The Concept of Global Health

Stefano Vella MD
Italian National Institute of Health
Global Burden of Disease
Global Burden of Disease

ITALY

Both sexes, All ages, 2016, DALYs per 100,000

DALYs attributable to All risk factors

IHD
Stroke
Lung C
Colorect C
Breast C
Leukemia
Pancreas C
Prostate C
Bladder C
Hypertension
Hypertension
A Fib
Depression
Anxiety
Back+Neck

Sense
Skin
Liver C
Colorect C
Breast C
Leukemia
Pancreas C
Prostate C
Bladder C
IHD
Stroke
Lung C
Colorect C
Breast C
Leukemia
Pancreas C
Prostate C
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Breast C
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Pancreas C
Prostate C
Bladder C
Hypertension
Hypertension
A Fib
Depression
Anxiety
Back+Neck

Oral
COPD
LRI
URR
Road Inj
Falls
Self Harm

Daly attributable to risk

Daly not attributable to risk
THE RISE OF LIFE EXPECTANCY

Life expectancy globally and by world regions since 1770

Source: Life expectancy – James Riley for data 1990 and earlier; WHO and World Bank for later data (by Max Roser)

OurWorldInData.org/life-expectancy/ • CC BY-SA
THE DRIVERS......1. CLEAN WATER

WORLDWIDE, 1 OUT OF EVERY 5 DEATHS OF CHILDREN UNDER 5 IS DUE TO A WATER-RELATED DISEASE.
THE DRIVERS......3. ADVANCES OF MEDICINE

1796
What Global Health is not

At least 30 million people die **prematurely** (half of them before the age of 5) in developing countries for lack of adequate access to basic health care. They die for causes that are very often **preventable or treatable**.

Despite the convergence on the concept of health as a human right, there still exist intolerable global inequalities in accessing health and health services and in terms of life expectancy and morbidity and mortality from **communicable and non-communicable diseases**.

The persistence of inequalities in terms of health - **not only between rich and poor countries, but also between different regions in the same country** - is also a contradiction to science, given the growing geographic interdependence of the biomedical causes and of the social determinants of health and diseases.
The unequal rise of «healthy» life expectancy
What Global Health is….not
What Global Health is....not
What Global Health is... not
Figure 1
Adult HIV Prevalence, 2017

Global HIV Prevalence = 0.8%

NOTES: Data are estimates. Prevalence includes adults ages 15-49.
SOURCES: Kaiser Family Foundation, based on UNAIDS, AIDSinfo, Accessed July 2018
What Global Health is....not

Prevalence of hepatitis B infection, adults 19-89 years, 2005


Prevalence of anti-hepatitis C virus

What Global Health is....not

2008 Global HPV-related burden:
607,000 annual cancer cases

- Cervical cancer
- Genital warts
- Anal cancer
- Oropharyngeal cancer
- Penile cancer

Vulva and Vaginal cancer

+ recurrent respiratory papillomatosis

International Agency for Research on Cancer
World Health Organization

De Martel et al. 2012 Lancet Oncol (cancers) and Dillner et al. 2010 BMJ (genital warts)
What Global Health is....not
Efficacy and effectiveness of an rVSV-vectorized vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Çà Suffit!)

Alo Marcel Fomba-Koné, Emma Caruso, Thomas W. Geisbert, Sara McQueen, Beatrice M. Dallaire, Lorna L. Carroll, Newland Cross, Anthonia Olatoba, Monica Otubia, Peter W. Byers, Samuel Issa, Jean-Michel Detalone, Marie-Claire Vanhems, Jonathan Jih, Florence Castel, Myriam L. Dikou, T. Alain Hantson, Nana A. Awe, Aboubakar Samoura, Sarah Tchinkende, Dimitri V. kulski, Jean-André Bassettes, Mohamed M. Youngham, Tom van der Werf, Fatimah Ismail, and the LUVVAK study group

Summary

Background rVSV-ZEBOV is a recombinant, replication-competent vesicular stomatitis virus-based candidate vaccine expressing a surface glycoprotein of Zaire Ebola virus. We tested the effect of rVSV-ZEBOV in preventing Ebola virus disease in contacts and contacts of contacts of recently confirmed cases in Guinea, west Africa.

Methods We did an open-label, cluster-randomised ring vaccination trial (Ebola Çà Suffit!) in the communities of Conacry and eight surrounding productive sites in the Basse-Guinée region of Guinea, and in Yambuku and Bombali in Sierra Leone. We assessed the efficacy of a single intramuscular dose of rVSV-ZEBOV (0.5 mL) plaque-forming units administered in the deltoid muscle in the prevention of laboratory confirmed Ebola virus disease. After confirmation of a case of Ebola virus disease, we definitively vaccinated on a list a ring (cluster) of all their contacts and contacts of contacts including named contacts and contacts of contacts who were absent at the time of the trial visit. The list was archived, then we randomly assigned clusters (1:1) to either immediate vaccination (delayed vaccination (21 days later) of all eligible individuals (i.e., those aged ≥18 years and not pregnant, breastfeeding, or severely ill). An independent statistician generated the assignment sequence using block randomisation with random varying block sizes, stratified by location (urban vs rural) and size of village, (≥20 individuals vs >20 individuals). Ebola response teams and laboratory workers were unaware of assignments. After a recommendation by an independent data and safety monitoring board, randomisation was stopped and immediate vaccination was also offered to children aged 4-17 years and all identified rings. The primary outcome was a laboratory confirmed case of Ebola virus disease within 10 days of more from randomisation. The primary analysis compared the incidence of Ebola virus disease in eligible and vaccinated individuals assigned to immediate vaccination versus eligible controls and controls of contacts assigned to delayed vaccination. This trial is registered with the Pan African ClinicalTrials Registry number PACTR201905010357393.

Findings In the randomised part of the trial we identified 4359 contacts and contacts of contacts in 51 clusters randomly assigned to immediate vaccination (of whom 2333 were eligible, 2281 consented, and 2219 were immediately vaccinated) and 4357 contacts and contacts of contacts in 47 clusters randomly assigned to delayed vaccination (of whom 2336 were eligible, 2289 consented, and 2218 were vaccinated 21 days after randomisation). No cases of Ebola virus disease occurred 10 days or more after randomisation among assigned contacts and contacts of contacts vaccinated in immediate vaccination versus 16 cases (7 clusters affected) among all eligible individuals in delayed clusters. Vaccine efficacy was 89.1% (95% CI 66.9-93.0; 0.001) with an estimated relative risk reduction of 0.51 (99.5% CI 0.35-0.70). All deaths occurred in the delayed group. Of the 17 clusters that showed no cases of Ebola virus disease occurred 10 days or more after randomisation among all immediately vaccinated contacts and contact of contacts versus 13 cases (7 clusters affected) among all eligible contacts and contacts of contacts in delayed plus all eligible contacts and contacts of contacts vaccinated in immediate clusters. The estimated vaccine efficacy here was 86.8% (95% CI 79.0-91.8; 0.001). 52% of contacts and contacts of contacts assigned to immediate vaccination and in non-randomised clusters received the vaccine immediately; vaccination protocol both vaccinated and unvaccinated people in these clusters. 5597 individuals in total received the vaccine (2643 adults and 194 children). and all vaccinated individuals reported receiving one dose of the vaccine. In 14 days after vaccination, there were typical mild (67.6% of all 7261 adverse events). Musculoskeletal (182 (25.4%), fatigue (164 (21.5%), and muscle pain (102 (13.5%)) were the most commonly reported adverse events in this period across all age groups. 80 serious adverse events were identified, of which two were judged to be
<table>
<thead>
<tr>
<th>Family</th>
<th>Prototype(s)</th>
<th>Licensed Vaccines</th>
</tr>
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<tbody>
<tr>
<td>Paramyxovirus</td>
<td>Measles, Mumps, Nipah, RSV</td>
<td>Live-attenuated</td>
</tr>
<tr>
<td>Togaviridae</td>
<td>Rubella, Chikungunya, WEVEE</td>
<td>Live-attenuated</td>
</tr>
<tr>
<td>Reoviridae</td>
<td>Rotavirus</td>
<td>Live-attenuated</td>
</tr>
<tr>
<td>Orthomyxovirus</td>
<td>Influenza A, B</td>
<td>Live-attenuated</td>
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<tr>
<td>Adenoviridae</td>
<td>Adenovirus 4, 7, 14</td>
<td>Live-attenuated, whole-inactivated</td>
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<tr>
<td>Rhabdoviridae</td>
<td>Rabies</td>
<td>Live-attenuated</td>
</tr>
<tr>
<td>Picornaviridae</td>
<td>Polio 1,2,3, Hepatitis A, EV71</td>
<td>Live-attenuated</td>
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<tr>
<td>Papillomaviridae</td>
<td>HPV 6, 11, 16, 18</td>
<td>Live-attenuated, whole-inactivated, Live-chimeric</td>
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<tr>
<td>Poxviridae</td>
<td>Variola</td>
<td>Live-attenuated</td>
</tr>
<tr>
<td>Hepadnaviridae</td>
<td>Hepatitis B</td>
<td>VLP</td>
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<tr>
<td>Herpesviridae</td>
<td>Varicella</td>
<td>VLP</td>
</tr>
<tr>
<td>Flaviviridae</td>
<td>Yellow Fever, TBE, JEV, Dengue, Zika</td>
<td>Live-attenuated, whole-inactivated, Live-chimeric</td>
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<tr>
<td>Hepepoviridae</td>
<td>Hepatitis E</td>
<td>VLP (China)</td>
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<tr>
<td>Filoviridae</td>
<td>Ebola, Marburg</td>
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<tr>
<td>Retroviridae</td>
<td>HIV-1</td>
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<td>Coronaviridae</td>
<td>SARS, MERS</td>
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<tr>
<td>Paroviridae</td>
<td>B19, Boca</td>
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<tr>
<td>Caliciviridae</td>
<td>Noro</td>
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<td>Polyomaviridae</td>
<td>JC, BK</td>
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<td>Arenaviridae</td>
<td>Lassa, Machupo</td>
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<tr>
<td>Bunyaviridae</td>
<td>Hanta, Rift Valley</td>
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<tr>
<td>Astroviridae</td>
<td>Astrovirus</td>
<td></td>
</tr>
</tbody>
</table>

Choose prototypic viruses within each family or each distinct genus:
- Define structures of surface proteins and particles
- Determine extent of genetic variability
- Define tropism, entry mechanisms, receptors
- Study pathogenesis and establish animal models
- Isolate human mAbs and determine mechanisms of neutralization
- Develop assays for diagnosis and immunogenicity testing
- Define immune correlates of protection
Nipah Virus, Rare and Dangerous, Spreads in India

The infection, an emerging threat, has killed virtually all of its victims so far in India.

By Emily Baumgartner

June 6, 2018

A rare, brain-damaging virus that experts consider a possible epidemic threat has broken out in the state of Kerala, India, for the first time, infecting at least 18 people and killing 17 of them, according to the World Health Organization.

The Nipah virus naturally resides in fruit bats across South and Southeast Asia, and can spread to humans through contact with the animals’ bodily fluids.

There is no vaccine and no cure.

The virus is listed by the W.H.O. as a high priority for research. Current treatment measures are insufficient, according to Dr. Stuart Nichol, the head of the viral special pathogens branch at the Centers for Disease Control and Prevention.
What Global Health is… not
Measles immunization coverage
(% of children ages 12-23 months) (2016)
Measles mortality

Measles
Both sexes, Under 5 years, 2016, Deaths per 100,000
60 percent through 2030. Dramatic improvements are needed to increase coverage and avoid leaving children behind in these settings.

The heatmap shows that even within countries that may be doing well, certain areas can be neglected. More than half of children haven’t received the necessary three doses of DTP in 26 percent of districts in sub-Saharan Africa.

The priority now is replicating successful strategies in the most challenging places so that all people everywhere receive lifesaving vaccines.
What Global Health is....not
What Global Health is...not

Probability of dying prematurely from non-communicable diseases

Probability of dying from the four main NCDs* between the ages of 30 and 70 2012, %

- Yellow (<15)
- Orange (15–19)
- Red (20–24)
- Dark Red (≥ 25)
- Gray (No data)

Source: WHO

*Non-communicable diseases: cardiovascular diseases, cancer, chronic respiratory diseases and diabetes
Mental and substance use disorders as a share of total disease burden, 2016

Mental health and substance use disorders as a share of total disease burden. Disease burden is measured in DALYs (Disability-Adjusted Life Years). DALYs measure total burden of disease, both from years of life lost and years lived with a disability. One DALY equals one lost year of healthy life.

Source: IHME, Global Burden of Disease
Globalization and Health
1. The current version of globalization has delivered economic growth.

2. But at enormous cost: massive environmental destruction, growing lawlessness, rising inequalities.

3. The causes of poor health for millions globally are rooted in political, social and economic injustices.
The Haves and the Have-Nots

Branko Milanovic

A BRIEF AND IDIOSYNCRATIC HISTORY OF GLOBAL INEQUALITY
Only 1% of people owns 50.4% of the global wealth; 2.4 billion adults own only 1%

ABSOLUTE POVERTY DECLINED; BUT NOT EVERYWHERE
The poor, the marginalised groups and the vulnerable populations are the most affected by health inequalities.
1.5 billion people live in slums
THE GREAT ESCAPE is a movie about men escaping from a prisoner-of-war camp in World War II. The Great Escape of this book is the story of mankind’s escaping from deprivation and early death, of how people have managed to make their lives better, and led the way for others to follow.
Migrants

Displaced
What Global Health is **not**

What Global Health actually **is**
Global Health

- Global health is the health of populations in a global context
- It transcends the perspectives and concerns of individual nations
- Global health is an extensive multisectorial domain that links health with the areas of development, humanitarian aid, and research
- It deals with:
  - worldwide improvement of health
  - reduction of disparities and inequalities, abroad and at home
  - protection against global threats
Global Health: lessons from the HIV/AIDS response

Advancing global health and strengthening the HIV response in the era of Sustainable Development Goals: the International AIDS Society—Lancet Commission report

Linda-Gail Bakhti, George Alinyo, Sifunard Band, Junior Copaga, Dorina-Dodokohia, David Cudd, Malek Djilali, Serge Droll, Peter Erasmus, Geoff Gurr, Anne Gwamaka, James Haskins, Diane Hatt, Michael Hlavac, Greg Iff, Adolfo Johnson, John Kasonde, Aaron Kihara, Muthoki Kiss, Michael Kobusingye, Malek Djilali, Maurice Kiwanuka, Steven Kwan, Clement Kwik, Natasha L Martin, Kenneth Mayhew, Grigoris Makris, Nikolaos Minci, Logan Prie, Casey Pili, Peter Platt, Anton Priedhorsky, Thomas C Quinn, Jefrey Radack, Jeanne Raffaelli, Graham Ryan, Gary Sper, Bern Brodie, Remi Skarpe, Anne Stor, Stefano Storme, Nicholas Thompson, Stefano Vella, Mounira Schettino, Peter Wawer, Brian Yik, Chris Byrne

Executive summary

In the unprecedented level of global solidarity and resolve, the trends that currently define our world in 2018 are in direct contrast with the sentiments that underpin the SDGs and with the ethos that generated such striking health and development gains in recent years. Democracy is in retreat, and the space for civil society is declining and the human rights environment deteriorating in many countries. Official development assistance for health has stalled, as an inward-looking nationalism has in many places supplanted recognition of the need for global collaboration to address shared challenges. The loss of momentum on global health ignores the urgent need to strengthen health systems in address the need of NCDs, which now account for seven out of 10 deaths worldwide.

Recent trends in the HIV response are especially concerning. Although the number of new HIV infections and AIDS-related deaths have markedly decreased since the epidemic peaked, little progress has been made in reducing new infections in the past decade. Without further reductions in HIV incidence, a resurgence of the epidemic is inevitable, as the largest generation of young people age into adolescence and adulthood. Yet where vigour and renewed efforts are needed, there are disturbing indicators that the world’s commitment is waning. Allowing the HIV epidemic to reemerge would be catastrophic for the communities most affected by HIV and for the broader field of global health. If the world cannot follow through on HIV, which prompted such an unprecedented global mobilisation, hopes for achieving the ambitious health aims outlined in the SDGs will inevitably diminish.

At this moment of uncertainty for the future of the HIV response and for global health generally, the International AIDS Society and the Lancet convened an

Key messages
- The HIV pandemic is not on track to end, and the prevailing discourse on ending AIDS has bred a dangerous complacency and may have hastened the weakening of global resolve to combat HIV.
- Existing tools and strategies are insufficient, and while dramatic gains can be made through existing existing prevention and treatment strategies, the HIV epidemic is likely to remain a major global challenge for the foreseeable future.
- Several millions of people will remain unserved by access to antiretroviral therapy for decades to come, vigilance will be needed to prevent a resurgence of the epidemic as the largest generation of young people age into adolescence and adulthood, and intensified efforts are required to address HIV among populations and settings that are being left behind.
- Allowing the pandemic to reemerge after achieving such remarkable progress would not only increase the human and financial costs of HIV, but it would potentially undermine the global health and development goals that support ambitious global health aspirations.
- An unprecedented global effort on HIV is essential to reverse and strengthen the global HIV response, the world’s imperative commitment to the scaling up of HIV treatment services must be matched by a similarly robust commitment to expanded access to HIV prevention.

The HIV epidemic must make concerted efforts with the broader global field to build a new era of global solidarity, and specific actions are urgently needed to respond to the rapidly rising health toll associated with non-communicable diseases, including taking health into account in the development of public policies of all kinds. HIV services should, where feasible, be integrated with broader health services, in an access where possible, with the aim of preventing both HIV-related and non-HIV-related health outcomes, greater integration of HIV and global health must presume and build on key attributes of the HIV response, including participatory community and civil society engagement and an ongoing commitment to human rights, gender equality, and equitable access to health and social justice.

The new era of global health solidarity should focus on the development of robust, flexible, people-centred health systems to end communicable diseases, develop effective responses to address the steady rise of non-communicable diseases, achieve universal health coverage, provide coordinated services tailored to the needs of health service users, and effectively address the social and structural determinants of health problems related to infectious and non-communicable diseases.
1950-1980
AIDS: a devastating impact in just a few years

40 million died

40 million live with HIV
Trends in Annual Rates of Death from Leading Causes of Death Among Persons 25-44 Years Old, USA

- **Unintentional injury**
- **Cancer**
- **Heart disease**
- **Suicide**
- **HIV infection**
- **Homicide**
- **Chronic liver disease**
- **Stroke**
- **Diabetes**
Antiretroviral Therapy for HIV Infection in 1996
Recommendations of an International Panel

Charles C. J. Carpenter, MD; Margaret A. Fischl, MD; Scott M. Hammer, MD; Martin S. Hirsch, MD; Donna M. Jacobson; David A. Katzenstein, MD; Julio S. G. Montaner, MD; Douglas D. Richman, MD; Michael S. Saag, MD; Robert T. Schooley, MD; Melanie A. Thompson, MD; Stefano Vella, MD; Patrick G. Yeni, MD; Paul A. Volberding, MD, for the International AIDS Society–USA

Objective.—To provide clinical recommendations for antiretroviral therapy for human immunodeficiency virus (HIV) disease with currently (mid 1996) available drugs. When to start therapy, what to start with, when to change to, and what to change to were addressed.

Participants.—A 13-member panel representing international expertise in antiretroviral research and HIV patient care was selected by the International AIDS Society–USA.

Evidence.—Available clinical and basic science data, including phase 3 controlled trials, clinical endpoint data, virologic and immunologic endpoint data, interim analyses, studies of HIV pathophysiology, and expert opinions of panel members were considered. Recommendations were limited to drugs available in mid 1996.

Process.—For each question posed, 1 or more member(s) reviewed and presented available data. Recommendations were determined by group consensus (January 1996); revisions as warranted by new data were incorporated by group consensus (February-May 1996).

Conclusions.—Recent data on HIV pathogenesis, methods to determine plasma HIV RNA, clinical trial data, and availability of new drugs point to the need for new approaches to treatment. Therapy is recommended based on CD4+ cell count, plasma HIV RNA levels, or clinical status. Preferred initial drug regimens include nucleoside combinations; at present protease inhibitors are probably best reserved for patients at higher progression risk. For treatment failure or drug intolerance, subsequent considerations include resistance to changing therapy, available drug options, disease stage, underlying conditions, and concomitant medication(s). Therapy for primary (acute) infection, high-risk exposures to HIV, and maternal-to-fetal transmission are also addressed. Therapeutic approaches need to be updated as new data continue to emerge.


IMPORTANT ADVANCES in understanding the biology and treatment of human immunodeficiency virus (HIV) infection have occurred during the past 18 months. As a result, new scientifically sound approaches to therapy have been developed that offer new options for persons with HIV infection. The relevant recent advances fall into 4 major categories: (1) better understanding of the replication kinetics of HIV throughout all stages of disease; (2) development of assays to determine the drug resistance profiles of infected patients; (3) availability of several new effective drugs; and (4) demonstration that combination therapy is more effective than zidovudine monotherapy. In light of these advances, the recommendations of earlier state-of-the-art guidelines are no longer applicable to clinical decision making in 1996. Therefore, an international panel of clinical investigators experienced in HIV patient care was selected and convened by the International AIDS Society–USA to develop current recommendations for the clinical management of HIV-infected individuals.

The panel addressed 4 central questions about antiretroviral therapy: when to initiate therapy, which types of drugs to use, when to change therapy, and which types of drugs to use when a change in therapy is indicated. In addition, the treatment of primary HIV infection, prevention of vertical transmission, and postexposure prophylaxis were addressed. The recommendations are not solely based on the outcomes of controlled clinical trials with well-defined clinical endpoints. Developing clinical guidelines in the HIV field at this time requires an approach firmly anchored in data from controlled, double-blind clinical trials when available, but also includes information from trials in progress and available virologic and immunologic endpoint data, as well as extrapolations from studies of the pathophysiology of HIV infection. Clinical decisions must be made for best use of up to 8 available antiretroviral drugs, as a time when long-term studies with clinical endpoints have been completed for only a few possible combinations.

The recommendations herein reflect the panel’s agreement on the importance of plasma HIV RNA measurements for predicting risk of clinical progression as well as the recent demonstration from clinical trials of combination therapies that reductions in plasma HIV RNA
Mortality vs. HAART Utilization

Palella F et al, HOPS Study
1998

April

November
Per Stefano Vella la prospettiva di cura è in un cocktail di farmaci dai costi devastissimi

Ma la terapia sarà solo per pochi

GIANCARLO ACGELONI

È una lotta a vista notte. Stefano Vella, un farmacista, lavora da 30 anni in un negozio di viale Roma a Milano. È teso, esaurito, senza un momento di respiro. La sua attività è impegnativa e critica.

Le ultime notizie dicono che l'80% dei farmaci per le malattie infettive sono prodotti in India. Vella lavora per garantire la qualità e l'affidabilità delle droghe che vende. È un posto di lavoro che richiede una grande responsabilità.

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Tuberecolosi più HIV, il "doppio problema" di domani

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YEAR 2000: difference in mortality between the rich north and the poor south

Annual AIDS deaths since 1982

- **1987:** First AIDS drug AZT slows deaths, but 16,000 still die in the United States and 10 times that many in Africa.
- **1999:** 10,100 AIDS deaths
- **1996:** AIDS deaths decline steeply with new three-drug treatment
- **2000:** 2.4 million AIDS deaths

Community mobilization
Global March for access to HIV treatment
Treatment Access Campaign (and others)

EVERYONE HAS THE RIGHT TO HEALTH!

All people with HIV/AIDS have a right to access treatments in addition to health care, employment, education, clean water, adequate nutrition, and housing. Denying people with HIV/AIDS access to affordable medicines in order to protect profits or intellectual property rights, is tantamount to genocide.
2001 – Global Commitment

Kofi Annan, UN Secretary General:
Call for 7 – 10 billion war chest against AIDS and the creation of the Global Fund (launched Jan 2002) “… we must put care and treatment within everyone's reach”.

UNGASS AIDS, June 2001
Declaration of Commitment:
“… make every effort to provide … the highest attainable standard of treatment for HIV/AIDS, including … the effective use of quality-controlled anti-retroviral therapy …”

Schwartländer et al, Science, June 2001

Resource Needs for HIV/AIDS

- Millions of prevention services delivered
- People tested
- MSMs reached
- STIs treated
- Blood screened
- SWs reached
- Harm reduction
- MTCT program

- Palliative care
- HAART
- OI treatment
- OI prophylaxis
- Orphan support

- Millions of people receiving care and support
UNGASS 2001: 
THE GLOBAL FUND WAS BORN

The Global Fund
To Fight AIDS, Tuberculosis and Malaria

<table>
<thead>
<tr>
<th>RESULTS 2018</th>
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<tbody>
<tr>
<td><strong>17.5 MILLION</strong> PEOPLE ON ANTIRETROVIRAL THERAPY FOR HIV</td>
</tr>
<tr>
<td><strong>79.1 MILLION</strong> HIV TESTS TAKEN</td>
</tr>
<tr>
<td><strong>9.4 MILLION</strong> PEOPLE REACHED WITH HIV PREVENTION PROGRAMS &amp; SERVICES</td>
</tr>
</tbody>
</table>

**27 MILLION LIVES SAVED**

| **5 MILLION** PEOPLE WITH TB TREATED |
| **102 THOUSAND** PEOPLE WITH DRUG-RESISTANT TB ON TREATMENT |

**US$ 4.2 BILLION** GLOBAL FUND GRANTS DISBURSED

| **197 MILLION** MOSQUITO NETS DISTRIBUTED |
| **108 MILLION** CASES OF MALARIA TREATED |

Lives saved are cumulative since 2002. All other results were achieved in 2017 in countries where the Global Fund invests.
Time to act: global apathy towards HIV/AIDS is a crime against humanity

Robert Hogg, Pedro Cahn, Elly Katabira, Joep Lange, NM Samuel, Michael O’Shaughnessy, Stefano Vella, Mark Wainberg, Julio Montaner
In June 2002, WHO includes 10 ARVs in the list of essential medicines.
HIV PHARMACEUTICAL INNOVATION

**FDA Approval of HIV Medicines**

<table>
<thead>
<tr>
<th>Year</th>
<th>Medication</th>
<th>Notes</th>
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<tbody>
<tr>
<td>1981</td>
<td>First AIDS cases reported in the United States</td>
<td></td>
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<tr>
<td>1987</td>
<td>Zidovudine (NRTI)</td>
<td></td>
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<tr>
<td>1991</td>
<td>Didanosine (NRTI)</td>
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<tr>
<td>1992</td>
<td>Zalcitabine (NRTI)</td>
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<td>1994</td>
<td>Stavudine (NRTI)</td>
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<td>Indinavir (PI) Nevirapine (NRTI) Ritonavir (PI)</td>
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<td>1997</td>
<td>Compliva (FDC) Delavirdine (NRTI) Nelfinavir (PI)</td>
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<td>1998</td>
<td>Abacavir (NRTI) Efavirenz (NRTI)</td>
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<td>Juluca (FDC)</td>
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<td>Biktarvy (FDC) Clindura (FDC) Symfri (FDC) Symfi to (FDC) Ibalizumab (PAI)</td>
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**Drug Class Abbreviations:**
- CA: CCR5 Antagonist
- FDC: Fixed Dose Combination
- PI: Fusion Inhibitor
- INSTI: Integrate Inhibitor
- NNRTI: Non- Nucleoside Reverse Transcriptase Inhibitor
- NRTI: Nucleoside Reverse Transcriptase Inhibitor
- PE: Pharmacokinetic Enhancer
- PI: Protease Inhibitor
- PAI: Post-Attachment Inhibitor

**Note:** Drugs in gray are not available in the United States and/or are no longer recommended for use in the United States by the HHS HIV/AIDS medical practice guidelines. These drugs may still be used in fixed-dose combination formulations.
Box 4: Access to medicines and the Doha Declaration on TRIPS and Public Health

Measuring access to medicines is a complex task, but price is one key factor among others. The Doha Declaration on TRIPS and Public Health recognized concerns about effects on prices while noting the need for innovation. Since the Declaration was adopted in 2001, prices for many treatments have fallen significantly, in part due to generic competition and tiered pricing schemes (see graph below). Surveys also show a marked increase in the use of TRIPS flexibilities to promote access to medicines.

Falling prices of first-line combinations of some first-line anti-retroviral therapies for HIV-AIDS since 2000

• “Each member has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted” and
• “to determine what constitutes a national emergency or other circumstances of extreme urgency”.

• Public health crises include “those relating to HIV/AIDS, tuberculosis, malaria and other epidemics” and “other circumstances of extreme urgency”.
Response to the AIDS Pandemic —
A Global Health Model

Peter Piot, M.D., Ph.D., and Thomas C. Quinn, M.D.

Just over three decades ago, a new outbreak of opportunistic infections and Kaposi's sarcoma was reported in a small number of homosexual men in California and New York. This universally fatal disease, which was eventually called the acquired immunodeficiency syndrome (AIDS), was associated with a complete loss of CD4+ T cells. Within the first year of its description, the disease was also identified in patients with hemophilia, users of injection drugs, blood-transfusion recipients, and infants born to affected mothers. Soon thereafter, a heterosexual epidemic of AIDS was reported in Central Africa, preferentially affecting women. Little did we know at the time that this small number of cases would eventually mushroom into tens of millions of cases, becoming one of the greatest pandemics of modern times.

Within 2 years after the initial reports of AIDS, a retrovirus, later called the human immunodeficiency virus (HIV), was identified as the cause of AIDS. Diagnostic tests were developed to protect the blood supply and to identify those infected. Additional prevention measures were implemented, including risk-reduction programs, counseling and testing, condom distribution, and needle-exchange programs. However, HIV continued to spread, infecting 10 million persons within the first decade after its identification.

The second decade of AIDS was marked by further intensification of the epidemic in other areas of the world, including the southern cone of Africa, which saw an explosive HIV epidemic. Asia and the countries of the former Soviet Union also reported a marked increase in the spread of HIV. However, by the mid-1990s, with the discovery of highly active antiretroviral therapy, rates of death in developed countries started to decline. The use of antiretroviral drugs during pregnancy also resulted in a substantial decline in mother-to-child transmission of HIV in high-income countries. However, without access to antiretroviral drugs in low- and middle-income countries, rates of death and mother-to-child transmission continued to increase, with 2.4 million deaths and more than 3 million new infections reported in 2001. Of these new infections, two thirds occurred in sub-Saharan Africa.

International Response to AIDS — A Global Health Model

It was not until the third decade of the epidemic that the world's public health officials, community leaders, and politicians united to combat AIDS. In 2001, the United Nations General Assembly endorsed a historic Declaration of Commitment on HIV/AIDS, a commitment that was renewed in 2011. These actions resulted in the formation of the Global Fund to Fight AIDS, Tuberculosis, and Malaria, which was established to finance anti-AIDS activities in developing countries. In 2003, President George W. Bush announced the President's Emergency Plan for AIDS
HIV AS A MODEL FOR GLOBAL HEALTH

1. It drew together towards the common objective of fighting health inequalities

✓ scientists,
✓ clinicians,
✓ public health officials,
✓ visionary politicians,
✓ economists,
✓ NGOs, faith based-organizations
✓ and patients
2. It recognized the supranational character of problems of disease and their amelioration, and the fact that no individual country can adequately address diseases in the face of the movement of people, trade, microbes, and risks.

3. It mobilized innovative drug production, pricing and procurement, both from generic and proprietary manufacturers.
HIV AS A MODEL FOR GLOBAL HEALTH

4. It focused on deeper knowledge of the burden of disease to **identify key health disparities and develop strategies for their reduction**.

5. It recognized that **people affected by disease have a crucial role** in the discovery and advocacy of new modes of treatment and prevention and their equitable access.

6. It based the action on **ethical and moral values that recognize that equity and rights are central** to the larger goals of preventing and treating diseases worldwide.
MAKE END AIDS by 2030
GOAL NO. 1 IN POST 2015 DEVELOPMENT AGENDA
HIV

New cases of HIV per 1,000 people

HIV treatment helps prevent new infections. An important step toward universal treatment is making sure that people living with HIV know their status. Currently, only 70 percent do. Studies from around the world demonstrate that people, especially those who are hard to reach and at risk, prefer self-testing to clinic-based testing. So far, approximately 40 countries have self-testing policies. If that number goes up, the number of new infections will go down.

SDG Target: End the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases. Target shown on chart has been extrapolated from UNAIDS target of 200,000 new infections among adults in 2030.
Addressing barriers to the end of AIDS by 2030

The introduction of combination antiretroviral therapy (ART) in 1996 was the first milestone in the fight against HIV/AIDS, and its impact has been huge. Today, we have solid proof that early ART initiation provides benefit for the health of the HIV-infected population and reduces the risk of HIV transmission. The concept of treatment as prevention is gaining ground, with decreasing HIV incidence in many countries. However, with HIV testing lagging behind, prevention cannot rely solely on expanded access to ART. Combination prevention will need to include both biomedical and non-biomedical interventions. On the biomedical side, the efficacy of pre-exposure prophylaxis (PrEP) has been confirmed by numerous randomized trials, with PrEP on demand adding convenience to the preventive strategy. Therapeutic developments are also on the way, with injectable, long-half-life antiretrovirals (possibly helping to increase ART adherence, definitely suitable for prevention). Finally, in the search for a cure, recent breakthroughs show that reactivation and killing of latently infected cells could be possible one day. Will a cure or remission strategy, whenever available, be accessible to the millions already infected? That’s another question.

In the year 2000, opening the Durban IAS Conference, Justice Edwin Cameron said that “our overriding and immediate concern should be to find ways to make accessible for the poor what is within reach of the affluent.” The subsequent creation of the Global Fund to Fight AIDS, Tuberculosis, and Malaria and of the Presidents Emergency Plan for AIDS Relief, the increase in funding for ART, and the availability of resources for countries’ AIDS programmes, held enormous promise. A promise that has actually delivered—with 15 million people on ART by the end of 2015, an accomplishment considered very difficult when this target was set in 2001 by UNAIDS. Unfortunately, despite the undeniable successes, 2 million new infections happen every year worldwide, and a significant proportion of the 40 million infected people remain untested, untreated, and undiagnosed. These numbers will be sobering for those with enthusiastic views regarding the third Sustainable Development Goal (SDG)—ensure healthy lives and promote well-being for all at all ages—which calls for an end to the AIDS epidemic by 2030. To make it happen, three major challenges are in front of us.

The first challenge is scientific: the discovery of an effective HIV vaccine. Treatment as prevention alone will not be able to stop the epidemic. Despite increasing ART access, there will be no end of ART without a preventive vaccine available for populations living in high prevalence areas and for key affected and marginalized populations around the world. New constructs of HIV vaccines eliciting broadly neutralizing antibodies, indicate that an HIV vaccine may be closer than thought just a few years ago. And a vaccine providing even relative weak protection might still have an important synergistic effect with increased ART coverage, because the number of potential HIV transmitters will be smaller.

The second challenge is operational. Expansion of HIV treatment programmes is expected to increase the demand for ART, however, with the switch of the eligibility criteria from starting treatment when CD4 count is less than 500 cells per μL to treatment at all stages. Although the risk in infection numbers may not be huge, it will still represent a challenge for already stressed health systems. Clinical and transmission benefits will become evident in the years to come, but the immediate benefits may not be so evident to programme managers. Wania El Said posited several important questions during the 2015 Vancouver Conference: Shall all populations start early? How will the START trial be interpreted in the real world? How will we sustain ART for all, and who will pay? And how do we minimise inequalities and disparities?

In addition, ART retention remains a substantial challenge. Therefore, the aspirational goal of maintaining the UNAIDS targets of 90% in care and 90% with viral suppression, barriers are not only biomedical (eg, ART toxicity) but also structural and behavioural. Because of the new entry criteria, the proportion of asymptomatic patients who will increase these patients may not receive short-term benefits from treatment, with consequent treatment cessation, especially in the face of onerous programmatic or toxic regimes. Therefore, the key to success is implementing a test-and-treat approach for millions of HIV-positive individuals will be to have a significant effect on HIV transmission at a population level. Unfortunately, even in UK, a high-income setting, data on the cascade of care shows that only 35% of the overall HIV population is fully suppressed. In the USA, the Centers for Disease Control estimate that only 25% of HIV-positive people are suppressed.

End of AIDS on the horizon, but innovation needed to end HIV

In the Lancet HIV, Viviane Lima and colleagues describe the encouraging progress achieved in the clinical care of HIV-infected patients in Brazil. Indeed, a number of deaths and AIDS defining events after the adoption of potent antiretroviral therapy (ART), are well documented. In fact, many potent drug combinations available today can only occur if the immune system remains functional and patients presenting at a very advanced stage. In high-income countries, 50% of patients treated with antiretroviral therapy can achieve a full viral suppression.

In resource limited settings, at least in countries where fees have been implemented, similar trends have been described. UNAIDS estimates that global mortality declined by 35% from 2005 to 2013. The picture may get progressively better, with further reduction of mortality, thanks to the adoption of WHO’s 2013 guidelines, which aligned the global standard of care by moving the CD4 count threshold for starting ART to 300 cell per μL and introducing a fixed-dose combination as the first-line treatment of choice.

However, an important conceptual difference exist between determining local AIDS incidence, and decreasing global HIV incidence. This latter goal, well described in the UNAIDS 90-90-90 strategic plan, is based on the ability of ART to prevent HIV transmission. Indeed, the vision of ending the HIV epidemic by 2030 may remain aspirational, without an honest reality check. The modelling exercise supporting the 90-90-90 strategy predicts that at least 75% of all HIV-positive individuals should be suppressed to have a significant impact on HIV transmission at a population level. Unfortunately, even in the UK, a high-income setting, data on the cascade of care shows that only 35% of the overall HIV population is fully suppressed. In the USA, the Centers for Disease Control estimate that only 25% of HIV-positive people are suppressed.

decentralisation, knowing your epidemic and reaching the right people, targeting of key populations, training of healthcare workers to recognize signature diseases, fully involving the community, destigmatization and human rights, and taking advantage of the new testing technologies.

Innovation will also be aggressively pursued through operational research—access and retention in care, the second lever: community and peer engagement and motivational counselling will be reinforced, particularly for earlier stages of infection. ART uptake and retention is indeed associated with perceptions of personal necessity for treatment and concerns about potential adverse events. These are key barriers to linkage, particularly now that we are thinking at a global test-and-treat approach again. This is an area where new technologies, like point of care CD4 and RNA diagnostics, but also mobile technologies will be key elements for success.

Finally, to reach the third 90, the therapeutic armamentarium available in high-income settings must be made available to all populations at affordable prices.

If this is not achieved, the extraordinary successes of the past two decades could be progressively lost. In a few years, an epidemic of treatment failures may emerge in low-income settings, because of patients’ non-adherence or frailty and side-effects of the currently used regimens (despite having saved millions of lives so far). In the absence of viral load monitoring, failures will not be diagnosed in time and will not be manageable with the few second-line treatments currently available.

As stated by the Lancet editorial team, we need to start now, and the benefits have to be sought for all ages—especially for all ages—which calls for an end to the AIDS epidemic by 2030.
"We have never ended a global epidemic without a vaccine or a cure and HIV will not be an exception"
A way forward: the agenda 2030
3 GOOD HEALTH AND WELL-BEING
SDG 3 - TARGETS

**TARGET 3·1**
Reduce Maternal Mortality

**TARGET 3·2**
End all preventable deaths under 5 years of age

**TARGET 3·3**
Fight communicable diseases

**TARGET 3·4**
Reduce mortality from non-communicable diseases and promote mental health

**TARGET 3·5**
Prevent and treat substance abuse

**TARGET 3·6**
Reduce road injuries and deaths

**TARGET 3·7**
Universal access to sexual and reproductive care, family planning and education

**TARGET 3·C**
Increase health financing and support health workforce in developing countries
The Sustainable Development Goals are interlinked
The Sustainable Development Goals are interlinked
500 million people worldwide lack health care including access to essential medicines, vaccines, diagnostics, medical devices, and health technologies that prevent and treat diseases
Access to medicines: lessons from the HIV response

Just two decades ago, HIV/AIDS treatments were prohibitively expensive and accessible in only a few affluent countries. But remarkable reductions in costs have enabled treatment expansion that has reduced mortality and transmission. Today, first-line HIV drugs cost less than US$100 per person per year, a 99% reduction from more than $10,000 in 2000. The number of people receiving HIV treatment doubled in just 5 years, from 9 million in 2011 to more than 18 million today.¹

In a world facing growing inequalities, the HIV response has lessons for low and middle-income countries (LMIC)—but also for high-income countries—on access to care and treatment for communicable diseases and for non-communicable chronic diseases, a global pandemic that dwarfs the HIV epidemic in scale.²

The transformative power of the HIV response was underpinned by moral rather than technical arguments. A unique coalition of activists, scientists, celebrities, and religious and community leaders from all over the world argued that no one should be denied life-saving treatment because of area of residence or income. The moral imperative was operationalised by activism for more urgent drug discovery, regulatory approval, and voluntary and compulsory licensing, followed by shifts towards large-scale generic production. Economies of scale underpinned a drive towards more efficient, cheaper production, and drove prices down. Major donors such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria and the US President’s Emergency Plan for AIDS Relief bought generic drugs. The Clinton Health Access Initiative negotiated price-volume discounts

The regimen which contains DTG (dolutegravir) is becoming extensively available in LMIC countries for about 1/100 of the current price – around US $75 per person per year.

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A New Deal to Close the Gap in Health Innovation and Access

The rising costs of health technologies and the lack of new tools to tackle health problems like disease outbreaks and antimicrobial resistance is a growing problem. Catalyzing innovation, especially for rare diseases, diseases of the poor, and the development of new antibiotics has proven very difficult without market incentives.

The twin challenges of innovation and access constrain health outcomes and hinder social and economic development in rich and poor countries.

The Imbalance Between Human Rights, Intellectual Property Rights and Public Health Objectives is Leaving People Behind
TARGET 3.8

ACHIEVE UNIVERSAL HEALTH COVERAGE
Universal Health Coverage (UHC) means that ALL PEOPLE can obtain the quality health services they need without suffering financial hardship.
The concept of “public good”

non exclusive: anyone can use them

non competitive: their use will not limit others to use them
The concept of “public good”

Progress of medicine and essential medicines shall be considered as global public goods and be accessible to all human beings living on our planet
Thank you

stefano.vella@iss.it