovation, mortality reduction and economic growth. In: Murphy K, Topel R, editors. *Measuring the gains from medical research. An economic approach*. Chicago: The University of Chicago Press; 2003. p. 74-109.
47. Cutler D, Kadiyala S. The return to biomedical research: Treatment and behavioral effects. In: Murphy K, Topel R, editors. *Measuring the gains from medical research. An economic approach*. Chicago: The University of Chicago Press; 2003. p. 110-62.
48. Heidenreich P, McClellan M. Biomedical research and then some: The causes of technological change in heart attack treatment. In: Murphy K, Topel R, editors. *Measuring the gains from medical research. An economic approach*. Chicago: The University of Chicago Press; 2003. p. 163-205.
49. Aikins M, Fox-Rushby J, D'Alessandro U, Langerock P, Cham K, New L, et al. The Gambian National Impregnated Bednet Programme: costs, consequences and net cost–effectiveness. *Social Science and Medicine* 1998;46:181-91.
50. Utzinger J, Tozan Y, Doumani F, Singer B. The economic payoffs of integrated malaria control in the Zambian copperbelt between 1930 and 1950. *Tropical Medicine and International Health* 2002;7:657-77.