#### Palazzo Reale Milano, 27 ottobre 2018

### Il diritto alla Salute

### nell'era della globalizzazione

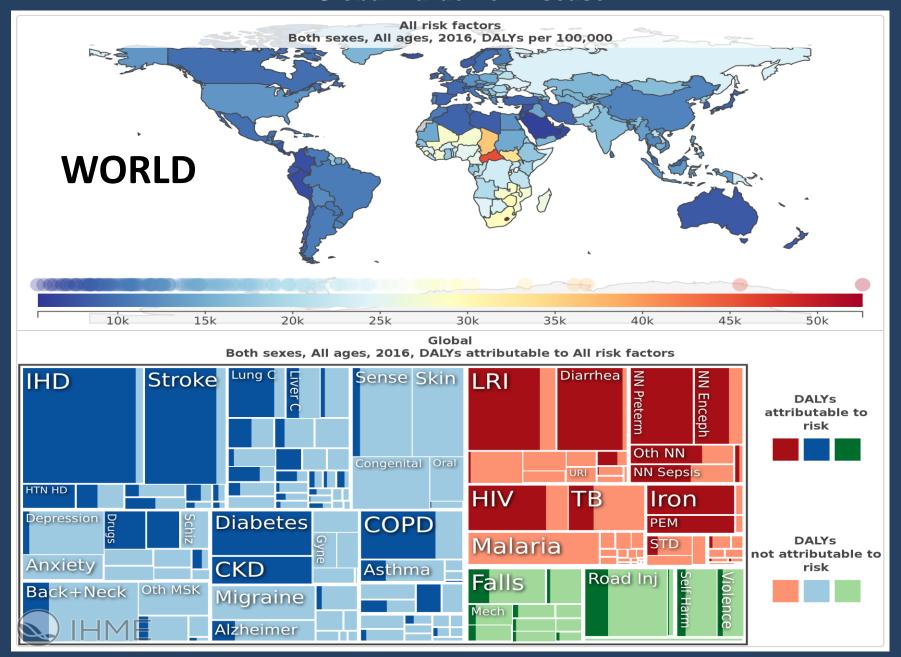
Stefano Vella

Centro Nazionale per la Salute Globale Istituto Superiore di Sanità - Rome

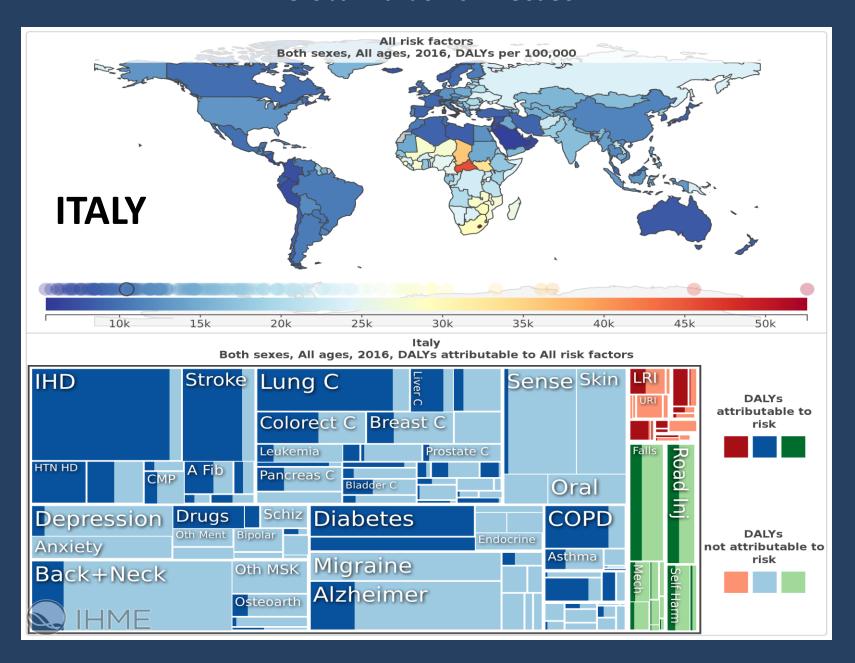




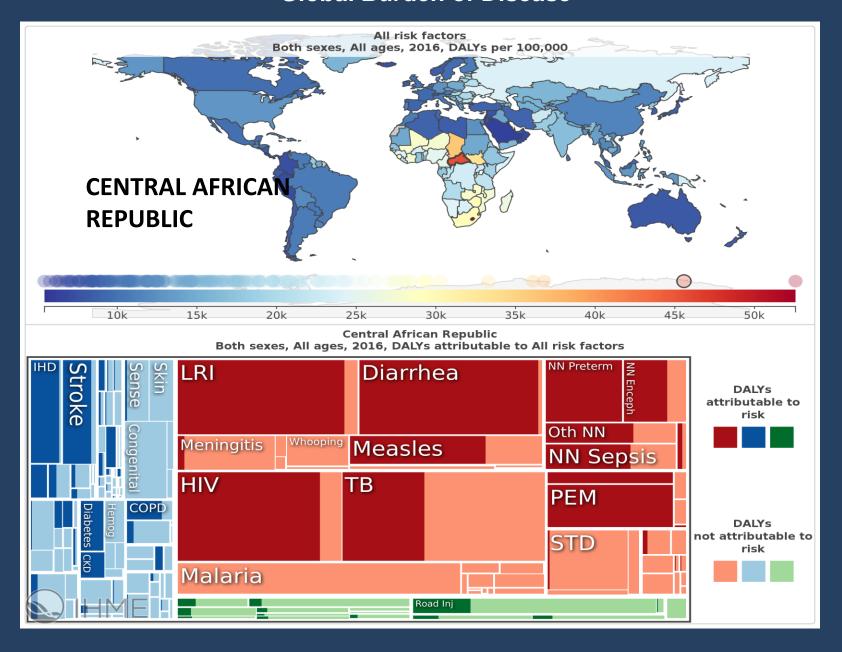
#### **Global Burden of Disease**



#### **Global Burden of Disease**



#### **Global Burden of Disease**



# OUTBREAK

Deadliest Pandemics in History

Bear age of visual aggent corr objects take lines as national pertiere. it can wipe out millions and span multiple continents rapidly. Here is a look at the infectious diseases the world has battled throughout history.

#### What is a Pandemic?

Derived from the Greek word pandemos meaning "pertaining to all people," a pandemic is a widespread disease that affects

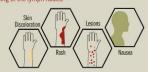


Key:

PANDEMIC DEATH TOLL



A bubo is an abnormal swelling of the lymph nodes



#### **Honorable Mentions**

Although the following viruses do not have a figure for total amount of lives claimed, they continue to terrorize various areas around the world.

#### MALARIA 1600 - Today

Chills, Headache, Fever, Jaundice, Muscle Pain, Nausea, Vomiting, Seizures

According to the World Health Organization's 2010 "World Malaria Report," an estimated 781,000 people are killed by the virus every year.

#### TUBERCULOSIS 700 BC - Today

Chest Pain, Cough, Fever, Chills, Fatigue

#### Death Toll

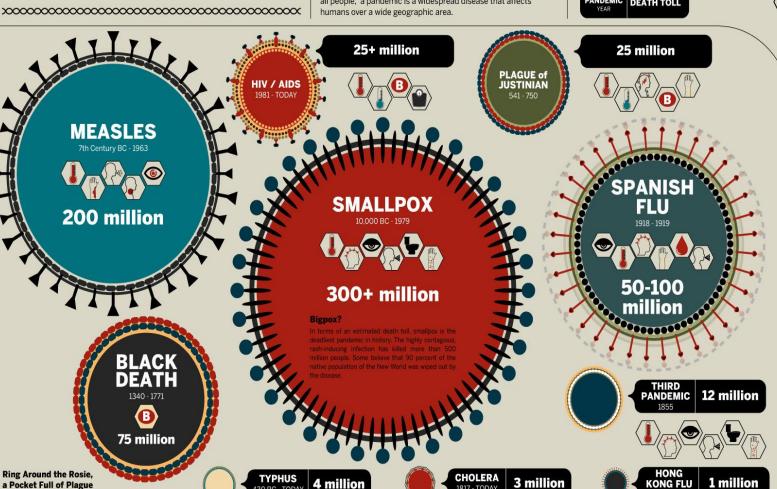
There are almost 2 million tuberculosis-related deaths worldwide every year.

#### YELLOW FEVER 16th Century - Today

#### Common Symptoms

Bleeding, Fever, Nausea, Vomiting, Delirium, Seizures, Jaundice

Worldwide, 30,000 deaths are caused by the infection every year.



a Pocket Full of Plague Legend says the Black Death plague inspired the children's rhyme "Ring Around The Rosy," which alluded to the rash-like rings and ashes of the deceased victims.

430 BC - TODAY

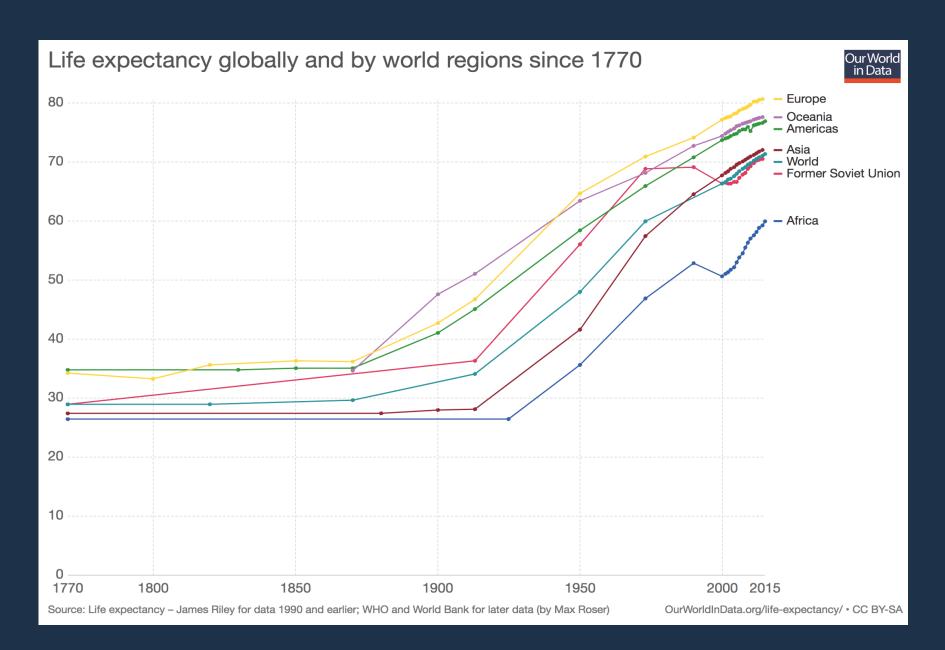




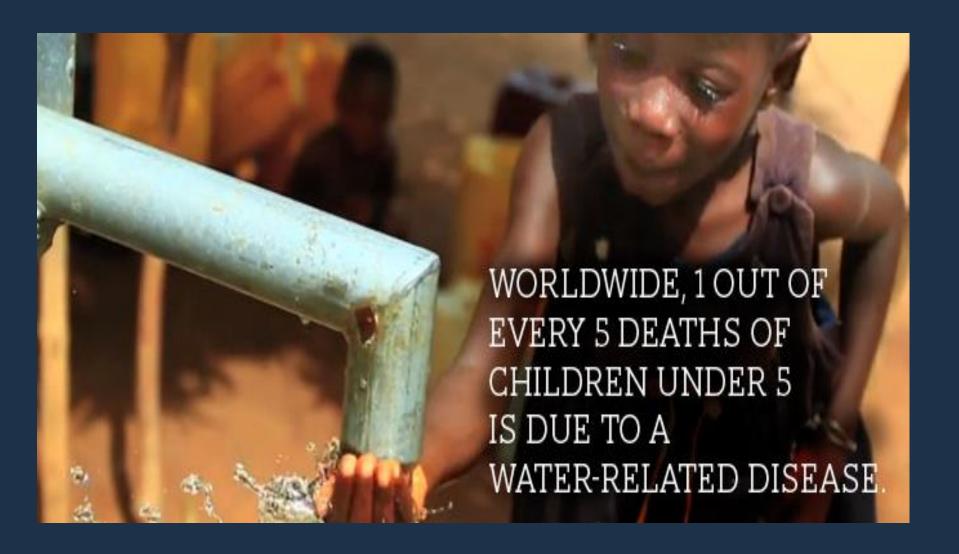




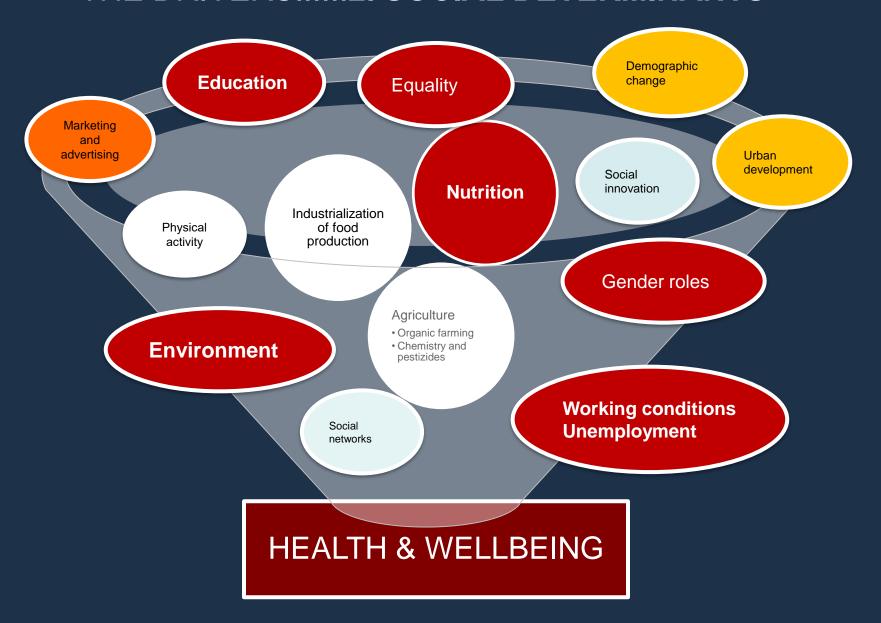
### THE RISE OF LIFE EXPECTANCY



# THE DRIVERS.....1. CLEAN WATER



### THE DRIVERS.....2. SOCIAL DETERMINANTS

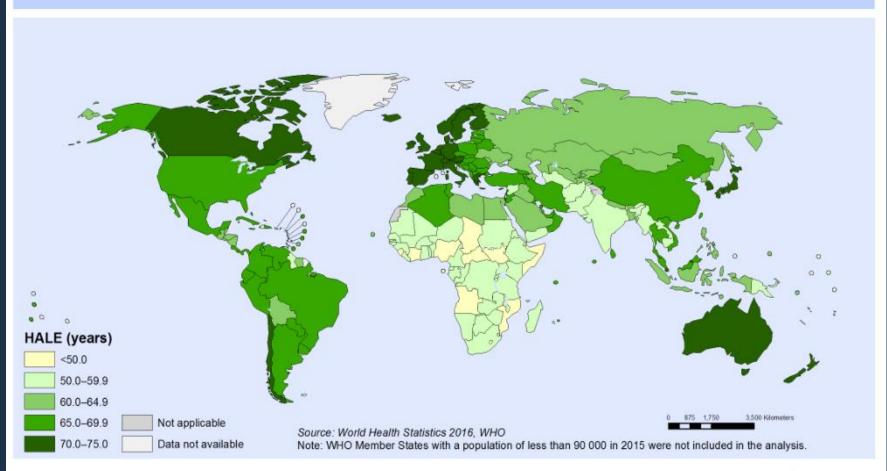


## THE DRIVERS.....3. ADVANCES OF MEDICINE



### The unequal rise of «healthy» life expectancy





The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization



#### Addio Millennio La medicina/Vaccini. antibiotici e soprattutto l'uso di acqua pulita: così il '900 ha allungato la durata della vita umana

Ma non nei paesi poveri

### CULTURA & SPETTACOLI

Nord e Sud, la salute non è uguale per tutti

di STEFANO VELLA

L NUMERO di anni che, in media, un bambino na-to in un qualsiasi Paese del-l'Occidente può sperare di vivere è progressivamente au-mentato nel corso dell'ultimo secolo, passando da circa 45 anni nel 1901 ad oltre 75. Se projettiamo nel ventunesimo secolo la crescita esponenzia-le delle conoscenze scientifi-che e la capacità della medici-na moderna di prevenire e curare un numero sempre più grande di malattie, un bambino che nascesse nel 2000 in Italia potrebbe avere una discreta possibilità di riu-scire a vedere anche un pezzetto del ventiduesimo se

lo. E questo senza tenere con-to della speran-za di riuscire un giorno a manipolare i geni che fisiologicamente determi-nano l'invec-chiamento delle nostre cellule.

Tuttavia, contrariamente a trariamente a quanto sarem mo portati a credere, l'au-mento della vi-ta media non è dovuto esclusivamente a grandi progressi della medicina del ventesimo secolo, ma so-prattutto all'abbattimento della mortalità pe-rinatale e al mi-glioramento delcondizioni igieniche gene-

#### delle malattie infettive

In un'ipotetica

classifica delle più importanti conquiste del-la medicina, ai primi posti dovremmo inserire la scoper-ta del valore dell'acqua pulita per la prevenzione di tan-te malattie infettive. Lo ave-vano ben capito i Romani, che per primi hanno dotato le loro città di reti idriche e fognarie di grande efficienza, e anche gli operatori sanitari che lavorano in molti Paesi africani sanno bene che una falda di acqua pulita è in gra-do di arrestare il diffondersi di un'epidemia di colera molto più rapidamente che dieci container" di farmaci.

Certo, senza la scoperta della vaccinazione e degli an-tibiotici, l'acqua corrente non sarebbe bastata per salvare l'umanità da tante altre malattie infettive che per secoli hanno rappresentato la principale caua di morte del-

E se molti considerano co-me paradigma dei grandi progressi della medicina la capacità di sostituire organi mala-ti, le tecniche cardiochirurgiche, i successi nella prevenzione e nella cura dei tumori (seppure ancora parziali), il controllo di malattie croniche come l'ipertensione e il diabete, il più grande risulta-to collettivo della medicina moderna è senz'altro costituito dalla battaglia vinta contro le malattie infettive, seb-bene sia azzardato ritenere la partita come definitivamente chiusa, vista l'improvvisa

comparsa dell'Aids e il ritor-no della tubercolosi. Da quando Jenner - era il 1796 - osservò che i mungitori delle vacche non contraeva-no il vaiolo, e pensò di inocu-lare il virus del vaiolo della

mucca (il cosiddetto "vaccino") per prevenire il vaiolo nell'uomo, il diffondersi della pratica della vaccinazione ha salvato miliardi di individui da malattie infettive come la poliomielte, la difterite, la pertosse, il tetano, la febbre gialla, il morbillo e, più recentemente, l'epatite B. Nel 1997, grazie ad una campagna di vaccinazione distrata dei si desci il desire. la pratica della vaccinazione durata alcuni decenni, il vaiolo, un flagello responsabile nei secoli passati di centinaia di milioni di morti, è stato didefinitivamente chiarato chiarato definitivamente scomparso dall'Organizzazio-ne Mondiale della Sanità, e in molti considerano questo evento come il più grande successo della medicina mo-

La nascita della genetica molecolare Certamente il grande protago-

nista della medicina del terzo millennio sarà la genetica molecolare. Per comprendere come questa branca della me dicina abbia in sé la potenzia-lità di curare e guarire tante malattie dell'uomo, compreso il cancro, dobbiamo partire dal concetto nuovo e rivo luzionario dell'origine "gene tica" della grande maggioran za delle malattie dell'uomo almeno di quelle non dovute a microrganismi patogeni. Grazie al Progetto Geno

sta disegnando la mappa completa del patrimonio ge netico dell'uomo, è stato sco-perto che non esistono soltan-to le classiche malattie genetiche ereditarie, come l'emofilia o la distrofia muscolare anche una parte rilevante del le comuni malattie croniche



# Global Health Inequalities

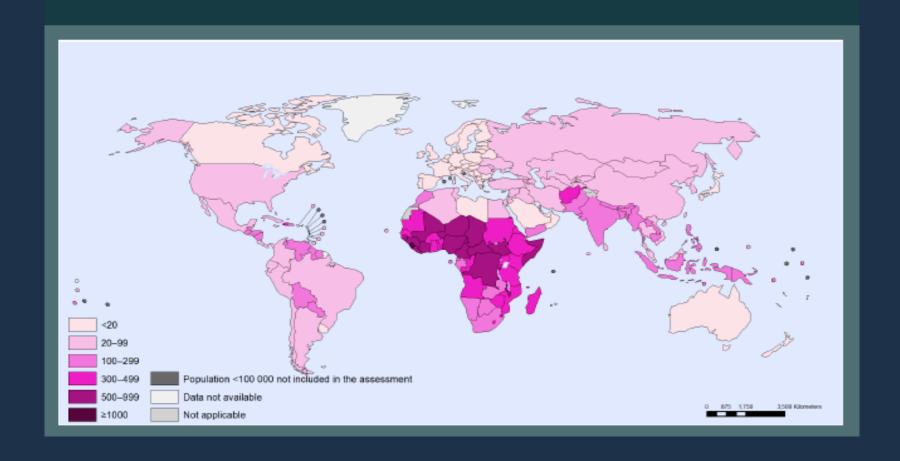
At least 30 million people die <u>prematurely</u> (half of then before the age of 5) in developing countries for lack of adequate access to basic health care. They die for causes that are very often <u>preventable or treatable</u>.

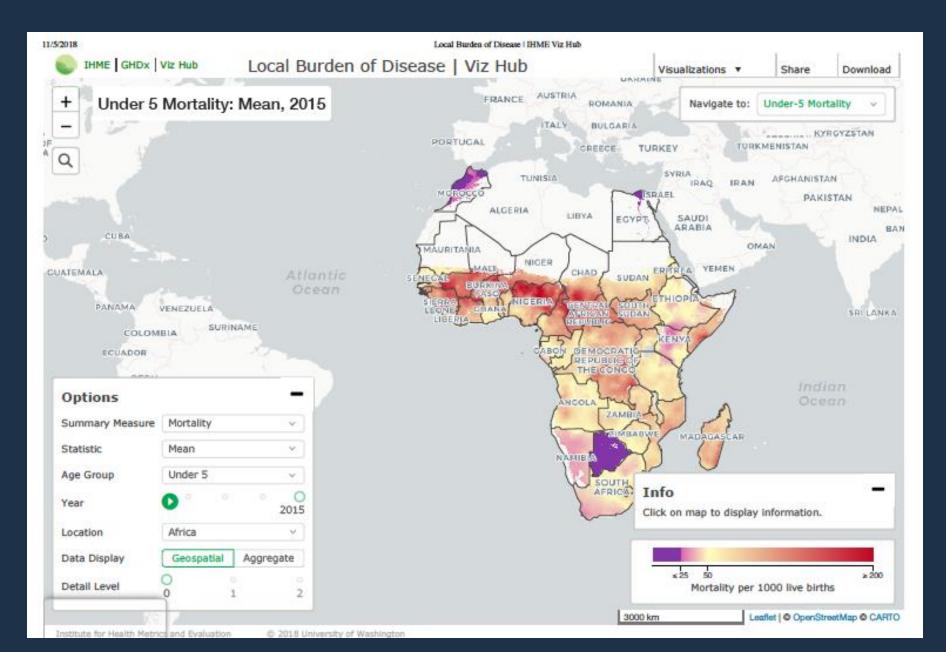
Despite the convergence on the concept of health as a human right, there still exist intolerable global inequalities in accessing health and health services and in terms of life expectancy and morbidity and mortality from **communicable and non-communicable diseases**.

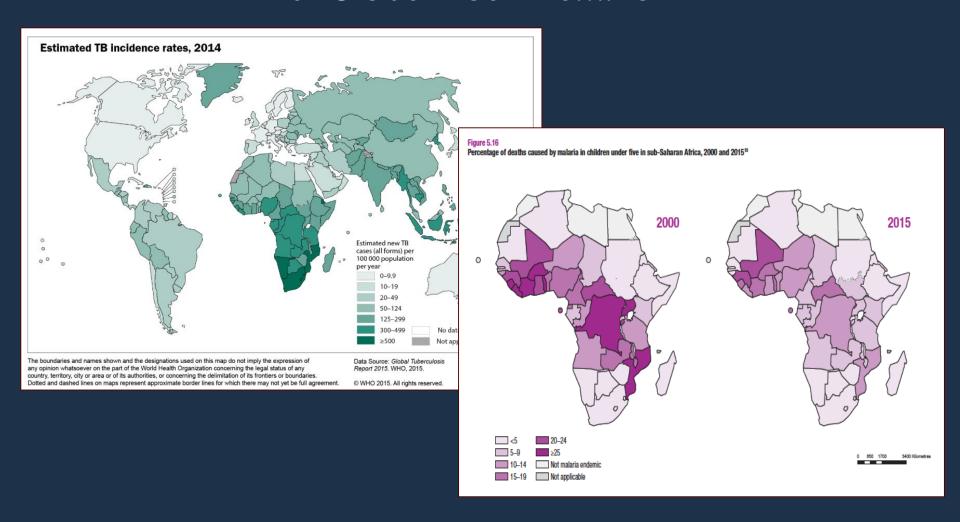
The persistence of inequalities in terms of health - not only between rich and poor countries, but also between different regions in the same country - is also a contradiction to science, given the growing geographic interdependence of the biomedical causes and of the social determinants of health and diseases.

### MATERNAL MORTALITY RATIO

per 100 000 live births, 2013

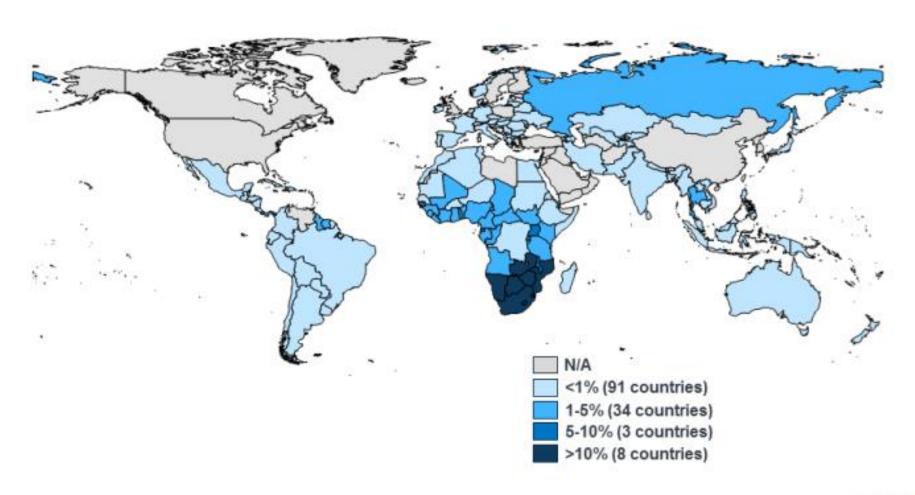






### Adult HIV Prevalence, 2017

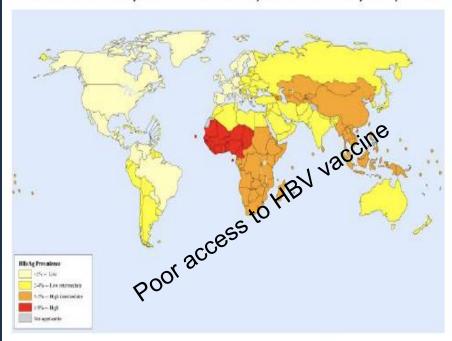
Global HIV Prevalence = 0.8%





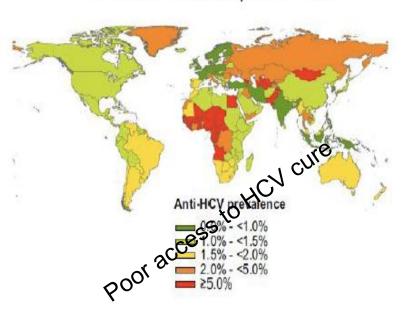
NOTES: Data are estimates. Prevalence includes adults ages 15-49. SOURCES: Kaiser Family Foundation, based on UNAIDS, AIDSinfo, Accessed July 2018.

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



Ott, J. J., G. A. Stevens, J. Groeger, and S. T. Wiersma. "Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity." *Vaccine* 30, no. 12 (2012): 2212-2219.

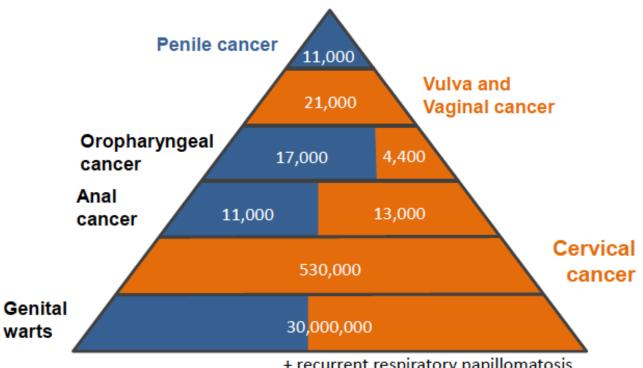
#### Prevalence of anti-hepatitis C virus

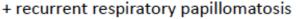


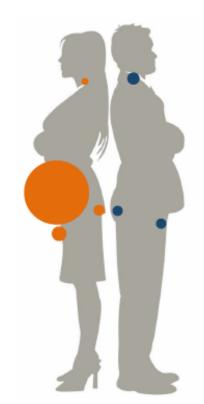
Gower, E., Estes, C., Blach, S., Razavi-Shearer, K., & Razavi, H. (2014). Global epidemiology and genotype distribution of the hepatitis C virus infection. Journal of hepatology, 61(1), S45-S57.

### 2008 Global HPV-related burden:

607,000 annual cancer cases







\*Circles proportional to annual burden

International Agency for Research on Cancer



De Martel et al. 2012 Lancet Oncol (cancers) and Dillner et al. 2010 BMJ (genital warts)



DDF 20

#### Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!)



Ana Maria Henao-Restrepo, Anton Camacho, Ira M Longini, Conall H Watson, W John Edmunds, Matthias Egger, Miles W Carroll, Natalie E Dean, Ibrahima Diatta, Moussa Doumbia, Bertrand Draquez, Sophie Duraffour, Godwin Enwere, Rebecca Grais, Stephan Gunther, Pierre-Stéphane Gsell, Stefanie Hossmann, Sara Viksmoen Watle, Mandy Kader Kondé, Sakoba Kétta, Souleymane Kone, Eewa Kuisma, Myron M Levine, Sema Mandal, Thomas Mauget, Gunnstein Norheim, Ximena Riveros, Aboubacar Soumah, Sven Trelle, Andrea SVicari, John-Arne Røttingen\*, Marie-Paule Kieny\*



Background rVSV-ZEBOV is a recombinant, replication competent vesicular stomatitis virus-based candidate vaccine Lencer 2017; 389:505-18 expressing a surface glycoprotein of Zaire Ebolavirus. We tested the effect of rVSV-ZEBOV in preventing Ebola virus Published Online 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 ça Suffit!) in the communities of Conakry and eight surrounding prefectures in the Basse-Guinée region of Guinea, and in Tomkolili and Bombali in Sierra Leone. We assessed the efficacy of a single intramuscular dose of rVSV-ZEBOV (2×107 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 enumerated 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 team visit. The list was archived, then we randomly assigned clusters (1:1) to either immediate vaccination or delayed vaccination (21 days later) of all eligible individuals (eg. those aged ≥18 years and not pregnant, breastfeeding, or severely ill). An independent statistician generated the assignment sequence using block randomisation with randomly varying blocks, stratified by location (urban vs rural) and size of rings (≤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 6-17 years and all identified rings. The prespecified primary outcome was a laboratory confirmed case of Ebola virus disease with onset 10 days or more from randomisation. The primary analysis compared the incidence of Ebola virus disease in eligible and vaccinated individuals assigned to immediate vaccination versus eligible contacts and contacts of contacts assigned to delayed vaccination. This trial is registered with the Pan African Clinical Trials Registry, number PACTR201503001057193.

Findings In the randomised part of the trial we identified 4539 contacts and contacts of contacts in 51 clusters randomly assigned to immediate vaccination (of whom 3232 were eligible, 2151 consented, and 2119 were immediately vaccinated) and 4557 contacts and contacts of contacts in 47 clusters randomly assigned to delayed vaccination (of whom 3096 were eligible, 2539 consented, and 2041 were vaccinated 21 days after randomisation). No cases of Ebola virus disease occurred 10 days or more after randomisation among randomly assigned contacts and contacts of contacts vaccinated in immediate clusters versus 16 cases (7 clusters affected) among all eligible individuals in delayed clusters. Vaccine efficacy was 100% (95% CI 68.9-100.0, p=0.0045), and the calculated intraclass correlation coefficient was 0.035. Additionally, we defined 19 non-randomised clusters in which we enumerated 2745 contacts and contacts of contacts, 2006 of whom were eligible and 1677 were immediately vaccinated, including 194 children. The evidence from all 117 clusters showed that no cases of Ebola virus disease occurred 10 days or more after randomisation among all immediately vaccinated contacts and contacts of contacts versus 23 cases (11 clusters affected) among all eligible contacts and contacts of contacts in delayed plus all eligible contacts and contacts of contacts never vaccinated in immediate clusters. The estimated vaccine efficacy here was 100% (95% CI 79-3-100-0, p=0-0033). 52% of contacts and contacts of contacts assigned to immediate vaccination and in non-randomised clusters received the vaccine immediately; vaccination protected both vaccinated and unvaccinated people in those clusters. 5837 individuals in total received the vaccine (5643 adults and 194 children), and all vaccinees were followed up for 84 days. 3149 (53.9%) of 5837 individuals reported at least one adverse event in the 14 days after vaccination; these were typically mild (87.5% of all 7211 adverse events). Headache (1832 [25.4%]), fatigue (1361 [18.9%]), and muscle pain (942 [13.1%]) 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

http://dx.dol.org/10.1016/ 50140-6736(16)32621-6

This online publication has bee corrected. The first corrected version appeared at thelancet. com on December 22, 2016. appeared on February 2, 2017

See Comment page 479

WHO Geneva Switzerland (A M Henao-Restrepo MD, M Doumbla M.D. G Enwere PWACP, P-S Gsell PhD S Kone MSc, T Mauget MBA, X Riveros MSc A SVicari PhD. M-P Klerry PhD); Faculty of **Epidemiology and Population** Health, London School of Hygiene & Tropical Medicine, London, UK (A Camacho PhD, C HWatson MFPH, ProfW | Edmunds PhD): Department of Biostatistics University of Florida Gainesville, FL, USA (Prof I M. Longini PhD, N E Dean PhD); Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland (Prof M Egger PhD); Centre for Infectious Disease Epidemiology and Research, University of Cape Town, Cape Town, South Africa (Prof M Egger); Public Health England, London, UK (M.W. Carroll PhD, S.Mandal M.D.);

Centre National d'Appul à la

Bamako, Mall (M Doumbia):

Institute for Tropical Medicine.

University of Hamburg,

Lutte contre la Maladie

Brussels, Belgium (B Draguez MD); Bernard Nocht

#### In Congo outbreak, Ebola vaccine faces reality tests

Friday, May 18, 2018 6:16 a.m. EDT



FILE PHOTO: Congolese Health Ministry officials carry the first batch of experimental Ebola vaccines in Kinshasa, Democratic Republic of Con

By Kate Kelland

LONDON (Reuters) - An experimental Ebola vaccine to be deployed in an outbreak in Democratic Republic of Congo has conquered some major scientific hurdles in giving high protection, but it now faces extreme real-

world tests including heat, humidity, language barriers and lack of roads.

Because it is not yet licensed, the Merck & Co vaccine has been offered to Congo under a "compassionate use" protocol agreed by national and international health and ethics authorities.

This means fully informed, signed consent is needed from every person who wants the shot. And in the current Ebola outbreak, that makes logistical, cultural and language barriers the ultimate challenges, global health specialists say.

The hurdles illustrate how hard it can be to move from laboratory to real life, especially in remote communities with no functioning health systems. The Congo outbreak is a chance to reality-test a vaccine against a disease epidemic that can't be replicated in controlled environments.

### Occhio alle epidemie prossime venture...



Family	10	ntial V	
Paramyxo	Prototype (s)	VIra	Pathon
Toga	Measles, Mumps, Nipoh, RSV	Licensed Vaccines	I Pathogens
Reo	Danisa, WEVEF	remated	
Orthomyxo	Influenza A, B	ttenuated	
Adeno	Adenovirus 4, 7, 14	attenuated	
Rhabdo	Rabies	Live-attenuated  Live-attenuated  Live-attenuated  Live-attenuated  Virus families with at least one representative licensed vaccine  Viruses with active vaccine research  Viruses with minimal vaccine research  Viruses with minimal vaccine research activity  VLP  Live-attenuated  VIP	
Picorna	Polio 1,2,3, Hepatitis A, EV68, 71		
Papilloma	HPV 6, 11, 16, 18		
Pox	Variola		
Hepadna	Hepatitis B		
Herpes	Varicella		
Flavi	Yellow Fever, TBE, JEV, Dengue, Z	ive-attenuated	
Нере	Hepatitis E	live-attenuated, whole-inactivat	ed, Live-chimeric
Filo	Ebola, Marburg	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 NT  Develop assays for diagnosis and immunogenicity testing  Define immune correlates of protection	
Retro	HIV-1		
Corona	SARS, MERS		
Parvo	B19, Boca		
Calici	Noro		
Polyoma	JC, BK		
Arena	Lassa, Machupo		
Bunya	Hanta, Rift Valley		
Astro	Astrovirus		

### **NIPHA VIRUS**



#### The New Hork Times

#### 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 Baumgaertner

June 4, 2018



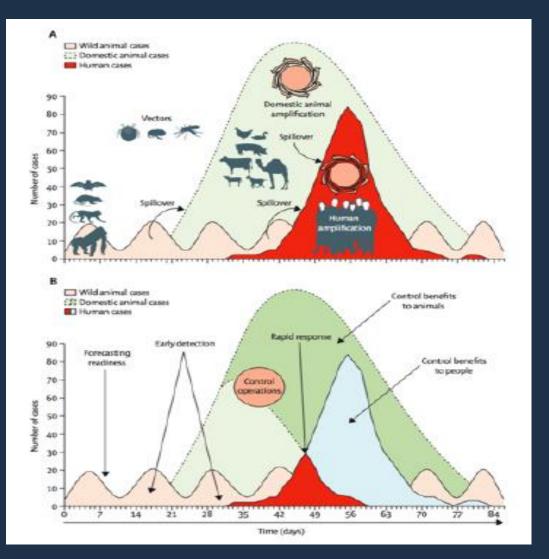
Burying a victim of the Nipah virus in Kozhikode, southern India. There is no vaccine and no cure for the disease. K.Shijith/Associated Press

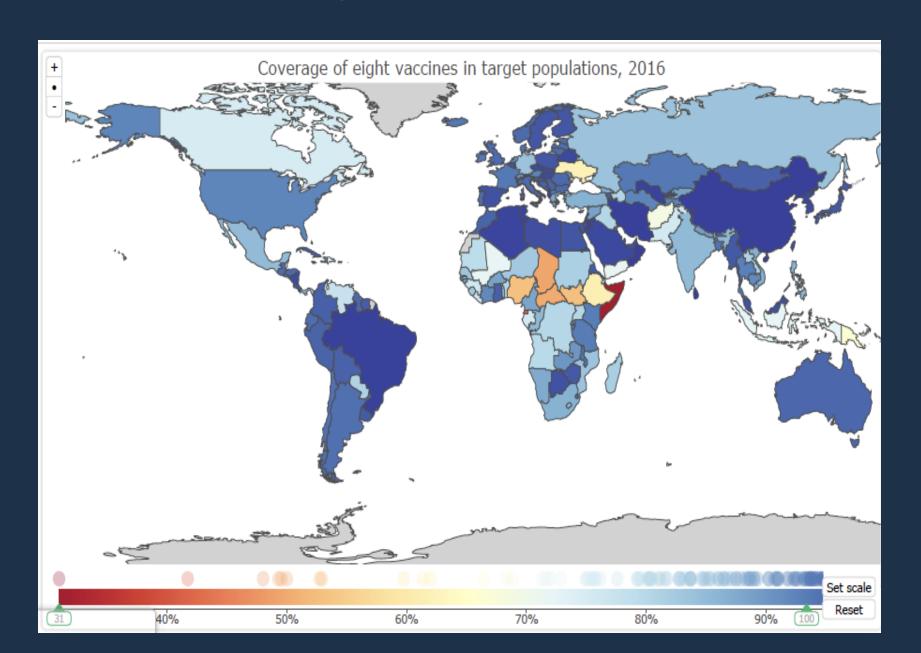
A rare, brain-damaging virus that experts consider a possible epidemic threat has broken out in the state of Kerala, India, for the first time, infecting at least 18 people and killing 17 of them, according to the World Health Organization.

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.



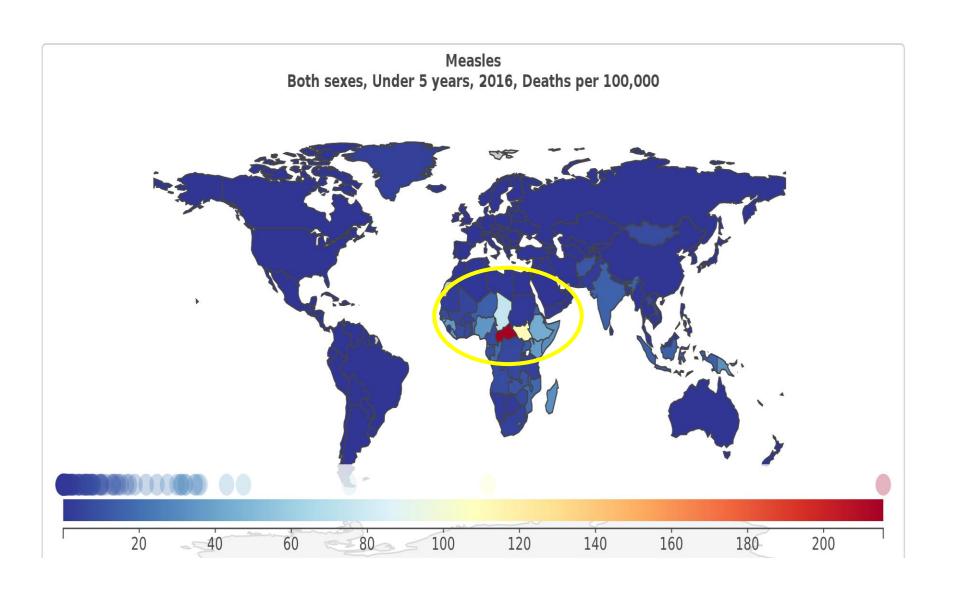




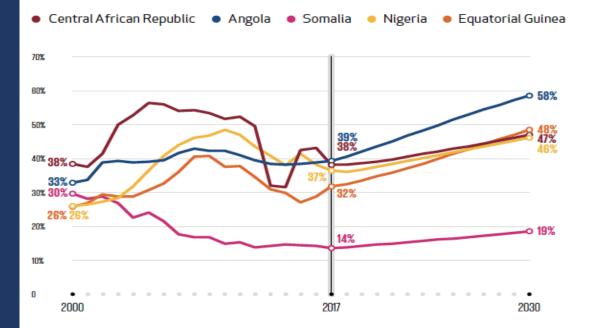
# Measles immunization coverage (% of children ages 12-23 months) (2016)



### **Measles mortality**



#### NATIONAL DTP3 COVERAGE

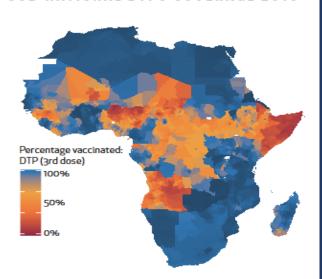


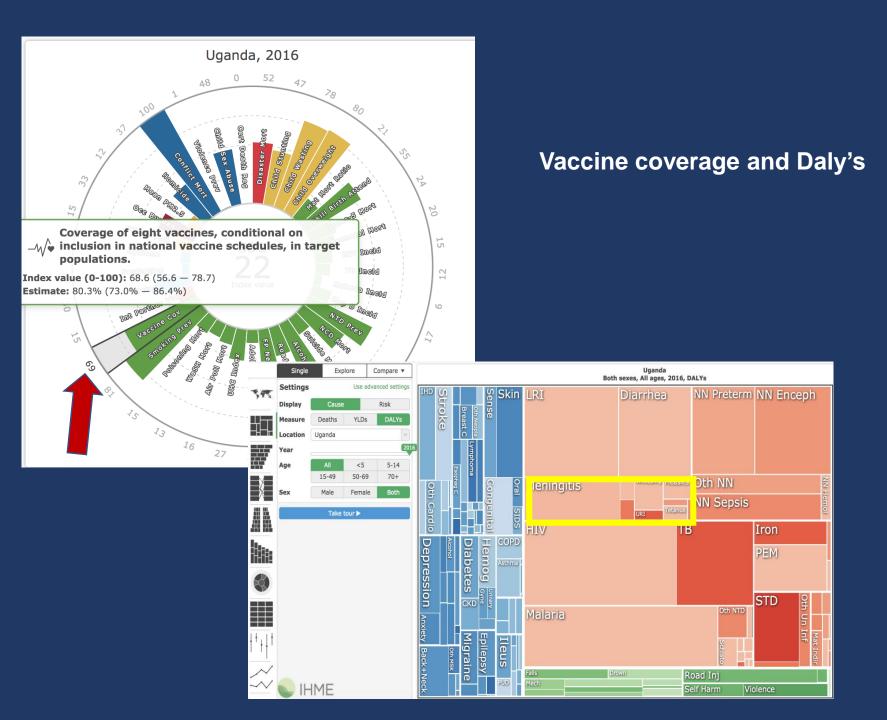
#### SUB-NATIONAL DTP3 COVERAGE 2016

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.

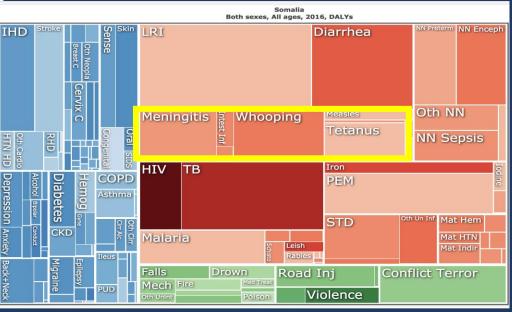




#### Somalia, 2016 Coverage of eight vaccines, conditional on \_//v inclusion in national vaccine schedules, in target neld populations. 18 Dood Index value (0-100): 0.2 (0.0 - 3.6)Estimate: 31.0% (23.6% - 40.1%) Bood Compare ▼ Settings Use advanced settings Deaths Measure Location Somalia <5 5-14 50-69 70+

IHME

#### Vaccine coverage and Daly's



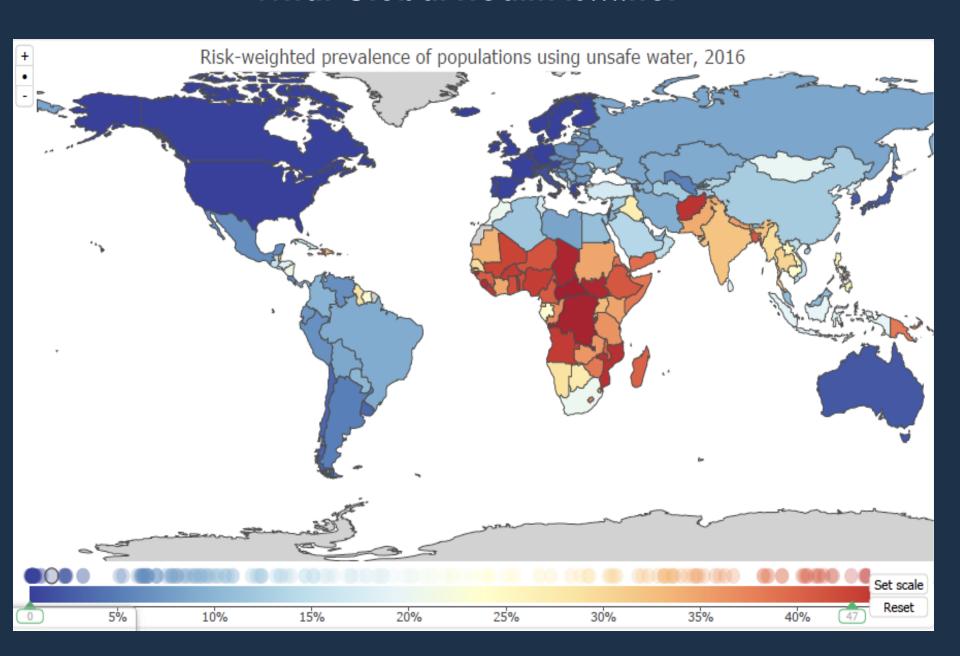
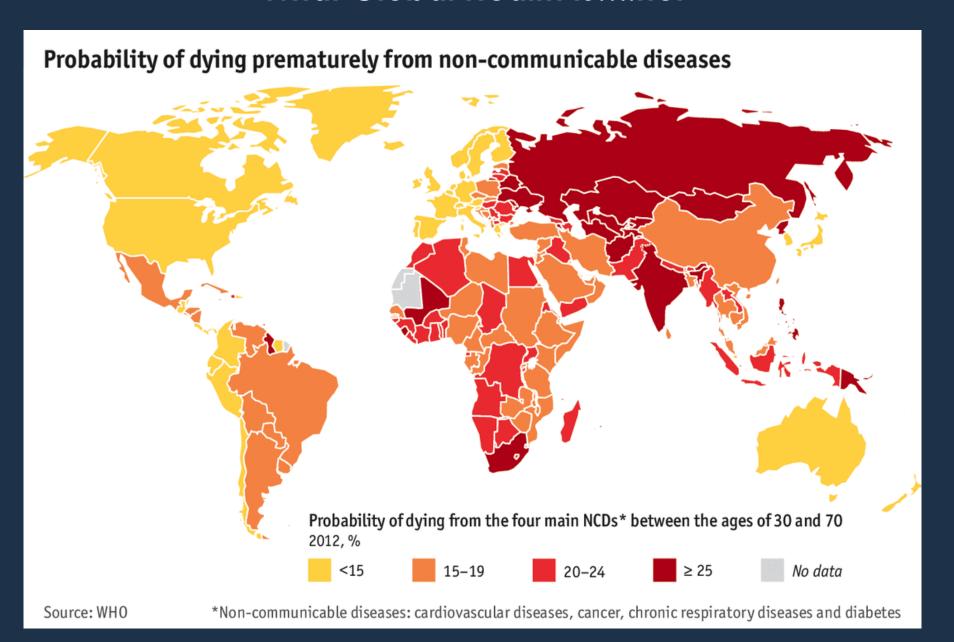


Fig. 3.4 Countries reporting cholera deaths and imported cases, 2016





# DISUGUAGLIANZE DI SALUTE: NON SOLO NEL SUD DEL MONDO......

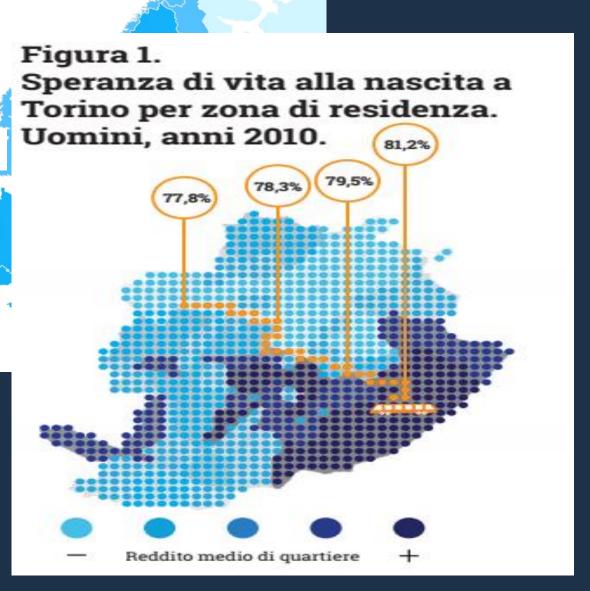
ASPETTATIVA DI VITA NEI PAESI DELLA REGIONE EUROPEA, 2010

#### **ASPETTATIVA DI VITA - QUINTILI**

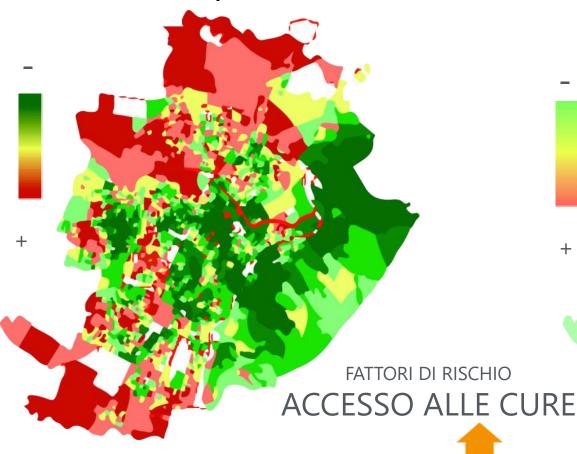
- PIÙ BASSO
- SECONDO
- TERZO
- QUARTO
- PIÙ ALTO

Dati: Who Regional Office for Europe

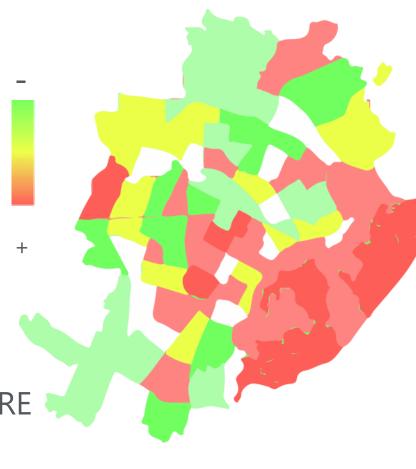
Giuseppe Costa



# Infarto miocardico acuto a Torino, 2009



# Rivascolarizzazione coronarica a Torino, 2009

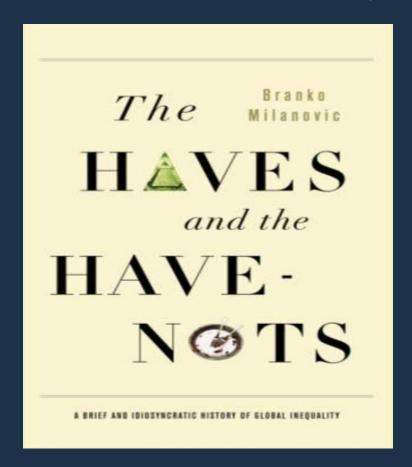


Giuseppe Costa



POSIZIONE SOCIALE = CONTROLLO

# The causes of poor health for millions globally are rooted in political, social and economic injustices



Only 1% of people owns 50.4% of the global wealth;
2.4 billion adults own only 1%
2015 Global Wealth Report - Credit Suisse.

#### Il lato oscuro della globalizzazione

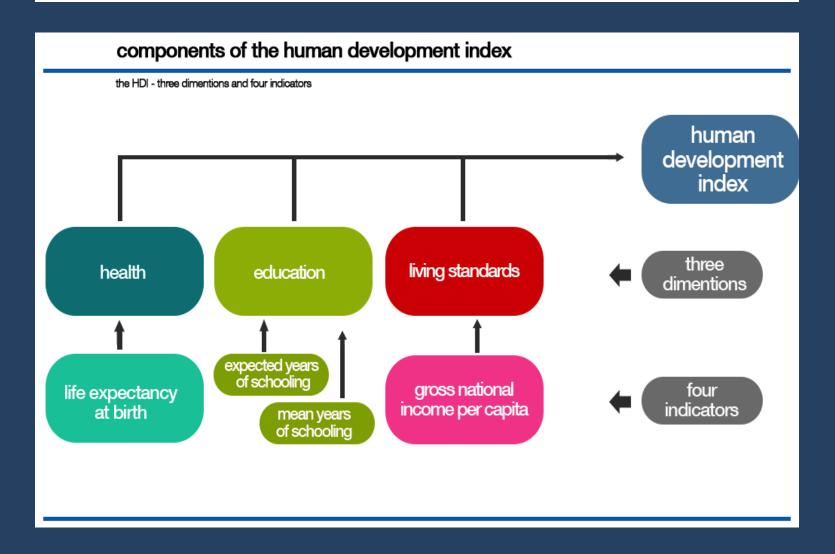
- ✓ urbanizzazione forsennata,
- ✓ nascita di nuove diseguaglianze sociali,
- ✓ nuovi poteri economici, fondamentalmente "finanziari",
  - ✓ geo-politica multi-polare,
  - ✓ mercato globale senza più regole,
  - ✓ uso smodato delle risorse naturali
  - ✓ e crescita del divario economico tra ricchi e poveri.

Secondo il corrente ma fuorviante paradigma dello sviluppo è la «crescita», non, ad esempio, la salute della popolazione o l'educazione, che viene considerata l'indice prevalente di successo di un Paese.

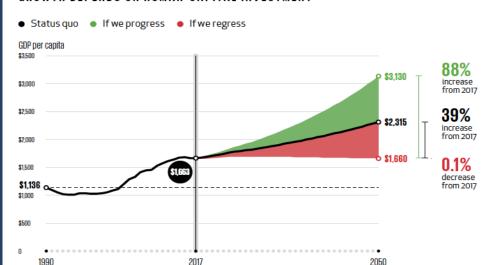
#### Human Development Report **2016**



#### **Human Development for Everyone**



#### THE MAGNITUDE OF SUB-SAHARAN AFRICA'S ECONOMIC GROWTH DEPENDS ON HUMAN-CAPITAL INVESTMENT



#### HUMAN CAPITAL: A BRIEF EXPLANATION

Economists generally think of three factors that contribute to economic growth:

- · Physical capital: Roads, bridges, factories, etc.
- Human capital: The sum total of the health, knowledge, and skills of the population.
- Total factor productivity: A broad category that captures an economy's efficiency, innovation, and level of technology.

In general, political leaders have preferred to invest in physical capital. When they build a piece of infrastructure, the impact is immediate and tangible. On the other hand, when they vaccinate and educate children effectively, the impact from an economic point of view comes decades later, and it's harder to see.

But the evidence is crystal clear: Human capital is a prerequisite for economic development. The data shows that differences in health and education levels explain as much as 30 percent of the variance in per capita GDP between countries.

It may be easier to capture the importance of investments in human capital by analyzing the impact they have on individuals. Consider height, which is a proxy for better health. Studies suggest that every additional centimeter boosts a person's income by 3.4 percent. Similarly, every additional year of schooling boosts it by 8 percent. When these individual effects are added up across a population, they can propel rapid economic growth.

# The poor, the marginalised groups and the vulnerable populations are the most affected by health inequalities



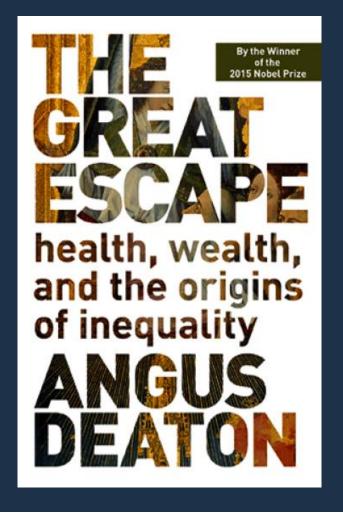






# 1.5 billion people live in slums





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.

## Quindi.....

...spesso si parte, volontariamente, in cerca di una vita migliore....

...oppure, forzatamente, lontano da guerre, violenze, disastri naturali...

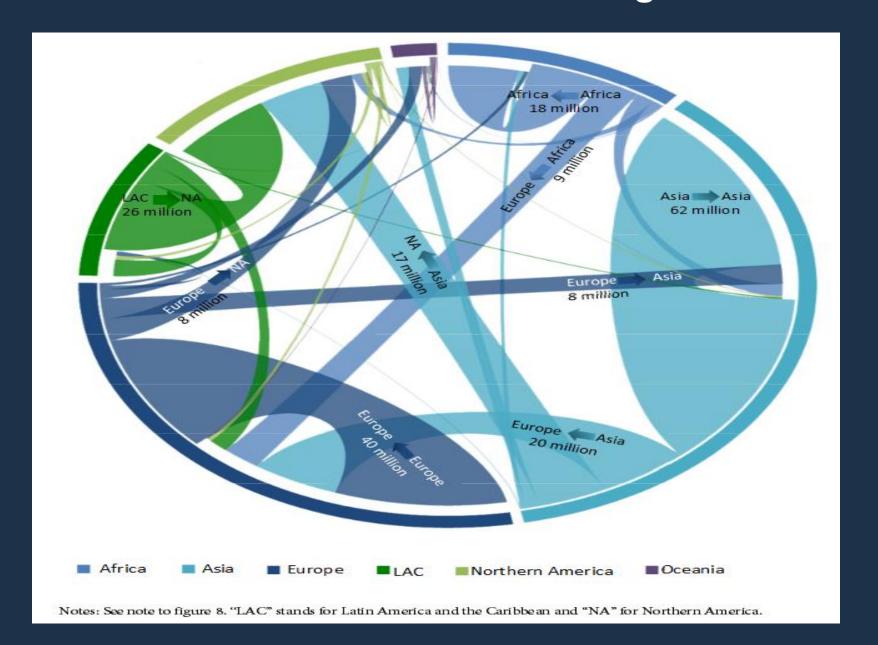
## **Migrants**



# **Displaced**

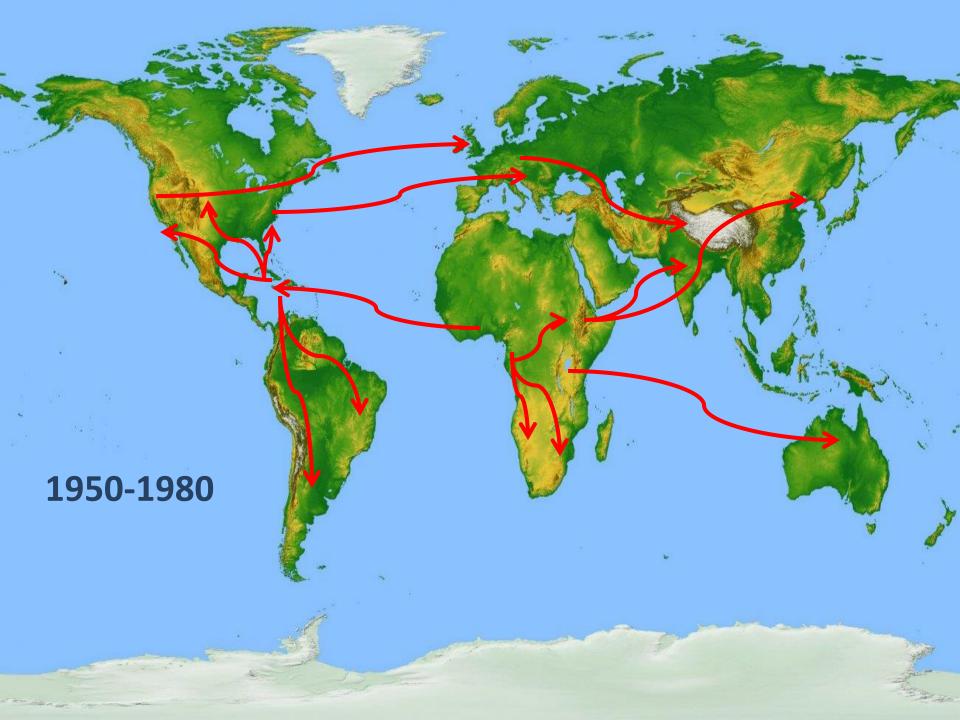


# ....un inarrestabile fenomeno globale



# Global Health: lessons from the response to HIV AIDS

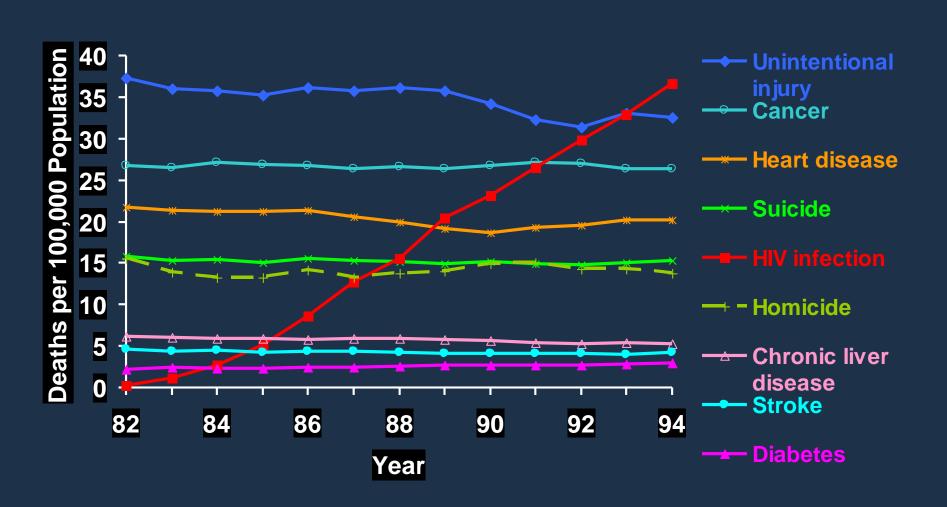




### AIDS: a devastating impact in just a few years

40 million live with HIV 40 million died

# Trends in Annual Rates of Death from Leading Causes of Death Among Persons 25-44 Years Old, USA



# 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. Jacobsen; 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, 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 level, 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 regimen considerations include reasons for 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.

JAMA, 1996;276:146-154

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) a better understanding of the replication kinetics of HIV throughout all stages of disease; (2) the development of assays to determine the viral load in individual patients; (3) the availability of several new effective drugs; and (4) the demonstration that combination therapy is more effective than zidovudine monotherapy.

In light of these advances, the recommendations of earlier state-of-the-art guidelines 12 are no longer applicable to clinical decision making in 1995. 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 results 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 must also include 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, at a time when longterm studies with clinical endpoints have been completed for only a few possible

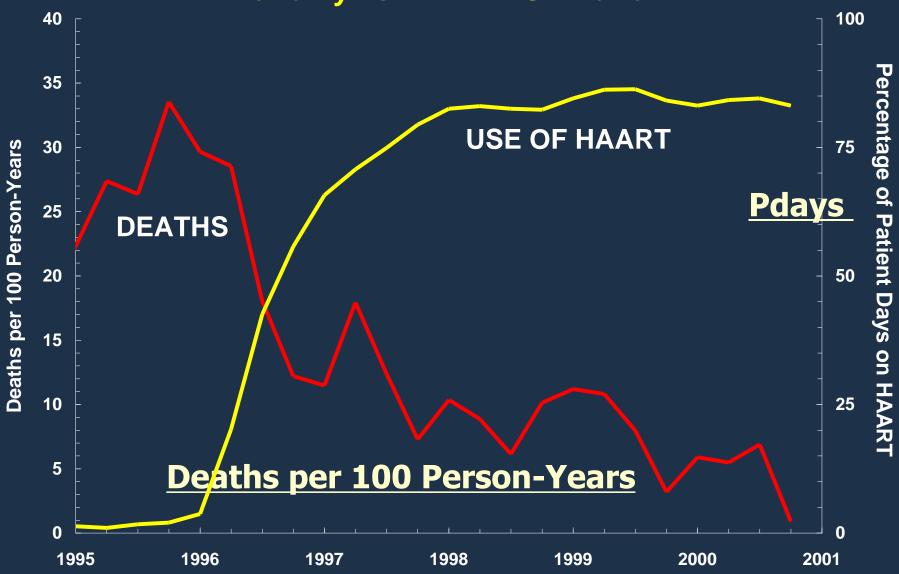
The recommendations herein reflect the panel's agreement on the importance of plasma HIV RNA measurements for predicting risk of clinical progression as well as of the recent demonstration from clinical trials of combination therapies that reductions in plasma HIV RNA

From Brown University School of Medicine, Providence, Ri (Dr Carpenter); the University of Miami (Ra) School of Medicine (Or Fischl), Harvard Medical Senool Beston, Mass (Ors Hammer and Hirsch): The International AIDS Society-USA, San Francisco, Calif. (Ms Jacobsen): Stanford (Calif) University Medical Center (Dr Katzenstein); St Paul's Hospital, Vancouver, British Columbia (Dr Montaner), University of California San Diego, and San Diego Veterans Affairs Medical Center (Dr Richman); the University of Alabama at Birmingham (Dr Saag); the University of Colorado School of Medicine, Denver (Dr Schooley); AIDS Research Consortium of Atlanta (Ga) (Dr Thompson), Istitute Superiore di Sanità, Rome, Italy (Dr Vella); Höpital Bichat-Claude Remard X. Richat Medical School, Paris. France (Dr Yeni); and the University of California San Francisco (Dr Volberdino).

Financial disclosures appear at the end of this article.

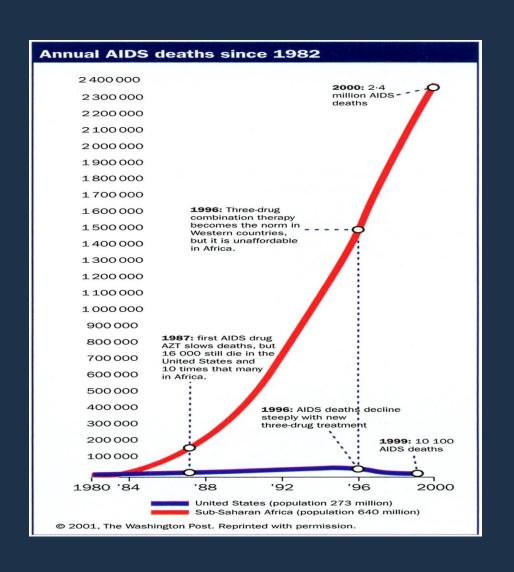
Reprints International AIDS Society-USA, 353 Kearny St. San Francisco, CA 94108

#### **Mortality vs. HAART Utilization**



Palella F et al, HOPS Study

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



# Ma la terapia sarà solo per pochi

#### GIANCARLO ANGELONI

 É una bella o bruita notizia. quella di Robert Gallo, secondo cui -entro dieci anni si curerà l'Aids-? È un'uscita elusiva e generica, che presta il fianco ad una certa informazione disimulta, interessata solo a conoscere «date» e «linee di traguardo», oppure contiene intuizioni autentiche dello scienziato? Cesto, è strano che ad ogni anno che passa, ci si debba nirovare a lare il gioco delle scommesse: e tanto più in questo 1995 che, anche a seguito della sospensione di tutte le sperimentazioni umane dei vaccini, ha fano agli inizi pensare al peggio. Facciamo un sano passo indietro, hanno detto alcuni. Si, per ricominciare e capire, hanno risposto altri: così, farento due passi in avanti. E, in effetti, se le cose nuove nascono davvero dalle crisi, il ripensamento ha funzionato, Quasi inaspettatamente, due latti, negli studi sulla patogenesi della malattia e sul fronte della terapia, hanno riportato un po' di sereno. Ma non è ancora il ciclo terso e azzuno - avverte Stefano Vella, direttore del reparto retrovirus nel laboraturio di virologia dell'Istituto superiore di sanità - perché non si devono scambiare i risultati ottenuti, pur importanti, con la cura dell'Aids: a dieci anni e più dall'inizio della pandemia, il ruolo dell'inlonnazione equilibrata in questo campo è ancora un problema non

sirolla.

Nette ultime settimane, Stefano Vella è stato invitato ad entrare, come uno dei tre membri per l'Europa, nell'organo di governo dello las, l'International Aids Society, che sovrintende alle conferenze internazionali, attualmente a cadenze biennale. Lo scorso anno ha tenuto, alla conferenza internazionale sull'Aids a Yokohama, la lettura inaugurale sulle terapie. E, di recente, al Congresso europeo di Copenaghen sull'Aids, ha discusso dei risultati dello studio europeoaustraliano Delta, che ha impegnato, lin dal '92, lo stesso Istituto superiore di sanità, e che si è alliancato a un altro «trial» molto importante. FActg 175, condotto negli Stati Uniti dai National Institutes of Health. Ora, a distanza di un paio di mesi da quell'incontro di Copenaghen, Sicano Vella ficordia: Cé stalo un riomento in sala, incrui tra i ricercatori è prevatsa l'emozione. Si, proprio l'emozione che prova un medico quando si accorge til poter cambiare finalmente la vita del proprio paziente, di essere sulla strada giusta».

E qual è questa strada, dottor Vella?

Veilar Noi abbiamo diviso lo studio Delta in due parti: nella prima abbiamo sperimentato una terapia combinata, Azt e ddi o Azt e ddC, su pazienti mai trattati in precedenza con antiettrovirali; nella seconda abbiamo invece arruulato, sempre per la stessa terapia combinata, pazienti che avevano avuto un trattamento con Azt di almeno tre mesi precedente all'arruolamento. Bene, sia per la progressione verso l'Aids, sia per la sopravvivenza, i risultati nel primo gruppo sono stati molto più lusinghieri che nel secondo, tanto che nei pazienti mai trattati prima attraverso la monoterapia con Azt, la riduzione di mortalità, mediante l'uso della terapia di combinazione, è stata stimata intorno al 40 per cento. Il confronto, dunque, è stato tra monoterapia e terapia di combinazione, ma il risultato vero dello studio Delta è stato quello di aver ottenuto una risposta sul come cominciare« occorre iniziare subito, e a dose piena, con la terapia

dovuto per il 30 % alla diffusione dell'filly (le sitre

cause sono l'aumento di povertà, quello del sonza

tetto e il difficile accesso alla cure del soggetti marginali), in alcuni paesi dell'Abico i casi di

tuberculosi sono addirittura racidoppiati. In Italia,

circs 1000 casi l'anno.

secondo uno studio condotto sul nostro territorio, questo fenomeno potrebbe portere a un aumento di

di combinazione, perché questa, al contrario della monoterapia, ha mostrato di poter modificare la storia noturale della malattia e ha stabilito, in un rapporto di causa el elfetto, che la replicazione del vius e la progressione della malatia sono legate tra di loro.

Ma, nella prospettiva, ci sono al-

tre optioni terapeutiche? Certo, Lo studio Delta e quello americano hanno tenuto conto solo degli antierciovirali già disponibili e non di quelli, sempte appartenenti alla forniglia dell'Azt, in via di approvazione da parte dell'Eda e delle stesse autorità europee, come il 3TC e il D41. Serza perisare, pol, che in strais molto avanzati ci sono gli indibitori delle proteasi, di diversa concezione e

di potenza di gran lunga superiore agli analoghi dell'Azt; e che in futuro, forse, si potrà contare su altri Înibitori, come quetti dell'integrasi. La prospettiva, dunque, è quella di usare tre o quattro farmaci contemporaneamente, e not di cambiare le combinazioni, regolamentandole, però, secondo un uso mirato e non selvaggio. Partroppo, c'è da dire che questa prospettiva riguardera solo il 5

per cento di coloro che nel memdo sono infetti, perche per le moltitudini dei sieroposini, che viuno in Alrica e in Asia nelle condizioni di miseria che sappiano, il così molto alti delle trrapie di combinazione saranno semple emente una cosa finazio.

E non c'é nessun altro interven to possibile?

to possibile et l'atti, l'unico intervento di tipo farmacologico è la prevenzione della trasmissione matemo-letale del visus, come sta cercando di verificare uno studio molto ampio, condinato dall'Oms, in praica, si vuol vedice se, somministrando farmaca: antretiosirati nelle fast più vicine al parto, si riesce ad evisare la trasmisione dell'I liv nel neonato. Il stradprevede una somministrazione che non superi i deci giorni, perche non superi i deci giorni, perche questo è il limite che le disponibilità economiche pong-no

Diversa sarebbe la situazione se

cl fosse un vaccino? St. per i suoi bassi costi. Ma. allustato attuale, non c'è davvero motto da sperare che il problema venga risolto, perché, nel caso dell'Itiv, il sistema immunistario, por funzionando, non è in grado di contrastare il virus con una risposta efficace. E poi, un'ulterrore complicazione è costituita dalla via di tasmissione, che è generalmente sessuale. Si dovrebbe costiluire, insomma, una protezione alla porta di ingresso del virus. cioè al livello delle mucose gentia- Ciò che oggi si pensa, in realtà. è che se un vaccino ci sarà, si tratterà di un «vaccino minore», che impediră solo la progressione dell'infezione, fin questo modo si rallenterebbe il corso della malattia. ma It daziente continuerable ad essere indettante

Un ultimo punto: la patogenesi, Qualt conoscenze nuove hamno portato i lavori pubblicati da -Nature- nel gennalo scorso, di cui si è tanto pariato?

cul s'étante partato? Hanno n'iconécito l'inféricine I fivin un quadro indetté o più classico, secondo un'inmagine dinamea che è più vicina alla realtà patolagica, e hanno dimostrato che moè vero che il sistema immontano no funziona a divere. Anti, essoregge benissimo all'attacco del virius, e lo da fino a quando, shopo anti, IT lor non riesce a siondare le linee. Se non trose cost, la persona intetta, morinetale entro qualche mess<sup>30</sup> in questo seno, di sofema immunitano va vato co me l'allesto esseritale della reagine.



mondo una persona al secondo e si stima che nel

prossimi dieci anni ucciderà 30 milioni di persone. Ma

però suments enormemente se la persona è infettata del virus dell'Alda. In quel caso la probabilità di

ammeleral aumente fino al 5 % all'enno. È qui si Innesta un circolo vizioso. Il contegio della IbC antiene

solo il 10 % degli infettati ha il 10 % di probeblità di aviluppare la molattia nel corso della vita, il rischio L'Usità - 1 dicembre 199



## World AIDS Conference - DURBAN, 2000

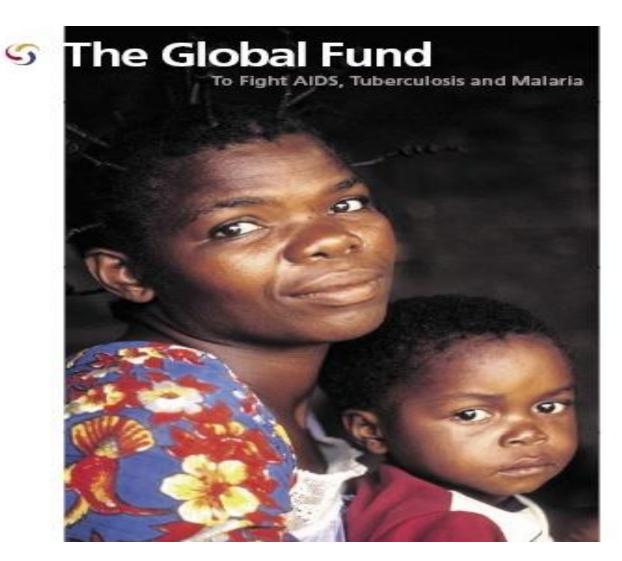


#### Community mobilization

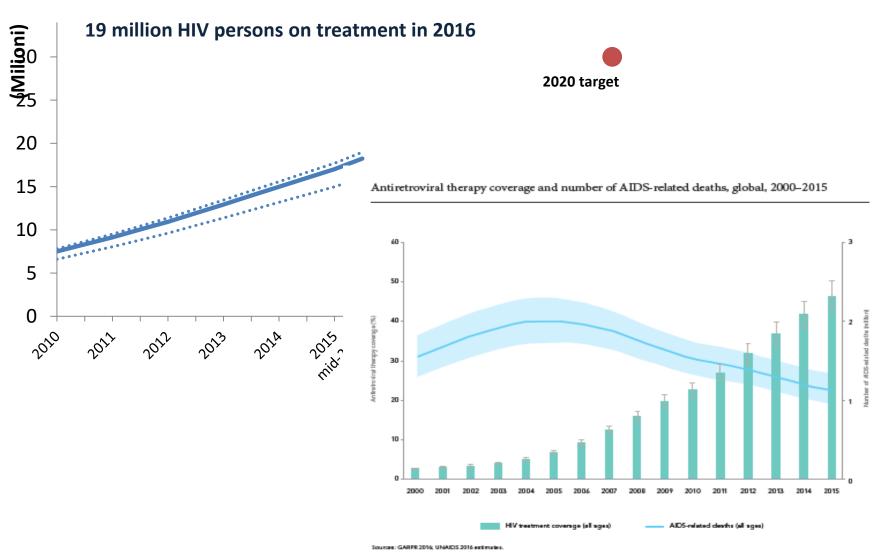


# **UNGASS 2001:** THE GLOBAL FUND WAS BORN



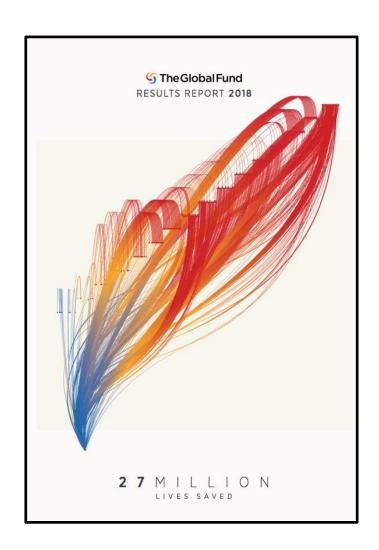


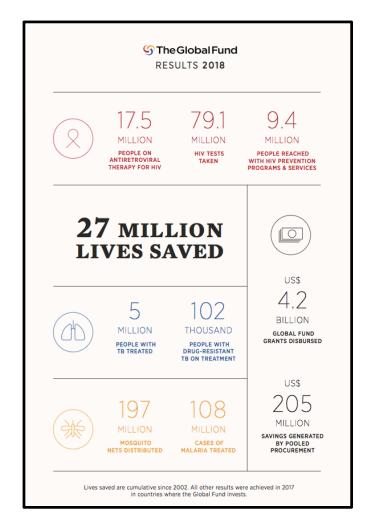
# The impact



Source: UNAIDS/WHO estimates.







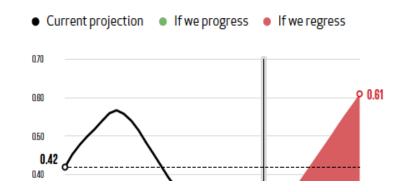


#### HIV

#### New cases of HIV per 1,000 people

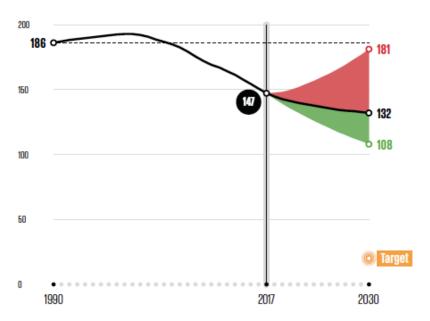
HIV treatment helps prevent new infections. An important step toward universal treatment is making sure that people living with LIVI know

their status. Currently, only 70 Studies from around the worl TUBERCULOSIS people, especially those who and at risk, prefer self-testing testing. So far, approximately self-testing policies. If that n the number of new infections



#### New cases of tuberculosis per 100,000 people

India has more TB cases than any other country in the world. The Government of India has responded by tripling its domestic funding to fight the disease and launching a plan to eliminate it by 2025, five years ahead of the Global Goals schedule. India's national plan includes commitments to dramatically increase the number of people tested and successfully treated, especially by focusing on patients who seek care in the private sector.



SDG Target: End the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases. Target shown on chart has been extrapolated from Stop TB Partnership target of <20 cases per 100,000 in 2030.

### L'agenda 2030: gli obiettivi per un mondo migliore

# SUSTAINABLE GEALS



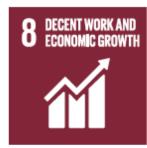
































# GOOD HEALTH AND WELL-BEING



#### **SDG 3 - TARGETS**



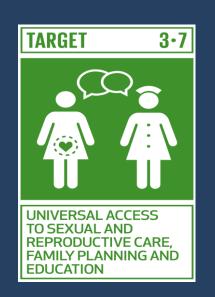






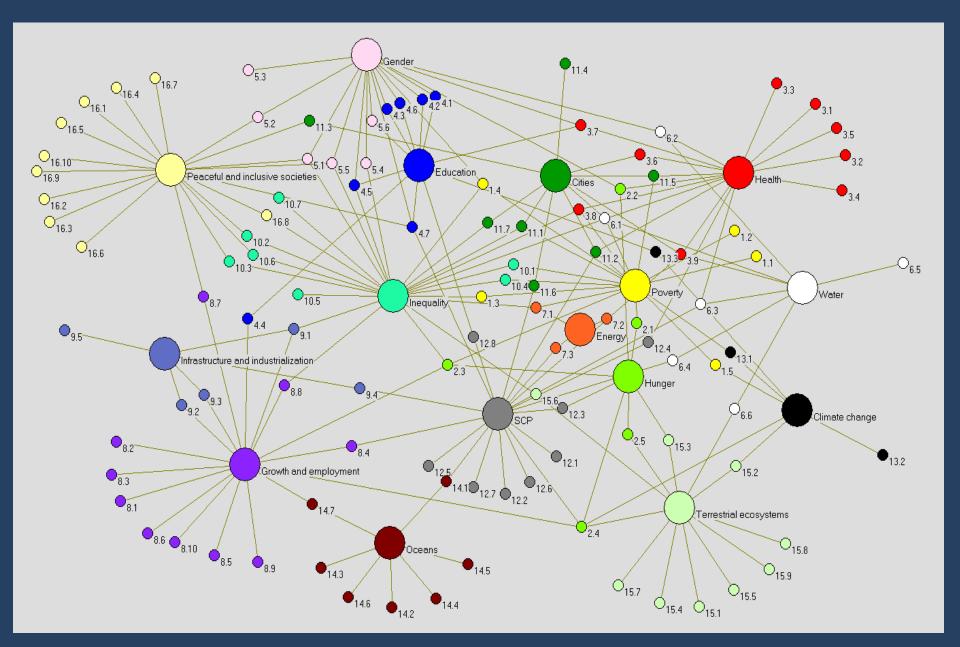






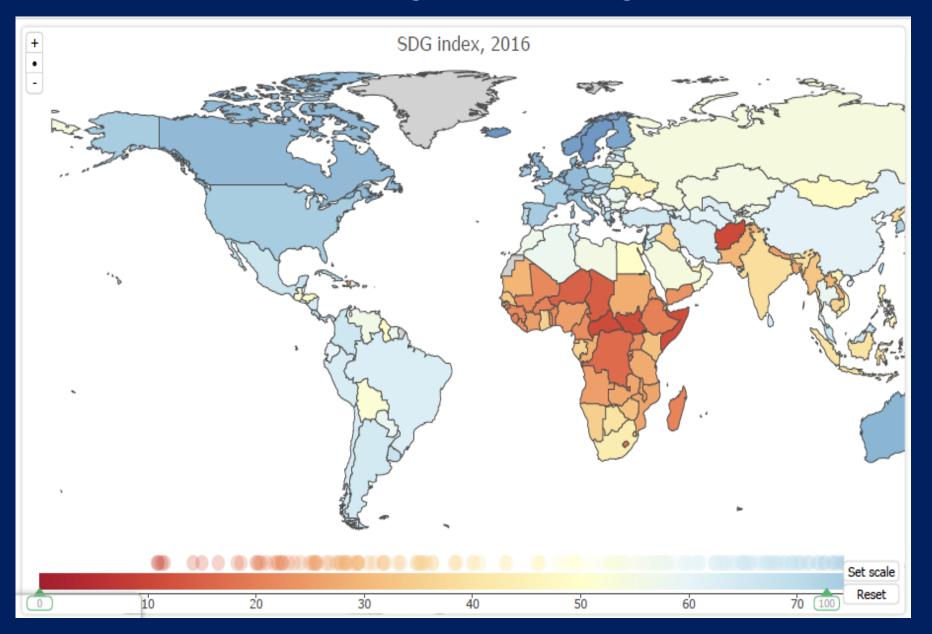


## I Sustainable Development Goals sono interconnessi

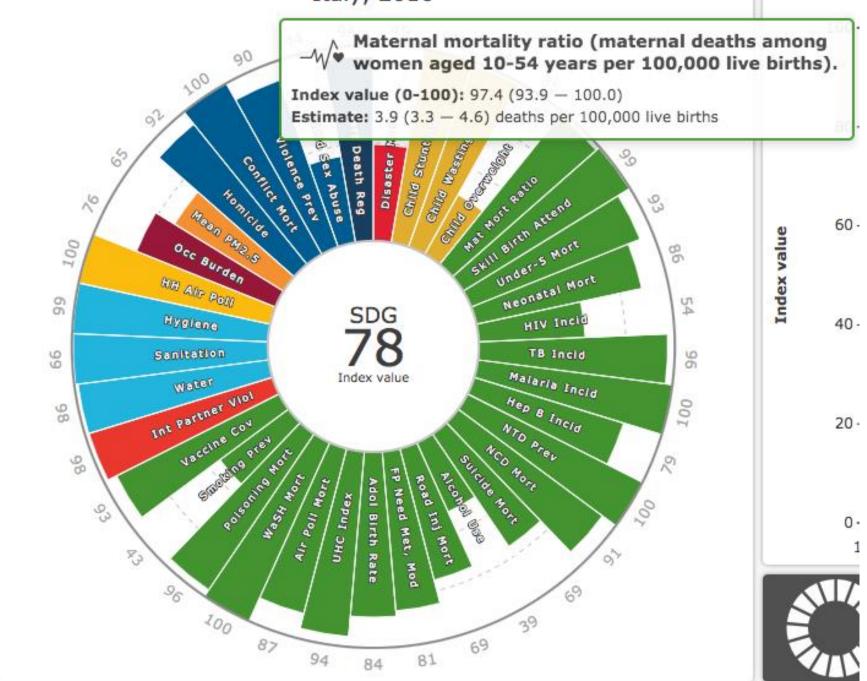


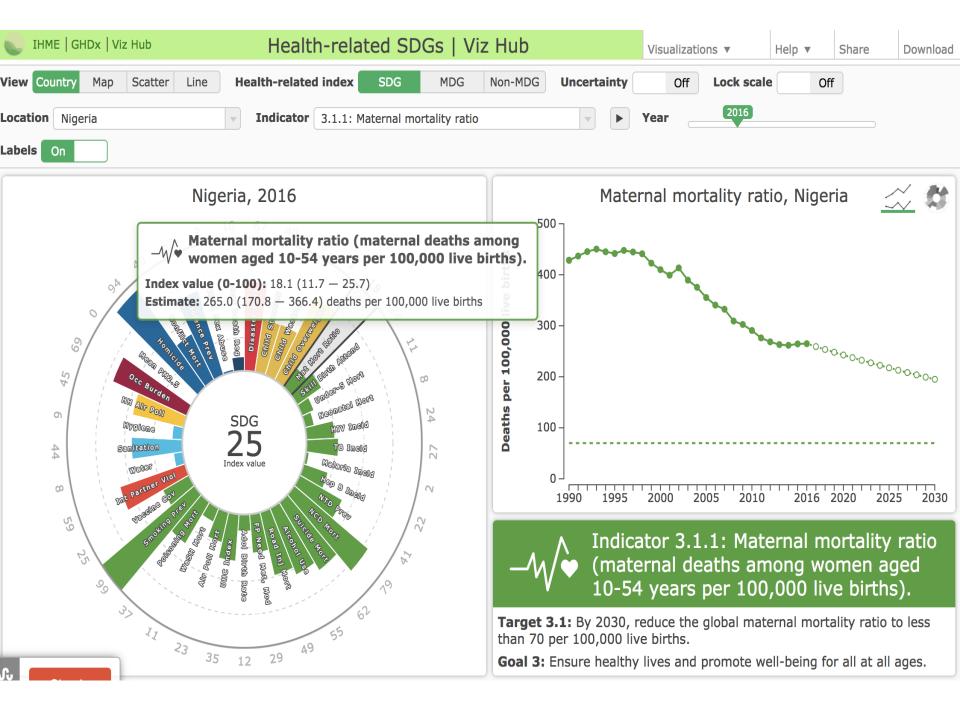


# Monitoring SDGs targets



#### Italy, 2016



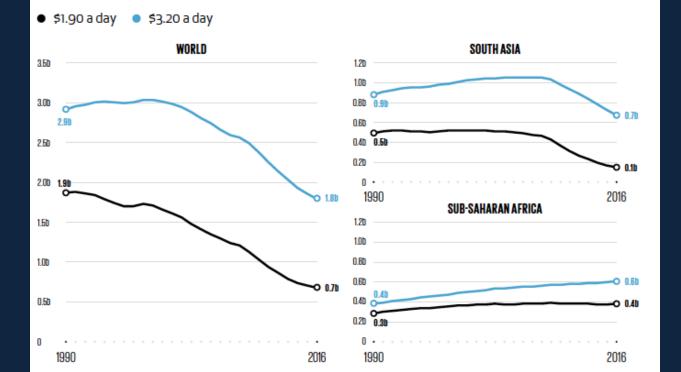


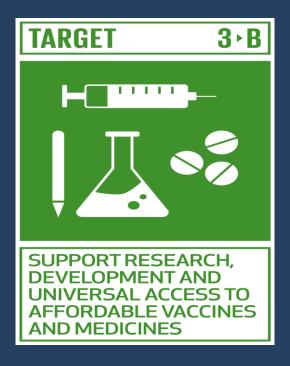


#### **POVERTY**

SDG Target: Eradicate extreme poverty for all people everywhere.

#### NUMBER OF PEOPLE LIVING AT DIFFERENT POVERTY THRESHOLDS





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.<sup>1</sup>

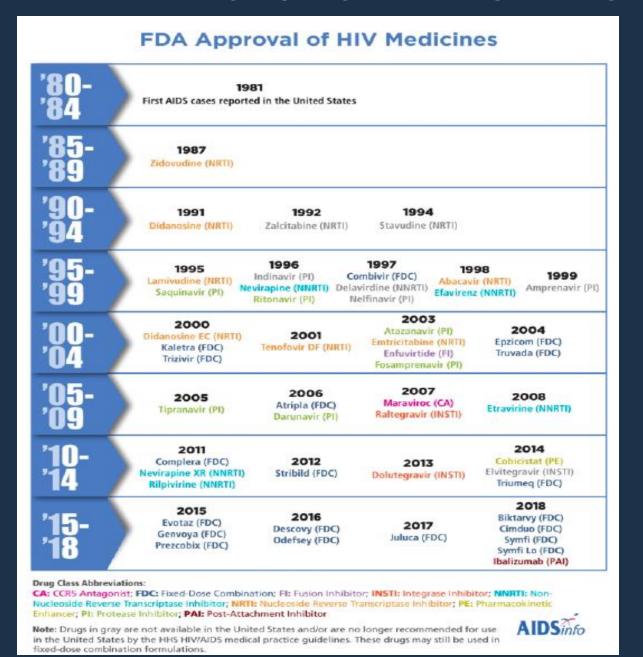
In a world facing growing inequalities, the HIV response has lessons for low and middle-income countries (LMIC)—but also for high-income countries—on access to care and treatment for communicable diseases and for non-communicable chronic diseases, a global pandemic that dwarfs the HIV epidemic in scale.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

The transformative power of the HV 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

www.thelancet.com/hiv Vol 4 April 2017 e147

Vella S, Wilson D. <u>Access to medicines: lessons from the HIV response.</u> Lancet HIV. 2017 Apr;4(4):e147-e149. doi: 10.1016/S2352-3018(17)30052-8.

#### HIV PHARMACEUTICAL INNOVATION



# WORLD TRADE ORGANIZATION

WT/MIN(01)/DEC/1 20 November 2001

(01-5859)

MINISTERIAL CONFERENCE Fourth Session Doha, 9 - 14 November 2001

#### MINISTERIAL DECLARATION

Adopted on 14 November 2001

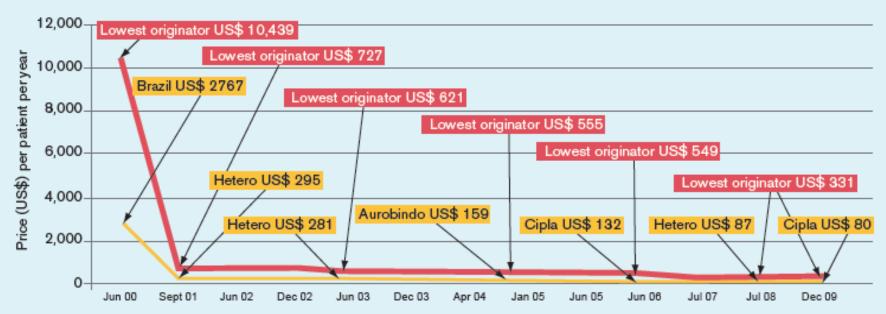
- "Each member has the right to grant compulsory licences and the freedom to determine the grounds upon which such licences are granted" and
  - "to determine what constitutes a national emergency or other circumstances of extreme urgency".
    - Public health crises include "those relating to HIV/AIDS, tuberculosis, malaria and other epidemics" and "other circumstances of extreme urgency".

#### HIV DRUG PRICING INNOVATION

#### 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



Source: Extract from MSF, Untangling the Web of Price Reductions, January 2010 at http://www.msfaccess.org.

## Cost Considerations and Antiretroviral Therapy

Last Updated: October 17, 2017; Last Reviewed: October 17, 2017

Coformulated Combination Products as Single Tablet Regimens				
Dolutegravir/Abacavir/Lamivudine	50/600/300 mg tablet	1 tablet daily	30 tablets	\$3,118.62
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine	600/300/200 mg tablet	1 tablet daily	30 tablets	\$3,057.89
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine	150/150/10/200 mg tablet	1 tablet daily	30 tablets	\$3,306.92

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.



# Promoting Innovation and Access

medicines • vaccines • diagnostics • health technologies

# 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

#### **Public-Private Partnerships and Product Development Partnerships (PDPs)**

Sharing the resources and strengths of the private and public sectors can accelerate innovation and allow investments to be made in health technologies that may lack a clear market incentive.









# **TARGET**

3.8



ACHIEVE UNIVERSAL HEALTH COVERAGE



# UNIVERSAL **HEALTH COVERAGE:** EVERYONE. **EVERYWHERE**

66 Health is a human right. No one should get sick and die just because they are poor, or because they cannot access the health services they need."

Dr Tedros Adhanom Ghebrevesus. WHO Director-General





# Universal Health Coverage (UHC)

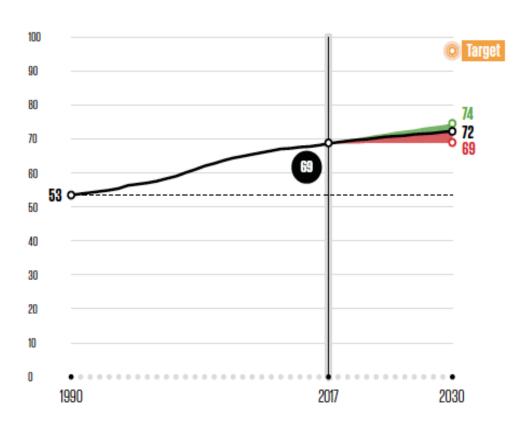
means that ALL PEOPLE can obtain the quality health services they need without suffering financial hardship.



#### UNIVERSAL HEALTH COVERAGE

## Performance score for coverage of essential health services

Last year, WHO made universal health coverage its top priority. Investing in primary health care, which can meet 90 percent of people's health needs, is the place to start. In fact, countries' performance on most indicators in this report depends on strong primary health care systems. The WHO director-general called it "the responsibility of every country ... to pursue universal coverage." The shape of this curve over time will reveal how governments responded to this challenge.



SDG Target: Achieve universal health coverage for all.

# The Challenge of Financing Universal Health Coverage: competing with emerging priorities

financial crisis,

conflict situations,

migration, security,

natural and human-made disasters

#### Investing in Health is very cost-effective

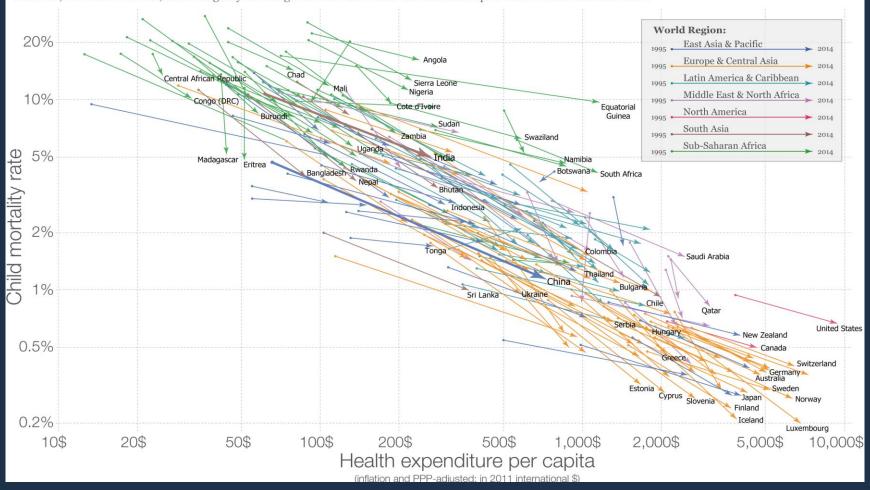
#### Fewer children die as more money is spent on health

Our World in Data

The arrows show the change for all countries in the world, from 1995 (earliest available data) to 2014 (latest available data). [Not all countries are labelled]

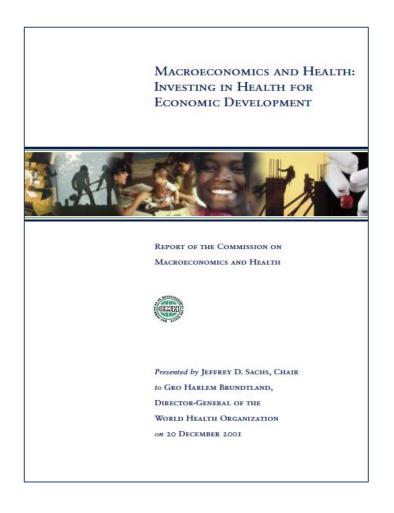
- Child mortality is the share of children that die before their 5th birthday.

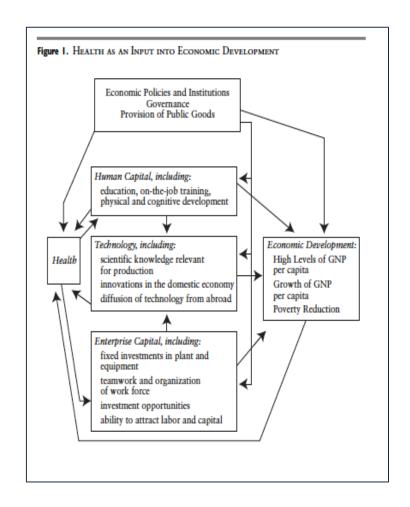
- Total health expenditure is the sum of public and private health expenditures. It covers the provision of health services (preventive and curative), family planning activities, nutrition activities, and emergency aid designated for health but does not include provision of water and sanitation.



# La salute non è soltanto un diritto fondamentale di ogni uomo che viva su questa terra,

#### ma è anche uno straordinario motore di sviluppo





# Allora, cos'e' la Salute Globale

- è un'area di ricerca e azione che si occupa di lottare contro le diseguaglianze di salute
- è intersettoriale: si occupa degli aspetti biomedici, ma anche di quelli economici, sociali e politici
- se ne occupa a livello globale, perché in un mondo così interconnesso, è ingenuo pensare alla salute come un problema di «casa nostra»
- perché la salute di tutti i popoli della terra è anche la «nostra»
   salute, ed è uno straordinario strumento di sviluppo, stabilità e di pace

DDF

## 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 87

# Grazie

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