Economic consequences of better health: insights from clinical data

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KEY MESSAGES

- There is strong evidence that good health in early life leads to better economic outcomes later in life.
- The body of evidence in support of this causal link is mostly related to the economic effects of better diets in utero and in early childhood.
- Although strong evidence exists on the economic consequences of some specific diseases and their treatments – such as HIV and antiretroviral treatment – for most diseases and treatments such evidence is lacking.
- Clinicians and researchers can generate powerful new insights on the economic consequences of specific diseases and treatments by incorporating economic outcomes in clinical trials and by identifying and exploiting natural experiments in routine clinical data.

Contributors and sources

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Patient involvement

No patients were involved in the preparation of article.

Conflicts of Interest

We have read and understood BMJ policy on declaration of interests and declare that all the authors have no relevant interest to declare.

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Standfirst

Osondu Ogbuoji and colleagues *discuss the state of available evidence of the causal links between health status and economic outcomes. They also propose ways for clinicians, economists, and other researchers to substantially improve our understanding of the economic consequences of specific diseases and their treatments.*

Introduction

Little could be more plausible than the proposition that healthier individuals and populations are likely to generate higher economic output than sickly ones: First, healthier individuals are more productive at work and less likely to be absent from work. Second, health promotes the accumulation of human capital. Healthier children are more likely to go to school, to learn and to develop to their full human and economic potential. Third, health promotes the accumulation of physical capital. Greater life expectancy increases the incentives to save for retirement. These savings, in turn, will be available for investment in the buildings, machinery and technology necessary for the production of goods and services. Fourth, declining child mortality often induces fertility reductions as parents realize that they require fewer children to ensure a comfortable old age. The lag between the mortality and the fertility decline lead to an increase ratio of working age population to young and old dependents – the so-called demographic dividence –, which provides favourable conditions for economic growth (1).

Box 1: Economic consequences of better health – pathways

Several authors have proposed theoretical frameworks in an attmpt to explain the causal link between health and future economic outcomes. Some common frameworks include the health to wealth framework by Bloom and Canning(1), subsequently expanded by Bärnighausen et. al. (2), and the social drift hypothesis for mental illness (3). We highlight some of the common pathways below.

Outcome-related productivity consequences: Healthier children learn better and perform better at school while healthier adults perform better at work and earn higher salaries. Another example is the social drift hypothesis in mental health research: a major mental health disorder, e.g. schizophrenia, prevents a person from earning a stable income leading to impoverishment.

Behaviour-related productivity consequences: Better health can induce individuals to change long-term behaviours that affect economic outcomes – such as fertility, education and saving for future spending. For instance, as life expectancy increases, so does the expected return on education. Life expectancy increases due to expanding vaccine coverage or access to HIV treatment should thus increase educational attainment in a community. In turn, higher educational attainment will increase wages for individuals and boost economic development at the community level.

Healthcare cost and care-related productivity consequences: Disease leads to the need for healthcare spending and reduces patients' and carers' productive time. Prevention and treatment can reduce future financial and monetary losses due to ill health. For instance, good glycaemic control among diabetic patients prevents future financial and time costs of care for diabetic complications. .

Community economic externalities: Healthier communities tend to attract more investment, such as foreign direct investment, and are more likely to provide the conditions for strong economic growth, such as social and political stability.

A combination of historical, macroeconomic, and household studies provide ample evidence of the association between health and economic outcomes, as well as inights into a range of potential pathways explaining these associations (**Box 1**) (4-6). Yet, causal (as opposed to associational) evidence remains sparse and inconclusive, particularly at the macroeconomic level. The *microeconomic research* on the causal link between health and economic outcomes has focused to a large degree on the wealth effects of two particular aspects of health: quasi-experimental evidence on in-utero exposure to mothers' health and both experimental and quasi-experimental evidence on reductions of various forms of malnutrition, such as stunting or nutrient deficiencies. These individual-level studies published in economic journals have been accompanied by a number of studies in medical journals examining the health effects of nutrition status and nutritional interventions. This research has moved from initial descriptions of associations to experiments providing strong causal evidence on the economic consequences of nutrition. What is largely lacking, however, perhaps surprisingly, are empirical individual-level studies establishing the economic consequences of specific diseases, such as malaria, hypertension, diabetes, pneumonia, diarrhoea or depression, and the economic returns to specific treatments. There are a few notable exceptions to this rule – in particular HIV treatment – but to date we lack strong causal evidence on the economic consequences of most diseases and most medical treatments.

Our purpose in this short note is twofold. First we provide three examples that illustrate the (already highly plausible) economic consequences of health. And, second, we point to a research agenda that would leverage clinical trials and routine data collection to provide, at relatively low cost, a mechanism for expanding the range, robustness, and practical utility of the literature on the economic consequences of better health.

Example of a specific medical treatment: HIV

HIV treatment can halt and reverse the progression of HIV disease, as well as reduce the spread of HIV. Untreated, HIV leads to physical suffering and eventually premature death. It is thus plausible that HIV treatment has important economic effects. Quasi-experimental studies over the past 15 years have established a number of these effects, mostly in sub-Saharan Africa: HIV treatment increases employment (7-10) and worker productivity (10) and decreases absenteeism (9). These effects are larger if treatment is initiated soon after HIV infection occurs rather than after the disease has progressed (11, 12). Based on the understanding of HIV disease, the directions of these effects may not be surprising. The main value of these findings could thus be seen primarily in quantifying the size of the effects within a particular context. Economic effects of treatment, however, may also manifest in unexpected directions. For instance, Patenaude and colleagues find that HIV treatment in rural South Africa decreased food security for a period of about three years following treatment initiation – despite positive effects of HIV treatment on employment in the same population (13). The likely explanation for this result is that the financial burden of treatment is immediate and large, while the economic benefits lag treatment initiation by three to five years. This study demonstrates that the empirical analysis of economic effects of a treatment may reveal unexpected directions of effects and stimulate further research into the mechanisms leading from treatment to economic outcomes.

Effects of in utero health on economic well-being in adulthood

The in-utero period was first linked to adult health outcomes by Barker (14, 15). Almond extended the Barker hypothesis – in utero conditions affect adult health – to economic outcomes. Using quasi-experimental variation in exposure to the 1918/19 Spanish flu in the United States, he estimated that the flu led to reduced educational attainment, substantially reduced income in

adulthood, and generally lower socio-economic status (16). Other studies have found similar effects for Brazil, Sweden, Switzerland and Taiwan (17-20). However, Vollmer and Wójcik show in a meta regression of census data that these findings do not translate to most other countries, although the Spanish flu was a global phenomenon (21). Almond and co-authors have investigated other natural experiments such as the exposure to Chernobyl's radioactive fallout in Sweden or temporal variation in Ramadan observance (22, 23). Their results consistently confirm the hypothesis that adverse in utero conditions negatively affect adult economic outcomes.

Economic effects of child health and nutrition

There is overwhelming evidence that, on average, healthy children enjoy better educational outcomes than unhealthy children, and that this educational advantage translates to higher earnings over their lifetime (24-27). Experiments done around the world found math and language scores and attendance rates to be significantly higher in schools that received a school feeding program compared to schools that did not (28-32). An experiment in a region of India with widespread iron deficiency anemia found that math and language scores were higher among children who regularly participated in a school feeding program that included iron fortified salt (33). A study conducted in Guatemala found that children who were randomly assigned to receive nutritional supplements in their first two years of life earned 46% more in wages than their counterparts in adulthood (34). However, randomized trials, which follow participants over very long periods are still rare and more evidence on the long-run economic effects of childhood interventions is needed.

Economic effects of adult nutrition

The quantity and quality of food intake affects the levels of productivity of workers. In separate studies conducted at different times, and in different countries, better diets were found to have a positive effect on the level of productivity of farm workers when measured as harvest yield or wages (35-38). Increased caloric intake in energy-deficient adults led to increased energy levels, which increased farm productivity in some studies (35, 39, 40), while in other studies it led to decreased farm productivity or no observable change in farm productivity (41, 42). There is some evidence that calories from protein seem to have a higher impact on productivity than

calories from other sources (40). Also workers with micronutrient deficiencies such as iron deficiency anemia show improvements in aerobic capacity, production efficiency, and work outputs once these specific deficiencies are addressed (43). These findings indicate that beyond simple calorie levels, the nutritional composition of adult diets may be a more important determinant of increased productivity.

Implications for clinical research

Overall, there is strong evidence of the general causal impacts of good health and nutrition on economic outcomes. Evidence on the economic consequences of specific diseases and treatments, however, is largely lacking. These knowledge gaps are important because they impede the optimal allocation of resources for healthcare – everything else equal, diseases leading to more severe economic harms and treatments with higher economic returns should be prioritized. These knowledge gaps also make it difficult to design policies and interventions to enhance the economic benefits and to mitigate economic harms that medical treatments can bring.

A first step in a clinical research agenda on economic returns to specific treatments could be the systematic description of the extant knowledge – for instance, in systematic reviews, scoping reviews, or evidence gap maps (44). What is our knowledge about the long-term productivity effects of headaches? What is the evidence on the effects of dementia on grandchildren's educational attainment? What do we know about the economic effects of empiric treatment of community-acquired pneumonia? These types of evidence bases are very different from standard health economic estimations of the direct and indirect costs of care – rather they focus on the downstream effects of health on economic and social outcomes.

Box 2: Evidence and gap maps and their potential contributions to research

What are evidence and gap maps?

An evidence and gap map (EGM) is a tool that visually summarizes all available evidence (meta-analysis, systematic reviews, and primary studies) about a particular subject (44). By doing this, it identifies important gaps that require future research, and can be used to prioritize investment of resources for research.

Why are they important?
EGMs are important because in addition to their role in determining future research priorities, they also promote the use of evidence in policy making. EGMs also prevents duplication of studies which in turn will promote more efficient use of limited resources for research.

How can EGM contribute to evidence generation on the economic consequences of better health?
The nature of the question of a causal link between health and economic outcomes necessitates cross-disciplinary research that will involve the clinical sciences, economics, and epidemiology, among others. Bringing together experts from these fields with evidence scattered around different databases, knowledge banks and repositories will be greatly facilitated by an exercise that consolidates all the information available in all disciplines related to the subject of interests. EGMs fulfill such a consolidating function. First, the process of developing an EGM will integrate all the information available on the economic consequences of health in an easy to use format. The visual summary of evidence gaps will focus researchers on what is and what is not available. Second, EGM will allow researchers to know the quality of evidence available on the economic consequences of health, and by implication the strengths of recommendations that can result from the existing evidence base. Third, it will enable researchers to identify gaps that need to be filled as well as prioritize the sequence for filling those gaps.

As a second step, clinical research infrastructures – in particular clinical trials and cohorts – could be leveraged to learn about economic consequences of specific diseases and treatments. All that would be needed to generate major new insights is measurement of economic outcomes in existing clinical research infrastructures – such as cognitive development in children, educational attainment in adolescents, labor productivity in middle-aged adults, and social functioning in older-aged adults.

Adding economic endpoints to clinical trials of novel treatments generates two powerful analytical opportunities. First, it allows empirical estimation of the causal effects of the treatment on economic outcomes. Second, it enables the estimation of the economic effects of the disease that the treatment affects. The latter purpose will require that the standard assumptions of instrumental-variable estimation are met – which in many cases will be likely in clinical trials: The treatment has been randomly assigned and many treatments (such as certain medicines) are unlikely to affect economic outcomes via pathways other than those running through the disease they are intended to affect. These opportunities that leverage already funded

clinical trials for major new insights apply to past trials – we can revisit trial cohorts and assess economic outcomes – as well as to future trials – we can make sure that the prospective endpoints include economic outcomes.

Adding economic outcome assessments to clinical cohorts will enable the estimation of the economic effects of diseases and routine healthcare. One strong quasi-experimental approach to analyzing clinical cohort data is regression discontinuity analysis around thresholds for treatment eligibility (45) – such as 140 mmHg for systolic blood pressure for antihypertensive treatment. Another quasi-experimental approach for clinical cohort studies is individual fixed effects analysis, comparing individuals to themselves in different treatment states over time (46). This latter approach allows control of all unobserved time-invariant individual confounders; the former approach allows control of all unobserved confounders – just like in a clinical trial.

Box 3: Opportunities for clinical science to contribute to the evidence on the economic consequences of better health

Adding economic endpoints to clinical trials
Past clinical trial cohorts can be revisited to assess economic endpoints, providing the data to measure economic consequences of diseases and treatments, such as th long-term wage effects of novel approaches to prevent stroke or treat depression. Economic outcomes should also be included in the design of relevant new clinical trials.

Adding economic assessments to clinical cohort studies
Clinical care has established cohorts of individuals that have been followed for many years and, in some situations, for several decades. If assessments of economic outcomes are added to these cohorts, they will generate the data to measure the economic consequences of specific diseases and treatments. For this purpose, a range of powerful quasi-experimental approaches can be used – such as regression discontinuity analyses around treatment thresholds (e.g, for diabetes mellitus, hypertension, or hypercholesterinemia), as well as instrumental variable analyses exploiting policy and clinical guideline changes, and fixed effects analyses comparing the same individuals in different disease and treatment states.

In conclusion, we see major opportunities for clinical research to contribute advances in our understanding of the causal effects of specific diseases and treatments on economic outcomes. This research would powerfully complement the existing economic literature, providing far

greater precision and detail in our evidence on effects of healthcare beyond effects on health. The investments for these scientific advances will not be very large, because past and future clinical trials and ongoing clinical cohorts can be leveraged for this research.

References

1. Bloom DE, Canning D. The health and wealth of nations. Science. 2000;287(5456):1207-9.
2. Bärnighausen T, Bloom DE, Cafiero-Fonseca ET, O'Brien JC. Valuing vaccination. Proceedings of the National Academy of Sciences. 2014;111(34):12313-9.
3. Saraceno B, Levav I, Kohn R. The public mental health significance of research on socio-economic factors in schizophrenia and major depression. World Psychiatry. 2005;4(3):181-5.
4. Preston SH. The changing relation between mortality and level of economic development. Population studies. 1975;29(2):231-48.
5. Deaton A. Health, inequality, and economic development. Journal of economic literature. 2003;41(1):113-58.
6. Jamison DT, Summers LH, Alleyne G, Arrow KJ, Berkley S, Binagwaho A, et al. Global health 2035: a world converging within a generation. The Lancet. 2013;382(9908):1898-955.
7. Bor J, Tanser F, Newell M-L, Bärnighausen T. In a study of a population cohort in South Africa, HIV patients on antiretrovirals had nearly full recovery of employment. Health affairs. 2012;31(7):1459-69.
8. Razzano LA, Hamilton MM, Perloff JK. Work status, benefits, and financial resources among people with HIV/AIDS. Work. 2006;27(3):235-45.
9. Habyarimana J, Mbakile B, Pop-Eleches C. The impact of HIV/AIDS and ARV treatment on worker absenteeism implications for African firms. Journal of Human Resources. 2010;45(4):809-39.
10. Rosen S, Larson B, Brennan A, Long L, Fox M, Mongwenyana C, et al. Economic Outcomes of Patients Receiving Antiretroviral Therapy for HIV/AIDS in South Africa Are Sustained through Three Years on Treatment. PLOS ONE. 2010;5(9):e12731.
11. Thirumurthy H, Chamie G, Jain V, Kabami J, Kwarisiima D, Clark TD, et al. Improved employment and education outcomes in households of HIV-infected adults with high CD4 cell counts: evidence from a community health campaign in Uganda. AIDS (London, England). 2013;27(4):627-34.
12. French D, Brink J, Bärnighausen T. Early HIV treatment and labour outcomes: A case study of mining workers in South Africa. Health Economics. 2019;28(2):204-18.
13. Patenaude BN, Chimbindi N, Pillay D, Bärnighausen T. The impact of ART initiation on household food security over time. Social Science & Medicine. 2018;198:175-84.
14. Barker DJ. The fetal and infant origins of adult disease. BMJ (Clinical research ed). 1990;301(6761):1111-.
15. Kalyanaraman K, Osmond C, Fall CHD. Early Origins of Cardiometabolic Disease. In: Prabhakaran D, Anand S, Gaziano TA, Mbanya J-C, Wu Y, Nugent R, editors. Disease Control Priorities (third edition): Volume 5, Cardiovascular, Respiratory, and Related Disorders. Washington, DC: World Bank.

16. Almond D. Is the 1918 Influenza Pandemic Over? Long-Term Effects of In Utero Influenza Exposure in the Post-1940 U.S. Population. Journal of Political Economy. 2006;114(4):672-712.
17. Karlsson M, Nilsson T, Pichler S. What doesn't kill you makes you stronger? The Impact of the 1918 Spanish Flu Epidemic on Economic Performance in Sweden. 2012.
18. Lin M-J, Liu EM. Does in utero exposure to Illness matter? The 1918 influenza epidemic in Taiwan as a natural experiment. Journal of health economics. 2014;37:152-63.
19. Nelson RE. Testing the Fetal Origins Hypothesis in a developing country: evidence from the 1918 Influenza Pandemic. Health Economics. 2010;19(10):1181-92.
20. Neelsen S, Stratmann T. Long-run effects of fetal influenza exposure: Evidence from Switzerland. Social Science & Medicine. 2012;74(1):58-66.
21. Vollmer S, Wójcik J. The long-term consequences of the global 1918 influenza pandemic: A systematic analysis of 117 IPUMS international census data sets. Available at SSRN 3083584. 2017.
22. Almond D, Edlund L, Palme M. Chernobyl's Subclinical Legacy: Prenatal Exposure to Radioactive Fallout and School Outcomes in Sweden*. The Quarterly Journal of Economics. 2009;124(4):1729-72.
23. Almond D, Mazumder B. Health Capital and the Prenatal Environment: The Effect of Ramadan Observance during Pregnancy. American Economic Journal: Applied Economics. 2011;3(4):56-85.
24. Behrman JR, Deolalikar AB. Chapter 14 Health and nutrition. Handbook of Development Economics. 1: Elsevier; 1988. p. 631-711.
25. Victora CG, Adair L, Fall C, Hallal PC, Martorell R, Richter L, et al. Maternal and child undernutrition: consequences for adult health and human capital. The Lancet. 2008;371(9609):340-57.
26. Alderman H, Hoddinott J, Kinsey B. Long term consequences of early childhood malnutrition. Oxford Economic Papers. 2006;58(3):450-74.
27. Dewey KG, Begum K. Long-term consequences of stunting in early life. Maternal & Child Nutrition. 2011;7(s3):5-18.
28. Glewwe P, Muralidharan K. Chapter 10 - Improving Education Outcomes in Developing Countries: Evidence, Knowledge Gaps, and Policy Implications. In: Hanushek EA, Machin S, Woessmann L, editors. Handbook of the Economics of Education. 5: Elsevier; 2016. p. 653-743.
29. Adrogue C, Orlicki ME. Do In-School Feeding Programs Have an Impact on Academic Performance and Dropouts? The Case of Public Schools in Argentina. education policy analysis archives. 2013;21:50.
30. Tan J-P, Lane J, Lassibille G. Student outcomes in Philippine elementary schools: An evaluation of four experiments. The World Bank Economic Review. 1999;13(3):493-508.
31. Kazianga H, De Walque D, Alderman H. Educational and health impacts of two school feeding schemes: Evidence from a randomized trial in rural Burkina Faso: The World Bank; 2009.
32. Chakraborty T, Jayaraman R. School feeding and learning achievement: Evidence from India's midday meal program. Journal of Development Economics. 2019.
33. Krämer M, Kumar S, Vollmer S. Improving Children Health and Cognition: Evidence from School-Based Nutrition Intervention in India. Courant Research Centre: Poverty, Equity and Growth-Discussion Papers; 2018.

34. Hoddinott J, Maluccio JA, Behrman JR, Flores R, Martorell R. Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults. The Lancet. 2008;371(9610):411-6.
35. Strauss J. Does Better Nutrition Raise Farm Productivity? Journal of Political Economy. 1986;94(2):297-320.
36. Deolalikar AB. Nutrition and Labor Producvivity in Agriculture: Estimates for Rural South India. The Review of Economics and Statistics. 1988;70(3):406-13.
37. Haddad LJ, Bouis HE. The Impact of Nutritional Status on Agricultural Productivity: Wage Evidence from the Philippines. Oxford Bulletin of Economics and Statistics. 1991;53(1):45-68.
38. Tiwasing P, Dawson P, Garrod G. The relationship between micronutrient intake and labour productivity: Evidence from rice-farming households in Thailand. Outlook on Agriculture. 2019;48(1):58-65.
39. Tiwasing P. Nutrition, labour productivity and food security in Thailand. Newcastle: Newcastle University; 2016.
40. Thomas D, Strauss J. Health and wages: Evidence on men and women in urban Brazil. Journal of econometrics. 1997;77(1):159-85.
41. Immink MDC, Viteri FE. Energy intake and productivity of Guatemalan sugarcane cutters: An empirical test of the efficiency wage hypothesis part II. Journal of Development Economics. 1981;9(2):273-87.
42. Immink MDC, Viteri FE. Energy intake and productivity of Guatemalan sugarcane cutters: An empirical test of the efficiency wage hypothesis part I. Journal of Development Economics. 1981;9(2):251-71.
43. Brownlie T, IV, Haas JD. Iron Deficiency and Reduced Work Capacity: A Critical Review of the Research to Determine a Causal Relationship. The Journal of nutrition. 2001;131(2):676S-90S.
44. Snilstveit B, Vojtkova M, Bhavsar A, Stevenson J, Gaarder M. Evidence & Gap Maps: A tool for promoting evidence informed policy and strategic research agendas. Journal of clinical epidemiology. 2016;79:120-9.
45. Bor J, Moscoe E, Mutevedzi P, Newell M-L, Bärnighausen T. Regression discontinuity designs in epidemiology: causal inference without randomized trials. Epidemiology. 2014;25(5):729-37.
46. Gunasekara FI, Richardson K, Carter K, Blakely T. Fixed effects analysis of repeated measures data. International Journal of Epidemiology. 2013;43(1):264-9.