A Global Perspective on Oncology

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2023 Debates and Didactics in Hematology and Oncology
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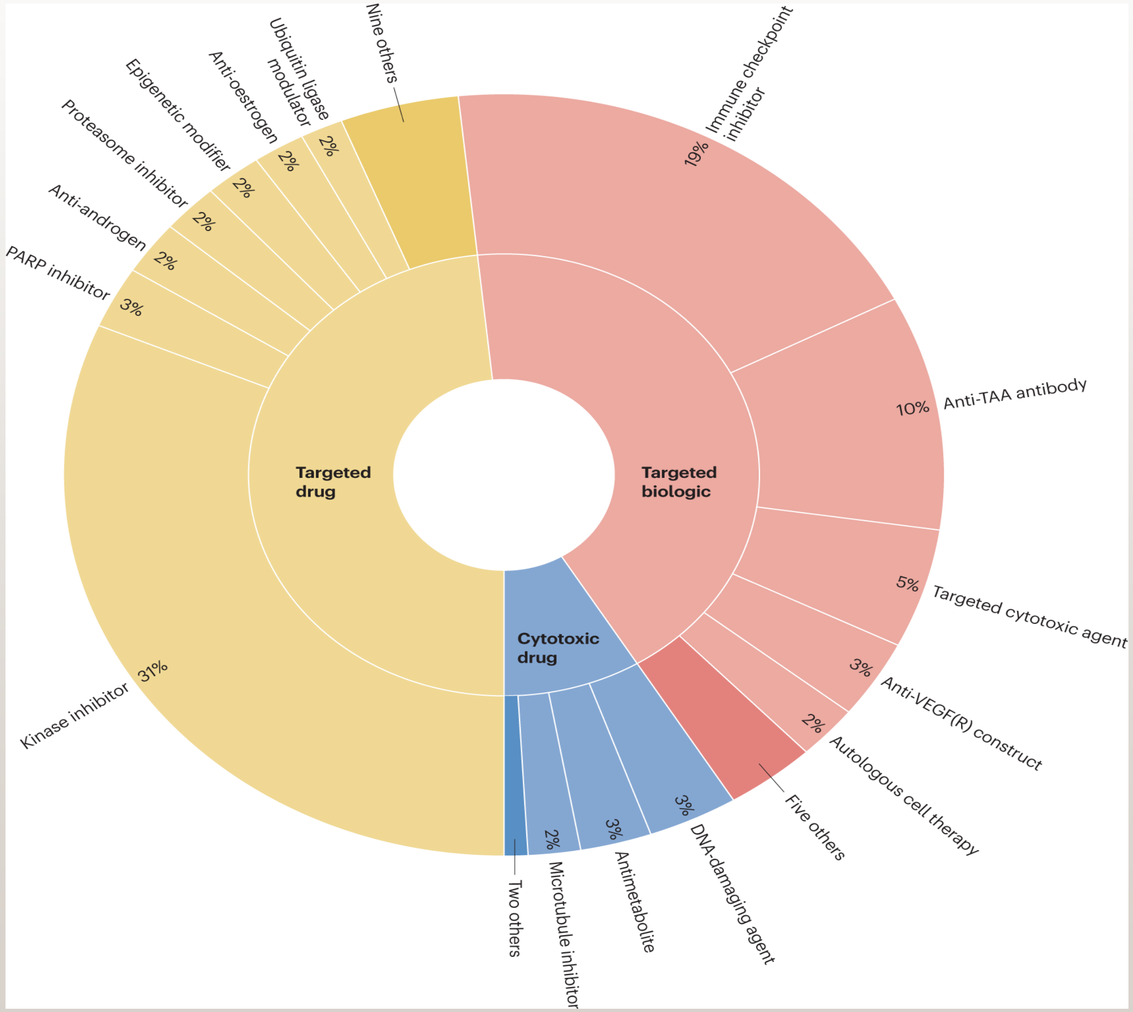
Office of the President | American University of Beirut

Outline

- Modern drug development and its financial implications
- High versus low-income countries cancer statistics
- Drug access in Lower Middle Income Countries (LMICs)
- Proposed solutions
- Conclusions

A Golden Age for Cancer Drug Development

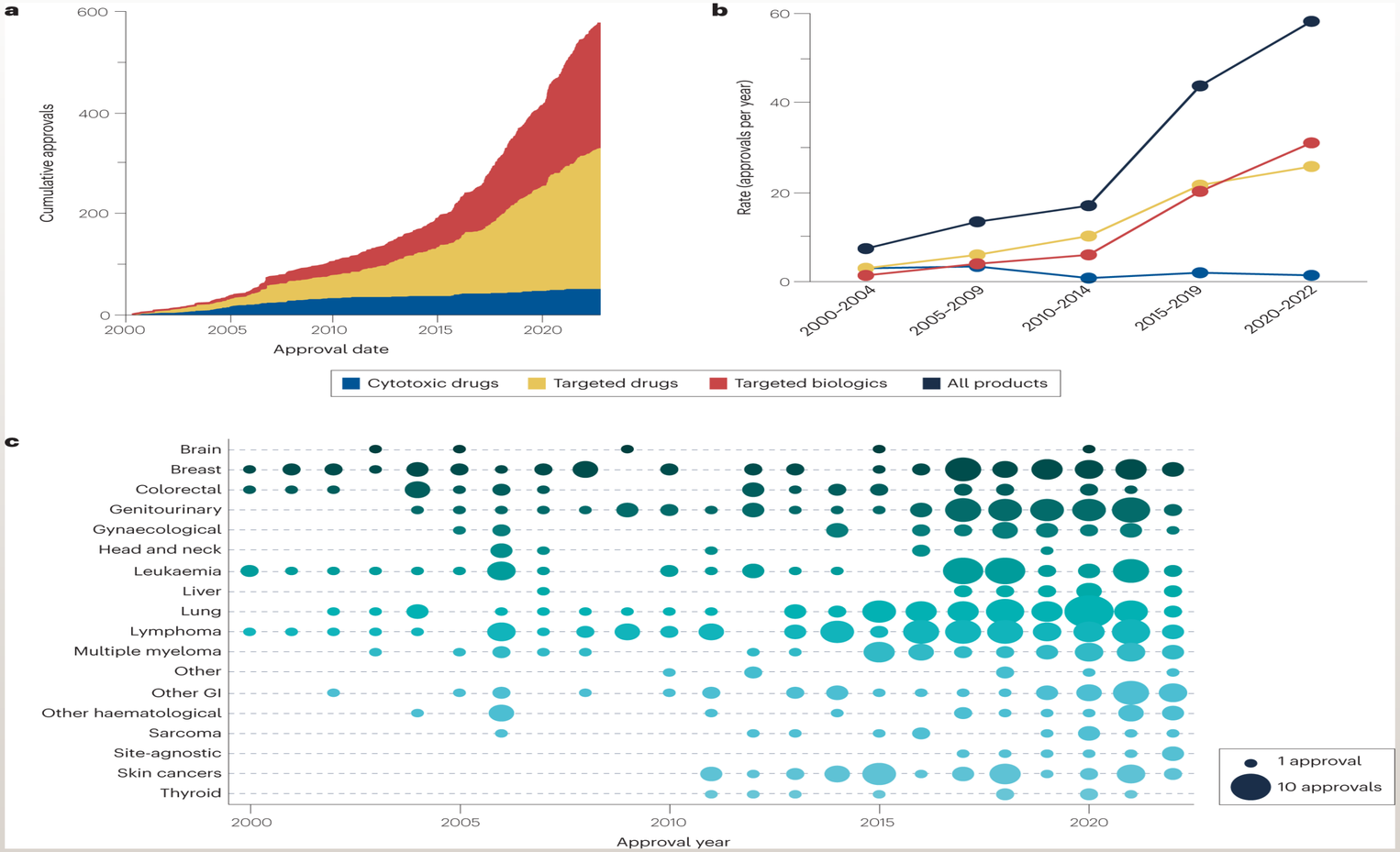
Fig. 1: Overview of oncology therapeutic products approved by the FDA since 2000 by mechanism of action.



https://doi.org/10.1038/s41573-023-00723-4

A Golden Age for Cancer Drug Development

Fig. 2: Trends in oncology therapeutic indication approvals since 2000.



a, Cumulative oncology approvals for the three product groups analysed: cytotoxic drugs, targeted drugs and targeted biologics. **b**, Rate of approvals (mean number of indication approvals per year) in the year bins shown, by product group and overall. **c**, Bubble plot of the number of annual approvals by disease site. Bubble size corresponds to number of annual approvals.

https://doi.org/10.1038/s41573-023-00723-4

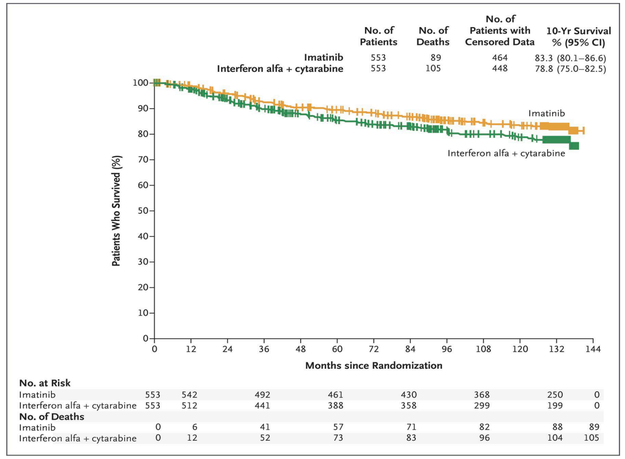
Clinical Decision Making in the Real World—The Perfect as the Enemy of the Good

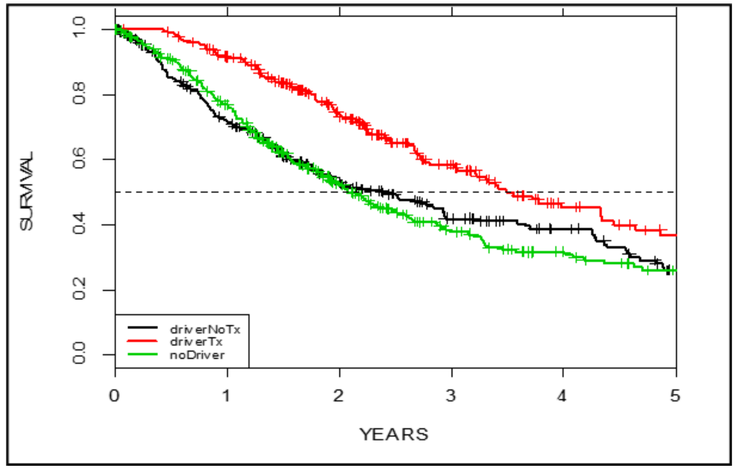
Howard (Jack) West, MD, MPhil[1,2]

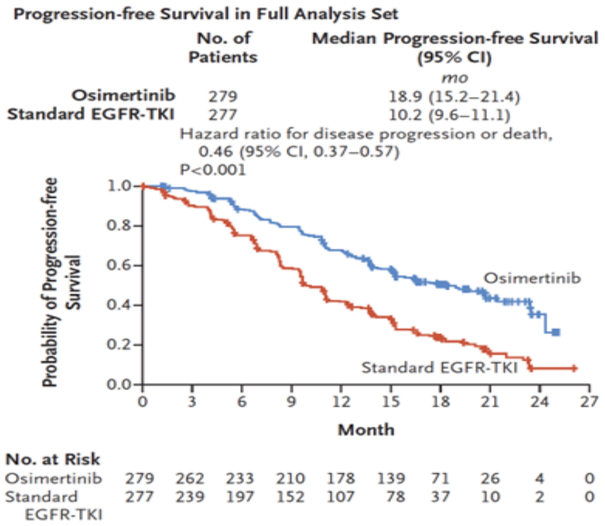
- Controversies remain regarding the optimal duration of Immunotherapy in NSCLC.
- With longer follow up, more and more data is emerging about the safety of stopping immunotherapy at 2 years.
- In practice, on the other hand, few patients are discontinuing therapy at 2 years as Oncologists continue to worry about disease progression.
- The perfect should not be the enemy of the good.

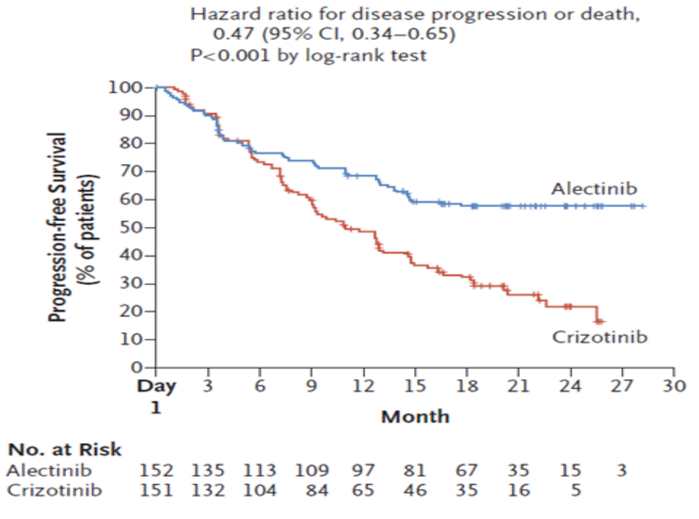
JAMA Oncol. Published online June 4, 2023. doi:10.1001/jamaoncol.2023.1811

Continued Survival Impact of Targeted Agents





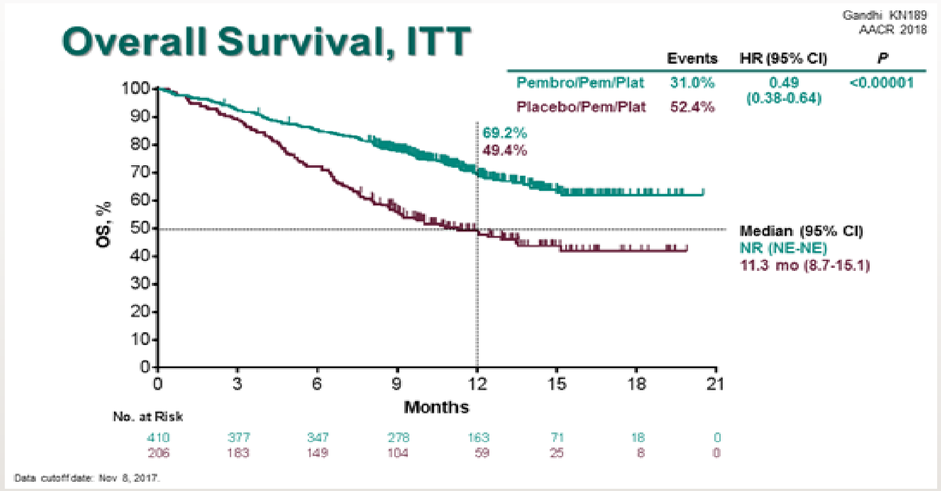


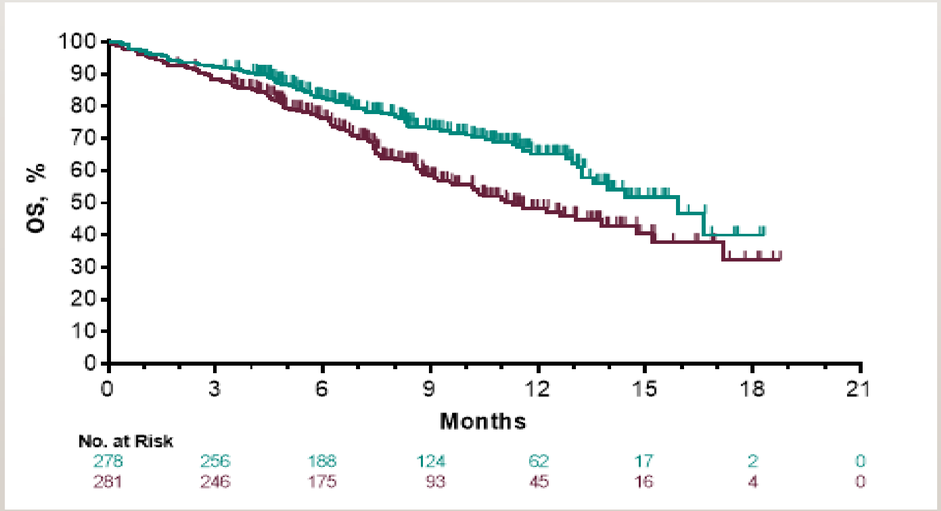


Hochhaus. N Engl J Med 2017; 376:917-927. Kris, M, et al, JAMA, 2014. Soria . N Engl J Med. 2018;378:113-125 Peters NEJM 2017.

Growing Survival Impact of Immunotherapy

KEYNOTE-189





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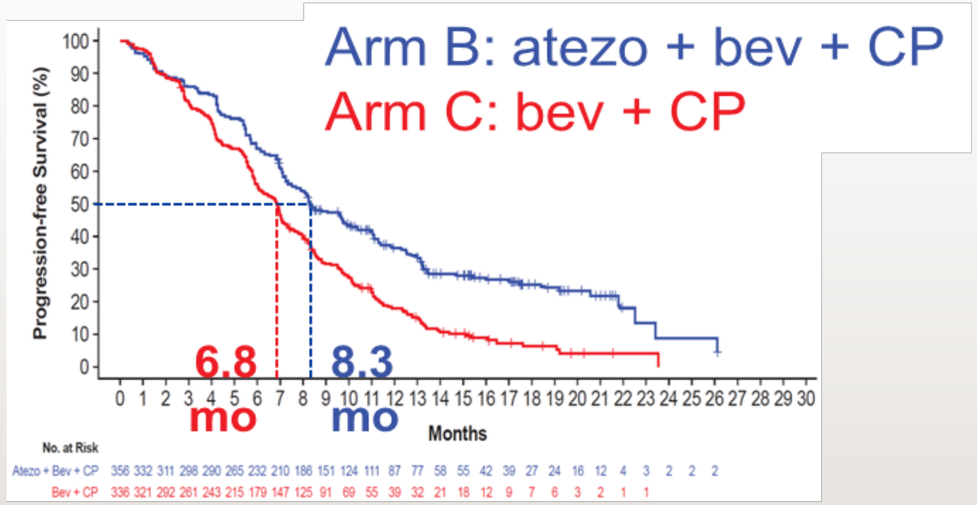
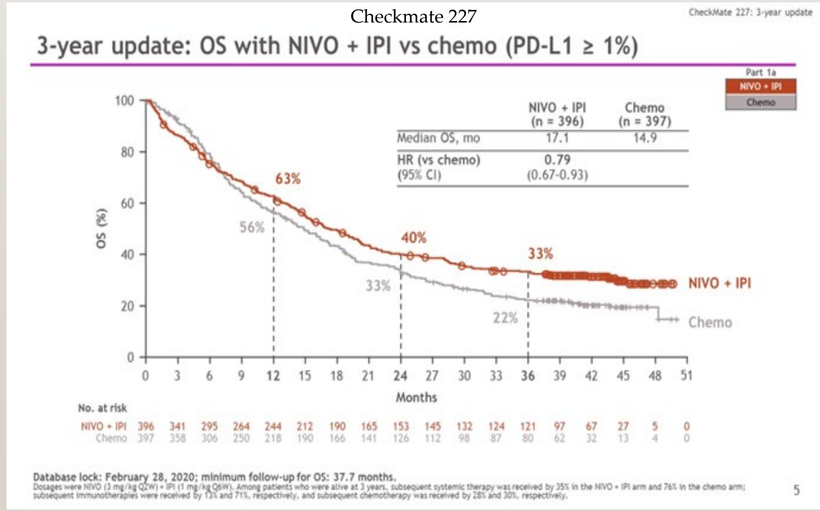
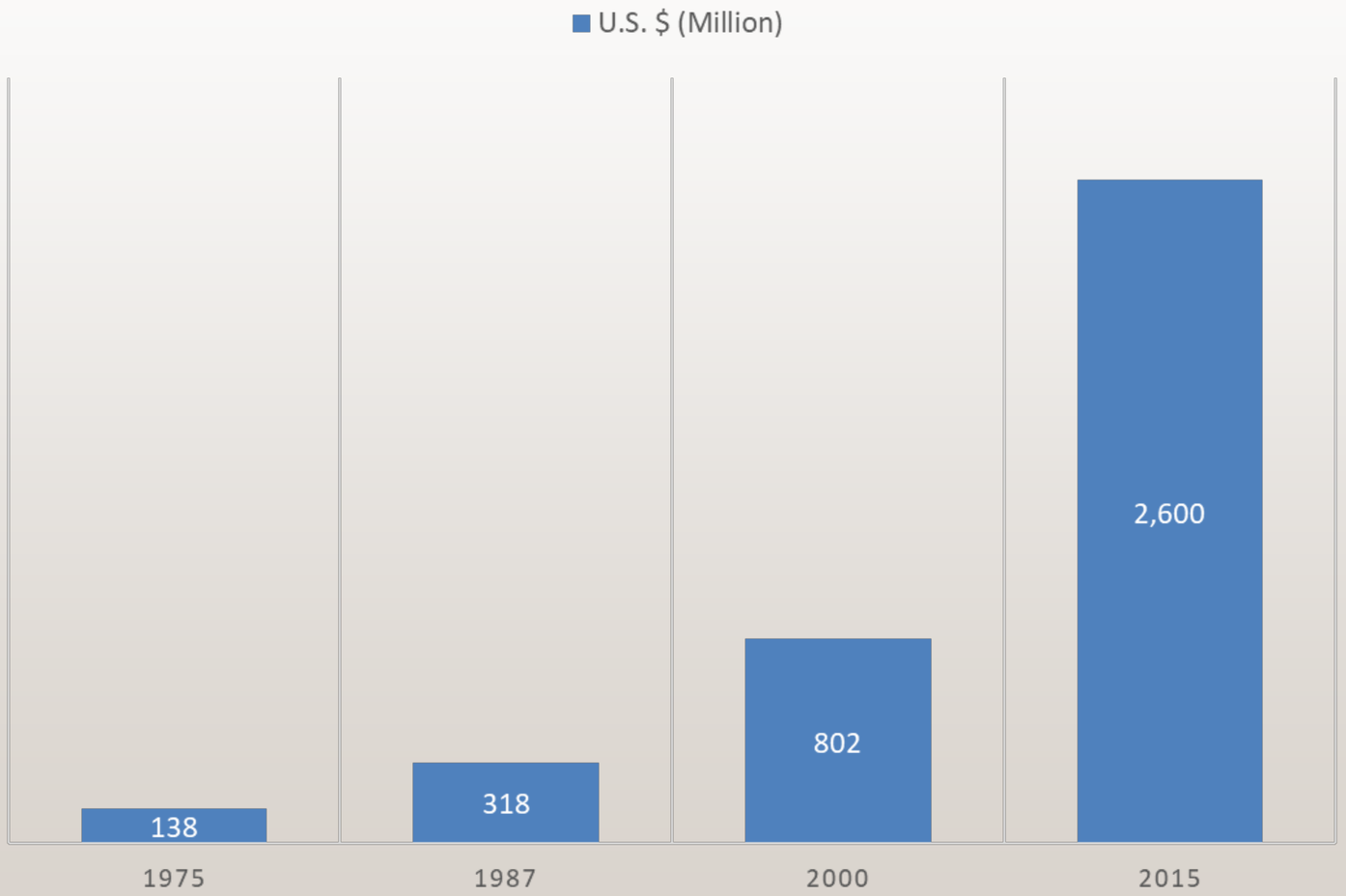


Checkmate 227



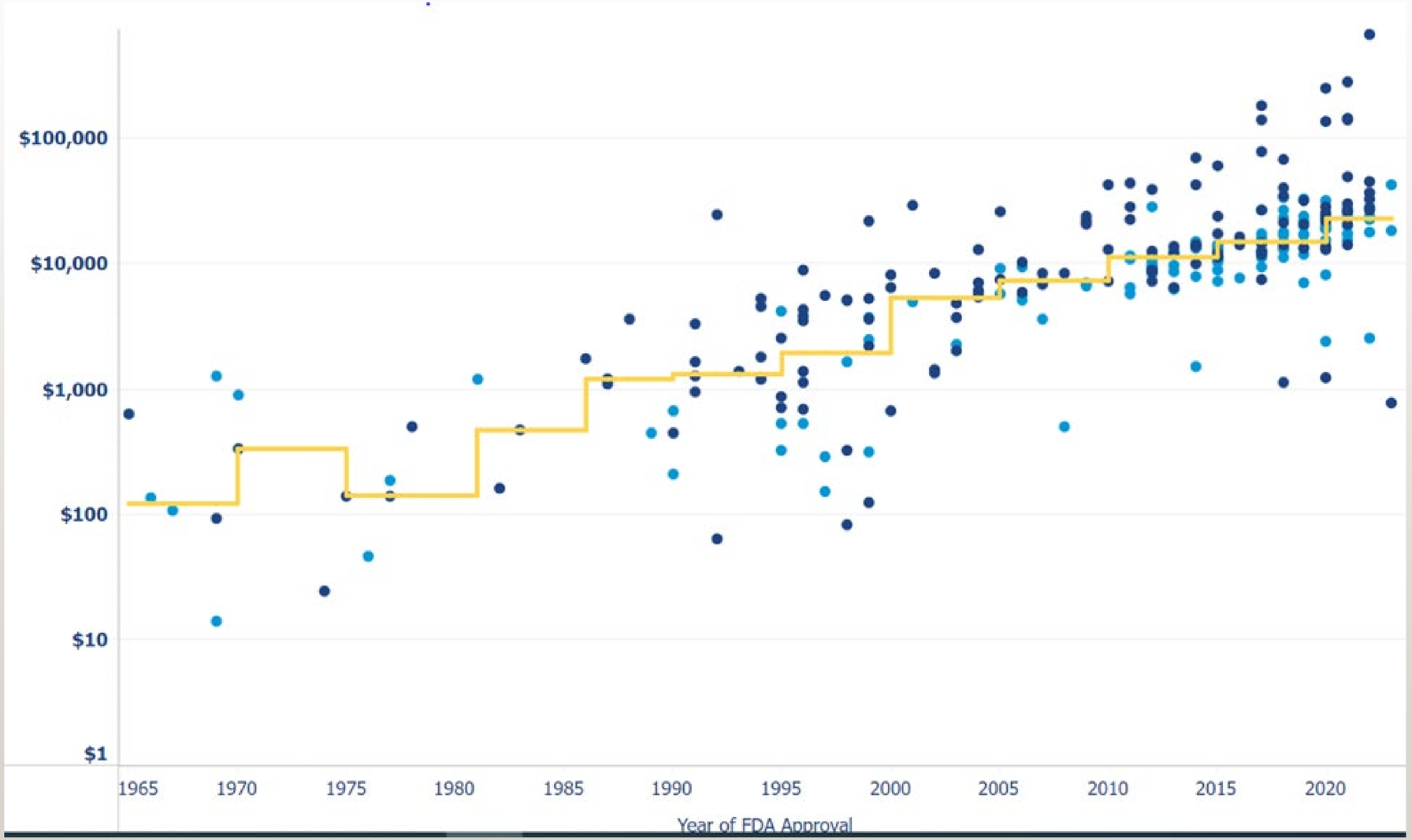
Gandhi L et al. *N Engl J Med.* 2018. Paz-Ares L et al. *N Engl J Med.* 2018. Reck, NEJM 2016. Hellmann MD, et al. *N Engl J Med* 2019;381:2020–2031

Mushrooming Cost of Developing A New Drug



DiMasi et al. J Heath Econ 2003 and press release from the Tufts group in 2015

Sale Price Change over Time



www. https://www.drugpricinglab.org/person/bach/

Cumulative Drug Sales

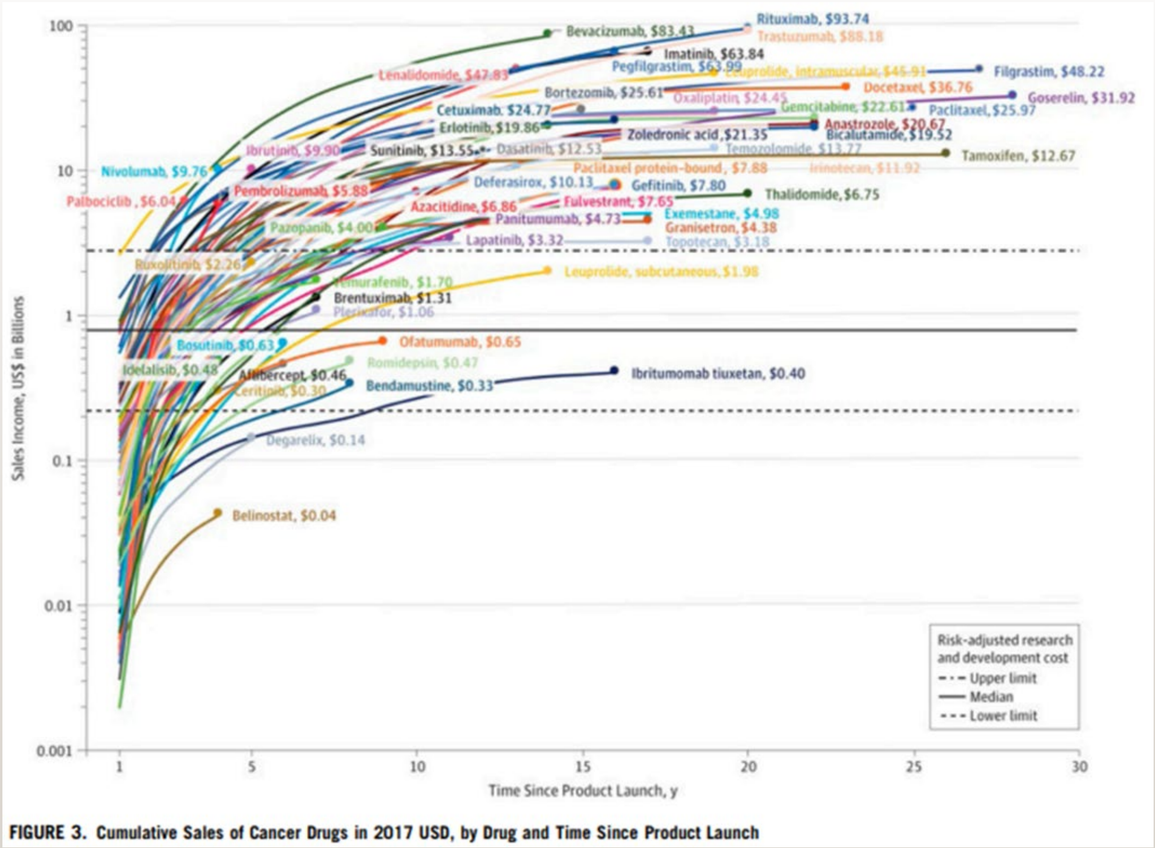
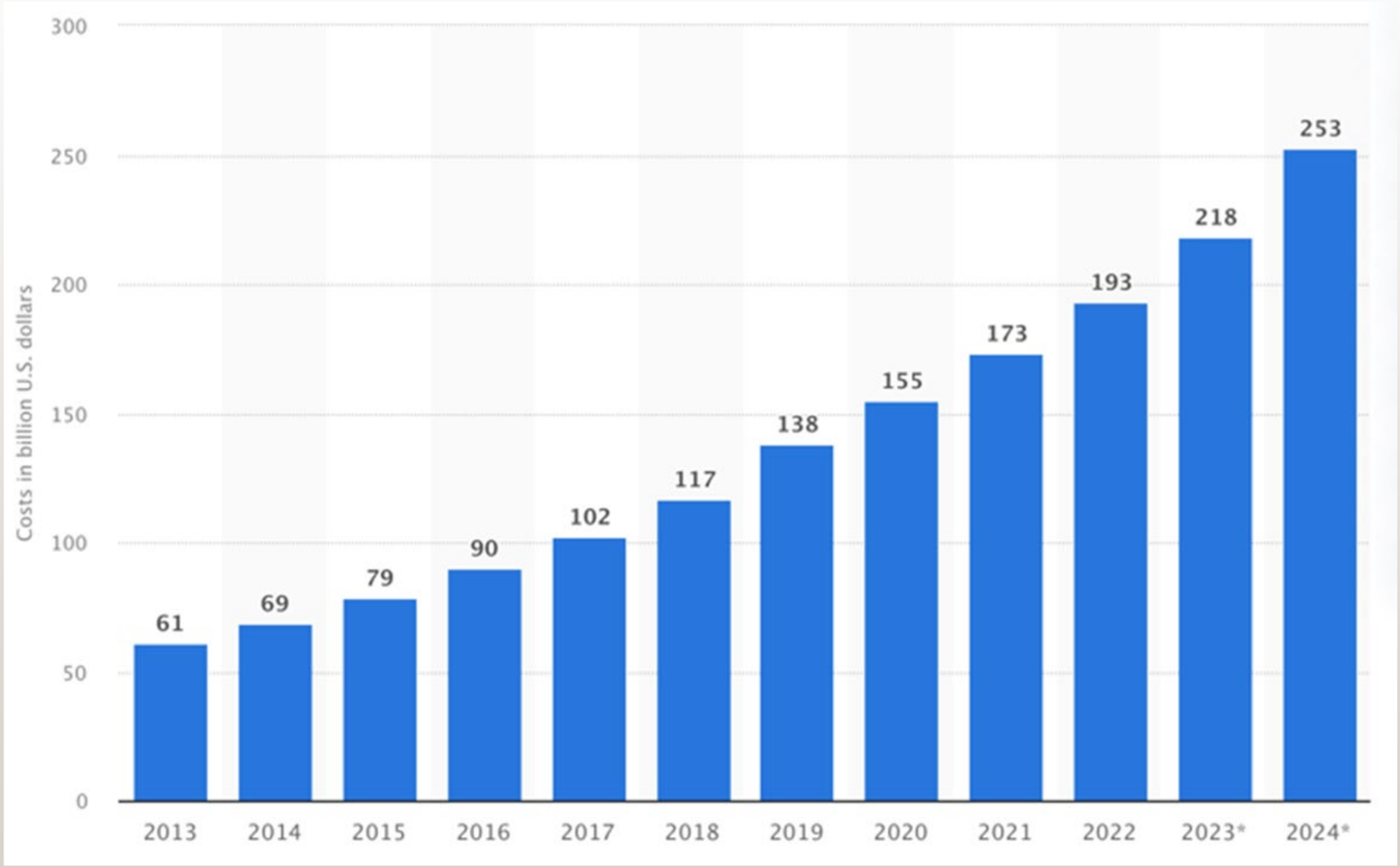


FIGURE 3. Cumulative Sales of Cancer Drugs in 2017 USD, by Drug and Time Since Product Launch

Tay-Teo K, Ilbawi A, Hill SR. JAMA Netw Open. 2019;2:e186875

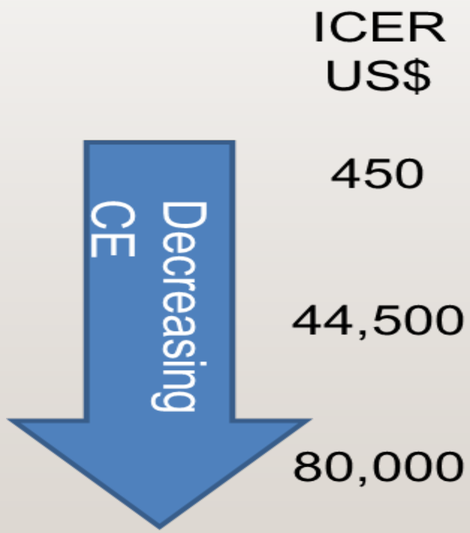
Global oncology spending from 2011 to 2024 (in billion U.S. dollars)



https://www.statista.com/statistics/696208/oncology-costs-worldwide/

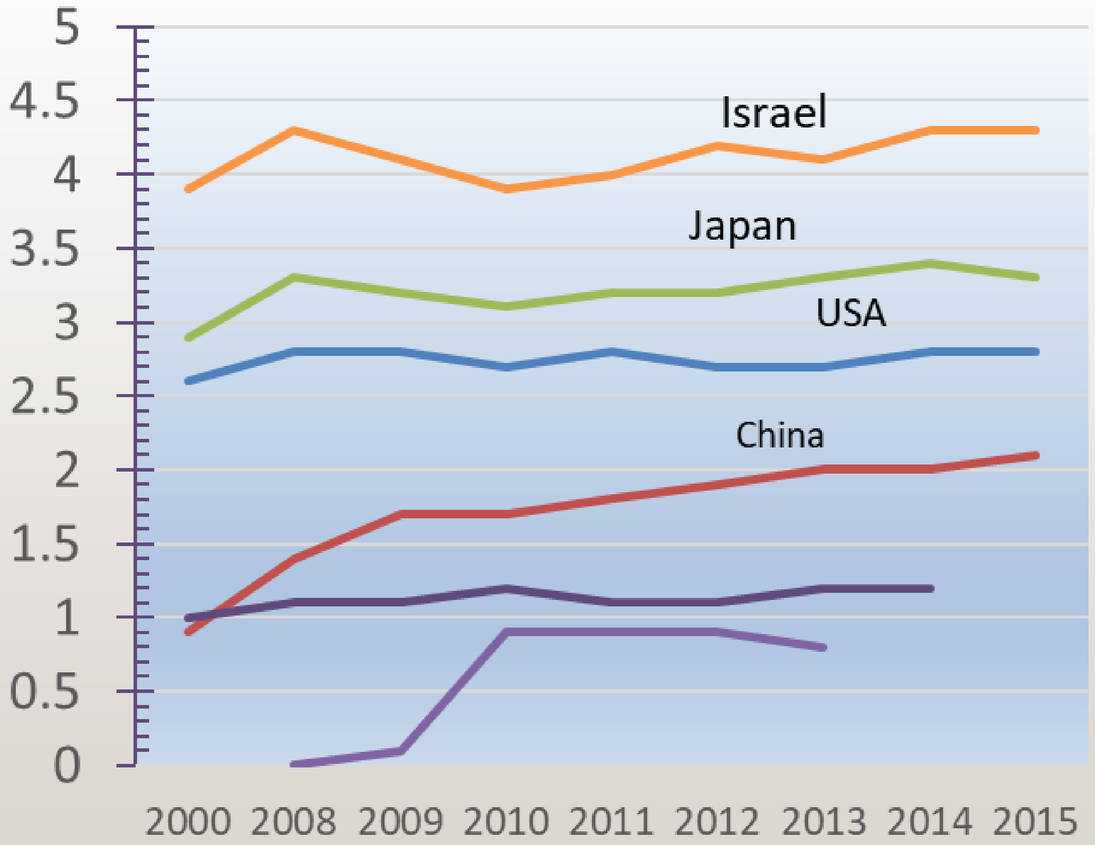
ICER in US$ (Colon Cancer)

Level	Drugs
Basic	BSC Alone
Limited	5FU Alone
Enhanced	+ Oxaliplatin, Irinotecan
Maximal	+ Cetuximab/Panitumumab, Bevacizumab



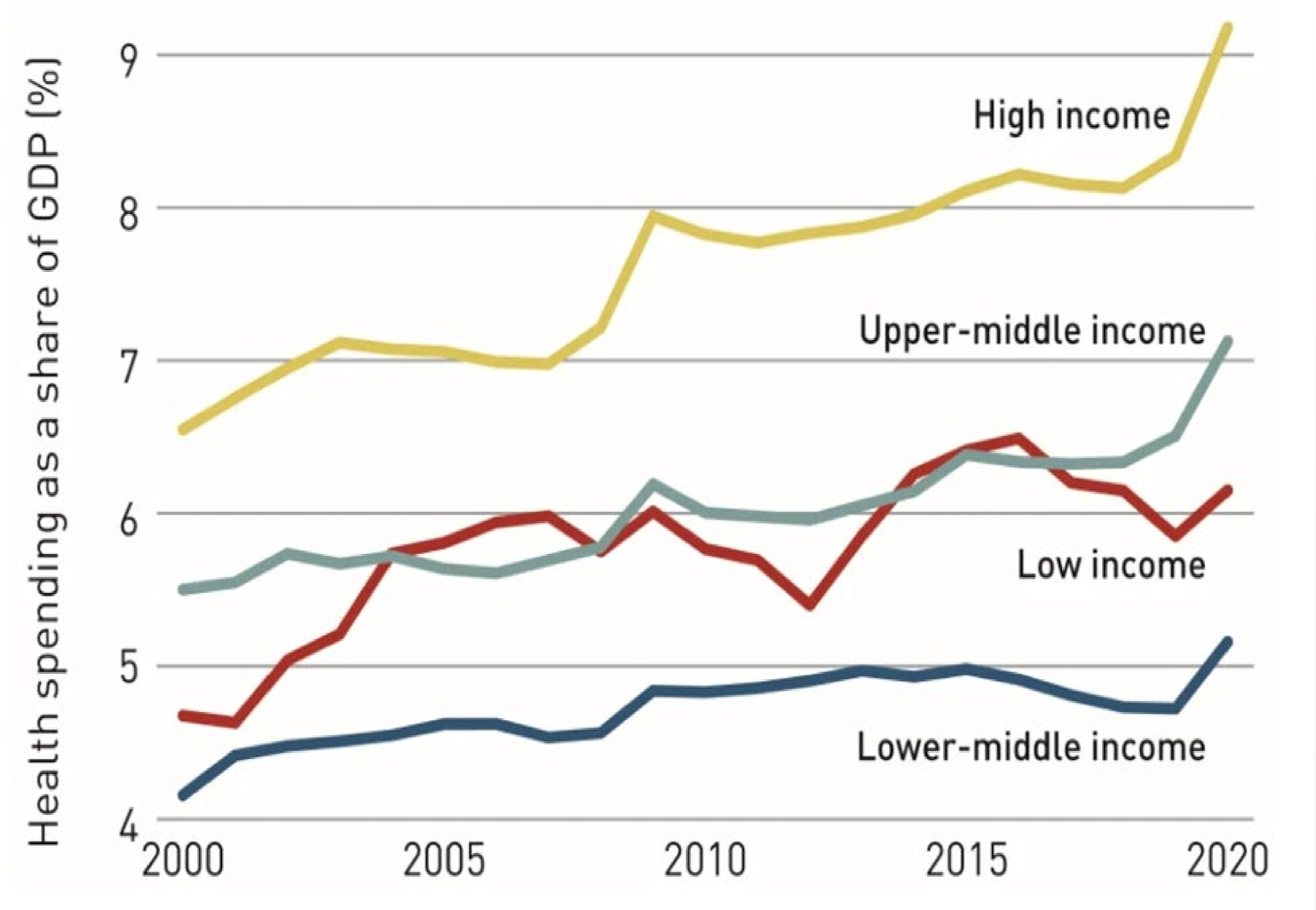
Lopes (Senior Author), Lancet Oncology 2012

R&D Expenditure (% of GDP)



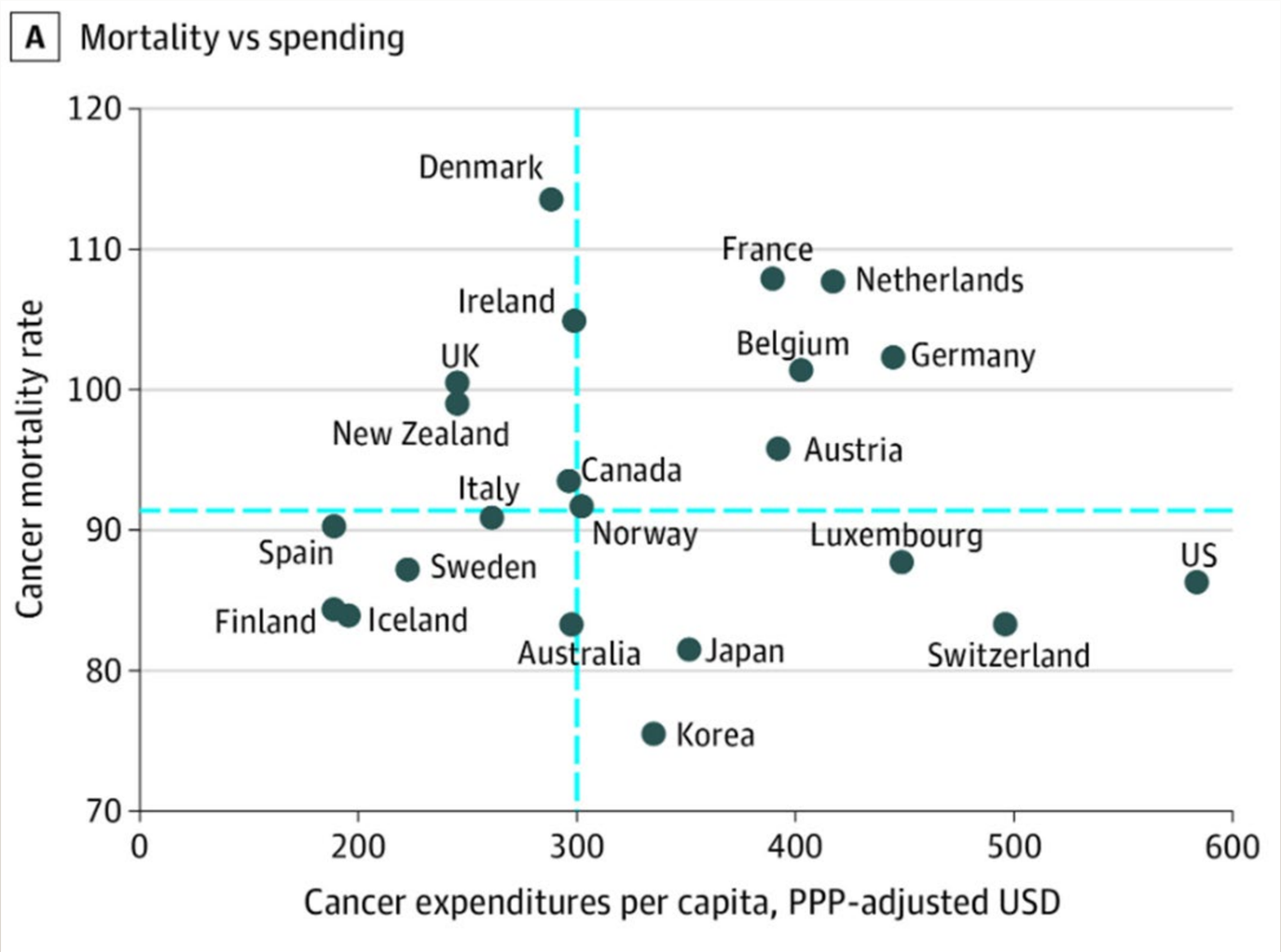
data.worldbank.org/share/widget?end=2015&indicators=GB.XPD.RSDV.GD.ZS&locations=US-CN-JP-LB-SA-BR-IL&start=1996&type=points&view=chart

Health Spending (% of GDP)

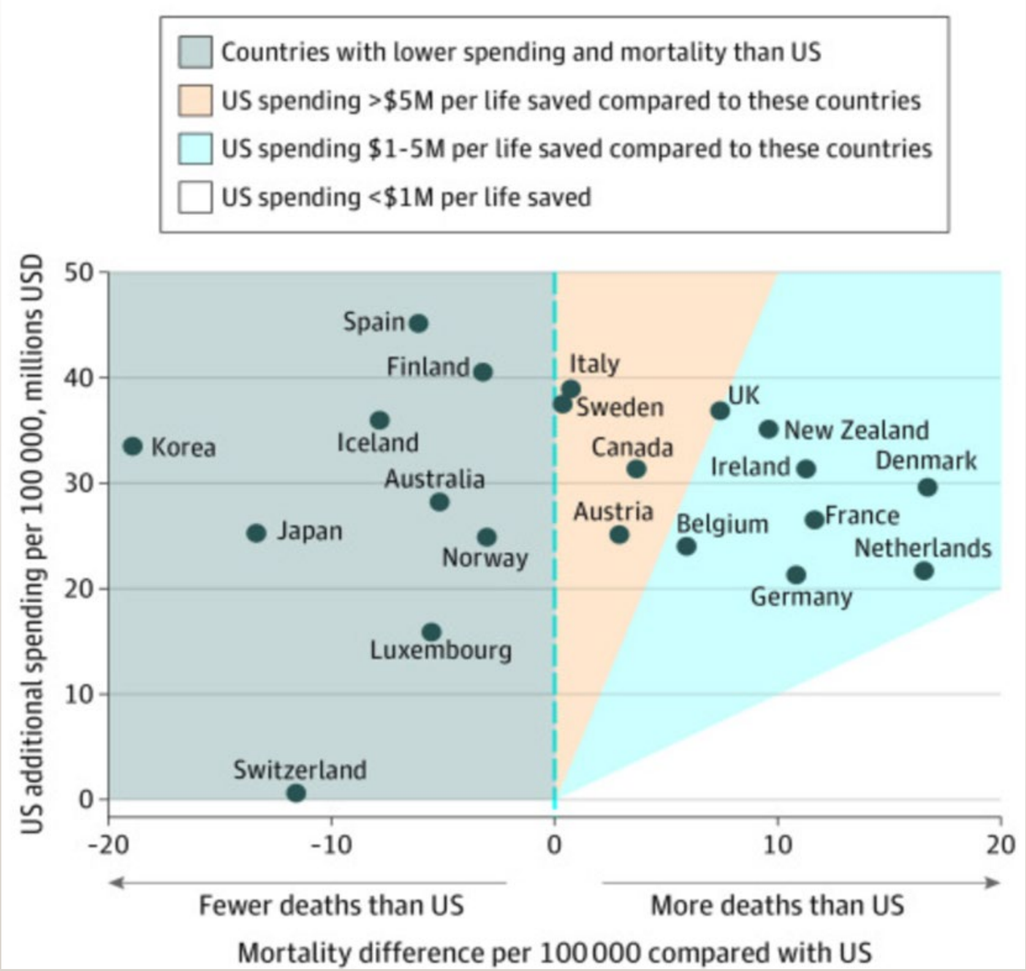


https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS

Cancer Spending versus Mortality



Cancer Spending versus Mortality



Chow et al.JAMA Health Forum. 2022 May 27;3(5):e221229

Cancer Spending per capita

Reality testing

For those of us who treat patients in low and middle income countries most of these advances are an inspiration and bring hope for the future...

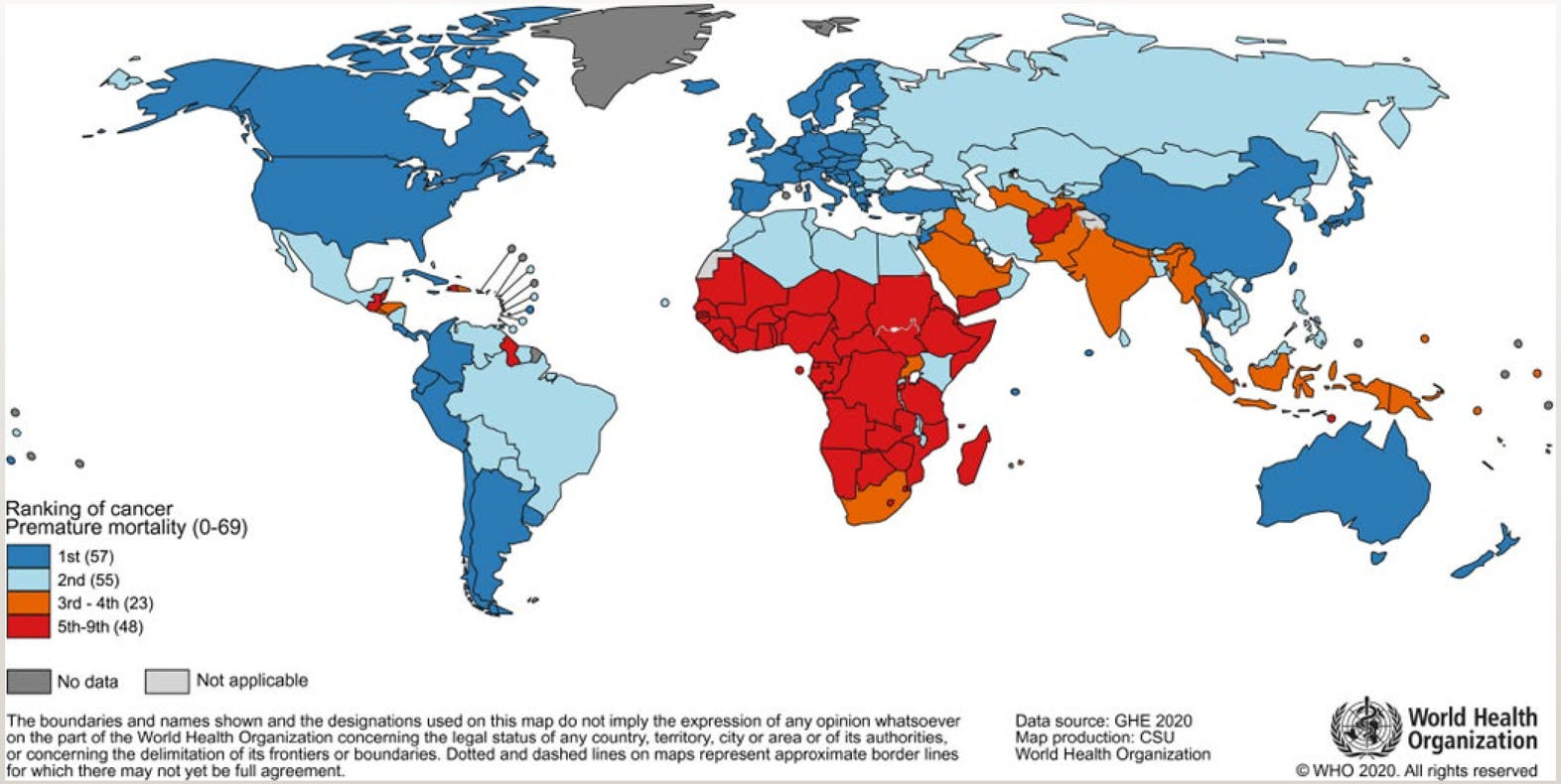
...but not our current reality

Cancer mortality to incidence ratios

USA	Europe	LMICs
0.36	0.48	0.68

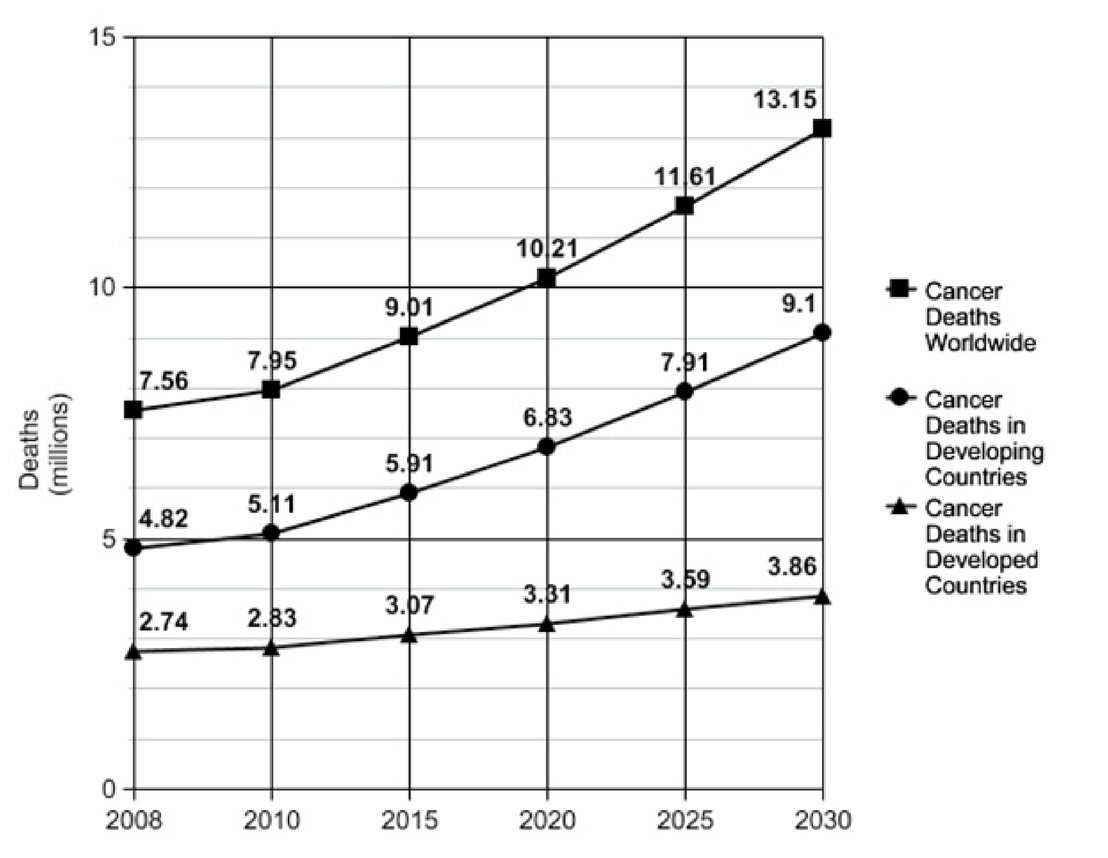
Lopes [Senior Author]: Global Health Equity: Cancer Care Outcomes Disparities in High, Middle and Low Income Countries. J Clin Oncol 2017. Based on Data from GLOBOCAN

Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries



CA A Cancer J Clinicians, Volume: 71, Issue: 3, Pages: 209-249, First published: 04 February 2021, DOI: (10.3322/caac.21660)

Countries in the developing world bear the greatest burden of new cancer cases as well as deaths.



By 2030, the developing world is expected to account for 70% of newly reported cancer cases

Moten et al. J Global Health 2014;4:010304.American Cancer Society. Global cancer facts & figures

Availability, Affordability, Access, and Pricing of Anti-cancer Medicines in Low- and Middle-Income Countries: A Systematic Review of Literature

Phyllis Ocran Mattila[1], Rabbiya Ahmad[2], Syed Shahzad Hasan[1] and Zaheer-Ud-Din Babar[1]*

[1] Department of Pharmacy, University of Huddersfield, Huddersfield, United Kingdom, [2] Faculty of Pharmacy, The Islamia University of Bahawalpur, Bahawalpur, Pakistan

- Wide variation in cancer medicines prices between countries
- Medicines are less affordable in LMICs as compared to High-income countries
- People with lower-income had lower access to cancer medicines
- Less availability of newer medicines
- More availability in private hospitals as compared to public ones.

Matilla et al. Front. Public Health 9:628744:2021

How to Increase Access

Most Important and Effective Options:

- Quality generics and biosimilars
- Price Discrimination, aka, Affordable Pricing or Price Tiering
- Adequate Healthcare Funding:
  - Universal Coverage
  - Value-Based Insurance Design
- Private Public Partnerships

Lopes. et al. Nature Rev Clin Oncol 2013

Generics

- Generic medicines account for 90% of all prescriptions dispensed in the United States, yet only 21% of all dollars spent on prescriptions. (source: IQVIA Institute)
- Cost of Medication may drop by 80% after introduction of generics.
- In the US the use of generics has saved greater than US$ 1.67 trillion over the decade through 2016.

Lopes G and colleagues. Ann Oncol 2013 and IJMPO 2017

Potential Savings with Generics

- Generic substitution for four commonly used drugs can amount to savings in excess of US$800 million in India every year.
- In one small retrospective study and one small prospective registry, efficacy and safety of commonly used drugs was equivalent with generic or originator drug in India.

Lopes G and colleagues. Ann Oncol 2013 and IJMPO 2017

Biosimilar competition and time to lowering of ASP

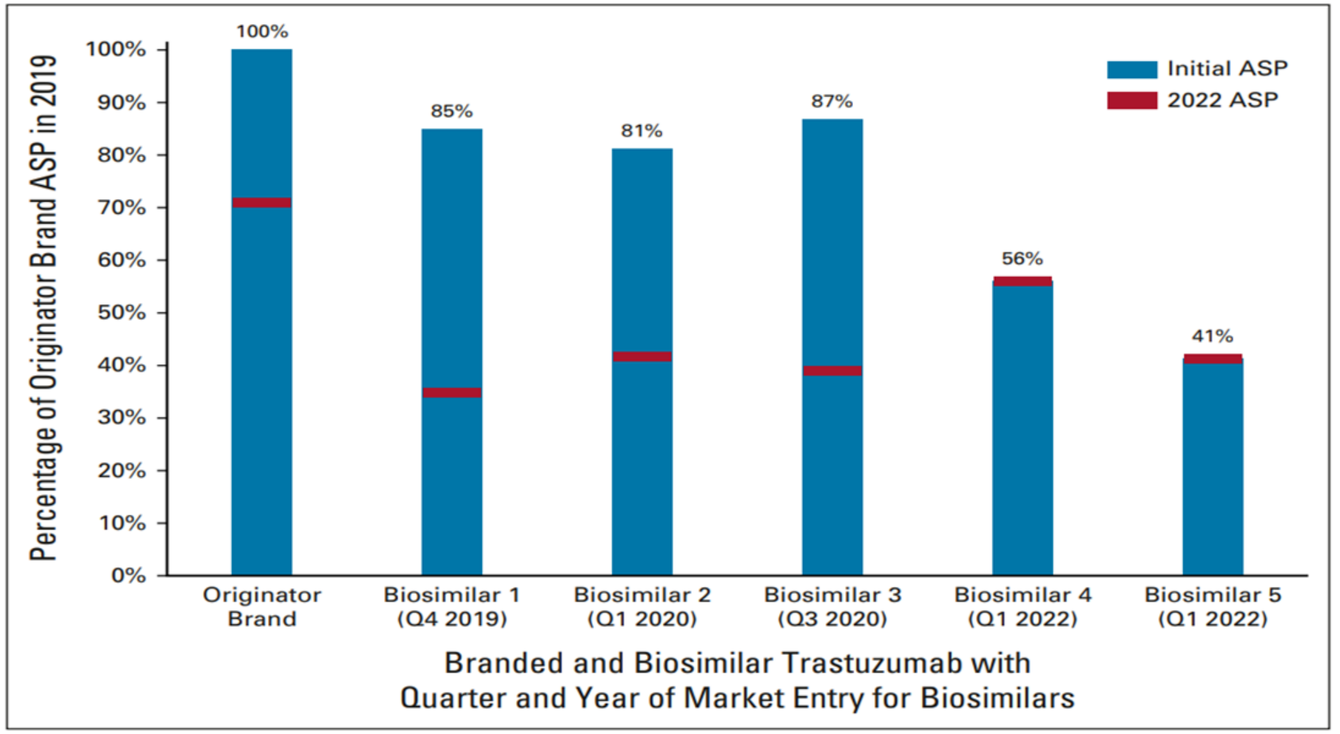


FIG 1. Average sales price of branded and biosimilar trastuzumab relative to the 2019 branded price. The ASP for 2022 represents January and July manufacturer ASP reports. ASP, average sales price; Q, quarter.

JCO Oncology Practice

Price Discrimination [including Access Programs]

Important concept in Economics and Business

Companies charge different prices in different markets or segments, increasing number of consumers able to afford a product or service widely used outside of health care.
[Think of discounts and rebates in electronics, for instance]

Price Discrimination [including Access Programs]

- Many pilot projects have led to an increase in access and, in some cases, revenue.
- Some companies now have specific policies to provide medications at a different cost in low and middle income countries.

Price Discrimination: Challenges

Parallel Imports

Political Backlash in higher income countries, especially in times of economic difficulties.

Lower prices might still not be low enough in the absence of Universal Coverage and Economic Development.

Medscape Saturday, June 10, 2023

COMMENTARY

Did an Unfair System Help ADAURA Win on Overall Survival?

H. Jack West, MD

DISCLOSURES | June 08, 2023

ADAURA Phase III study design

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
- ≥18 years (Japan / Taiwan: ≥20)
- WHO performance status 0 / 1
- Confirmed primary non-squamous NSCLC Ex19del / L858R‡
- Brain imaging, if not completed pre-operatively
- Complete resection with negative margins§
- Maximum interval between surgery and randomization:
  - 10 weeks without adjuvant chemotherapy
  - 26 weeks with adjuvant chemotherapy

Stratification by:
Stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
Race (Asian vs non-Asian)

Randomization
1:1
(N=682)

Osimertinib 80 mg, once daily

Placebo, once daily

Planned treatment duration:
3 years

Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

Endpoints

- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

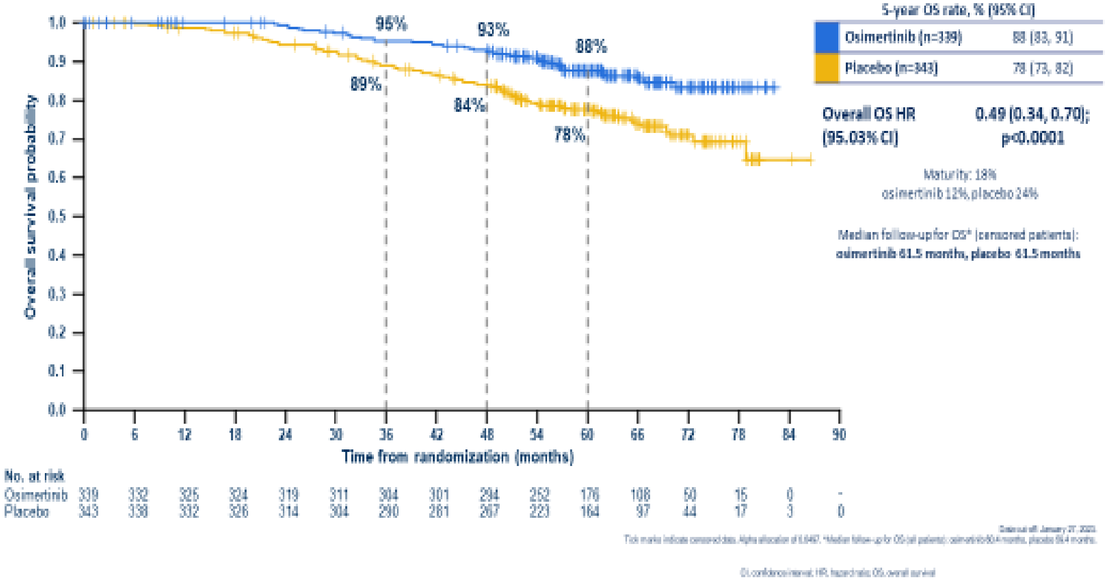
*At the time of recruitment, staging was determined by the AJCC / UICC Staging Manual 7th edition. Patients with stage IB disease were not eligible in Japan. †Pre-operative, post-operative, or planned radiotherapy was not allowed.
‡Centrally confirmed in tissue. §Patients received a CT scan after resection and within 28 days prior to treatment.

AJCC, American Joint Committee on Cancer; CT, computerized tomography;
DFS, disease-free survival; EGFRm, epidermal growth factor receptor-mutated;
Ex19del, exon 19 deletion; NSCLC, non-small cell lung cancer; OS, overall survival;
UICC, Union for International Cancer Control; WHO, World Health Organization

Tsuboi et al. NEJM June 4, 2023

Overall survival: patients with stage IB / II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the overall population of stage IB–IIIA disease



Tsuboi et al. NEJM June 4, 2023

Subsequent treatments

- At data cut-off for this final OS analysis, 76 patients (22%) in the osimertinib arm and 184 patients (54%) in the placebo arm had received any subsequent anti-cancer treatment
- EGFR-TKIs were the most common subsequent anti-cancer treatment received across both arms; most frequently osimertinib

Subsequent treatments, n (%)	Osimertinib (n=339)	Placebo (n=343)
Patients who received subsequent anti-cancer treatment*	76 (22)	184 (54)
EGFR-TKIs	58 (76)	162 (88)
Osimertinib	31 (41)	79 (43)
Other EGFR-TKIs	28 (37)	114 (62)
Chemotherapy	20 (26)	46 (25)
Radiotherapy	30 (39)	53 (29)
Other anti-cancer treatments	12 (16)	29 (16)

Data cut-off: January 27, 2023.

Percentages of patients by treatment type are calculated from the number of patients who received a subsequent anti-cancer treatment. *Subsequent anti-cancer treatments were identified by medical review and included anti-cancer treatments with a start date on or after the date of discontinuation of study treatment, and before withdrawal from the study. Surgeries and procedures were not included. Patients could have received more than one subsequent anti-cancer treatment.

EGFR-TKI, epidermal growth factor receptor-tyrosine kinase inhibitor; OS, overall survival

Article

The illusion of moral decline

- A series of surveys on around 12.5 million people over a 20-year period
- Assessed their perception of morality and its change over time
- Most believed there is less morality in 2020 compared to 2005
- However, most believed their personal morality did not change over time

Mastroianni et al. Nature, June 2023.

Article

The illusion of moral decline

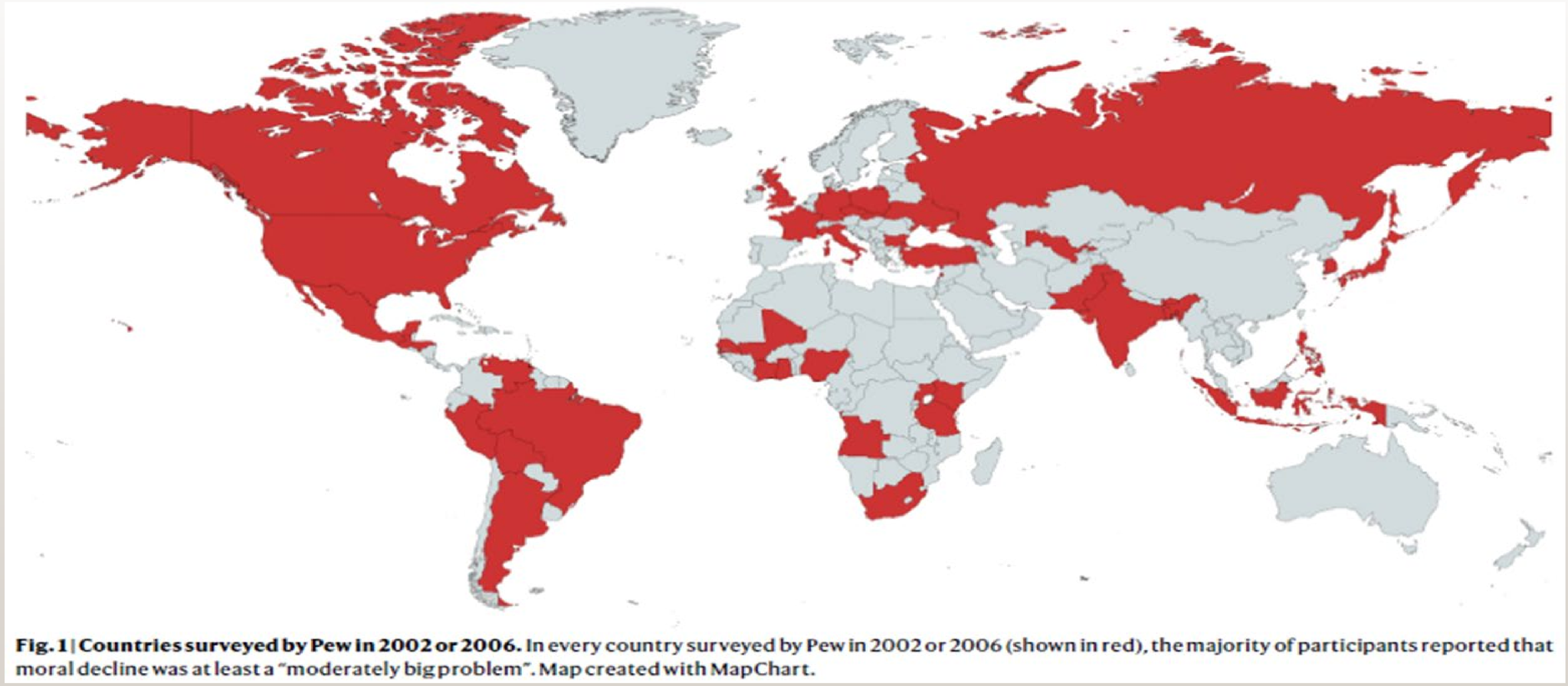


Fig. 1 | Countries surveyed by Pew in 2002 or 2006. In every country surveyed by Pew in 2002 or 2006 (shown in red), the majority of participants reported that moral decline was at least a "moderately big problem". Map created with MapChart.

Mastroianni et al. Nature, June 2023.

Article

The illusion of moral decline

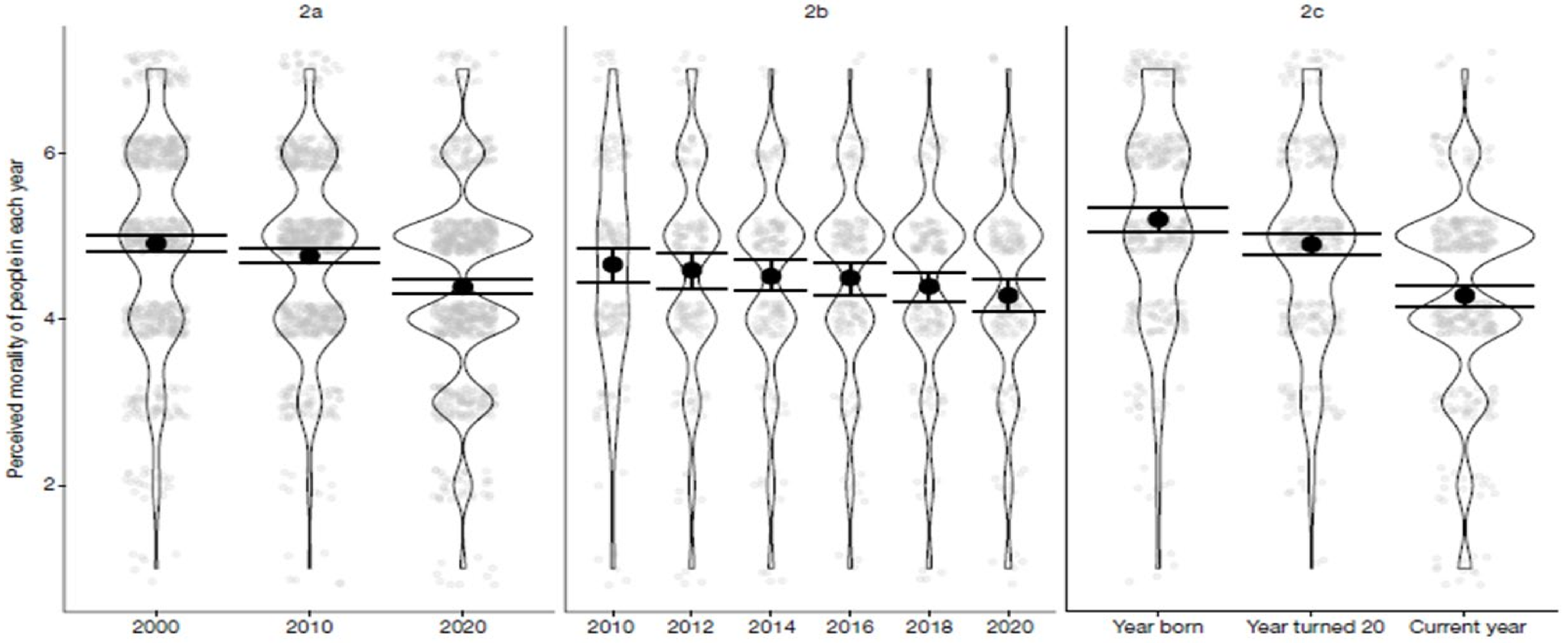
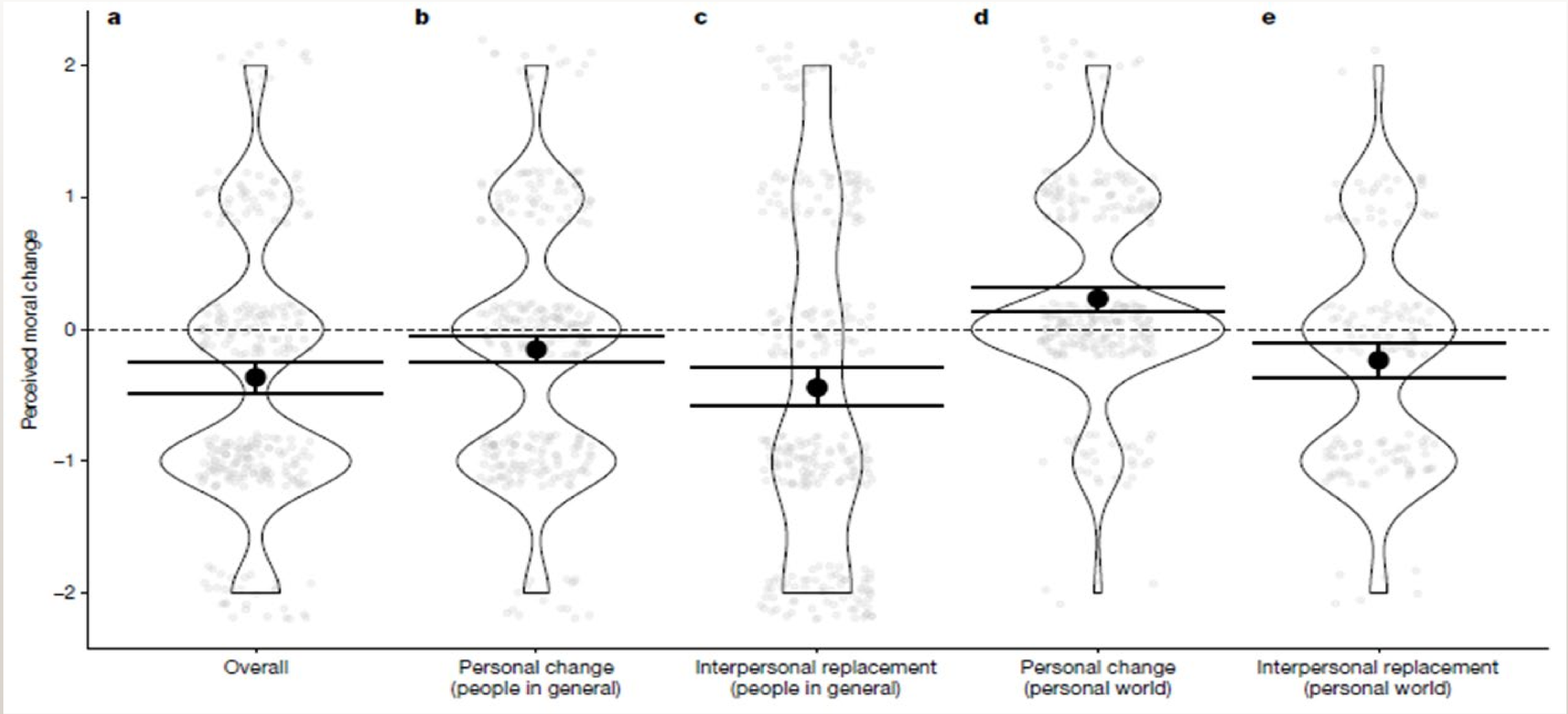


Fig. 2 | Results of studies 2a–c. The panels show the results of studies 2a (left panel), 2b (middle panel) and 2c (right panel). Opaque points represent means. Transparent points represent individual observations jittered for legibility. Error bars represent 95% CIs. Study 2a $n = 698$, study 2b $n = 148$ and study 2c $n = 347$.

Mastroianni et al. Nature, June 2023.

Article

The illusion of moral decline

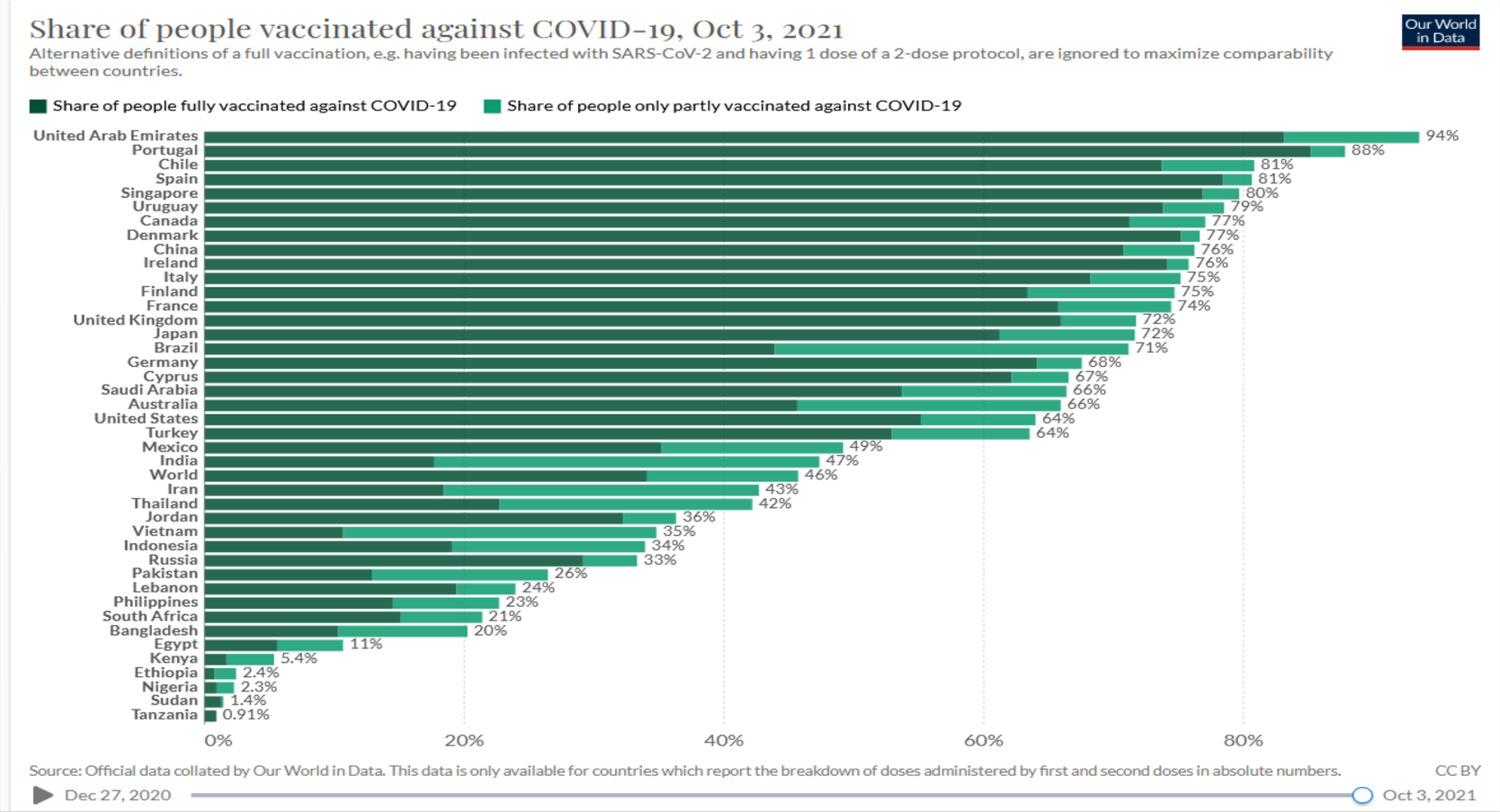


Mastroianni et al. Nature, June 2023.

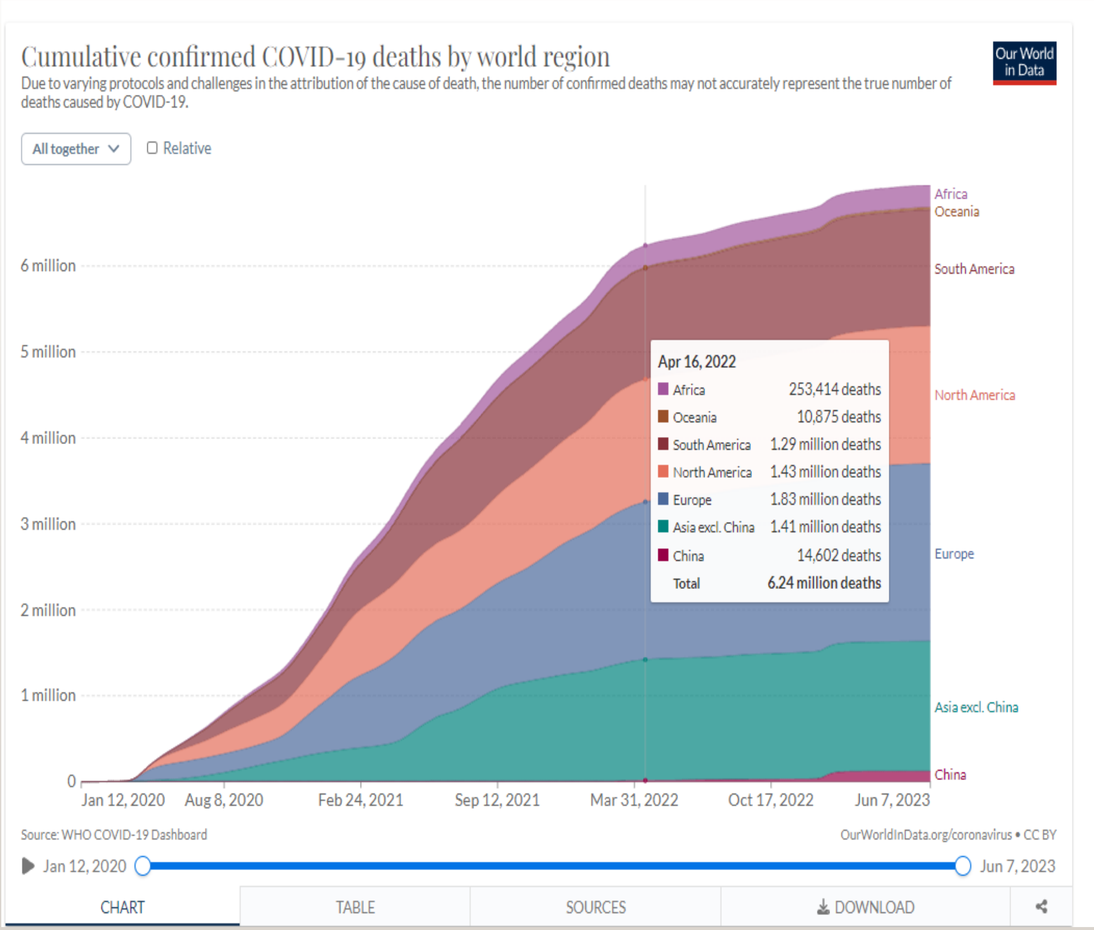
Ethical Dilemmas in Resource Allocation and Global Impact

- Is it ethical for the world's wealthiest economies to utilize the vast majority of cancer therapeutics with relatively stable cancer incidence?
- At the peak of the COVID-19 pandemic, 10 countries utilized 90% of the world's supply of COVID-19 vaccine.
- Disease control and outcomes improved in those 10 countries but the infections kept spreading.
- LMICs are expected to face an epidemic of cancer cases in the next few decades
- Several programs have made huge impact in LMICs with affordable budgets: They include Ivermectin for onchocerciasis, universal Hep B vaccinations, but best recent example is PEPFAR

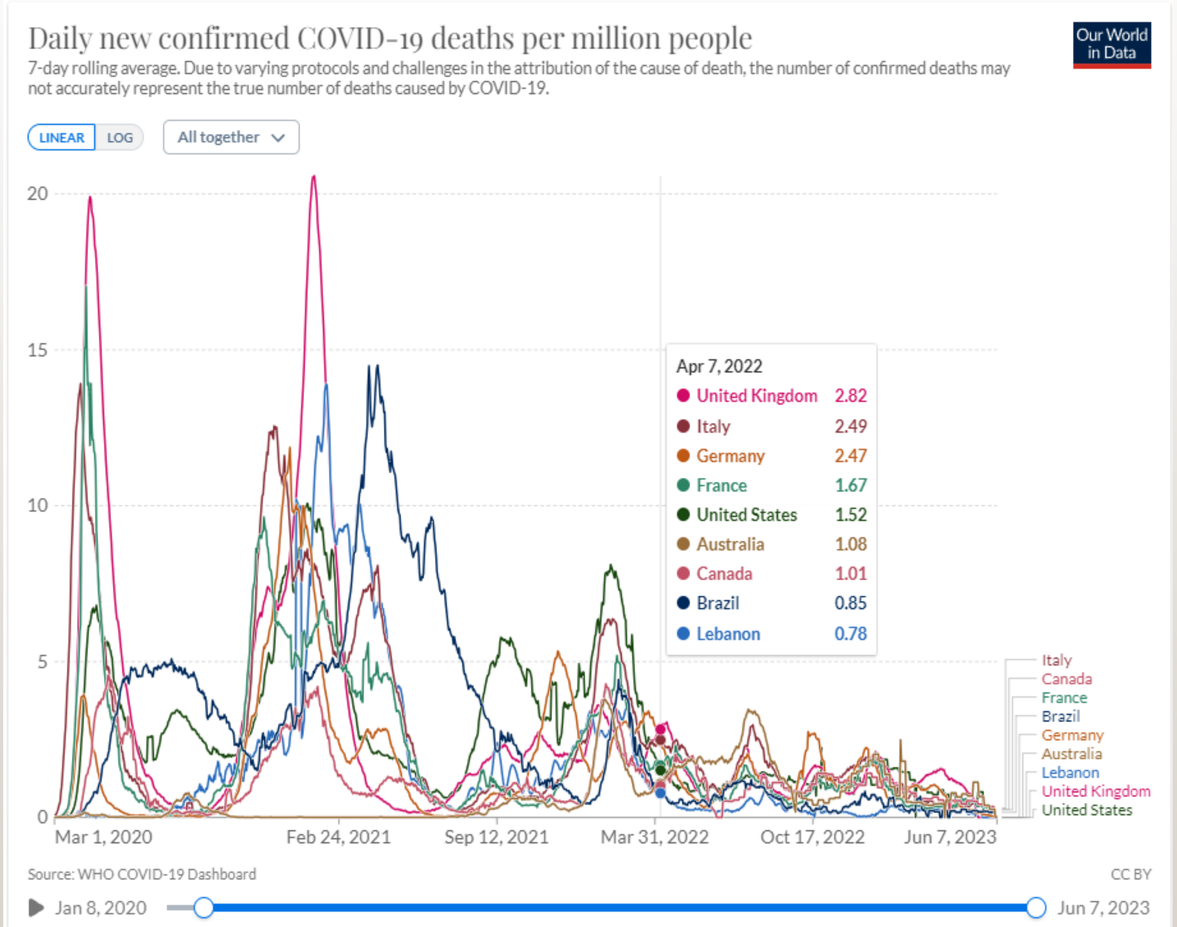
Uneven distribution of COVID-19 vaccines and mortality between the Global North and Global South



Uneven distribution of COVID-19 vaccines and mortality between the Global North and Global South



https://ourworldindata.org/grapher/cumulative-covid-deaths-region



https://ourworldindata.org/covid-deaths

PEPFAR at 20 — A Game-Changing Impact on HIV in Africa:
Selected PEPFAR Achievements, Remaining Challenges, and Approaches for Solutions

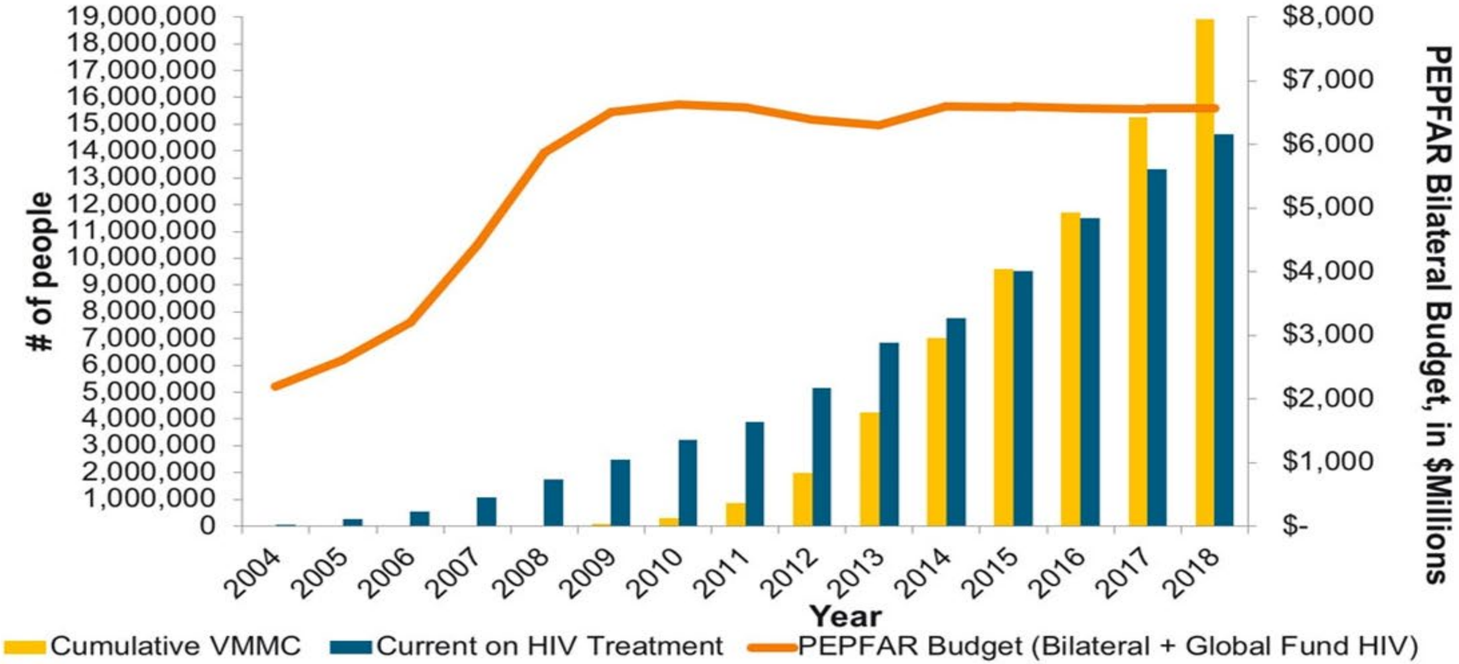
Selected PEPFAR Achievements, Remaining Challenges, and Approaches for Solutions.*

Selected Achievements	Remaining Challenges	Approaches for Solutions
Initiated ART in more than 20 million people. Enabled 20 countries with high HIV burden to achieve UNAIDS 90/90/90 treatment targets; a few are near or have achieved new 95/95/95 targets. Performed 27.7 million voluntary male circumcisions to reduce risk of HIV transmission.	There are persistent gaps in access to HIV services among men who have sex with men, transgender people, and sex workers. New HIV infections are still highest among adolescent girls and young women 15 to 24 years of age (three times higher than among adolescent boys and young men). There is increased risk of HIV infection among migratory, refugee, and internally displaced populations.	Increase advocacy against laws that criminalize members of marginalized groups, such as men who have sex with men, sex workers, and people who inject drugs. Develop and implement new interventions to address social and structural barriers to HIV-service access, uptake, and continuity.
Averted 5.5 million perinatal HIV infections. Achieved perinatal transmission of <5% in selected countries (e.g., Botswana).	Sub-Saharan Africa is home to 90% of the global population of children with HIV. There is heterogeneity in ART coverage during pregnancy and in mother-to-child transmission in West and Central vs. East and southern Africa. There is suboptimal HIV testing, ART coverage, and viral-load suppression among children as compared with adults; rates are lower in West and Central Africa than in East and southern Africa.	Implement point-of-care early HIV virologic diagnostic tools for infants and new approaches for HIV screening and diagnosis in older children (i.e., at immunization clinics and in inpatient and outpatient settings). Improve access to new ART pediatric formulations and pediatric viral-load testing. Initiate home-based ART and integrate HIV services into maternal and child health services. Use long-acting ART, when available.
Saved 25 million lives; led to countries regaining up to 20 years of life expectancy lost because of HIV/AIDS.	Moving toward country-level ownership with responsible transfer of program oversight and management to governmental and nongovernmental organizations is a work in progress.	Fast track country-level management, leadership, and ownership using specific metrics and milestones.
Strengthened health systems (70,000 facilities strengthened, 340,000 health workers trained, 3000 laboratories strengthened). Added more than 250,000 health care workers as part of PEPFAR-supported MEPI and NEPI programs.	In some countries and regions, the quality and size of the health workforce is limited.	Scale up patient-centered approaches to simplify and adapt HIV services throughout the care cascade to align with patients' preferences, expectations, and needs while reducing unnecessary burdens on health systems. Increase training and support for the community health workforce; increase the size of the field workforce trained in epidemiology, laboratory, and digital health data.
Leveraged HIV platform and infrastructure to respond to emerging and reemerging pathogens (e.g., SARS-CoV-2, Ebola, mpox).	There is an unmet need to integrate noncommunicable disease (e.g., diabetes) models to promote person-centered HIV care in the context of limited resources. Long-term funding is needed for sustainability.	Work with governments to integrate vertical AIDS programing more efficiently and effectively into local health service delivery for tuberculosis and noncommunicable diseases. Strategically align core HIV and broader health resources to support maximum effect and value of PEPFAR, GFATM, partner-country, and other donor investments.

* ART denotes antiretroviral therapy, GFATM the Global Fund to Fight AIDS, Tuberculosis, and Malaria, MEPI the Medical Education Partnership Initiative, NEPI the Nursing Education Partnership Initiative, PEPFAR the President's Emergency Plan for AIDS Relief, and UNAIDS Joint United Nations Program on HIV/AIDS.

Jean B. Nachega, M.D., Ph.D., M.P.H., David Serwadda, M.B., Ch.B., M.P.H., Alash'le Abimiku, Ph.D., Izukanji Sikazwe, M.B., Ch.B., M.P.H., and Quarraisha Abdool Karim, Ph.D. PEPFAR at 20 — A Game-Changing Impact on HIV in Africa. *The NEW ENGLAND JOURNAL of MEDICINE*, July 2023.

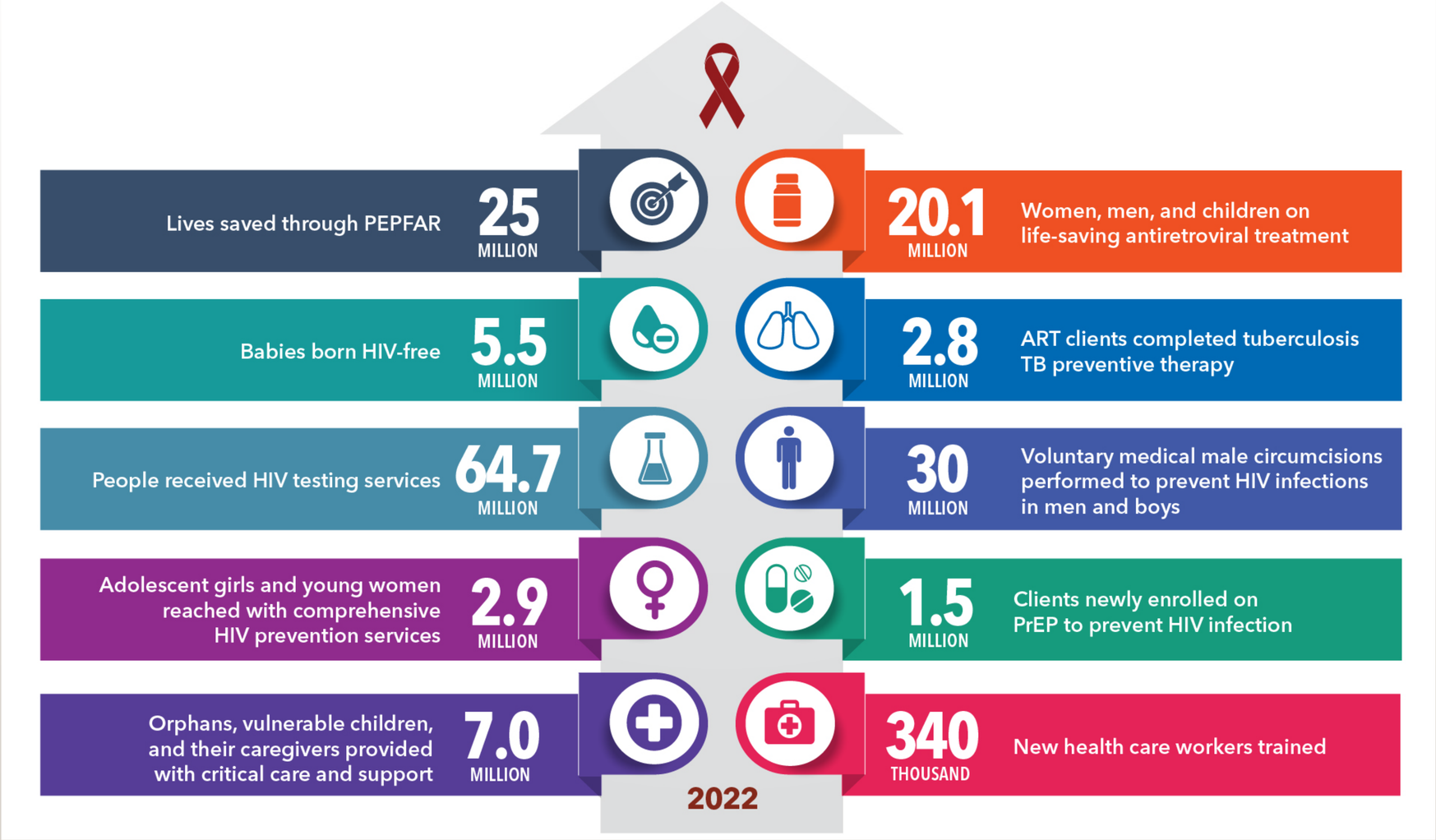
PEPFAR's remarkable expansion of lifesaving services with flat budgets



PEPFAR
U.S. President's Emergency Plan for AIDS Relief

https://www.state.gov/about-us-pepfar

PEPFAR's remarkable lifesaving results over the past 20 years



As of September 30, 2022, the U.S. President Emergency Plan for AIDS Relief (PEPFAR) supported antiretroviral treatment for 20.1 million people.

https://www.state.gov/results-and-impact-pepfar/

Conclusions

- It is both our moral obligation and our advantage to work together.
- Hippocrates Oath: ***I will prevent disease whenever I can, for prevention is preferable to cure. I will remember that I remain a member of society, with special obligations to all my fellow human beings.***
- We live in a world that is increasingly interconnected, in which no nation can isolate itself from the outside world.
- Metastatic spread of non-communicable diseases through “financial toxicity, emigration waves, and other universally negative consequences of maldistribution of resources.
- Cancer treatment, prevention and control are a global priority. Treating them as such needs to be a social, economic, and global priority.
- PEPFAR shows what we can do when we think of others as a part of us. It needs to be the model for future therapeutic and preventive models.

"FOOLS" SAID I, "YOU DO NOT KNOW
SILENCE LIKE A CANCER GROWS
HEAR MY WORDS THAT I MIGHT TEACH YOU
TAKE MY ARMS THAT I MIGHT REACH YOU"
BUT MY WORDS LIKE SILENT RAINDROPS FELL
AND ECHOED IN THE WELLS OF SILENCE

AMERICAN
UNIVERSITY
OF BEIRUT

Simon, P. The Sound of Silence. 1964

THANK YOU!

AMERICAN UNIVERSITY OF BEIRUT