Economic consequences of better health: insights from clinical data

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Economic consequences of better health: insights from clinical data

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KEY MESSAGES

- We have strong evidence that good health in early life leads to better economic outcomes later in life.
- The evidence supporting this causal link is mostly related to the economic effects of better diets in utero and in early childhood.
- We lack strong evidence on the economic consequences of most specific diseases and treamtents over the life course, with a few exceptions – such as HIV and antiretroviral treatment.
- 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 (i.e. knowledge, skills, and experience) – 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 (i.e. tools of production such as buildings, machines and technology) – because greater life expectancy increases the incentives to save for retirement and these savings, in turn, will be available for investment in physical capital. Fourth, declining child mortality often induces fertility reductions as parents realize that they require fewer children to ensure a comfortable old age. The fertility decline, however, typically lags behind the child health improvement that triggers it, leading to an increase in the ratio of working-age adults to the young and the old who depend on them for sustenance and care, which provides favourable conditions for economic growth – the so-called demographic dividend [1].

Box 1: Economic consequences of better health – pathways

Several authors have proposed theoretical frameworks in an attmpt to categorize the most important causal pathways from health to 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: 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 monetary and time losses due to ill health. For instance, good glycaemic control among diabetic patients reduces the costs of care to treat 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 economic consequences of two particular aspects of health: 1) quasi-experimental evidence on in-utero exposure to mothers' health and 2) 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 effects of nutrition status and nutritional interventions on health and economic outcomes.[7-10] This research has moved from initial descriptions of associations to experiments providing strong causal evidence of 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 net economic returns to specific medical interventions. There are a few notable exceptions – 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 paper is twofold. First we provide examples that demonstrate and quantify the – highly plausible – economic consequences of health. These examples were selected because they provide the strongest causal evidence yet of the link between health and future economic outcomes. 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. Our analysis focuses on economic outcomes, such as income, employment, education, or earnings.

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

The in-utero period was first linked to adult health outcomes by Barker.[11 12] Almond extended the Barker hypothesis – in utero conditions affect adult health – to explain economic outcomes in adulthood. Using quasi-experimental variation in in-utero 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.[13] Other studies have found similar effects for Brazil, Sweden, Switzerland and Taiwan.[14-17] 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.[18] 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.[19 20] The Chernobyl study found that children exposed to radiation fallout performed worse than others in mathematics.[19] The Ramadan study showed that children whose mothers observed the Ramadan fast during their pregnancy exhibited higher rates of learning disabilities.[20] Their results consistently confirm the hypothesis that adverse in utero conditions negatively affect adult economic outcomes.

Effects of child health and nutrition on economic outcomes

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.[7-9 21] 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.[22-26] An experiment conducted 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.[27] Another 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 in adulthood than their counterparts.[10] 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.

Effects of adult nutrition on productivity at work

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.[28-31] Increased caloric intake in energy-deficient adults led to increased energy levels, which increased farm productivity in some studies,[28 32 33] while in other studies it led to decreased farm productivity or no observable change in farm productivity.[34 35] There is some evidence that calories from protein seem to have a higher impact on productivity than calories from other sources.[33] 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.[36] These findings indicate that beyond simple calorie levels, the nutritional composition of adult diets may be a more important determinant of increased productivity. By contrast, there is no causal evidence that obesity – which lies at the opposite end of the spectrum of nutrition disorders – has an effect on long term economic outcomes. Several studies show statistical associations between obesity and decreased worker productivity, and earning potential,[37 38] but no study has as yet provided evidence of a causal link.

Intergenerational and multigenerational effects of health on economic outcomes

Intergenerational (e.g. from parent to children) and multi-generational (e.g. from grand-parents to grand-children) effects of health on economic outcomes have also been studied. Research in this space is relatively new, but increasing in number and quality – partly because of the growing availability of long-run data and increased sophistication of research methods. However, current evidence in support of any link is mostly associational, *not causal*. As expected, the proposed causal links between health status in one generation and economic outcomes in a future generation are complex. In separate reviews of the extant literature in economics, demography, and sociology, Janet Currie[39] and Alberto Palloni[40] conclude that early child health plays a role in the transmission of intergenerational inequalities in economic status. Plausible causal pathways run – first – from parental health status to a child's health status, which in turn affects the child's economic outcomes, and – second – from parental health status to parental economic outcomes, which then influences child health. While there have been few causal studies that demonstrate these pathways end-to-end , there are many that provide causal evidence for steps along the causal chain.[39-42]

Example of a specific medical intervention: HIV treatment

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 consequences. Quasi-experimental studies over the past 15 years have established a number of these effects, mostly in sub-Saharan Africa: HIV treatment increases employment[43-46] and worker productivity[46] and decreases absenteeism.[45] These effects are larger if treatment is initiated soon after HIV infection occurs rather than after the disease has progressed.[47 48] 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.[49] The likely explanation for this result is that the financial burden of treatment is immediate and large, while the economic benefits, such as a boost to employment, 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.

Implications for clinical research

Overall, there is strong evidence in support of a causal effect of good health status on economic outcomes. Evidence on the economic consequences of specific diseases and treatments, however, is sparse. We know from studies that have investigated the fetal origins hypothesis that exposure to harmful conditions in-utero have a profoundly negative effect on future earnings potential.We also know that the quality of diets in early childhood has a noticeable effect on cognitive development, academic achievement, and future earnings potential, while the quality of diets in adults directly impacts productivity at work. However, apart from existing research on the effect of HIV and its treatment on employment and income, there is little *causal* evidence of the economic consequences of specific diseases and treatments. These knowledge gaps are important because they impede the optimal allocation of resources for healthcare and scientific discovery – all else equal, diseases leading to more severe economic harms and treatments with larger economic benefits should be prioritized. The present knowledge gaps make it difficult to design health policies and interventions to support economic thriving and human development.

A first step in a clinical research agenda on economic consequences of specific treatments could be evidence synthesis of the extant knowledge – for instance, in systematic reviews, scoping reviews, and evidence gap maps.[50] For example, what do we know about the long-term productivity effects of headaches or chronic back pain? 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. A good heuristic for selecting diseases to focus on first when conducting this type of evidence synthesis are diseases that affect large numbers of people and last for long times – e.g., chronic diseases such as hypertension, diabetes and depression worldwide, or HIV in sub-Saharan Africa

–, because these diseases are likely to have major economic effects both at the individual and the population level.

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

What are evidence and gap maps?
An evidence and gap map (EGM) visually summarizes all available evidence (meta-analysis, systematic reviews, and primary studies) about a particular subject.[50] It identifies the important knowledge gaps on a scientific topic.

Why are they important?
EGMs promote the use of all available evidence to guide research investment and health policy. EGMs also prevent duplication of studies, ensuring efficient use of research funds.

How can EGMs contribute to establishing the economic consequences of diseases and treatments?
EGMs integrate evidence on the economic consequences of diseases and treatments from different scientific fields. The process of developing EGMs can bring together experts from clinical medicine, epidemiology and economics and ensures that data scattered around different databases, knowledge banks and repositories are consolidated in an easily accessible form. The visual summary of evidence gaps focuses researchers – quickly – on those areas where their activities can add greatest value. EGMs can also visualize the quality of the evidence – e.g., through colour coding – adding important nuance to the evidence synthesis.

As a second step, *existing* 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 in intent-to-treat analyses. Second, it enables the estimation of the economic effects of the disease that the treatment affects. This opportunity arises if the treatment changes the disease duration or intensity. In this case, the random variation in disease duration or intensity induced by the randomly assigned treatment could be used to estimate the causal effects of the disease on economic outcomes using instrumental-variable (IV) analyses. This approaches requires that the standard assumptions of IV analyses are met, in particular the so-called exclusion restriction – the treatment may only affect the outcome through its effects on disease duration or intensity.[51 52] In many trials, this assumption will likely be met, e.g., in trials that randomly assign people to different medicines with few or similar side effects.

Adding economic outcome assessments to clinical cohorts will enable the estimation of the economic effects of diseases and routine healthcare through quasi-experimental analysis. One strong quasi-experimental approach to analyzing clinical cohort data is regression discontinuity,[53] which exploits the fact that clinical medicine assigns many treatments by applying a threshold to continuously measured indicators, such as systolic blood pressure, low-density lipoprotein cholesterol or haemoglobin A1C.[54] In a small neighborhood around this threshold, regression discontinuity designs quasi-randomly assign individuals to treatment versus control conditions, because measurement error introduces randomness into the threshold-based assignment. As a result, regression discontinuity designs allow control of all unobservable confounders, similar to randomized controlled trials.[55]

< insert Table 1 around here >

A third step in the clinical research agenda on economic consequences of specific treatments is to exploit *previous* clinical RCTs. In this approach, cohorts of individuals that participated in RCTs that were concluded years (or decades) ago are traced and an assessment of their economic outcomes is conducted. This allows sufficient time for the manifestation of any long-term economic consequences that the treatment might have on the individuals who were previously randomly assigned to receive (or not receive) an intervention. An example of this is the follow-up study in Guatemala to assess the economic outcomes of adults (aged 25 to 42 years) who had received a nutritional intervention in an RCT conducted when they were children (aged 0 to 7 years).[10] The study found 46% higher wages, on average, in adults that received the nutrition intervention as children compared to those that did not get the intervention. Due to the long intervals between the original and follow-on studies, a potentially significant challenge with this approach is the difficulty in tracing all individuals who participated in the original study – the Guatemalan study was able to reach 1,424 (60%) of the 2,392 individuals who participated in the original study. Nevertheless, this approach holds promise to generate powerful evidence on long-term causal effects of treatments on economic outcomes.

In conclusion, there is convincing evidence on the causal effects of health on economic outcomes for a few medical domains, but for many important diseases and treatments we lack strong causal knowledge of economic effects. We see major opportunities for clinical research to contribute to filling these knowledge gaps. Clinical research could 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 would not be very large, because past and future clinical trials and ongoing clinical cohorts could be leveraged for this research.

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Table 1: Studies to estimate the economic consequences of diseases and treatments

	Contribution	Rationale	Challenges	Further reading
Adding economic outcomes to trials data				
Intent-to-treat estimation	Estimation of causal effects of treatments on economic outcomes	• The assignment to treatment vs. control conditions in randomized controlled trials can be used for intent-to-treat estimation of causal treatment effects on economic outcomes. • Economic outcomes – such as income, employment or education – could be routinely added to future trials and measured during re-visits of cohorts that participated in past trials.	• Changes to economic outcomes may manifest themselves only in the long term, requiring follow-up many years after the assessment of clinical endpoints has been completed. • Long-term follow-up of trial cohorts may suffer from substantial attrition due to mortality, migration or name changes associated with marriage.	*Methods:* Moher D, Hopewell S, Schulz K, Montori V, Gøtzsche P, Devereaux P, Elbourne D, Egger M, Altman D (2010). CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomized trials. *BMJ*; **340**: c869. *Domain example:* Hoddinott J, Maluccio J, Behrman J, Flores R, Martorell R (2008). Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults. *Lancet*; **371**(9610): 411-416.
Instrumental-variable estimation	Estimation of causal effects of diseases on economic outcomes	• If randomly assigned treatments induce significant changes in a disease, the treatments can be used as an instrumental variable to estimate the effects of the	• The exclusion restriction needs to be met – the treatments can only affect the economic outcomes through their effect on the	*Methods:* Sussman J, Hayward R (2009). An IV for the RCT: using instrumental variabels to adjust for treatment contamination in

		disease on economic outcomes. • Economic outcomes – such as income, employment or education – could be routinely added to future trials and measured during re-visits of cohorts that participated in past trials.	disease and not through any other pathway. • Changes to economic outcomes may manifest themselves only in the long term, requiring follow-up many years after the assessment of clinical endpoints has been completed.	randomized controlled trials. *BMJ*; **340**: c2073 *Domain example:* Daepp M, Arcaya M (2017). The effect of health on socioeconomic status: using instrumental variables to revisit a successful randomized controlled trial. Economics and Human Biology; **27**: 305-314.
Adding economic outcomes to cohort data				
Regression-discontinuity estimation	Estimation of causal effects of treatments on economic outcomes	• Eligibility for many treatments is determined by applying a threshold to a continuously measured indicator (such as blood pressure or CD4 count). In these cases, we can estimate treatment effects by comparing outcomes among people whose indicator value fell just below the threshold with outcomes among those whose indicator value fell just above the threshold.	• Clinical cohorts may only provide an opportunity to measure economic outcomes among those who were deemed treatment eligible – and not among those on the other side of the treatment threshold –, because only the former return regularly to health facilities for clinical follow-up. • We need large numbers of people whose indicator value falls in a small window around the treatment eligibility threshold to ensure sufficient statistical power in the effect estimation. Regression discontinuity analyses may thus not be a useful study design to	*Methods:* Imbens G, Lemieux T (2008). Regression discontinuity designs: a guide to practice. Journal of Econometrics; **142**: 615e34. Bor J, Moscoe E, Mutevedzi P, Newell N, Bärnighausen T (2014). Regression discontinuity designs in epidemiology: causal inference without randomized trials. *Epidemiology*; **25**(5): 729-737. *Substantive example:* Chen S, Sudharsanan N, Huang F, Liu Y, Geldsetzer P,

			estimate economic outcomes of rare diseases and treatments.	Bärnighausen T (2019). Causal impact of community based screening for hypertension on blood pressure after two years: regression discontinuity analysis in a national cohort of older adults in China. *BMJ*; **366**: l4064. *Domain example:* Patenaude B, Chimbindi N, Pillay D, Bärnighausen T (2017). The impact of ART initiation on household food security over time. *Social Science & Medicine*; 198: 175-184.
Instrumental-variable estimation	Estimation of causal effects of treatments on economic outcomes	• We can estimate the economic effects of a treatment using a variable that significantly affects treatment but is as good as randomly assigned to patients in a clinical cohort (i.e. an instrumental variable), such as physician's prescribing preference or treatment guideline changes.	• The exclusion restriction needs to be met – the instrumental variable can only affect the economic outcomes through its effect on treatment and not through any other pathway. • The exchangeability condition needs to be met – the instrumental variable does not share common causes with the economic outcomes.	*Methods:* Angrist J, Imbens G, Rubin D (1996). Identification of causal effects using instrumental variables. *Journal of the American Statistical Association*; **91**: 444e55. *Domain example:* Finkelstein A, Taubman S, Wright B, Bernstein M, Gruber J, Newhouse J, Allen H, Baicker K, Oregon Health Study Group (2012) The Oregon health insurance

				experiment: evidence from the first year. *The Quarterly Journal of Economics*; **127**(3): 1057-1106.

The readings on methods provide methodological background for the estimation; the substantive examples are applications of the methods but not within the health-to-wealth domain; the domain examples are applications within the health-to-wealth domain.