L'INITIATIVE
sida, tuberculose, paludisme

IMPLEMENDED BY EXPERTISE FRANCE GROUPE AFD

FUNDED AND UNDER THE SUPERVISION OF MINISTÈRE DE L'EUROPE ET DES AFFAIRES ÉTRANGÈRES
Liberté
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AS PART OF THE FRENCH CONTRIBUTION TO THE GLOBAL FUND

REGIONAL MEETING OF L'INITIATIVE'S PARTNERS IN SOUTH-EAST ASIA

Pullman Hotel G, Bangkok - June 10 and 11, 2024

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PRIORITY PUBLIC HEALTH ISSUES IN THE GREAT-MEKONG SUB-REGION: VISION AND EXPERIENCE SHARING

Key-note speech

Dr. Weerawat Manosuthi, Department of Disease Control, Ministry of Public Health (Thailand) and Dr. Patrice Piola, MD PhD, expert (France)

Introduction

- In Greater Mekong Sub-region (GMS), significant progress has been made in reducing the burden of HIV, TB, and malaria.
  - Notable achievements regarding increased PLHIV access to antiretroviral therapy and malaria prevention interventions.
  - All countries continue to face challenges with other emerging infectious diseases (EIDs) and antimicrobial resistance (AMR).
- Several noncommunicable diseases (NCDs), principally cardiovascular diseases, diabetes, cancer and chronic respiratory diseases impose a major and growing burden on health and development in the GMS.
- GMS is one of the regions most vulnerable to the adverse impacts of climate change, where rising sea levels, heat waves, floods, and droughts, as well as increasingly intense and unpredictable weather events.
  - This phenomenon affect millions of people in densely populated areas and coastal zones.
- This sub-region is confronted with pressing global challenges related to human health issues-stemming from the intersection of the humans, animals and the ecosystem.
  - This requires a collaborative one health approach by sectors that recognize this interdependency.

Outlines

HIV/AIDS

- Latest situation
- Strategy
- Update relevant clinical data

Tuberculosis

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AMR

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MDRO: Multi-drug resistance organisms

EID: Mpox

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EID: Emerging infectious diseases

Latest HIV/AIDS Situation in Greater Mekong Sub-region in 2023

Countries	HIV testing and treatment cascade			Pregnant women and children	
	PLHIV who know their status	PLHIV receiving ART	PLHIV with viral load suppression	% Pregnant women living with HIV with PMTCT (2022)	Estimated ART coverage among children 0-14 years
Cambodia	86%	86%	84%	89%	59%
Lao PDR	76%	58%	57%	54%	62%
Myanmar	N/A	74%	N/A	43%	69%
Thailand	90%	81%	79%	97%	76%
Viet Nam	89%	73%	72%	77%	87%

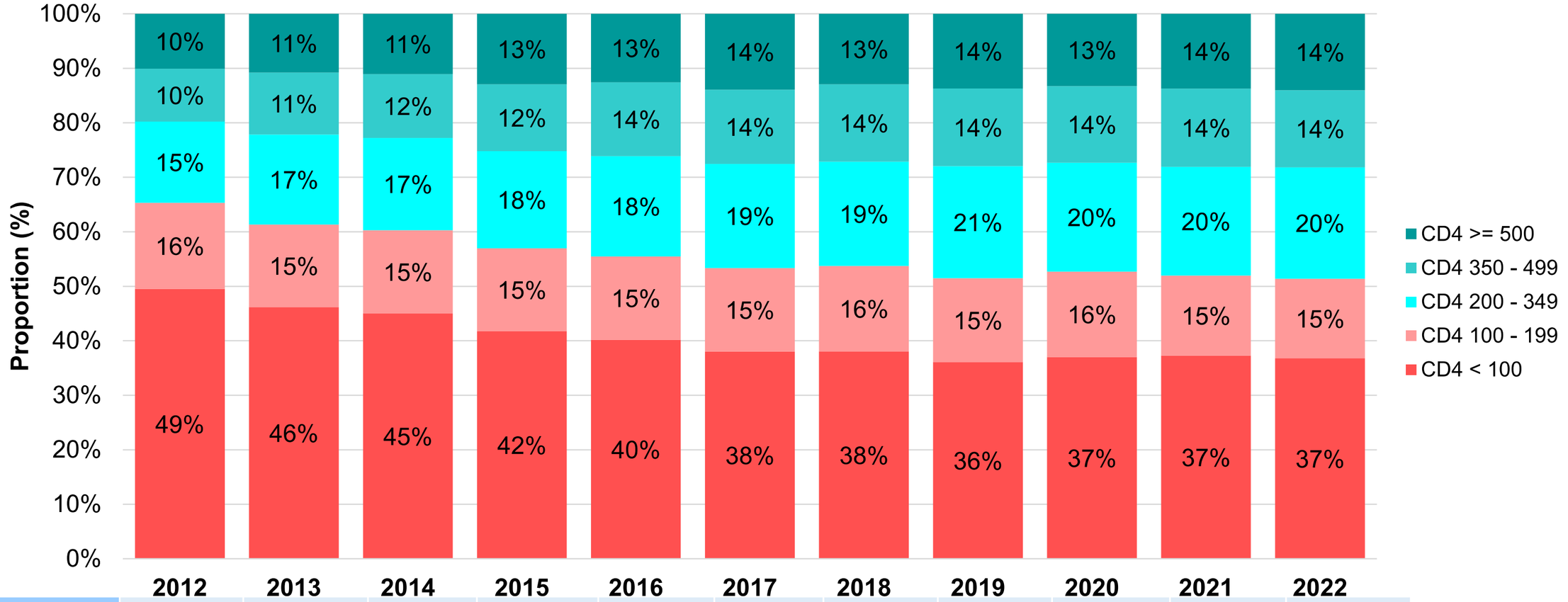
Key challenges in HIV program and ways forward

- Stigma towards HIV, leading to late access to testing and getting to know HIV states
- High proportion of AIDS related death
- Increasing number of adolescents with STIs and HIV infection and ARV coverage

- Improve communication and promote U=U awareness
- Scale up HIV self-test
- Improve access and primary care capacity for STIs & HIV services.
- Scale up TB preventive therapy and advance HIV disease package

https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/strategic-information/hiv-data-and-statistics

CD4 Levels Upon HIV Diagnosis in Thailand between 2012-2022



	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
% CD4 < 200	**65%**	**61%**	**60%**	**57%**	**55%**	**54%**	**53%**	**51%**	**53%**	**52%**	**52%**
# CD4 Tested	9,231	11,213	12,057	12,406	17,950	21,882	21,045	21,096	19,313	18,019	17,809

Source: NAP database, National Health Security Office (NHSO), November 2022

Strategy on AIDS in Greater Mekong Sub-region

Reduce new HIV infection

- Expedite effective package of services for populations and locations with high HIV transmission
  - PrEP, index testing, self test
- Strengthen and integrate current effective prevention efforts into existing system ensuring quality and sustainability
  - Condom strategy, HIV&STIs health literacy

Reduce AIDS related deaths

- Develop and enhance differentiated Tx, care and social support, ensuring quality, comprehensiveness and sustainability
  - Same day result, same day or rapid ART, quality improvement
  - National guideline for TB, TB/HIV, TPT, HIV/HBV, HIV/HCV

Reduce HIV and gender related discrimination

- Adjust HIV perceptions and build capacity of individuals, families and communities along with strengthen rights protection mechanism
  - Stigma & discrimination reduction in community and health care setting, self stigma reduction program

Update Data on “HIV PrEP” and “Treatment among PLHIV with Suboptimal response”

HIV PrEP

HPTN 083 and 084: LA IM Cabotegravir Q2m vs. Daily Oral FTC/TDF

- International, randomized, double-blind phase IIb/III (083) and phase III (084) tria

HPTN 083[1]

- N = 4566 MSM and transgender women
- HR for CAB vs FTC/TDF: 0.34 (0.18-0.62)
- 12 incident infections on LA CAB 4 with on-time injections
- 18 additional infections identified up to 1 yr after study unblinding (2 with on-time injections)[2,3]

HPTN 084[4]

- N = 3224 cisgender women
- HR for CAB vs FTC/TDF: 0.12 (95% CI: 0.05-0.31)

Suboptimal Response or Nonadherence to Oral ART

ACTG A5359: LA Cabotegravir + Rilpivirine Q4wk vs. SOC

- RCT to evaluate People living with HIV with poor viral response after ≥6 mo of ART or loss to f/u with ≥6 mo of nonadherence[5]
- 1ry outcome: treatment regimen failure at wk 52
  - LA CAB + RPV 24% vs. SOC 38% (Tx difference -14% (-30% to 0.8%).
- 2nd outcome: Virologic Failure
  - LA CAB + RPV 7% vs. SOC 25%
- Study was terminated early due to superior efficacy of LA CAB + RPV in secondary endpoints

Treatment regimen failure = earliest confirmed virologic failure or discontinuation

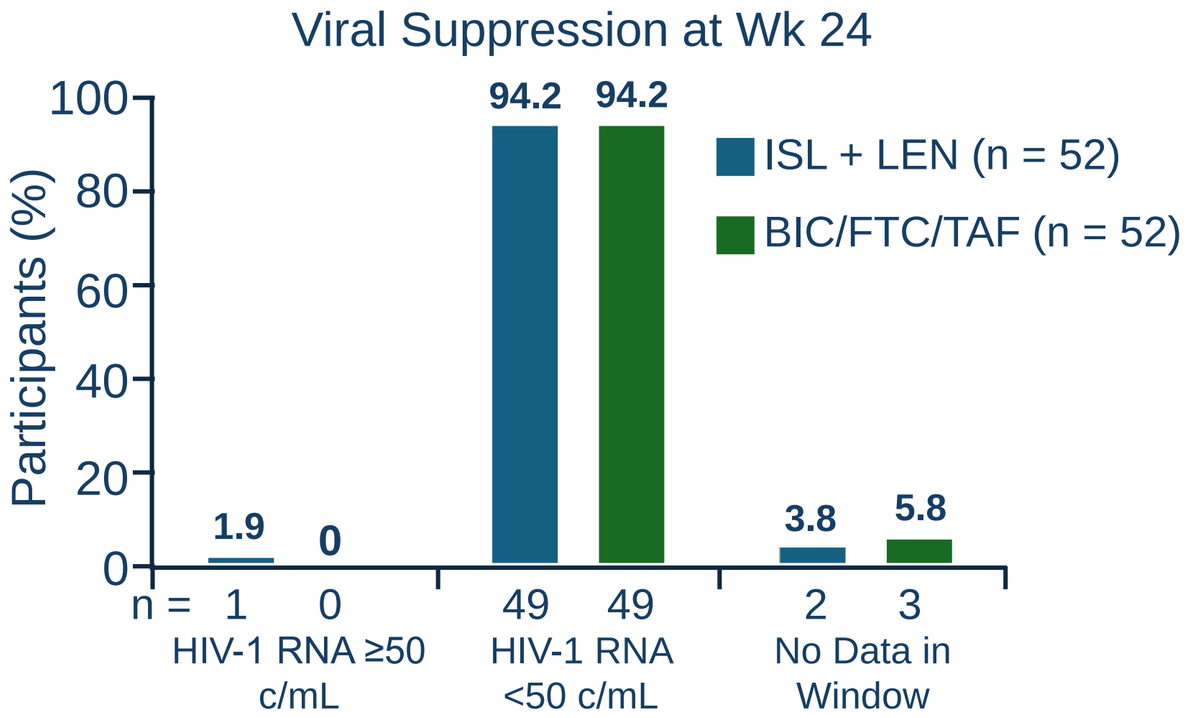
1. Landovitz. NEJM. 2021;385:595. 2. Landovitz. Lancet HIV. 2023;10:E767. 3. Marzinke. Antimicrob Agents Chemother. 2023;67:e0005323. 4. Delany-Moretlwe. Lancet. 2022;399:1779. 5. Rana. CROI 2024. Abstr 212.

Future Directions for Long-Acting ART:

"Oral Weekly Islatravir + Lenacapavir" in PLHIV with Virologically Suppressed

Open-label, active-controlled phase II trial

- High rates of virologic suppression maintained in both treatment arms



- No significant differences between groups in CD4 cell counts and ALC alterations at Wk 24

Mean Change in CD4+ Cell Count, cells/µL	ISL + LEN (n = 52)	BIC/FTC/TAF (n = 52)
Day 1	755	818
Wk 24	755	761
▪ 95% CI; *P* value	-57 to -4; .3477	

Colson. CROI 2024. Abstr 208.

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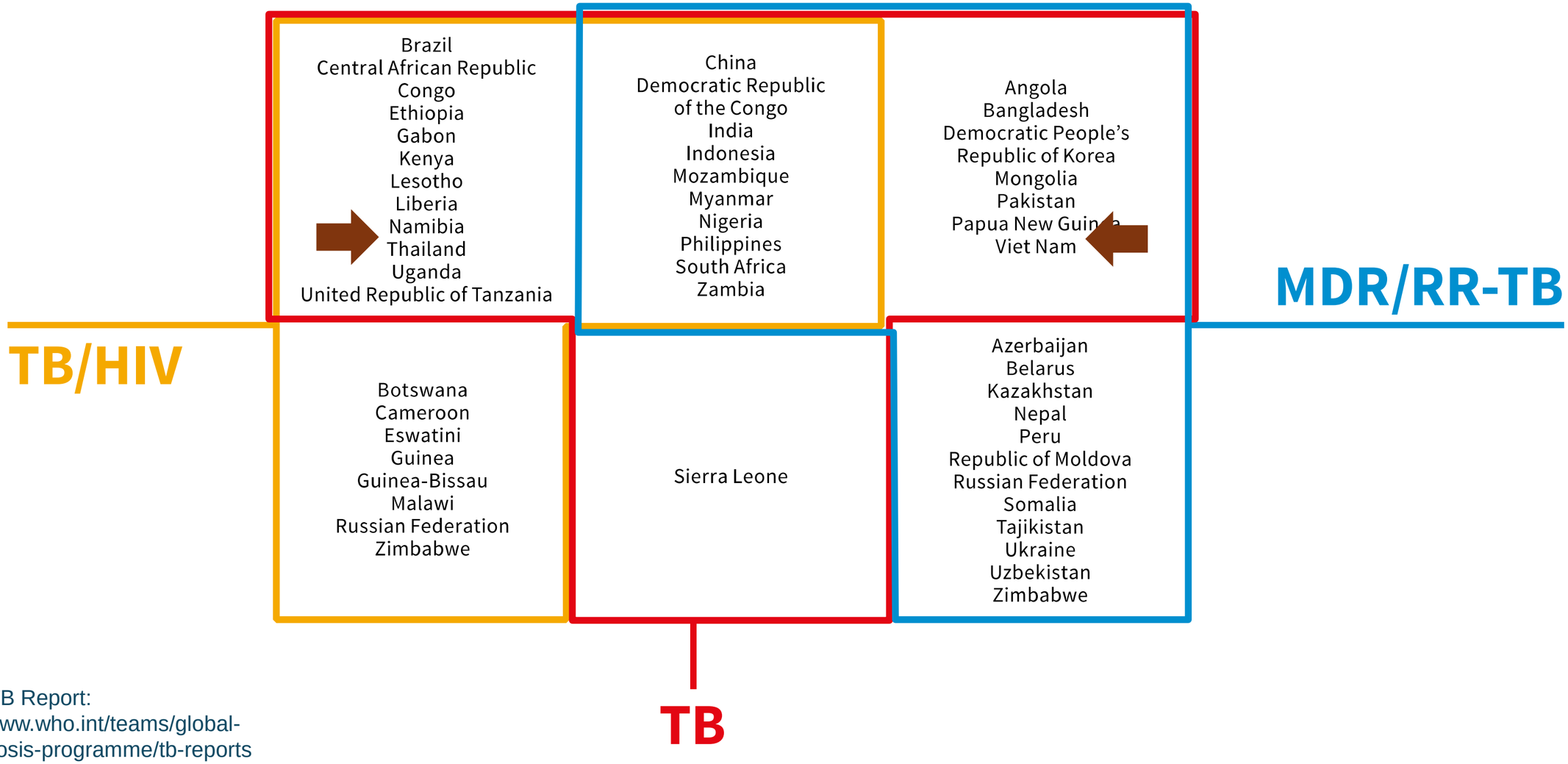
Three Global Lists of High-burden Countries for TB, HIV-associated TB and MDR/RR-TB 2021–2025



Global TB Report:
https://www.who.int/teams/global-tuberculosis-programme/tb-reports

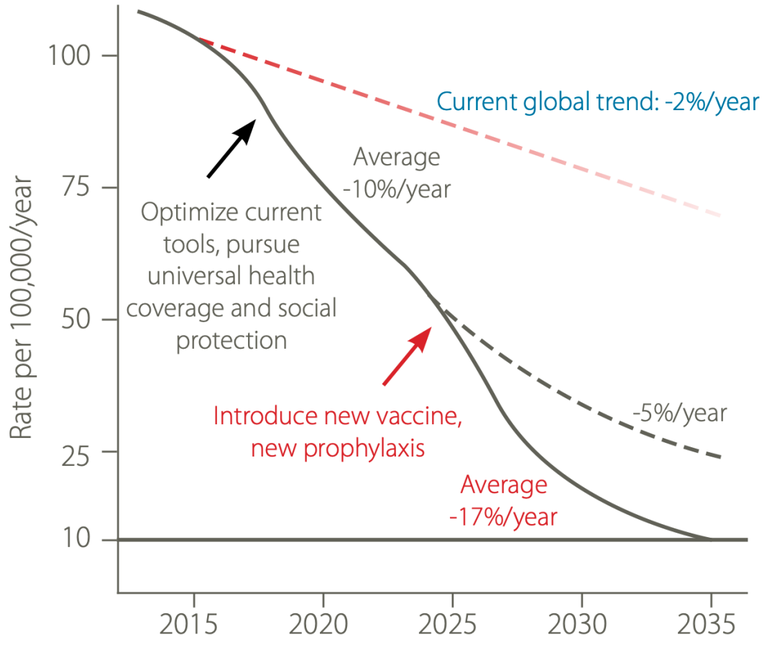
Latest TB Situations in Greater Mekong Sub-region

	Cambodia	Lao PDR	Myanmar	Thailand	Viet Nam
TB Incidence, rate per 100,000 population	320	138	475	155	176
Treatment success: New and relapse cases registered in 2021	95%	87%	87%	85%	90%
HIV-positive TB incidence, rate per 100,000 population	3.6	6.2	29	13	4.4
MDR/RR-TB incidence, rate per 100,000 population	4.1	1	24	3.7	9.4
HIV-negative TB mortality, rate per 100,000 population	23	13	80	16	11
HIV-positive TB mortality, rate per 100,000 population	3.9	1.3	11	2.9	2.7
TB preventive treatment - % of new HIV-positive people on preventive treatment - % of household contacts on preventive treatment	 53% 34%	 36% 1.2%	 21% 1.1%	 - 15%	 49% 6.4%

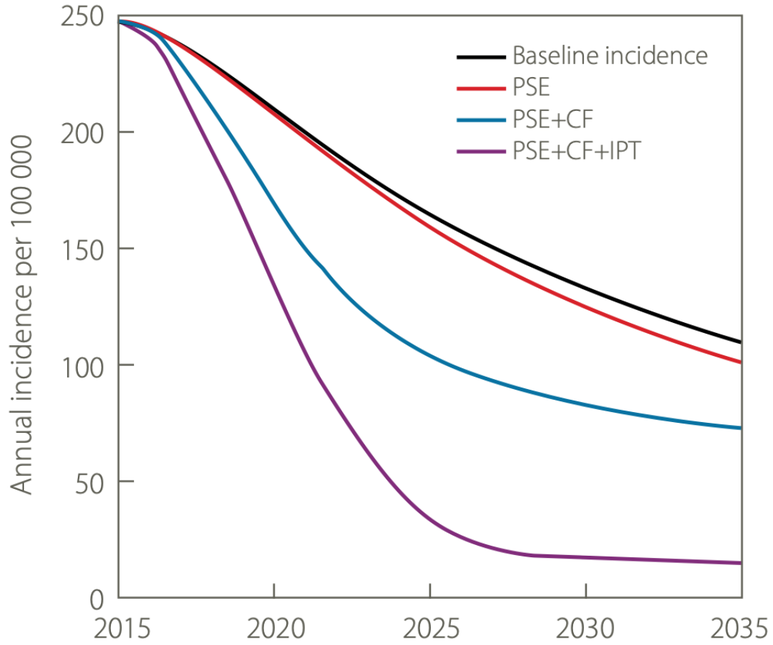
https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023

“Incidence Rate of TB” and “Impact of Tuberculosis Preventive Therapy (TPT)” in SEARO

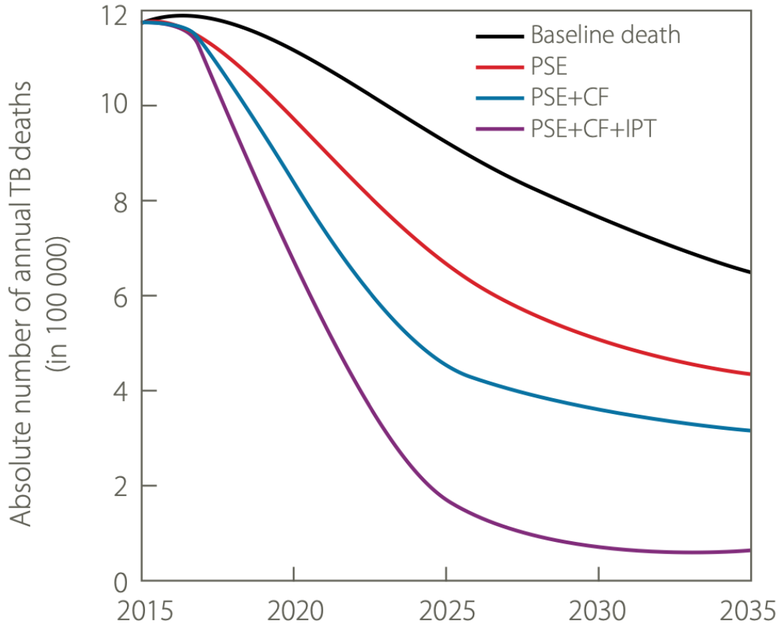
Desired decline in global TB incidence rates to reach 2035 targets



Impact on TB incidence



Impact on TB mortality



TPT in addition to program sector engagement (PSE) + Intensified case finding(CF) affects the curve comes down steeply.

https://iris.who.int/bitstream/handle

TB Strategy in Greater Mekong Sub-region

Screening	Diagnosis	Treatment	Prevention
Scale up screening and evaluation of high-risk groups for DS-TB and DR-TB infection, especially prisoners and migrants.	Early detection of drug-resistance	Use more patient-friendly treatment regimen, including 4-m regimen (2HRZ(E)/2HR) for children or pediatric FDC	Expand and decentralize testing facilities, i.e., IGRAs
	LF-LAM tests in diagnosing TB in selected groups of PLHIV with presumed TB	New, 4-m DS-TB regimen (2HPMZ/2HPM) for people aged ≥12 y	Improve access to dCXR and computer-aided detection
		Scale up the use of shorter, safer, all-oral treatment regimens for DR-TB, i.e., 6-month all-oral regimens (BPaLM or BPaL) and 9-month all-oral bedaquiline-containing regimens	Provision of TPT to all eligible PLHIV and household contacts of people with bacteriologically confirmed pulmonary TB
		Psychosocial support through counselling services, nutritional and transport support	Updated national guidelines to align with the latest recommendations to offer newer, shorter TPT combination therapies (3HP, 1HP, 3HR, and 6 Lfx for DR-TB),
			New shorter, combination therapies (3HP, 1HP, 3HR)

Clinical Trials Evaluating Possible Shorter Treatment for Drug-susceptible (DS) TB and DR-TB

Trial name	Study details	Condition/disease	Phase	Recruitment status
SimpliciTB	Bedaquiline–pretomanid–moxifloxacin–pyrazinamide (BPaMZ)	DS-TB and DR-TB	3	Completed
endTB	Bedaquiline and delamanid with various existing regimens for MDR-TB and XDR-TB	MDR-TB	3	Completed
endTB-Q	Bedaquiline–delamanid–linezolid–clofazimine for fluoroquinolone-resistant MDR-TB	Pre-XDR-TB	3	Completed
TRUNCATE-TB	Several 2-month regimens for DS-TB	DS-TB	3	Completed
RIFASHORT	High-dose rifampicin with standard regimen for DS-TB treatment	DS-TB	3	Completed
ZeNix	Safety and efficacy of various doses and treatment durations of linezolid plus bedaquiline and pretomanid in participants with pulmonary, XDR-TB, pre-XDR-TB or non-responsive/intolerant MDR-TB	XDR-TB, pre-XDR-TB, or treatment-intolerant or non-responsive MDR-TB	3	Completed
Study 31/A5349	Rifapentine-containing TB treatment-shortening regimens	DS-TB	3	Completed
Nix-TB	Safety and efficacy of bedaquiline plus pretomanid plus linezolid in subjects with DR pulmonary TB	XDR-TB and MDR-TB	3	Completed
TB-PRACTECAL	Bedaquiline and pretomanid with existing and repurposed anti-TB drugs for MDR-TB	RR-TB	2–3	Completed
MDR-END	Treatment shortening of MDR-TB using existing and new drugs	MDR-TB	2	Completed
BEAT-TB	Bedaquiline–delamanid–linezolid–levofloxacin–clofazimine (6-month oral regimen for RR-TB) or bedaquiline–delamanid–linezolid–clofazimine (6–9-month oral regimen for pre-XDR-TB and XDR-TB)	Pre-XDR-TB, XDR-TB, MDR-TB and RR-TB	3	Active, not recruiting
TB-TRUST	Ultra-short treatment for fluoroquinolone-sensitive MDR-TB	RR/MDR-TB	3	Active, not recruiting
DRAMATIC	Efficacy and tolerability of bedaquiline, delamanid, levofloxacin, linezolid and clofazimine	MDR-TB	2	Recruiting
Hi-DoRi-3	High-dose rifampicin to shorten DS-TB treatment	DS-TB	3	Not yet recruiting
CLO-FAST/ A5362	Shorter regimens including clofazimine and rifapentine for DS-TB	DS-TB	2	Suspended (temporarily closed (paused) to accrual)

Francesca Saluzzo, et al. Breathe 2023; 19: 230028. https://doi.org/10.1183/20734735.0028-2023

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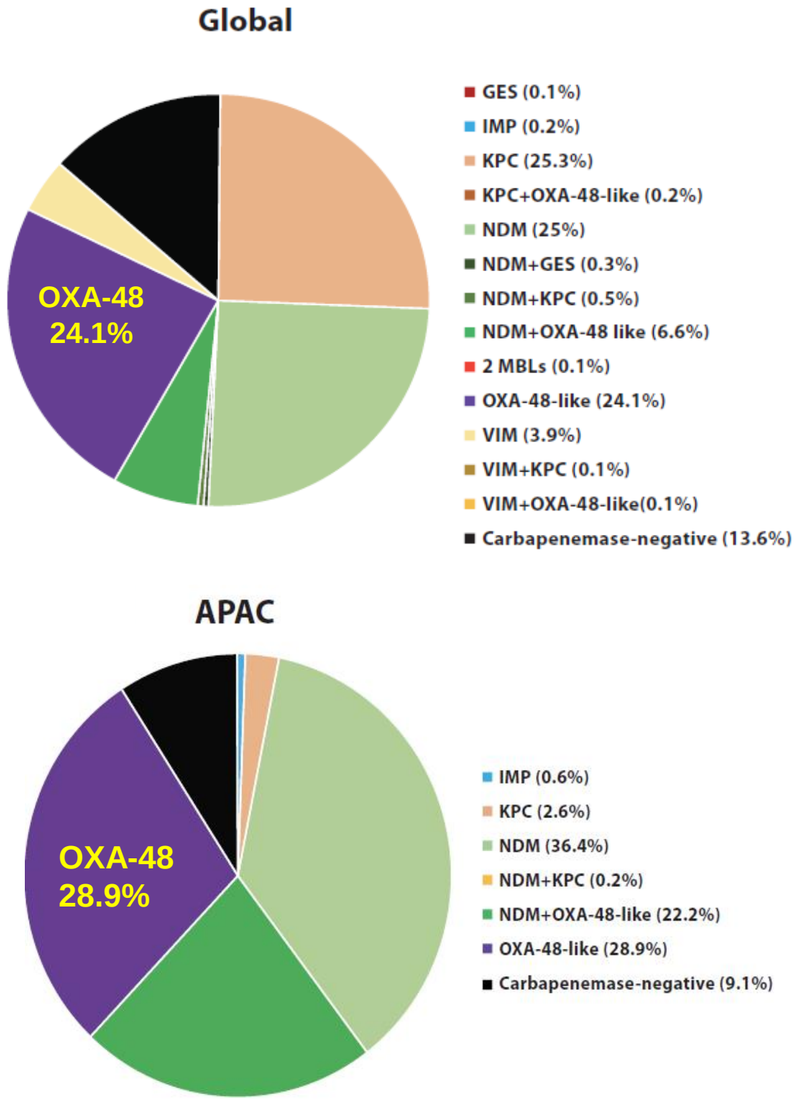
Meropenem-nonsusceptible Enterobacterales and Mechanisms Identified in Between 2018-2019



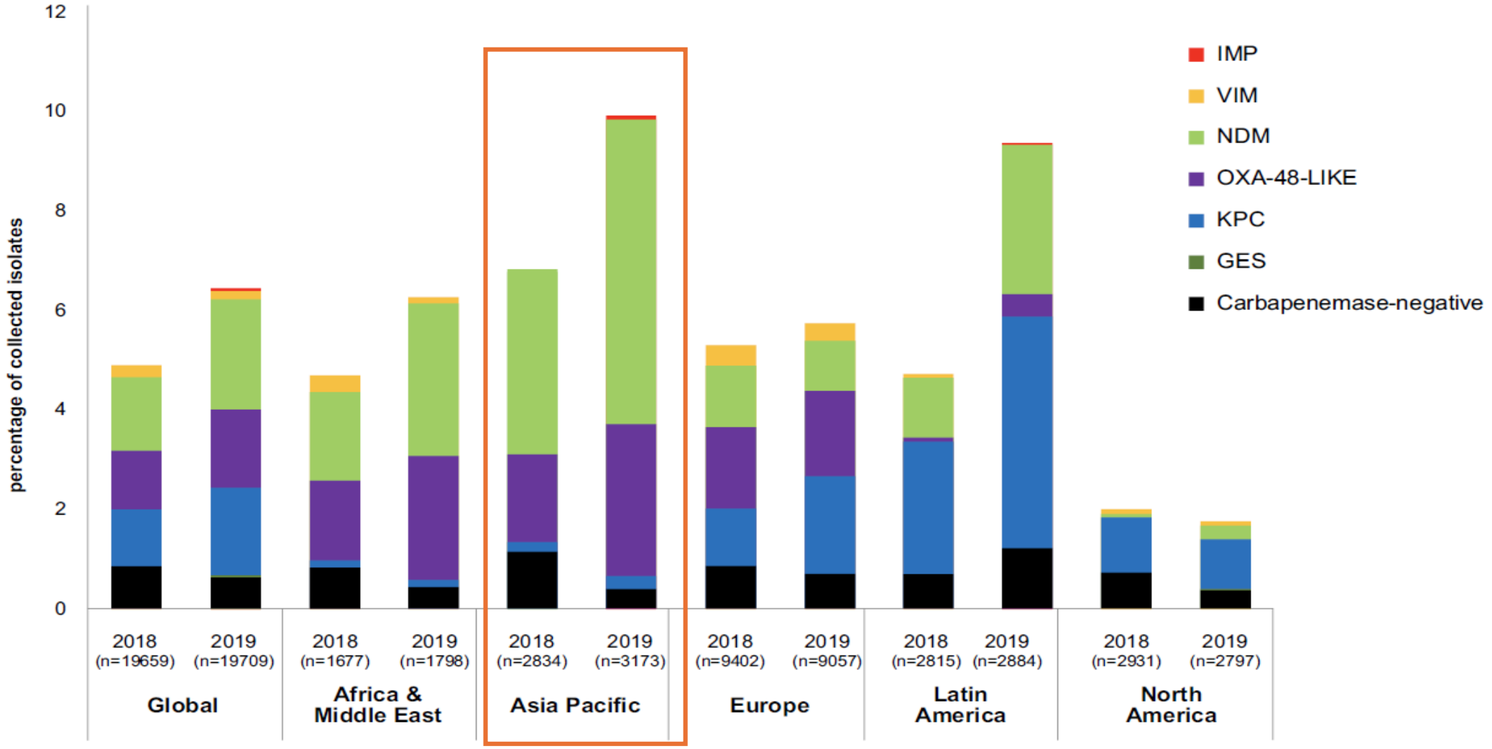
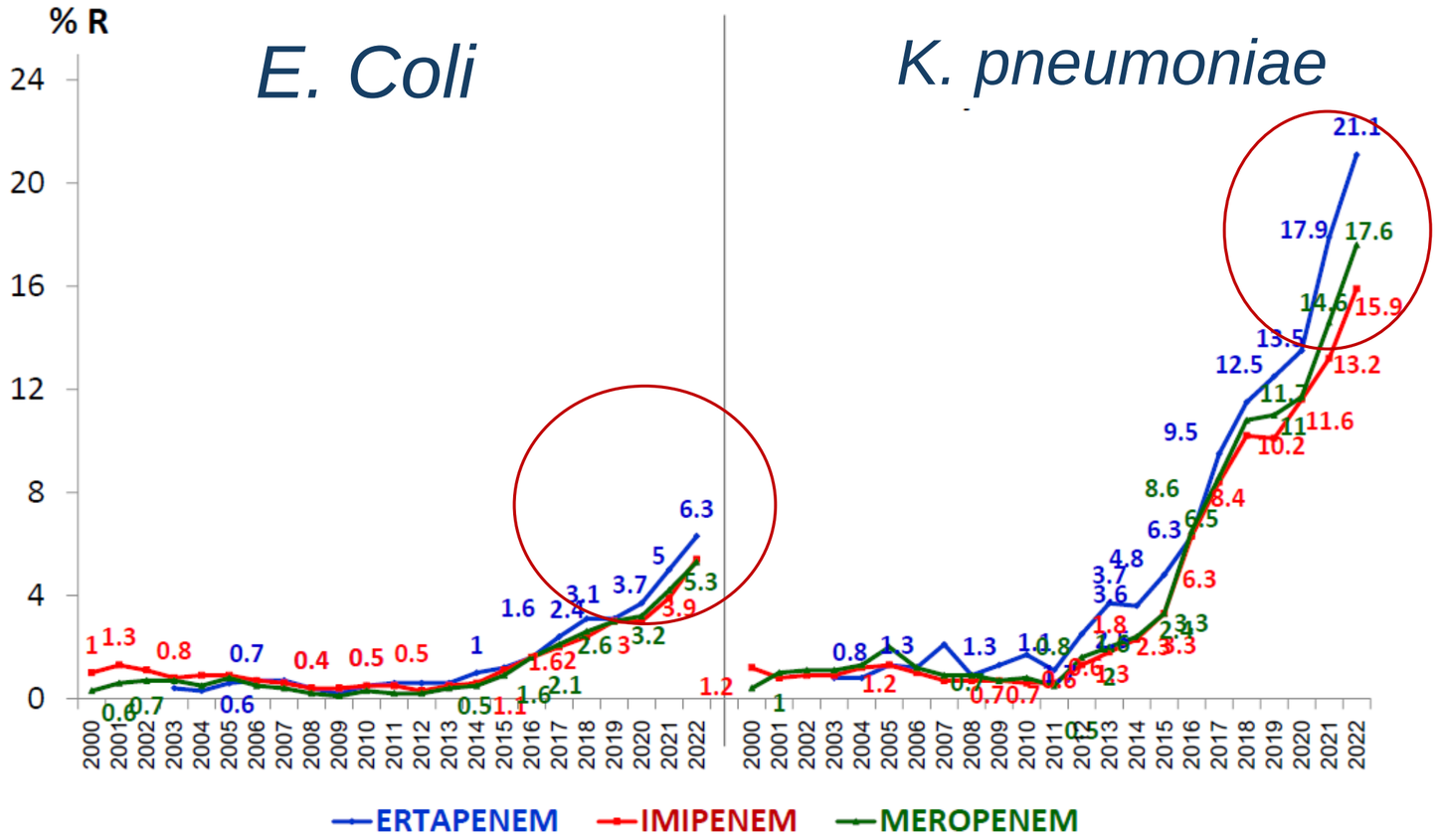


Figure: Proportion of carbapenem resistance mechanisms identified in meropenem-nonsusceptible Enterobacterales isolates collected globally and across different regions in 2018 and 2019.
n, total number of isolates collected.

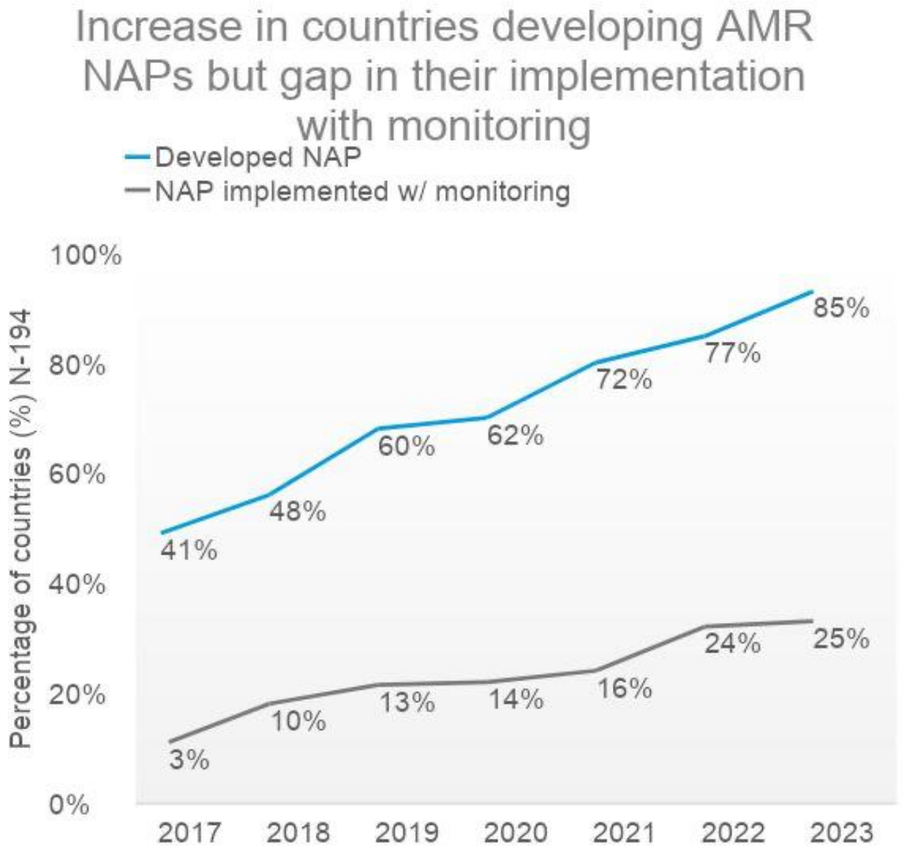
Adapted from Estabrook et al. Antimicrob Agents Chemother 2023 doi/10.1128/aac.01406-22

Thai NARST 2022: Carbapenem Resistance in *E. coli*, *K. pneumoniae, P. aeruginosa*



(68 hospitals)

AMR and Implementation of National Action Plans



- **Implementation** of NAPs is fragmented, ad-hoc, not costed and budgeted, not resourced
- **Interdependence** of various AMR interventions is not being considered
- A more **comprehensive and programmatic approach** is needed **putting people and their needs at the center**

http://narst.dmsc.moph.go.th National Antimicrobial Resistance Surveillance Center, Thailand. (accessed on 14 Sep 2023)

Health System Challenges to Addressing Antimicrobial Resistance for Human Health in Greater Mekong Sub-region

Prevention of infection

- Limited health worker education on AMR
- Poor IPC programs and practices

Health services

- Limited health service coverage and lack of financial protection for the entire population
- Lack or insufficient health-care services, diagnostics and antimicrobials and trained health workers
- Use of substandard or falsified diagnostics and antimicrobials

Diagnosis

- Limited laboratory capacity
- Limited health worker education in appropriate

Treatment

- Weak regulation of over-the-counter sales
- No standardized treatment guidelines or AMS programs
- Inappropriate prescribing of antimicrobials
- Limit treatment option for MDR organisms in GMS

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EID: Emerging infectious diseases

Seven EIDs: WHO Declared Public Health Emergency of International Concern (PHEIC) After 2005

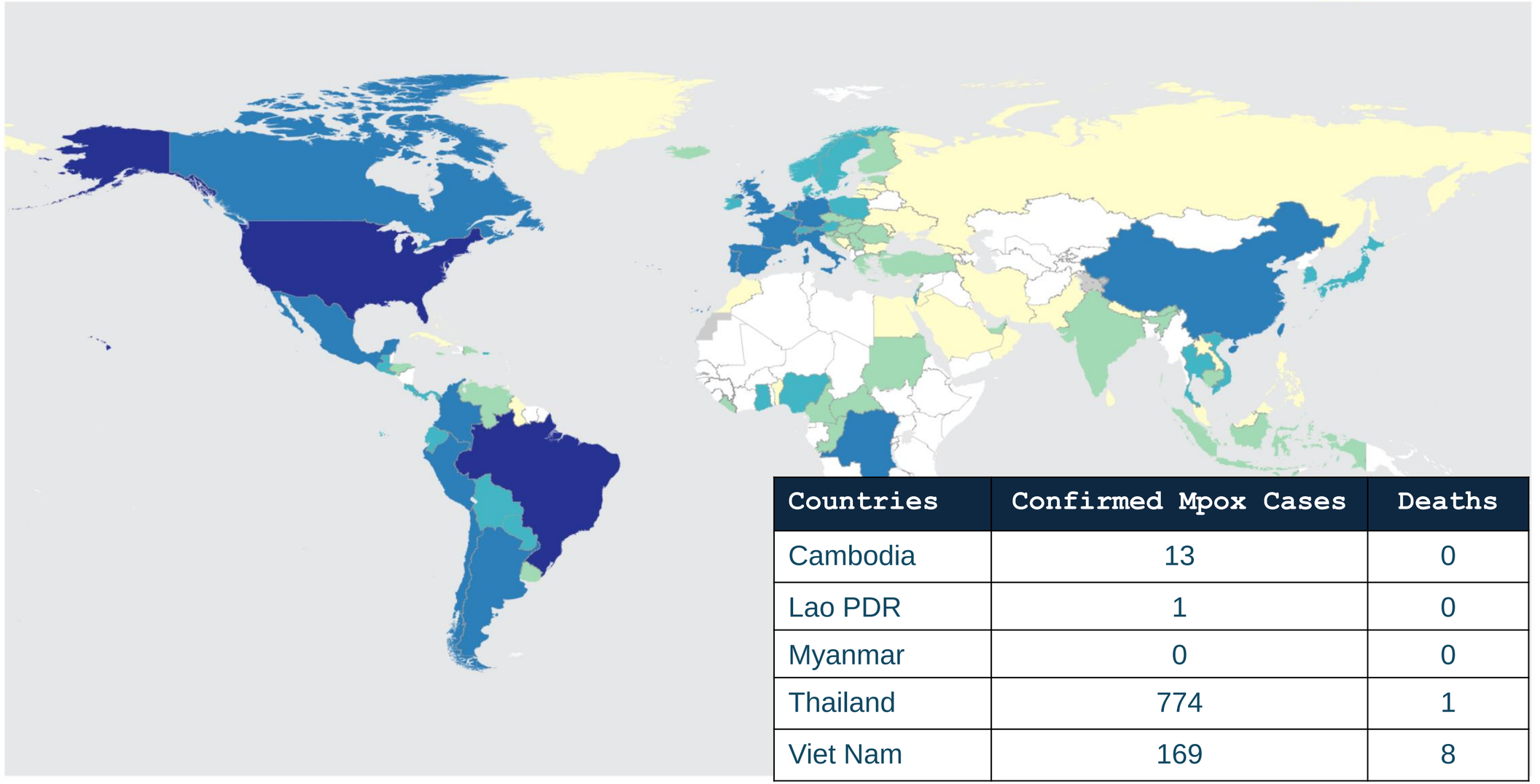
- 2009: H1N1 (Swine flu) originates in Mexico and spreads to the United States.
- 2014: Polio resurges in Afghanistan, Pakistan and Nigeria.
- 2014: Ebola virus infections spread throughout Guinea, Sierra Leone and Liberia.
- 2016: Zika virus epidemic causes microcephaly and other neurological disorders in the Americas
- 2019: Ebola outbreak spreads in a conflict zone in the Democratic Republic of the Congo
- 2020: The first cases of COVID-19 appear in China in late 2019, and the SARS-CoV-2 coronavirus spreads to many other countries, becoming a pandemic.
- 2022: Monkeypox infections pop up and spread widely in countries outside Central and West Africa, where they had been slowly circulating for 50 years.

Annelies Wilder-Smith, et al. Journal of Travel Medicine. doi: 10.1093/jtm/taaa227

Total mpox cases

from 1 Jan 2022, as of 30 Apr 2024

World Health Organization



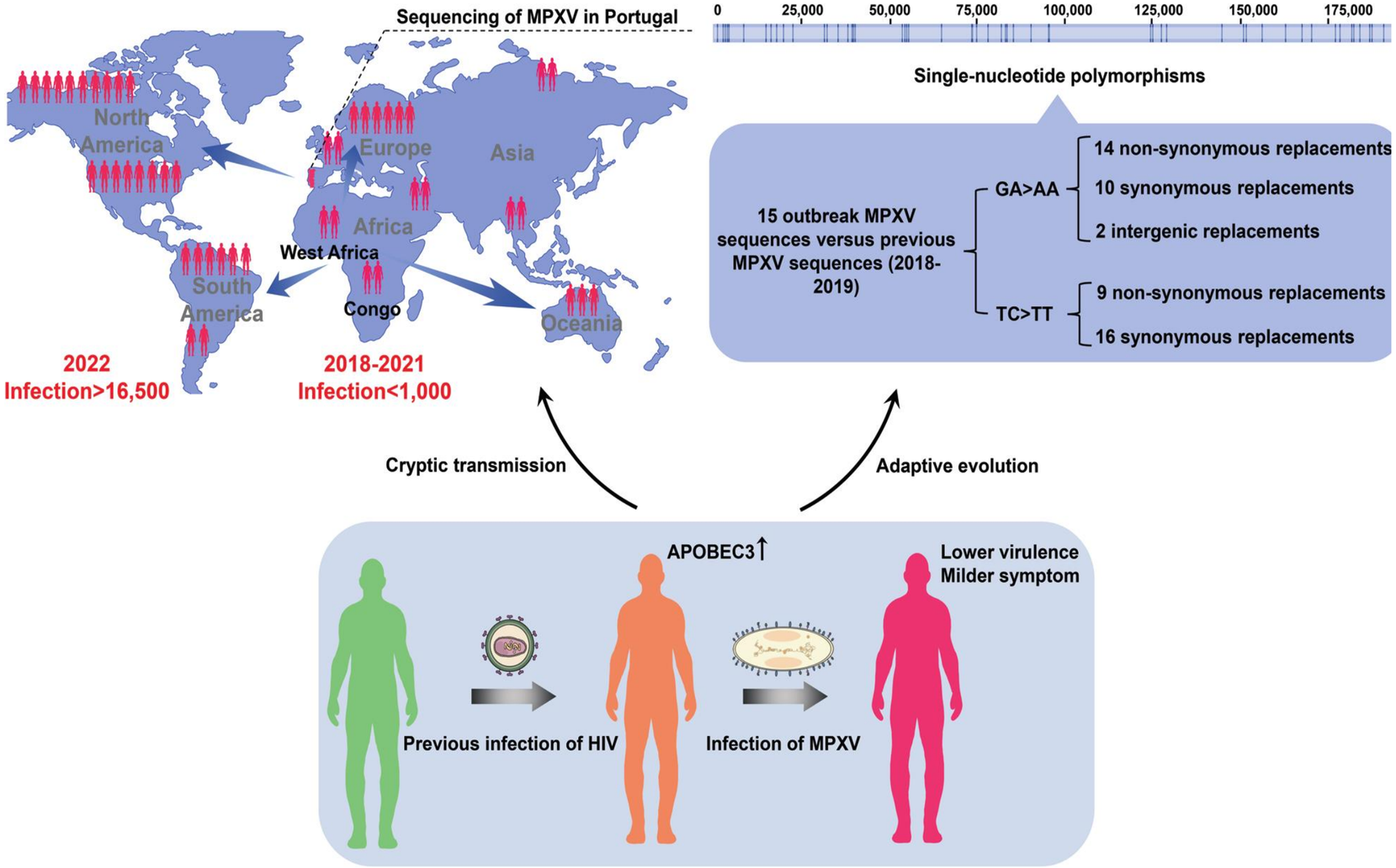
Countries	Confirmed Mpox Cases	Deaths
Cambodia	13	0
Lao PDR	1	0
Myanmar	0	0
Thailand	774	1
Viet Nam	169	8

https://worldhealthorg.shinyapps.io/mpx_global/

Mpox 2022 Outbreak:
Adaptive Evolution Associated with APOBEC3

- 50 genetic differences identified in viral genomes of recent cases compared with 2018-2019, esp 3 amino acid changes (D209N, P722S, and M1741I) in surface glycoprotein B21.
  - B21 is an important immune target and its mutation is beneficial for virus immune evasion and transmission.

- 46 SNPs presenting mutation, with 26 and 15 replacements with GA > AA and TC > TT.



APOBEC3= Apolipoprotein B mRNA- editing catalytic polypeptide-like 3

Yangzhen Chen, et al. Signal Transduction and Targeted Therapy 2022;7:323.

Mpox Vaccines

Generation	Vaccine name	Strain name	Preparation method	Advantages	Disadvantages
First-generation live virus vaccine	Dryvax	NYCBH strain	Unattenuated live vaccinia virus	Made significant contributions to the global eradication of smallpox campaign.	Live virus safety and reliability are lower, can produce serious side effects.
	Lister	Lister strain			
	Tiantan	Tiantan strain			
Second-generation live virus vaccine	ACAM2000	NYCBH strain	Unattenuated live vaccinia virus	Improved and simplified the production process of the first-generation vaccine, enhancing safety.	There is a certain probability of exhibiting serious adverse reactions, performing poorly in patients with compromised immune function.
	Elstree-BN	Lister strain			
	CJ-50300	NYCBH strain			
Third-generation attenuated vaccine	MVA	Ankara strain	Attenuated live vaccinia virus	Significantly improved safety, the strain's replication capability is reduced, suitable for patients with compromised immune function.	Situations with relatively low levels of neutralizing antibodies in vaccinated individuals exist, clinical reliability needs to be verified.
	LC16m8	Lister strain		Compared to the first and second-generation smallpox vaccines, enhanced safety, reduced theovvurrence of adverse reactions.	Clinical reliability needs to be verified.
	NYVAC	Copenhagen strain		Enhanced safety.	
	dVV-L	NYCBH strain			

Xinlong Wang, et al. CCDC Weekly,6:118-125.

Update New Generation of Mpox Vaccines

- Potential vaccine targets and highlighted effective immunogens.
  - Such as L1R, B5R, A27L, and A33R

Mpox Vaccines	Characteristics
Mpox DNA Vaccine	- 4pox DNA vaccine targets immunogenic sites L1, A27, B5, and A33.[1] - Compared to mRNA vaccines, greater stability and do not require drug delivery systems such as lipid nanoparticles to deliver mRNA to target cells.
Mpox multivalent mRNA Vaccines	- MPXVac-097 targets 5 antigens: A29L, E8L, M1R, A35R, and B6R.[2] - Demonstrated specific T-cell responses against MPXV and protection against vaccinia virus attacks in mouse models.
Mpox protein-based Subunit Vaccines	- Contain only antigenic components, such as proteins or polysaccharides, eliminating the risk of causing the disease. - Require adjuvants or booster shots to achieve the desired efficacy - Experimented in mice using CpG-ODN and aluminum as adjuvants, containing envelope proteins from MV and EV.[3] - Mice vaccinated with these showed significantly lower viral titers compared to the unvaccinated control group.

1. Mutcker EM, et al. J Virol 2022;96(3): e0150421. 2. Zhang NB, et al. Sci China Life Sci 2023;66(10):2329-41. 3. Vaccine 2007;25(7):1214 − 24

ASEAN Center for Public Health Emergency and Emerging Disease (ACPHEED)

Pillars: Prevent-Detect-Respond

Soft Launch of ACPHEED on 26th August 2022

- Secretariat Office in Thailand
- Governing Board: 10 ASEAN Members
- 3 centers in Vietnam, Indonesia and Thailand (Response Center)

Journal of Health Science 2022;6:1151.

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One Health

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Climate & Environment

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Malaria

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NCDs

- Latest situation
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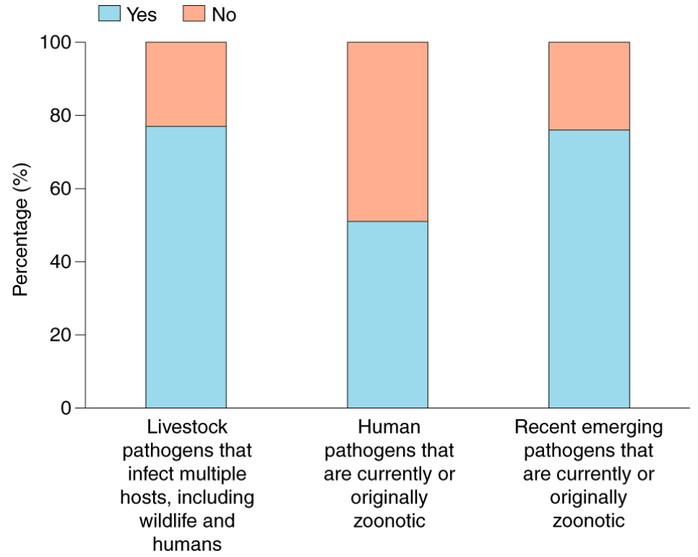
NCD: non-communicable diseases

One Health: In an evermore interconnected health

- **Key Drivers:**
  - **Zoonotic diseases: 75% of emerging infectious diseases are zoonotic.**
  - **Environmental changes: Deforestation, climate change, urbanization.**
  - **Wildlife trade: High-risk factor for zoonotic spillover.**
- **Malaria:** Wildlife trade brings forest workers into forests with malaria transmission.
- **Tuberculosis:** TB from usually captive elephants can be transmitted to Humans (and from humans to captive elephants).
  Note: occupational risk, tiny fraction of total human TB cases.



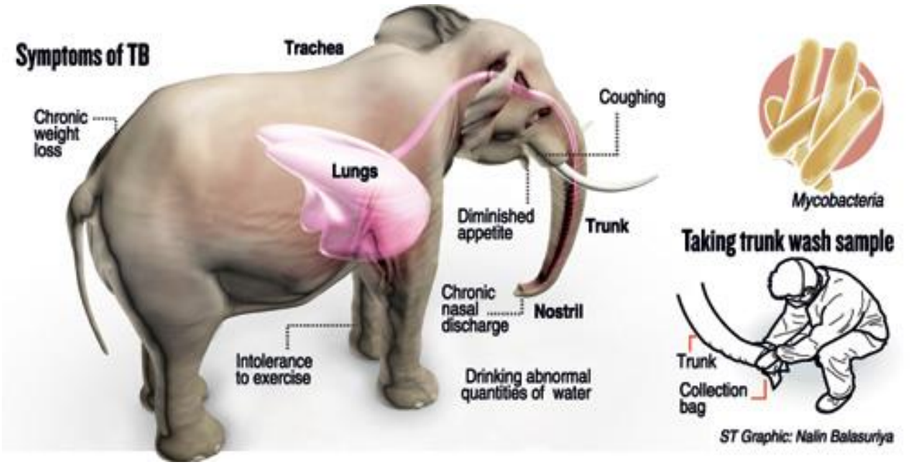


Table 4 Antibiotic resistance of Salmonella in animals and meats in the GMS

Year	Sample origin	Province, country	Sample size	Percentage of resistance										Source
				TET	AMP	NAL	CEP	STR	CHL	SXT	FLO	SUL	AMX	
Chicken														
2012	Wet market and super-market	Ha Noi, Ho Chi Minh, Phu Tho and Lam Dong, Vietnam	457	59	42	–	–	–	37	35	–	–	–	Ta et al., 2014 [50]
2010-2011	Super-market	Bangkok, Thailand	14	21	79	–	0	–	–	17	–	–	–	Chaisatit et al., 2012 [57]
2010	Retail market	Phatthalung, Thailand	38	60	68	76	5	92	68	5	–	–	–	Lertworapreecha et al., 2013 [106]
2004	Market and supermarket	Ho Chi Minh City, Vietnam	18	39	22	39	0	28	11	–	–	–	22	Van et al., 2007 [47]
2003	Retail market	Khon Kaen, Thailand	30	100	–	–	–	100	27	20	–	100	30	Angkititrakul et al., 2005 [48]
2000-2002	Farm (fecal)	Chiang Mai and Lamphung, Thailand	11	100	0	100	–	–	–	–	27	–	–	Padungtod and Kaneene, 2006 [51]
	Market		57	33	0	43	–	–	–	–	0	–	–	
	Slaughter-house		87	16	0	16	–	–	–	–	0	–	–	
2000-2001	Wet market	Mekong Delta, Vietnam	20	–	5	35	–	20	25	–	–	–	–	Ogasawara et al., 2008 [107]
Pigs and Pork														
2011	Market	Champasak, Laos	35	63	60	14	–	57	11	37	–	–	–	Boonmar et al., 2013 [108]
2010	Retail market	Phatthalung, Thailand	45	77	51	4	28	71	11	17	–	–	–	Lertworapreecha et al., 2013 [106]
2010	Farm (fecal)	Sa Kaew, Thailand	3	33	33	0	–	33	33	0	–	–	–	Pulsrikarn et al., 2013 [109]
	Retail market		42	69	50	0	–	31	14	36	–	–	–	
2004	Market and supermarket	Ho Chi Minh City, Vietnam	32	78	50	25	0	16	0	–	–	–	50	Van et al., 2007 [47]
2003	Retail market	Khon Kaen, Thailand	26	89	–	–	–	100	15	15	–	100	15	Angkititrakul et al., 2005 [48]
2000-2001	Farm (fecal)	Chiang Mai and Lamphung, Thailand	51	98	0	2	–	–	–	–	6	–	–	Padungtod and Kaneene, 2006 [51]
	Market		155	60	0	21	–	–	–	–	8	–	–	
	Slaughter-house		48	89	1	39	–	–	–	–	15	–	–	
2000-2001	Wet market	Mekong Delta, Vietnam	48	–	6	–	–	15	13	–	–	–	–	Ogasawara et al., 2008 [107]
Cattle and Beef														
2011	Market	Champasak, Laos	20	75	70	5	–	80	15	30	–	–	–	Boonmar et al., 2013 [108]
2009	Retail market	Hanoi, Vietnam	63	46	32	18	–	30	22	–	–	–	–	Thai et al., 2012 [110]
2005-2007	Farm (fecal)	Nakhonpathom, Thailand	160	9	4	–	–	64	2	–	–	11	–	Chuanchuen et al., 2010 [111]
2004	Market and supermarket	Ho Chi Minh City, Vietnam	32	13	0	6	0	6	0	–	–	–	0	Van et al., 2007 [47]
2000-2001	Wet market	Mekong Delta, Vietnam	35	–	–	–	–	6	3	–	–	–	–	Ogasawara et al., 2008 [107]

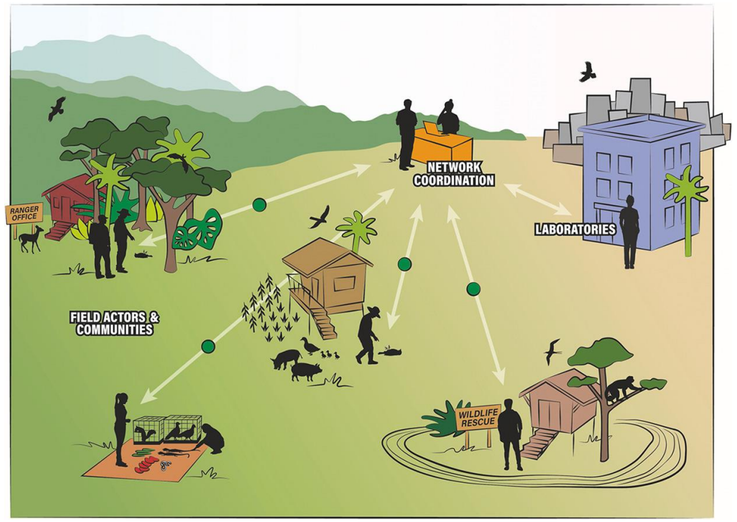
TET tetracycline, *AMP* ampicillin, *NAL* nalidixic acid, *CEP* cephalothin, *STR* streptomycin, *CHL* chloramphenicol, *SXT* trimethoprim/sulfamethoxazole, *FLO* florfenicol, *SUL* sulfamethoxazole, *AMX* amoxicillin

EXPERTISE FRANCE GROUPE AFD

L'INITIATIVE sida, tuberculose, paludisme

Intensified food production and correlated risks to human health in the Greater Mekong Subregion

- Pesticides,
- Livestock infection with antibiotic-resistant pathogens
- Disease vector proliferation in irrigated agroecosystems



WAYS FORWARD for ONE HEALTH

- Develop innovative and automated **surveillance** technologies to improve real-time **data sharing** and with geo-integration
- Support, develop, and implement **standardized protocols** for cross-sectoral and cross-national collaboration
- Stimulate community engagement and education **to**

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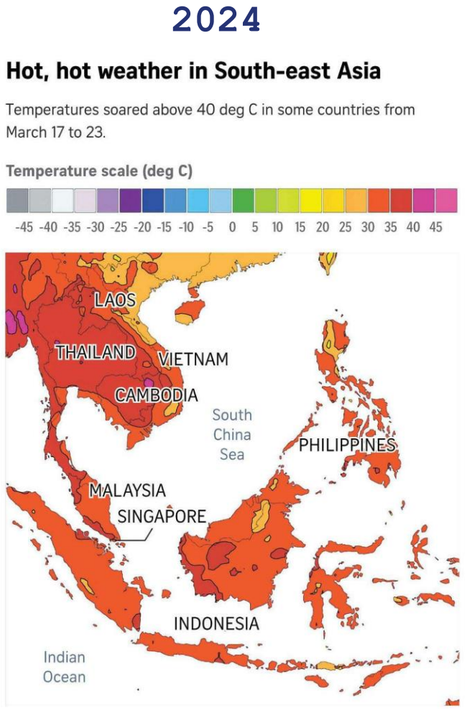
NCD: non-communicable diseases

Climate & Environment: A Region at High Risk



GMS is one of the world's most biodiverse regions

Deforestation

Air Pollution in cities

Water Pollution (industrial waste, agricultural runoff)

.**Rising heat:** 0.2-0.3°C per decade.

.Increased frequency and intensity of **floods, droughts,** and **heatwaves.**

.**Heat-related illnesses and deaths.**

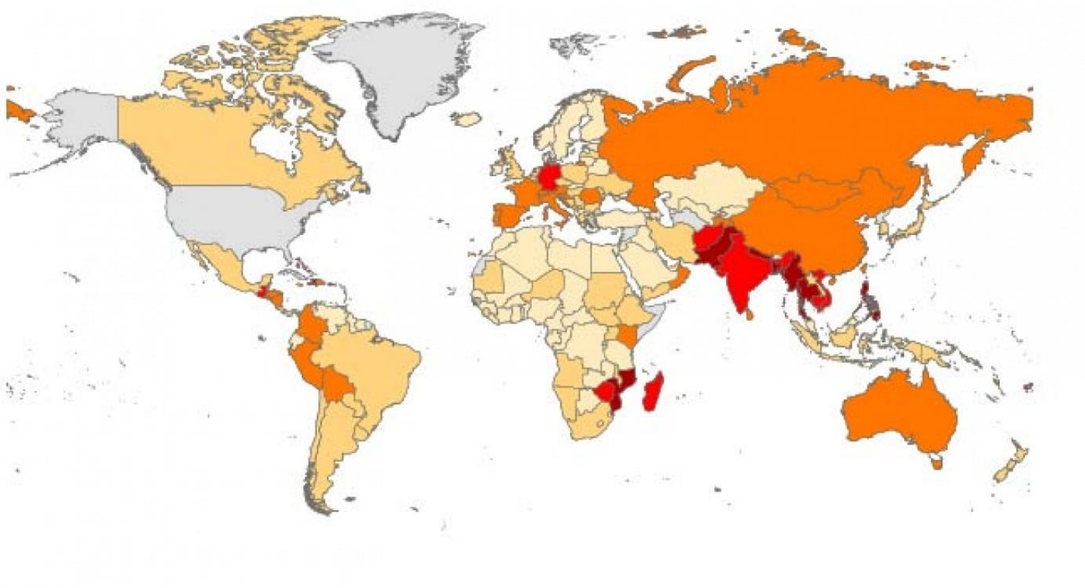
.Increased prevalence of vector-borne diseases

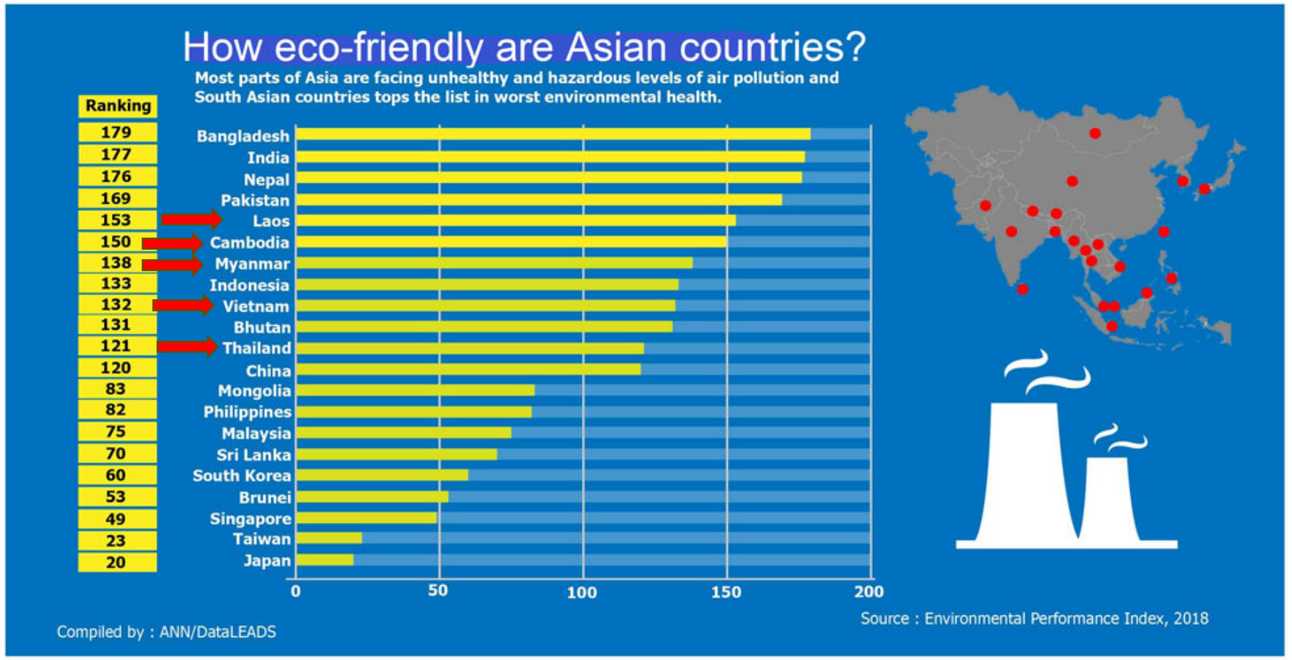
.(e.g., dengue, CHK, ZIKV)

.Respiratory diseases from air pollution

.Food and water insecurity

GMS: A climate- vulnerable region

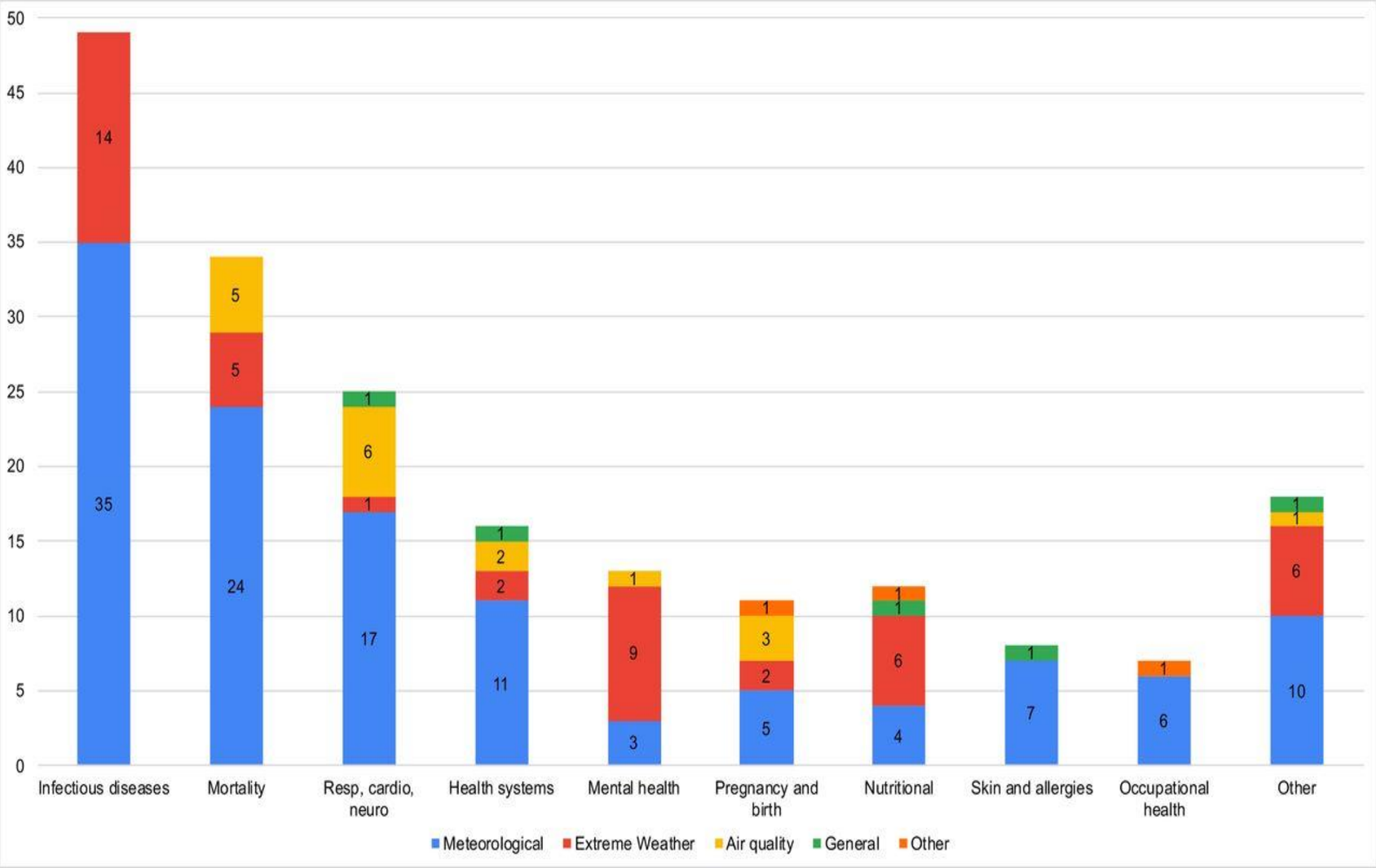




Source: Global Climate Risk Index (GermanWatch)

The annually published Global Climate Risk Index analyses to what extent countries have been affected by the impacts of weather-related loss events (storms, floods, heat waves etc.).

Impact of Climate Factors on Various Health Outcomes: Study Frequencies



- **Infectious Diseases**: Most studied under meteorological impacts and extreme weather events.

- **Mortality**: Commonly investigated in relation to meteorological impacts.

- **Respiratory, Cardiovascular, Neurological Outcomes**: Frequently linked to meteorological impacts.

- **Health Systems**: Often explored concerning meteorological impacts.

- **Mental Health**: Significant focus on impacts from extreme weather events.

- **Nutritional Outcomes**: Notable studies on the effects of extreme weather.

Rocque RJ, Beaudoin C, Ndjaboue R, et al. Health effects of climate change: an overview of systematic reviews. BMJ Open 2021;11:e046333. doi:10.1136/ bmjopen-2020-046333

Climate & Environment: impact on malaria, tuberculosis and HIV

MALARIA

- Temperature Increases: Faster mosquito and parasite development.
- Rainfall Variability: More mosquito breeding sites.
- Humidity Changes: Extended mosquito lifespan.

➔ Spread to new areas

TUBERCULOSIS

- Poverty and Displacement: Increased overcrowding.
- Healthcare Infrastructure: disrupted services.
- Air Pollution: Compromised respiratory health.
- Food Security: Malnutrition and weakened immunity

HIV

- Healthcare Disruption: Reduced treatment access.
- Migration and Displacement: Increased transmission risk.
- Food Insecurity: Malnutrition weakens immunity

BUT

Scarce scientific evidence *demonstrating* causality
from climate change
<u>through dedicated studies</u>

Research should better identify climate and environmental factors with the highest impact on health

Climate change adaptation strategies should be tailored to the specificities of ecosystems, hence for the GMS

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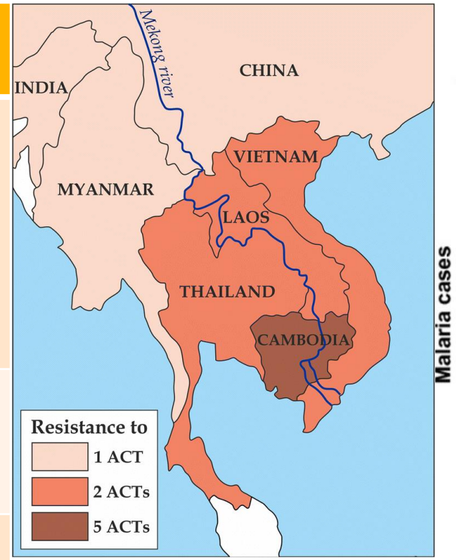
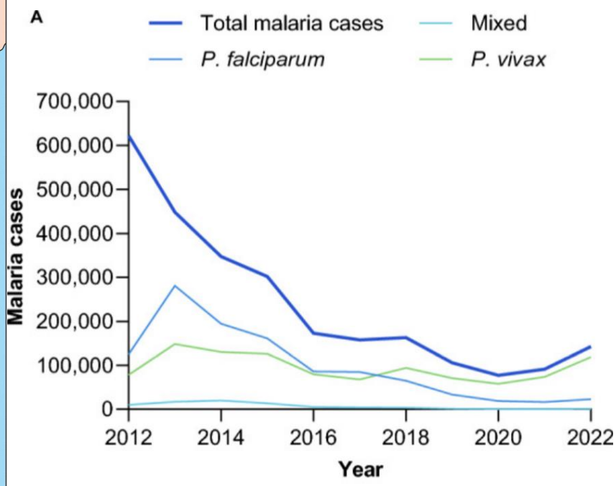
MALARIA IN THE GMS: MAJOR PROGRESS, YET PERSISTANCE

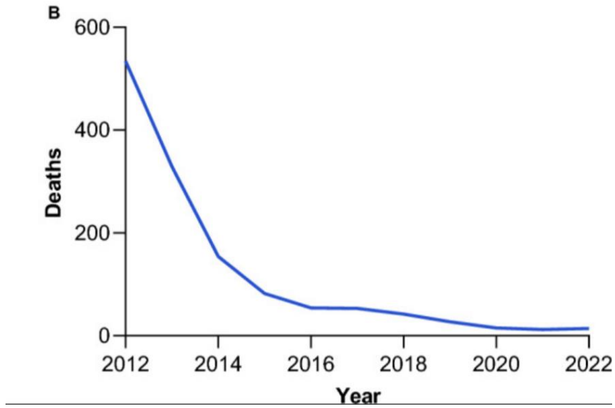
Achievements	Challenges	Way forward
77% decrease in malaria cases across GMS, 94% for P. falciparum cases	- Pockets with high transmission persist mostly **forested** areas, hence along **borders** - Recent increase in Myanmar (political instability), spilling to Thailand	Geographically targeted interventions are needed to address remaining hotspots
Containment of Artemisinin Resistance and Multi-drug Resistance	Continued threat of drug resistance	Keep malaria
Deployment of Malaria Workers in high transmission areas	Malaria vectors remain in forests and immediate surroundings	Intensify targeted Interventions for High-risk Populations: TDA, IPTf
Stronger surveillance systems for timely detection of drug resistance and malaria cases	Fewer cases complicate surveillance system	Increase granularity of data to identify and respond to malaria foci
Focus on high-risk groups: Forest Workers	Mobile Populations	Intensify Community Engagement and Cross-border collaboration
Political Commitment and Strategic Planning	Vivax more resilient to elimination than falciparum	Vivax: new drugs, point-of-care diagnostics, personalized treatment approaches



Geographical spread of resistance to ACTs for malaria.

Incidence across the GMS of malaria cases and malaria deaths



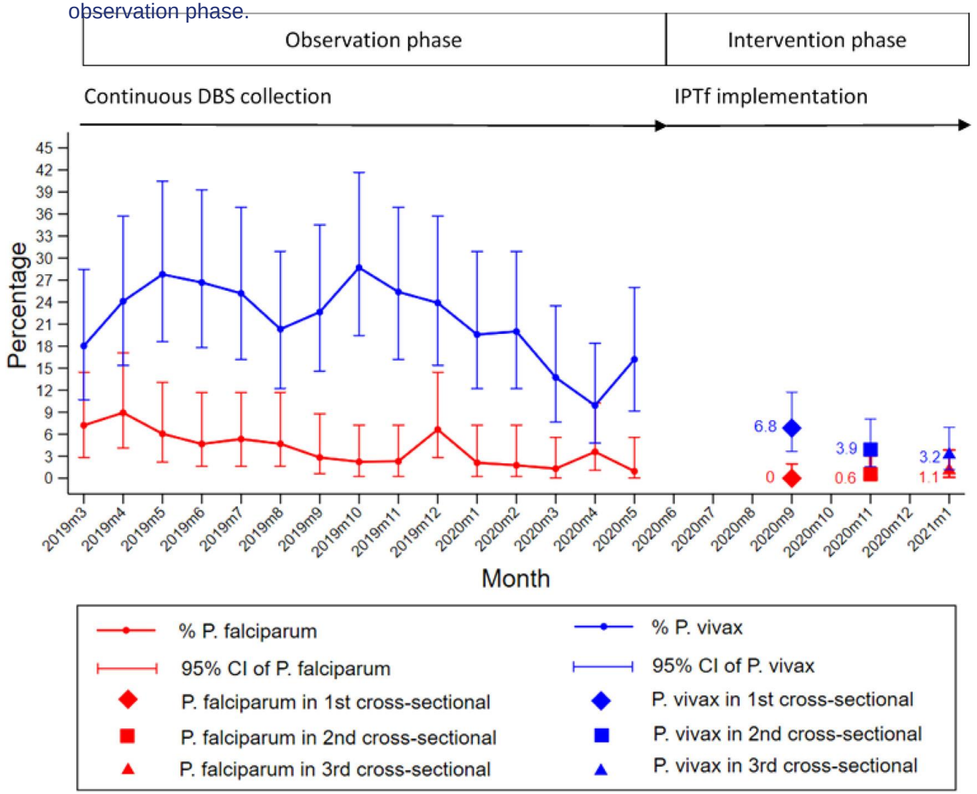


Source: MEDB database; Manzoni, Giulia et al.
"Progress towards malaria elimination in the Greater Mekong Subregion: perspectives from the World Health Organization."
Malaria journal vol. 23,1 64. 1 Mar. 2024, doi:10.1186/s12936-024-04851-z)

Malaria: from research to policy

Targeted Interventions for High-risk Populations: TDA, IPTf

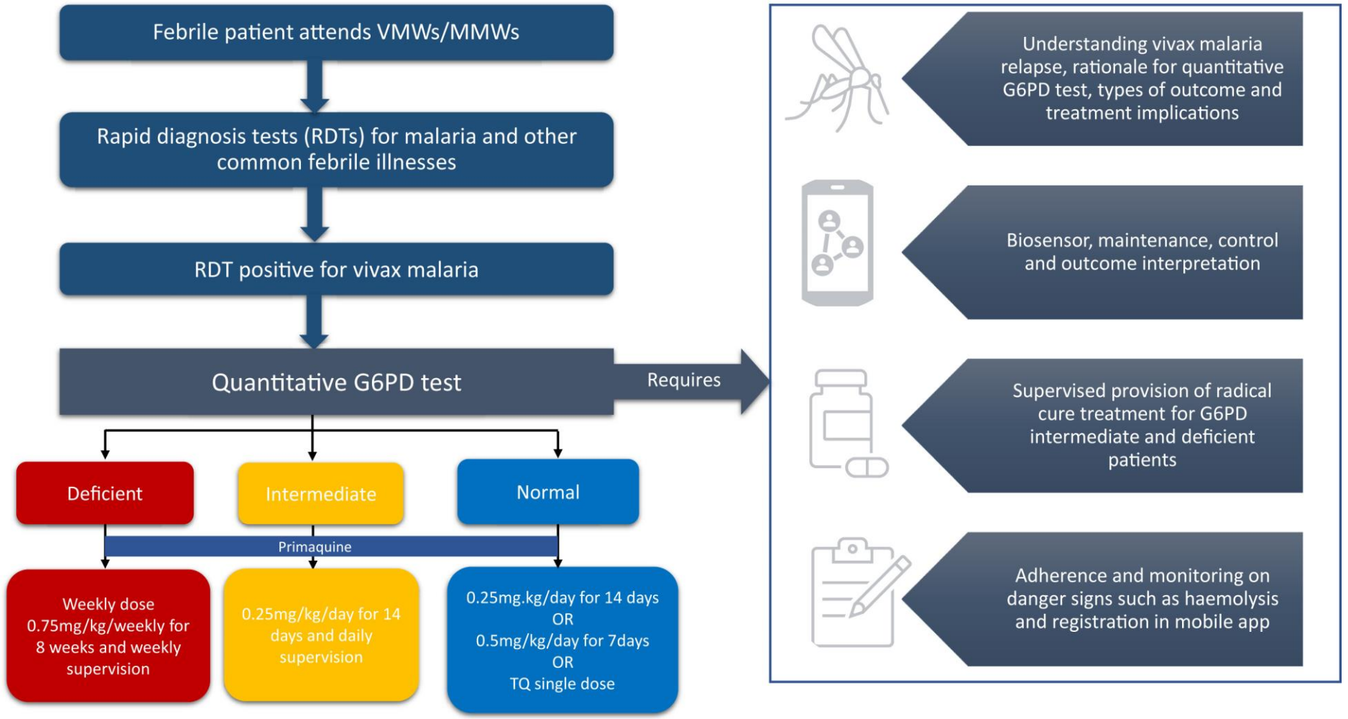
Trend of malaria prevalence inside the study forests in the observation and intervention phase. Mixed cases were added in each P. falciparum and P.vivax prevalence during the observation phase.



Iv, S., et al. (2024). "Intermittent preventive treatment for forest goers by forest malaria workers: an observational study on a key intervention for malaria elimination in Cambodia." Lancet Reg Health West Pac **47**: 101093.

Community-based vivax malaria management

How village malaria workers and their network could be trained and supervised for community-based vivax malaria management



Adhikari, Bipin, et al. "Village malaria workers for the community-based management of vivax malaria." *The Lancet Regional Health-Southeast Asia* 9 (2023).

Malaria:
Questions for action

How to adapt **surveillance** in remote areas for a disease becoming rare, surveillance being instrumental to elimination?

Can such surveillance of rare events be mutually beneficial with EID surveillance?

How to keep monitoring antimalarial drug resistance when cases are very few and scattered ?

How to reinforce Targeted DA or prophylaxis (IPTf) for high-risk populations in forested and border areas?

How to reach a high coverage of a safe radical cure for Vivax malaria?

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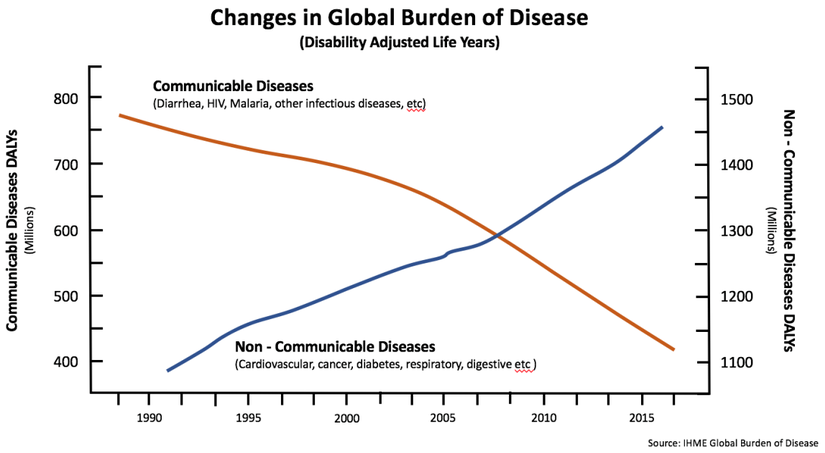
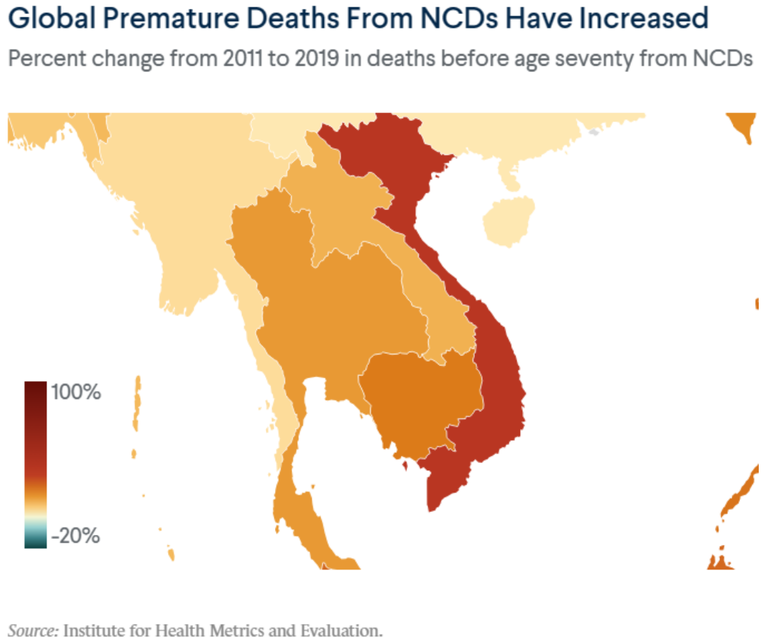
NCD: non-communicable diseases

NCDs:
The Rising Threat

- Unhealthy lifestyles of HICs now in GMS: poor diets, physical inactivity
- Aggravated by air pollution and environmental challenges
- Epidemiology:

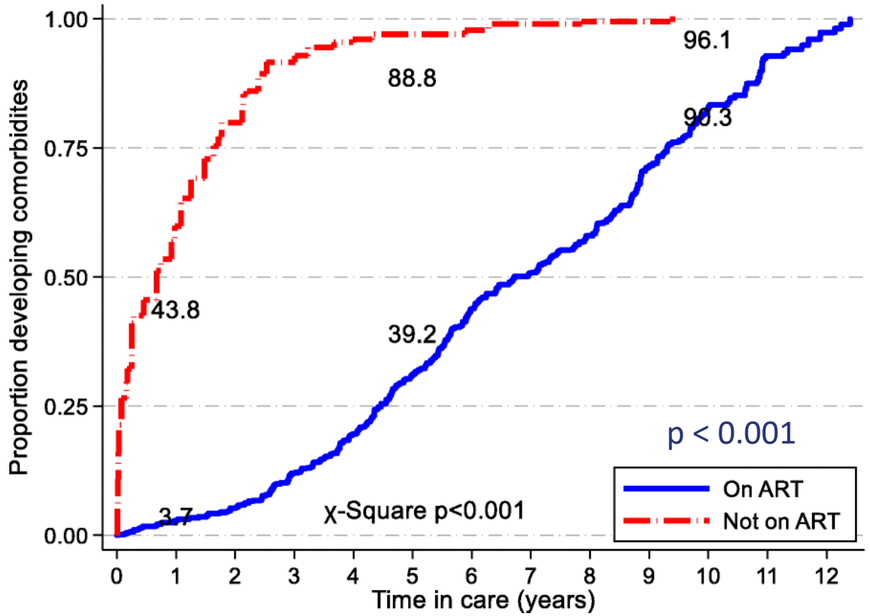


Proportion of noncommunicable disease (NCD) deaths occurring among middle-aged (45–59 years old) and older people (≥60 years old), by WHO region, 2016. *Source:* WHO (2018b).



NCDs in PLHIV

Proportion of patients developing comorbidities any time and during follow-up by ART status, Longitudinal Surveillance of Treatment in Kenya, 2016 (*N* = 3170)

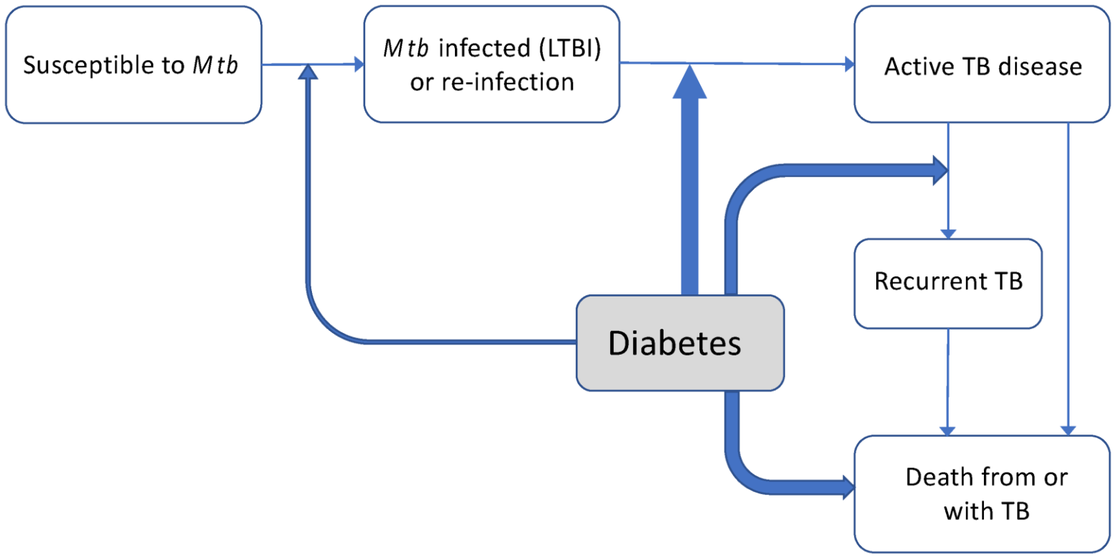


- Sharp rise in NCD diagnosis in PLHIV not on ART initially.
- Gentle trajectory for PLHIV on ART.
- 1-year follow-up: 43.8% NCD in non-ART vs. 3.7% in ART.
- 5-year follow-up: 88.8% NCD in non-ART vs. 39.2% in ART.

Achwoka, Dunstan et al. "Noncommunicable disease burden among HIV patients in care: a national retrospective longitudinal analysis of HIV-treatment outcomes in Kenya, 2003-2013." BMC public health vol. 19,1 372. 3 Apr. 2019, doi:10.1186/s12889-019-6716-2

NCDs and TB

Impact of diabetes on TB's natural history

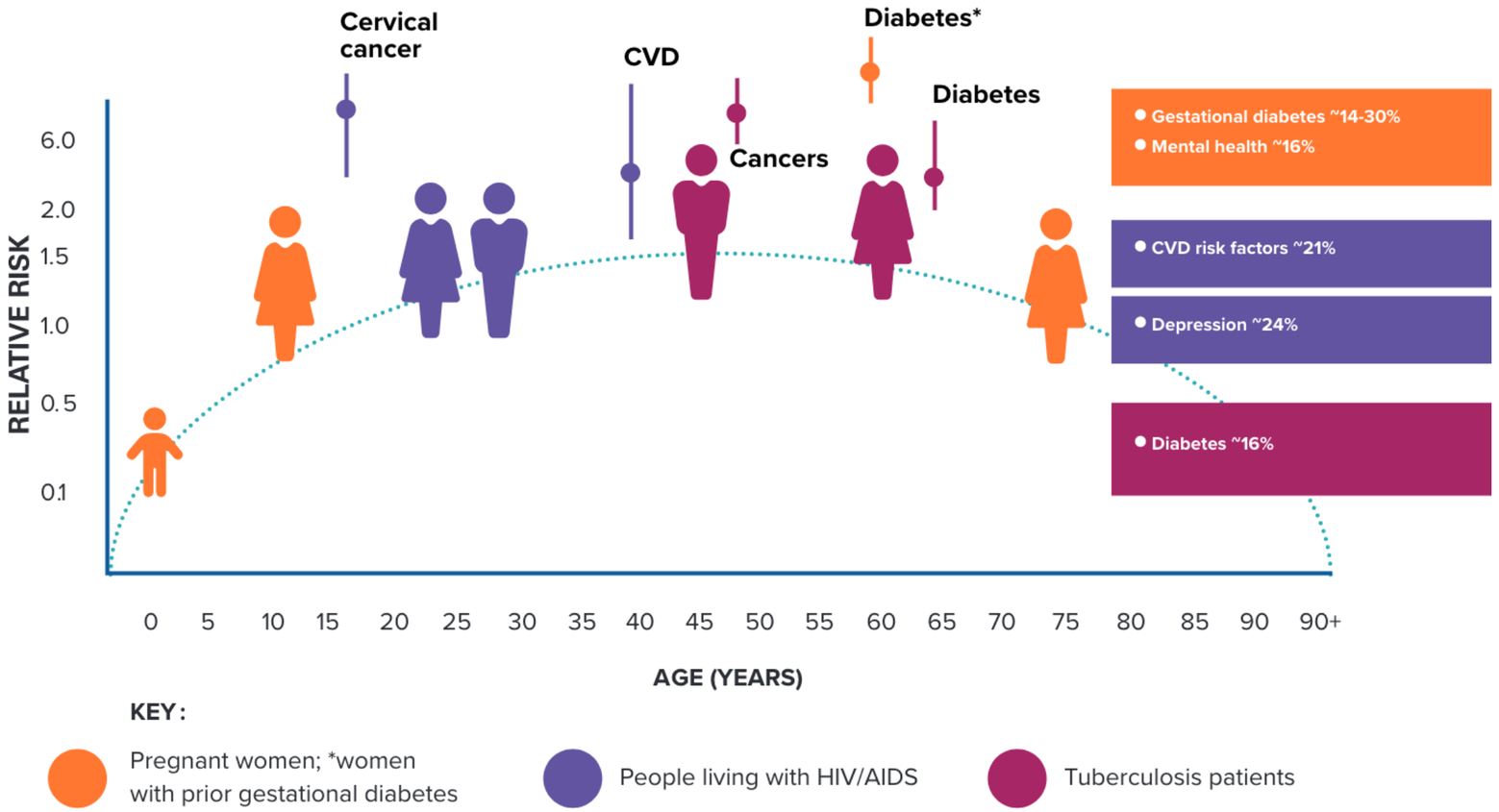


- TB pathways with diabetes impact.
- Line width indicates evidence magnitude and certainty.
- Refer to references for evidence and relationship details.
- Relationships: diabetes and TB susceptibility, disease, prognosis.

van Crevel, R.; Critchley, J.A. The Interaction of Diabetes and Tuberculosis: Translating Research to Policy and Practice. Trop. Med. Infect. Dis. 2021, 6, 8. https://doi.org/10.3390/tropicalmed6010008

Integration of NCD care and HIV/TB care

NCD prevalence and risk at different stages of life provide windows of opportunity to help address the NCD epidemic

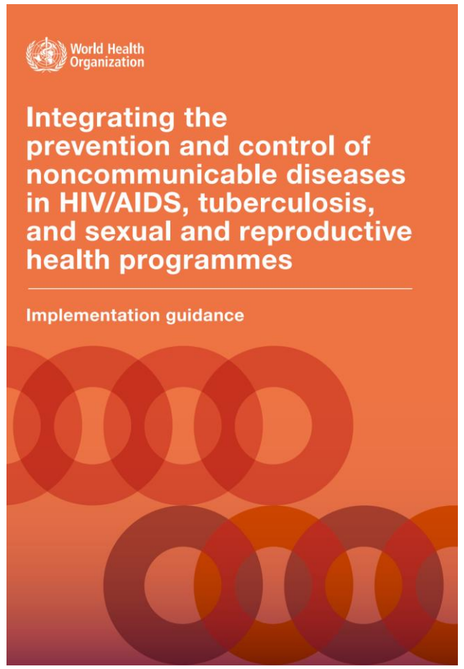


- 2x higher risk of cardiovascular disease (CVD) for people living with HIV.
- 1 in 4 people living with HIV have moderate to severe depression.
- 1 in 5 people living with HIV have one or more modifiable CVD risk factors.
- Type 2 diabetes prevalence among people living with HIV ranges from 1.3% to 18%.
- Ageing cohort of people living with HIV heightens chronic health conditions.
- Depression affects ART adherence and HIV outcomes.

NCDs: Questions for action

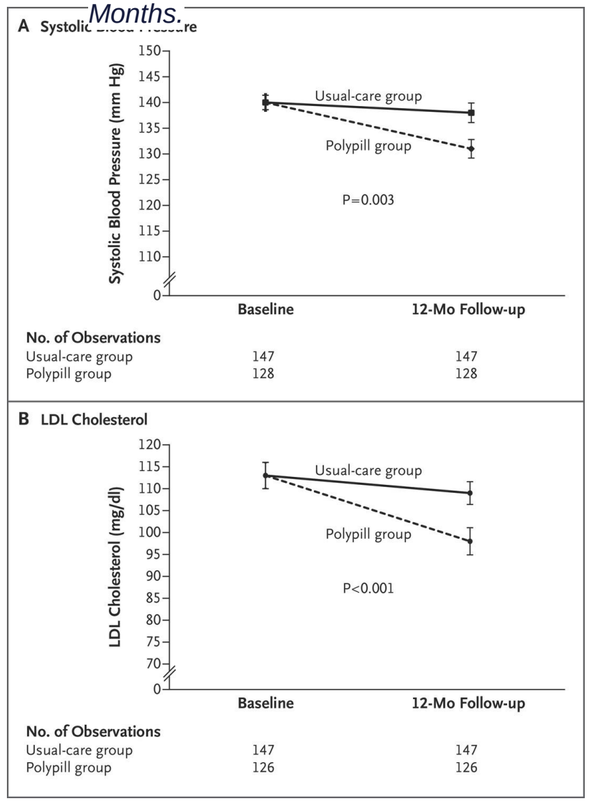
How to improve early detection and screening for NCDs in rural

How to integrate NCD care and HIV/TB care?



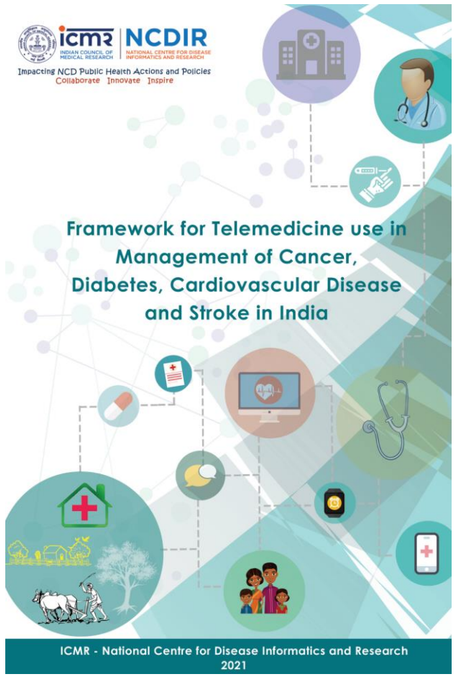
Is "polypill " deployment an adequate and feasible option in the CMS?

Changes in Systolic Blood Pressure and LDL Cholesterol Level at 12 Months.



N Engl J Med 2019;381:1114-1123

How could AI and telemedicine compensate for inequities and the uneven distribution of healthcare professionals in the



Conclusions

Key Achievements

- Significant reductions in the burden of HIV, TB, and malaria in the GMS.
- Increased access to ARTs and effective malaria interventions.
- Notable advancements in combating EIDs and AMR.

Persistent Challenges

- Stigma with HIV and improvable access to testing and treatment.
- Inadequate LTBI screening and preventive short-therapy scale-up.
- Ongoing threat of MDR TB and AMR.
- Managing rising NCDs and intersection HIV, TB.
- Mitigating health impacts of climate change in at-risk region.

Priorities

- Surveillance: Essential for monitoring and response across all diseases. Regional data-sharing enables consistency + efficiency.
- **HIV**: Enhance access to testing, treatment, and reduce stigma through community engagement.
- **TB:** Scale up screening and diagnosis in high-risk groups (IGRA), promote safer short-course preventive therapies (1HP/3HP) for LTBI, and prescribe TB preventive treatment to PLHIV as part of an integrated comprehensive management.
- **Malaria**: Intensify targeted interventions in high-risk areas and strengthen surveillance systems.
- Integration: Strengthen One Health collaborations/data sharing and efforts to address environmental changes and wildlife trade.
- Promote community engagement in health interventions.
- Migrants: provide health care to economic or insecurity (Myanmar) related migrants for disease control and altruism.
- Innovation: Advanced surveillance technologies for real-time data sharing, AI + telemedicine against health gaps in rural areas.

EXPERTISE FRANCE
GROUPE AFD

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L’INITIATIVE
sida, tuberculose, paludisme

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L’Initiative
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www.initiative.expertisefrance.fr/en

Expertise France
40 boulevard de Port-Royal
75005 Paris
01 70 82 70 82

ef.linitiative
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MISE EN ŒUVRE PAR EXPERTISE FRANCE GROUPE AFD

FINANCÉE ET PLACÉE SOUS LA TUTELLE DU MINISTÈRE DE L’EUROPE ET DES AFFAIRES ÉTRANGÈRES
Liberté
Égalité
Fraternité

DANS LE CADRE DE LA CONTRIBUTION FRANÇAISE AU LE FONDS MONDIAL