Infectious Diseases and Antimicrobial Resistance: Combined challenge to Nepal's Health System

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POPULATION AND THE SUSTAINABLE DEVELOPMENT GOALS

SDG Target 3.3 End the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases

HIV incidence

1.3 million

people were newly infected with HIV worldwide in 2022

Malaria cases

249 million

cases of malaria were estimated in 85 malaria endemic countries in 2022

TB incidence

10.6 million

people fell ill with TB in 2022

NTD treatment and care

1.62 billion

people were reported to require mass or individual care for neglected tropical diseases (NTDs)

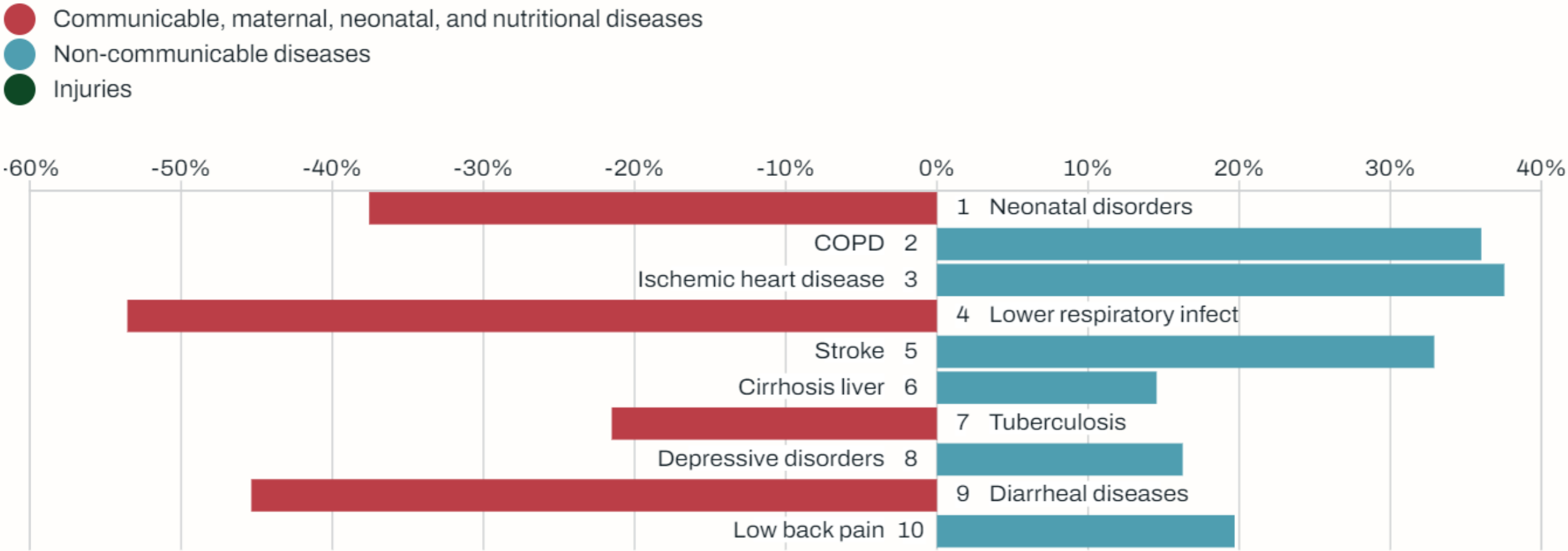
Goal	Diseases
Eradication	Dracunculiasis; malaria; polio; yaws
Elimination of transmission	Human African trypanosomiasis (HAT) (gambiense); leprosy; onchocerciasis
Elimination as a public health problem	Cervical cancer; Chagas disease; cholera; gonorrhoea; hepatitis B & C; HIV; HAT (rhodesiense); visceral leishmaniasis; lymphatic filariasis; maternal and neonatal tetanus; measles; meningitis; rabies; rubella (including CRS); schistosomiasis; STH/strongyloidiasis; syphilis; trachoma; TB; Japanese encephalitis; yellow fever

What causes the most deaths?

Communicable, maternal, neonatal, and nutritional diseases
Non-communicable diseases

Cause	2009 rank	2019 rank	Change in deaths per 100k, 2009–2019
COPD	1	1	↑ +22.1
Ischemic heart disease	2	2	↑ +18.4
Stroke	5	3	↑ +10.2
Lower respiratory infect	4	4	↓ −19.6
Neonatal disorders	3	5	↓ −26.0
Cirrhosis liver	8	6	↑ +2.8
Tuberculosis	6	7	↓ −6.6
Asthma	9	8	↑ +1.8
Diarrheal diseases	7	9	↓ −11.5
Chronic kidney disease	13	10	↑ +5.8

What causes the most death and disability combined?

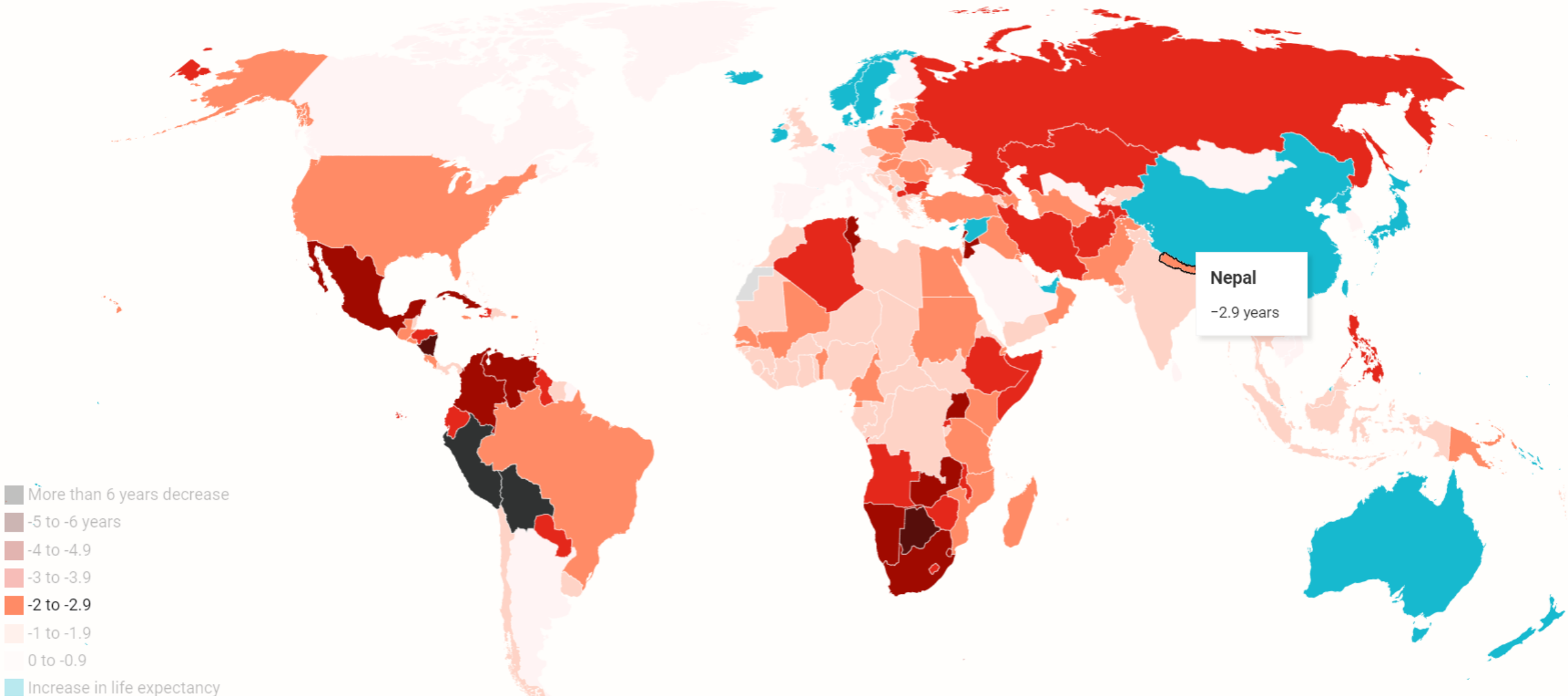


What risk factors drive the most death and disability combined?

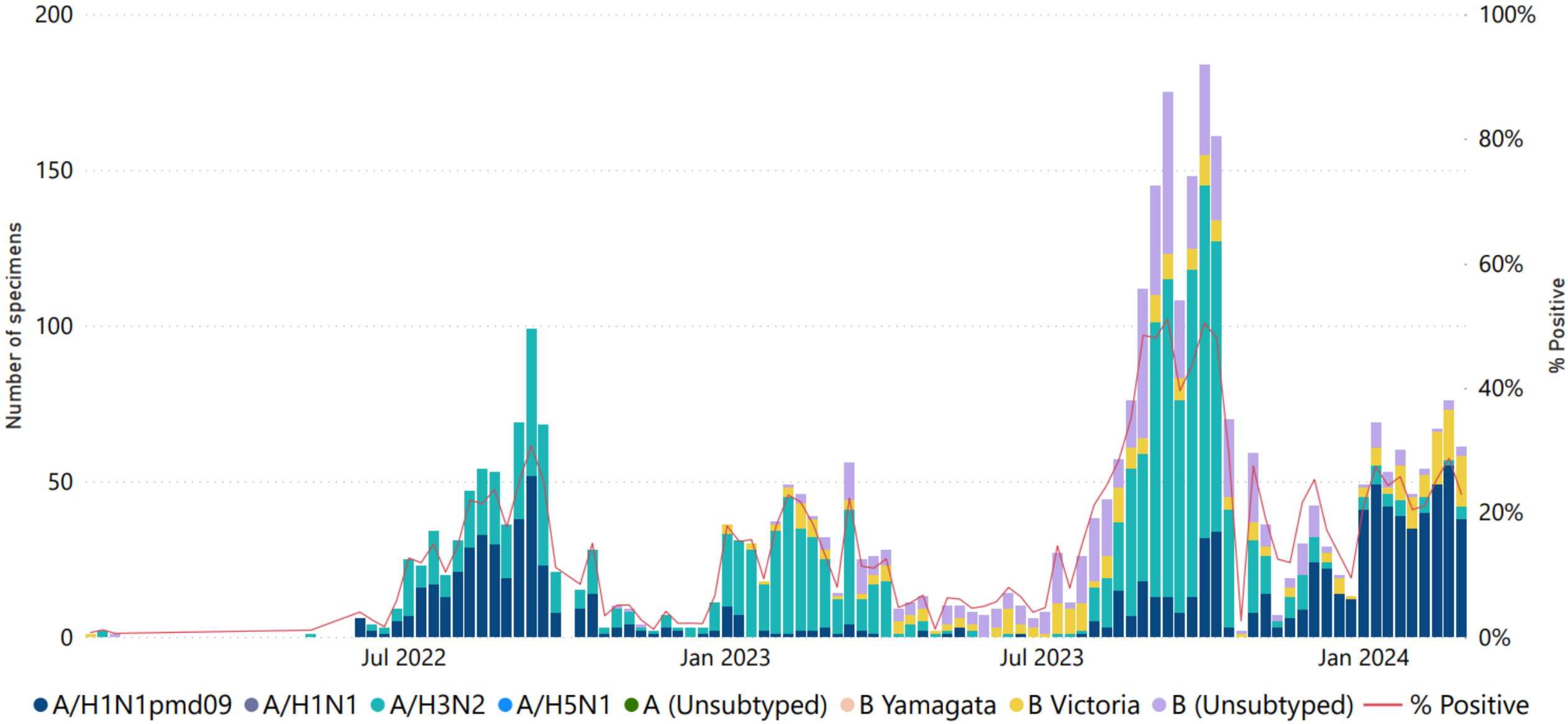
- Metabolic risks
- Environmental/occupational risks
- Behavioral risks

Risk	2009 rank	2019 rank	Change in DALYs per 100k, 2009–2019
Malnutrition	1	1	↓ −4,584.0
Air pollution	2	2	↓ −1,186.6
Tobacco	3	3	↓ −31.5
High blood pressure	5	4	↑ +144.9
Dietary risks	7	5	↑ +303.0
Occupational risks	6	6	↓ −3.3
High fasting plasma glucose	8	7	↑ +529.2
High body-mass index	12	8	↑ +465.3
Alcohol use	9	9	↑ +129.1
WaSH	4	10	↓ −1,100.3

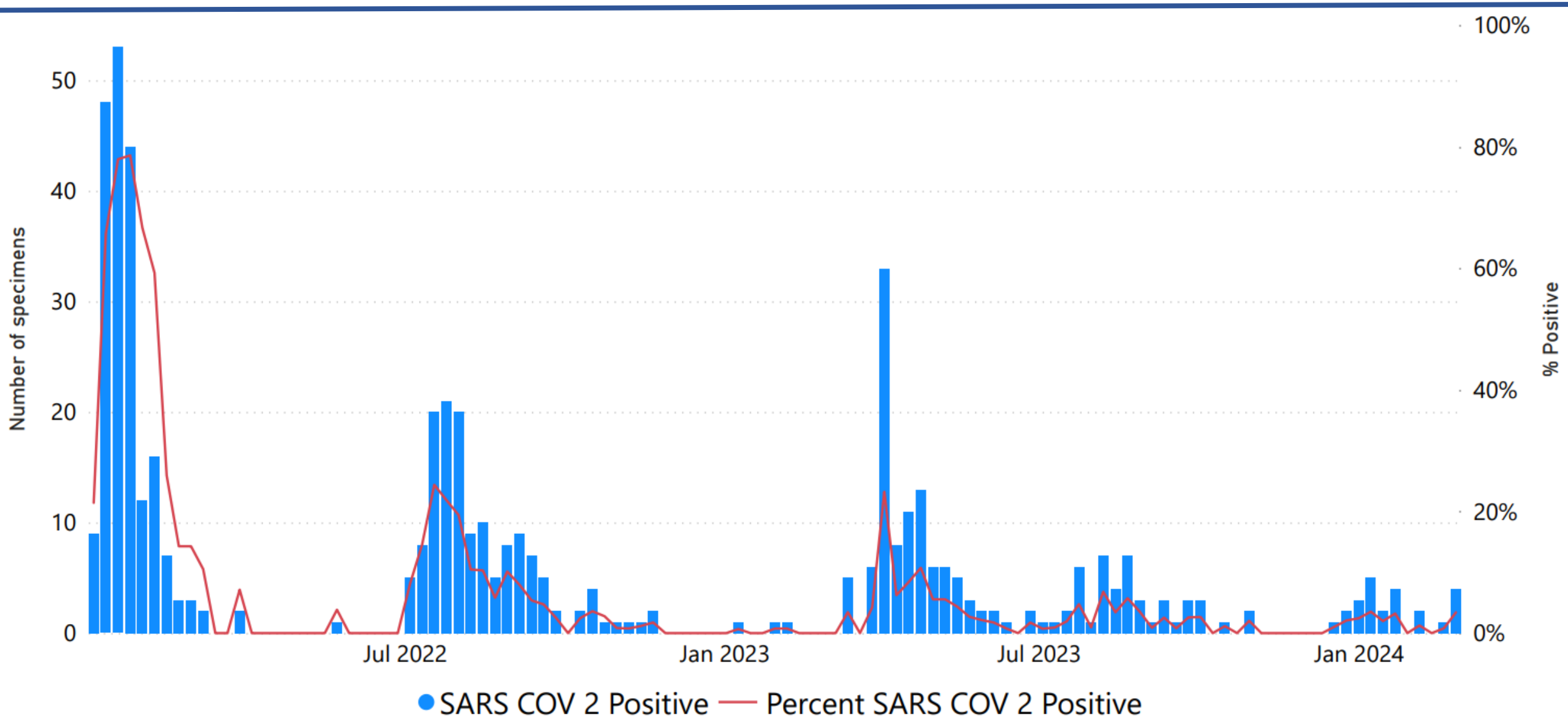
Change in life expectancy amid the COVID-19 pandemic, 2019-2021



Number of specimens positive for influenza by subtypes and the percentage positive, Nepal

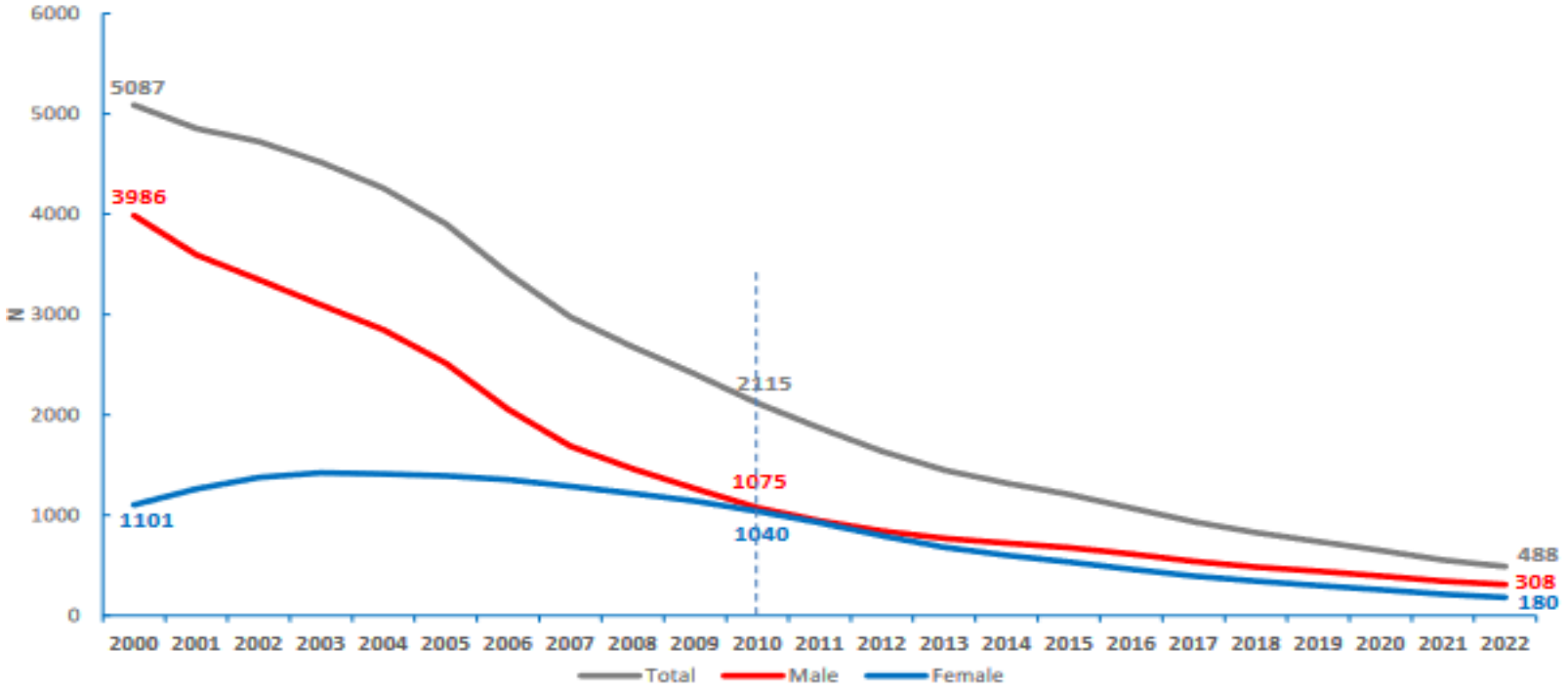


Number and the percentage of ILI/SARI specimens positive for SARS COV-2, Nepal

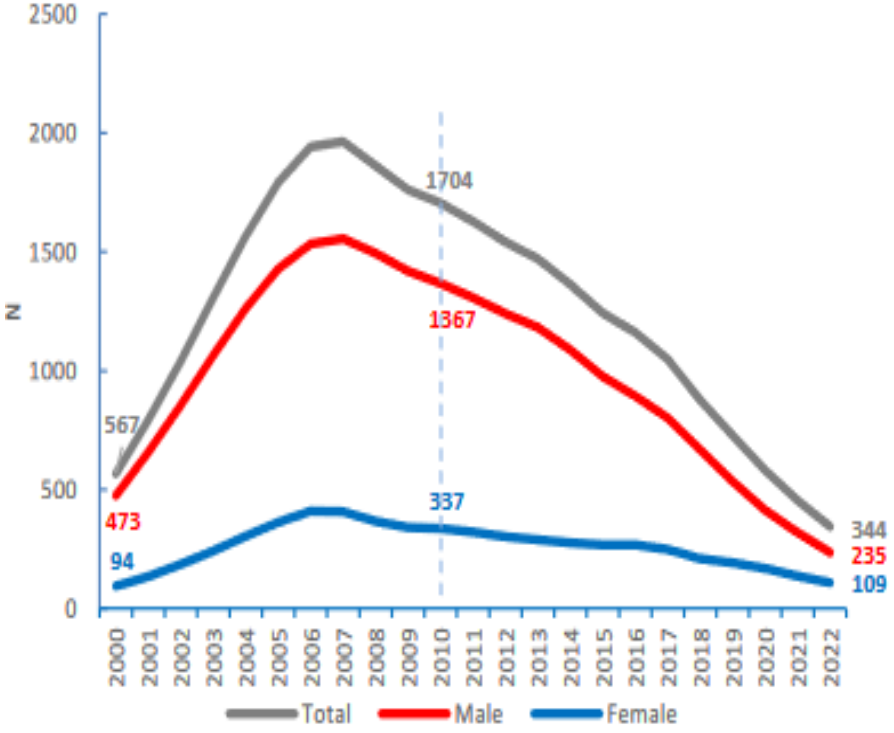


HIV/AIDS in Nepal

Trends of new HIV infections in Nepal (2000-2022)

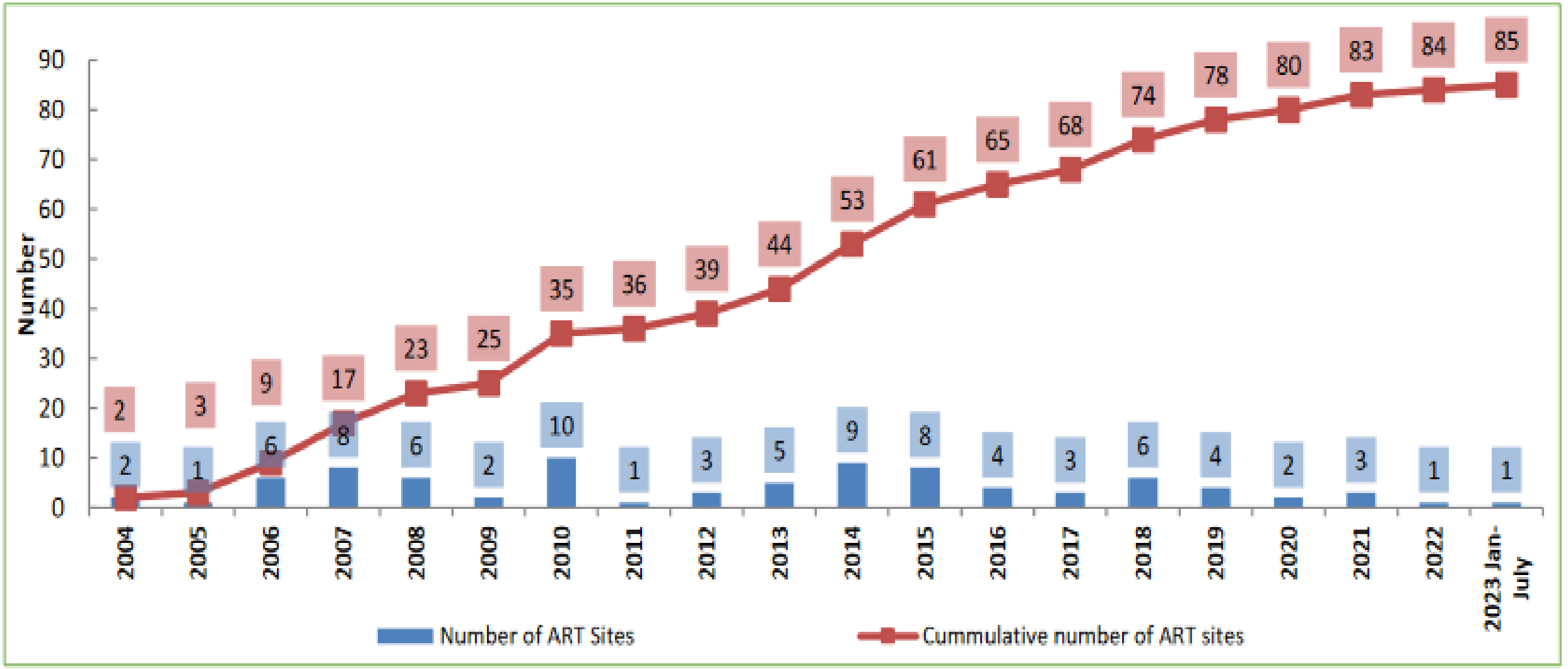


Number of AIDS deaths in Nepal



Long way to reach to 95,95,95 target

ART sites expansion every year for treatment & care



Tuberculosis including MDR-TB cases in Nepal

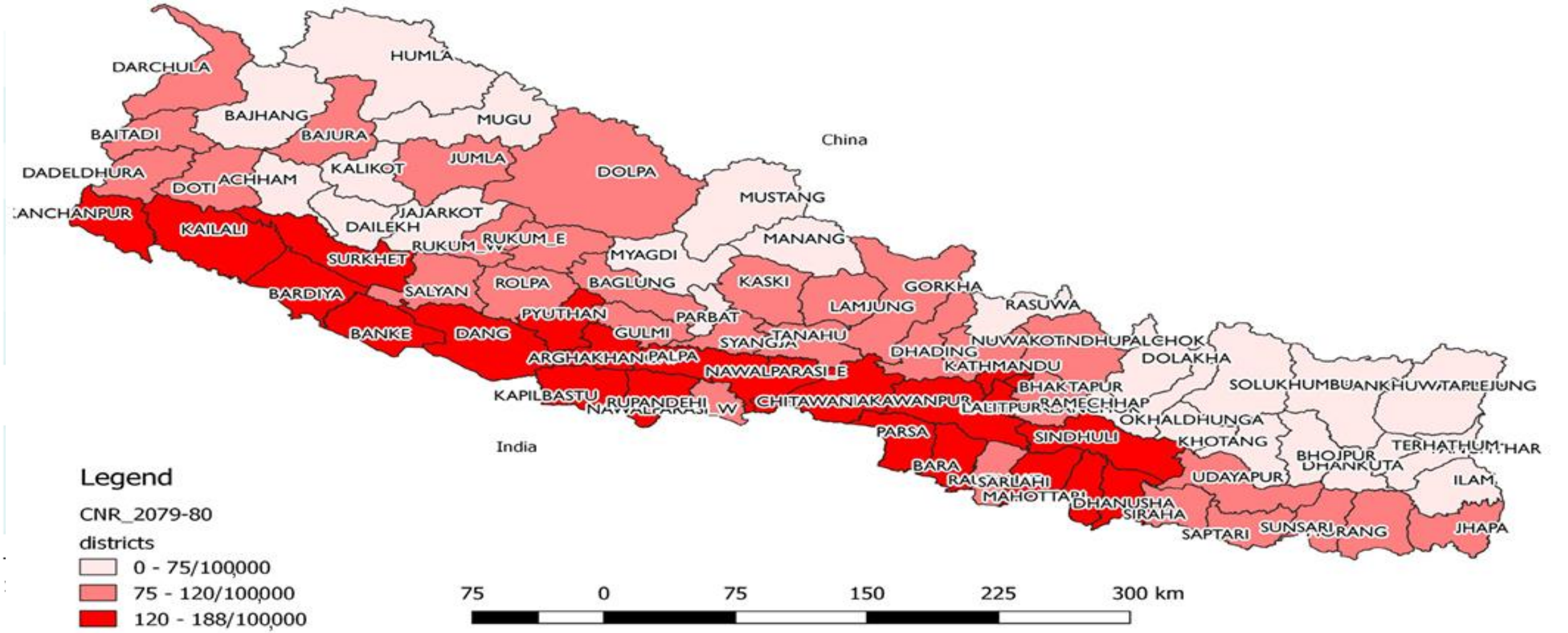


Figure 11.7 District wise tuberculosis case notification rate, 2079/80

Source: HMIS/NTCC/DoHS

Malaria in Nepal

- Significant progress has been made
  - 74% decline in total malaria cases and 98% decline in indigenous malaria cases in last 10 yrs
- Endemic districts are in the **Western Terai** region along India border
- Imported malaria cases increased from 42% to 97%, between 2010 to 2023.

UNITED NATIONS

WORLD HEALTH ORGANIZATION

BIBLIOTHEQUE OMS WHO 20 AOUT 1954

NATIONS UNIES

ORGANISATION MONDIALE DE LA SANTÉ

MALARIA CONFERENCE FOR WESTERN PACIFIC AND SOUTH-EAST ASIA REGIONS

15-27 November 1954 - Taipei

a 60531

WHO/Mal/103.5
Taipei Conf./2.5
19 August 1954

ENGLISH ONLY

The Secretary of the Expert Committee on Malaria has the honour to communicate hereunder the following note:

INFORMATION ON THE MALARIA CONTROL PROGRAMME IN NEPAL

1. Present status of malaria control:

1.1 Recently estimated population of the country about 9,000,000.

1.2 Number of inhabitants living in malarious regions:

Low Terai - 4.0 million pop. - Malaria involves 80%

Mid Terai - 0.6 million pop. - Malaria involves 100%

Hill area - 4.5 million pop. - Malaria involves 10%

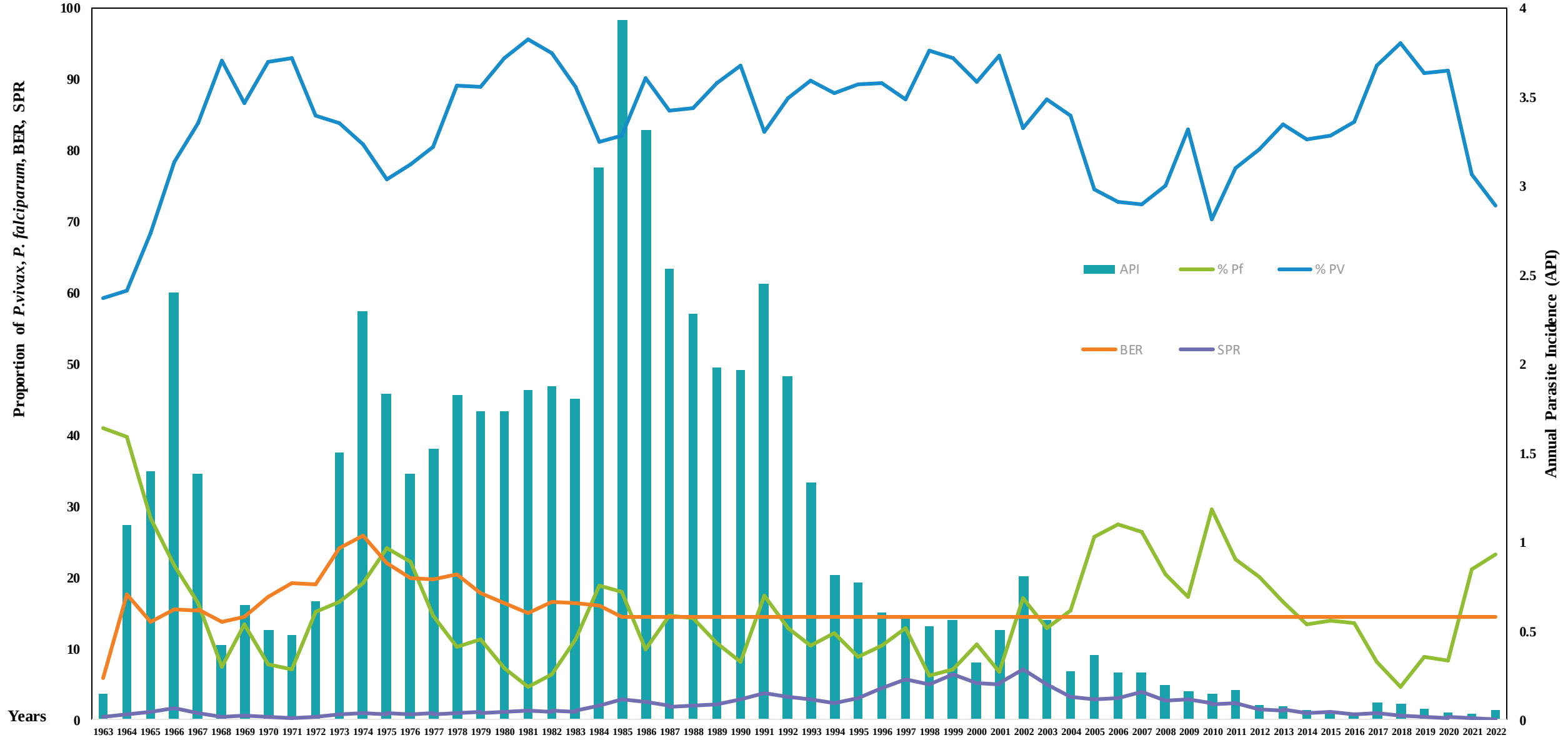
About 5.1 million people live in malarious area.

1.3 Estimated cases of malaria per year (1952) - 3,445,000

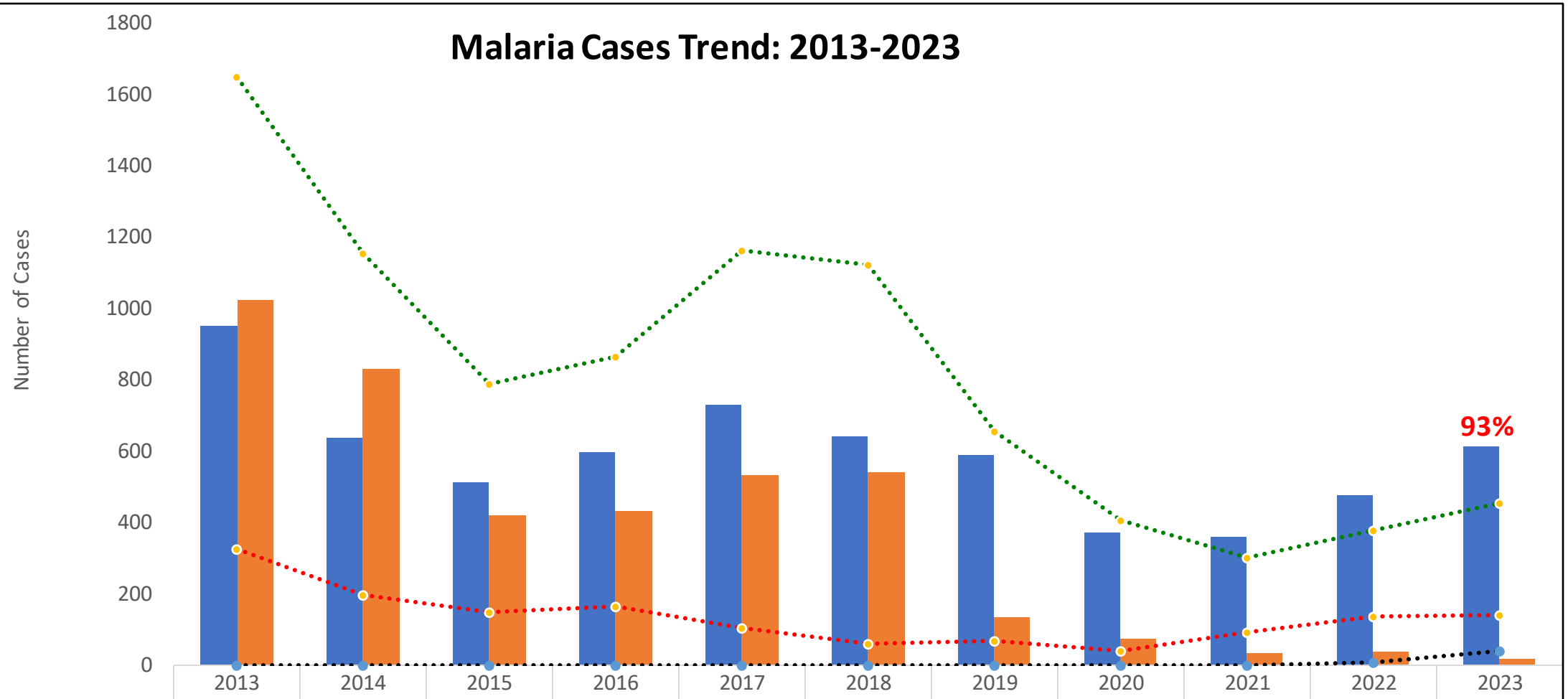
Estimated deaths from malaria per year (1952) - 38,450 directly and 38,450 indirectly.

Malaria is not notifiable.

Key malariometric indices of malaria epidemiology in Nepal, 1963-2022



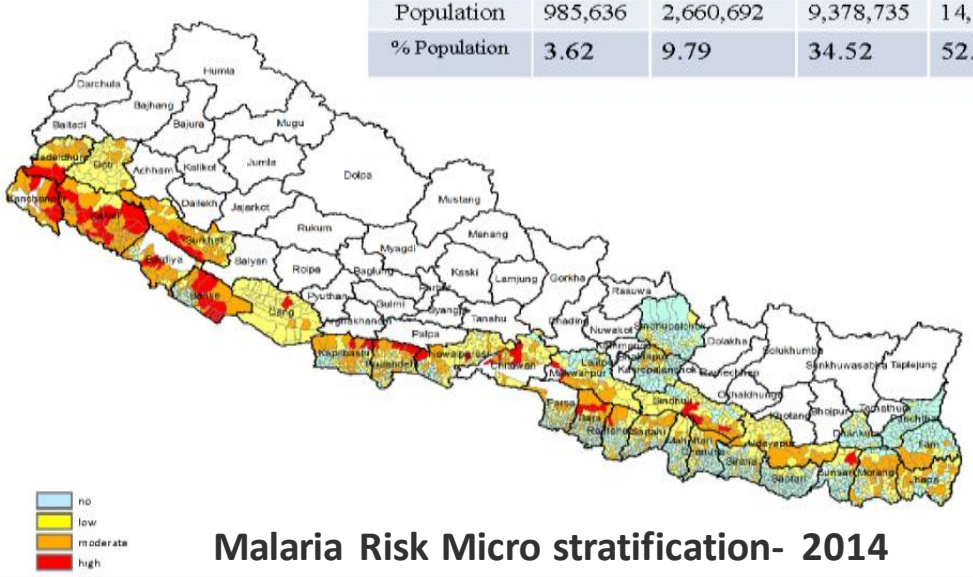
Malaria Cases Trend: 2013-2023



	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
IMP	950	637	514	595	731	641	587	373	359	476	613
IND	1024	832	420	432	534	541	134	74	32	36	17
Pv	1649	1154	788	863	1162	1123	655	407	300	376	452
Pf	325	195	146	164	103	59	66	40	91	136	140
Po	0	0	0	0	0	0	0	0	0	7	38

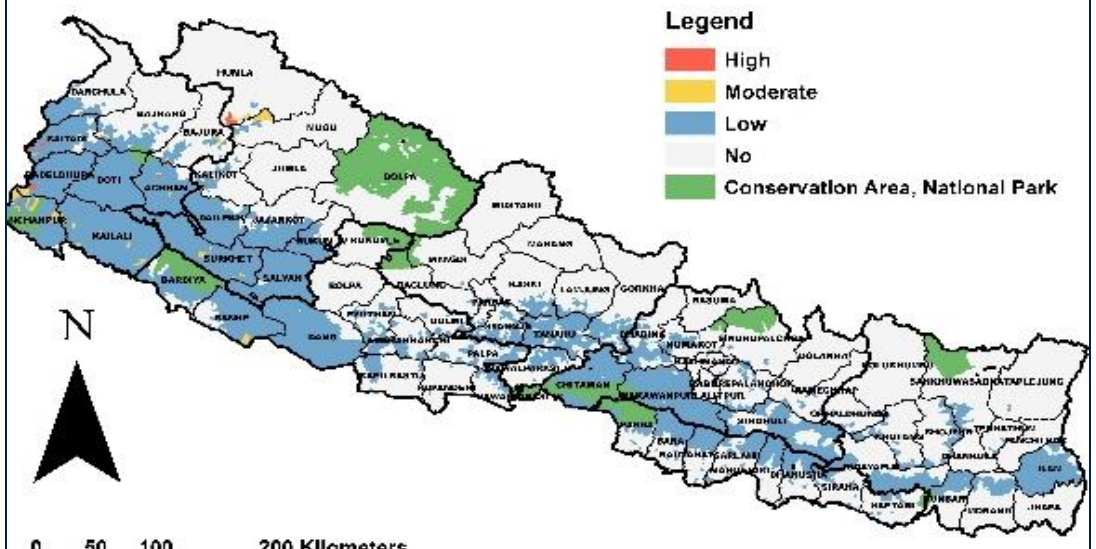
630

Particulars	High	Moderate	Low	No
No. of VDCS	54	201	999	2718
Population	985,636	2,660,692	9,378,735	14,139,920
% Population	3.62	9.79	34.52	52.05

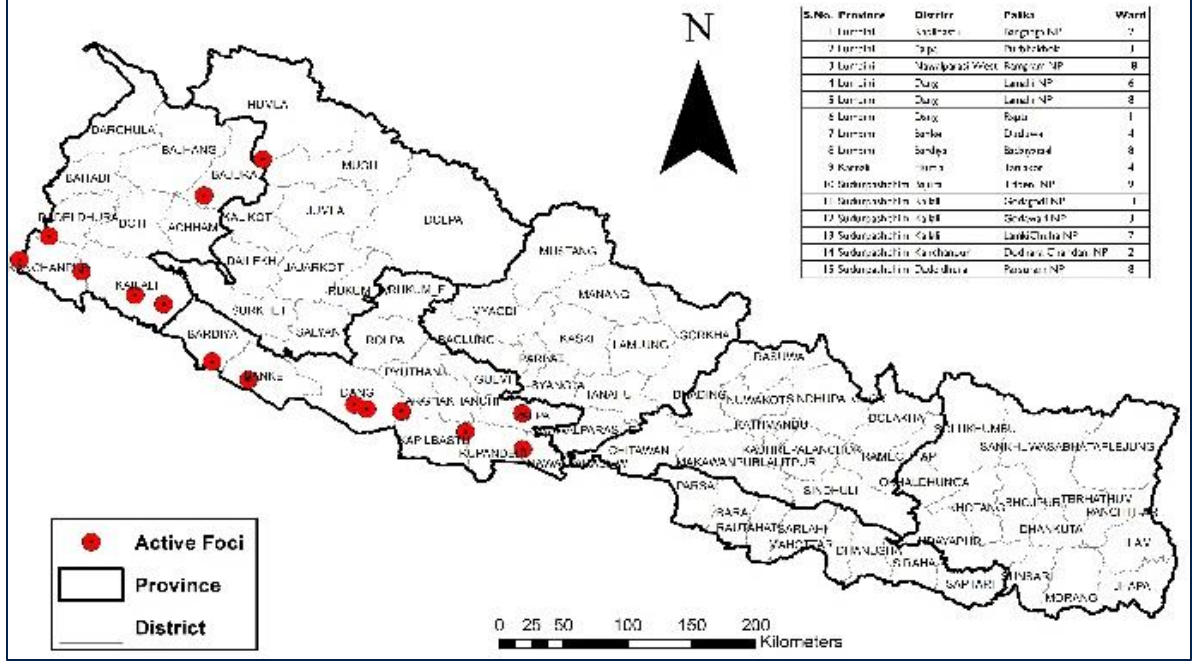


Malaria Risk Micro stratification- 2014

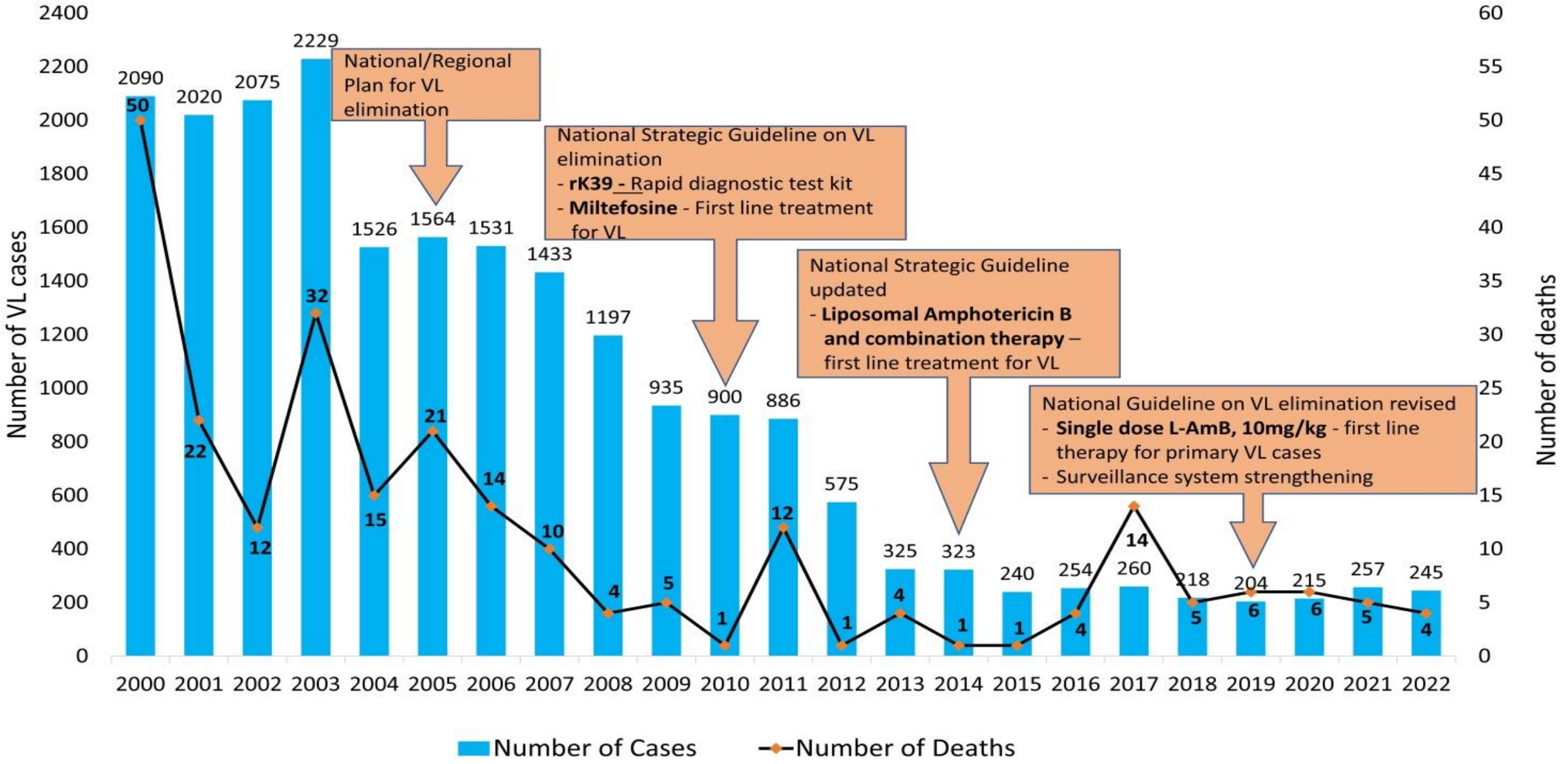
Malaria Risk Area as per Microstratification 2023



Malaria Active Foci in 2023



Visceral leishmaniasis in Nepal



Dengue in Nepal

SITUATION REPORT ON DENGUE IN NEPAL- 2023

1-Jan to 15-Dec

Reported Dengue Cases	51243
Confirmed Deaths	20
Affected Districts	77
No. of Districts with >500 cases	16

DENGUE: SYMPTOMS AND CARE

ANNUAL TRENDS OF DENGUE CASES (2004-2023)

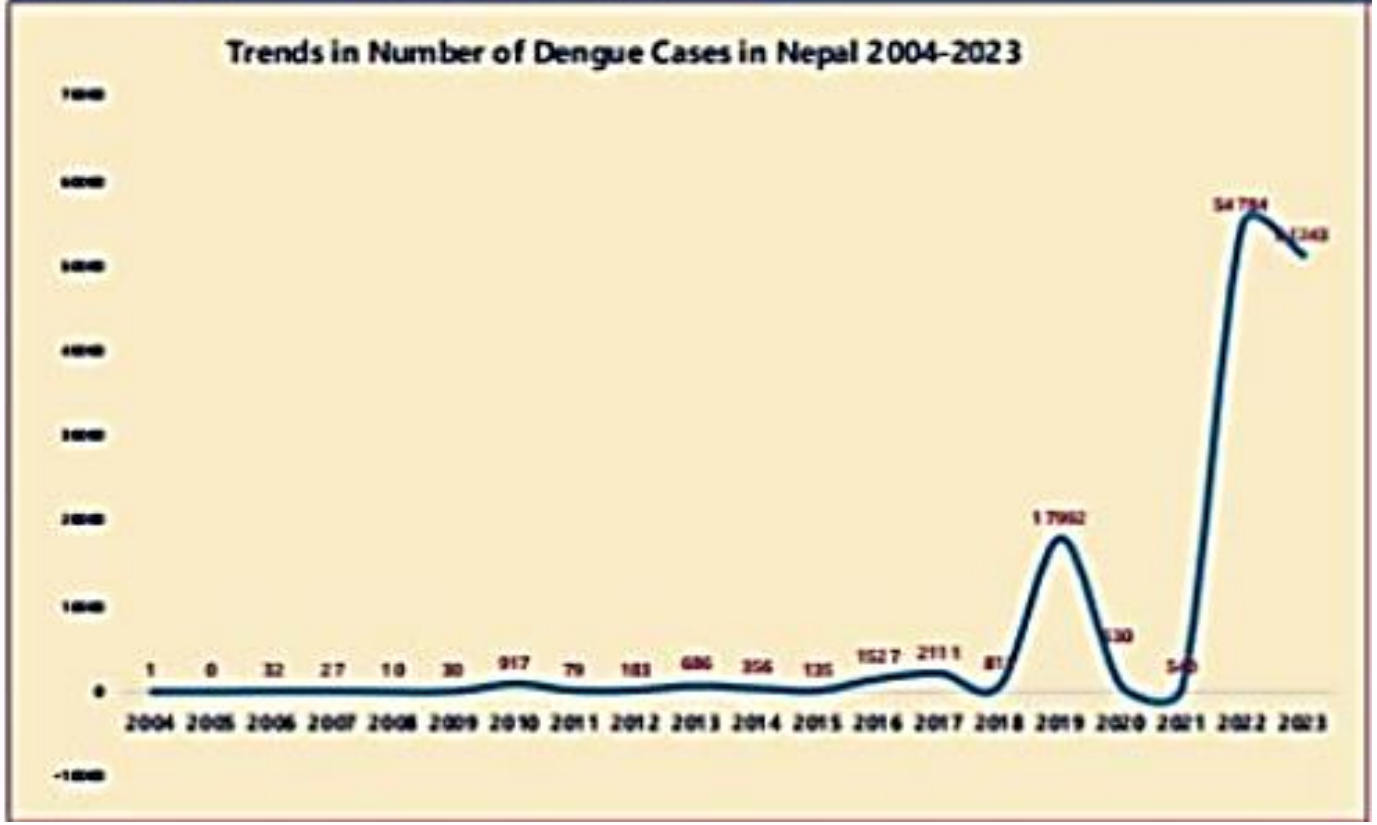
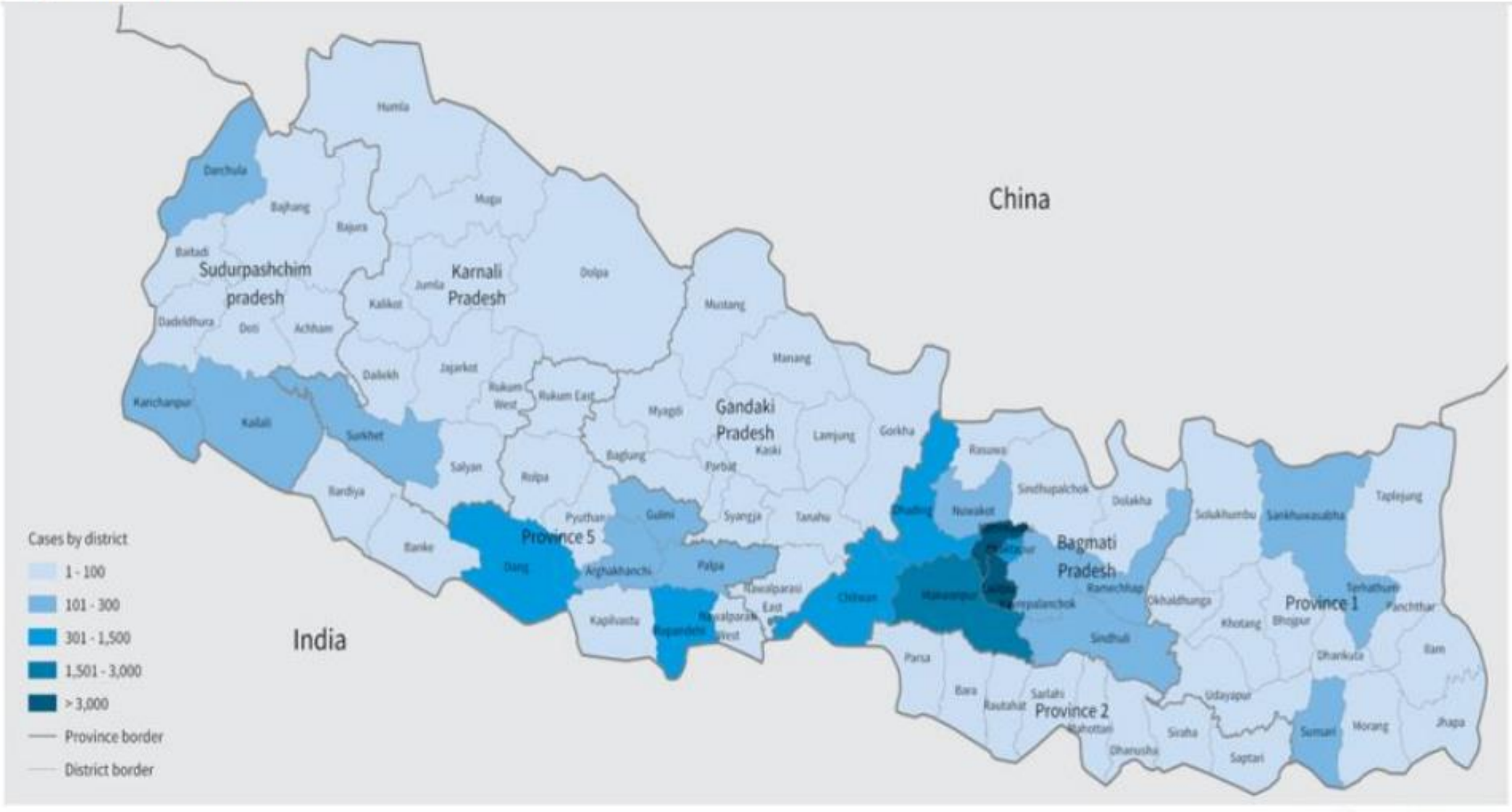


Figure 1. Number of Dengue cases reported from districts of Nepal from 1 January- 28 September 2022.



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Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme
Map Date: 5 October 2022

0 50 100 Km

World Health Organization

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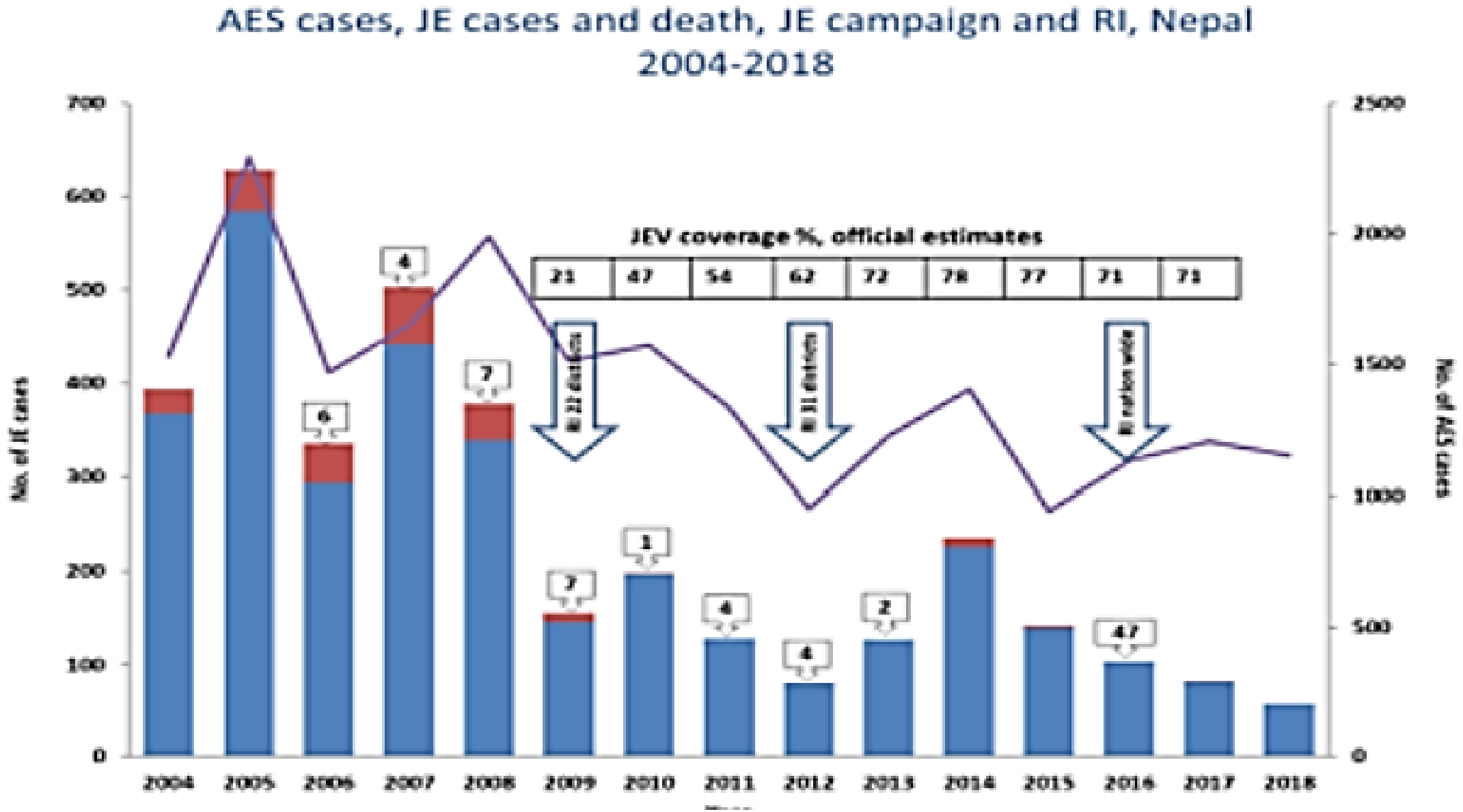
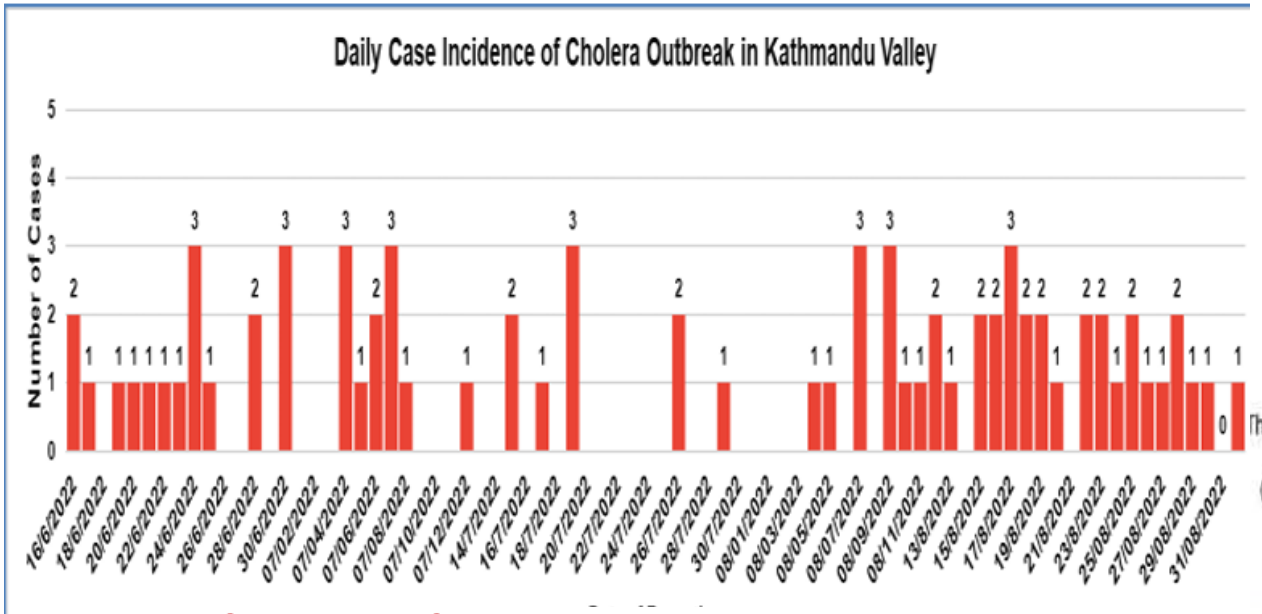
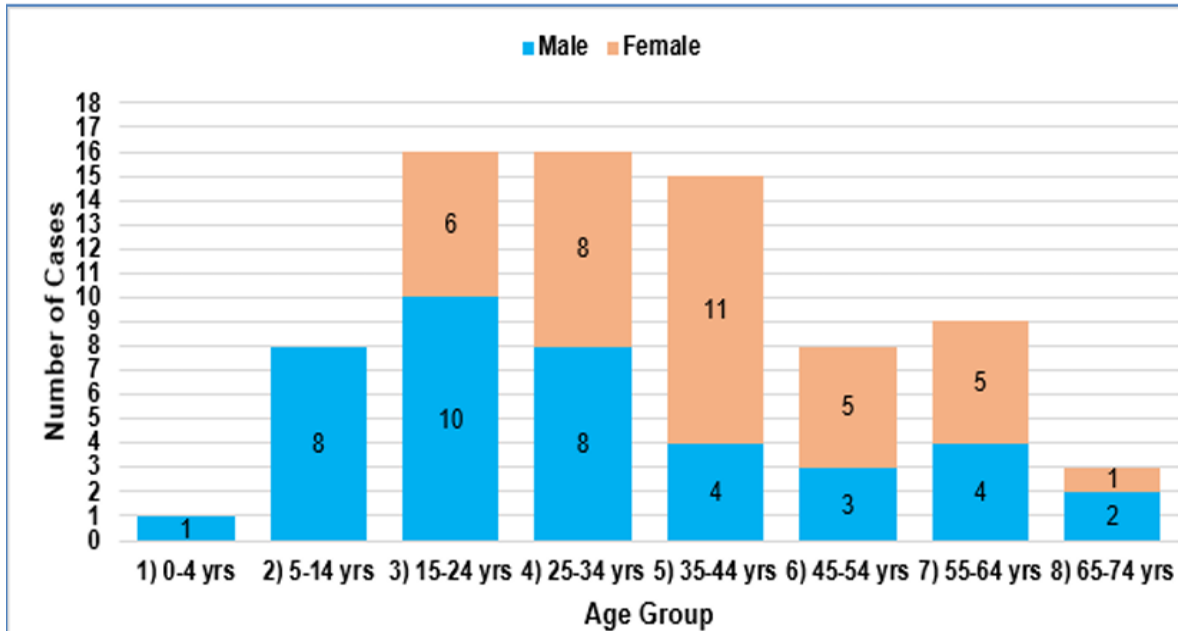
Japanese encephalitis



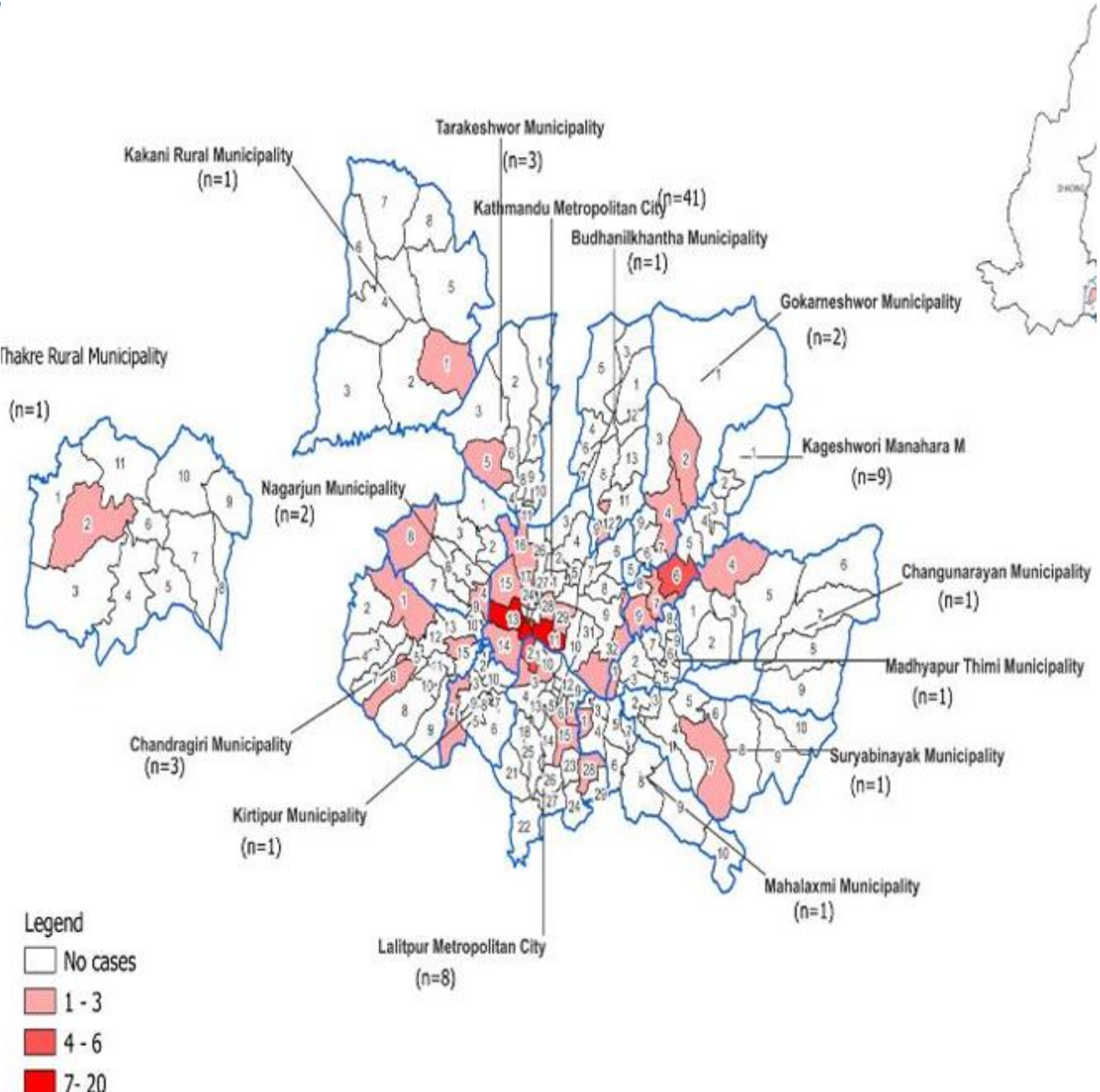
Epidemic curve of reported cases of Cholera in Kathmandu Valley, as of 5th September 2022 (n=76)



Age and Sex Distribution



Map showing cholera cases in Nepal: 16th June to 1 Sep 2022



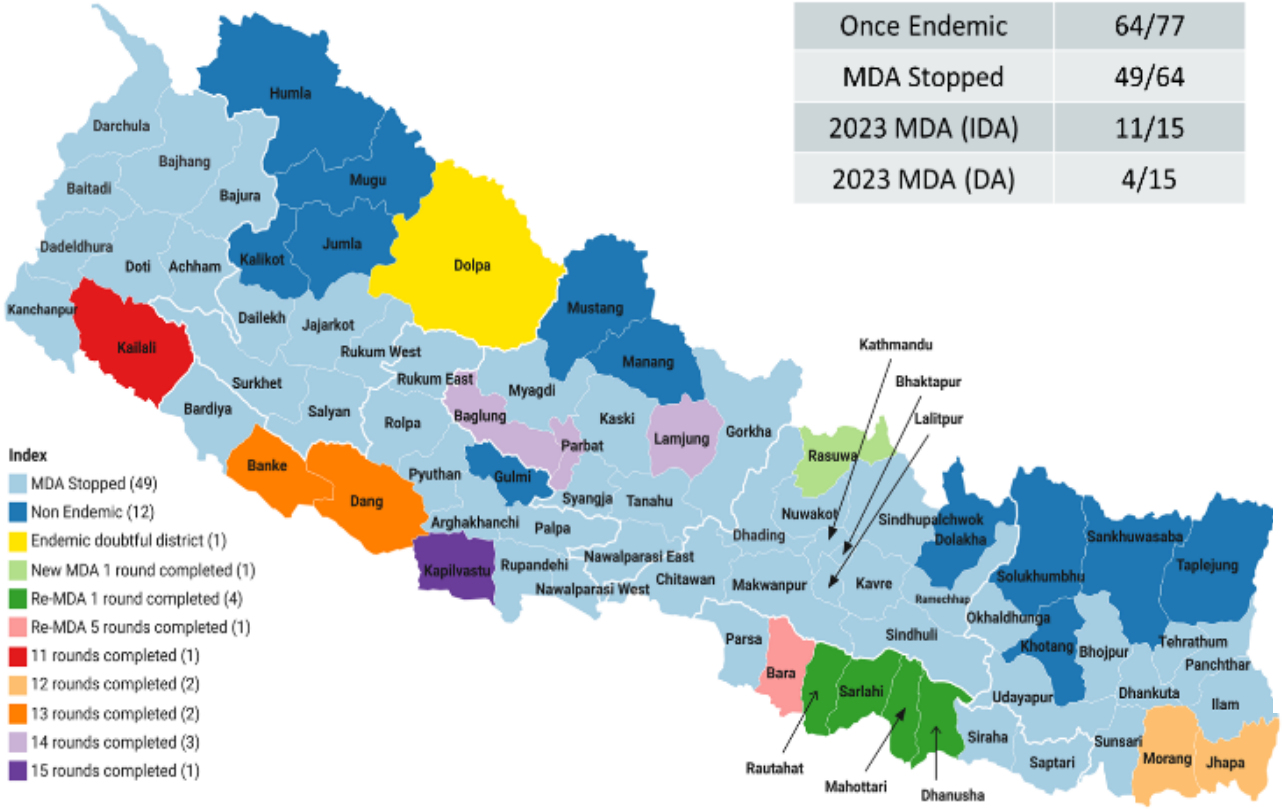
Lymphatic Filariasis

Province wise distribution of morbid cases of LF (as of September 2023)

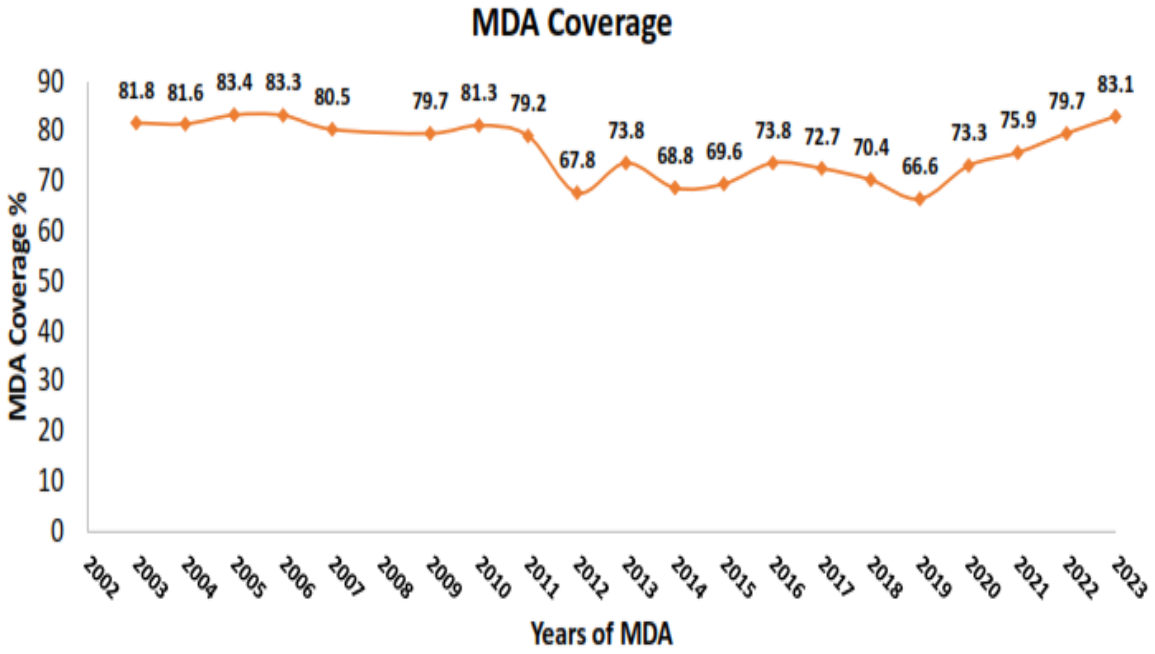
Province	Total population	Total districts	# districts having morbidity information	# lymphedema cases	# hydrocele cases	Both	Total
Koshi	5045125	14	6	689	1035	8	1732
Madhesh	6248281	8	8	2614	5363	71	8048
Bagmati	6169841	13	10	3968	4046	86	8100
Gandaki	2512938	11	6	502	563	3	1068
Lumbini	5220383	12	11	2872	6854	123	9849
Karnali	1725340	10	2	41	53	1	95
Sudurpaschim	2760121	9	8	1624	3914	37	5575
Total	29682029	77	51	12310	21828	329	34467

MDA coverage for LF

LF MDA Status of Nepal (2023)



MDA Status	# Districts
Once Endemic	64/77
MDA Stopped	49/64
2023 MDA (IDA)	11/15
2023 MDA (DA)	4/15



Leprosy

Province wise new leprosy cases and NCDR of FY 2078/79

Provinces	New Leprosy Cases	NCDR
Koshi	345	6.9
Madhesh	910	14.8
Bagmati	83	1.4
Gandaki	93	3.7
Lumbini	581	11.3
Karnali	68	4.0
Sudur Paschim	205	7.5
National	**2285**	**7.8**

Districts with PR>1 (16 districts) : Jhapa, Morang, Siraha, Dhanusha, Mahottari, Sarlahi, Rautahat,Bara, Parsa, Rupandehi, Parasi, Banke, Bardiya, Kailali, Kanchanpur and Achham

Scrub Typhus

- Underreported and often misdiagnosed acute febrile illness
- *Orientia (*formerly *Rickettsia) tsutsugamushi*
- First described in Japan in 1899
- Zoonotic disease but human is accidental host

Province wise scrub typhus cases reported to EWARS from 2077/78 -2078/79

S.N.	Province	2077.78	2078.79
1	Koshi	125	264
2	Madesh	6	89
3	Bagmati	159	240
4	Gandaki	102	163
5	Lumbini	382	687
6	Karnali	19	42
7	Sudurpaschhim	980	989
National Total		1773	2474

- Banke, Palpa, Kathmandu, Dhading, Morang, Chitwan, Kaski, Rupandehi, Dadeldhura, Kailali, Ilam, Kavrepalanchowk and Makawanpur (Source: EDCD)

Major programmatic activities

- Capacity strengthening of medical doctors and health workers
- Diagnostic support to health facilities
- IEC activities

Rabies

Status of reported animal bites and rabies in Nepal

Fiscal year	Number of cases of dog bites	Number of cases of other animal bites	No. of cases of animal bites (dog+ Other animal)	Number of ARV vials consumed	Reported Deaths
2073/74	37,226	2,518	39,744	227,639	8
2074/75	33,204	2,477	35,681	281,718	32
2075/76	32,882	2,368	35,250	236022	18
2076/77	52,610	4,009	56,619	-	15
2077/78	54,996	4,418	59,414		18
2078/79	75,562	9,921	85,483		13

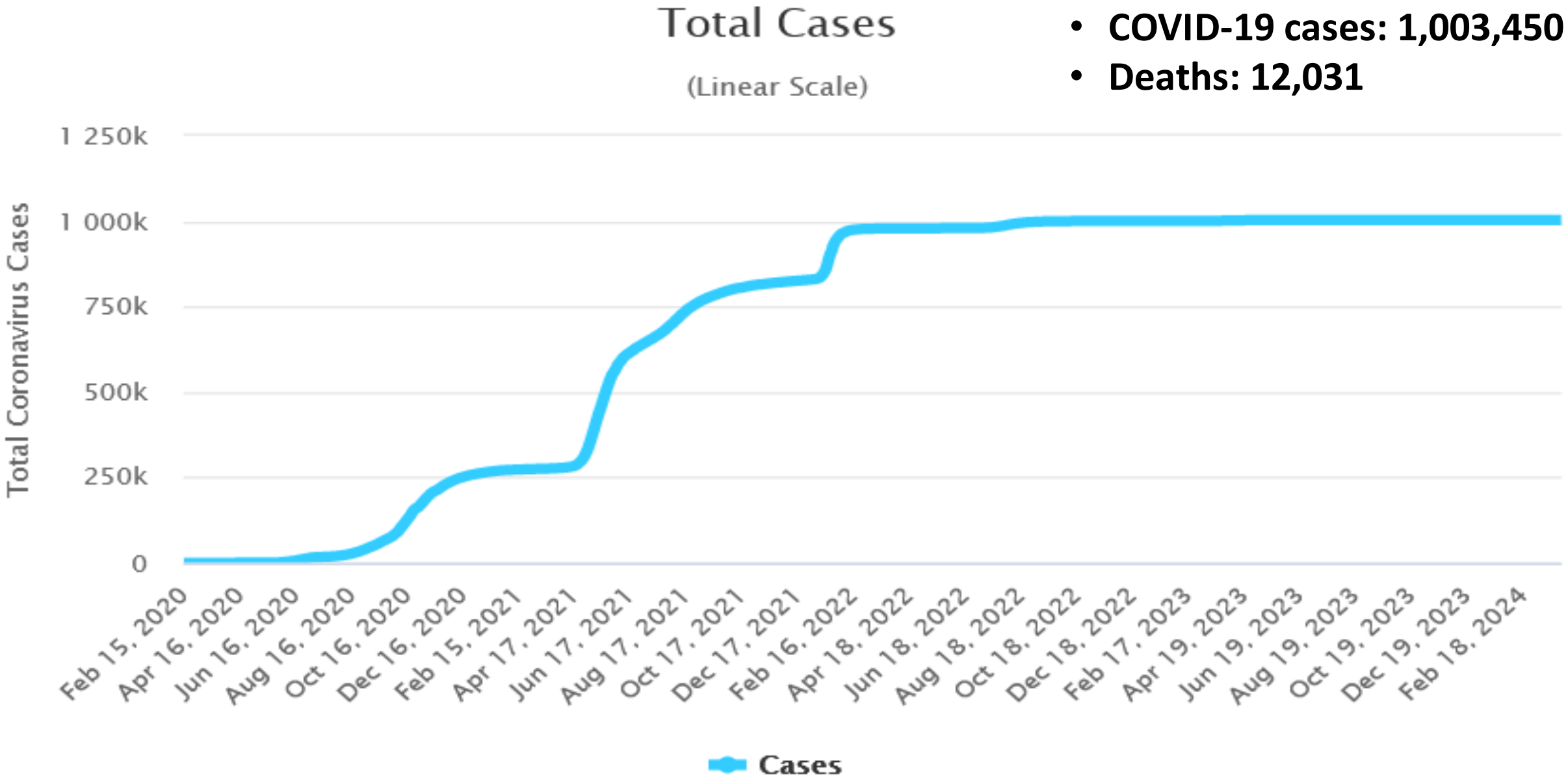
Source: EDCD/DoHS

Cell culture and embryonated egg-based rabies vaccines (CCEEVs) from Institute Pasteur du Cambodge (IPC) is now used for rabies in Nepal.

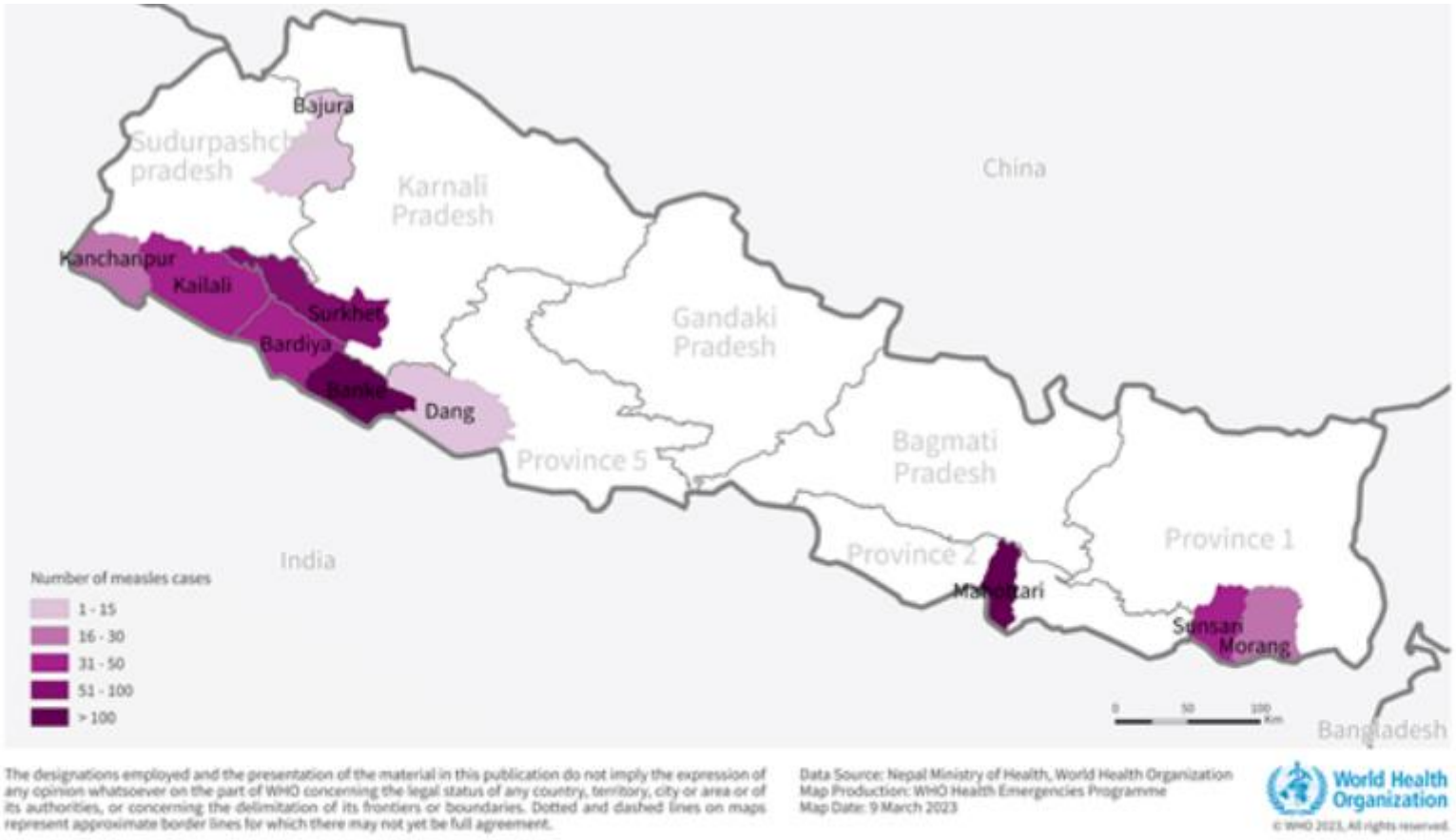
Dose	Route	Duration	No of Injection Sites Per Clinic Visit	Sites
0.1ml Each site	Intradermal	1 week • Day 0 • Day 3 • Day 7	2-2-2-0-0	• Deltoid OR • Lateral thigh

Outbreaks/Pandemics of Coronavirus

- **COVID-19 cases: 1,003,450**
- **Deaths: 12,031**



Measles cases & outbreaks in Nepal 2022-2023

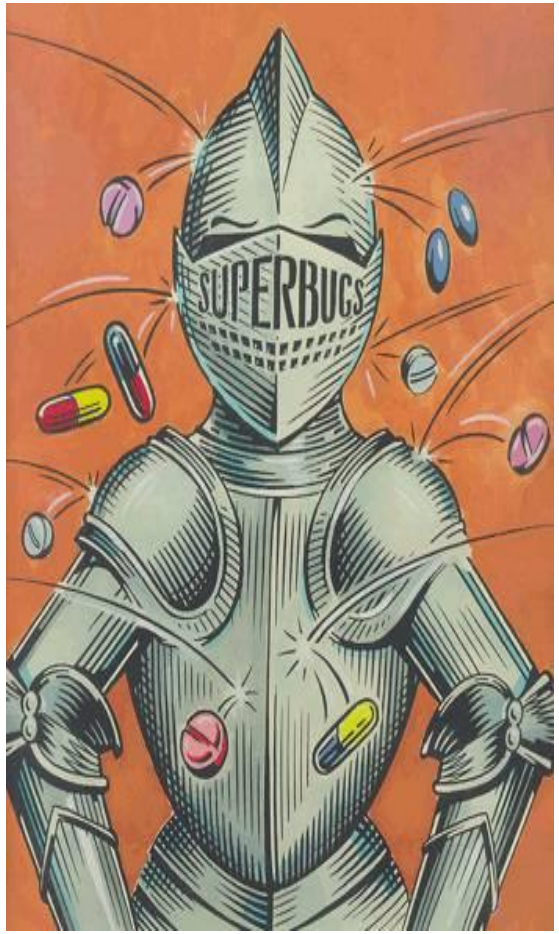


measles cases (n= 690) reported by district in Nepal between 24 November 2022 to 10 March 2023

https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON446

Most of the cases (n=327; 47%) were reported from Banke district, Lumbini province, which borders India. Additionally, the routine immunization outreach session sites and microplan[1] were not developed with community involvement, leading to very few outreach session sites, a lack of awareness, and a large number of children who missed the vaccination.

Alexander Fleming's Nobel Prize Lecture



"It is not difficult to make microbes resistant to penicillin ….

"The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under-dose himself and by exposing his microbes to nonlethal quantities of the drug make them resistant."

1929

ON THE ANTIBACTERIAL ACTION OF CULTURES OF A PENICILLIUM, WITH SPECIAL REFERENCE TO THEIR USE IN THE ISOLATION OF *B. INFLUENZÆ*.

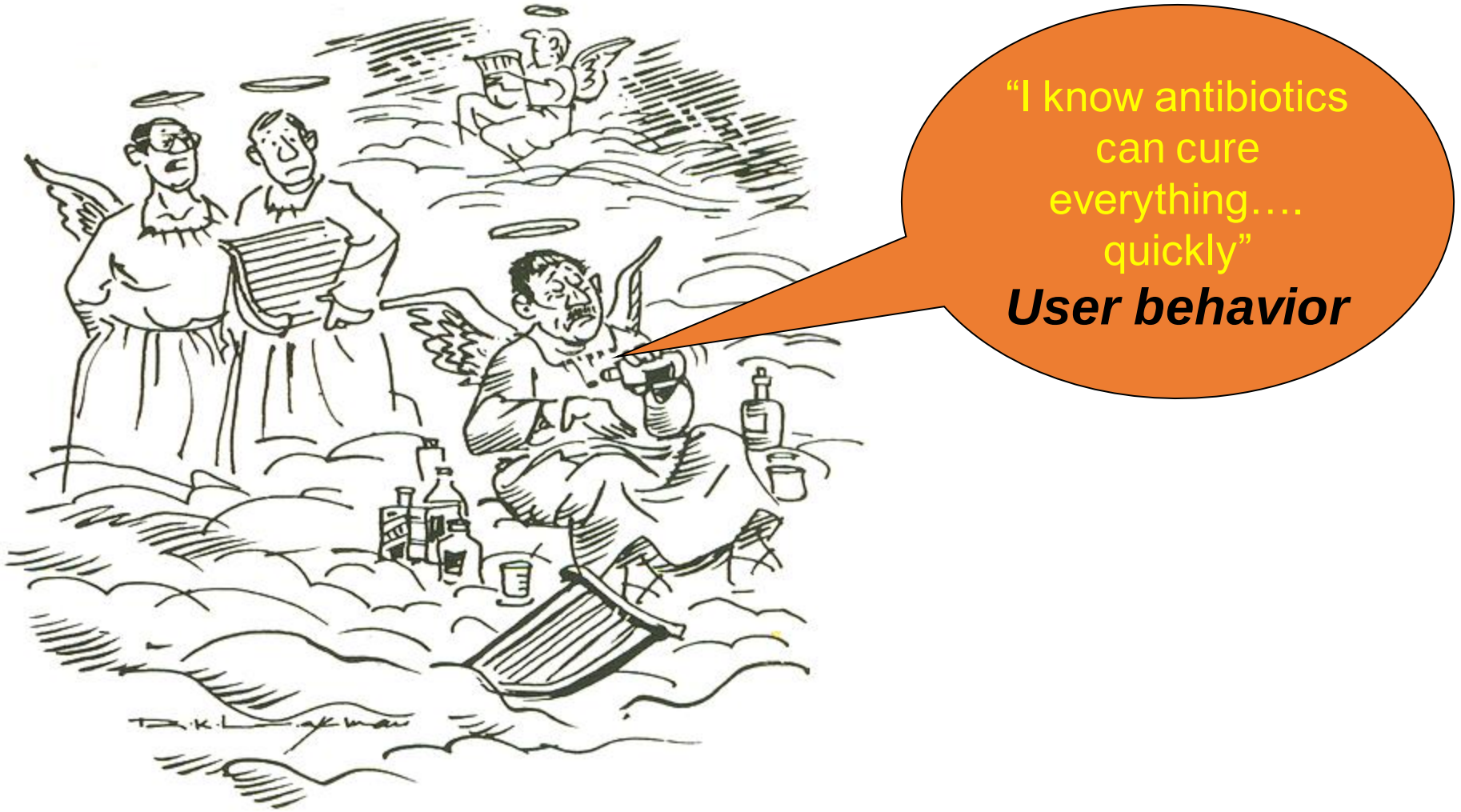
ALEXANDER FLEMING, F.R.C.S.

From the Laboratories of the Inoculation Department, St. Mary's Hospital, London.

Received for publication May 10th, 1929.

WHILE working with staphylococcus variants a number of culture-plates were set aside on the laboratory bench and examined from time to time. In the examinations these plates were necessarily exposed to the air and they became contaminated with various micro-organisms. It was noticed that around a large colony of a contaminating mould the staphylococcus colonies became transparent and were obviously undergoing lysis (see Fig. 1).

Subcultures of this mould were made and experiments conducted with a view to ascertaining something of the properties of the bacteriolytic substance which had evidently been formed in the mould culture and which had diffused into the surrounding medium. It was found that broth in which the mould had been grown at room temperature for one or two weeks had acquired marked inhibitory, bactericidal and bacteriolytic properties to many of the more common pathogenic bacteria.


"I know antibiotics can cure everything…. quickly"
User behavior

“All fevers require injections
Followed by colorful capsules”
Unauthorized prescribers

"Empirically: GPs
Prevent superinfection
Hidden focus
Patient demands
Prescribe something"

Prescribers' dilemma

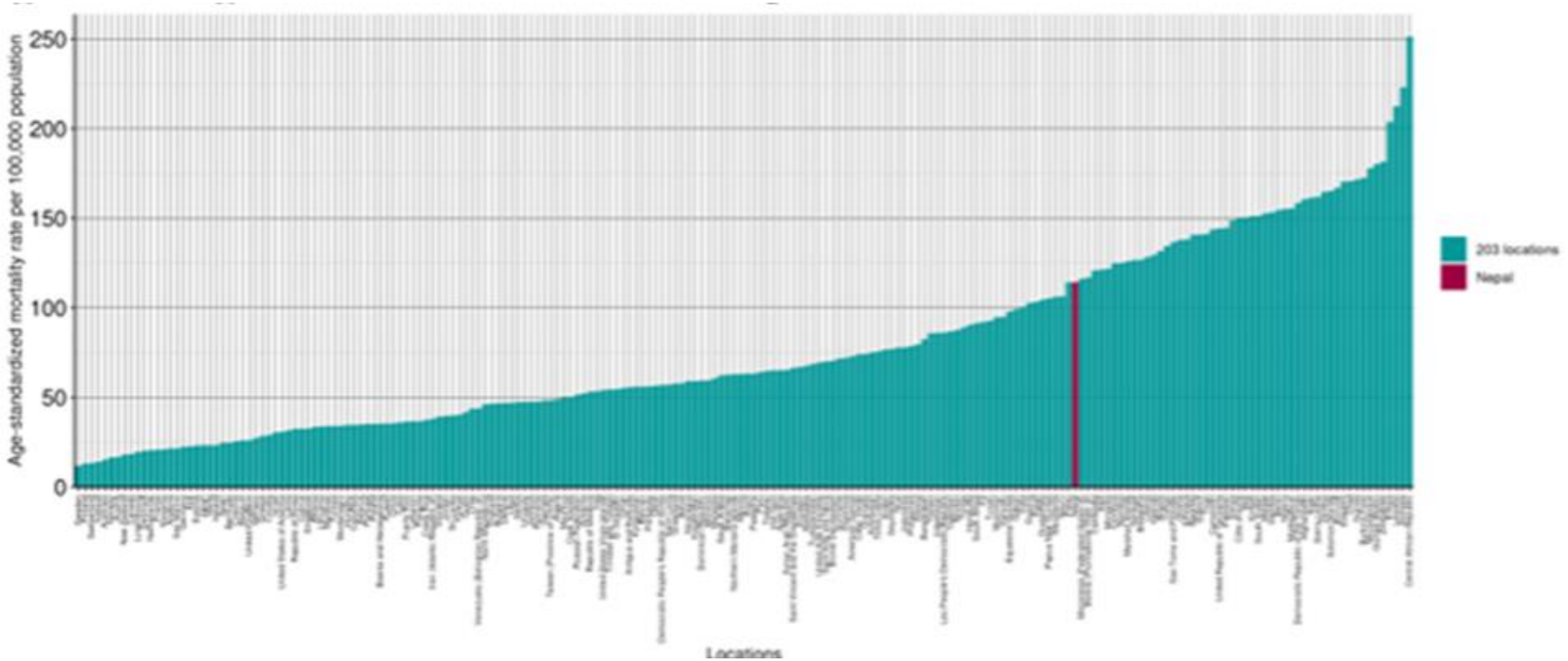
"Full course costs 100/-!!
I have only 40/-
Give me as much as you can in 40/-…or some other brand……
But I have to go to work".

Economic and regulatory issues

Counterfeit drugs
21 billion
US$/year

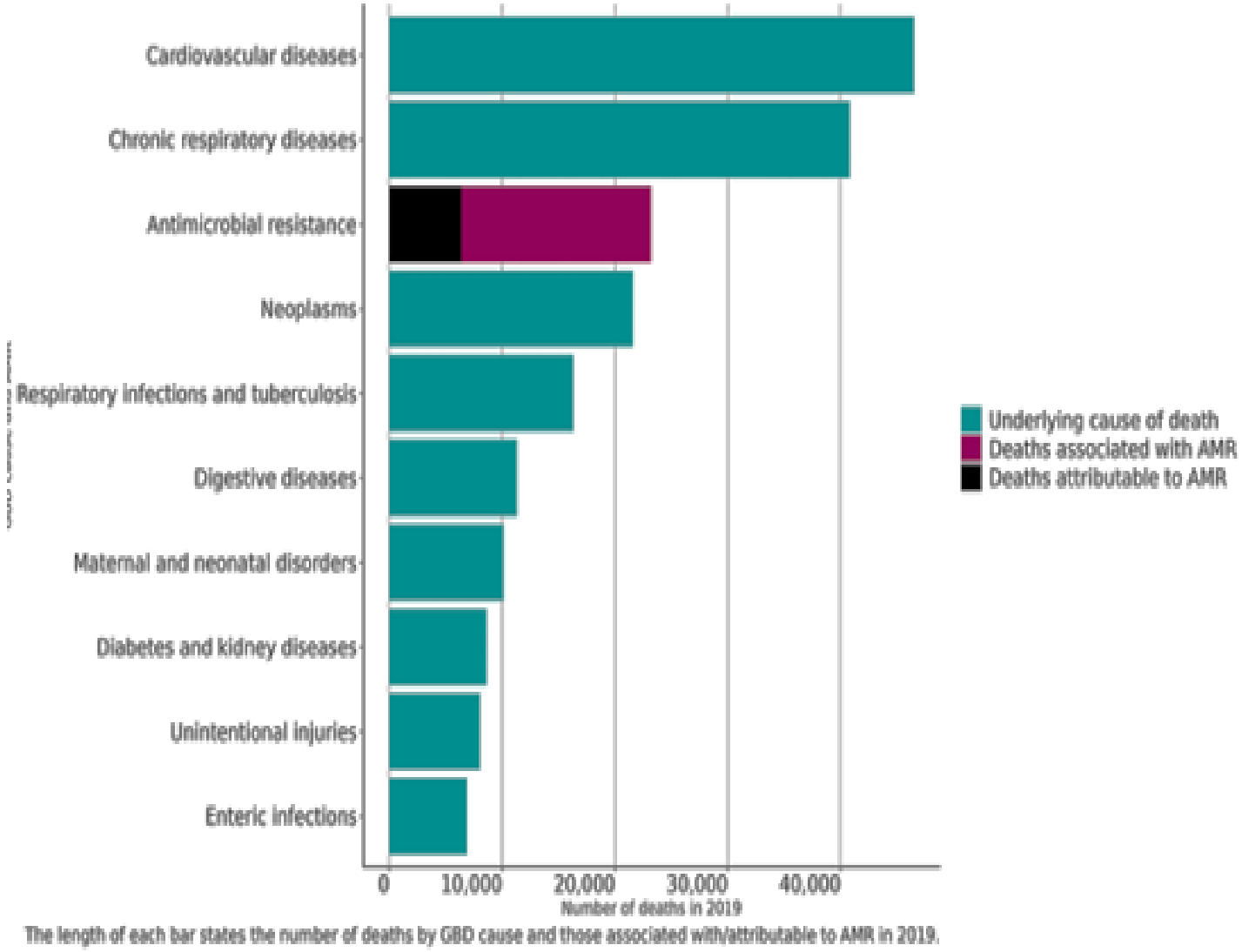
Antimicrobial Resistance in Nepal

- **In 2019, there were 6,400 deaths attributable to AMR and 23,200 deaths associated with AMR.**
- **Nepal has the 52nd highest age-standardized mortality rate per 100,000 population associated with AMR across 204 countries.**
- **In the GBD region of South Asia, Nepal has the 2nd highest age-standardized mortality across 5 countries.**



Position of AMR in context with other causes of death in 2019 in Nepal

- **AMR- Third largest killer in Nepal**
- **Five pathogens to be aware of in Nepal: *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae***
- **National Action Plan on AMR - endorsed & waiting for effective implementation.**



Commonly Prescribed Antibiotics (2003-2020)

Year	Name of the antibiotics/class	Prescription (%)	References
2003	Beta-lactams (Penicillin)	49.6	Shankar et al., 2003
	Metronidazole	13.2	
	Quinolones	11.5	
	Others	25.7	
2004	Beta-lactams (Penicillin)	40.0	Palikhe, 2004
	Cephalosporin	34.0	
	Aminoglycoside	16.0	
	Quinolones	6.0	
	Macrolides	1.0	
	Others	3.0	

Year	Name of the antibiotics/class	Prescription (%)	References
2005	Beta-lactams (Penicillin)	47.7	Dawadi, 2005
	Tetracycline	43.2	
	Macrolides	4.2	
	Quinolones	3.1	
	Cephalosporin	2.1	
2006	Beta-lactams (Penicillin)	36.6	
	Quinolones	19.6	
	Macrolides	11.7	Lamichhane et al., 2006
	Tetracyclines	8.8	
	Aminoglycosides	4.5	
	Ciprofloxacin	2.2	

Year	Name of the antibiotics/class	Prescription (%)	References
2008	Macrolides	40.5	Baral et al., 2013
	Quinolones	27.8	
	Beta-lactams (Penicillin)	20.3	
	Cephalosporin	5.4	
	Others	6.0	
2011	Cephalosporins	41.5	Choudhury and Bezbaruah, 2013
	Beta-lactams (Penicillin)	35.5	
	Aminoglycosides	20.0	
	Macrolides	2.0	
	Fluroquinolones	1.0	

Year	Name of the antibiotics/class	Prescription (%)	References
2013	Cephalosporins	35.1	Khan et al., 2013
	Quinolones	31.9	
	Nitroimidazoles	14.8	
	Aminoglycosides	12.0	
	Macrolides	6.2	
2015	Cephalosporins	100.0	Thapaliya et al., 2015
	Macrolides	26.2	
	Others	3.6	

Year	Name of the antibiotics/class	Prescription (%)	References
2017	Cephalosporins	62.1	Gupta et al., 2017
	Quinolones	15.9	
	Macrolides	8.8	
	Beta-lactams (Penicillin)	8.3	
	Aminoglycoside	3.9	
	Tetracycline	1.0	
	Others	10.9	
2018	Cephalosporins	23.2	Shrestha and Dixit, 2018
	Beta-lactams (Penicillin)	19.0	
	Macrolides	10.0	
	Others (37 antibiotics)	47.3	

Year	Name of the antibiotics/class	Prescription (%)	References
2019	Cephalosporin	40.0	Shakya, 2021
	Aminoglycosides	21.0	
	Beta-lactams (Penicillin)	11.7	
	Fluroquinolone	9.9	
	Macrolides	5.5	
	Others	11.3	
2020	Cephalosporin	29.9	Nepal et al., 2021
	Beta-lactams (Penicillin)	24.9	
	Quinolones	15.0	
	Antiprotozoal	13.0	
	Sulfonamides	7.2	
	Macrolides	4.6	
	Tetracycline	1.6	
	Others	3.7	

Commonly Dispensed Antibiotics (2013 to 2021)

Year	Name of the antibiotics/class	Dispensed percent	Sources
2013	Beta-lactams (Penicillin)	32.3	Ansari, 2013
	Cephalosporins	32.2	
	Macrolides	16.7	
	Fluoroquinolones	15.6	
	Others	3.8	
2016	Cephalosporins	69.8	Ansari, 2017
	Beta-lactams (Penicillin)	68.3	
	Marcolides	57.1	
	Fluoroquinolones	49.1	
	Sulfonamide	19.3	
2017	Cephalosoprins	38.0	Nepal et al., 2019
	Beta-lactams (Penicillin)	29.3	
	Quinolones	13.7	
	Macrolides	8.1	
	Antiprotozal	7.9	
	Others	3.0	

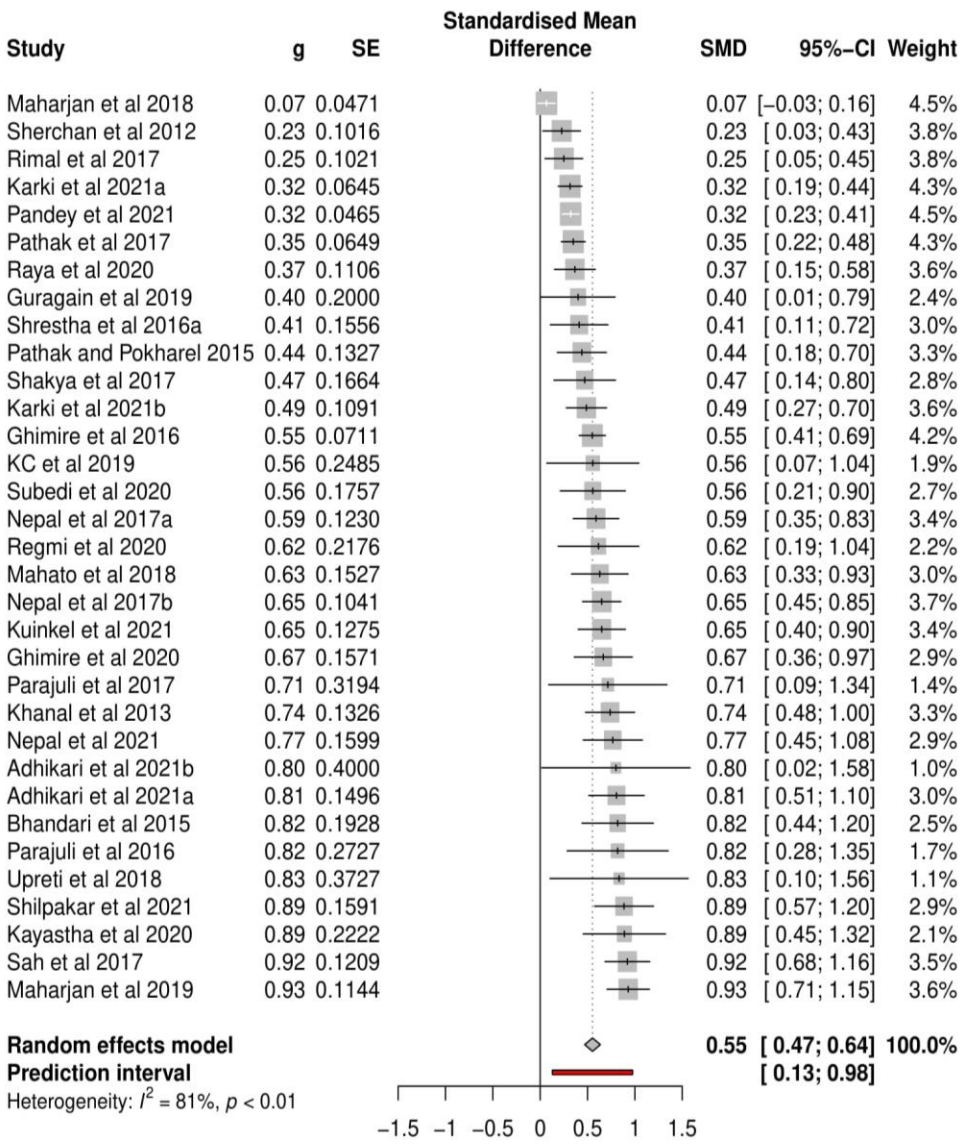
Year	Name of the antibiotics/class	Dispensed percent	Sources
2020	Beta-lactams (Penicillin)	46.0	Jha et al., 2020
	Macrolides	23.0	
	Cephalosporins	19.0	
	Quinolones	9.0	
	Sulfonamide	2.0	
	Others	1.0	
2021	Macrolides	67.6	Acharya et al., 2021
	Beta-lactams (Penicillin)	21.6	
	Cephalosporins	9.0	
	Fluoroquinolone	1.8	

Antibiotic resistance pattern of *S. aureus* (2003 - 2019)

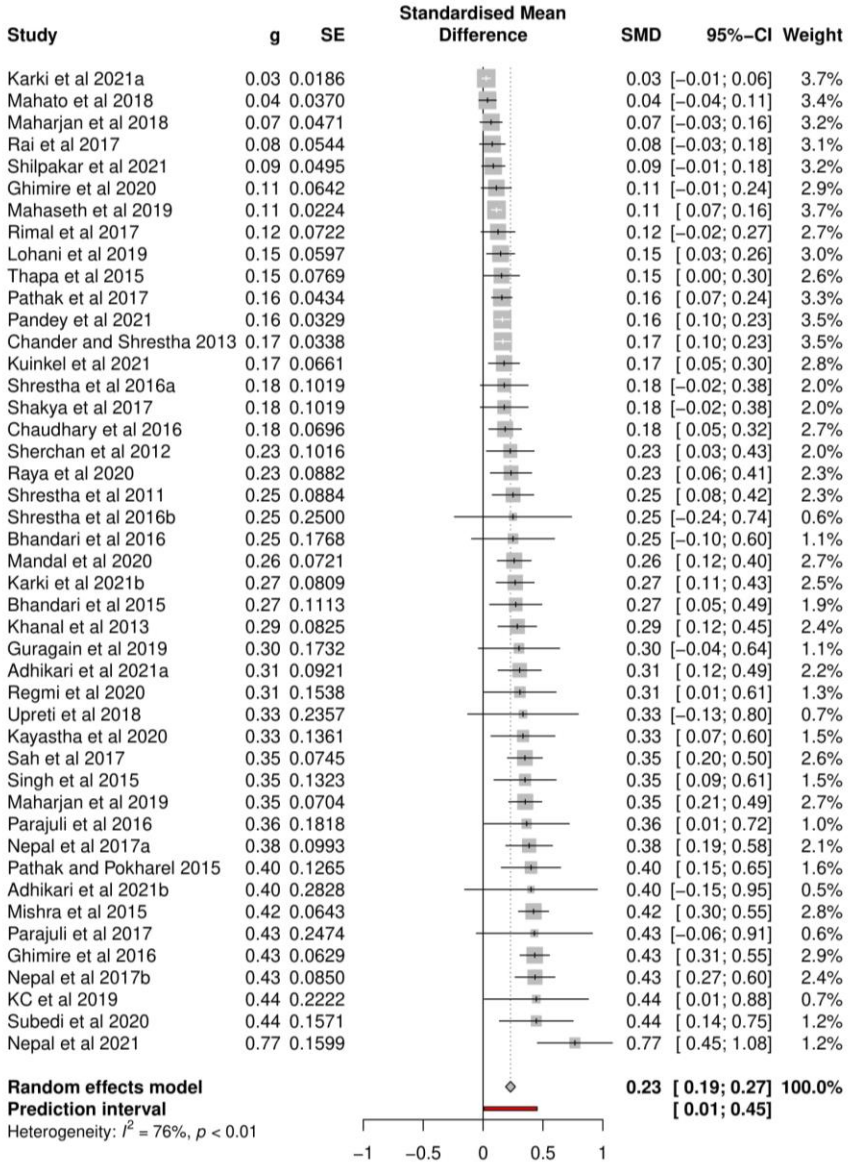
Antibiotics	2003	2005-2007			2009-2010	2015-2016		2018-2019
	S. aureus	*MRSA*	*S. aureus*	*MDR MRSA*	*MRSA*	*MRSA*	*MSSA*	*S. aureus*
Penicillin	100	100	81.5	100	-	47.2	52.8	-
Norfloxacin	-	43.4	30.6	58.8	-	-	-	-
Kanamycin	-	-	40.0	64.8	-	-	-	-
Erythromycin	-	-	71.7	5.4	-	62.5	37.5	**91.6**
Cloxacillin	-	100	69.1	100	100	-	-	**50.0**
Ampicillin	-	90.0	87.5	100	100	-	-	-
Amoxicillin	80.0	91.1	91.8	91.8	-	-	-	**91.6**
Tetracycline	-	52.3	39.6	64.3	20.7	85.7	-	-
Trimethoprim	--	-	77.0	-	-	-	-	-
Cephalexin	-	57.6	55.5	58.8	-	-	-	-
Clindamycin	-	-	-	-	44.8	32.2	30.3	**41.6**
Gentamicin	25.0	-	-	-	20.8	73.5	26.5	-
Amikacin	-	-	-	-	24.1	100	-	**83.0**
Cotrimoxazole	100	-	-	-	44.82	71.4	71.4	**58.3**
Ciprofloxacin	25	-	-	-	17.0	62.8	31.8	**83.3**
References	Shankar et al, 2003	Tiwari et al., 2009			Pandey et al., 2013	Raut et al., 2017		Prajapati, 2020

Pooled prevalence of MDR and ESBL *Klebsiella pneumoniae* in Nepal

MDR *K. pneumoniae*



ESBL *K. pneumoniae*



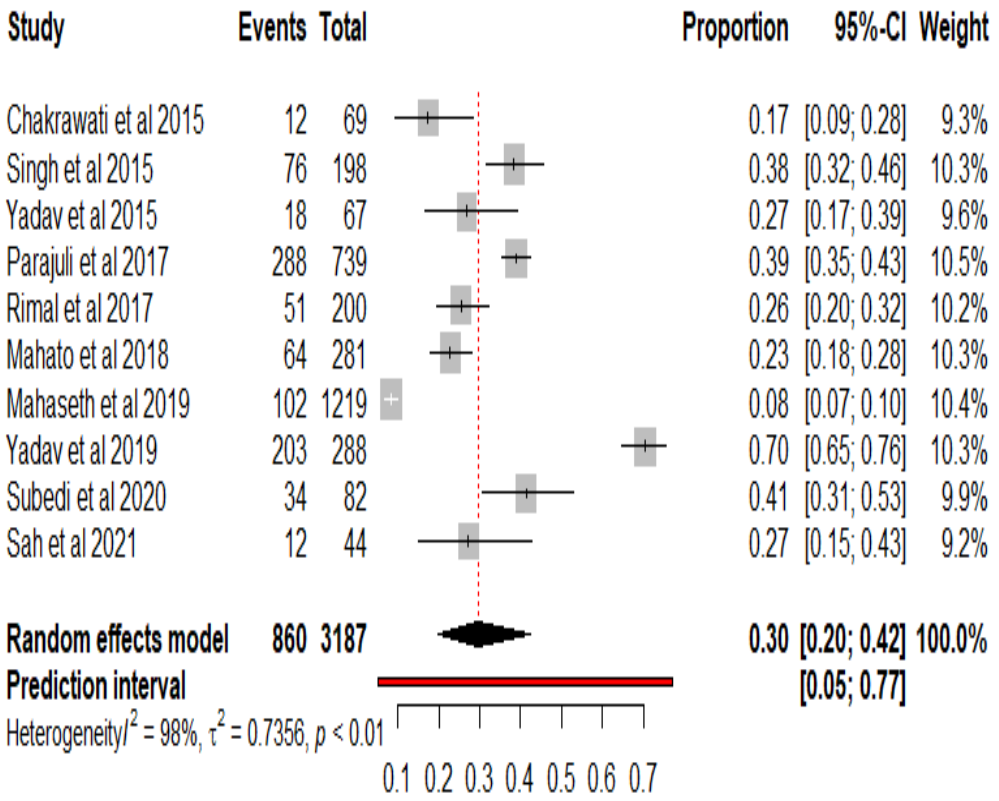
(Shyaula et al., 2023)

Antibiotic resistance profile of ESBL-KP

Antibiotics	Resistance (Pooled estimation)	95% CI	Test of heterogeneity		Number of studies reviewed (34)
			I^2 (%)	p-value	
Ampicillin	99.90	[0.9990; 0.9990]	0.0	<0.0001	3
Trimethoprim-sulfamethoxazole	60.22	[0.4825; 0.7218]	0.0	<0.0001	6
Ofloxacin	56.69	[0.2249; 0.9090]	48.3	0.0100	5
Gentamicin	50.90	[0.2796; 0.7383]	0.0	0.0058	4
Nitrofurantoin	31.97	[-0.0004; 0.6398]	40.3	0.0502	4
Amikacin	7.30	[-0.0100; 0.1559]	47.9	0.0750	7
Imipenem	0.10	[0.0010; 0.0010]	0.0	0	5

(Shyaula et al., 2023)

Prevalence of ESBL *E.coli* in urine specimens in Nepal

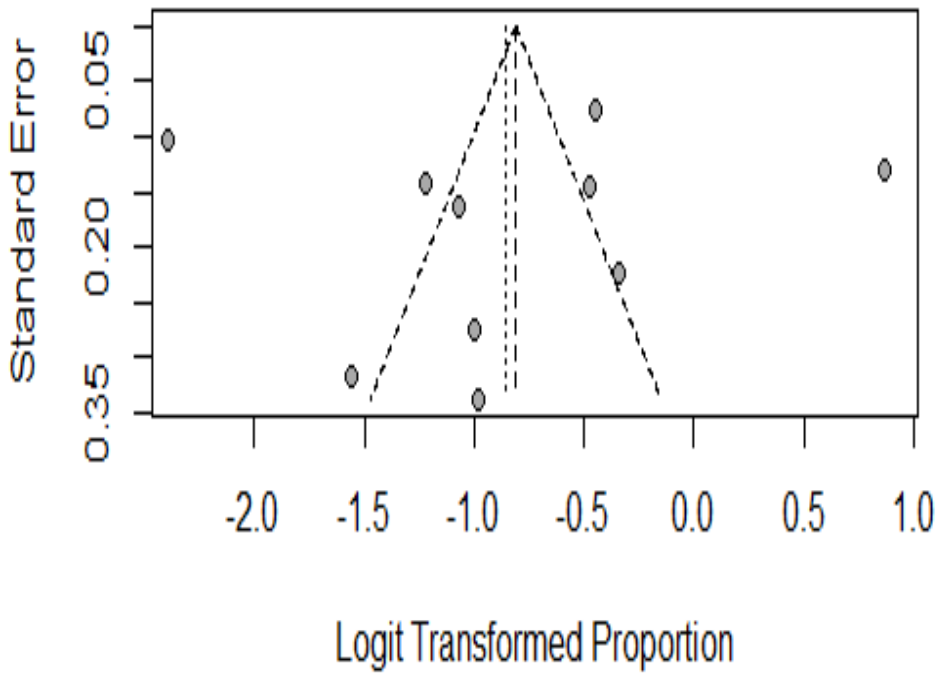


Heterogeneity test

I^2 = 98% (p<0.01)

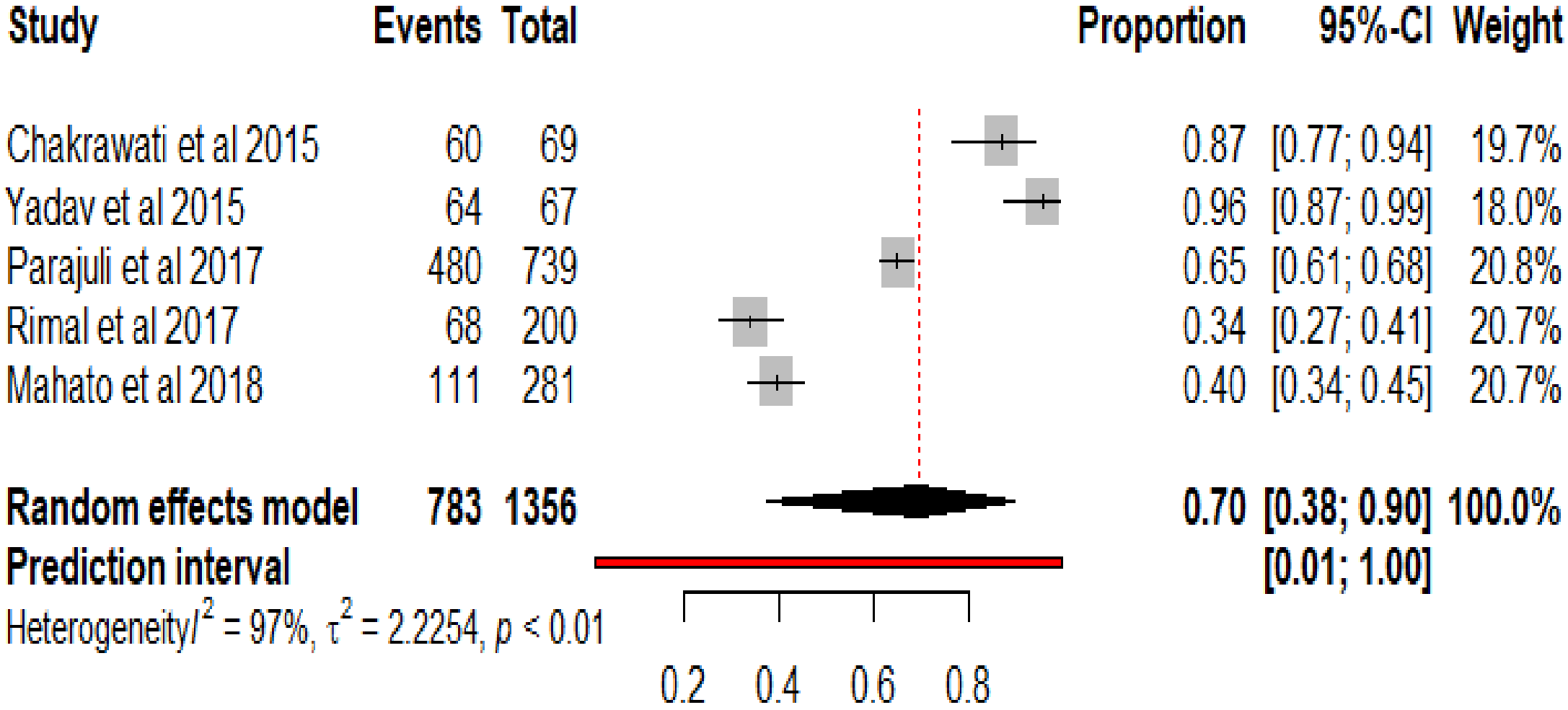
Egger's Test

t = -0.11 (p=0.9140)



(Rana Chhetri et al., 2023)

Forest plot of pooled prevalence of MDR *E.coli* in urine samples in Nepal



(Rana Chhetri et al.[46], 2023)

Antibiotic resistance profile of *ESBL-E coli* isolated from urine

Antibiotics	Resistance (Pooled estimation)	95% CI	Test of heterogeneity		Number of studies reviewed
			I^2 (%)	p-value	
Ampicillin	99.99	[99.98;99.99]	0	<.0001	3
Cefotaxime	96.46	[89.55;103.37]	99.99	<.0001	5
Nalidixic Acid	88.22	[75.74;100.69]	99.97	<.0001	3
Ceftazidime	85.66	[65.53;105.79]	100	<.0001	8
Ceftriaxone	85.64	[60.35;110.93]	100	<.0001	7
Ciprofloxacin	84.43	[76.90;91.96]	99.97	<.0001	5
Ofloxacin	80.90	[72.04;89.77]	99.95	<.0001	4
Norfloxacin	79.45	[65.79;93.11]	99.98	<.0001	4
Cefepime	79.48	[59.86;99.10]	99.99	<.0001	4
Cotrimoxazole	70.60	[61.72;79.48]	99.98	<.0001	8
Levofloxacin	63.92	[51.91;75.93]	99.96	<.0001	4
Gentamicin	45.27	[36.71;53.83]	99.94	<.0001	5
Nitrofurantoin	30.98	[12.67;49.29]	99.99	0.0009	6
Amikacin	19.87	[2.82;32.91]	99.99	0.0199	6
Meropenem	13.91	[-3.5937;31.4308]	99.99	0.1193	3
Imipenem	10.71	[4.43;17.00]	99.90	0.0008	3

(Rana Chhetri et al., 2023)

CAUSES OF ANTIBIOTIC RESISTANCE

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

Over-prescribing of antibiotics

Patients not finishing their treatment

Over-use of antibiotics in livestock and fish farming

Poor infection control in hospitals and clinics

Lack of hygiene and poor sanitation

Lack of new antibiotics being developed

Message

- Infectious diseases still causes significant morbidity and mortality in Nepal.
  - Preventive measures are important to control these diseases.
  - Continuous efforts are essential to control the diseases using effective measures.
  - Effectiveness of the programs may be increased through maximizing synergies between the programs and health system governance.
  - Multi-disease elimination requires multisectoral approaches (e.g. WASH, IVM, COMBI) to address social, economic and behavioral determinants of health.
- Antimicrobial resistance is a public health threat with increased burden to the health system, requiring effective antibiotic stewardship measures for timely containment.

Thank You !