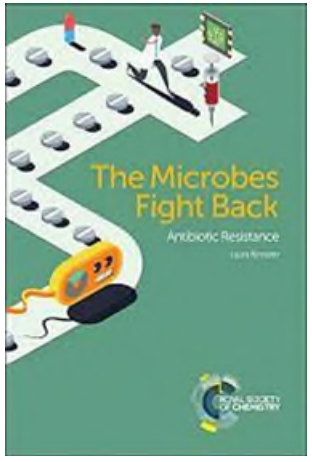
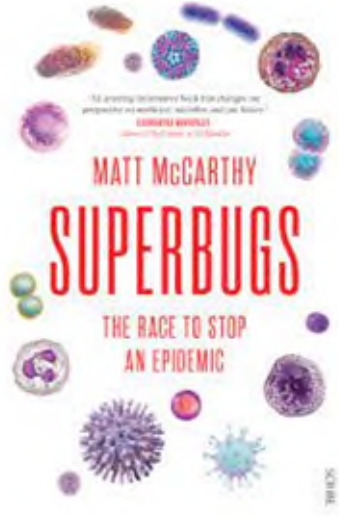
The Unending Human Battle with the Microscopic World

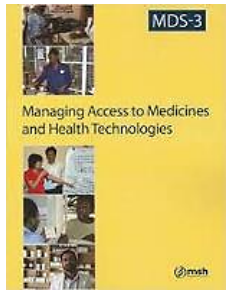
- And my small part in it





Speaker:

Prof. Andy Barraclough
Global Public Health Expert



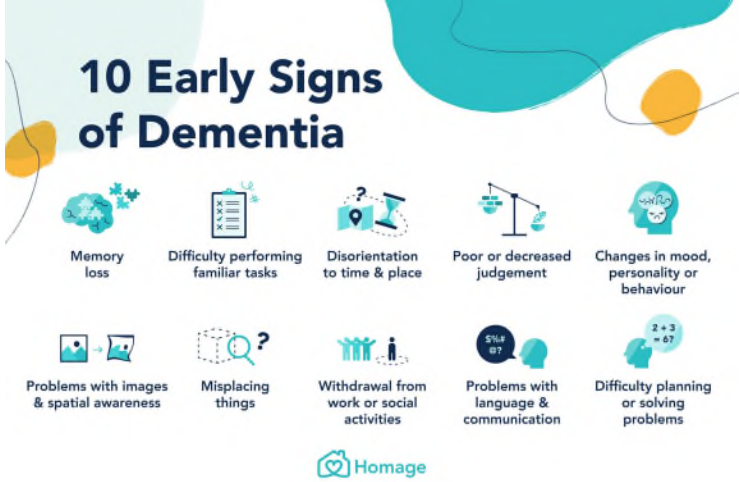
He is the Professor of Public Health and Director of Training at the Empower School of Health.
Andy is one of the co- authors of the 'Yellow Book', Managing Access to Medicines and Health technlogies by MSH and WHO, and the e-Handbook of Health Systems in Action.

He has over 30 years of experience of working in low and middle income countries. The main focus of previous experience includes effective management of pharmaceuticals, vaccines and medical commodities, and especially the implementation of programs for the introduction of new medicines and rapid diagnostics for neglected tropical diseases.

He has presented on Rational Use of Medicines (RUM) and Anti-Microbial Resistance (AMR) at many conferences, seminars and webinars in the SE Asia region, and has authored the RUM and AMR training courses for the Empower School of Health Master's Degree Course in Healthcare Procurement and Supply Chain Management.

Most recently, he has authored the Global Outbreak Alert and Response Network (GOARN) Medical Supply Chains for Emergency Response Covid-19 Platform, pandemic preparedness training modules and presented at a series of webinars on RUM and AMR in the era of Covid-19.

ADVISORY



- I am old.
- I am in the early stages of dementia – I may slur my words, stumble over some words, repeat myself and at times veer off subject and ramble.
- Your patience and understanding is required.
- I have personally suffered from some of the Neglected Tropical Diseases I mention:
  - Latent TB, probably from childhood milk
  - Malaria – 4 times – I know global warming is real and its impact on disease patterns, and the treatment failures that Anti-Microbial Resistance causes
  - Dengue and Dengue Hemorrhagic Fever
  - Amoebic dysentery, Amoebic hepatitis
- So, I know the battle with microbes is real, and not over yet

Disclaimer

•The views and opinions expressed in this presentation are those of the Presenter and do **not** necessarily represent official policy or position of any of the organizations and bodies to which he is, or has been associated;

•The material in this presentation is general background information. This information is given in outline and summary form and does not purport to be complete. In particular there are aspects of diseases which I do not mention which might be appropriate to you. This presentation was created for informational purposes only.

It MUST not be considered or used as medical/clinical advice or a personal recommendation.

•The content of this presentation is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your physician or other qualified health provider with any questions you may have regarding a medical condition. Never disregard professional medical advice or delay in seeking it because of something you have read in this Presentation.

Declaration of Interests

Prof. Andy Barraclough:

I do **NOT** practice clinical medicine in Thailand.

I do **NOT** provide individual medical/clinical advice.

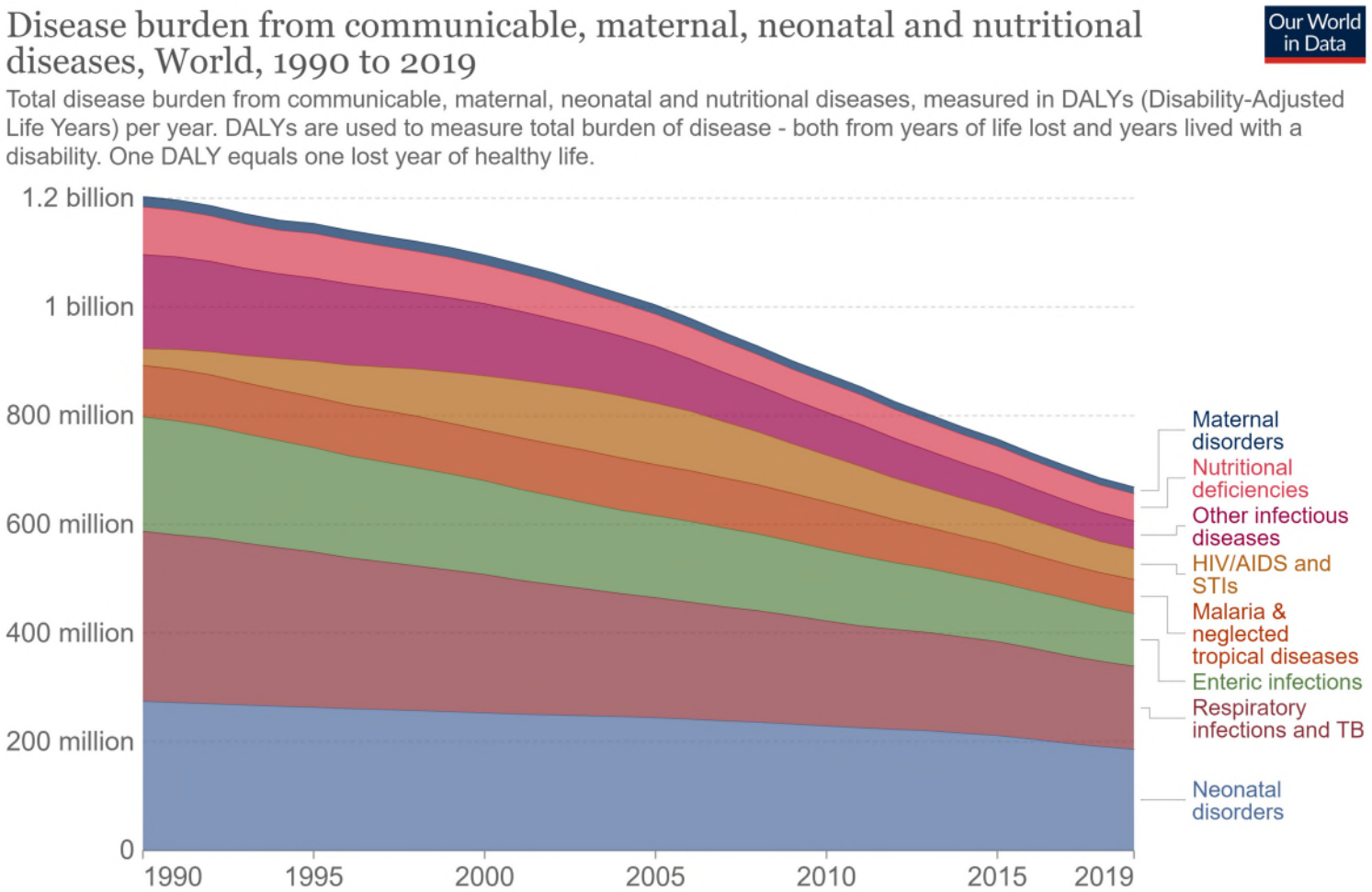
- I have the following financial interest or relationship(s) to disclose with regard to the subject matter of this presentation:
- I have received funding from, and/or worked in various capacities with the following organizations which have enabled my activities:
- Empower School of Health
- UN agencies, World Health Organization especially WHO SEARO
- GOARN Global Outbreak Alert Response Network

Acknowledgments

- The majority of the materials contained in this presentation are extracted from published information which is freely available in the public domain, from such bodies as:
  - Empower School of Health
  - World Health Organization
  - UK NHS
- Wherever possible I have cited the internet link to the published information.

Microbes: Surely it's a battle that is already won?

There has been a significant reduction in global burden from communicable, neonatal, maternal and nutritional diseases in recent decades, falling from 1.2 billion in 1990 to below 670 million in 2019 (around a 44 percent reduction).

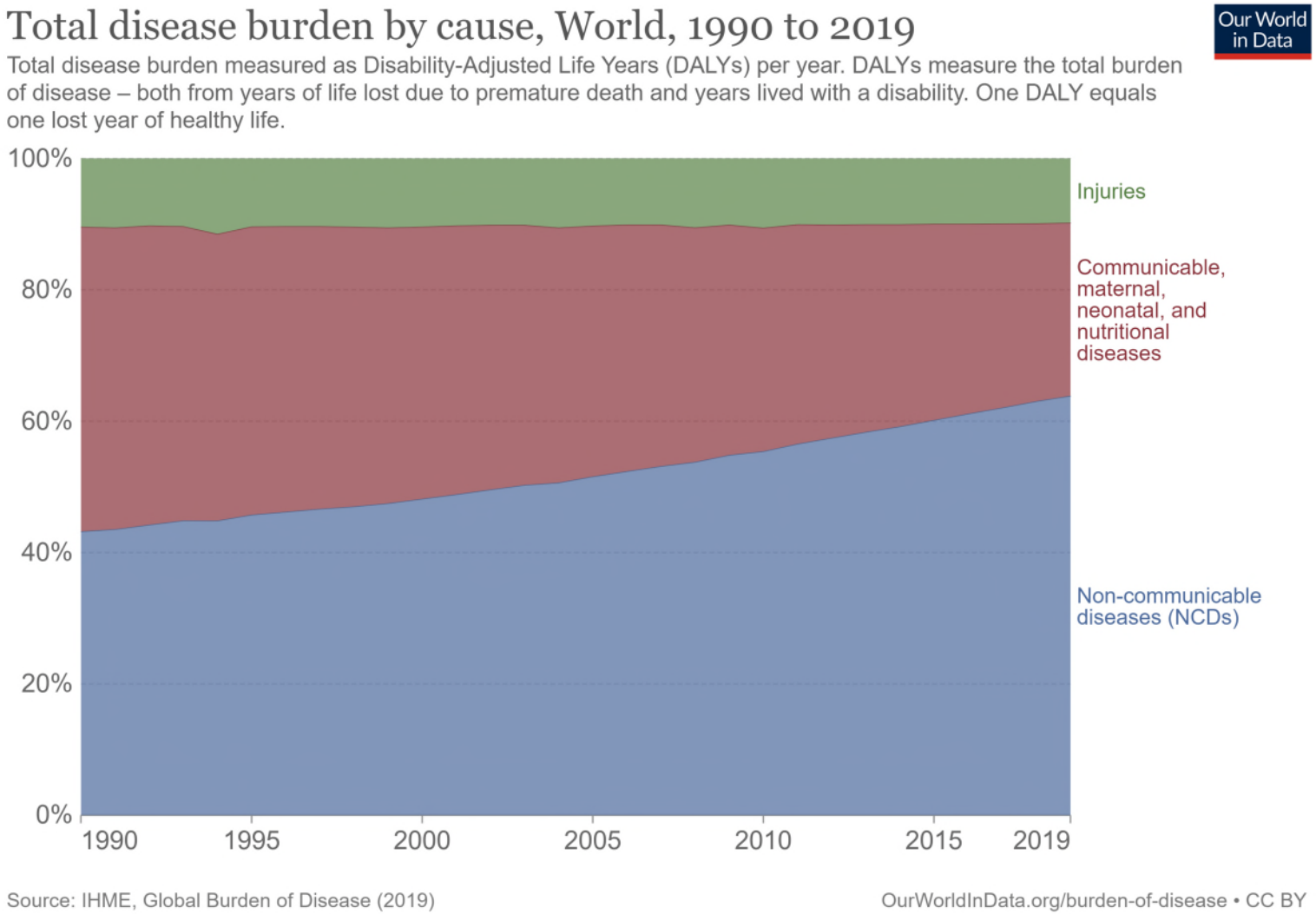


https://ourworldindata.org/burden-of-disease#:~:text=There%20has%20been%20a%20significant,around%20a%2044%20percent%20reduction).

Its no longer infectious diseases that are the prime killers – its Non Communicable Diseases (NCDs)

At a global level, in 2017 more than **60 percent of the burden of disease results from non-communicable diseases** (NCDs), with 28 percent from communicable, maternal, neonatal and nutritional diseases, and just over 10 percent from injuries.

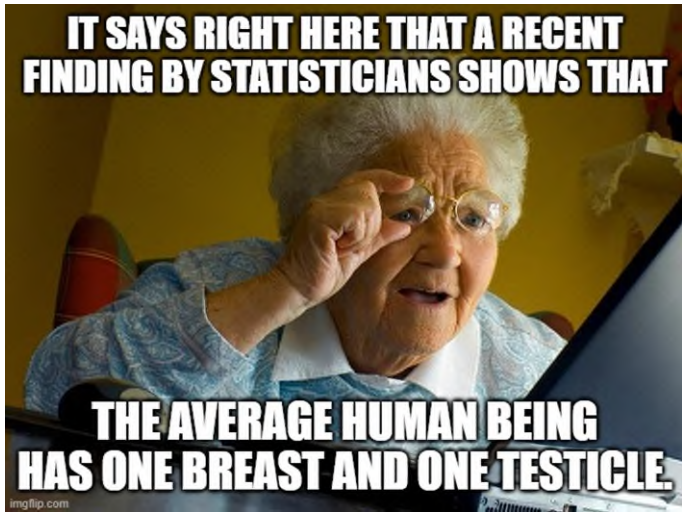
The chart also shows a notable shift since 1990, when communicable diseases held the highest share at 46 percent.

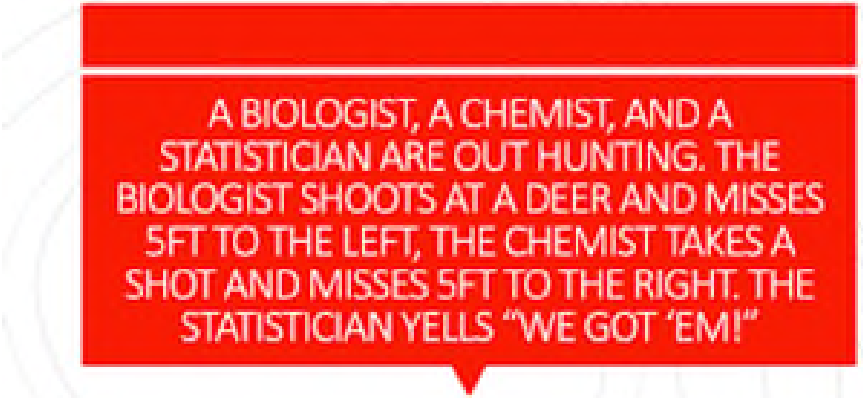


How averages can be misleading

- Many of you in this room will be over 60 years old
- ALL of you are in SE Asia
- Many (most) of you will have some underlying chronic medical condition – diabetes, hypertension, digestive issues, reduced immune system, etc.

- The situation for YOU looks VERY different from the average

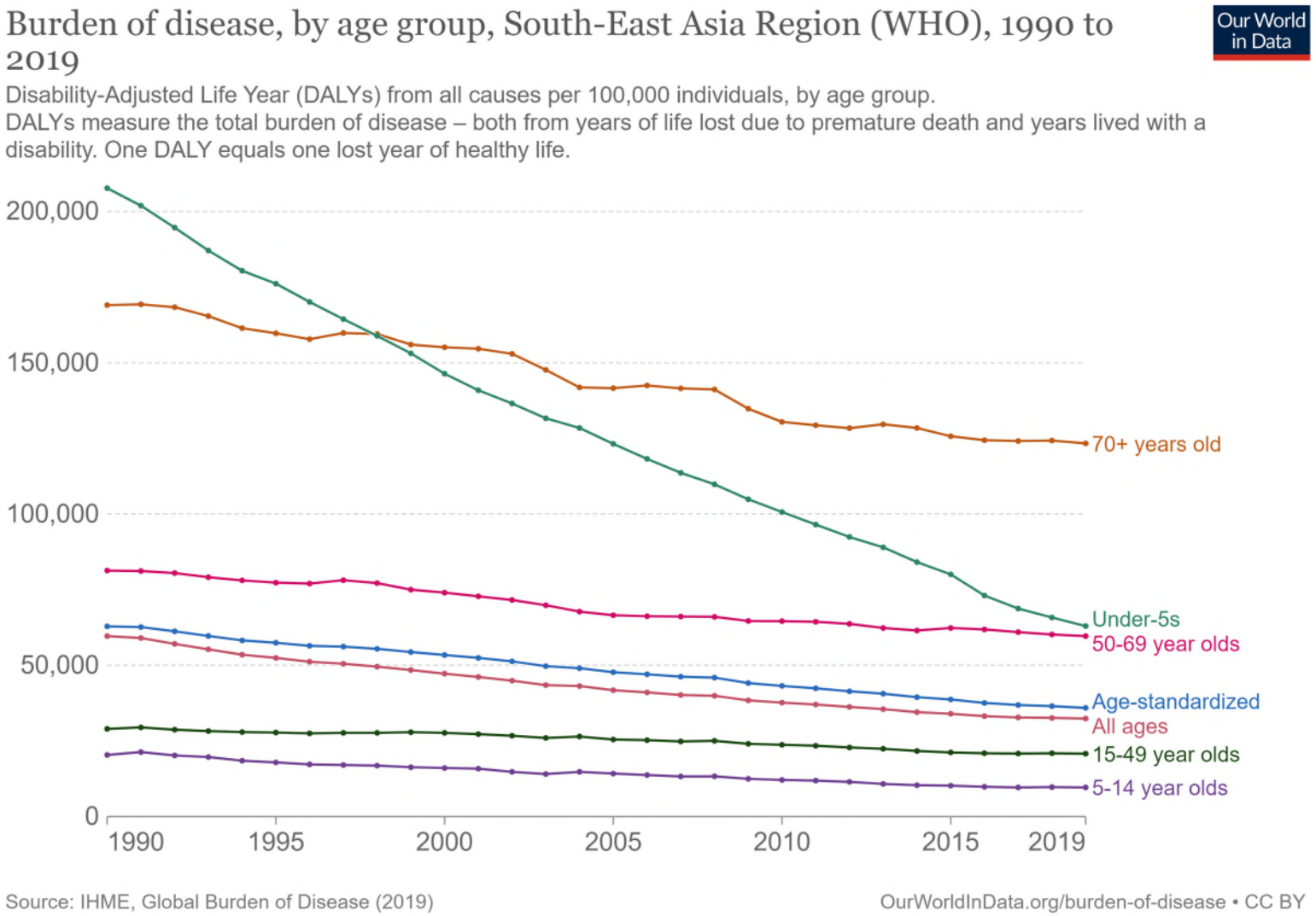




Disease burden by age over time in SE Asia

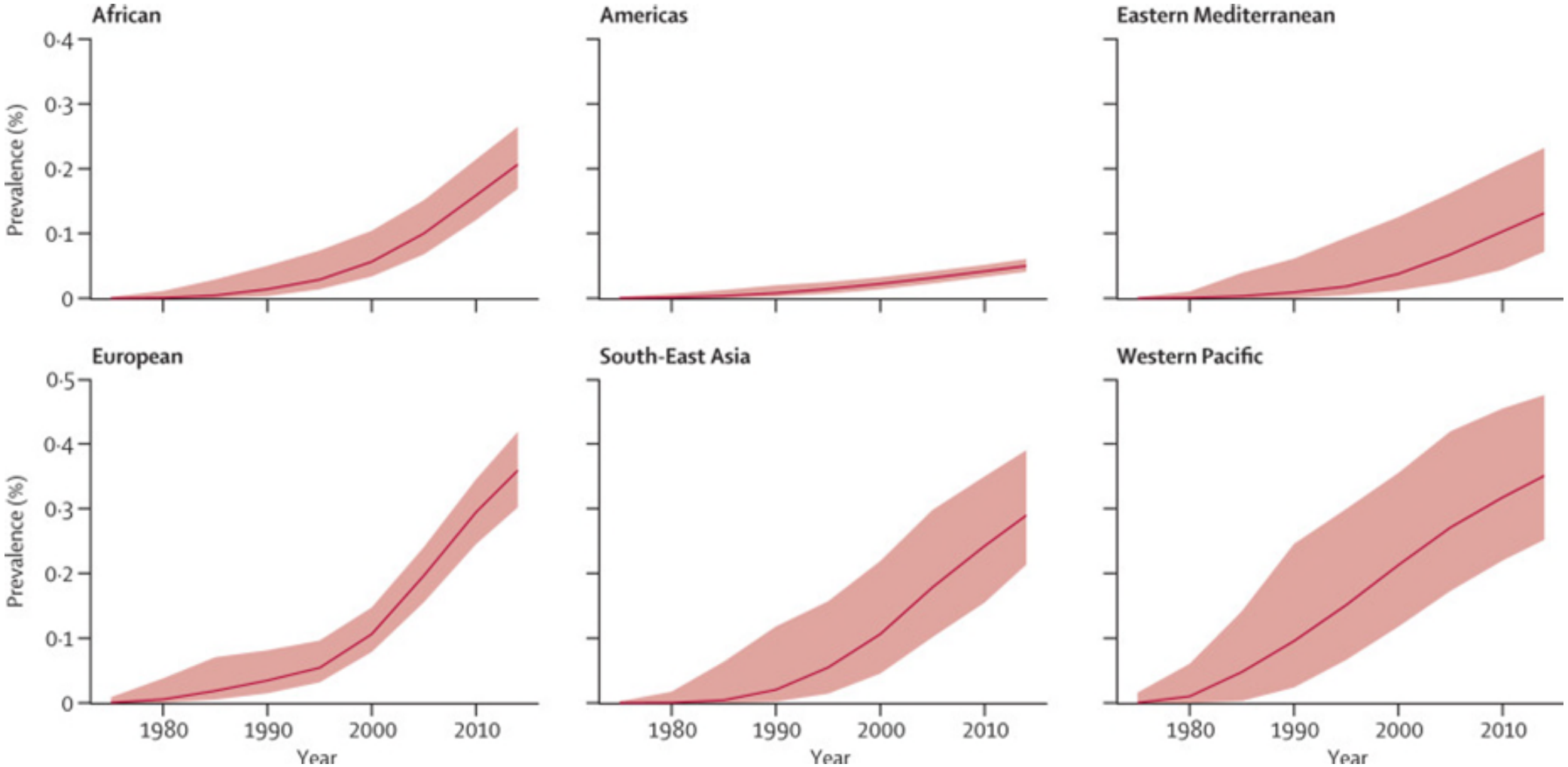
Disease Burden in Under-5s (green line) has fallen massively BUT disease burden in over 50s (red line) has fallen NOT by much

https://ourworldindata.org/burden-of-disease#the-disease-burden-by-age



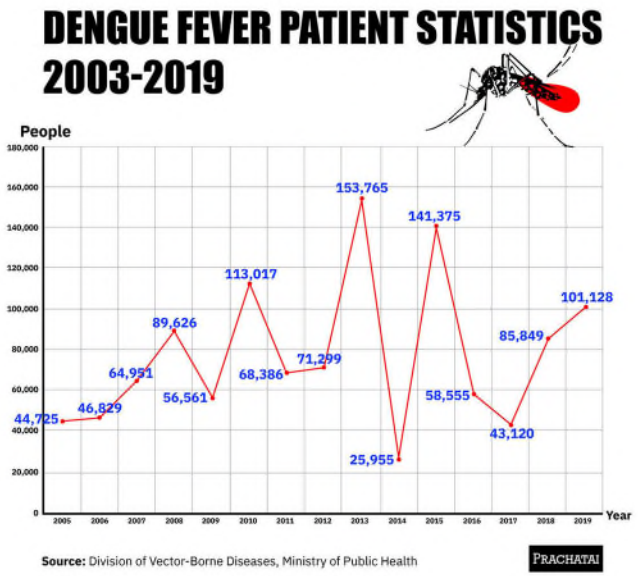
Some Diseases are on the increase

Prevalence of latent multidrug-resistant tuberculosis infection, by WHO region



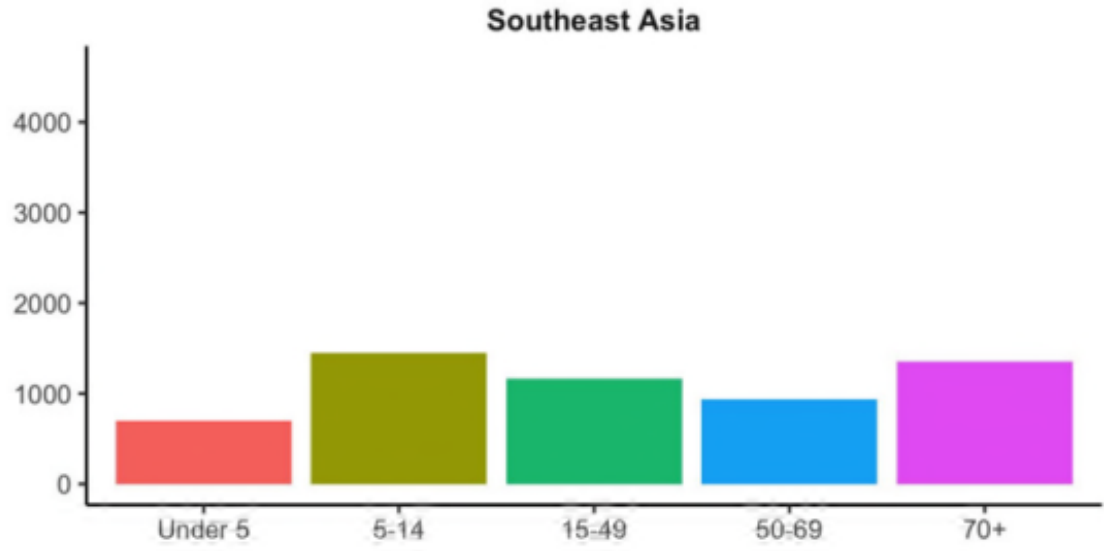
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2819%2930307-X/fulltext

Dengue



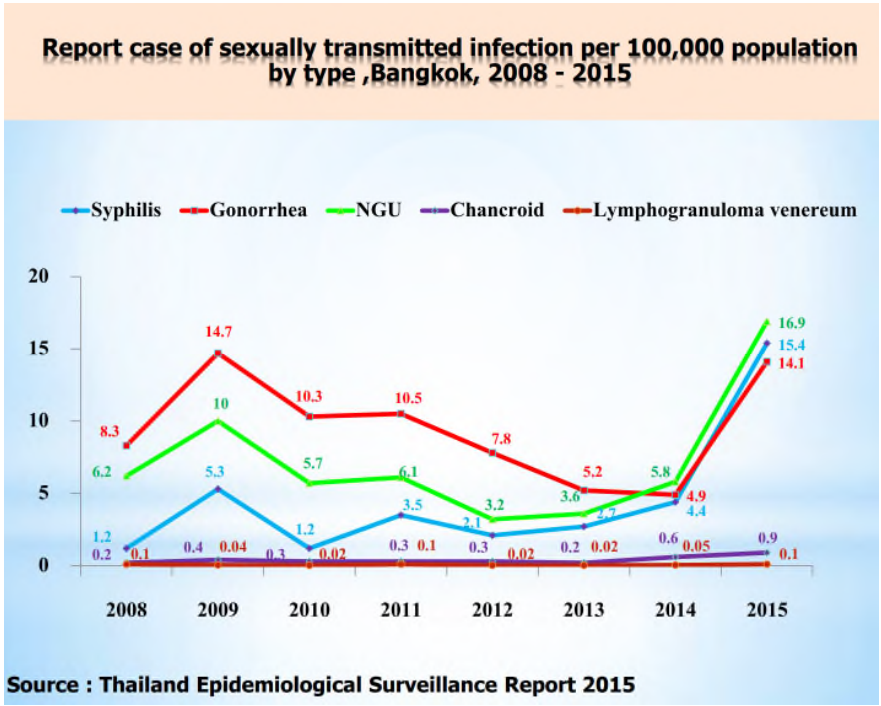
- From 2015 to 2019, dengue cases in SEA region increased by 46% (from 451,442 to 658,301) whereas deaths decreased by 2% (from 1,584 to 1,555).
- Five countries (India, Indonesia, Myanmar, Sri Lanka and Thailand) are among the 30 most highly endemic countries in the world. In spite of the control efforts, there has been a significant increase in the number of dengue cases over the years, though improvement has been made in case management and reduction of CFR to below 0.5%

Incidence 2019 from
Dengue Incidence Trends and Its Burden in Major Endemic Regions from 1990 to 2019



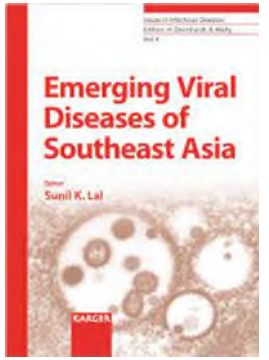
Sexually Transmitted Infections

- Every single day, more than one million sexually transmitted infections (STIs) are contracted across the world, a report by the World Health Organization (WHO) suggests.
- The report was released in early June 2019, suggesting that four STDs top the list in terms of most common infection – chlamydia, gonorrhoea, trichomoniasis and syphilis.
- Thailand has been seeing a steady increase in the number of new syphilis cases since 2013. In 2018, the number of new diagnoses in the mentioned young adults age group was 36.9 per cent higher than the number of new syphilis cases in 2017.
- In Thailand, 0.7 per cent of the sex workers carry an active syphilis infection, as per the WHO statistics.



- https://www.shimclinic.com/blog/number-of-syphilis-diagnoses-in-thailand-goes-up-what-are-the-dangers

New Emerging Diseases

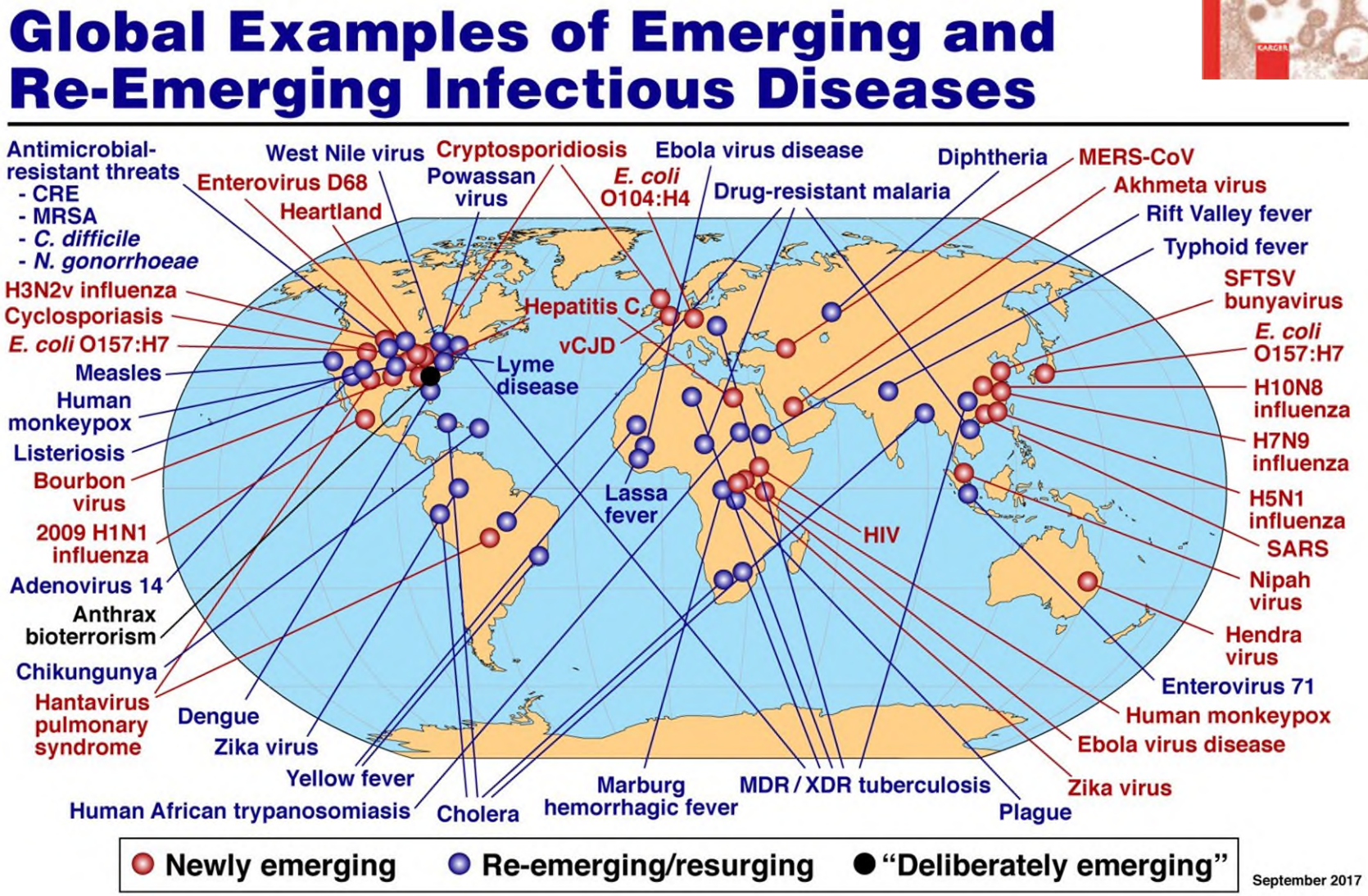


For Thailand:

Nipah virus (NiV) infection causes encephalitis and has > 75% mortality rate, making it a WHO priority pathogen due to its pandemic potential.

Both Malaysian and Bangladeshi NiV strains have been found in fruit bats in Thailand.

High identity shared between the NiV genome from Thai bats and the Bangladeshi patient highlights the outbreak potential of NiV in Thailand.



Climate Change

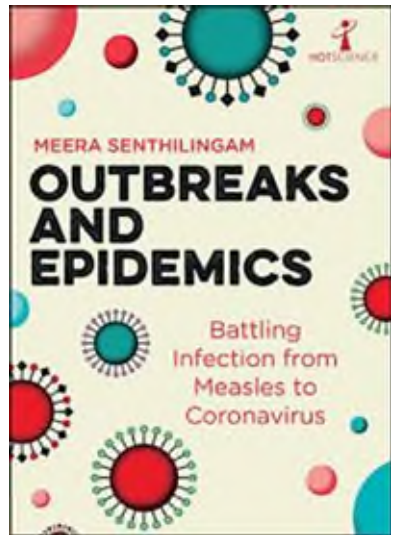
As the climate changes, the risk also increases for health threats such as:

- Anaplasmosis
- Antibiotic-resistant infections
- Dengue
- Fungal diseases like valley fever and histoplasmosis
- Hantavirus
- Lyme disease
- Rabies
- Salmonellosis
- West Nile virus disease
- Anthrax
- Cryptosporidiosis
- Ehrlichiosis
- Giardiasis
- Harmful algal bloom-associated illness
- Plague
- Spotted fever rickettsiosis
- Vibriosis

https://www.cdc.gov/ncezid/what-we-do/climate-change-and-infectious-diseases/index.html

What Does This Mean?

- The battle between human health and the microscopic world is far from over.
- ‘Old’ diseases are re-emerging
- New diseases are emerging
- Climate change is driving different disease patterns
- Resistance to medicines is increasing, and they are becoming less effective



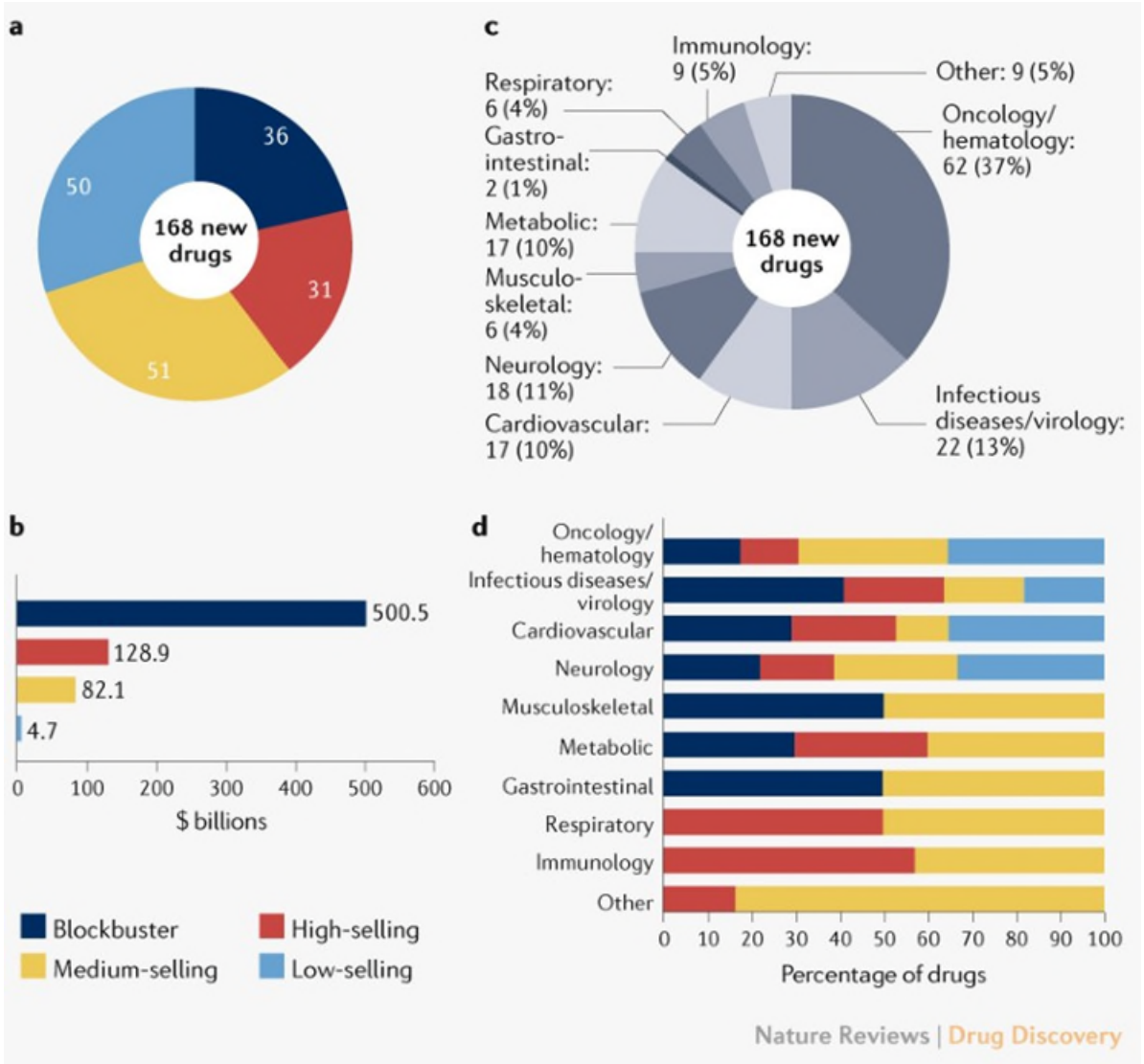
Infectious Diseases

- Infectious diseases are caused by microscopic organisms that penetrate the body's natural barriers and multiply to create symptoms that can range from mild to deadly. Although progress has been made to eradicate or control many infectious diseases, humankind remains vulnerable to a wide array of new and resurgent organisms.

Obstacles in Infection Treatment

- New, potentially dangerous bacteria, viruses, fungi and parasites such as severe acute respiratory syndrome (SARS) emerge every year.
- Previously recognized pathogens can evolve to become resistant to available antibiotics and other treatments.
- Population crowding and easy travel also make us more vulnerable to the spread of infectious agents.
- Recent concerns about bioterrorism have focused new attention on eradicated or rare infectious diseases such as smallpox and anthrax.
- Types of Infection

Well OK – but its just about inventing some new medicines – isn't it?



- Less than 13% of new drugs are for infectious diseases
- A 2015 analysis by Philipsborn et al. found that poverty-related diseases represent 14% of the global burden of disease, yet only attract 1.3% of global R&D expenditure
- Neglected Tropical Diseases remain neglected

Its not just new medicines
Its getting the medicines to the patients

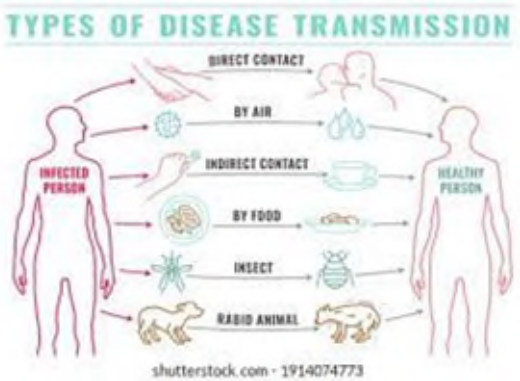
- Nearly 2 billion people have no access to basic medicines, causing a cascade of preventable misery and suffering.
- WHO has struggled to improve access to medicines throughout its nearly 70-year history

- https://cdn.who.int/media/docs/default-source/essential-medicines/fair-price/chapter-medicines.pdf?sfvrsn=adcffc8f_4&download=true

- The UN Commission noted that addressing barriers and ensuring access could save up to 6 million lives over five years and contribute to reductions in maternal mortality rates and under-5 deaths.

- https://gcgh.grandchallenges.org/challenge/health-systems-strengthening-ensuring-effective-health-supply-chains-round-19

Why Access matters in the fight

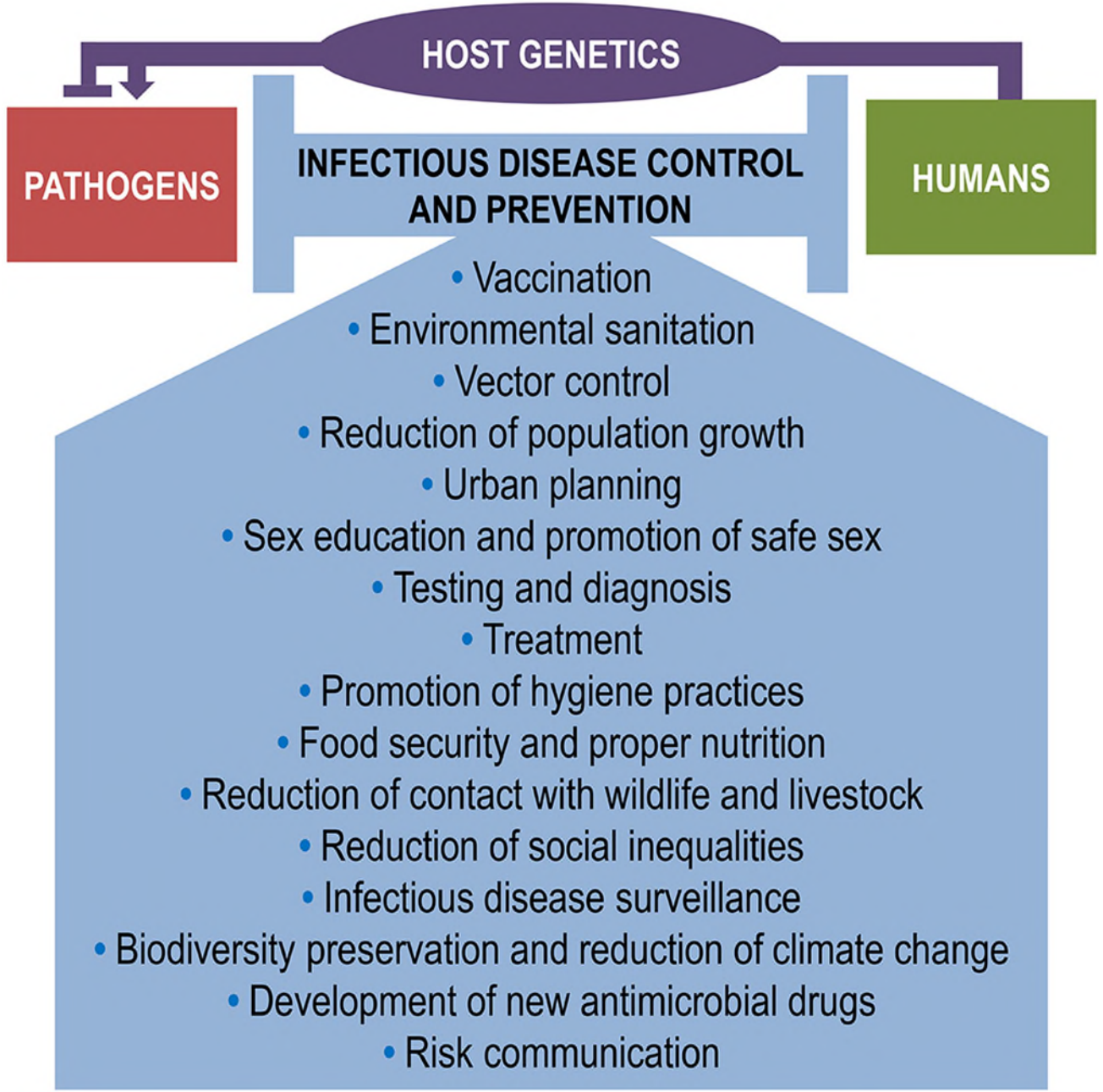


- Of course there are ethical, human rights and equality and humanity issues

BUT, there are also clinical issues

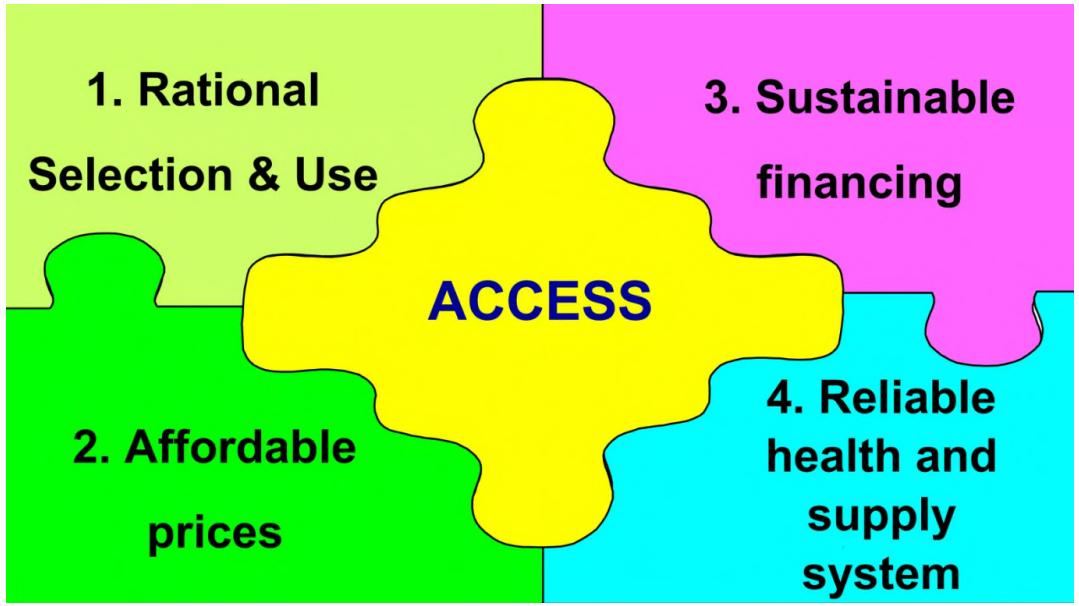
- Many diseases do not arrive spontaneously – they are transmitted
- If no one has malaria no one gets malaria – treating malaria benefits the whole community
- If no one has TB no one gets TB – treating TB benefits the whole community – after around one month of treatment patients are no longer infectious
- If no one has HIV no one gets HIV – after around 3 months of treatment patients are no longer infectious

The fight


HOST GENETICS
PATHOGENS
INFECTIOUS DISEASE CONTROL AND PREVENTION
HUMANS
• Vaccination
• Environmental sanitation
• Vector control
• Reduction of population growth
• Urban planning
• Sex education and promotion of safe sex
• Testing and diagnosis
• Treatment
• Promotion of hygiene practices
• Food security and proper nutrition
• Reduction of contact with wildlife and livestock
• Reduction of social inequalities
• Infectious disease surveillance
• Biodiversity preservation and reduction of climate change
• Development of new antimicrobial drugs
• Risk communication

My roles in the fight

- Advocacy
- Access
- Availability
- Awareness
- Education
- Rational Medicine Use
- Pharmacovigilance

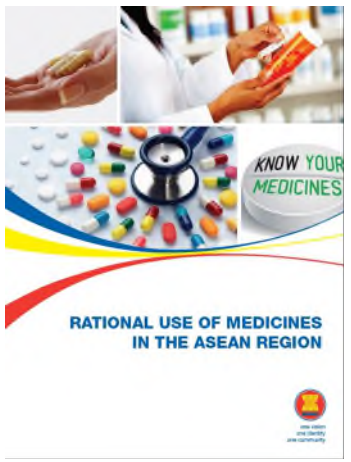


World Health Organization SE Asia
The South-East Asia Region Antimicrobial Stewardship 2022, Webinar Series

Rational Use of Medicines and Anti-Microbials

Empower School of Health

EMPOWER SCHOOL OF HEALTH



Advocacy – New Medicines

- Prior to 2010 there had been no new medicine to treat TB in forty years
- After extensive campaigning over 20 years, the organization Stop TB was formed
- The Stop TB Partnership brings together expertise from a broad spectrum of country, regional, and global partners in our shared mission to revolutionize the TB space and end TB by 2030.
- Founded in 2001, the Stop TB Partnership is a United Nations hosted organization that takes bold and smart risks to serve the needs and amplify the voices of the people, communities, and countries affected by TB.
- On December 31, 2012, the FDA approved the first new tuberculosis drug in four decades. SIRTURO™ (bedaquiline) was approved on the basis of phase two efficacy and safety data to treat multidrug-resistant tuberculosis (MDR-TB). Bedaquiline is manufactured by Johnson and Johnson and is the first medication exclusively manufactured for MDR-TB
- Global TB Report 2022 launch: Stop TB Partnership sounds the alarm on the TB funding crisis as TB deaths increase
- https://www.stoptb.org/

Sponsored by the Bill and Melinda Gates Foundation, the PAN-TB, or “Project to Accelerate New Treatments for Tuberculosis”, collaboration brings together non-profit, philanthropic, and private sector partners for a common mission to develop novel TB medicines that are better-tolerated, shorter in duration, and simpler to use than existing options.

2022 Global New TB Drug Pipeline[1] Updated 11/3/2022

Discovery | Preclinical Development | Clinical Development

Lead Optimization → Early Stage Development → GMP / GLP Tox. → Phase 1 → Phase 2 → Phase 3 → Regulatory Market Approvals

Indazole sulfonamides
Diarylthiazoles
DprE1 Inhibitors
Direct InhA Inhibitors
Mtb energy metabolism
Gyrase Inhibitors
Arylsulfonamides
Inhibitors of MmpL3, Translocase-1, ClpC1, PKS13, F-ATP synthase
Oxazolidinones
DnaE1 / Nargenicin analogs

TBD-09, TBD-10 (MK-7762, -3854)
MPL-447*
JSF-3285*
CPZEN-45*
NTB-3119*
MBX-4888A (1810)*
FNDR-10045*, FNDR-20364*

GSK-839*
OTB-658

BVL-GSK098*
GSK-286*
TBAJ-876
TBAJ-587
TBI-223
Macozinone* (PBTZ-169)

Sanfetrinem
Delpazolid
Sutezolid
Sudapyridine (WX-081)
BTZ-043*
TBA-7371*
OPC-167832*
GSK-656* (070)
Telacebec*
Pyrifazimine (TBI-166)
SPR720*
SQ-109*

Results Reported / Expected in 2022/23

TB Practecal
ZeNix
Simplici TB (4-month regimen)
Truncate TB (2-month regimens)
STREAM 2

Bedaquiline*
Delamanid*
Pretomanid*

*New chemical class. Known chemical classes for any indication are color coded: rifamycin, oxazolidinone, nitroimidazole, diarylquinoline, benzothiazinone, imidazopyridine amide, beta-lactam.

[1] New Molecular Entities not yet approved, being developed for TB or only conditionally approved for TB. Showing most advanced stage reported for each. Details for projects listed can be found at http://www.newtbdrugs.org/pipeline/clinical

Ongoing projects without a lead compound identified: http://www.newtbdrugs.org/pipeline/discovery

Underline = updates since May 2022

WORKING GROUP ON NEW TB DRUGS
www.newtbdrugs.org

Updated: November 2022

Understanding Access - Leprosy

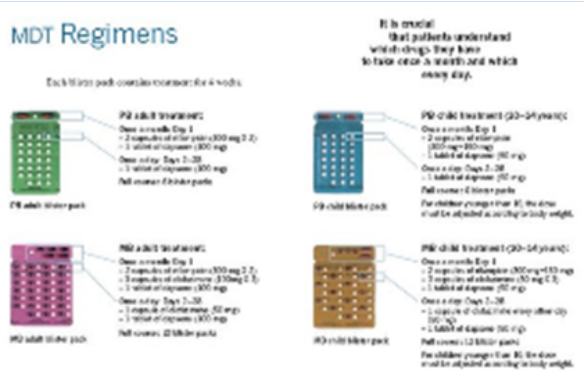
- In the 80s I was working at the Hospital Conde S. Januário in Macau
- I am called down to a ruckus to find a dentist refusing to treat a patient because they have leprosy – to then find that there is a Leper Colony on Colane Island.
- In the 1980s, thirty years after leprosy became curable, Macau was still running a leper colony. I considered it an utter disgrace.
- On the island of Colane – linked by a bridge to the Macau peninsular.

About 100 lepers lived in the Ka Ho leprosy, abandoned to themselves and in urgent need of care. The village was isolated and it could only be reached by boat.
https://www.indiegogo.com/projects/a-life-dedicated-to-the-lepers-in-macau#/

The lepers of Our Lady's Village

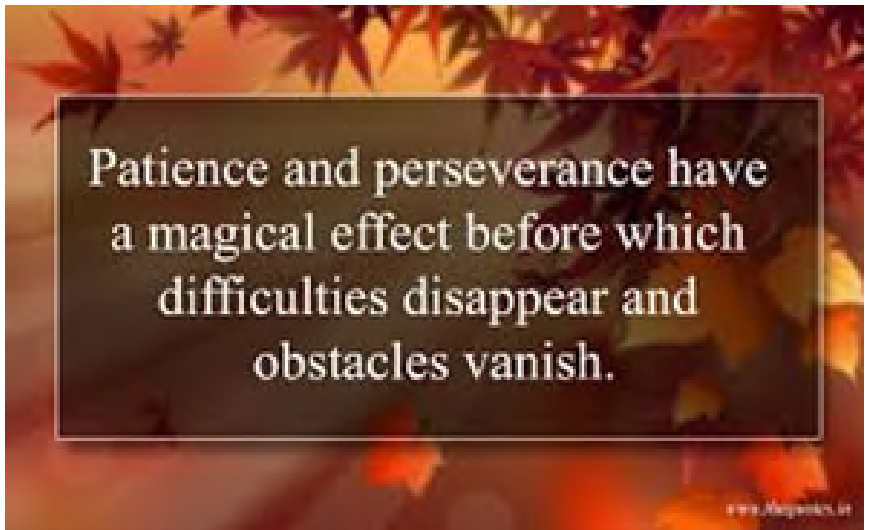
- *“In the early morning, a handful of men and women shuffle into a little stone church on a desolate and windswept point in the Portuguese-run territory of Macao.*
- *It's still dark as they file into the church, much as they have done every morning for more than 30 years. These are the lepers of Our Lady's Village. They have spent their lives in exile on the island of Coloane, one of the many tiny specks on the South China Sea.*
- *Their shadows, cast by meager candlelight, dance across a peaked ceiling. There are no deformities in this light.*
- *The 29 men and women are the remnants of a century-old leper colony which in its heyday housed several hundred.*
- *Most have been here since early childhood, cast out by families in southern China and loaded on to rickety boats that traveled under the dignity of darkness to Coloane.*
- *They have little memory of life outside their remote leprosarium, let alone the families that abandoned them.*
- ***Their enforced isolation should have ended in the 1950s with a cure for leprosy, but it did not……”***

Basel, January 29, 2021 — A renewed partnership agreement signed by Novartis and the World Health Organization (WHO) will drive the global push towards making leprosy history. The five-year extension of the partnership – which was first signed in 2000 – will see Novartis continue to donate multidrug therapy (MDT) medicines to treat leprosy up to the end of 2025.
https://www.novartis.com/news/media-releases/novartis-renews-who-medicine-donation-pledge-aim-ending-leprosy



Medicines Access

- So I thought there was a winning combination of medicines and BUT as I was to find – it was not enough
- You also need Patience, perseverance and a deep understanding of the realities of human nature to overcome stigma and discrimination



Access to medicines
Millions of yearly childhood deaths from diseases that could have been prevented or cured by existing medical products would be unthinkable in a fair and just world.
The world is neither
WHO has struggled to improve access to medicines throughout its nearly 70-year history…. Good health is impossible without access to pharmaceutical products.

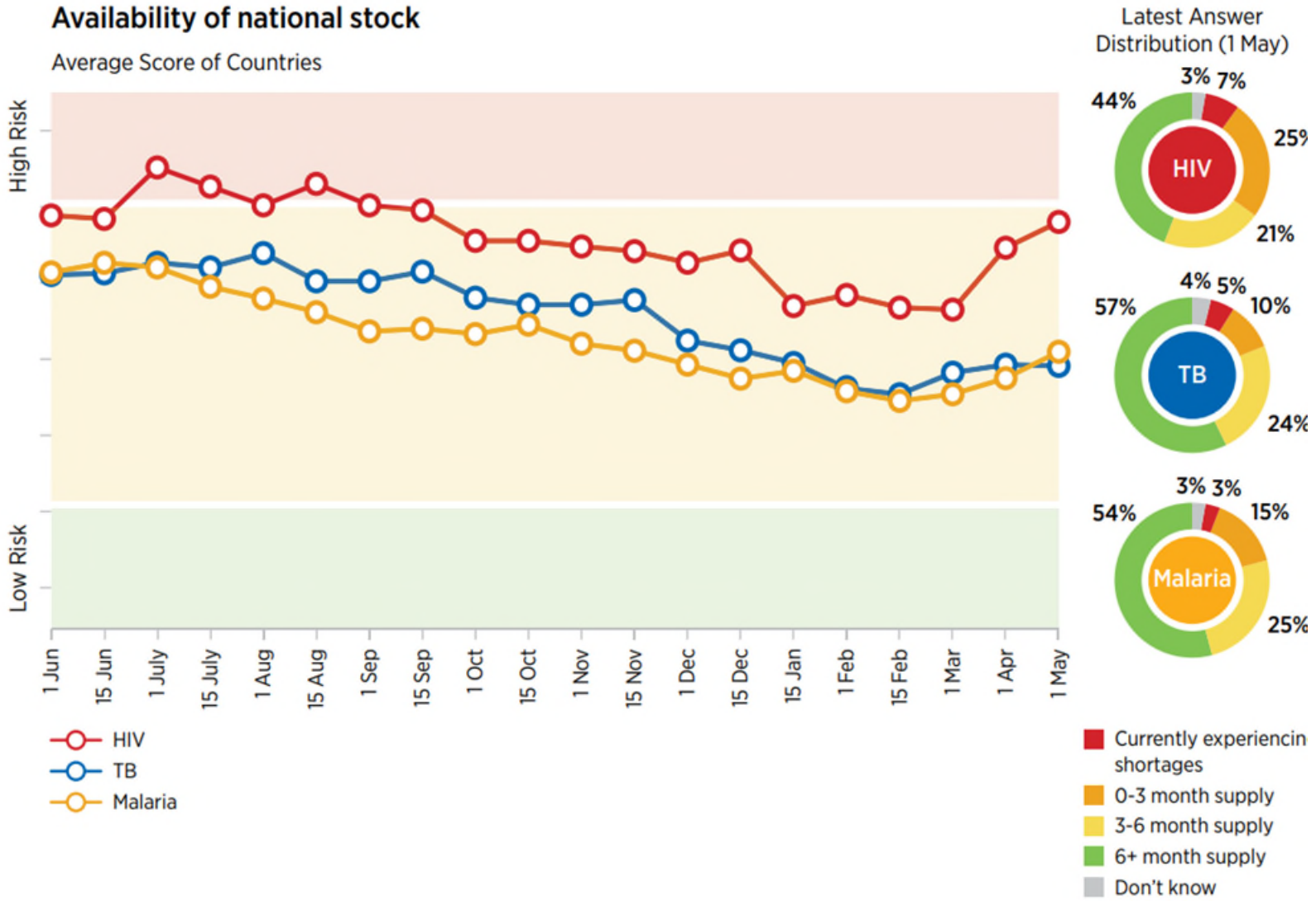
ACCESS TO MEDICINES
- Problems and Solutions -

"An estimated 2 billion people have no access to essential medicines, effectively shutting them off from the benefits of advances in modern science and medicine."
Dr Chan, WHO Director-General
https://www.who.int/publications/10-year-review/medicines/en/

Availability

- Medicines shortages have become a complex global issue, putting lives at risk and creating difficulties for health care professionals. There is evidence that these shortages are worsening with time; in some countries, medicine shortages tripled between 2005 and 2010. The causes of these shortages are multidimensional in the context of a complex global supply chain. As a result, there is a growing concern among health care professionals about the future of medicines availability worldwide.
- Dec 2022: We've run out of cholera vaccines, WHO official says as disease surges

Availability of HIV/TB/Malaria medicines stocks

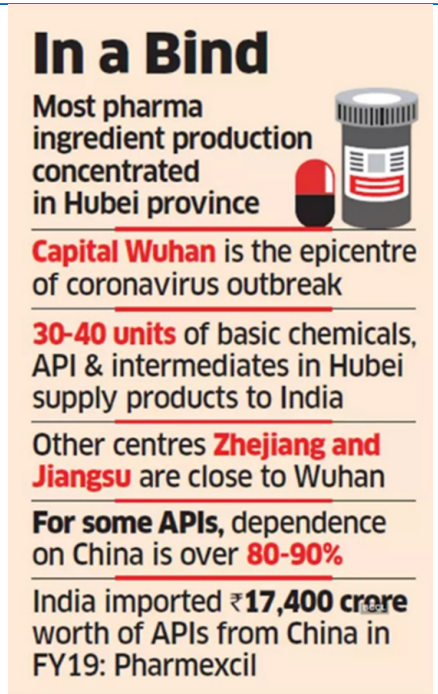


https://www.theglobalfund.org/media/10915/covid19_2021-05-20-situation_report_en.pdf

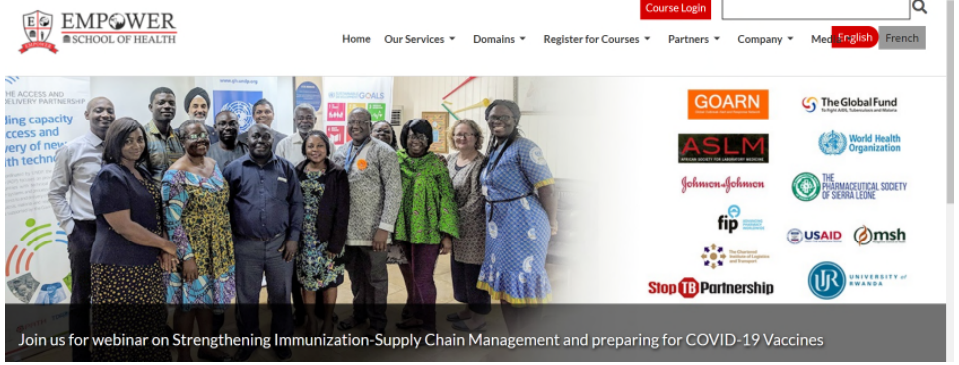
2023 target

<15% of African countries with any ART medicine stockout during a 12-month period.

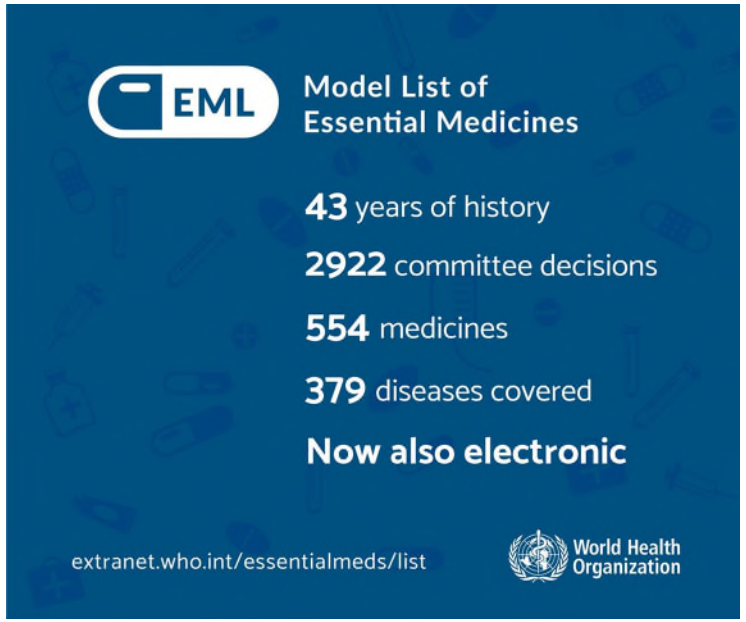
https://www.afro.who.int/sites/default/files/2019-04/HIV_DrugRes_FINAL_01_04_19_online.pdf



Awareness



- Which treatments are available for each disease?



Almost ten years ago, bedaquiline (BDQ) was approved use in treatment of multidrug-resistant tuberculosis (MDR-TB) in adults.
This critical development in the fight against TB offered the first promise since the 1960s that humanity could overcome the rapid increase in strains of deadly MDR-TB.
Currently, while approximately half a million people globally are estimated to become ill with rifampicin-resistant (RR-) or MDR-TB annually, barely a third are diagnosed and receive appropriate second-line drug treatment.

Tafenoquine can cure a type of malaria caused by Plasmodium vivax, which is most common in South and Southeast Asia, South America and the Horn of Africa. P. vivax causes up to 5 million malaria infections every year. Children aged 2 to 6 are four times more likely than adults to contract it, MMV said.

World Health Organization South-East Asia

GOARN Global Outbreak Alert and Response Network

EMPOWER SCHOOL OF HEALTH

THE EMERGENCY OUTBREAK RESPONSE PLATFORM

STRENGTHENING THE CAPACITY OF PUBLIC HEALTH SUPPLY CHAIN PROFESSIONALS IN WHO SOUTH EAST ASIA REGION (SEAR)

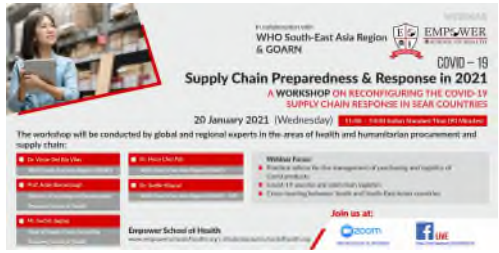
Department of Health Emergencies Programme (WHE) at WHO Southeast Asia Regional Office (SEARO), along with Empower School of Health and GOARN, are pleased to announce the launch of The Emergency Outbreak Response Platform. The Emergency Outbreak Response Platform is created to propagate the optimal design of resilient supply chains that can withstand pandemic challenges.

The Platform has 5 key features including Learners, Mentors, Courses, Resources and Collaboration. It will allow you to easily access peers, national and international mentors, take any number of courses and access any type of resources (videos, PDFs, podcasts).

The courses and resources have been categorised according to the following areas:

- PSM Preparedness and Planning
- Forecasting
- Procurement
- Supply Chain Logistics

The platform also features a Procurement and Supply Chain Management (PSM) Course on Pandemic Response and Preparedness. The course is designed to capacitate PSM personnel in WHO South East Asia Region (SEAR) to fight the current and future pandemics by building awareness, knowledge and skills related to pandemic response and preparedness.



Managing Non-vaccine Health Product Waste Disposal in the Era of COVID

EDUCATION

6th – 9th
December, 2018

International Workshop on
Scientific Writing

Bangkok, Thailand

EMPOWER
SCHOOL OF HEALTH

9th International Workshop
on Global Health Procurement, &
Supply Chain Management

18th – 22nd June, 2018

Bangkok, Thailand

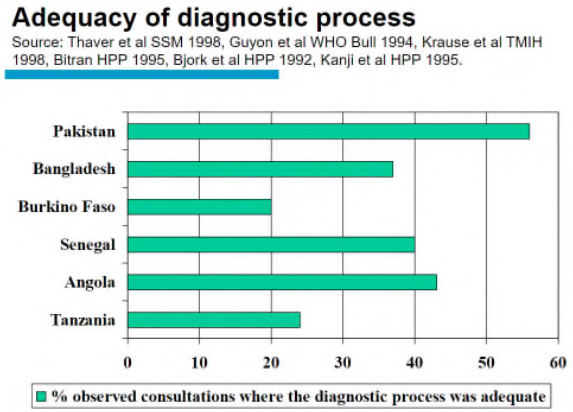
EMPOWER
SCHOOL OF HEALTH

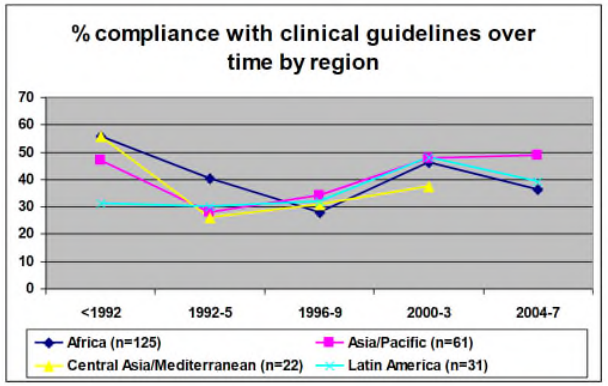
What is rational use of drugs?

The rational use of drugs requires that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and the community (WHO 1985)

This audit of 1406 newly registered hypertensive patients attending 16 Thai hospitals demonstrated that half of patients had their hypertension controlled at six months and around two thirds of newly diagnosed cases had their blood pressure controlled during their last reading over 1 year.

https://onlinelibrary.wiley.com/doi/full/10.1111/jch.14193





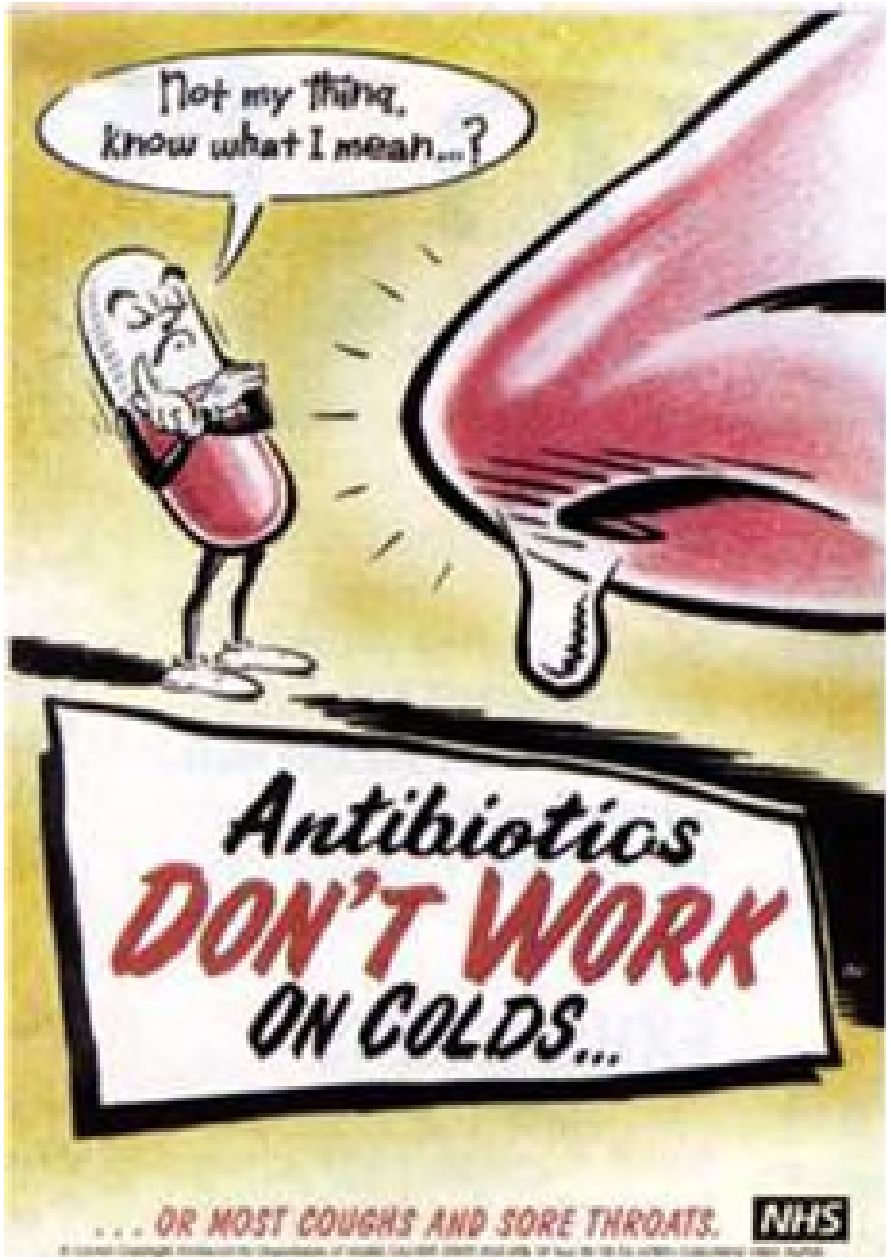
Department of Essential Medicines and Pharmaceutical Policy TBS 2008 World Health Organization

Global epidemic of irrational use of medicines

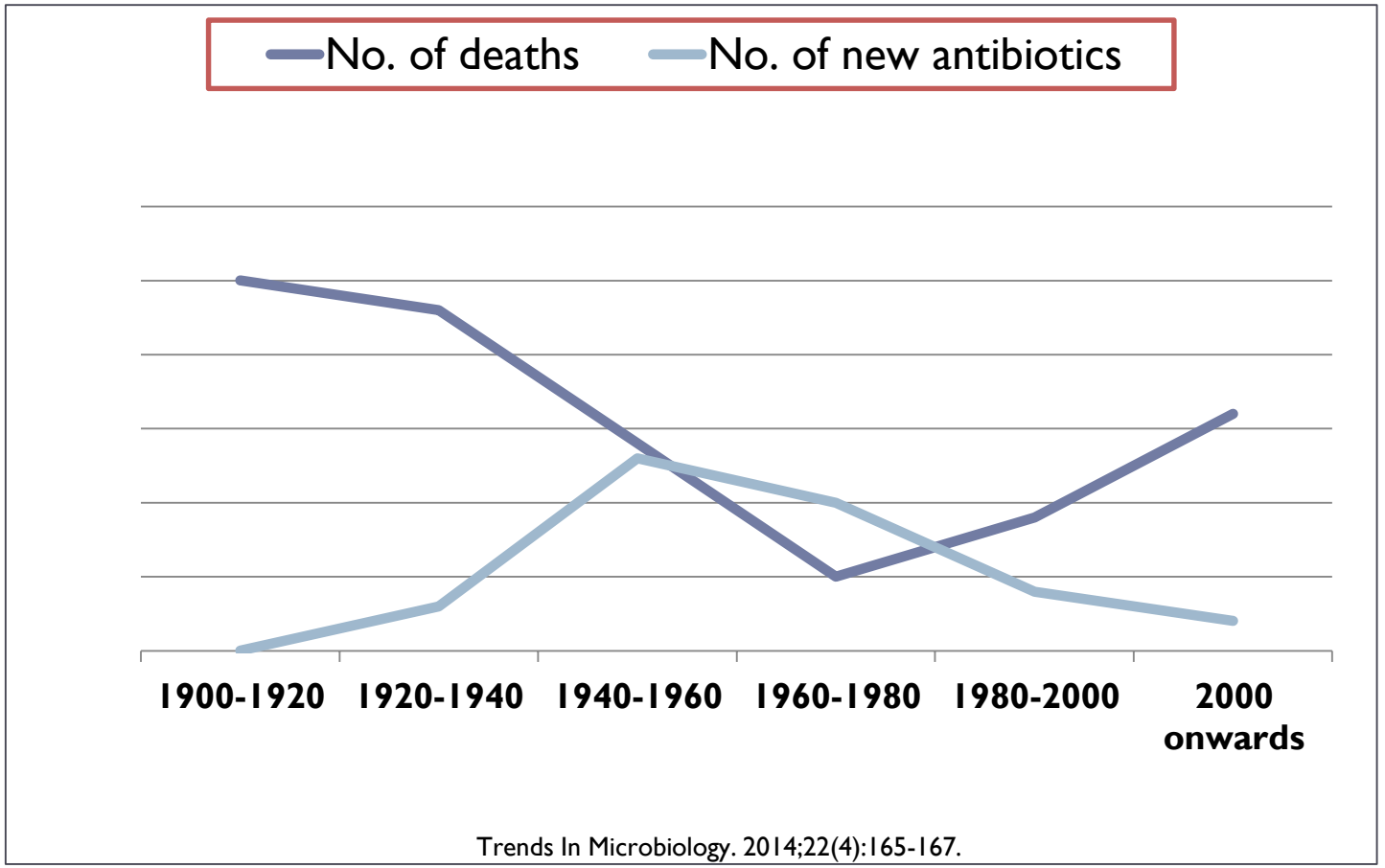
Irrational prescribing = pathological prescribing

Overuse (using Drugs for conditions where they are ineffective)

- **Misuse of antibiotics**
- **Overuse of injections**



The Rise & Fall of Antibiotics



Trends In Microbiology. 2014;22(4):165-167.

Problem with new antibiotics

Antibiotics R & D has not responded to the urgent need of new antibiotics

Lack of investment in antibiotics R & D

Falling clinical and preclinical antibiotic pipelines

Development process is not economical as antibiotics are costly to produce, low prices with restricted use

Regulatory hurdles

A Failing Market – Between 1960-2000, No Major Classes were Introduced

Antibiotic resistance getting worse globally but fixes could be simple

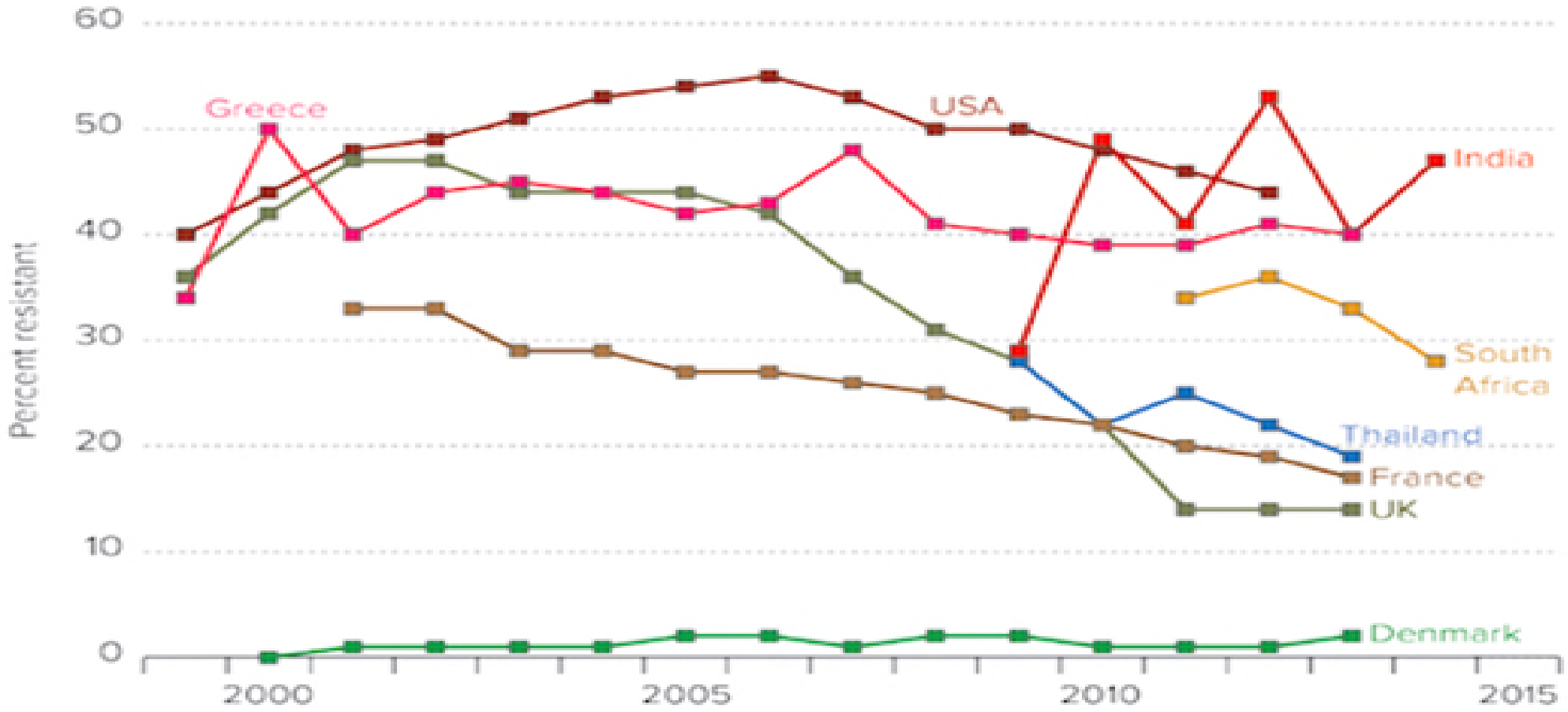
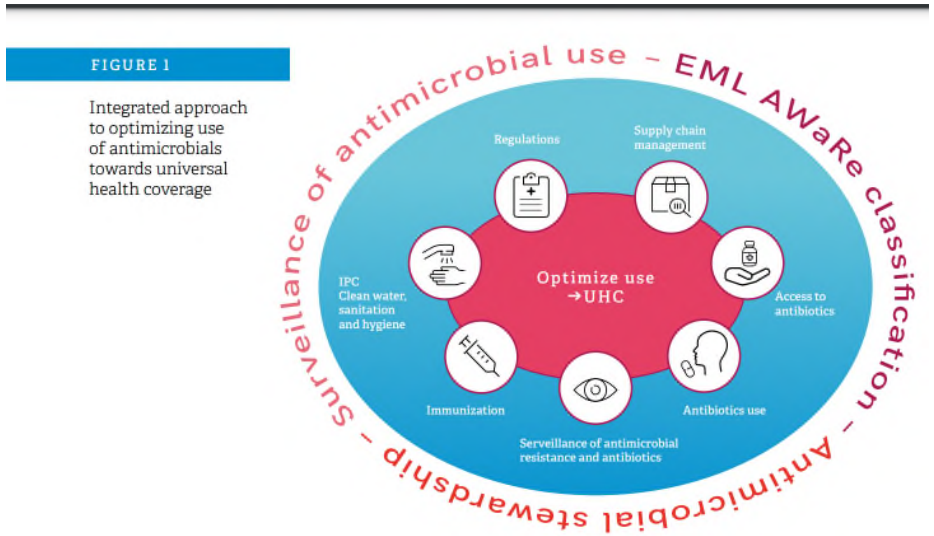


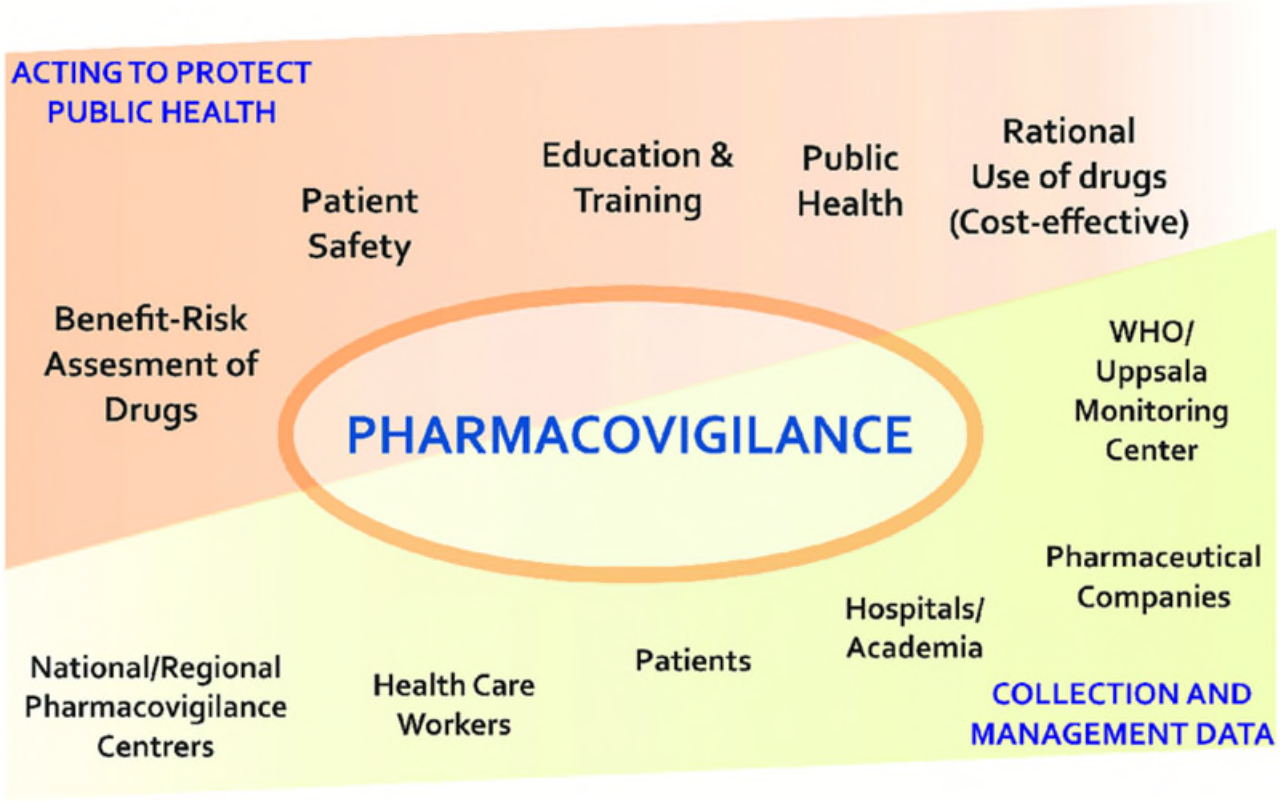
FIGURE ES-1[1]: Percentage of *Staphylococcus aureus* isolates that are methicillin resistant (MRSA) in selected countries, 1999–2014

New Concept of ‘stewardship’ of medicines

- Stewardship is defined as “the careful and responsible management of something entrusted to one’s care”.
- It was originally applied in the health-care setting as a tool for optimizing antimicrobial use, termed “antimicrobial stewardship” (AMS).



Pharmacovigilance



Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem.

Treatment failures must be investigated.

1 in 10 medical products in developing countries is substandard or falsified – WHO.

What's my Point ?

- Science and new medicines are wonderful, but will only ever get you so far – if they are ever to have significant impact, then management and stewardship need to be applied with humanity, spirituality, perseverance, and a very big bucket of patience.

The battle with microbes is not over and probably never will be; but it can be brought to a position of disease control.

New medicines can help, but it needs a whole lot more of the 'soft' arts if we are to keep the bugs, beasties and other nasties at bay.

DON'T be mislead be averages
Even in Pattaya not many adults have one breast AND on testicle.

DO look for age specific and geographically relevant information.

Thank You

- For allowing me to share a little of my life with you
- I Bid you now to go forth with Peace Light and Tranquility, and arrive home with Joy and Happiness