

Defining Success and Failure in Life Sciences



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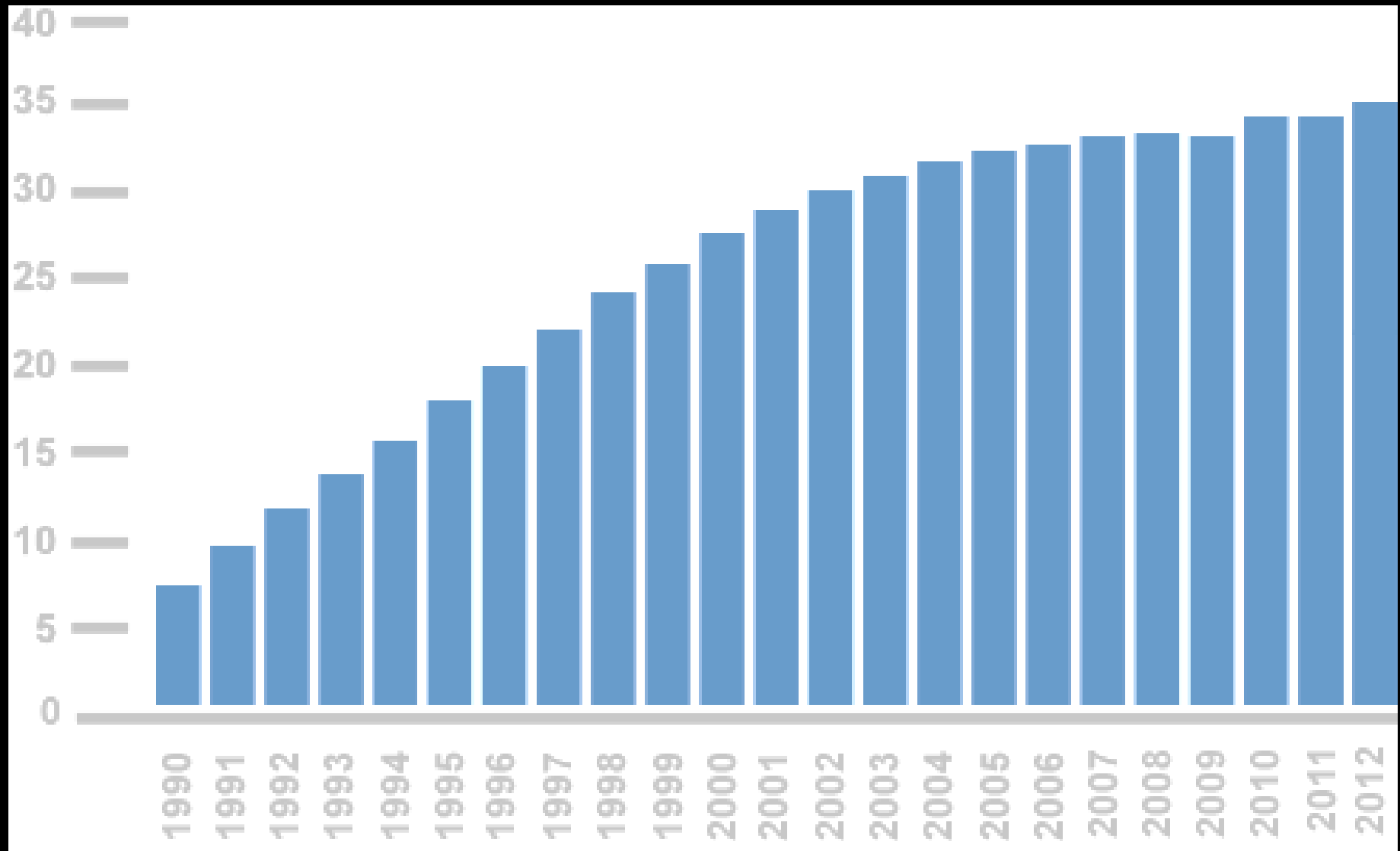
CRUCELL
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What is the use of life sciences research?

to improve health

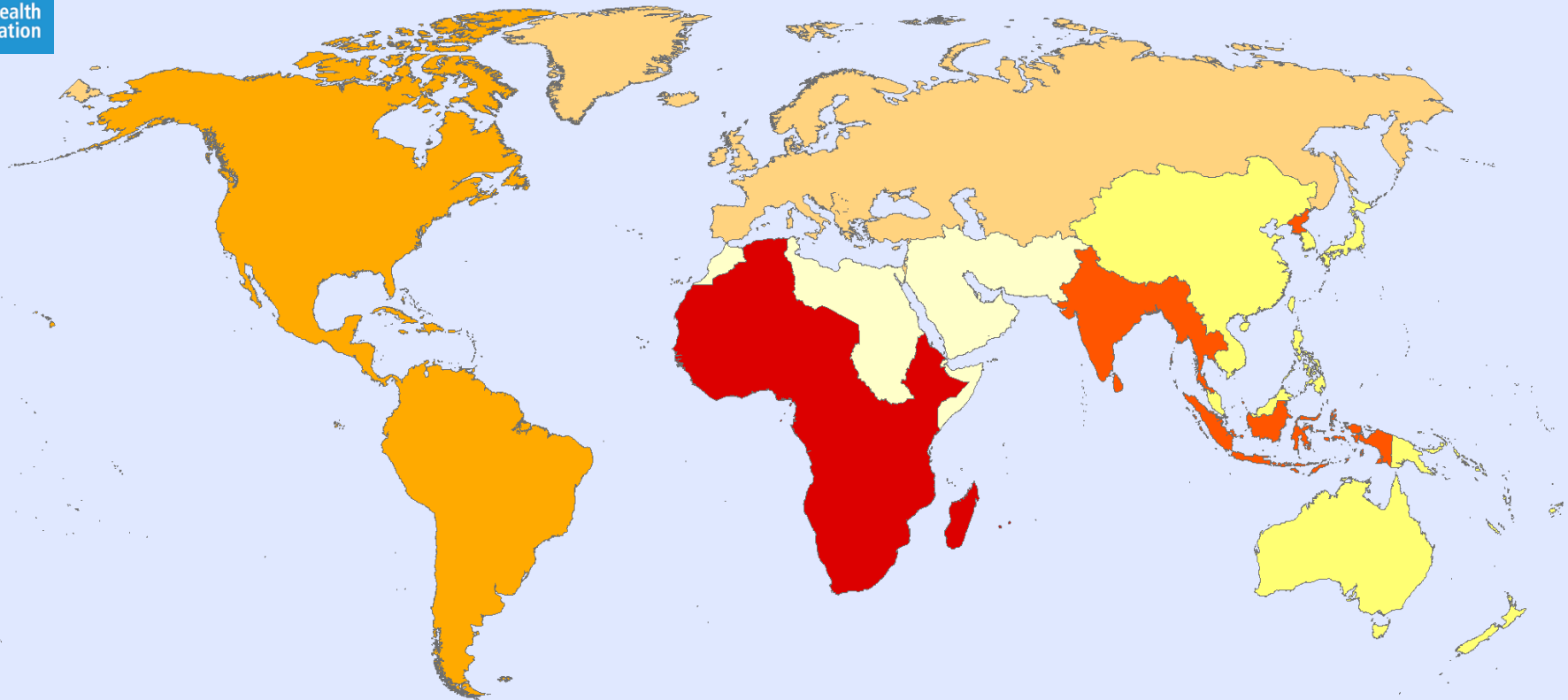
Number of people living with HIV (millions)



South-East Asia and Africa are most affected by AIDS, 2011



World Health Organization



Number of people (millions), by WHO region

Eastern Mediterranean: 0.56 [0.41-0.80]	Americas: 3.00 [2.50-3.70]
Western Pacific: 1.30 [1.10-1.60]	South-East Asia: 3.5 [2.60-4.60]
Europe: 2.30 [2.00-2.70]	Africa: 23.00 [22.00-25.00]

Total: 34.00 [31.40-35.90]

0 875 1,750 3,500 Kilometers

A Lifetime of HIV

infection

asymptomatic

AIDS



Reduce Incidence and Prevent Transmission

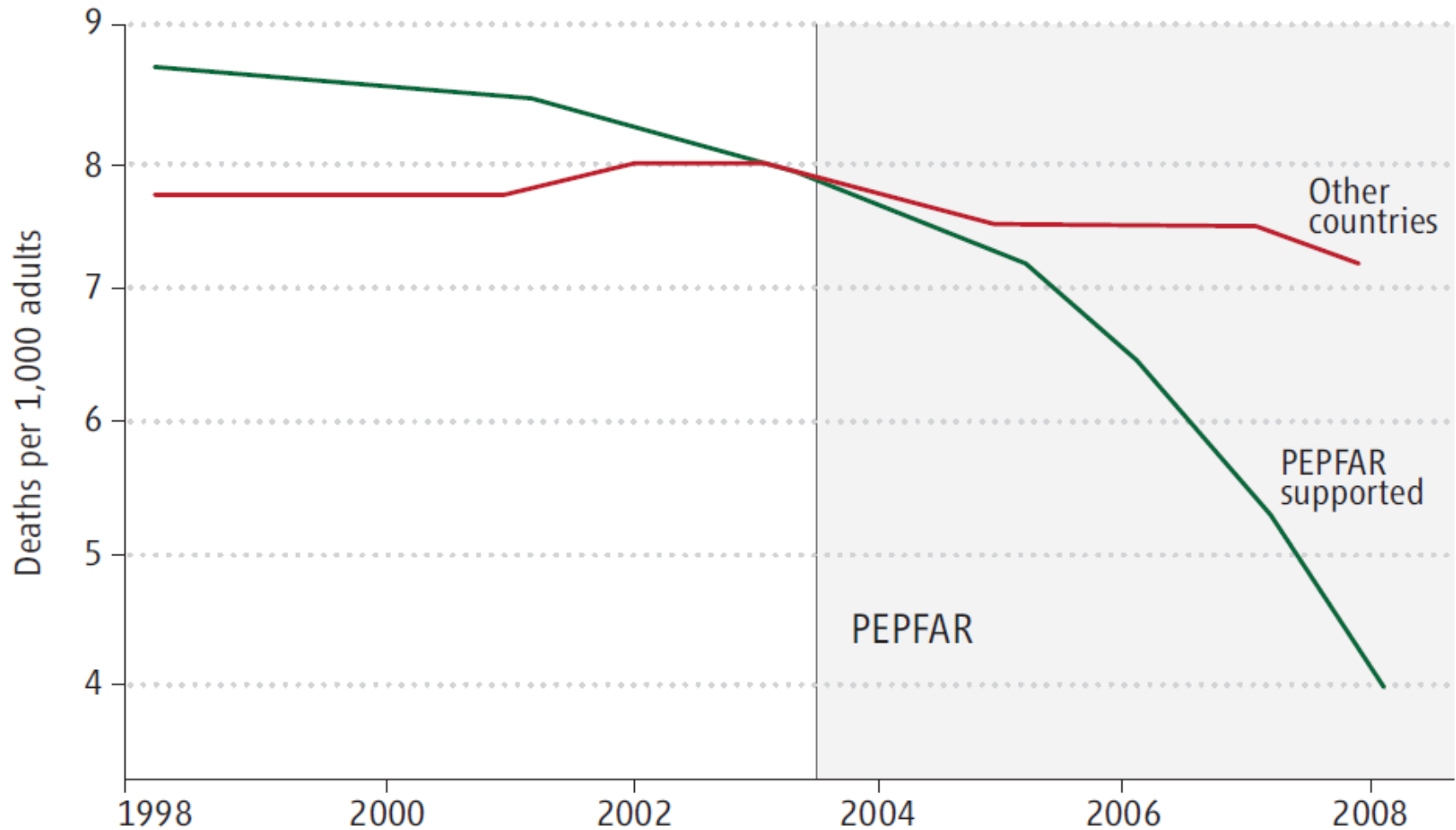
US President's Emergency Plan for AIDS (PEPFAR)



“...it was invented...by President George W. Bush, whose reputation in international affairs is dominated by his war on terrorism, military interventions in Iraq and Afghanistan, and the antagonism he displayed to the United Nations and to several of our traditional partners”

Harold Varmus, Director
US National Cancer Institute

Deaths in PEPFAR-Supported Countries in Africa





EXPRESSION OF HUMAN IMMUNODEFICIENCY VIRUS ANTIGEN (HIV-Ag) IN SERUM AND CEREBROSPINAL FLUID DURING ACUTE AND CHRONIC INFECTION

Jaap Goudsmit^a, Deborah A. Paul^c, Joep M. A. Lange^a, Hans Speelman^b, Jan Van Der Noordaa^a, Hayo J. Van Der Helm^b, Frank De Wolf^{a, f}, Leon G. Epstein^d, Willy J. A. Krone^a, Eric Ch. Wolters^e, James M. Oleske^d, Roel A. Coutinho^f

THE LANCET

BMJ

Declining incidence of AIDS dementia complex after introduction of zidovudine treatment

BMJ VOLUME 299 30 SEPTEMBER 1989

Peter Portegies, Jan de Gans, Joep M A Lange, Mayke M A Derix, Hans Speelman, Margreet Bakker, Sven A Danner, Jaap Goudsmit

Human herpesvirus 8 infections in the Amsterdam Cohort Studies (1984–1997): Analysis of seroconversions to ORF65 and ORF73

4838–4843 | PNAS | April 25, 2000 | vol. 97 | no. 9

PNAS

Proceedings of the National Academy of Sciences of the United States of America

Jaap Goudsmit^{*†}, Neil Renwick^{*}, Nicole H. T. M. Dukers[‡], Roel A. Coutinho[‡], Siem Heisterkamp[§], Margreet Bakker^{*}, Thomas F. Schulz[¶], Marion Cornelissen^{*}, and Gerrit J. Weverling[§]

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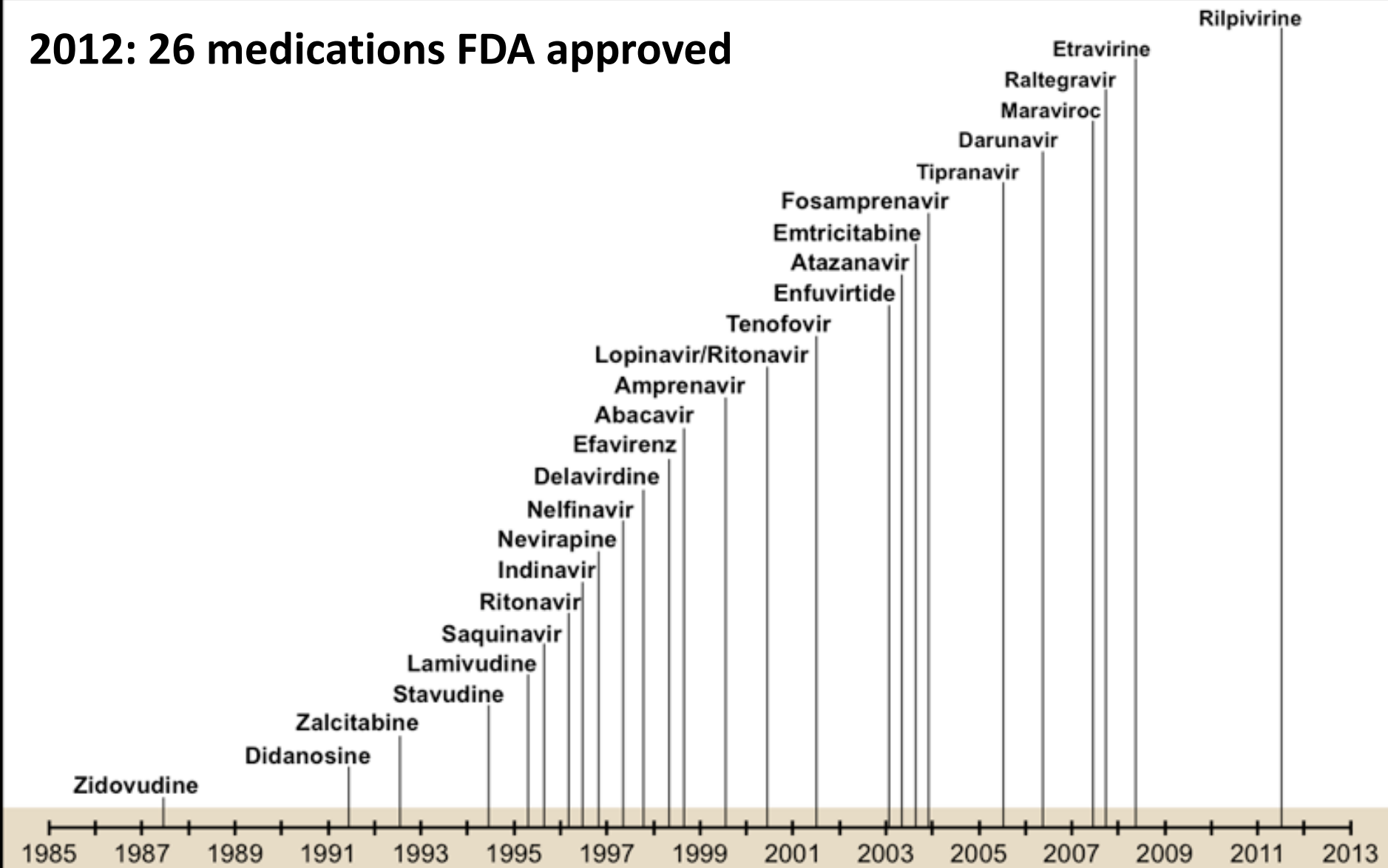


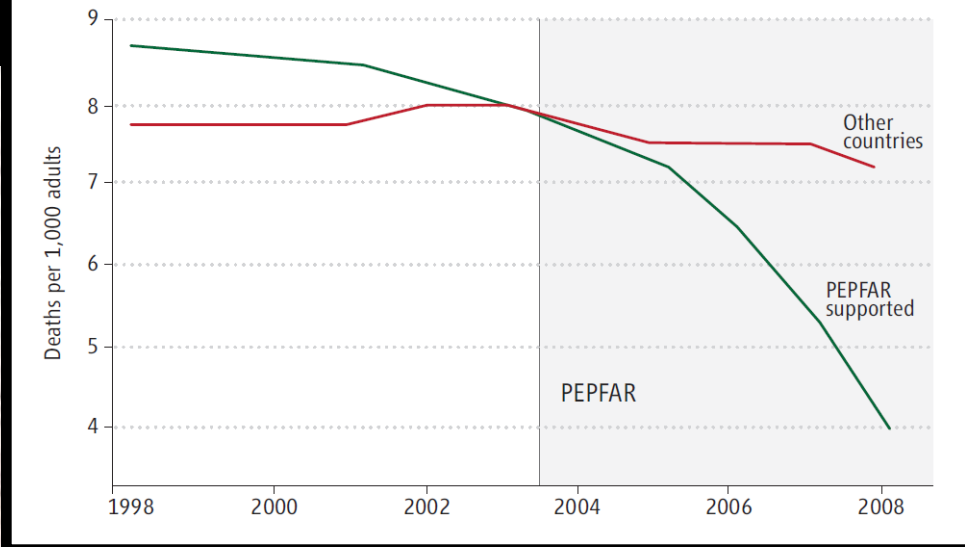
Zidovudine sensitivity of human immunodeficiency viruses from high-risk, symptom-free individuals during therapy

C.A.B. Boucher, MD,^a J.M.A. Lange, MD,^{a, b} Prof J. Goudsmit, MD^a, J.W. Mulder, MD^{b, d}, M. Tersmette, MD,^c R.E.Y. de Goede^c, P. Kellam, BSc^e, G. Darby, PhD,^e B.A. Larder, PhD^e

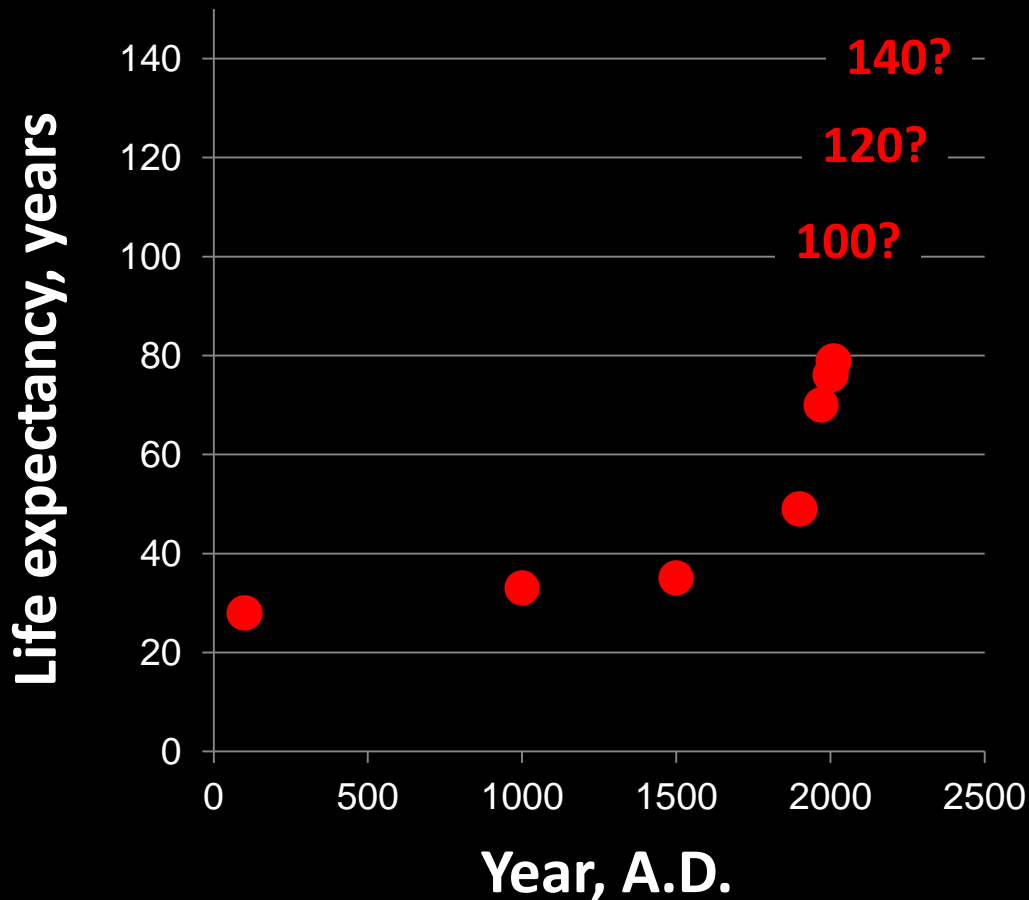
Timeline FDA approval of antiviral & retroviral drugs

2012: 26 medications FDA approved

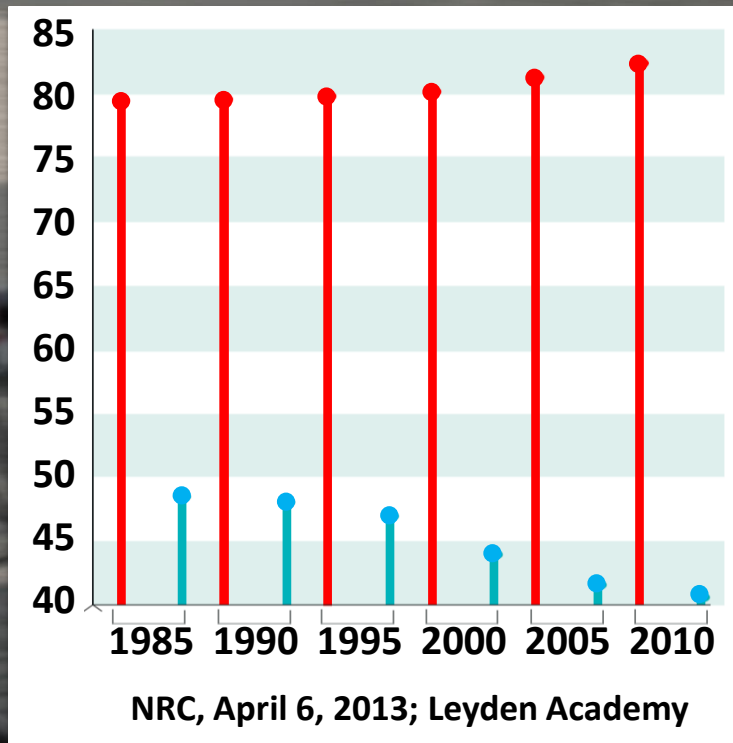
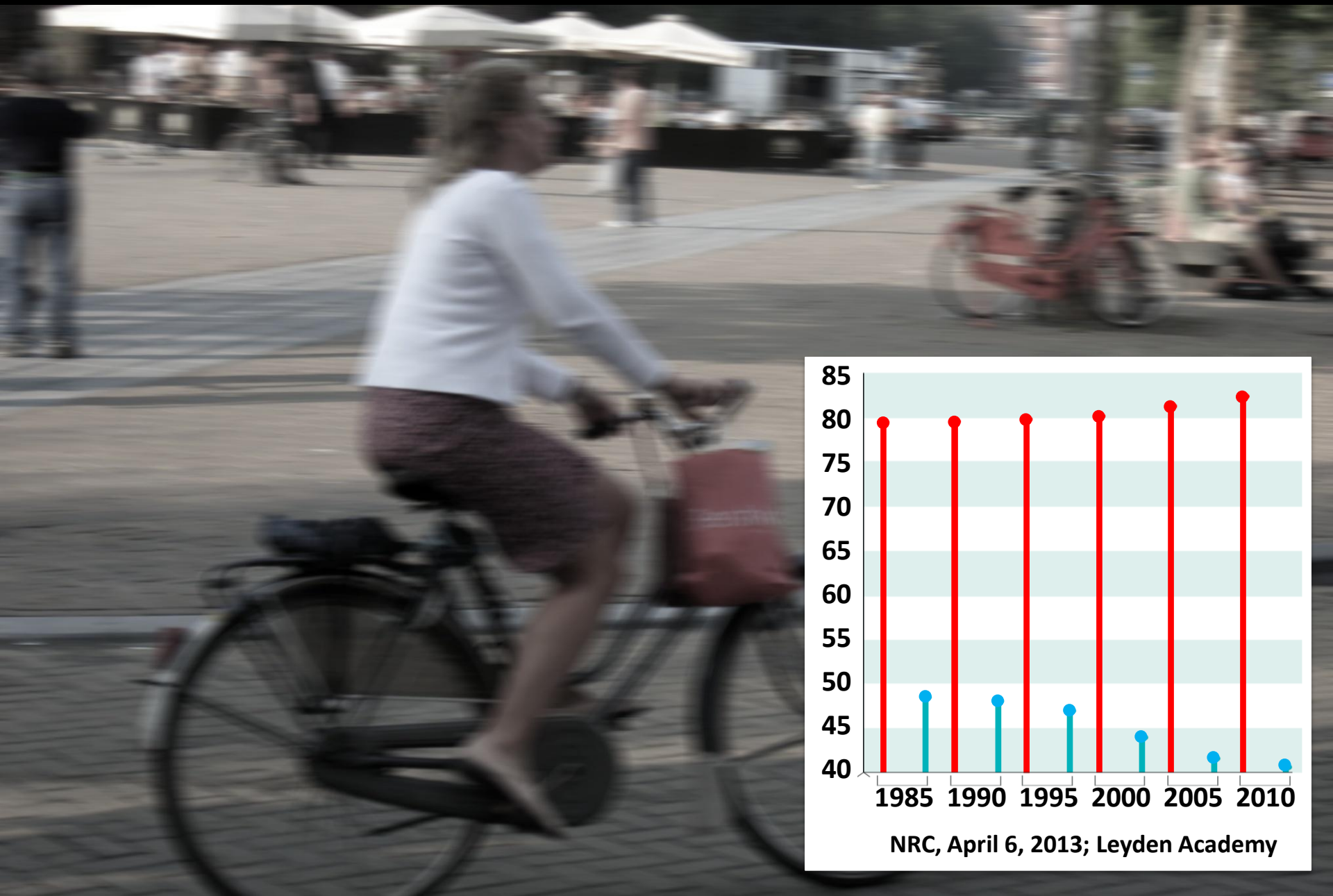




Life expectancy almost doubled in one century



Are we dying more slowly?



Will all of us live a longer life of suffering?

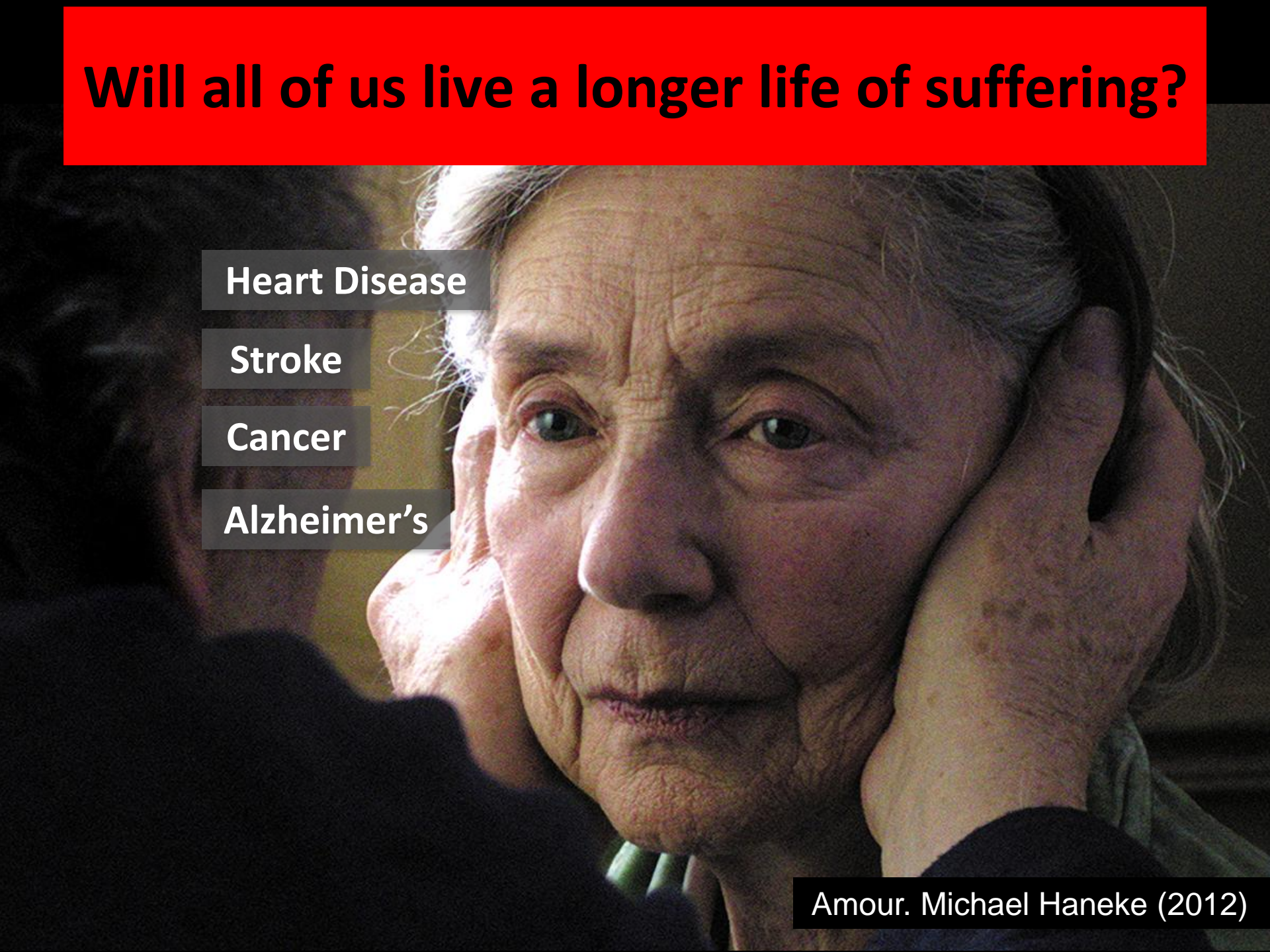
Heart Disease

Stroke

Cancer

Alzheimer's

Amour. Michael Haneke (2012)



6/53 landmark cancer studies are reproducible

COMMENT

ADAM BRUGENGA Shift expertise to track mutations where they emerge p.534

CAROL SYSTEMS Past climates give valuable clues to future warming p.537

HISTORY OF SCIENCE Descartes' lost letter tracked using Google p.540

OUTLOOK Wythe Vale and an elusive stress hormone p.542

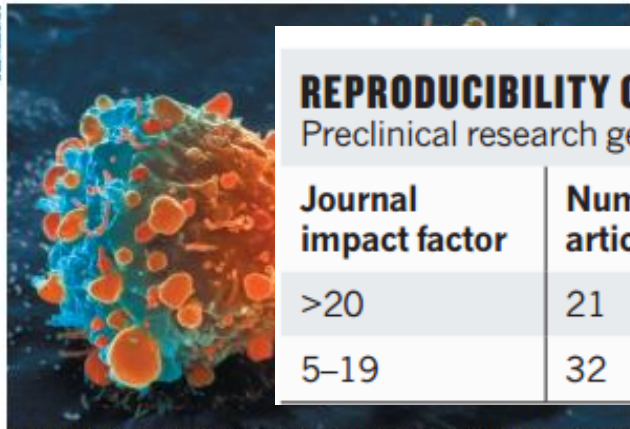


nature

REPRODUCIBILITY OF RESEARCH FINDINGS

Preclinical research generates many secondary publications, even when results cannot be reproduced.

Journal impact factor	Number of articles	Mean number of citations of non-reproduced articles*	Mean number of citations of reproduced articles
>20	21	248 (range 3–800)	231 (range 82–519)
5–19	32	169 (range 6–1,909)	13 (range 3–24)



Many landmark findings in preclinical oncology research are not reproducible, in part because of inadequate cell lines and animal models.

Raise standards for preclinical cancer research

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

Efforts over the past decade to characterize the genetic alterations in human cancers have led to a better understanding of molecular drivers of this complex set of diseases. Although we in the cancer field hoped that this would lead to more effective drugs, historically, our ability to translate cancer research to clinical success has been remarkably low¹. Sadly, clinical

trials in oncology have the highest failure rate compared with other therapeutic areas. Given the high unmet need in oncology, it is understandable that barriers to clinical development may be lower than for other disease areas, and a larger number of drugs with suboptimal preclinical validation will enter oncology trials. However, this low success rate is not sustainable or acceptable, and

investigators must reassess their approach to translating discovery research into greater clinical success and impact.

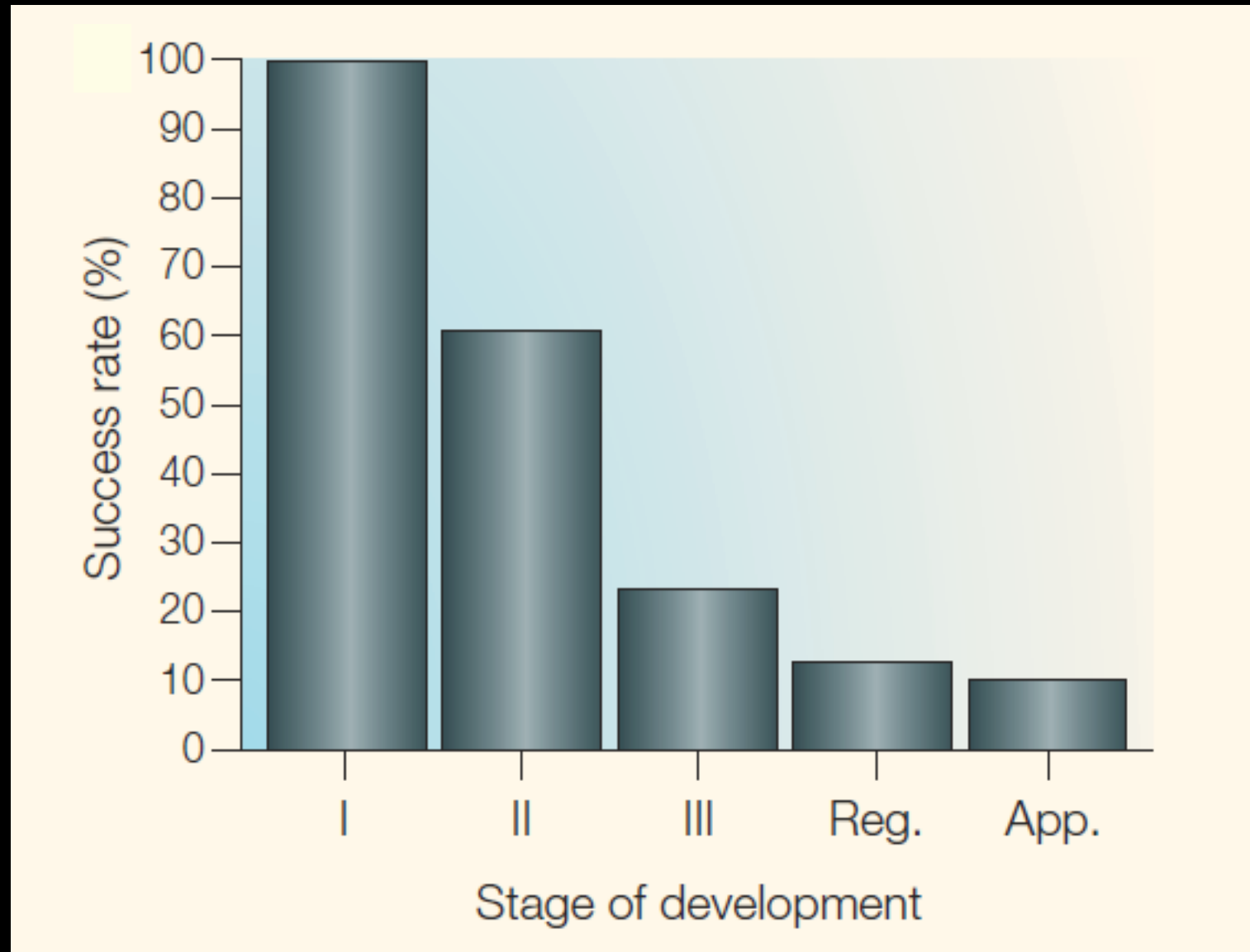
Many factors are responsible for the high failure rate, notwithstanding the inherently difficult nature of this disease. Certainly, the limitations of preclinical tools such as inadequate cancer-cell-line and mouse models² make it difficult for even

“The NIH is firmly committed to making systematic changes...”

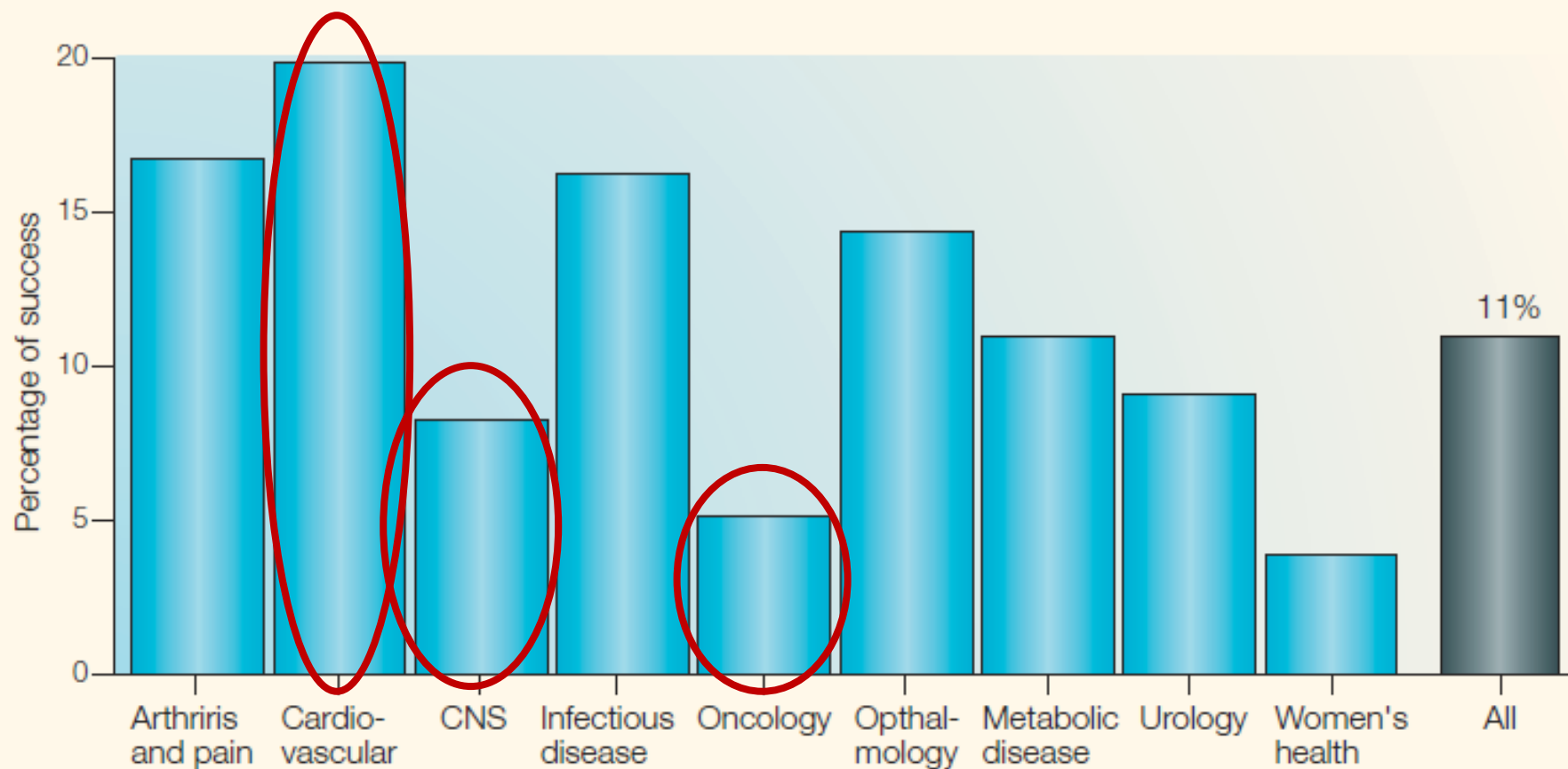


- poor training of scientists
- reward for provocative statements (not for reporting design)
- publication bias for positive and headline-grabbing results
- overvaluation of publications in high-profile journals
- difficulty accessing unpublished results
- problem of academics, industry researchers, funders, publishers

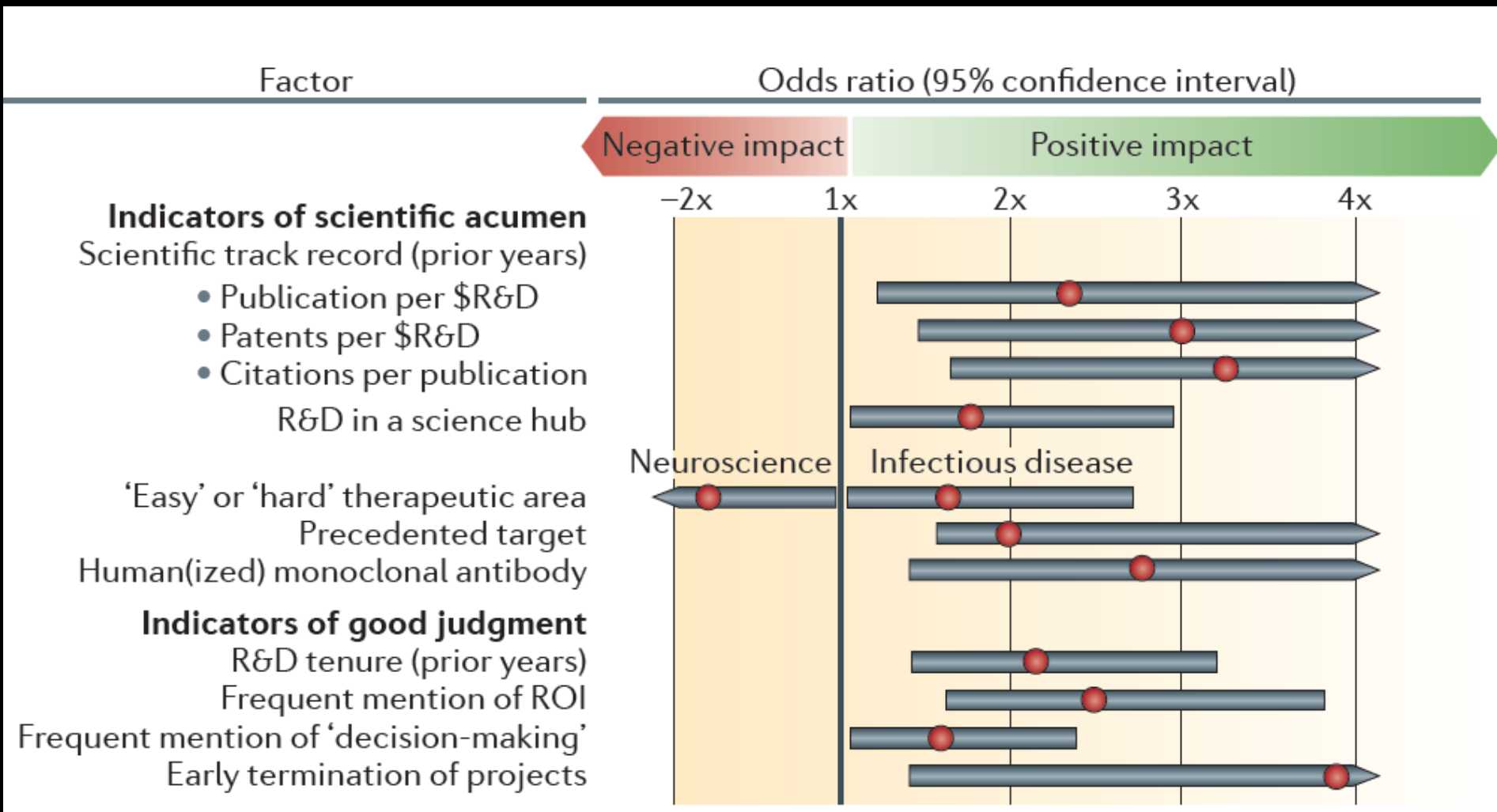
Drug success rate by phase of development to registration and approval



Drug success rates to registration by therapeutic area



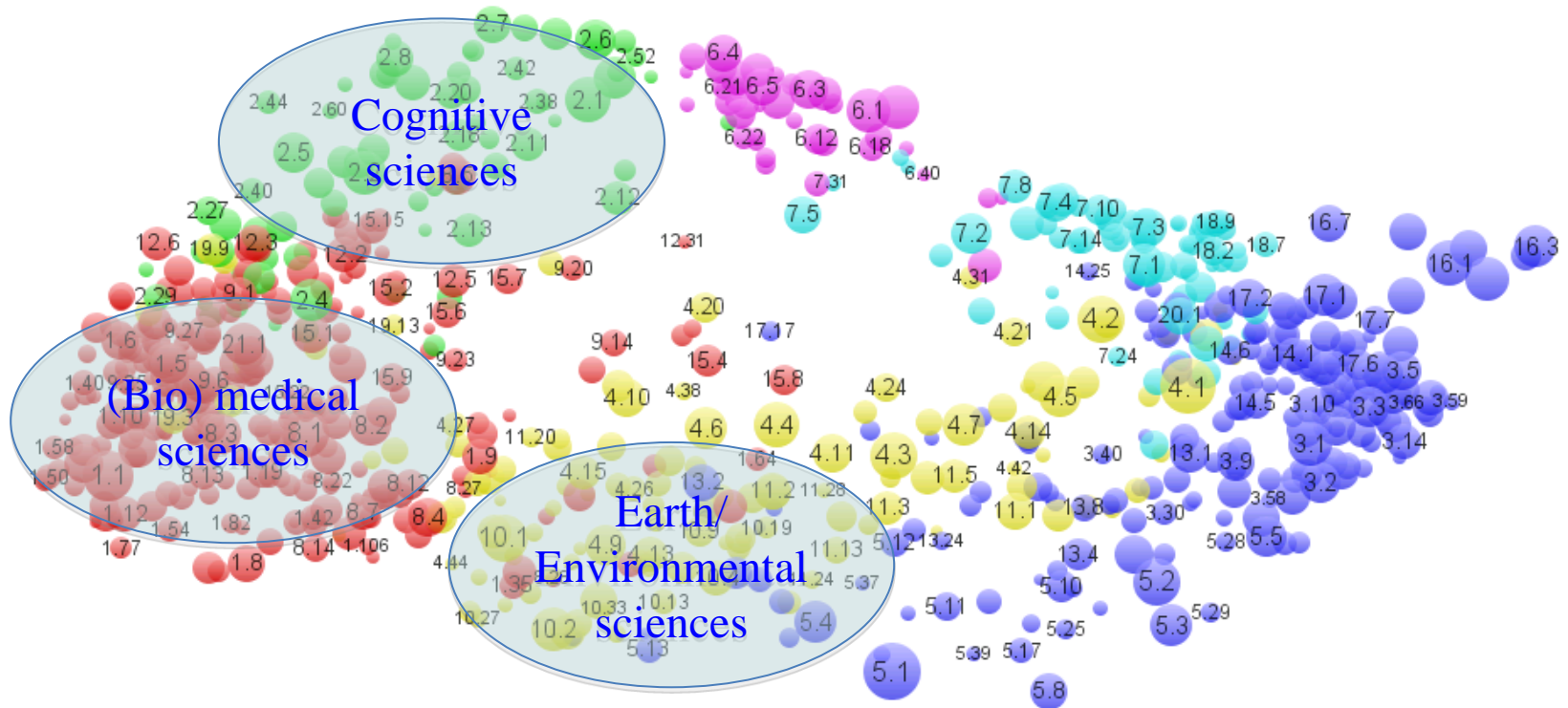
Factors correlated with success or failure in drug development (842 molecules, 637 failures)



Top Dutch Scientists

1,3 million Life Science scientists

36,500 Dutch



Web of Science based 1993-2012



Drug success rates to registration by therapeutic area

