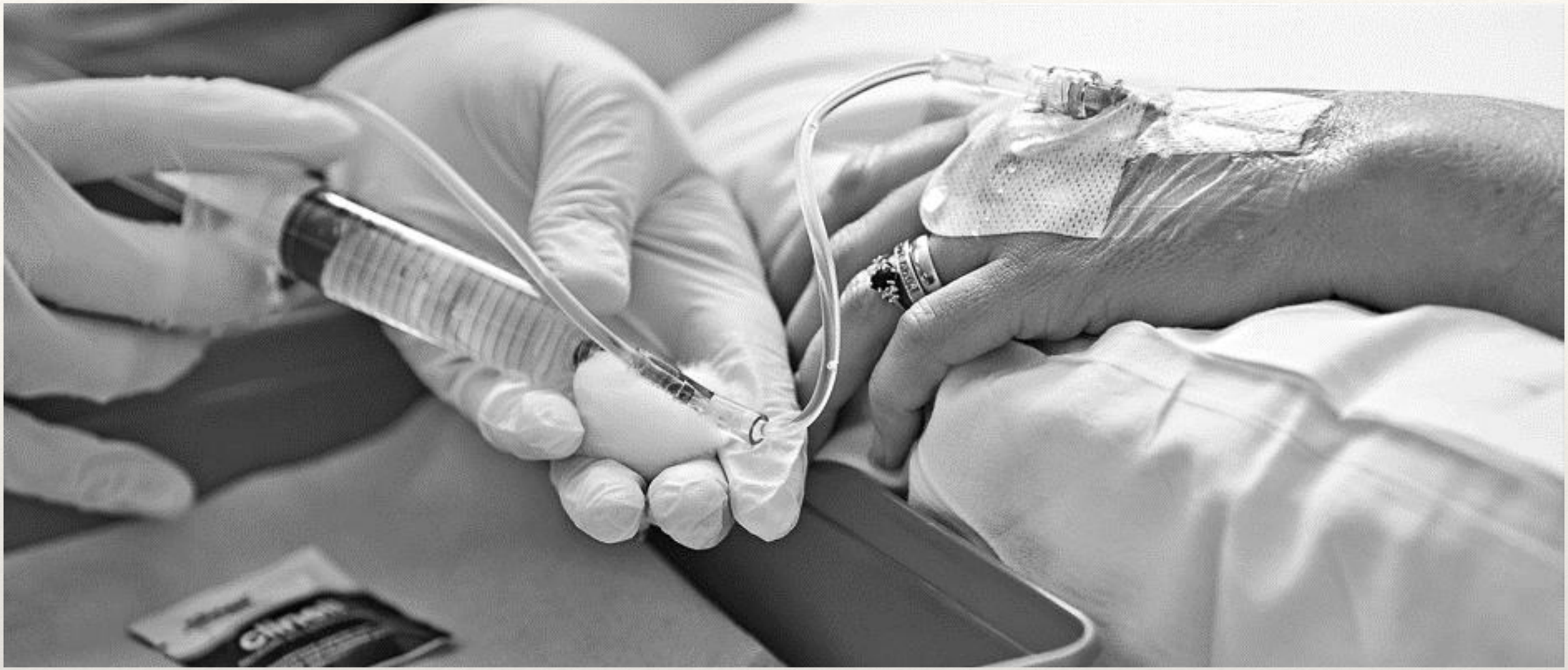

How the Health and Human Rights Framework Evolved *And How That Affects Clinical Research*

Stephen Inrig
Associate Professor,
Health Policy and Management
Mount Saint Mary's University

The need: problems facing health systems and the need for clinical research

Innovation in medicine, science, and technology has transformed global access to medicines.

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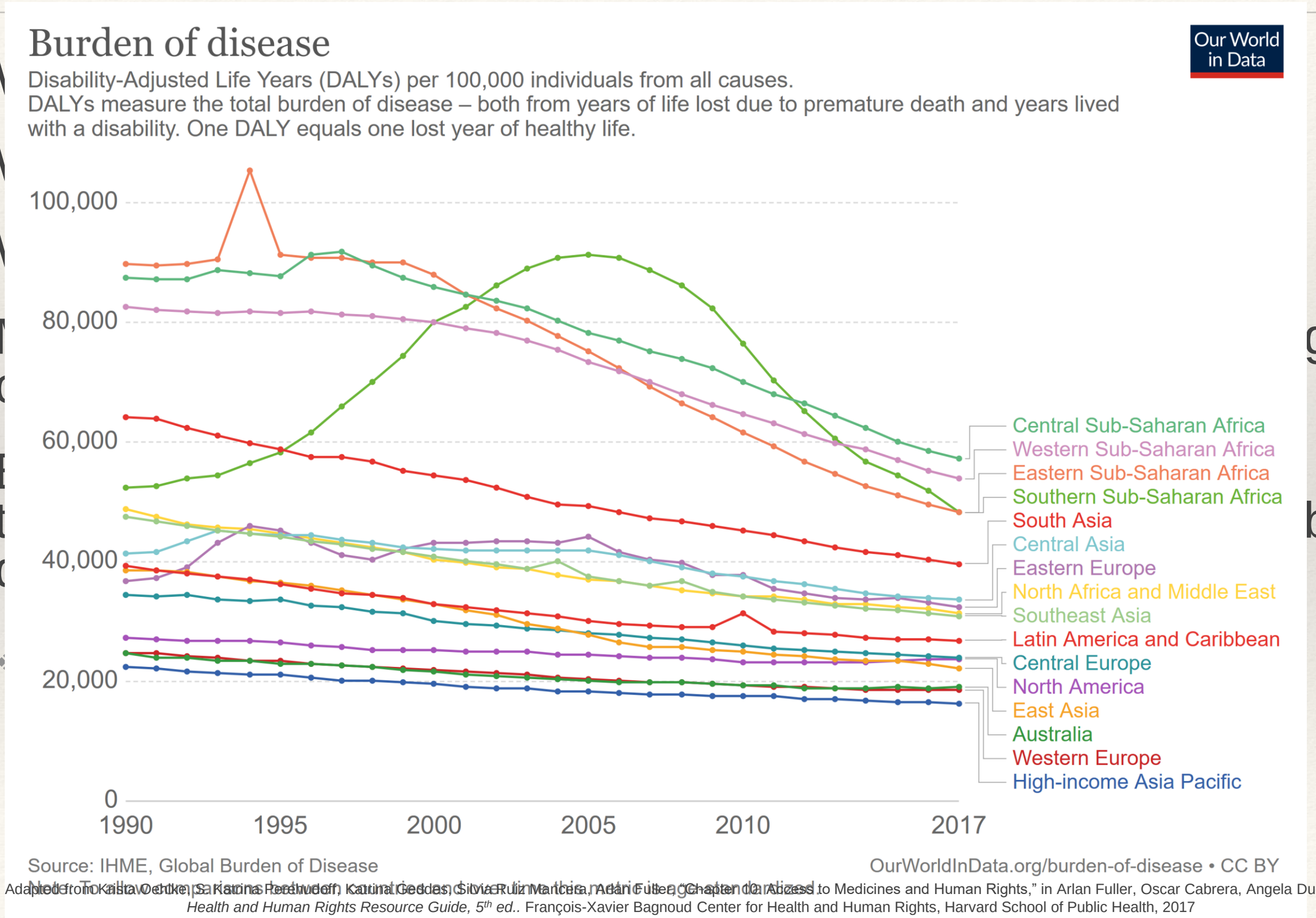


Adapted from Krista Oehke, S. Katrina Reedhoff, Katuna Geddes, Silvia Ruiz Manrique, Arlan Fuller, "Chapter 10. Access to Medicines and Human Rights," in Arlan Fuller, Oscar Cabrera, Angela Duger, eds., *Health and Human Rights Resource Guide, 5th ed.*. François-Xavier Bagnoud Center for Health and Human Rights, Harvard School of Public Health, 2017

Nonetheless, tremendous challenges remain

- Approx. 2 Billion people have inadequate access to needed medicine[1]
- Funding from public-private partnerships did bring 37 new treatments for neglected diseases to market between 2000 and 2011[2]
- Neglected diseases account for about 11% of the global burden of disease, but this represented just 4% of all new therapies during that period.
- Except for Ebola and other African viral haemorrhagic fevers, “funding for product development for neglected diseases has shown a downward trend since 2009.”[3]

1. Access to Medicine Foundation, “The 2016 Access to Medicine Index: Methodology 2015,” 2016, http://apps.who.int/medicinedocs/documents/s22176en/s22176en.pdf
2. Gavin Yamey, Amie Batson, Peter H Kilmarx, and Marcel Yotebieng, “**Funding innovation in neglected diseases**,” *BMJ*. 2018; 360: k1182
3. Gavin Yamey, Amie Batson, Peter H Kilmarx, and Marcel Yotebieng, “**Funding innovation in neglected diseases**,” *BMJ*. 2018; 360: k1182, citing Chapman N, Doubell A, Oversteegen L, et al. Neglected disease research and development: reflecting on a decade of global development. G-Finder. 2016

Nonetheless, tremendous challenges remain

- The current market driven R&D model is ill-equipped to address gaps in essential medicines and neglected tropical diseases
- HIV medicines (as we will see) have become an example of success
- The purchasing power of the populations most affected by Zika, Ebola, and Neglected Tropical Diseases is insufficient to incentivize R&D in many of these diseases
- Many have looked to other incentives – including the health and human rights framework – to resolve these concerns and realign priorities

Unequal access to health and the problem of the WHO

- Launched in April 1945,
  - during the conference held at San Francisco to set up the United Nations.
  - Proposed by representatives of Brazil and China
- Constitution drawn up at an international health conference in New York in 1946.
  - "Interim Commission" established to address urgent needs until UN Member States ratified constitution.
- Constitution ratified on April 7, 1948;
- Established as **a specialized, non political, health agency of the United Nations, with headquarters at Geneva;** a single worldwide inter-governmental health agency.
- Annually, the WHO's World Health Assembly evaluates global disease burdens and votes on actions and programs "to bring relief, and so improve the quality of life of populations at risk."
- Its first resolution – in 1949 – focused on what are now termed NTDs

Adapted from Lorenzo Savioli, Denis Daumerie, et al., First WHO report on neglected tropical diseases: working to overcome the global impact of neglected tropical diseases. Geneva: World Health Organization, 2003.

Membership in WHO

- Membership in WHO is open to all countries.
- Most countries belong both to the UN and WHO, but some don’t
  - Ie. - Switzerland belongs to WHO, but not the United Nations.
- Territories not responsible for the conduct of their international relations may be admitted as Associate Members.
  - Associate Members participate but do not vote in WHO deliberations.
- Each Member State contributes the annual budget
- Each Member State is entitled to the services and aid the organization can provide.
  - In 1948, WHO had 56 Members
  - Since 2003, WHO has had 192 Member States and two Associate Members.

Countries launched the WHO within the larger UN global governance system to prevent conflict and protect rights

What are Human Rights according to the UN?

- Human rights are legally guaranteed by human rights law, to protect individuals and groups against actions of the state that interfere with fundamental freedoms and dignity,
  - Enshrined in the 1948 Universal Declaration of Human Rights (UDHR)
- Human Rights encompass what are known as civil, political, cultural, economic and social rights that were codified in the following legally binding treaties (1966):
  - The International Covenant on Economic, Social and Cultural Rights (ICESCR)
  - The International Covenant on Civil and Political Rights (ICCPR).

The World Health Organization considers “health” a human right

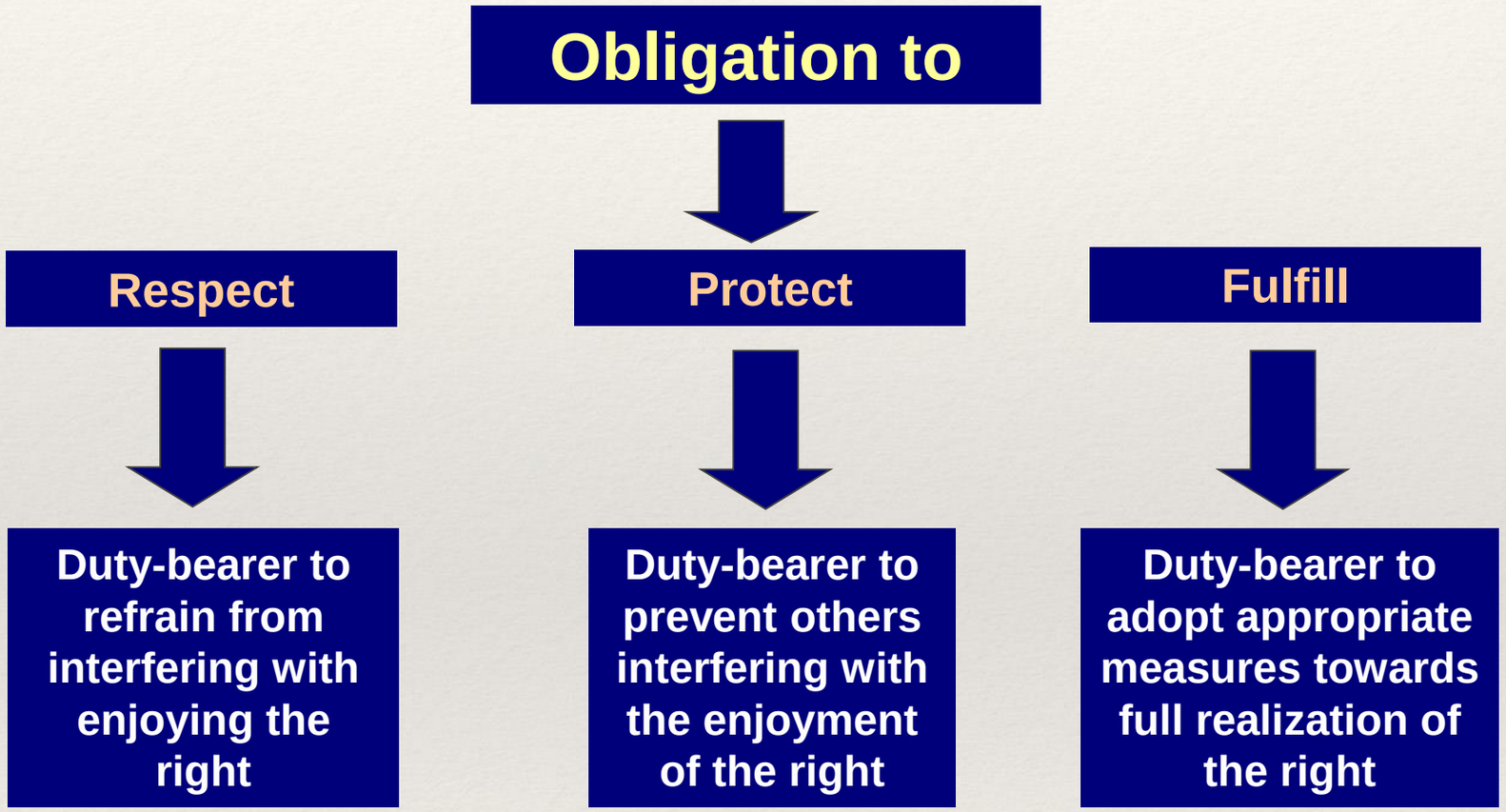
- The WHO Constitution (1946) envisages “…the highest attainable standard of health as a fundamental right of every human being.”
- “Health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.”
- Understanding health as a human right creates a legal obligation on states to ensure access to timely, acceptable, and affordable health care of appropriate quality as well as to providing for the underlying determinants of health, such as safe and potable water, sanitation, food, housing, health-related information and education, and gender equality.

World Health Organization, “Human Rights and Health,” December 29, 2017
World Health Organization, “What is the WHO definition of health?” 2020

WHO understood the “Right to Health” as a process

- Progressive realization
  - Concrete steps e.g. national strategy
  - Using maximum of available resources, international assistance
- Core minimum obligation
  - Beginning point: non-discrimination
  - Minimum essential food
  - Shelter, housing, sanitation, safe drinking water
  - Provision of essential drugs
  - Equitable distribution of health facilities, goods, services

Types of obligations the UN in general and the WHO in particular associate with state obligations



But what if you – as a state – lack power to obtain essential medicines? How do you meet your obligations?

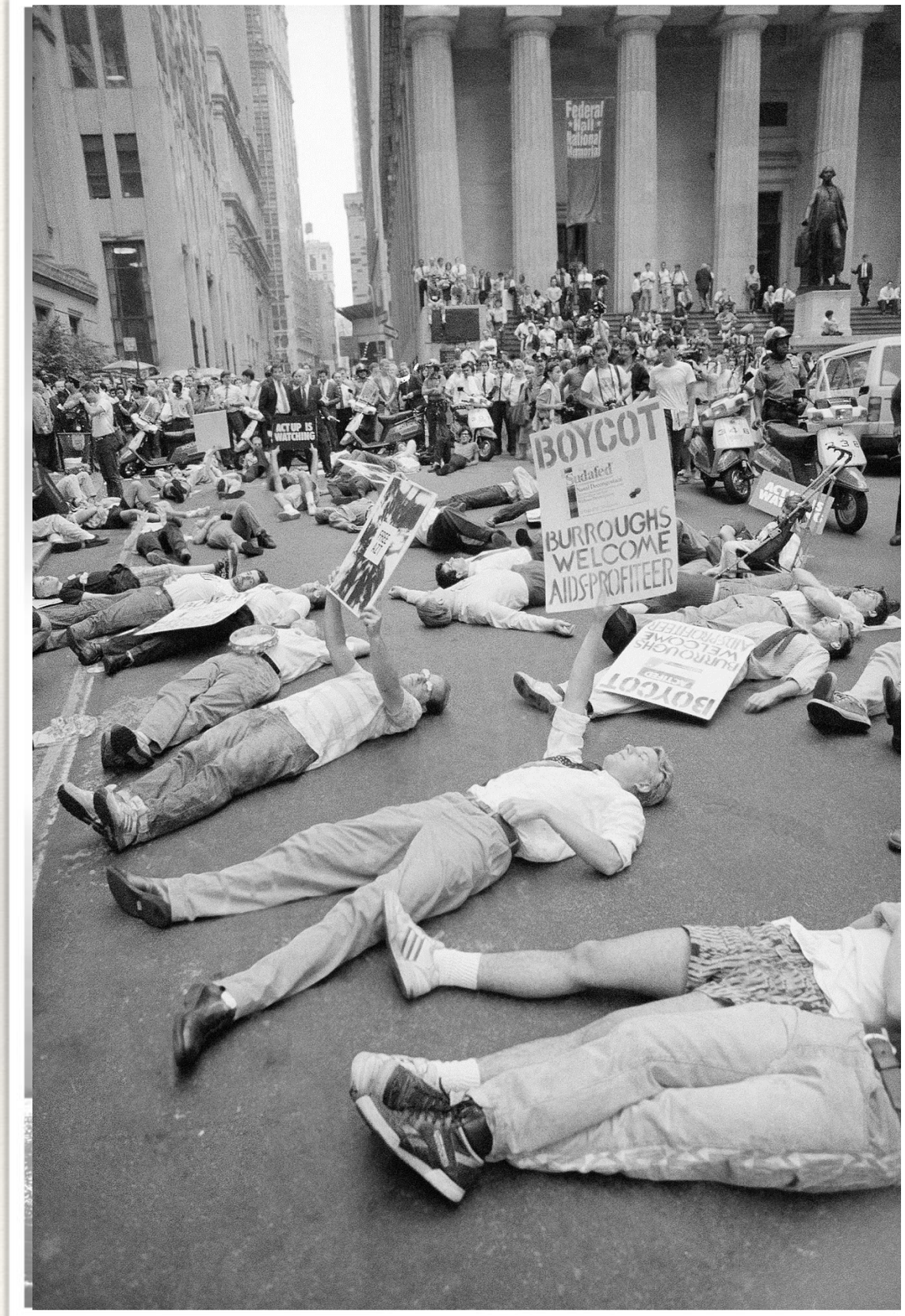
The problem of essential medicines

- “Essential medicines” are those medicines that “satisfy the priority healthcare needs of the population.”
- The WHO selected them on the basis of their estimated current and future public health relevance, evidence of efficacy and safety, and comparative cost-effectiveness.
- WHO publishes medicines that meet these principles in WHO’s model list of essential medicines (EML).
- Countries can use national lists as a tool to prioritize their most pressing public health needs by focusing on public sector procurement and treatment of a limited and high-priority set of medicines.
- At the start of the 21st Century, 30% of the world’s population lacked access to essential medicines and in countries 27 low income countries that did have essential medicines available, they were only available for 34.9% of the served population[1]
- For states to fulfill their human rights obligations, they need to solve this “essential medicines” dilemma which they do not control.

1. Hiroko Yamane, Interpreting TRIPS: Globalization of Intellectual Property Rights and Access to Medicines (Portland: Hart Publishing, 2011)

Clinical research and the challenge of human rights: AIDS, ART, and the “health and human rights” framework.

AIDS served as the key impetuous for reflecting on clinical research and R&D from a human rights perspective

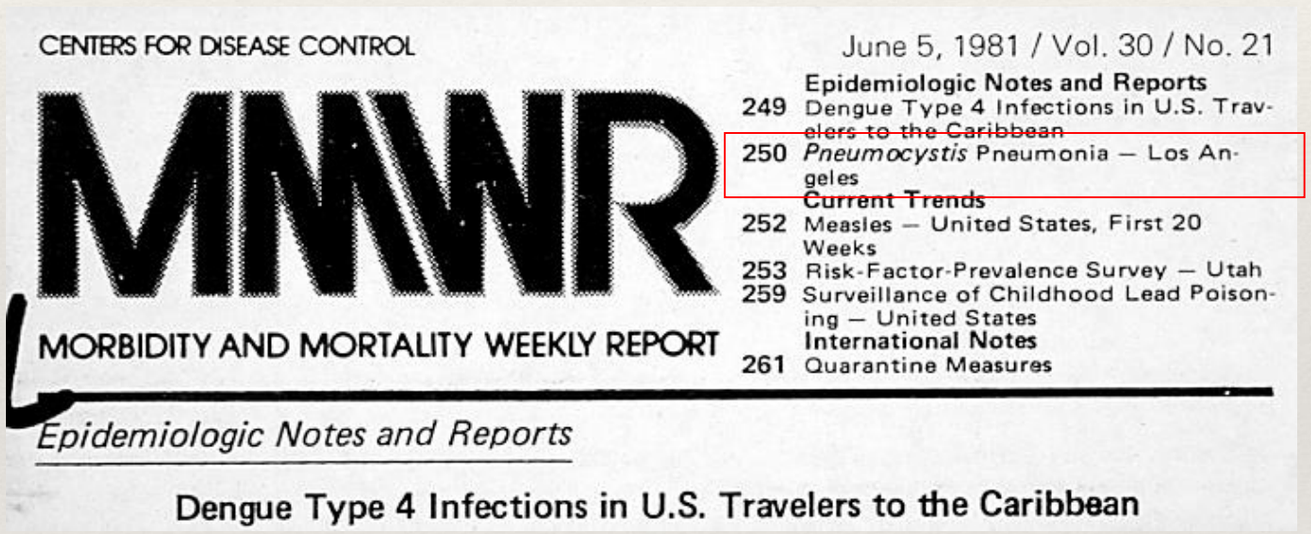


Many groups had started to think about health and human rights before HIV/AIDS

- Between the 1960s and 1980s, several NGOs mobilized to research, generate action, prevent, and end grave human rights abuses.
  - International Committee of the Red Cross (1863)
  - Amnesty International (1961)
  - *Medecins Sans Frontieres* (1971)
  - *Medecins Du Monde* (1980)

HIV emerged seemingly out of nowhere in 1981

- June 1981: ***Pneumocystis carinii*** **pneumonia *in LA***



CENTERS FOR DISEASE CONTROL

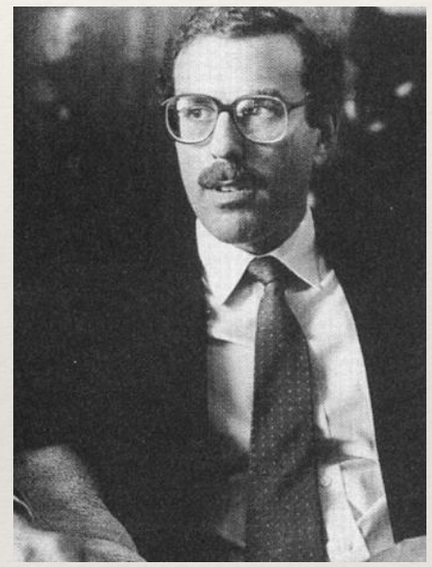
June 5, 1981 / Vol. 30 / No. 21

MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

Epidemiologic Notes and Reports

Dengue Type 4 Infections in U.S. Travelers to the Caribbean



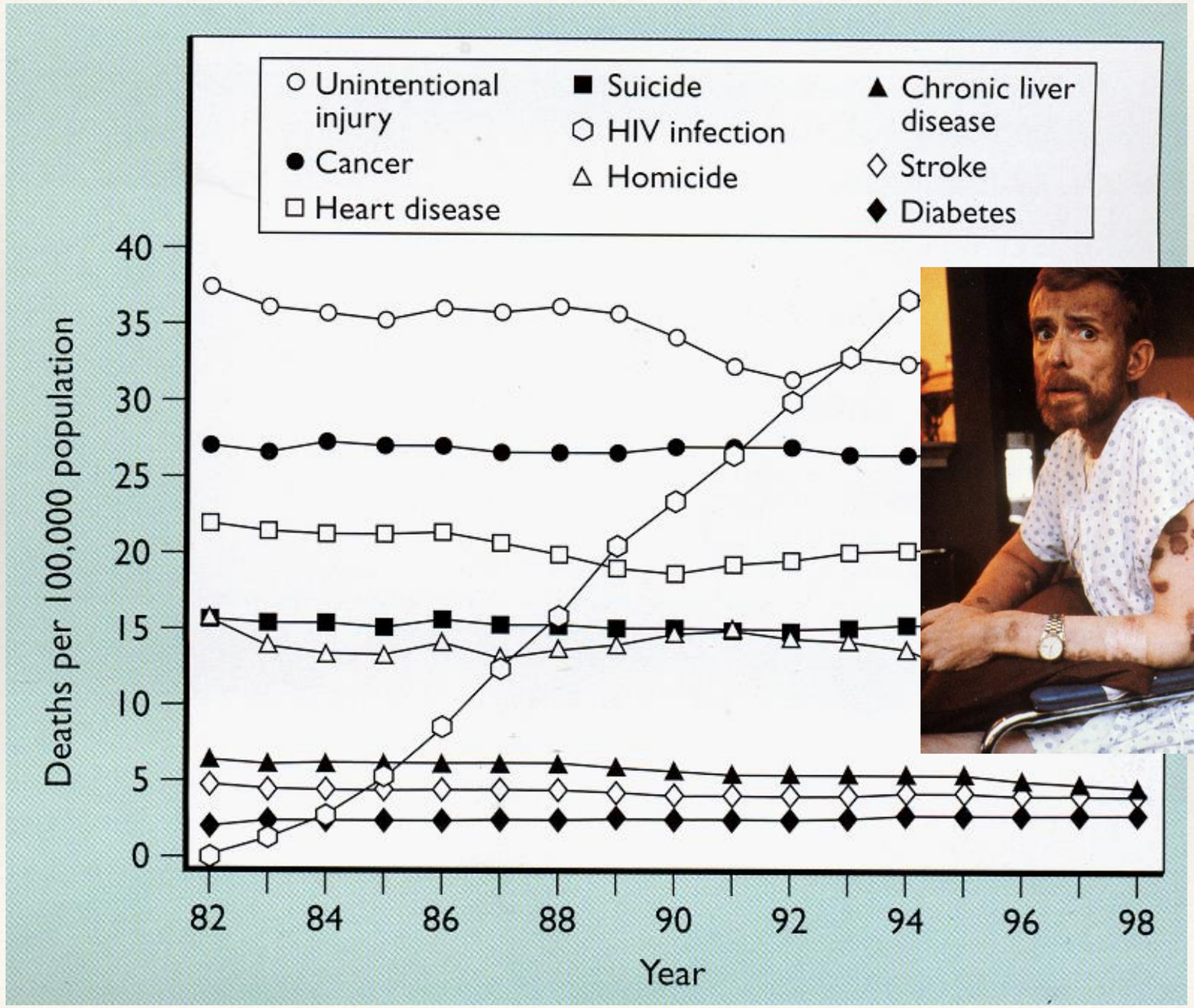
Michael Gottlieb MD
Los Angeles

- **"an association between some aspects of the homosexual lifestyle or disease acquired thru sexual contacts and *Pneumocystis* pneumonia in this population"**
- **"the observations suggest the possibility of a cellular-immune dysfunction that predisposes individuals to opportunistic infections such as pneumocystosis and candidiasis"**

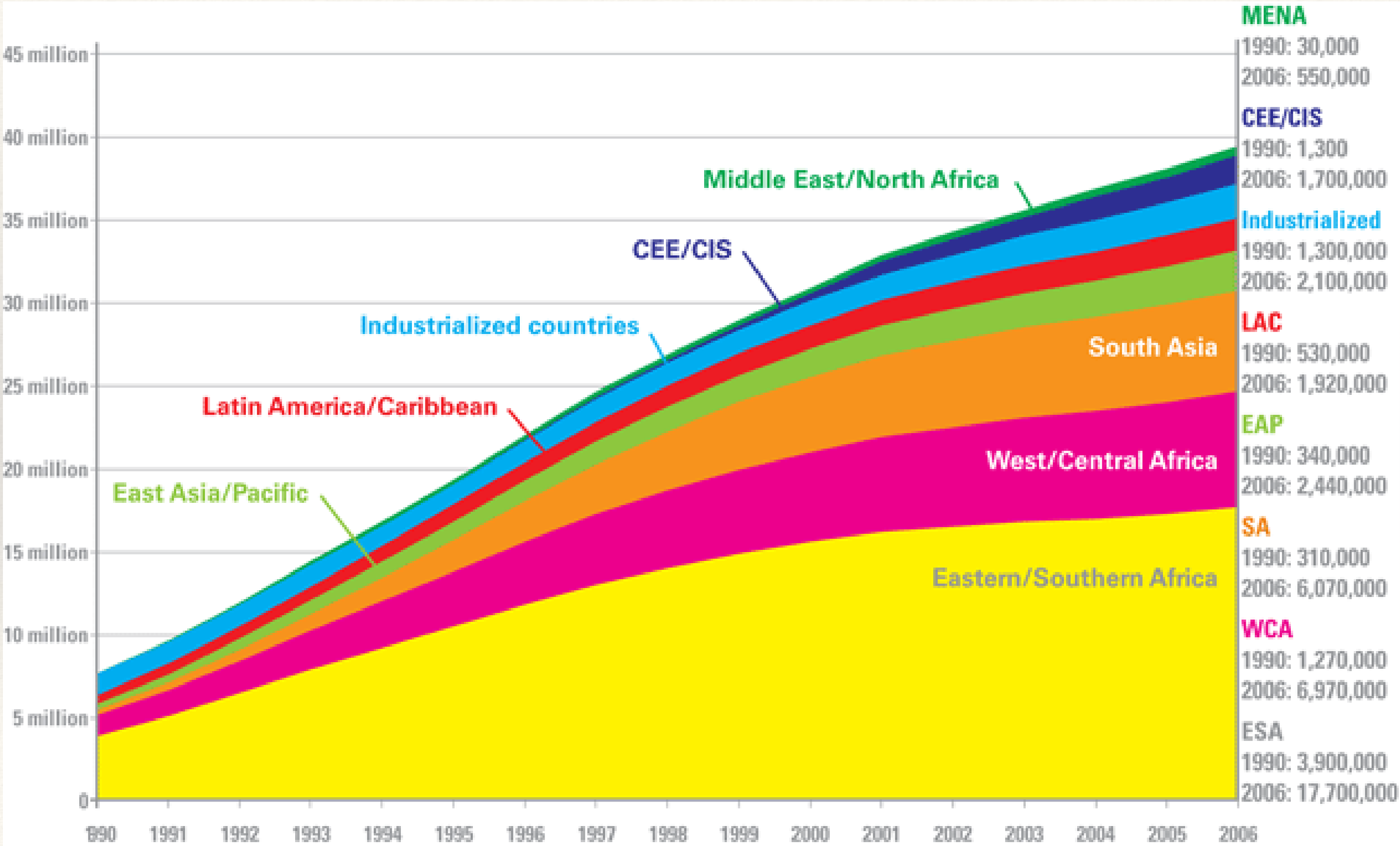
Sandra Panem, *The AIDS Bureaucracy* (Cambridge, MA, 1988). pp. 9, 11

The disease had a rapid and profound impact in the US

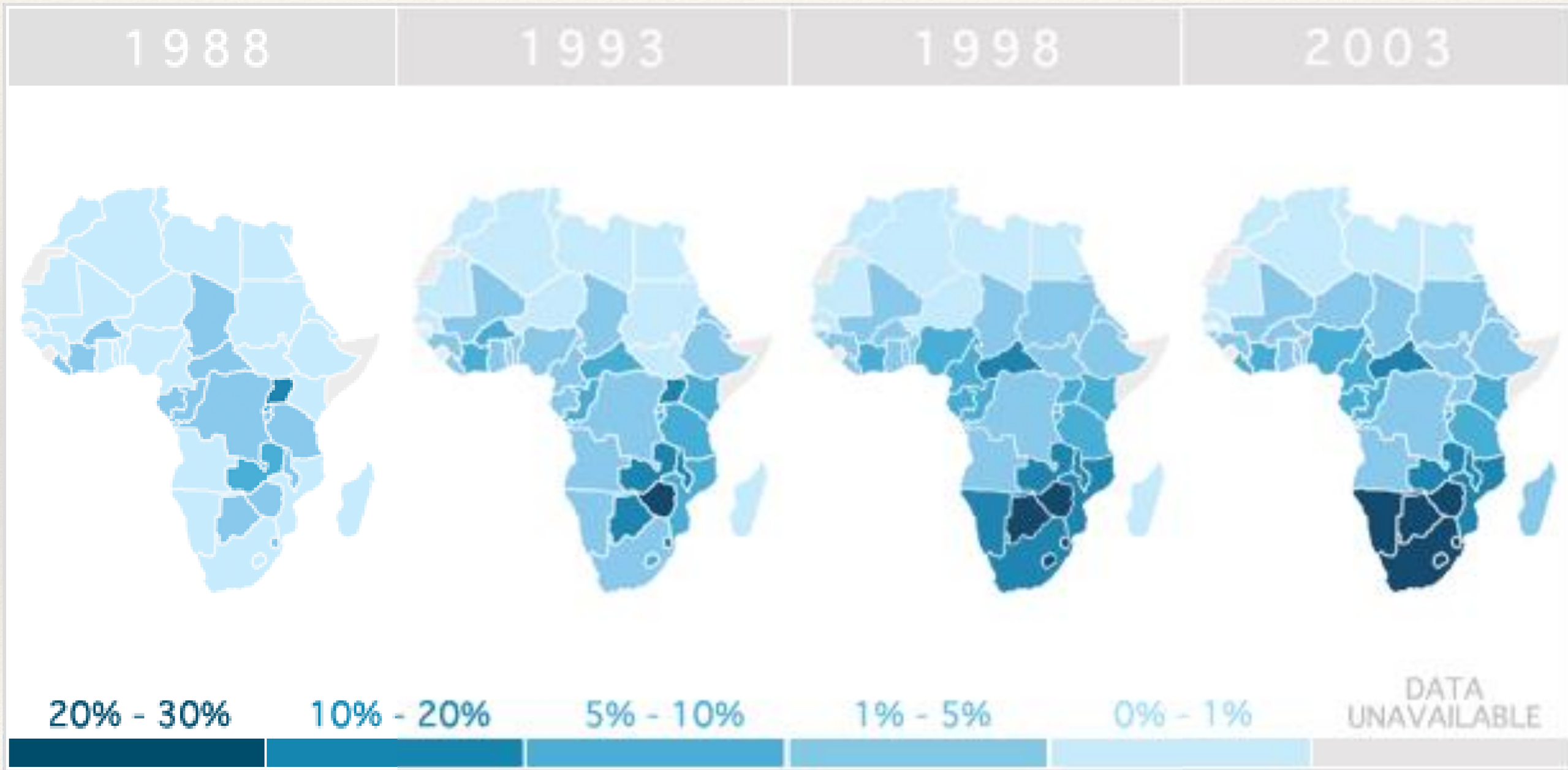
Causes of death, ages 25-44, USA, 1982-1994



And an even more profound affect across the globe



Wreaking particular havoc and devastation across Africa



AIDS led to intense discrimination but groups responded immediately

- Loss of insurance
- Closure of MSM establishments
- Denied insurance
- Loss of job
- Housing discrimination
- Violence
- Loss of parental rights
- Etc.

Many of the early debates encouraged people to think from a “rights perspective”

- Relevant commissions
  - Blood product safety
  - Gay rights
- Issues resolution in 1983 on human rights aspects of discrimination
- 1983 – 1985 issues several calls
  - for non-discriminatory policy,
  - Denunciation of gay discrimination
  - For exploration of ethics issues around blood donor screening

COUNCIL OF EUROPE

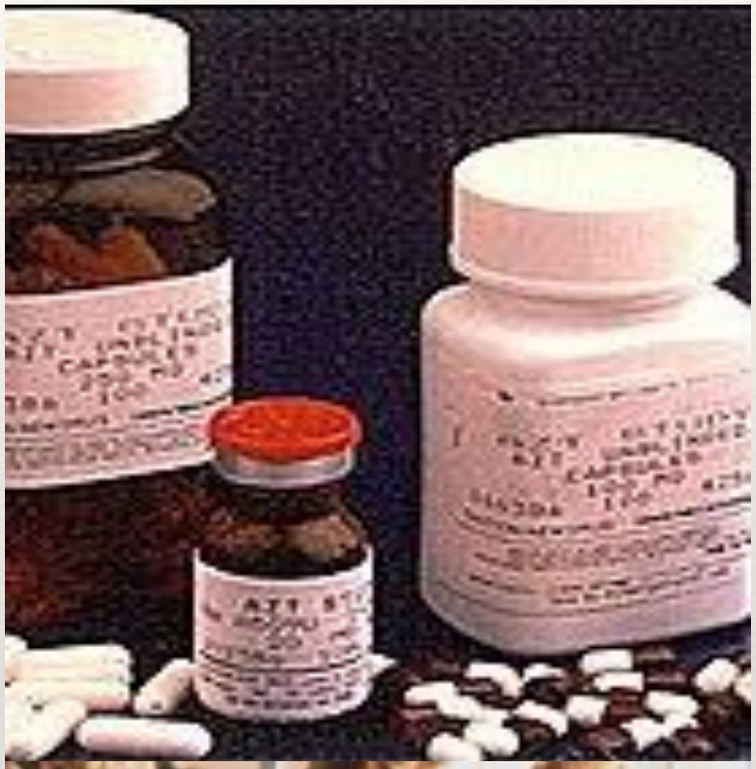
CONSEIL DE L’EUROPE

At the WHO, AIDS discrimination initially manifest itself in issues around migration and travel

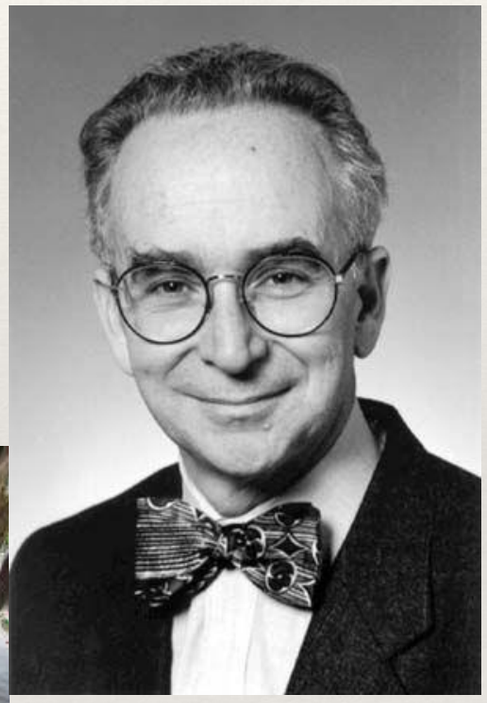
AP/Getty

Until AZT in 1987, clinicians lacked AIDS therapies

- AZT developed in 1964 as a possible anti-cancer agent; it did not work and proved too toxic
- Burroughs Wellcome, a British non-profit with a US office in North Carolina, secured the drug in the late 1970s and began testing it against a murine virus in 1984
- Clinical trials move rapidly as it shows efficacy and, by 1987, Burroughs Wellcome had brought it to market.
- Annual price tag of $10,000 - $12,000
- AIDS activists launch ACT-UP in response to this perceived price-gauging (among other things)



Assaad died in 1986 and was replaced at WHO by Jonathan Mann



Mann's response to AIDS initially did not focus on drug access

- Strategic Consultations with Countries
- Removal of travel restrictions
- Promote national policies and testing regimens aligned with ethics and human rights protections

Combatting AIDS led Mann to identify what he called the “third epidemic”

- Mann begins talking about the “third epidemic”
  - First epidemic = epidemic of the virus
  - Second epidemic = Epidemic of AIDS (the end-stage disease)
  - Third epidemic = The enormous social, cultural, economic, and political pandemic.

- The “third epidemic” highlighted the structural implications of AIDS:
  - One cannot hope to prevent the reuse of disposable injection equipment in many African countries when many hospital budgets are insufficient for the purchase of antibiotics or pentamidine.
  - Health providers cannot reduce the risk among vulnerable populations if those populations are deemed illegal or lack access to the full panel of AIDS-related services and therapies.

The heart of the third epidemic - discrimination

Mann initially focused on “the public health rationale” of protecting human rights

- Rationalize anti-discrimination efforts on public health grounds

AIDS

Discrimination and Public Health

Jonathan M. Mann, MD, MPH
Director, Global Programme on AIDS
World Health Organization

An address presented 13 June 1988 at the
IV International Conference on AIDS
Stockholm, Sweden
by

Kathleen Kay
Executive Assistant to the Director
Global Programme on AIDS

Moving beyond nondiscrimination

- Continued operationalizing nondiscrimination policies
- Address conflation of AIDS discrimination against associated risk groups
- Recognize barriers to individual behavior change
  - You may want to use condoms but can’t afford them
- Began exploring positive environments for healthy behaviors: adequate health and social systems

Human rights beyond the "individual"

1. Recognize that discrimination falls on groups not just individuals

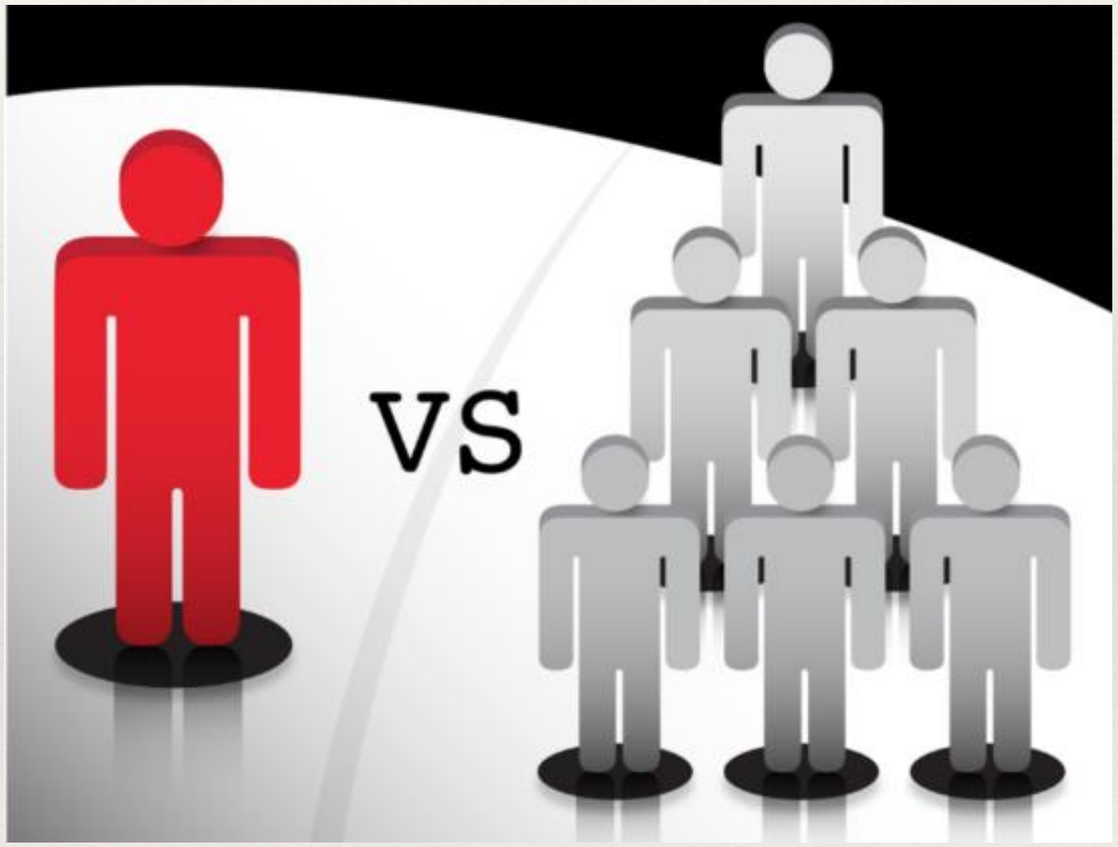
2. Bolster support systems because nondiscrimination was not the same as positive access

    1. Supportive social environments

    2. Explore the role that clinical research plays in providing drugs and therapies to vulnerable populations

    3. Address the extent to which low income countries have access to treatments of opportunistic infections (and whether some of them – particularly Tuberculosis and Malaria – had ongoing robust research efforts)

3. AIDS-related support would remain inadequate in a given country if the larger system of health inequities and inequality remained.



Structural rights

- the right to a good health system
- the right to a continuum of care
- the right to accessible therapies
- the right to accessible care

- Initially, Mann’s argument was that we needed these things to fight HIV/AIDS

Flipping the script:
- AIDS as a means to an end

- As Mann pushed the international health community to envision the public health rationale for promoting human rights, other observers pushed him to realize he had it backwards.

The key issue: AIDS and the place of women in society

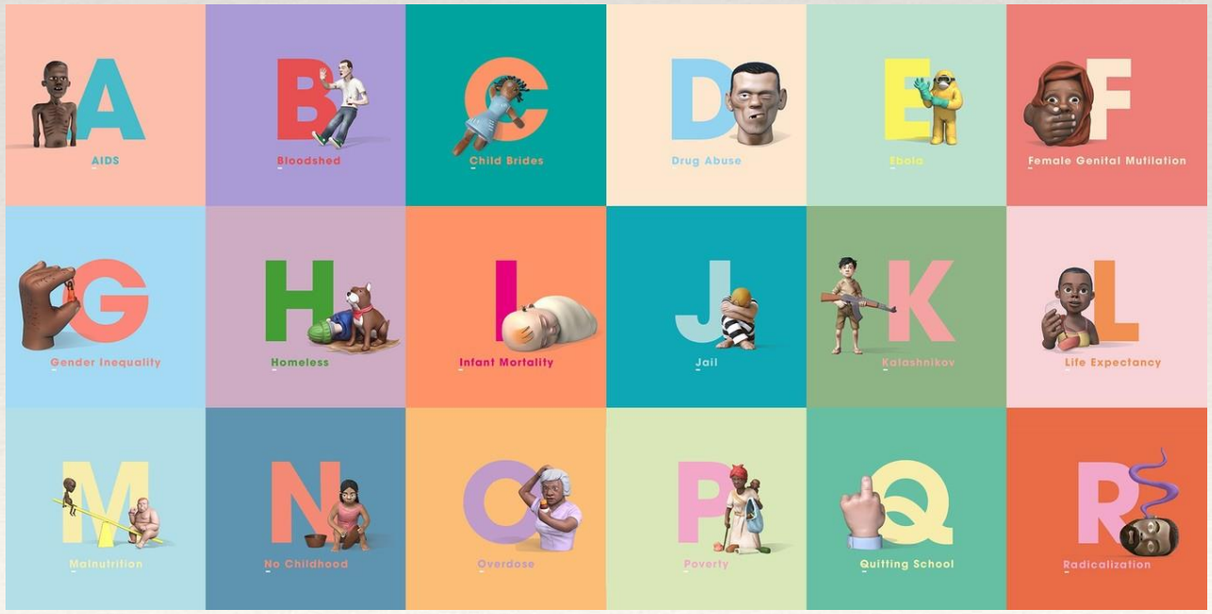
Public Health Perspective

- Make AIDS education materials for illiterate women

Human Rights perspective

- Teach women to read and include AIDS and other health information in the reading assignments

But … why can't women read?

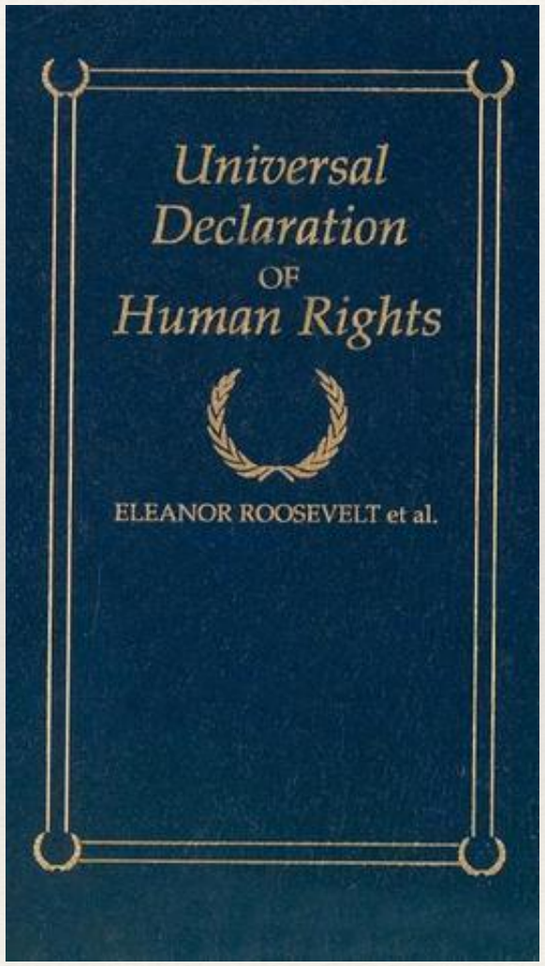


Women and the health and human rights framework

- Highlight growing burden of AIDS on women
- Include and involve women at all levels within national AIDS programs
- Target women's organizations; develop education materials that address the needs of women

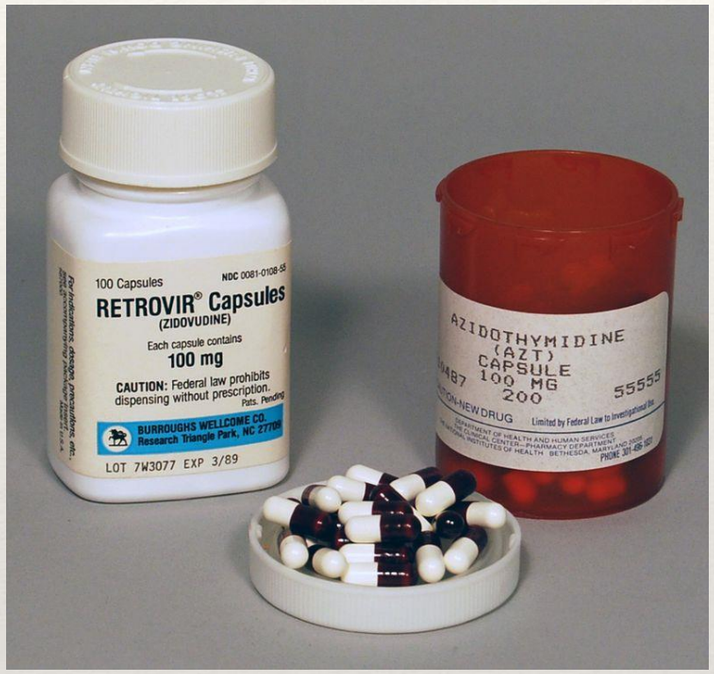
- From: "we should fight rape so women don't get AIDS" to "Women shouldn't be raped."
- The corollaries, with respect to HIV and drug access, were:
  - Why were women at greater risk for HIV?
  - Why were HIV drugs inaccessible to the majority of women with HIV?
  - Why were the diseases that affected the majority of women at risk for HIV so understudied and lacking therapies?
- This became the foundation for the Health and Human Rights perspective on AIDS and global health: The right to health means addressing the structural barriers that make people vulnerable to disease and likewise limits their access to care once they succumb to those diseases.

The problem, Merson found, is that “human rights” had lots of rhetorical power …



But how do you operationalize it?

Safe, Effective, and Affordable interventions – AZT



- October 1990 meeting between WHO and BW
  - Won't lower price
  - Promote short-term MTCT use
- Late 1990 meeting
  - Some price drops
  - Intellectual property protections
- February 1991 meeting
  - Gave options based on price drop; minority only covered
- May 21, 1991
  - BW won't drop price
  - GPA recommends flex pricing
- 1992 – 1993 – partial coverage through donation; GPA rejects

Research in Resource-Limited Settings

- Short Course AZT trials to prevent MTCT

Short-Course AZT Studies

- **Short-course AZT prophylaxis is effective.**
- **Longer (28 weeks) antepartum treatment is more effective than shorter (36 weeks) antepartum therapy, showing that a significant proportion of *in utero* infection occurs between 28 and 36 weeks.**
- **Efficacy of prophylaxis is diminished by breastfeeding, but still persists at 24 months with short-course AZT.**

Key Human Research Cases

The "Short-Course" AZT Trials

- Trials of a "short-course" AZT regimen to prevent mother-to-child transmission of HIV
- Opponents noted trials not permitted in high-income countries, where a more complex "076 regimen" was the standard of care
- Debated ethical double standard
- Studies remain controversial

Affordable HIV drug costs and the absence of North American activists

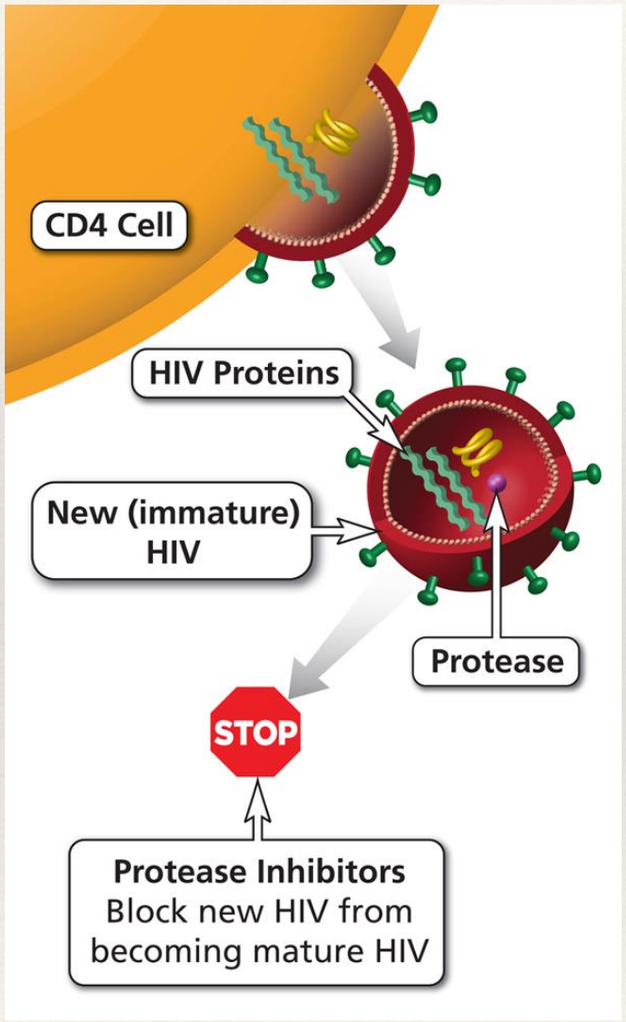
Eric Sawyer, PLWA; Health Global Access Program

Into this breach steps the Rockefeller Foundation: IAVI

- In 1994, Rockefeller Foundation works with WHO and other UN entities, convening a meeting in Italy of AIDS researchers and philanthropies to create clinical trial and research partnerships with academic, biotech, pharma, and governmental entities.

- IAVI helps launch the Global Health Technologies Coalition, a group of 30 non-profit groups aimed at addressing the gaps in therapies for AIDS and other diseases.

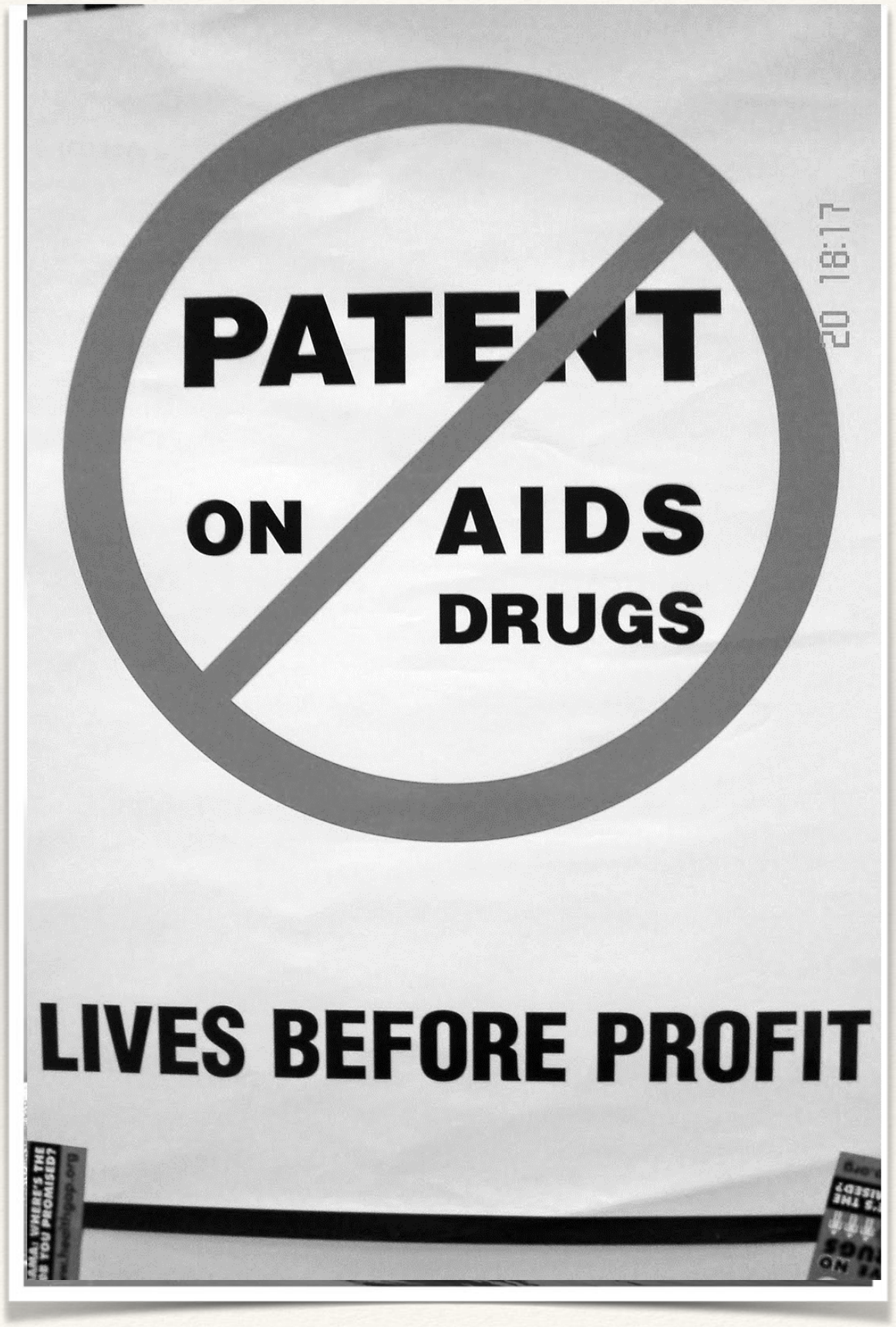
In the wake of protease inhibitors (in 1996), UNAIDS pushed treatment access



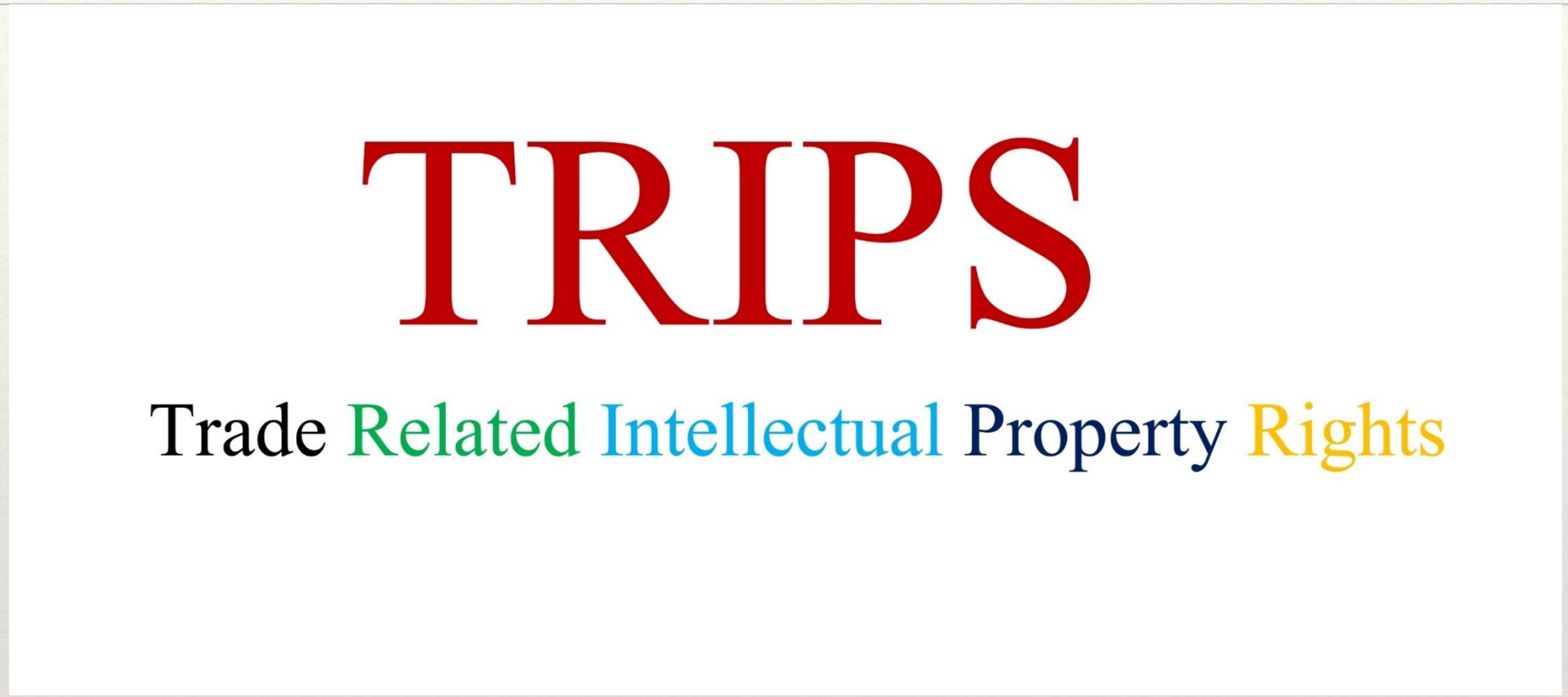
- UNAIDS launches HIV Drug Access Initiative in 1997
  - Focuses on increasing access to ARTs in four countries.
  - Concern about affordability gap, and north-south gap in treatment access

How can UNAIDS help lower prices?

Rights in conflict: intellectual property rights, new clinical research models, and human rights



TRIPS



- The **TRIPS Agreement** when into effect in 1995
- It established minimum standards for regulating intellectual property. First time international property law in multilateral trade system
- High income countries interpreted these standards very narrowly. This meant rigorous patent protection thwarted efforts to create generic drugs or reduced pricing for low income countries.

Doha Declaration (2001)

- Doha was an intellectual property declaration made by low income countries during the 2001 TRIPS talks.
- The declaration recognized certain “flexibilities” in the TRIPS agreement that allowed member states to grant compulsory licenses for pharmaceuticals to address national emergencies.
- Gave countries the right to determine what constituted a national emergency.
- It expressly included public health emergencies such as HIV/AIDS, Malaria, and Tuberculosis or other pandemics.
- The Doha declaration raises the right to health – that patent rights do not trump human rights:
  - TRIPS can and should be interpreted in light of the goal "to promote access to medicines for all."

Lorem Ipsum Dolor

Emerging solutions and thoughts for the future

But by the late 1990s and early 2000s, several things changed

- Leadership changes at several UN agencies fostered collaboration
- The Rockefeller Foundation sponsored a massive Public Private Partnership called International AIDS Vaccine Initiative
- Social and political conservatives in the US became concerned about the impact of AIDS and other diseases on Africa
- The Clinton Administration backtracked on its strong intellectual property rights stance, sees AIDS as a global security threat.
- Al Gore addresses AIDS before the UN Security Council
- Pharmaceutical companies begin facing pressure to find flexible ways to the gaps in essential medicines, especially with respect to AIDS

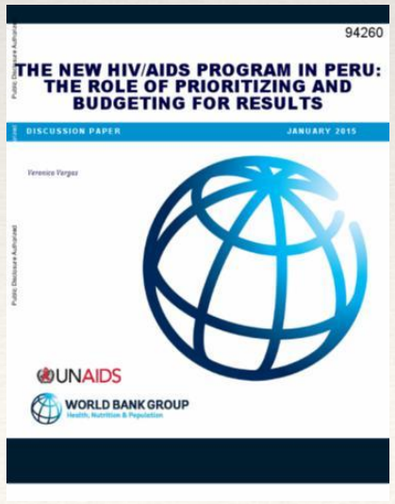
In 2000, people continue thinking beyond HIV/AIDS

- Gates Foundation

- Global Alliance for Vaccines and Immunization (GAVI)

Gates Foundation and others join in to launch the Global Fund

- Caribbean nations launch pan-Caribbean Partnership against AIDS
- OAU declares AIDS and emergency
- UN sec. gen. announces call to action on AIDS
- Bush meets with Annan and announces US commitment to a global fund to fight AIDS
- Gates Foundation, UNAIDS, UNGASS, and others make AIDS a UN Development Goal and announce support
- Launches January 2002 as public private partnership



At the same time, the US launches PEPFAR

WHO rejoins the fight

2000s

Treat

3 million

by 2005

Naisiadet Mason

HIV/AIDS Department, WHO, Geneva, Switzerland

CCIH, May 2004

World Health Organization

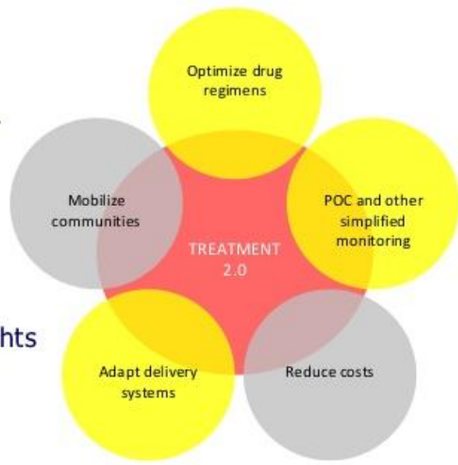
"3 by 5" Initiative

http://www.who.int/3by5

2010s

Treatment 2.0 Priority Work Areas

1. Optimize **drug regimens**
2. Provide access to **point of care** and other simplified **diagnostics**.
3. Reduce **costs**
4. Adapt **delivery systems**
5. Mobilize **communities**, protect human rights

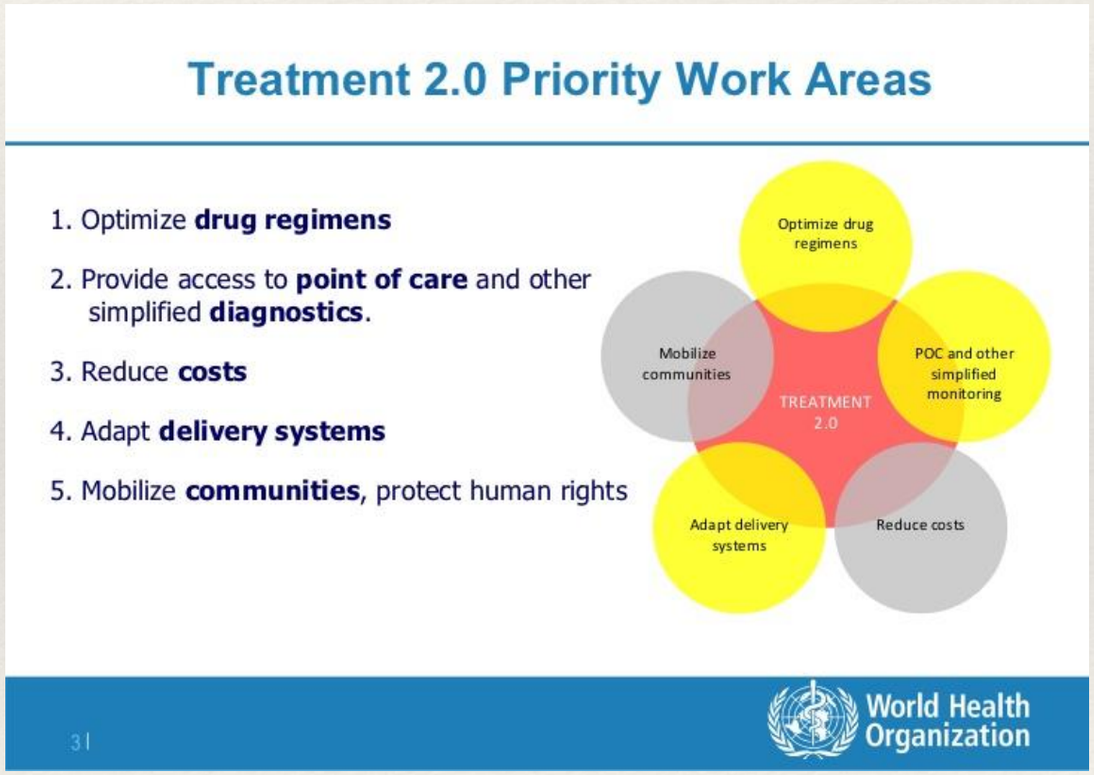


World Health Organization

WHO rejoins the fight against HIV/AIDS

- 2000s

- 2010s



Drug companies step up efforts in Africa

- Not wanting countries to implement compulsory licensing and parallel tracking, pharmaceutical companies launch their own programs to offset costs

Bristol-Myers Squibb Foundation

SECURE THE FUTURE®

Care and Support for Communities Affected by HIV/AIDS in Africa

STF

Clinton Foundation joins, working on drug prices

UNAIDS spearheads a “getting to zero” campaign with its 90-90-90 program

“Getting to Zero”
UNAIDS 2011-2015 Strategy

Dr. Paul De Lay,
Executive Director, Programme
UNAIDS

UNAIDS
JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS
UNHCR UNICEF WFP UNDP UNFPA UNODC ILO UNESCO WHO WORLD BANK

90–90–90: Treatment for all

There are 36.9 million people living with HIV

75% know they are HIV-positive. The rest do not

Three out of five people living with HIV are on antiretroviral therapy

And only 47% have undetectable levels of HIV

90–90–90 HIV treatment targets

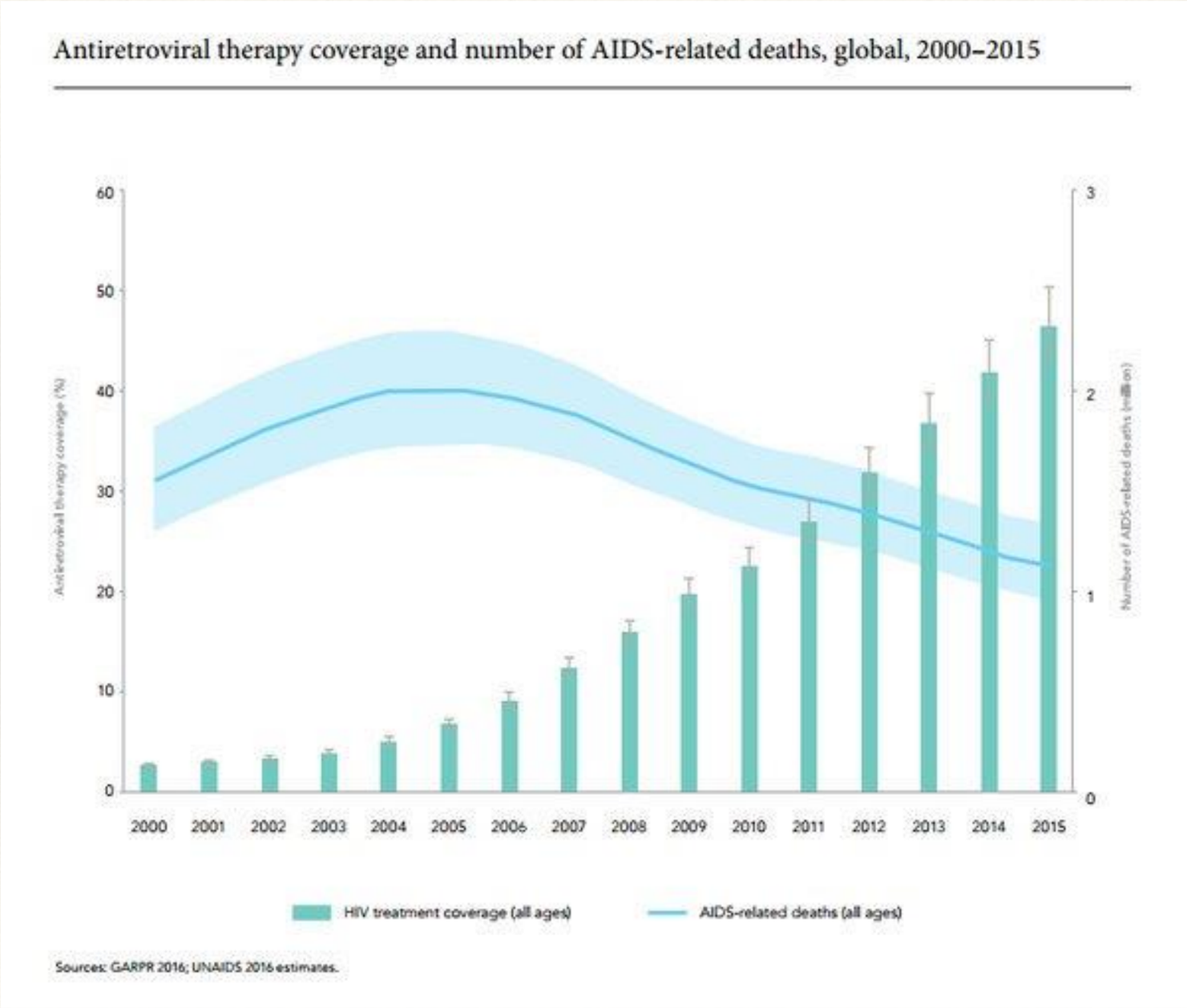
30 million people on treatment by 2020

90% of people living with HIV know their status

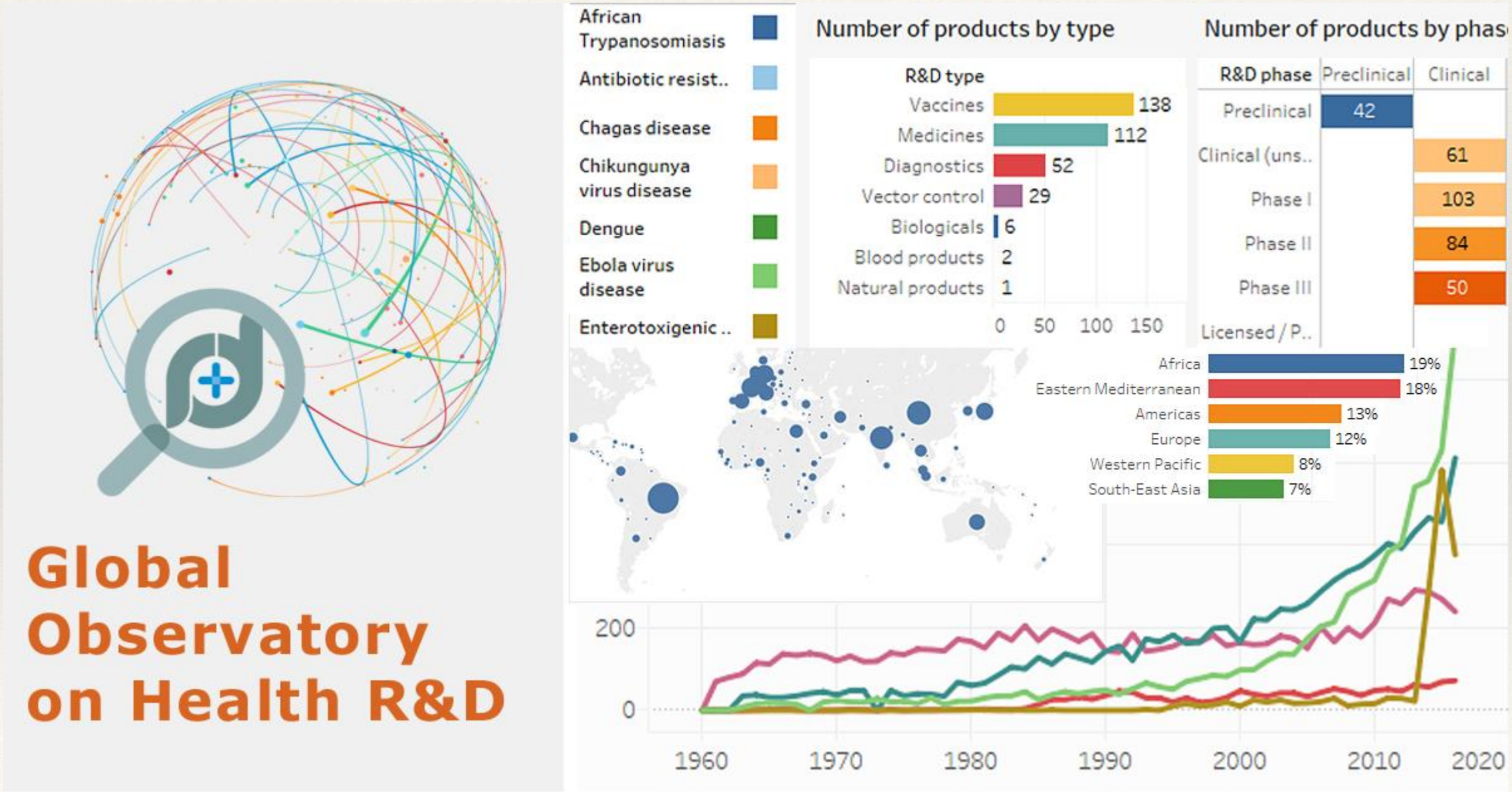
90% of people who know their status are on antiretroviral therapy

90% of people on antiretroviral therapy achieve viral suppression

UNAIDS saw huge success



The WHO's Global Observatory on Health R&D



Global Observatory on Health R&D

The Millennium Development Goals

- The right to health, and access to medicines within a full health system, built into the UN's Sustainable Development Goals (SDGs) in 2015

Accountability to improve access

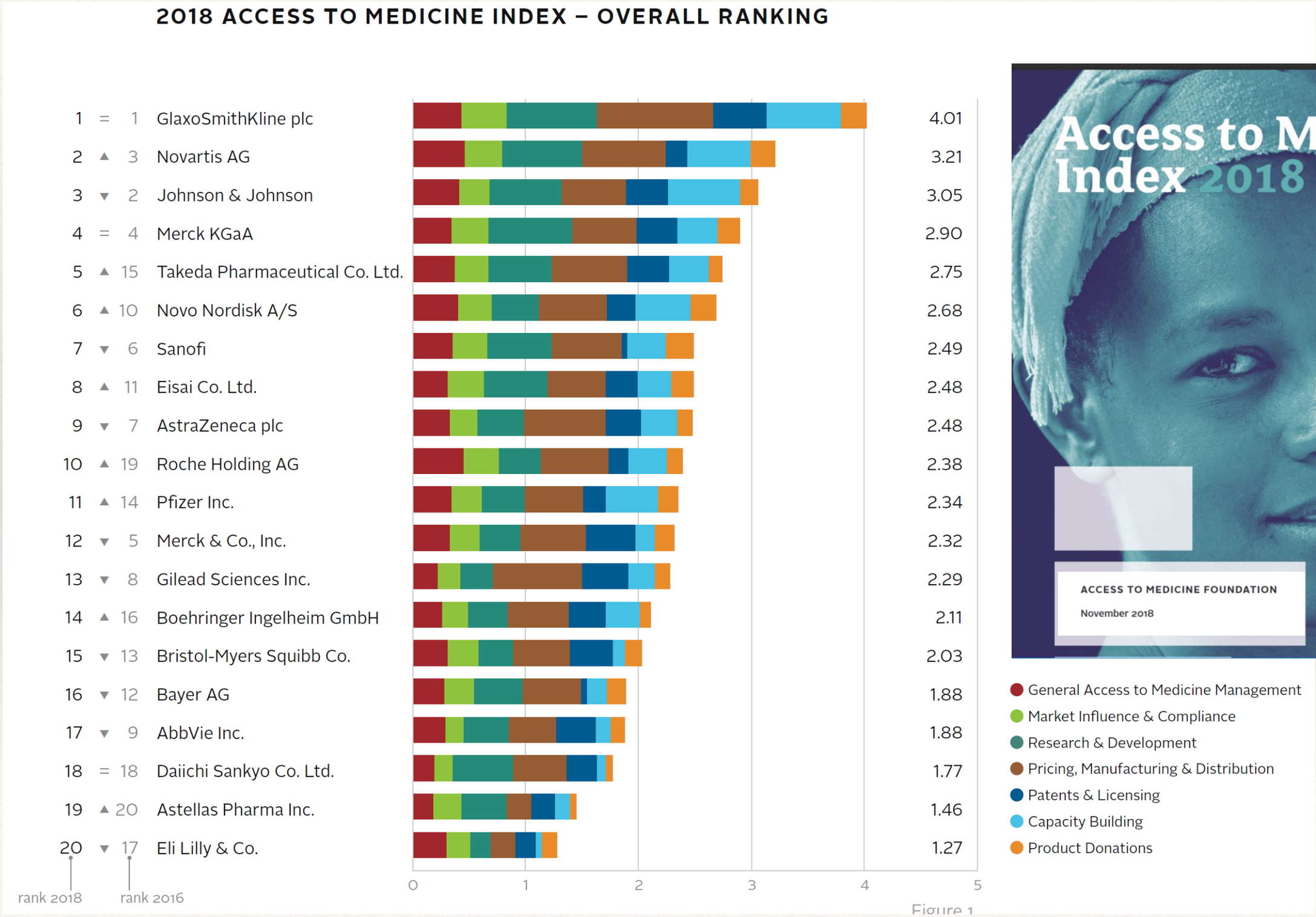


Figure 1

Partnerships to improve access

- 1987 – Merck & Co donated ivermectin to treat river blindness
- Medicines for Malaria venture (MMV)
- Institute for One World Health (OWH)
- EU supported Innovative Medicines Initiative (IMI)
- Drugs for Neglected Disease Initiative (DNDi)
- European Lead Factory (ELF) waives fees for non-profit drug discovery programs

- Drugs for Neglected Disease Initiative (DNDi) has raised $290 million from public and philanthropic funds and put 26 candidate products into the development pipeline and has brought 6 drugs to market in the past 10 years.
- Because DNDi covers the costs of research, these drugs sell for the cost of production.

Partnerships to improve access: Innovations

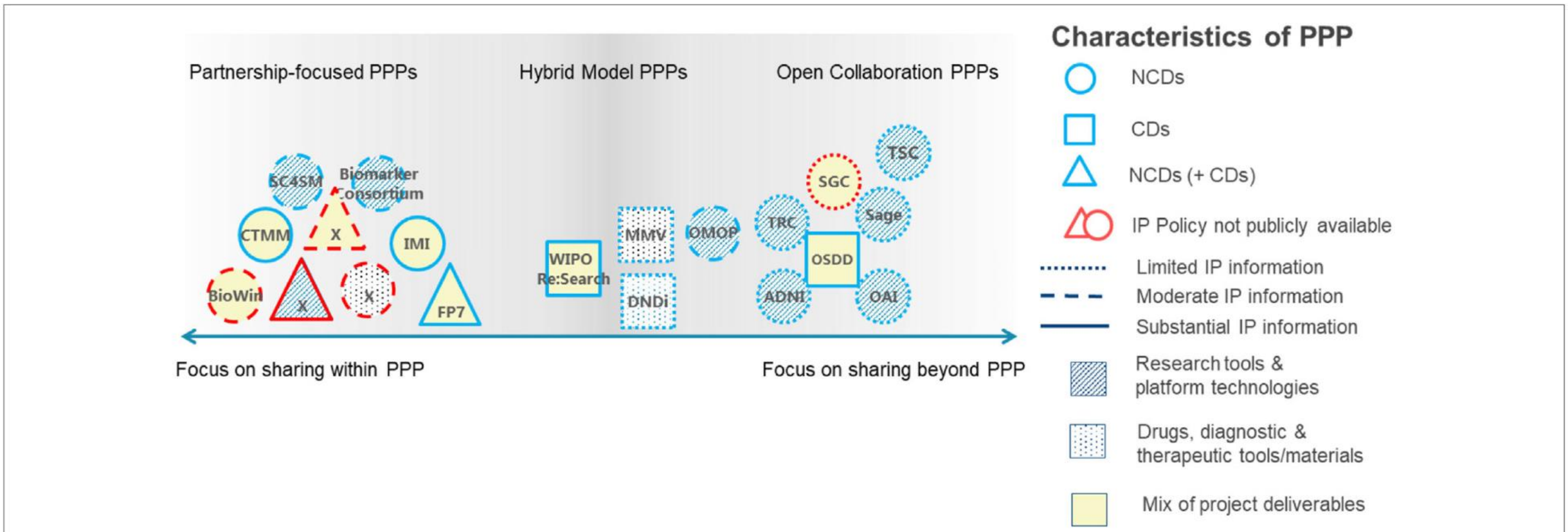


FIGURE 1 | Link between intellectual property (IP) frameworks as defined in the IP policies of the public–private partnership (PPPs) analyzed, the information provided in the IP policies, project focus, and project deliverables. PPPs are categorized by research focus [non-communicable diseases (NCDs, circles), communicable diseases (CDs, squares), or a mix (triangles)]; availability of IP information [unavailable (gray outlines) and limited, partial, or substantial availability (black outlines)]; and deliverables [research tools and platform technologies (striped shading), drugs, diagnostic, and therapeutic tools or materials (dotted shading) or a mix (no shading)]. ADNI, Alzheimer's Disease Neuroimaging Initiative; BioWin, Biotechnologies Wallonie Innovation; CTMM, Center for Translational Molecular Medicine; DNDi, Drugs for Neglected Diseases Initiative; FP7, European Framework Programmes; IMI, innovative medicines initiative; MMV, medicines for malaria venture; ND, not disclosed by PPP request; OAI, Osteoarthritis Initiative; OMOP, Observational Medical Outcomes Partnership; OSDD, Open Source Drug Discovery; SC4SM, Stem Cells for Safer Medicines; TSC, the SNP Consortium; TRC, the RNAi Consortium; SGC, Structural Genomics Consortium. [Figure adapted from Stevens et al. (34) with permission from the authors.]

Using intellectual property as an access mechanism

- Compulsory License Flexibility and other mechanisms

- Other mechanisms

Pricing models as an access mechanism

- Funding innovations
  - Low income countries as investors
- Other mechanisms

Health, Human Rights, & Clinical Research

- We have a long way to go, and many gaps remain.
- The health and human rights perspective is imperfect, but it has promoted strong efforts to reduce gaps in health access and increase the availability to essential medicines.
- There are emerging models with pricing, partnerships, and patents that are delinking research financing from end-product prices which hold tremendous potential for increasing the vision of health for all.

Questions