Valuing Vaccination

David E. Bloom
Harvard School of Public Health, Boston

January 19, 2015
Fondation Mérieux
Veyrier-du-lac, France
Vaccination ecosystem health check: achieving impact today and sustainability for tomorrow

EARLY REPORT

Early report

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associ... by the parents, with measles, mumps, and rub... vaccination in eight of the 12 children, with meas... infection in one child, and otitis media in ac... All 1... children had intestinal abnormalities ranging from lymphoid nodular hyperplasia to ... Histology showed patchy chronic infla... in 11 children and reactive ileal lymph... perplasia in seven, but no granulomas. Be... oural disorders included autism (nine), disintegrative ... sis (one), a... possible postviral or vaccinal encephalitis ...). There were no focal neurological ab... malities and ... and EEG tests were normal. Abno... laboratory results ... significantly raised urinary ...thylmal... acid compared with age-matched contr... ...03), low ... haemoglobin in four children, a... low s... IgA in ... children.

Interp...tation ... identi... associated gastrointestinal dis...se and ...evelopmental regression in a group of previ... ...ly ...mal chi...n, which was generally associated in time ... possible environmental triggers.

Lancet 199... **351:** 637–41
See Commentary page

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB, J Linnell PhD, A P Dhillon MRCPath, S E Davies MRCPath) **and the University Departments of Paediatric Gastroenterology** (S H Murch MB, D M Casson MRCP, M Malik MRCP, M A Thomson FRCP, J A Walker-Smith FRCP,), **Child and Adolescent Psychiatry** (M Berelowitz FRCPsych), **Neurology** (P Harvey FRCP), **and Radiology** (A Valentine FRCR), **Royal Free Hospital and School of Medicine, London NW3 2QG, UK**

Correspondence to: Dr A J Wakefield

Introduction

We saw several children who, after a ... of apparent normality, lost acquired skills, includi... ...g com...unication. They all had gastrointestinal ...mptoms, ...luding abdominal pain, diarrhoea, and ...ating and, ... some cases, food intolerance. We ...scribe... the clinical f...dings, and gastrointestinal featur... of these chi...ren.

Patients and meth...ds

12 children, con...ecutive... ...ferred to ... department of paediatric gastr...terology ... a hi...y of a pervasive developmental ...der with loss ...ca...red skills and intestinal symptoms ...arrh... abdominal ...in, bloating and food intolerance), were in...pitalised. All children were admitted to the ward for ... week, accom...ied by their parents.

...nical investigations

... took histor... including details of immunisations and ...posure to infec...us diseases, and assessed the children. In 11 ca...the histor... was obtained by the senior clinician (JW-S). Neur...d psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria.[1] Developmental ... included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

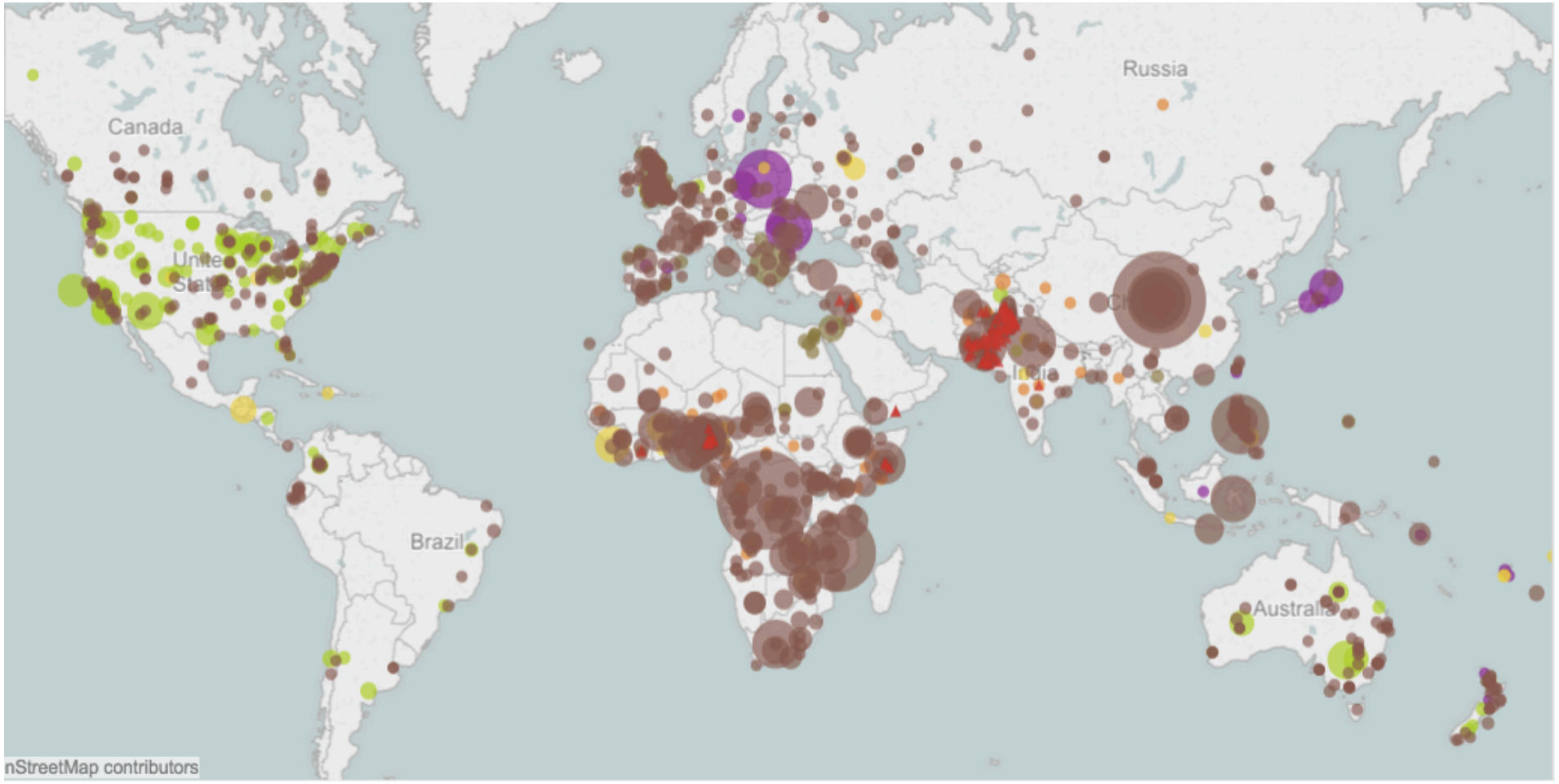
Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, by a modification of a technique described previously.[2] Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid concentrations in patients and controls were compared by a two-sample *t* test. Urinary creatinine was estimated by routine spectrophotometric assay.

Children were screened for antiendomyseal antibodies and boys were screened for fragile-X if this had not been done

Vaccine preventable disease outbreaks



What we will cover today…

1) **Review key links between health and wealth**

2) **Discuss the role of vaccination as a driver of <u>both</u> health and wealth**

3) **Operationalizing the VOV framework**

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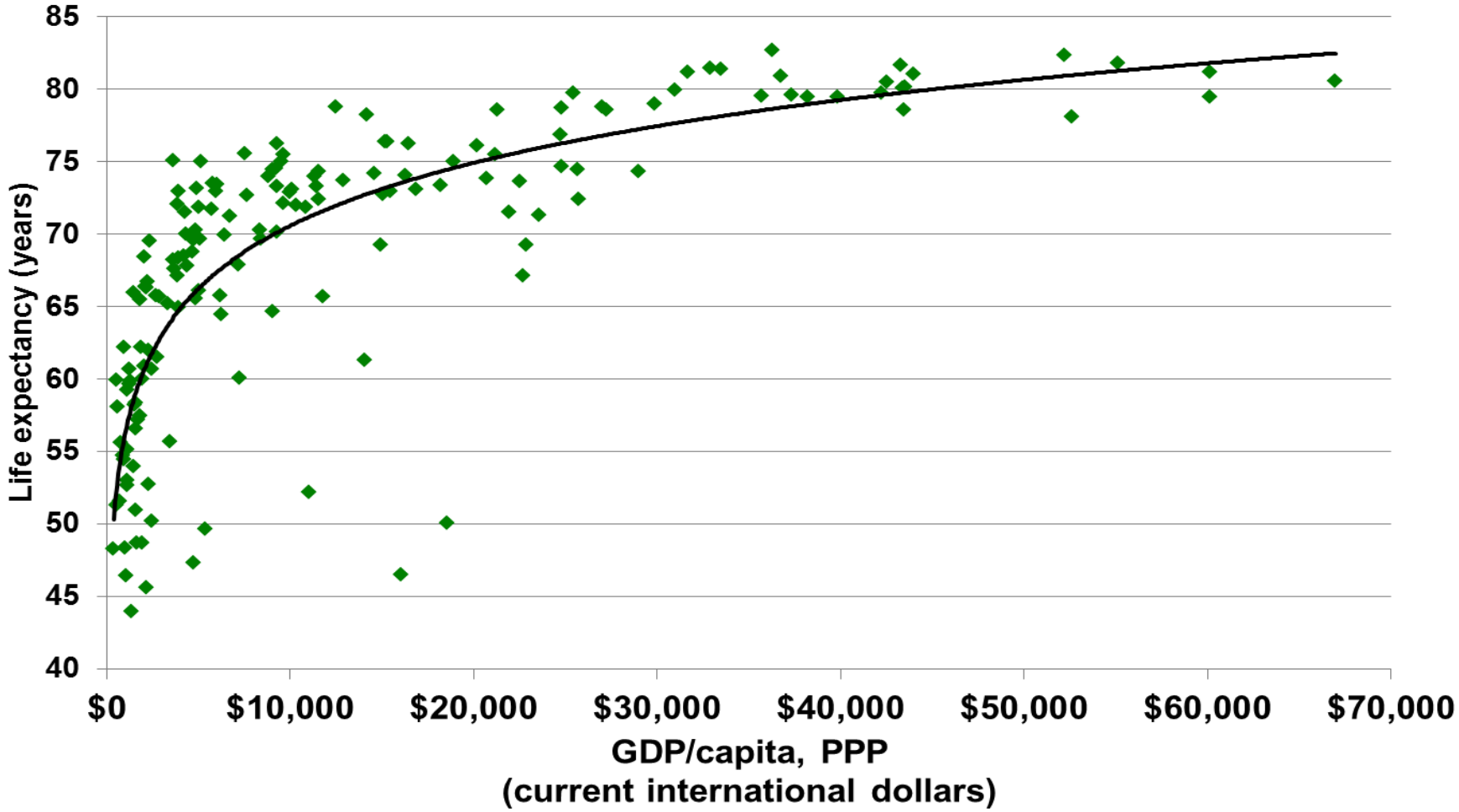
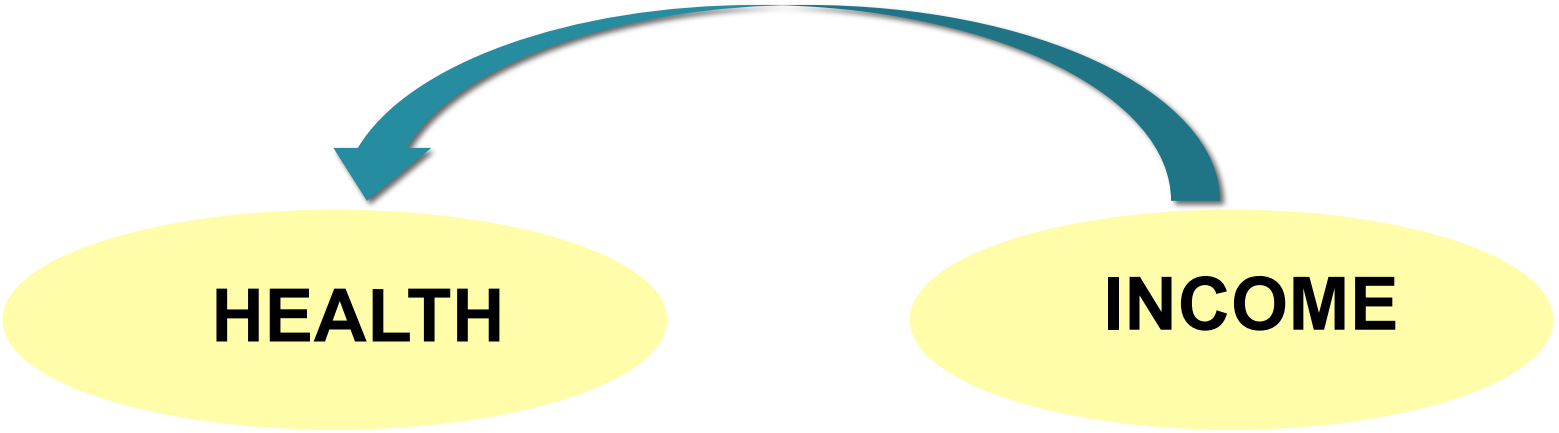
Life expectancy and income



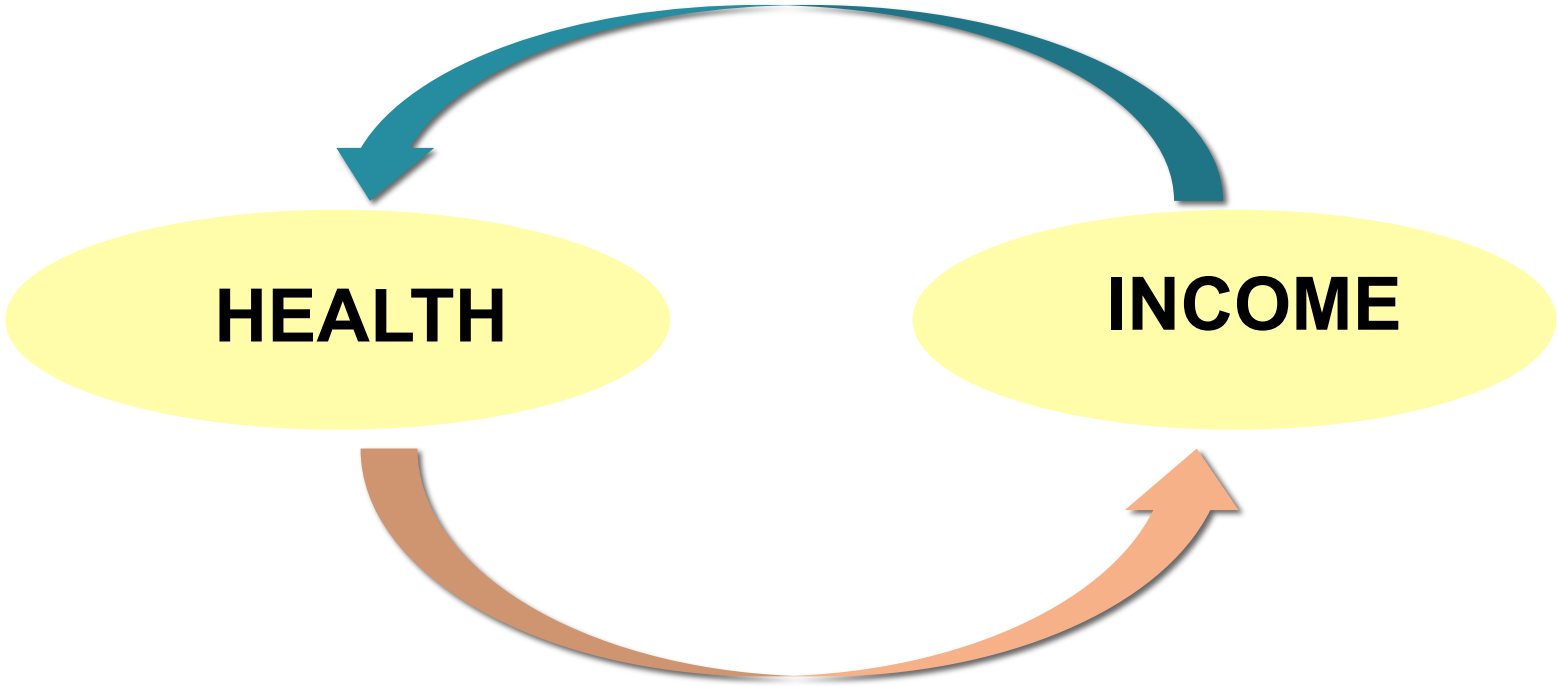
Sources: Life expectancy data: United Nations. World Population Prospects: The 2012 Revision (data for 2010);
GDP/Capita: World Bank. World Databank (data for 2012).

From income to health…

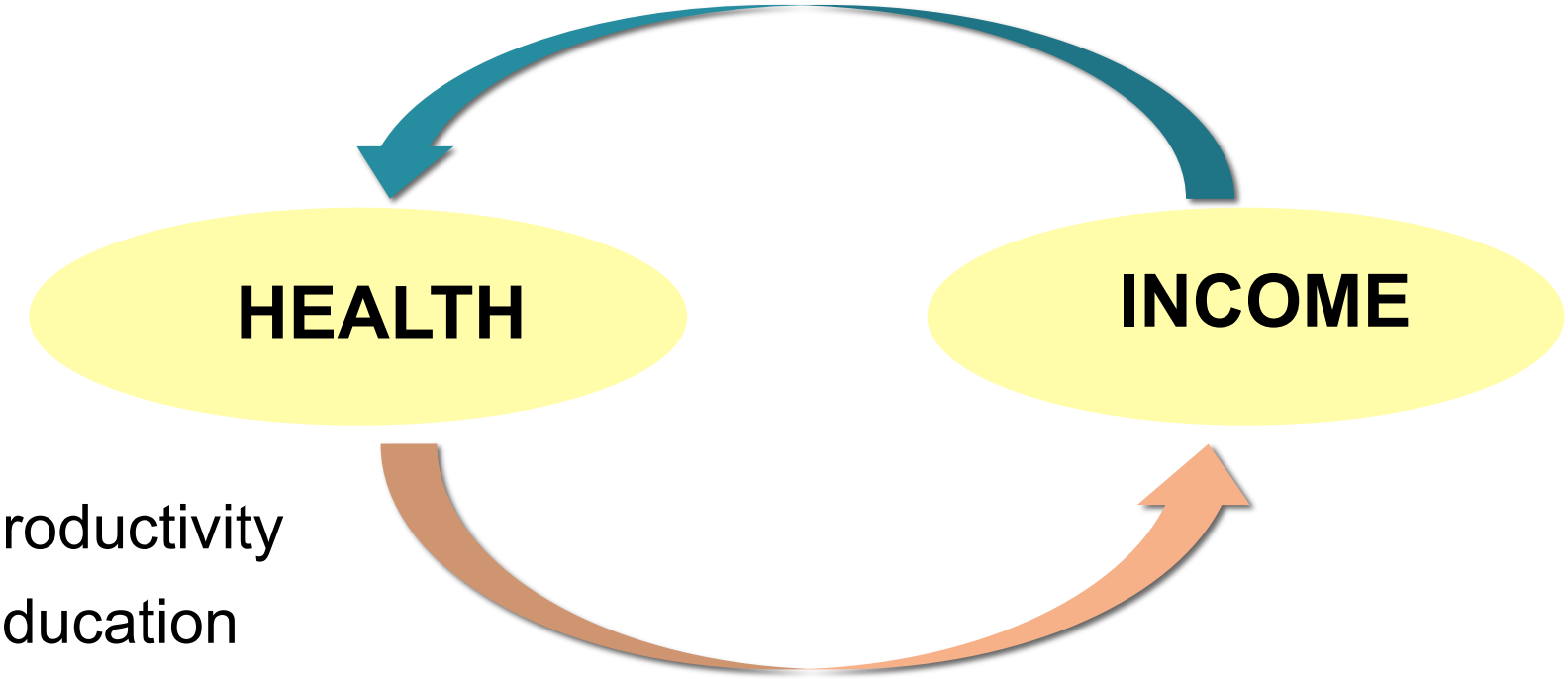


- Nutrition
- Safe water
- Sanitation
- Health care
- Psycho-social resources

… and from health to income



… and from health to income



- Productivity
- Education
- Investment
- Demographic dividend

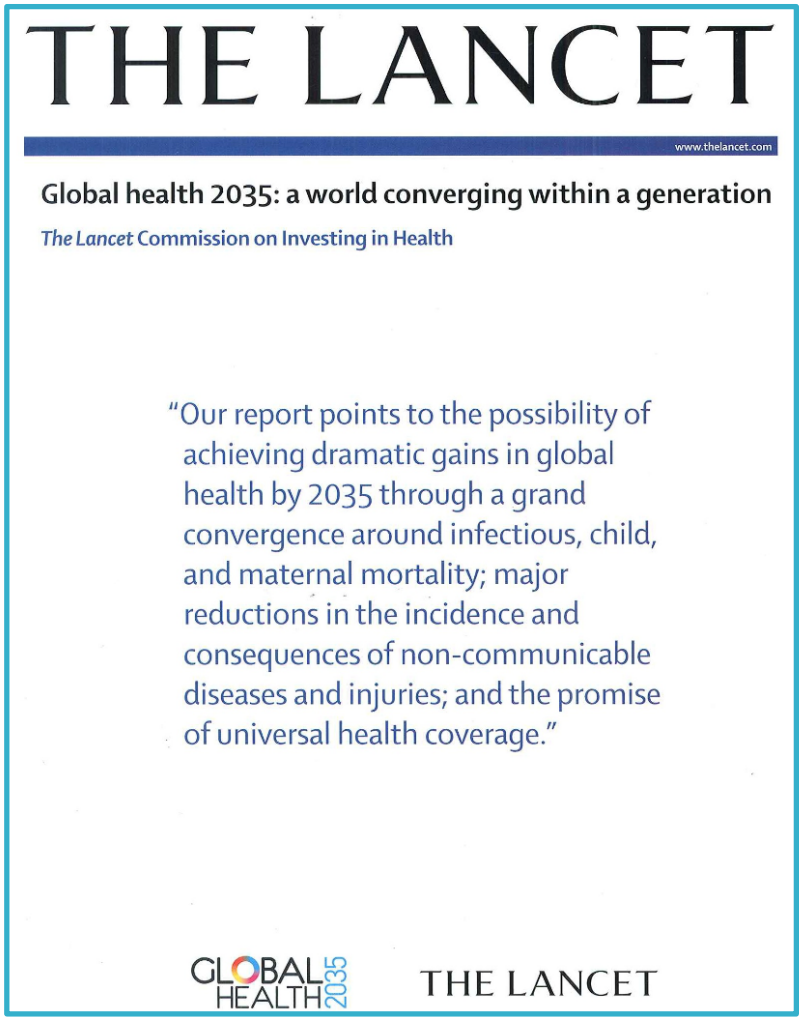
Sources: Bloom DE & Fink G. (2013). "The Economic Case for Devoting Public Resources to Health" in Jeremy Farrar, Nicholas White, David Lalloo, Peter Hotez, Thomas Junghanss and Gagandeep Kang, eds., *Manson's Tropical Diseases 23rd Edition*, Elsevier.
Bärnighausen T, Bloom DE, Cafiero ET, O'Brien JC. (2012). Economic evaluation of vaccination: capturing the full benefits, with an application to human papillomavirus. *Clinical Microbiology and Infection* 18 (Suppl. 5): 1–7

Stage decorations of the public health lecture. Source: Bu (2009) from Strother F. (1918) 'An American Physician-Diplomat in China', *The World's Work*, New York: Doubleday, page and Co., p. 546.

Turbo-charging the economy

A 10 year gain in life expectancy translates into as much as 1 additional percentage point of annual growth of income per capita

Investing in health


THE LANCET

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Global health 2035: a world converging within a generation

The Lancet Commission on Investing in Health

"Our report points to the possibility of achieving dramatic gains in global health by 2035 through a grand convergence around infectious, child, and maternal mortality; major reductions in the incidence and consequences of non-communicable diseases and injuries; and the promise of universal health coverage."

GLOBAL HEALTH 2035

THE LANCET

“A healthy population is a prerequisite for growth as much as a result of it.

Dr. Gro Harlem Brundtland
Director-General, WHO 1998-2003
On the occasion of the launch of the Report of the WHO Commission on Macroeconomics and Health

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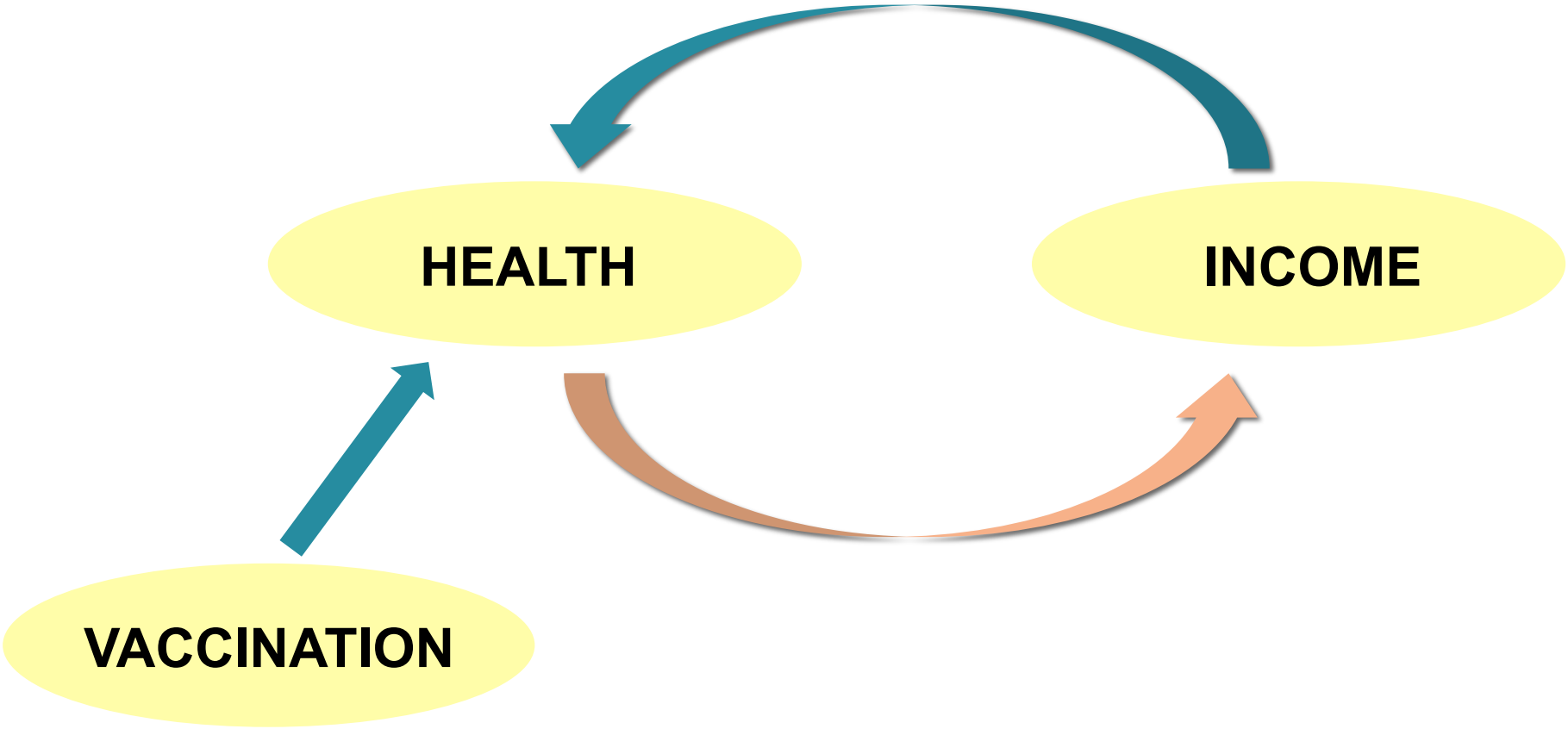
Health and income: application to vaccination



Inattention to the full economic benefits…

Valuing vaccinations: the traditional perspective

Perspective		Benefit categories
	Narrow	Health care cost savings
		Care-related productivity gains

Valuing vaccinations: a broader perspective

Perspective		Benefit categories
Broad	Narrow	Health care cost savings
		Care-related productivity gains
		Outcome-related productivity gains
		Behavior-related productivity gains
		Community externalities
		Utilitarian value of health gains

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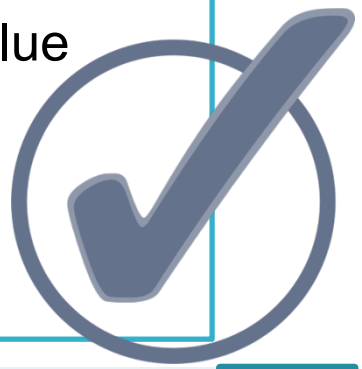
Valuing vaccinations: selecting the right tool

- **Cost-effectiveness analysis**
  - Compares 2 or more health interventions with a common health outcome
  - Outcomes expressed in terms of DALYs or gain in life years

- **Benefit-cost analysis**
  - Looks at a range of health and non-health outcomes
  - Outcomes expressed in terms of a dollar value



Evolving evidence base

- 'The value of vaccination', *World Economics*, 2005.
- 'Do we fully understand the economic value of vaccines?', *Vaccine*, 2007.
- 'Accounting for the full benefits of childhood vaccination in South Africa', *South African Medical Journal*, 2008.
- 'The effect of maternal tetanus immunization on children's schooling attainment in Matlab, Bangladesh: follow-up of a randomized trial.' *Social Science & Medicine,* 2011.
- 'Rethinking the benefits and costs of childhood vaccination: the example of the *Haemophilus influenza* type b vaccine', *Vaccine*, 2011
- 'Estimated economic benefits during the 'Decade Of Vaccines' include treatment savings, gains in labour productivity.' *Health Affairs* 2011.
- 'The effect of vaccination on children's physical and cognitive development in the Philippines', *Applied Economics*, 2012
- 'Economic evaluation of vaccination: Capturing the full benefits, with application to HPV', *CMI*, 2012.
- 'Systematic review of studies evaluating the broader economic impact of vaccination in low and middle income countries', *BMC Public Health,* 2012.
- 'Valuing the broader benefits of dengue vaccination, with a preliminary application to Brazil', *Seminars in Immunology*, 2013
- 'Valuing vaccination,' *Proceedings of the National Academy of Sciences*, 2014

GAVI:
The power of productivity …

A drop of pure gold

"A group of researchers attempts to estimate the economic benefits of vaccination."

Reuters
Oct 13th 2005
From *The Economist*
print edition

12% by 2005

18% by 2020

Source: Bloom DE, Canning D, and Weston M. "The Value of Vaccination". *World Economics* **8**:15-39, July-September 2005

Philippines: cognitive development

Cognitive development improvements generate an estimated rate of return to investment in a basic immunization program of 21%

Source: Bloom DE, Canning D, and Seiguer E. “Childhood Immunization as Human Capital”, (*working manuscript*)

‘Rethinking the benefits and costs of childhood vaccination: the example of the Hib vaccine’

Vaccine 29 (2011) 2371–2380

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Rethinking the benefits and costs of childhood vaccination: The example of the *Haemophilus influenzae* type b vaccine☆

Till Bärnighausen[a,b], David E. Bloom[a,*], David Canning[a], Abigail Friedman[a], Orin S. Levine[c], Jennifer O'Brien[a], Lois Privor-Dumm[c], Damian Walker[d]

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ARTICLE INFO

Article history:
Received 11 April 2010
Received in revised form
29 November 2010
Accepted 30 November 2010
Available online 13 December 2010

Keywords:
Childhood vaccination
Economic evaluation
Review
Haemophilus influenzae type b vaccine

ABSTRACT

Economic evaluations of health interventions, such as vaccinations, are important tools for informing health policy. Approaching the analysis from the appropriate perspective is critical to ensuring the validity of evaluation results for particular policy decisions. Using the example of cost–benefit analysis (CBA) of *Haemophilus influenzae* type b (Hib) vaccination, we demonstrate that past economic evaluations have mostly adopted narrow evaluation perspectives, focusing primarily on health gains, health-care cost savings, and reductions in the time costs of caring, while usually ignoring other important benefits including outcome-related productivity gains (improved economic productivity due to prevention of mental and physical disabilities), behavior-related productivity gains (economic growth due to fertility reductions as vaccination improves child survival), and community externalities (herd immunity and prevention of antibiotic resistance). We further show that potential cost reductions that could be attained through changes in the delivery of the Hib vaccine have also generally been ignored in economic evaluations. Future economic evaluations of childhood vaccinations should take full account of benefits and costs, so that policymakers have sufficient information to make well-informed decisions on vaccination implementation.

Valuing the broader benefits of dengue vaccination, with a preliminary application to Brazil

Seminars in Immunology 25 (2013) 104–113

Contents lists available at SciVerse ScienceDirect

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Review

Valuing the broader benefits of dengue vaccination, with a preliminary application to Brazil

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ARTICLE INFO

Keywords:
Dengue
Vaccine
Vaccination
Immunization
Economic evaluation

ABSTRACT

The incidence of dengue has been on the rise since at least the 1960s, bringing greater urgency to the need for a vaccine to prevent the disease. Recent advances suggest that the scientific world is moving closer to an effective dengue vaccine. However, there are concerns that the price of a future vaccine could limit its uptake. High prices, in addition to other challenges, have already weighed negatively in government decisions to include other new vaccines in national immunization programs, e.g., the pneumococcal, rotavirus, and human papillomavirus vaccines. Recent research on the value of vaccination, however, suggests that vaccination confers benefits that are often neglected by traditional economic evaluations. In the case of dengue, commonly overlooked benefits are likely to include reduced spending on outbreak control, averted losses in tourism flows, and avoided productivity losses due to long-term dengue sequelae. Accounting for these and other broader benefits of dengue vaccination could reveal significantly greater economic value and strengthen the case for inclusion of dengue vaccination in national immunization programs. In this article we discuss a framework for the broader value of vaccination and review its application in the context of dengue vaccination for Brazil.

Dengue in Brazil

Sao Paulo Dengue Fever Outbreak Concerns World Cup Visitors, Officials

By Connor Adams Sheets @ConnorASheets
on June 20 2014 6:38 PM

The Rio Time
News in Rio de Janeiro, Brazil

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Issue CCXVIII - Weekly Edition: May 15 - May 21, 2013

Dengue Fever Cases Triple in Brazil: Daily

February 26, 2013 | Filed under Daily Update, Politics | Posted by Contributing Reporter

By Leo Byrne, Contributing Reporter

RIO DE JANERIO, BRAZIL – The ministry of health reported today that the number of dengue fever cases in the country was three times higher than during the same period last year. Although the number of serious cases and deaths decreased by 44 and 20 percent respectively, the total number of cases rose to 204,650 in the first seven weeks of the year.

The Secretary of Health Observation, Jarbas Barbosa attributed the increase to a different strain of the disease, known as DENV-4 which has been circulating Brazil since 2011. A higher than usual incidence of mosquitoes was also to blame.

"Every time we have a new strain in a place where it has never previously circulated, more people are susceptible. In 2013,[DENV-4] hit big cities and this [illegible]ease in the number of cases,"

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26 February 2013 Last updated at 10:26 GMT

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Brazil dengue cases almost triple as new strain spreads

Health authorities in Brazil say there has been a steep rise in the confirmed cases of dengue fever this year.

More than 200,000 people were infected in the first seven weeks of 2013 compared to 70,000 in the same period last year, official figures suggest.

The southern state of Mato Grosso do Sul has been hardest hit.

Officials said the cases were likely to rise as the rainy season increases

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‘Economic evaluation of vaccination: Capturing the full benefits, with application to HPV’

ORIGINAL ARTICLE 10.1111/j.1469-0691.2012.03977.x

Economic evaluation of vaccination: capturing the full benefits, with an application to human papillomavirus

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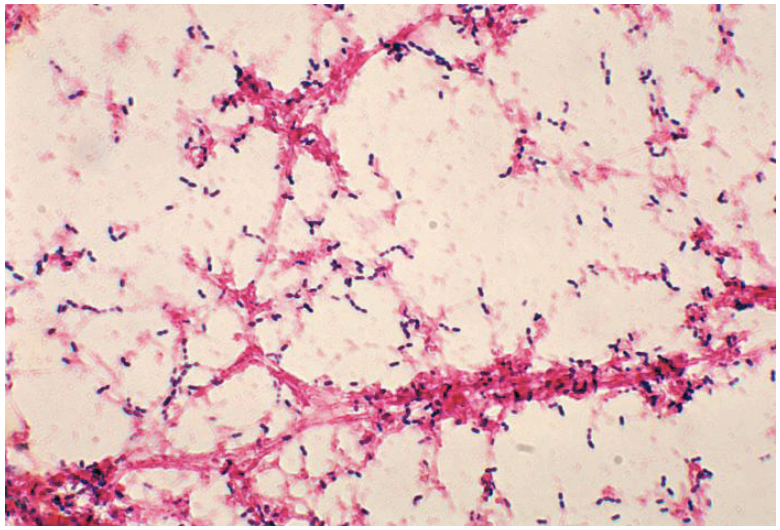
Abstract

Vaccination has been among the greatest contributors to the past century’s dramatic improvements in health and life expectancy. Recent advances in vaccinology have resulted in new vaccines that will likely lead to substantial future health gains. However, the high cost of these new vaccines, such as the human papillomavirus (HPV) vaccine, poses an obstacle to their widespread adoption in many countries. Economic evaluation can help to determine if investment in vaccine introduction is worthwhile. However, existing economic evaluations usually focus on a narrow set of vaccination-mediated benefits—most notably avoided medical-care costs—and fail to account for several categories of potentially important gains. We consider three sources of such benefit and discuss them with respect to HPV vaccination: (i) outcome-related productivity gains, (ii) behaviour-related productivity gains, and (iii) externalities. We also highlight that HPV vaccination protects against more than just cervical cancer and that these other health gains should be taken into account. Failing to account for these broader benefits of HPV vaccination could result in substantial underestimation of the value of HPV vaccination, thereby leading to ill-founded decisions regarding its introduction into national immunization programmes.

Keywords: Benefit–cost analysis, economic evaluation, economics, externalities, human papillomavirus vaccine, vaccination
Original Submission: 5 May 2012; **Revised Submission:** 18 June 2012; **Accepted:** 23 June 2012

Pneumo vaccination in Ontario



Final remarks

- **Don't focus on costs in isolation**
- **Need better alignment on a defined range of potential prices**
- **Need better data and more evidence**

The New York Times

HEALTH | PAYING TILL IT HURTS : Vaccines

COMMENTS

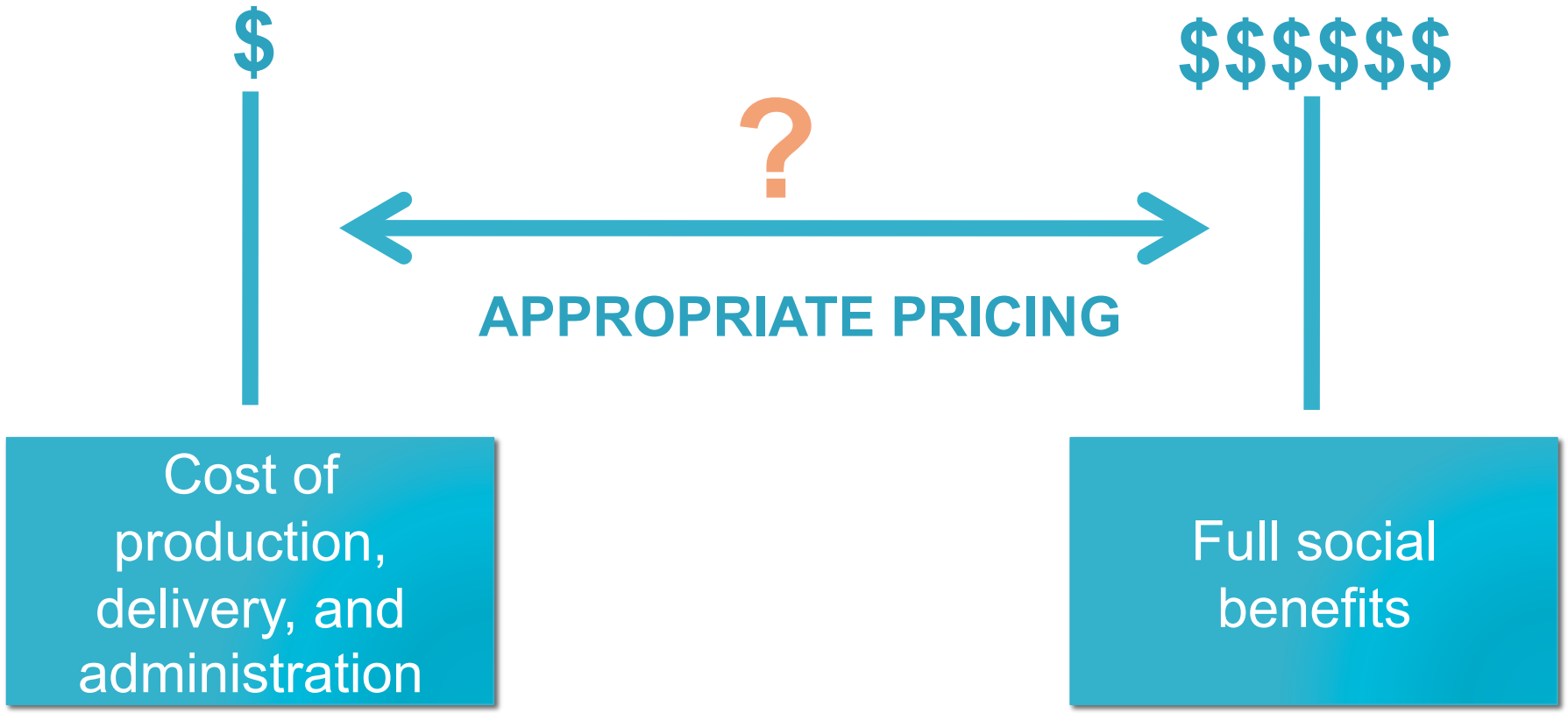
The Price of Prevention: Vaccine Costs Are Soaring

By ELISABETH ROSENTHAL JULY 2, 2014

PAINFUL MEDICINE Rachel Chavez, left, and Beth Barnhart administer vaccines to Caius Sims as his mother, Cedra Sims, helps hold him at Dr. Lindsay Irvin's office.

Ben Sklar for The New York Times

Debate on pricing: resource costs or value-based?



"I'll have an ounce of prevention."