



Best strategies for global HCV eradication

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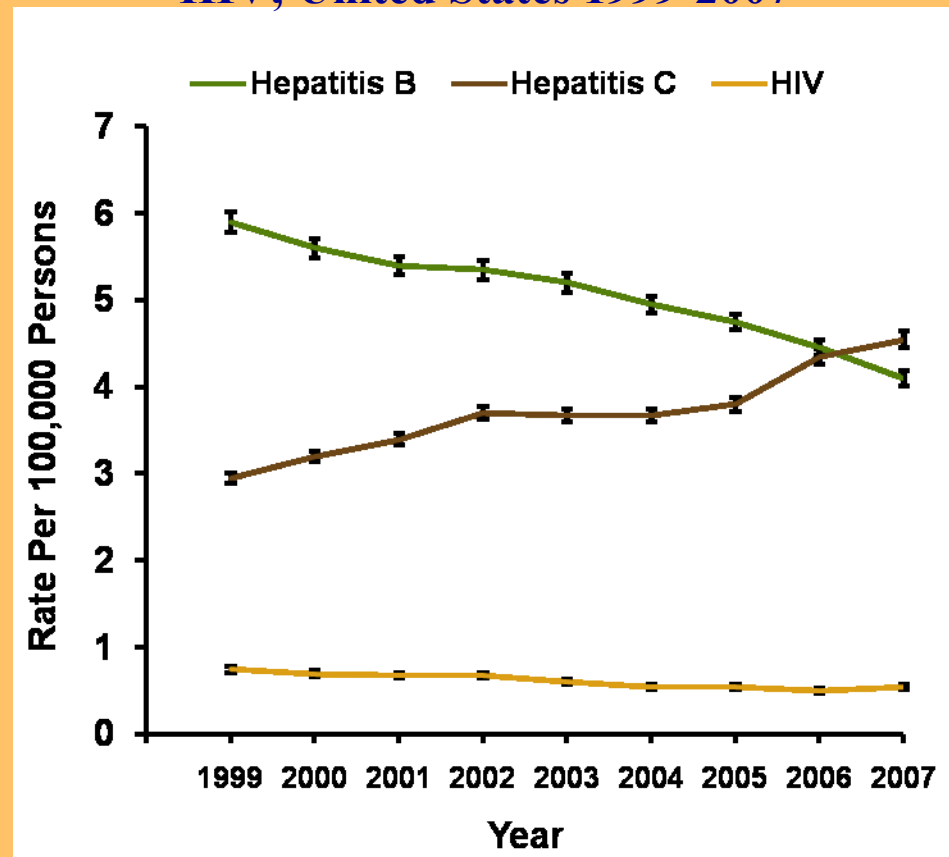
Since 2007, more Americans die from HCV than HIV infection (Similar in Europe)

- National multiple-cause mortality data

By 2007 hepatitis C-associated deaths had **overtaken** HIV as a cause of mortality in the United States.

- Co-morbidities associated with increased odds ratio of mortality
 - Alcohol related (4.6; HCV and 3.7; HBV)
 - HIV co-infection (1.8; HCV and 4.0; HBV)

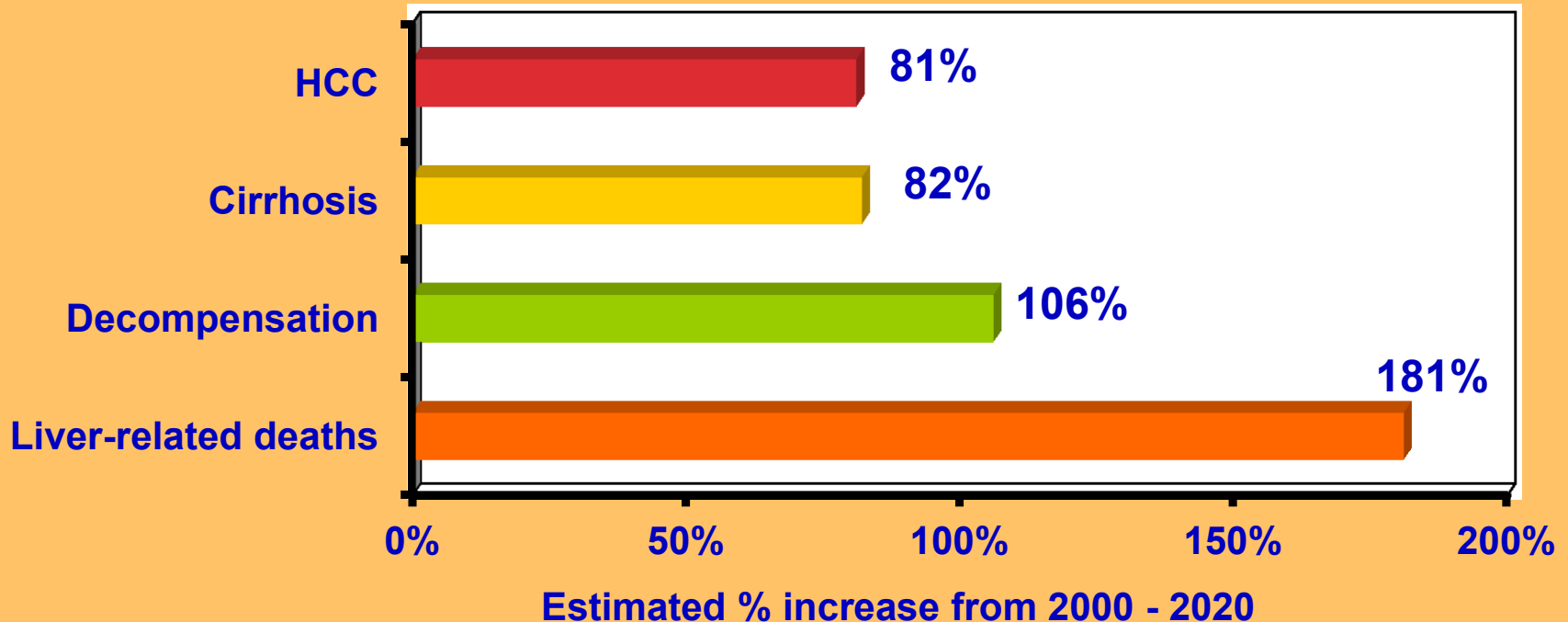
Mortality rates of HBV, HCV, and HIV; United States 1999-2007



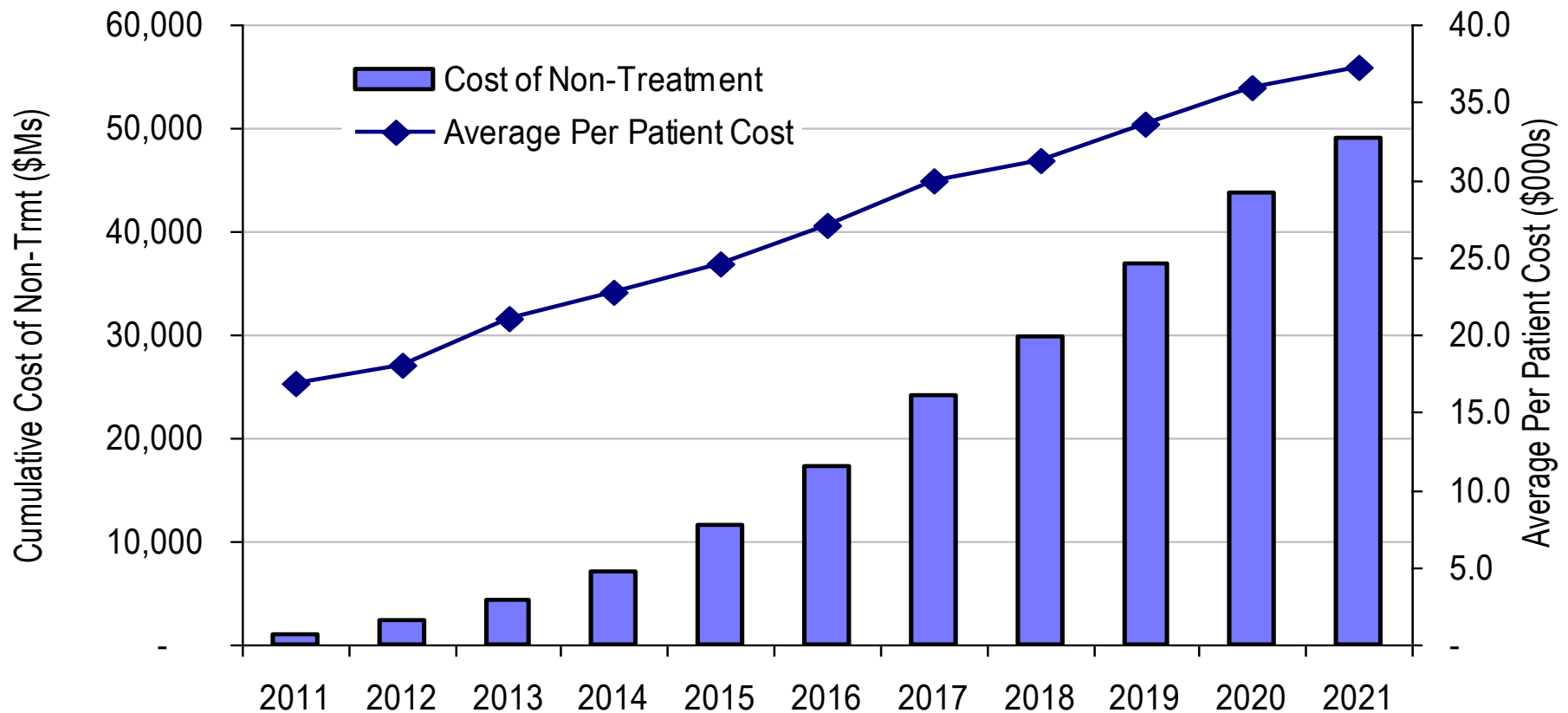
HCV Related Illness

Expected to Increase Significantly in the Coming Years

In the absence of novel treatments it's going to be a tsunami of HCV related liver failure, transplant, death & increased financial burden



A New Analysis of Dx and Rx of HCV Infections



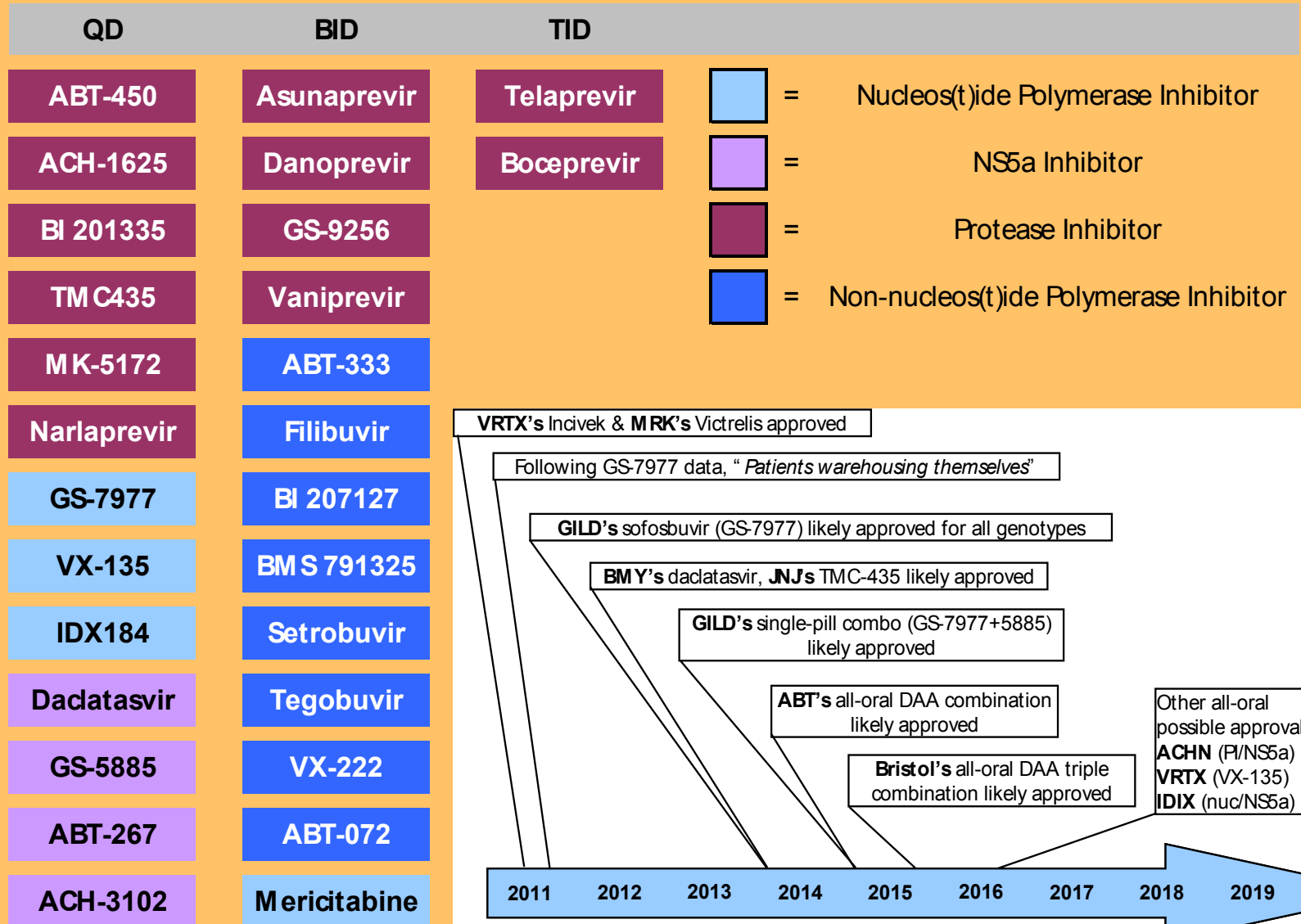
HCV Therapies: Changing Landscape

Advances for Unmet Medical Needs

“The times, they are a-changin’”

Bob Dylan

Market Will See An Influx of New Drugs Over the Next Few Years



Market Time Lines: Shaping the Future

VRTX's Incivek & MRK's Victrelis approved

Following GS-7977 data, "*Patients warehousing themselves*"

GILD's sofosbuvir (GS-7977) likely approved for all genotypes

BMJ's daclatasvir, JNJ's TMC-435 likely approved

GILD's single-pill combo (GS-7977+5885) likely approved

ABT's all-oral DAA combination likely approved

Bristol's all-oral DAA triple combination likely approved

Other all-oral possible approvals:
ACHN (PI/NS5a)
VRTX (VX-135)
IDIX (nuc/NS5a)

2011

2012

2013

2014

2015

2016

2017

2018

2019

The Game is not over

- ❖ Assuming Sofosbuvir (PSI/GS-7977) is approved by Q4 2013; new IND are behind by 3 years.
- ❖ Gilead may be able to treat at most half a million people per year With only 1.5 – 2 MM people treated over 3 yrs, there is still majority of the world and US market available.
- ❖ > 60 MM people who can pay will be available for treatment

There is still another opportunity: Shift in focus to difficult to treat persons

Several unmet needs remain:

- **Cirrhosis**
- **DAA/PR failures**
- **co-infected with HIV or HBV**
 - **non-GT1**
- **IFN intolerant or contraindicated**
- **bleeding disorders**
- **pediatrics**
- **opiate substitution therapy**
- **null-responders**

Too few Tx persons to come to any conclusion

Three Waves of Treatment with Leading Drug Sofosbuvir Leading to Cure Tsunamis

- Sofosbuvir as a single DAA plus Riba
- Sofosbuvir/NS5a or PI for genotype 1
- Final regimen, short in duration, one size fits all that is pangenotypic and SVR rates $> 90\%$ in the real world (nuc as backbone + PI/NS5a or two nucs)



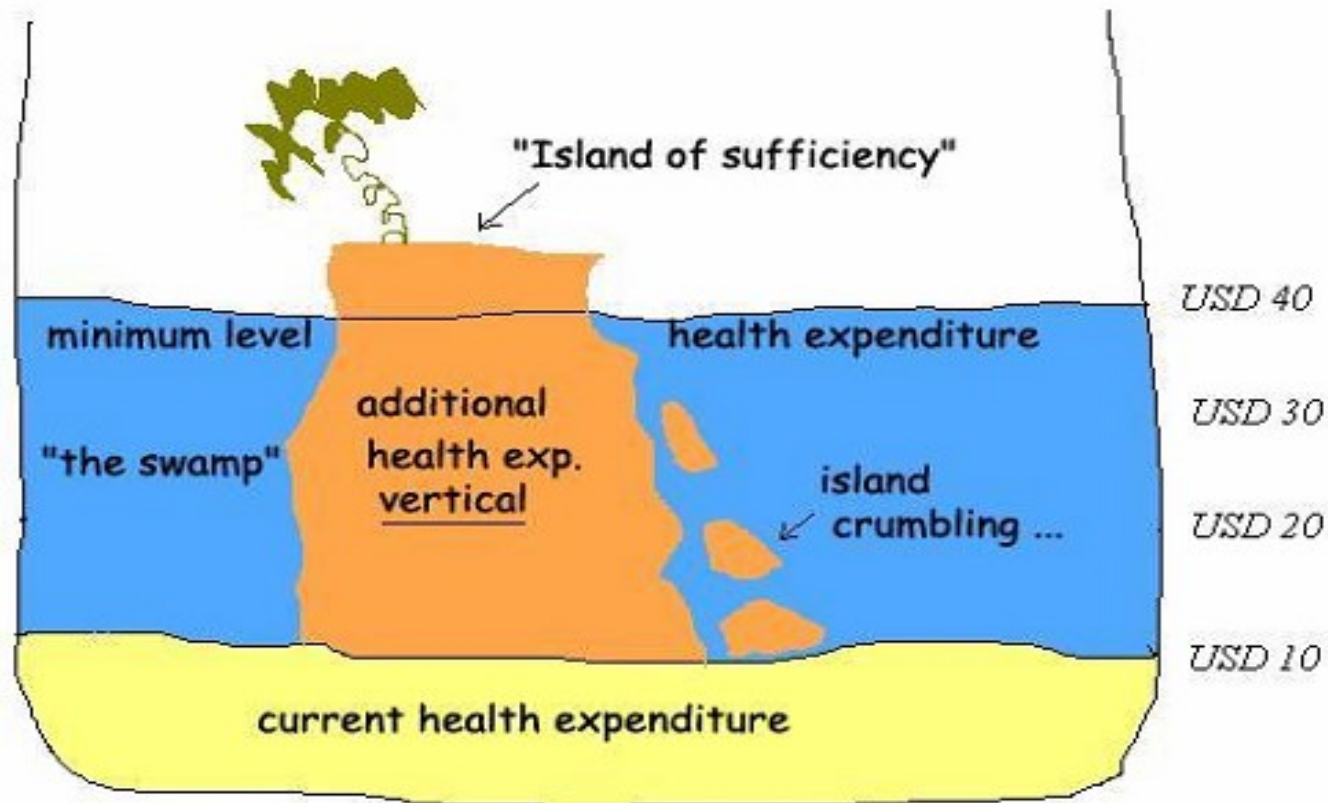
....The US and EU are Only ~5% of the Total Worldwide HCV Population



170MM People HCV Infected Worldwide

The HCV response will create islands of sufficiency in a swamp of insufficiency

The "vertical approach"

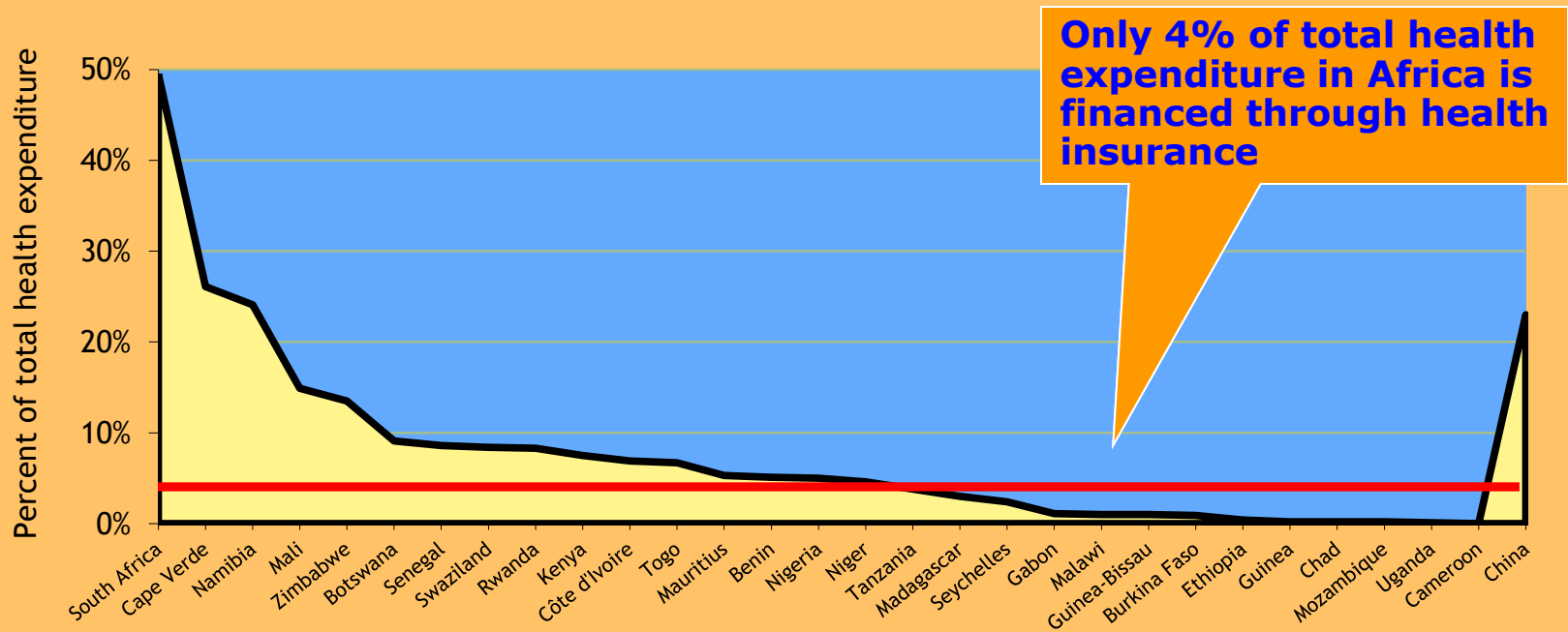


Health systems in Africa

Risk pooling is very scarce

Africans lack protection against medical costs; solidarity is limited

Social security and private prepaid health care spending



The Gaza Problem / What to Eat Now / The New Wii

TIME

Africa

It's the world's next economic powerhouse. But huge challenges lie ahead By Alex Perry

Rising



INSIDE THIS WEEK: TECHNOLOGY QUARTERLY

The Economist

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Economist.com

President Newt? Brace yourselves

Britain's coming recession

Why India needs Walmart

France tries to stay AAA

The science of ethical foie gras

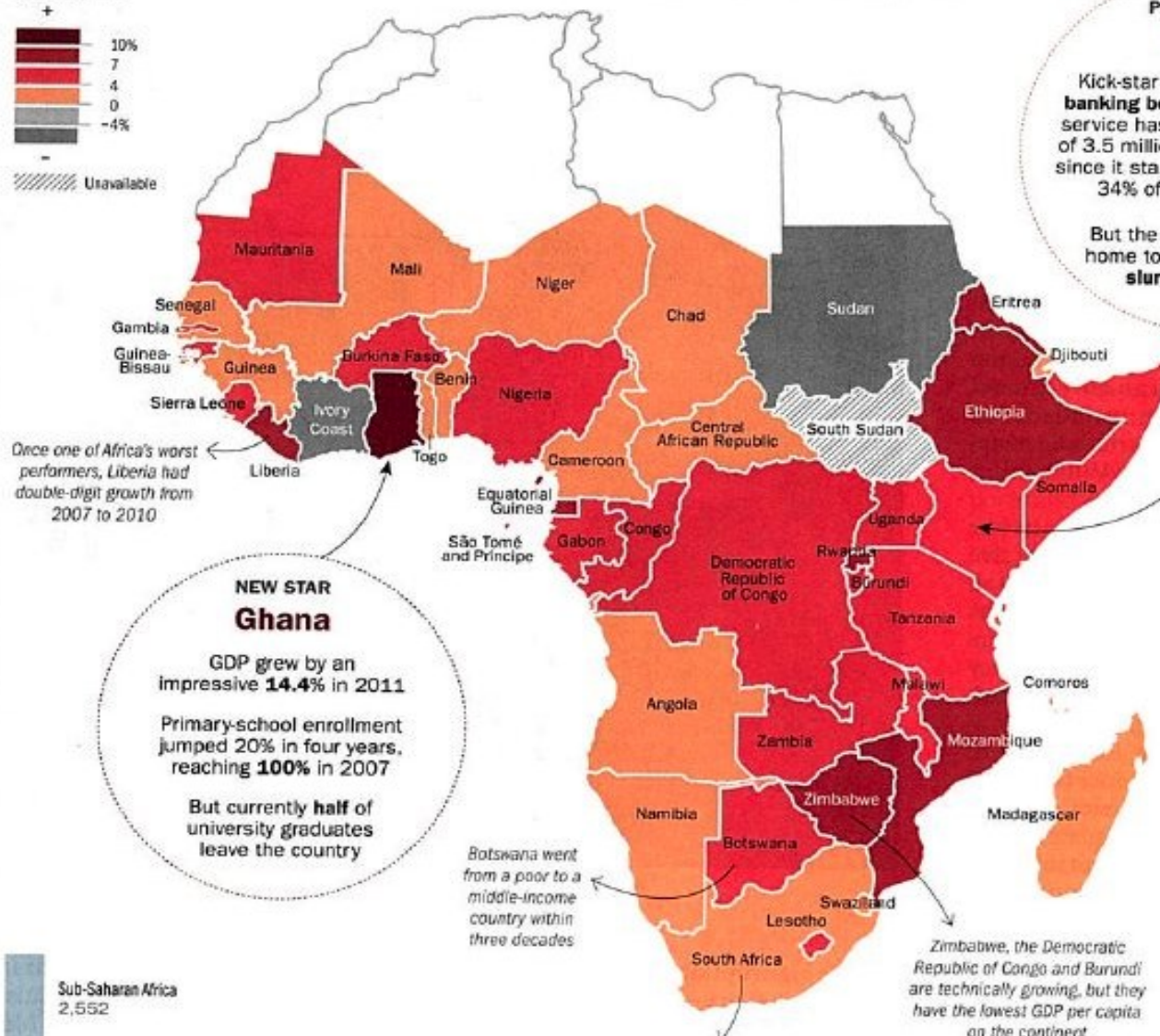
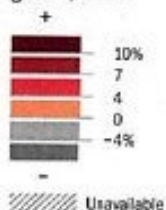
Africa rising



Growing Pains

Sub-Saharan Africa has the second fastest growing regional economy in the world, after Asia. But huge challenges remain, even in countries that are experiencing boom times

Real GDP growth, 2011



Once one of Africa's worst performers, Liberia had double-digit growth from 2007 to 2010

NEW STAR Ghana
 GDP grew by an impressive **14.4%** in 2011
 Primary-school enrollment jumped 20% in four years, reaching **100%** in 2007
 But currently **half** of university graduates leave the country

Botswana went from a poor to a middle-income country within three decades

POWERHOUSE Kenya
 Kick-starting Africa's **mobile-banking boom**, Kenya's M-PESA service has grown by an average of 3.5 million customers per year since it started in 2007, reaching 34% of Kenyans in 2011
 But the capital, Nairobi, is home to **one of the largest slums** in the world

QUIET ACHIEVERS
 These island countries boast solid economic growth and high scores in health and education



Zimbabwe, the Democratic Republic of Congo and Burundi are technically growing, but they have the lowest GDP per capita on the continent

Although classified as an upper-middle-income country by the World Bank, South Africa has one of the most unequal societies in the world

Sub-Saharan Africa
 2,552

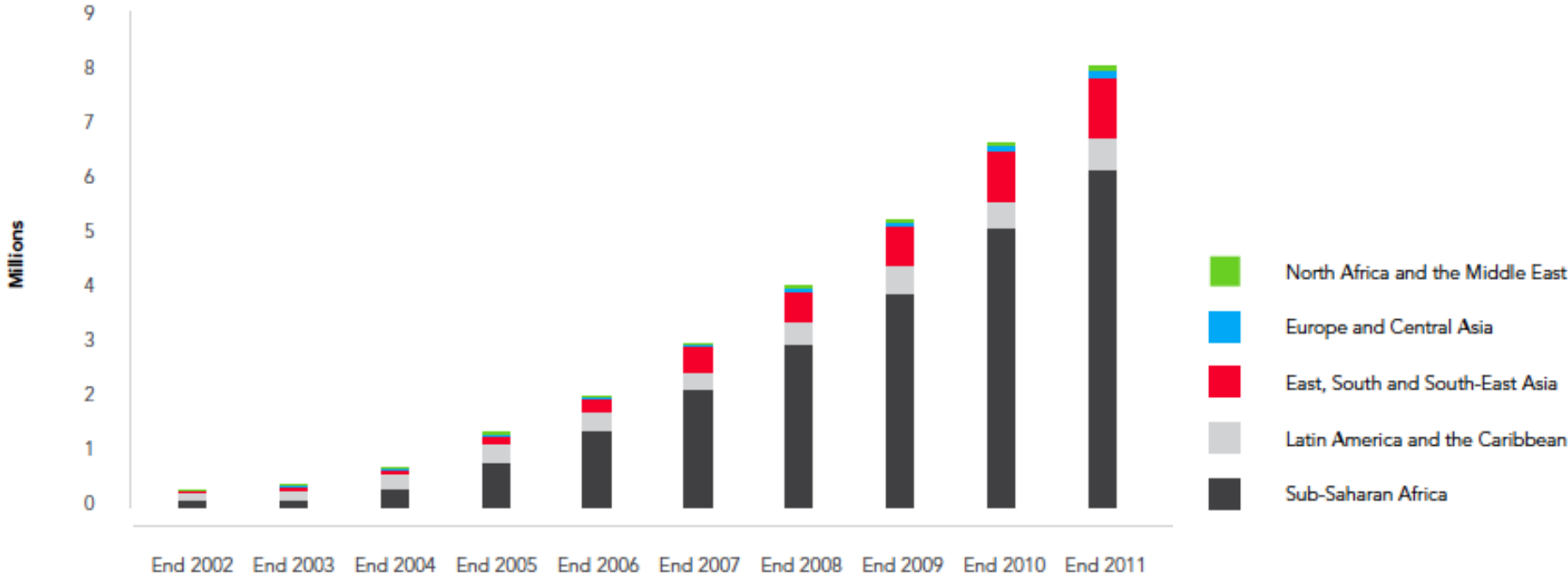
Lessons from HIV:
Reasons not to introduce HAART in
resource-poor settings in 1996

- **Too expensive**
- **Too complex**
- **Prevention more important than treatment**

Positive developments (“milestones”) by 2012-13 bringing HAART to resource poor settings

- **Price reduction of antiretroviral agents (Accelerating Access Initiative, etc) (2000)**
- **Declaration of Commitment of the United Nations General Assembly Special Session on HIV/AIDS (UNGASS) (2001)**
- **Establishment of funding mechanisms:**
 - World Bank Multicountry AIDS Program (MAP, 2000)
 - Global Fund to fight AIDS, TB and malaria (GFATM, 2002)
 - President’s Emergency Plan for AIDS Relief (PEPFAR, 2003/2004)
- **WHO Treatment Guidelines + uptake of antiretroviral agents in WHO Model List of Essential Medicines (2002)**
- **WHO’s “3by5” initiative: “3 million people in resource-poor settings on antiretroviral therapy by the end of 2005”**

Number of people receiving antiretroviral therapy in low- and middle-income countries, by region, 2002–2011



Source: 2012 country progress reports (www.unaids.org/cpr).

Before ...



HCV shows no visible scars like HIV that inspire the public to advocate solutions

After ...



Global Eradication Solutions

We must meet the silence of HCV's forward march with resonant opposition

Keys to successful eradication:

- ❖ **Public awareness**
- ❖ **Government action** (local, state, national, international)
- ❖ **Emphasize that new drugs can cure**

Increase awareness through:

- ❖ **Universal screening to unmask “silent” infections**
- ❖ **Education that empowers**
- ❖ **Care for prisoners, drug addicts, children & the poor**

Global Eradication Solutions

Translate education to **advocacy**

- ❖ Confront government with the **ethical and moral responsibility** to screen and treat
- ❖ Intensify government, UN & WHO action to become proportional to burden of HCV
- ❖ Governments must cultivate **financial and political will** to step up to the opportunity to eradicate another global plague (e.g., smallpox, polio)

HCV ERADICATION WORLDWIDE IS POSSIBLE

*A pessimist sees the difficulty in
every opportunity;*

*An optimist sees the opportunity
in every difficulty*

Winston Churchill

“The ultimate benefit of cures for HCV will be measured by the costs they avoid, but by the lives they save”



*Supported by NIH, CFAR, and the Department of Veterans Affairs
COI: I am a founder & shareholder of Idenix & RFS Pharma LLC*