Health, Growth, and Finance

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Health

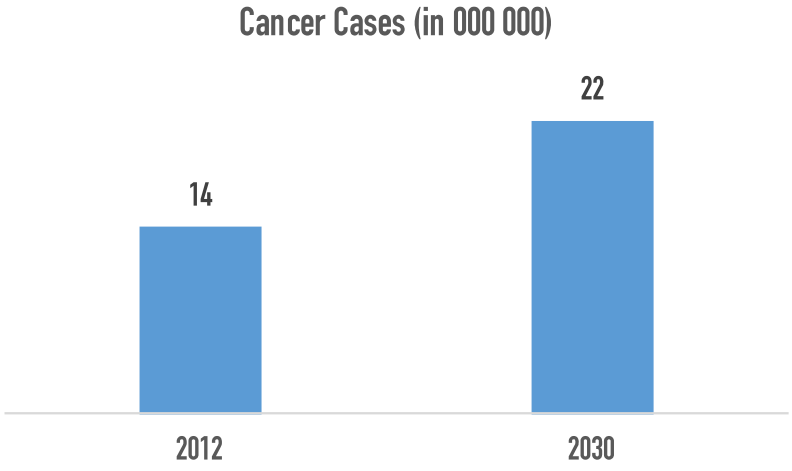
Health

1. Healthconomic Crises

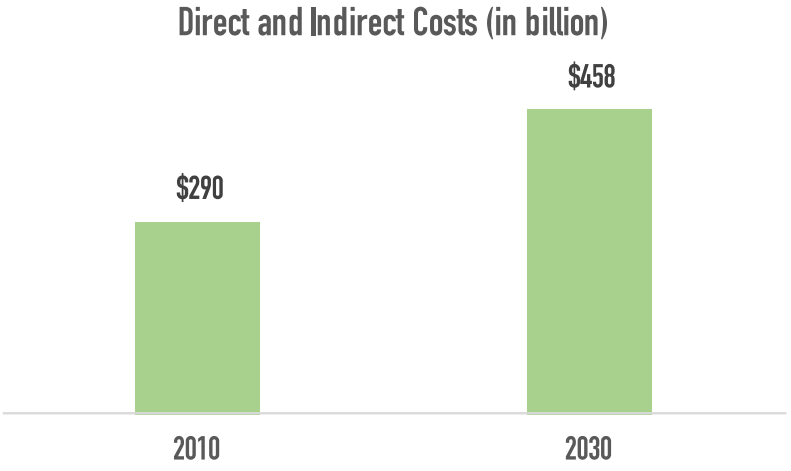
- Rises in unemployment caused many countries to cut public-sector expenditure on health care
- Increases in mortality rates
  - suicide rates
  - cardiovascular disease incidence

⇢This is due to increased behavioural, mental, and physiological stress

2. Cancer (worldwide)



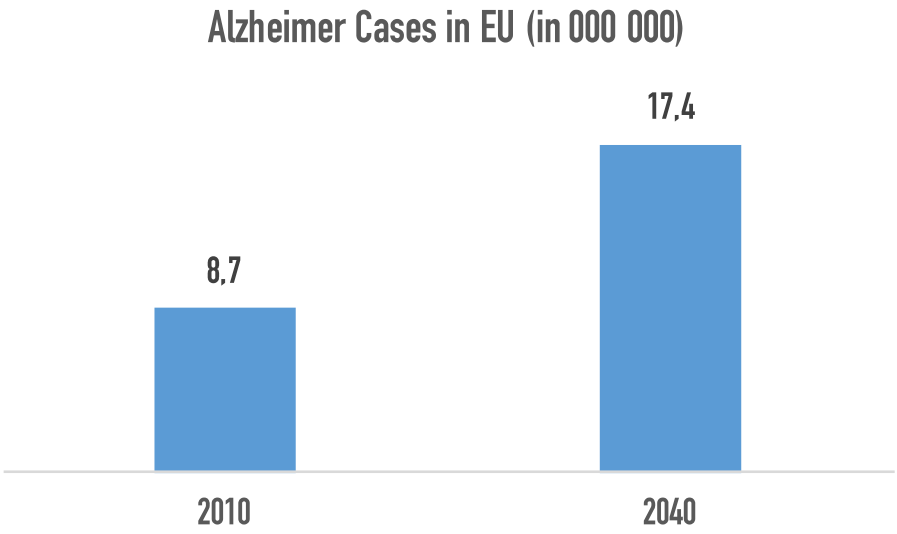
Source: GLOBOCAN 2012 (IARC)

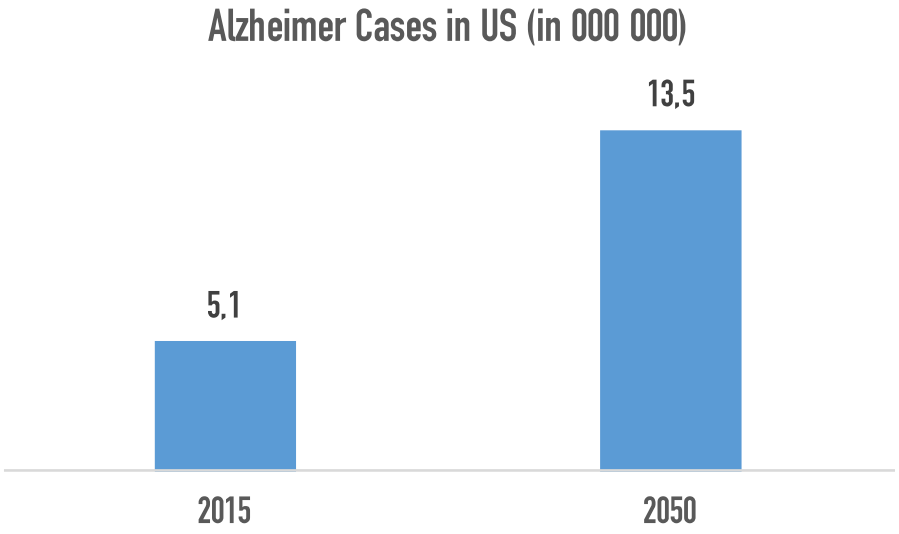


Source: American Association of Cancer Research (AACR)

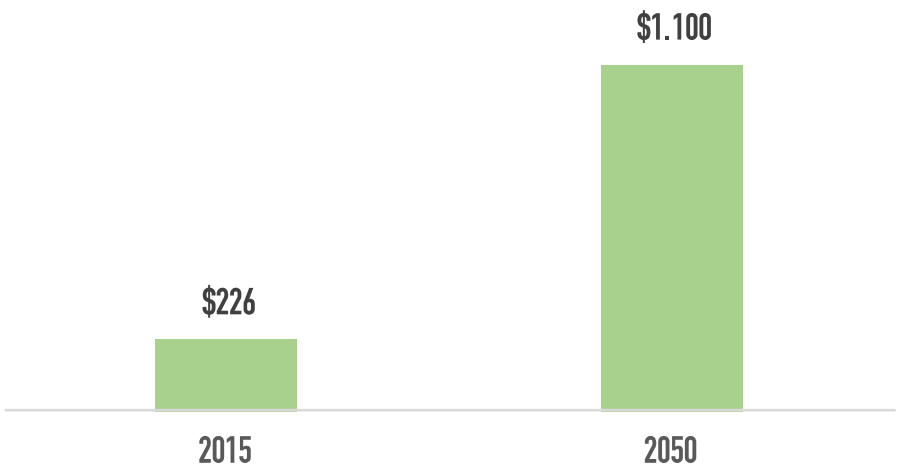
Health

3. Alzheimer (European Union and US)





Cost per person with dementia
€22,000 per year



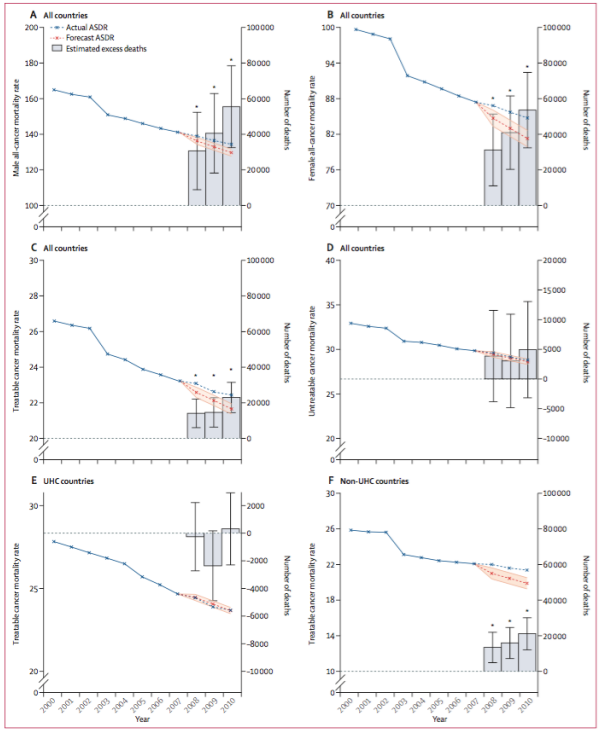
Source: http://www.alzheimer-europe.org/

Source: http://alz.org/

Health

4. The Lancet

- Unemployment increases are associated with rises in cancer mortality
- the 2008–10 economic crisis was associated with about 260 000 excess cancer-related deaths in the OECD countries



Economic downturns, universal health coverage, and cancer mortality in high-income and middle-income countries, 1990–2010: a longitudinal analysis

Mahiben Maruthappu*, Johnathan Watkins*, Aisyah Mohd Noor, Callum Williams, Raghib Ali, Richard Sullivan, Thomas Zeltner, Rifat Atun

Summary

Background The global economic crisis has been associated with increased unemployment and reduced public-sector expenditure on health care (PEH). We estimated the effects of changes in unemployment and PEH on cancer mortality, and identified how universal health coverage (UHC) affected these relationships.

Methods For this longitudinal analysis, we obtained data from the World Bank and WHO (1990–2010). We aggregated mortality data for breast cancer in women, prostate cancer in men, and colorectal cancers in men and women, which are associated with survival rates that exceed 50%, into a treatable cancer class. We likewise aggregated data for lung and pancreatic cancers, which have 5 year survival rates of less than 10%, into an untreatable cancer class. We used multivariable regression analysis, controlling for country-specific demographics and infrastructure, with time-lag analyses and robustness checks to investigate the relationship between unemployment, PEH, and cancer mortality, with and without UHC. We used trend analysis to project mortality rates, on the basis of trends before the sharp unemployment rise that occurred in many countries from 2008 to 2010, and compared them with observed rates.

Results Data were available for 75 countries, representing 2·106 billion people, for the unemployment analysis and for 79 countries, representing 2·156 billion people, for the PEH analysis. Unemployment rises were significantly associated with an increase in all-cancer mortality and all specific cancers except lung cancer in women. By contrast, untreatable cancer mortality was not significantly linked with changes in unemployment. Lag analyses showed significant associations remained 5 years after unemployment increases for the treatable cancer class. Rerunning analyses, while accounting for UHC status, removed the significant associations. All-cancer, treatable cancer, and specific cancer mortalities significantly decreased as PEH increased. Time-series analysis provided an estimate of more than 40 000 excess deaths due to a subset of treatable cancers from 2008 to 2010, on the basis of 2000–07 trends. Most of these deaths were in non-UHC countries.

Interpretation Unemployment increases are associated with rises in cancer mortality; UHC seems to protect against this effect. PEH increases are associated with reduced cancer mortality. Access to health care could underlie these associations. We estimate that the 2008–10 economic crisis was associated with about 260 000 excess cancer-related deaths in the Organisation for Economic Co-operation and Development alone.

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Introduction

The economic crisis beginning in 2008 saw substantial rises in unemployment, and caused many countries to cut public-sector expenditure on health care (PEH).[1,2,3] Several studies[4–14] have shown the impact of such macroeconomic changes on outcome indicators such as suicide rates, cardiovascular disease incidence, and all-cause mortality, with economic downturns leading to increases in respective mortality rates, likely due to increased behavioural, mental, and physiological stress—so-called healthconomic crises.[15]

Cancer is a leading cause of death worldwide, accounting for 8·2 million deaths in 2012, with estimates suggesting a rise in annual cancer cases from 14 million in 2012, to 22 million by 2030.[16] As such, an understanding of the effects of macroeconomic changes on cancer outcomes worldwide is important. However, few studies have analysed the relation between economic downturns and cancer outcomes, especially in countries with underdeveloped social security and health-care systems, which can be particularly susceptible to economic shocks.

Establishment of a causal relation between an economic change, such as aggregate unemployment, and cancer mortality has been challenging because downstream effects of unemployment-induced behavioural changes on lifestyle-related cancers manifest much later (after 20–30 years) than, for example, suicide or acute stress-related cardiovascular events. However, access to health care and PEH might act as mediating factors with more immediate effects on health outcomes.

We examined the association between changes in aggregate unemployment and PEH with deaths due to specific cancers, groups of cancers, and all cancers for countries with available data for 1990–2010 deemed to be of sufficient quality. Mortality was regarded as a more reliable measure of health outcomes than incidence

Growth

Growth

What economists say about health and economic growth

- Health is an **important determinant** of economic growth (Barro, 2013)
  1. better health tends in various ways to stimulate economic growth
  2. economic growth encourages further accumulation of health capital

- **No clear** relationship (Acemoglu, Johnson, 2006)
  - Medical innovations from 1940 to 1980:

- Other **empirical findings** on the impact of health on GDP
  - 1 extra year of life expectancy ⇢ 4% increase in GDP per capita (Bloom et al., 2004)
  - 1% increase in life expectancy ⇢ 6% increase in total GDP in the long run, and 5% increase in GDP per capita (Swift, 2011)

Growth

When one considers developing countries, the **assumption that income growth will automatically lead to health improvement is unwarranted**; and the assumption that income growth is the best way to achieve health improvement is even more unwarranted.

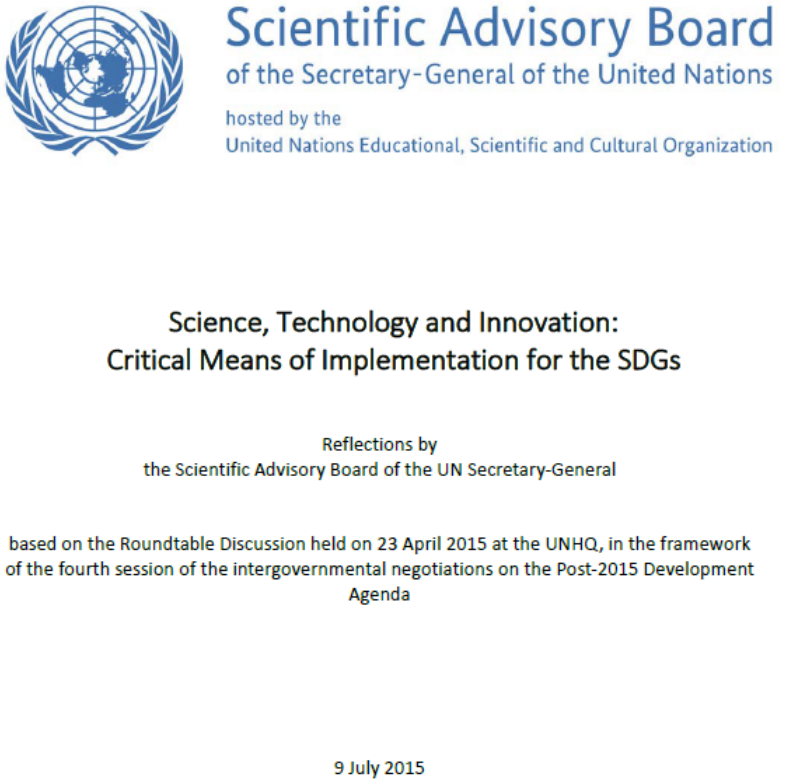
Deaton (2006) writes, "**Economic growth frequently needs help to guarantee an improvement in population health**"

David N. Weil (2014)

Investing in Science

9 July 2015
Scientific AB – UN Secretary-General

- Investing up to **3.5% of GDP** in science, technology and innovation can be "the game changer" for development
- Science, technology and innovation can help alleviate poverty, **reduce inequalities, increase income and improve health**, scientists advising U.N. Secretary-General Ban Ki-moon on sustainable development said
- Closing the gap between developed and developing countries depends on first **closing the gap on science, technology and innovation**



Scientific Advisory Board
of the Secretary-General of the United Nations
hosted by the
United Nations Educational, Scientific and Cultural Organization

Science, Technology and Innovation:
Critical Means of Implementation for the SDGs

Reflections by
the Scientific Advisory Board of the UN Secretary-General

based on the Roundtable Discussion held on 23 April 2015 at the UNHQ, in the framework of the fourth session of the intergovernmental negotiations on the Post-2015 Development Agenda

9 July 2015

How to Invest in Science?

Big vs. Small Science Conundrum

- We just don't know" whether it is "**better to spend $3 billion on the Human Genome Project or to support 6,000 researchers each to the tune of $500,000**" Megaprojects, like epidemiological cohorts, that "provide inputs for more research down the road" but don't by themselves, provide answers "are especially difficult to evaluate.

Paula Stephan. How Economics Shapes Science. Harvard University Press, 2012

Investing in Distant Reward

- Would you spend money today to make the world a substantially better place for your children and grandchildren?

  Most of us would.
- But what if the benefit would accrue only to your great-great-great-great-grandchildren, not born until the 22nd century?

William Press, Science, 2013

EDITORIAL

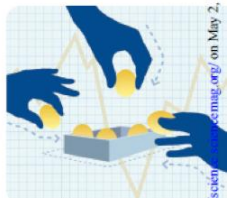
Investing in Distant Rewards

William H. Press is the president of the American Association for the Advancement of Science and the Warren J. and Viola M. Raymer Professor in Computer Science and in Integrative Biology at the University of Texas, Austin, TX, USA. E-mail: wpress@cs.utexas.edu.

WOULD YOU SPEND MONEY TODAY TO MAKE THE WORLD A SUBSTANTIALLY BETTER PLACE FOR YOUR children and grandchildren? Most of us would. But what if the benefit would accrue only to your great-great-great-great-grandchildren, not born until the 22nd century? That's an awfully distant time horizon for most people. Many would probably spend today's resources on more immediate concerns.

Economists model this preference as a "social discount rate," a form of reverse compound interest that assesses future benefits or catastrophes as exponentially less important than immediate ones. Mathematical arguments favor this model over several alternatives. But when applied to the question "How much should we spend today on basic science research?", the model often gives the answer "Not much!" This is because the returns from basic research, although possibly large, can be quite distant. Reverse compound interest thus knocks out the returns. But, I argue here, exponential discounting is both mathematically and practically inappropriate when applied to basic science. Also, importantly, the public appears to know instinctively why it does not apply.

In its broad range, from useful incremental advances to world-changing discoveries, scientific research exhibits what statisticians call a "heavy-tailed" probability distribution. Such distributions have the property that more important events are only mildly less probable, a so-called power law. A consequence is that rare events can have truly huge magnitudes, in comparison to typical ones. The discovery of penicillin was no typical incremental advance, and the confluence of fundamental discoveries in quantum mechanics and atomic structure that led to modern electronics was surely world-changing. Yet both occurred in a single century. Science's heavy tail allows us to expect even greater future



Investing in Science

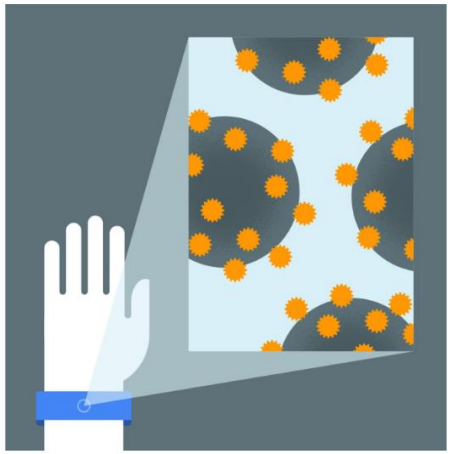
- Benefits of scientific discovery are heavy-tailed and can play paradigmatic changes, but need financial resources

One of the projects Google eventually settled on was what Conrad calls the "Nanoparticle Platform," an effort to build a cancer-detecting pill, publicly revealed last week. The idea is that this pill will contain magnetic nanoparticles that can latch onto certain cancer-related molecules in the bloodstream—and that a wearable device could then use magnetic properties to recognize when this happens. As Gambhir points out, this is just one of many efforts to detect cancer *in vivo*—i.e. within the body, without drawing blood. But he'll also tell you that Google brings something new to such a project.

Part of it, he explains, is that Google has built an unusually talented team that spans multiple disciplines, including physics, chemistry, and biology. "They have brought on a lot of very smart people that are thinking about these problems in very unique ways, " Gambhir says, pointing out the company has hired some researchers from his lab. Certainly, some academic centers have built their own multi-discipline teams, but on top of this, Google provides a new kind of corporate leverage. It aims to push this sort of thing into the market at speed.

CADE METZ BUSINESS 11.05.14 6:30 AM

WHY GOOGLE'S CANCER-DETECTING PILL IS MORE THAN JUST HYPE



Google is hoping to build nanoparticles that can detect cancers inside your body—and notify a wearable computer on your wrist. Google

NEWS & VIEWS

doi:10.1038/nature18443

IMMUNOTHERAPY

Cancer vaccine triggers antiviral-type defences

An immunotherapy approach targets nanoparticles to dendritic cells of the immune system, leading to an antitumour immune response with antiviral-like features. Initial clinical tests of this approach show promise.

JOLANDA DE VRIES & CARL FIGDOR

Preventive vaccines are perhaps the most effective form of immunotherapy. But in a paper online in *Nature*, Kranz *et al.*[1] describe a vaccination strategy against cancer that targets existing tumours by recruiting immune mechanisms normally used against viral infection. The authors used nanoparticles carrying tumour RNA to simulate the intrusion of a viral pathogen into the bloodstream. When the nanoparticles reach lymphoid tissues, including the spleen and lymph nodes, they activate antiviral defence mechanisms in immune cells such as dendritic cells. The dendritic cells translate RNA obtained from the nanoparticles to express and present tumour antigens (molecules used by the immune response as attack targets) to the T cells of the immune system, priming these cells to launch an antitumour immune response.

Why is it so difficult to effectively vaccinate against cancer? One reason is that cancer cells are similar in many ways to normal cells and the immune system avoids attacking the self. Only relatively modest immune responses occur with vaccines containing antigens that are also expressed on healthy tissue. Strong immune responses can be expected only when cancer cells express antigens that are not usually expressed in normal adult cells.

Another reason is that the growth of a cancer is not accompanied by strong inflammatory signals such as those that occur during microbial infection and which initiate a strong immune response. This leads to tumour microenvironments in which immune cells tolerate, or even promote, cancer growth[2]. Antitumour vaccines must therefore work when the disease has already taken hold, and often when it has spread throughout the body. Last, and in a key contrast to preventive vaccinations against viruses, most cancers coexist and coevolve with our immune systems over years, resulting in an immunosuppressive tumour microenvironment that adds an extra obstacle for immunotherapy.

In vaccine approaches for a range of diseases, specialized antigen-presenting cells have a pivotal role. Dendritic cells in particular are extremely well suited to handling and presenting antigens to activate T cells. Cultured dendritic cells that have been loaded with antigens *in vitro* can boost immunity when given to patients with cancer, but up to now the clinical efficacy of this strategy has been limited[3]. Most of these vaccines use dendritic cells that have been derived *in vitro* from white blood cells called monocytes. *Ex vivo* activation of different dendritic-cell subsets that naturally circulate in the blood has also been investigated, using several types of dendritic cell including plasmacytoid dendritic cells, which produce high levels of the immune-response protein interferon-α (IFNα) upon viral infection[4].

Immunologists have also explored vaccines aimed at directly activating the patient's own dendritic cells *in vivo*, which avoids laborious and expensive *in vitro* culture[5]. Such a vaccine requires at least three components: an 'address label' (a dendritic-cell-specific antibody or ligand molecule such as a carbohydrate)[6–8] that targets the dendritic cell; a tumour antigen; and a compound that readies the dendritic cells to fully activate T cells (usually a ligand for a Toll-like receptor (TLR)). Nanoparticles containing antigen and TLR ligands, along with targeting antibodies or other ligands, have proved effective in animal models[9], and initial clinical trials using conjugates of dendritic-cell-targeting antibodies bound to a tumour antigen are under way (see ref. 10 for examples).

Kranz *et al.* have developed a different type of nanoparticle vaccine that does not require antibodies or ligands to target the dendritic cells. Instead, they made nanoparticles consisting of RNA–lipid complexes[11]. They first demonstrated that, by making the nanoparticles

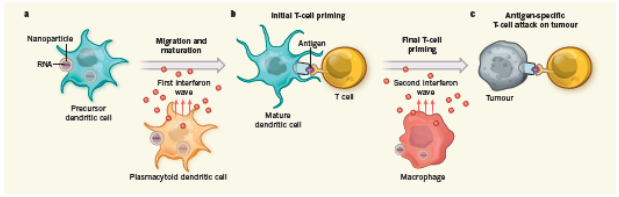


Figure 1 | An antitumour nanoparticle vaccine. a, Kranz *et al.*[1] prepared nanoparticles (lipid complexes containing RNA that encodes tumour antigens), and report that they target dendritic cells and macrophages in mice. Nanoparticle uptake by precursor dendritic cells causes them to develop into mature antigen-presenting dendritic cells that migrate to the T cells. Uptake of nanoparticles by plasmacytoid dendritic cells promotes secretion of an initial wave of interferon protein that helps to prime the first steps of T-cell activation. b, Translating the RNA within the nanoparticles, the mature dendritic cells express tumour antigens and present them to the T cells. Nanoparticle uptake by macrophages leads to a second wave of interferon release, which fully primes the T cells against specific antigens. c, The primed T cells then attack tumour cells.

Big vs. Small Science Investing

- We should make **risky research-based investments "in distant rewards"** **feasible also in the short-run**

- Maybe we could reformulate the question as:

HOW CAN WE MIX BIG WITH SMALL SCIENCE PROJECTS?

Finance

Finance

Fernandez, Stein, Lo (2012)

- Do not invest in one single project, instead consider investing in a number of projects simultaneously
- Issuing Research Backed Obligations (RBOs) with research programs as collateral

PERSPECTIVE

nature biotechnology

Commercializing biomedical research through securitization techniques

Jose-Maria Fernandez[1], Roger M Stein[1,2] & Andrew W Lo[1,3,4]

Biomedical innovation has become riskier, more expensive and more difficult to finance with traditional sources such as private and public equity. Here we propose a financial structure in which a large number of biomedical programs at various stages of development are funded by a single entity to substantially reduce the portfolio's risk. The portfolio entity can finance its activities by issuing debt, a critical advantage because a much larger pool of capital is available for investment in debt versus equity. By employing financial engineering techniques such as securitization, it can raise even greater amounts of more-patient capital. In a simulation using historical data for new molecular entities in oncology from 1990 to 2011, we find that megafunds of $5–15 billion may yield average investment returns of 8.9–11.4% for equity holders and 5–8% for 'research-backed obligation' holders, which are lower than typical venture-capital hurdle rates but attractive to pension funds, insurance companies and other large institutional investors.

Consensus is growing that the bench-to-bedside process of translating biomedical research into effective therapeutics is broken. A confluence of factors is responsible for such pessimism but one of the most widespread is the sense that the current business model for life sciences R&D is flawed[1–3]. The productivity of big pharmaceutical companies—as measured by the number of new molecular entity and biologic license applications per dollar of R&D investment—has declined in recent years[4], and their stock-price performance over the past decade—an annualized return of −1.2% for the New York Stock Exchange Arca Pharmaceutical Index during the period from 2 January 2002 to 4 January 2012—has been equally disappointing.

years, including gene therapies for previously incurable rare diseases, molecularly targeted oncology drugs, new modes of medical imaging and radiosurgery, biomarkers for drug response or for such diseases as prostate cancer and heart disease, and the use of human genome sequencing to find treatments for diseases that have confounded conventional medicine, not to mention advances in bioinformatics and computing power that have enabled many of these applications. Moreover, there are many life-threatening diseases for which the number of afflicted individuals continues to increase—if for no other reason than population growth—implying a growing demand for therapeutics from a grateful and price-insensitive clientele. Why, then, does the industry appear to be so challenged?

Here we propose one explanation for this apparent inconsistency and a possible solution. Our proposed explanation is the trend of increasing risk and complexity in the biopharma industry. This trend can be attributed to at least two distinct sources: scientific advances and economic circumstances. That biomedicine is far more advanced today than even a decade ago is indisputable, but breakthroughs such as molecular biomarkers for certain diseases generate many new potential therapies to be investigated, each of which requires years of translational research at a cost of hundreds of millions of dollars and has a substantial likelihood of failure. Although such complexity offers new hope to the afflicted, it also presents an enormous number of uncertain prospects that must be triaged by researchers, biopharma business executives, investors, policymakers and regulators.

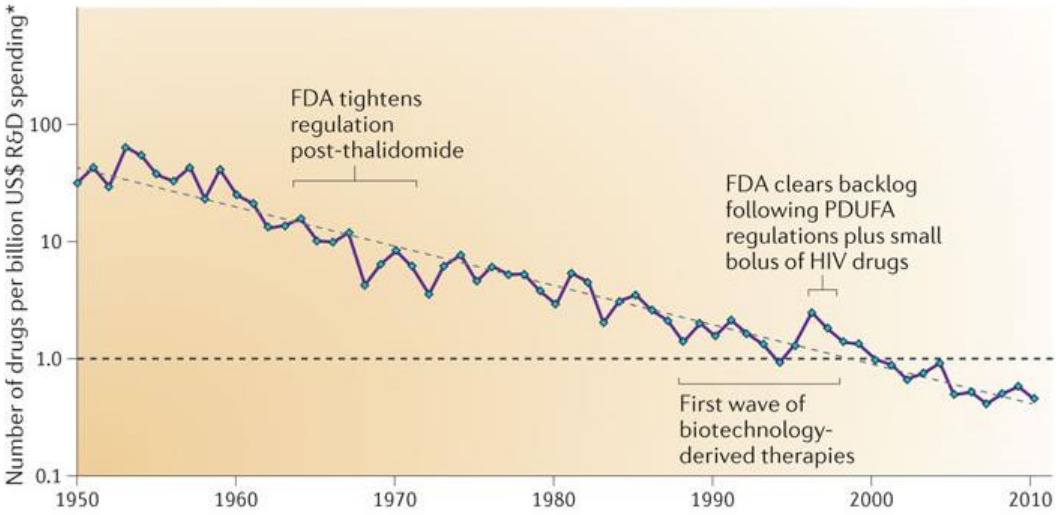
A host of economic and public-policy conditions has also contributed to this uncertainty, including declining real prescription-drug spending; rising drug-development costs and shrinking R&D budgets; the 'patent cliff' of 2012 during which several blockbuster patents will expire; increased public-policy and regulatory uncer-

Indeed

There is "missing" private R&D on scientifically feasible projects that would be developed but for their long commercialization lags

Finance

- **Eroom's Law**: Even with the tremendous and continued advancements in the R&D cost to bring a new drug to market is still increasing linearly



Jack W. Scannell, Alex Blanckley, Helen Boldon & Brian Warrington
Nature Reviews Drug Discovery 11, 191-200 (March 2012)

- **Reforming (and digitizing?) clinical trials** could help lower R&D costs, reduce time to approval and save lives

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