Burden of infectious diseases and bacterial antimicrobial resistance in India: a systematic analysis for the global burden of disease study 2019 and 2021(60-95+ age group):

### Summary:

<u>Background:</u> Infectious diseases and antimicrobial resistance (AMR) has become pressing concerns in India. We aimed to comprehensively investigate the burden of them. Infectious diseases remain a major public health concern in India, contributing significantly to morbidity and mortality. The rising threat of bacterial antimicrobial resistance (AMR) exacerbates this burden, undermining treatment efficacy and increasing healthcare costs. This study systematically analyzes the burden of infectious diseases and the impact of bacterial AMR in India, leveraging data from the Global Burden of Disease (GBD) Studies 2019 and 2021.

Findings: There were an estimated 2.70 million (95% UI: 2.15–3.24) infection-related deaths, accounting for 27.2% of the total deaths in India 2019 and 2.6 million (95% uncertainty intervals, UI 2.0-3.1) infection-related deaths, accounting for 17.4% of the total deaths in India 2021. Males(1359735) and females(1335854) were effected in 2019 and males(1305998) and females (1245855) were effected in 2021. Bloodstream infections (BSIs) were most lethal infectious syndrome, associating with 558754 deaths (499993, 617514), followed by lower respiratory infections (724219), and peritoneal and intra-abdominal infections (78747) in 2019. These five leading pathogens were tuberculosis, pathogen of diarrhea, S.pneumonia, E.coli and K pneumoniae which were associated with 47.4%% (1223407/2583188) of all infectionrelated deaths. The pathogens of different infectious syndromes exhibited significant heterogeneity. In 2019, more than 1050 thousand deaths were associated with AMR, including 283 thousand deaths attributable to AMR. The top 3 AMR attributable to death were carbapenems-resistance A baumannii (25,316), carbapenems-resistance Streptococcus pneumoniae (21,766) and third-generation carbapenems-resistance klebsiella pneumoniae (19804). For individuals aged 60 to 95 and older, the most affected infectious syndromes include bloodstream infections, lower respiratory infections, tuberculosis, and diarrhoea. These syndromes account for a significant proportion of infectious disease mortality in this age group.

<u>Interpretation</u>: Infectious diseases and bacterial antimicrobial resistance were serious threat to public health in India, related to 2.7 million and 2.6 million total deaths in 2019 and 2021 respectively.

Keywords: Burden of infectious diseases; Antimicrobial resistance; Death; DALYs; India

#### **Introduction:**

Among the top ten global health threats released by World Health Organization (WHO) in 2019, six were related to infectious diseases (global influenza pandemic; antimicrobial resistance; Ebola and other high-threat pathogens; vaccine hesitancy; dengue; HIV). It was estimated that in 2019, the number of deaths due to infectious diseases was 13.7 million (95% uncertainty intervals, UI 10.9–17.1), while deaths associated with bacteria ranked as the second leading cause of death globally. Whether on a global scale or within India, the issue of bacterial antimicrobial resistance (AMR) has become a pressing concern. It was estimated that AMR cause 1.27 million (95% UI 0.911–1.71) deaths directly, and contribute to 4.95 million (95% UI 3.62–6.57) deaths indirectly worldwide. Globally, lower respiratory infections were responsible for over 1.5 million deaths associated with resistance, making it the most burdensome infectious syndrome. In 2019, India experienced a significant burden from infectious diseases and antimicrobial resistance: An estimated 2.7 million deaths were attributed to infectious diseases in India. Approximately 1.04 million deaths in India were directly attributable to antibiotic-resistant bacterial infections. 2.99 million sepsis-related deaths in India, about 33.4% were linked to bacterial AMR. An estimated 325,000 sepsis deaths in children under five were associated with bacterial infections.

#### Overview and data sources

In this study, we used a subset of input data describing India from the Global Antimicrobial Resistance Burden (GARB) study to estimate the burden of infectious diseases and bacterial antimicrobial resistance. 2,3 The global overall input data from 471.3 million sample size and 9324 number of study-location-years. The data input sources (could be found at: https://ghdx.healthdata.org/record/ihme-data/global-bacterial-antimicrobial-resistanceburdenestimates-2019) in the GARB study included nine categories: administrative data, demographic surveillance, epi surveillance, estimate, modeled data, report, scientific literature, survey, and vital registration. The data for this study were obtained from a publicly available database and did not require ethical review or informed consent. In this study, the input data sources for India: https://vizhub.healthdata.org/microbe/?settings=eyIxIjoic3luZHJvbWVzIiwiMiI6ImJhciIsIjMiOiJz ZXBzaXMiLCI0IjoyMiwiNSI6MSwiNiI6MywiNyI6MSwiOCI6MTYzLCI5IjoxLCIxMiI6MSwiM TMiOjEsIjE0IjoxLCIxNSI6MiwiMTYiOjIsIjE3IjozLCIxOCI6MjAxOSwiMTkiOmZhbHNlLCIy MCI6ZmFsc2UsIjIyIjoxLCIyNCI6ImVuIiwiMjUiOiJzeW5kcm9tZSIsIjI2IjpbMSwyLDMsNCw1 LDYsNyw4LDksMTAsMjJdLCIyNyI6WzQsMzEsNjQsMTAzLDEzNywxNTgsMTY2XSwiMjgi OlsyLDMsNCw1LDYsNyw4LDksMTAsMTEsMTIsMTNdLCIyOSI6WzEsMl0sIjMwIjpbMSw 3LDExLDE3LDIzLDIyXSwiMzEiOlsiMS0xIiwiMS0yIl0sIjMyIjoiMS0xIiwiMzMiOlsxLDJdfQ==

#### Analysis steps:

Our analysis consisted of 5 main steps. In step 1, we estimated the disease burdens (death number/rate, DALYs number/rate) of the total and 12 infectious syndromes in India in 2019 by age and sex. In step 2, we described the disease burden (death number/rate, DALYs number/rate) caused by 43 pathogens and estimated the proportion of pathogens in differentinfection syndromes. These 43 microorganisms were in 6 major categories: 34 bacteria, 4 viruses, 2 protozoa, fungi, polymicrobial, and other pathogens. In step 3, we calculated the disease burden of total and 12 infection syndromes caused by bacterial AMR in two scenarios (AMR associated deaths, AMR attributable deaths), respectively. Associated deaths were the inclusive estimate of AMR burden, which measures people with a drug-resistant infection that contributed to their death. The infection was implicated in their death, but resistance may or may not have been a factor. Attributable deaths were the conservative estimate of AMR burden, which measures people who would not have died of infection if it was treatable (i.e., if there was no AMR).12 In step 4, we estimated the AMR burden (death number/rate, DALYs number/rate) of 22 bacteria in aforementioned two scenarios. In step 5, we calculated the burden of AMR by 22 bacteria and 19 antibiotics combinations Health Estimates Reporting (GATHER) statement. Role of the funding source.

#### **Estimation:**

#### 1. Data Extraction and Cleaning

Relevant epidemiological data for India were extracted from the GBD database, focusing on major infectious diseases such as lower respiratory infections, diarrheal diseases, tuberculosis, and bloodstream infections

### 2. Stratification by Demographics

The data were stratified by age, sex, and geographical region (state/union territory) to assess disparities in disease burden and AMR impact across population subgroups. This allowed us to identify vulnerable populations such as children under five, the elderly, and residents of urban areas.

#### 3. Estimation of Disease Burden

The burden was estimated using key GBD metrics:

- o Incidence and Prevalence of each infectious disease.
- Mortality rates (deaths per 100,000 population).
- Disability-Adjusted Life Years (DALYs), which include both Years of Life Lost (YLLs) and Years Lived with Disability (YLDs).
- Attributable burden due to AMR, calculated by comparing health outcomes in resistant versus susceptible infections.

#### 4. Statistical Analysis and Visualization

We performed statistical analysis using R software, employing packages such as dplyr and ggplot2 for data wrangling and visualization. To enhance interpretability:

- **Heatmaps** were created to display the geographical distribution of disease and AMR burden across Indian states.
- Bar charts and line graphs illustrated time trends and demographic variations in disease and resistance patterns.
- Cluster plots were used to show relationships among pathogens and resistance levels.

#### Visual representation of Age-Wise deaths for 2019 and 2021:

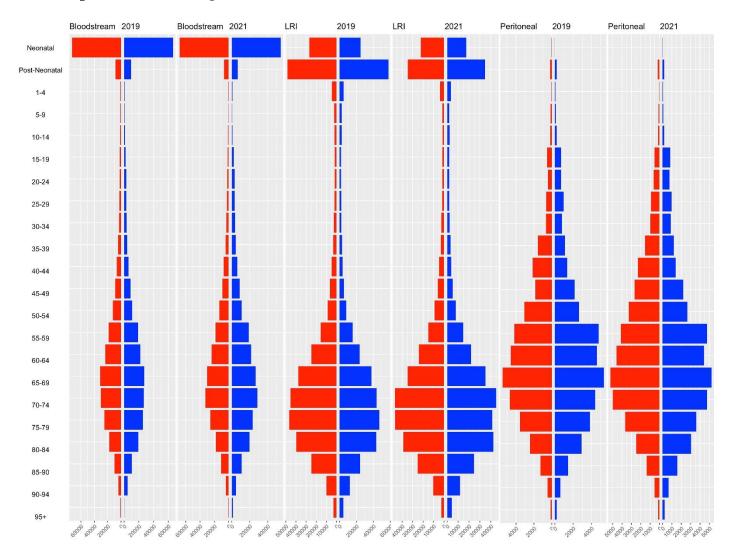


Fig1: Age-wise Population pyramid for the year 2019 and 2021 (Bloodstream, LRI, Peritoneal)

## Interpretation: (60 to 95+)

For the 60–95+ age group, mortality due to infectious syndromes remains high across Bloodstream infections, Lower Respiratory Infections (LRI), and Peritoneal infections in both 2019 and 2021. LRI caused the highest deaths, peaking in the 70–84 age range for both males and females, maintaining a major impact with only slight variation over the years. Bloodstream infections show consistently high mortality that increases steadily with age, especially after 85, with a slight rise in female deaths in 2021 (+~3%). Peritoneal infections had the lowest mortality overall but showed a notable increase (+~5%) in the oldest age group (85–94) in 2021, mainly among females. Gender differences were minor but visible, with males and females affected almost equally across infections. These trends highlight age as a critical risk factor and emphasize the need for targeted infection control and prevention strategies, especially for LRI and bloodstream infections, in elderly populations.

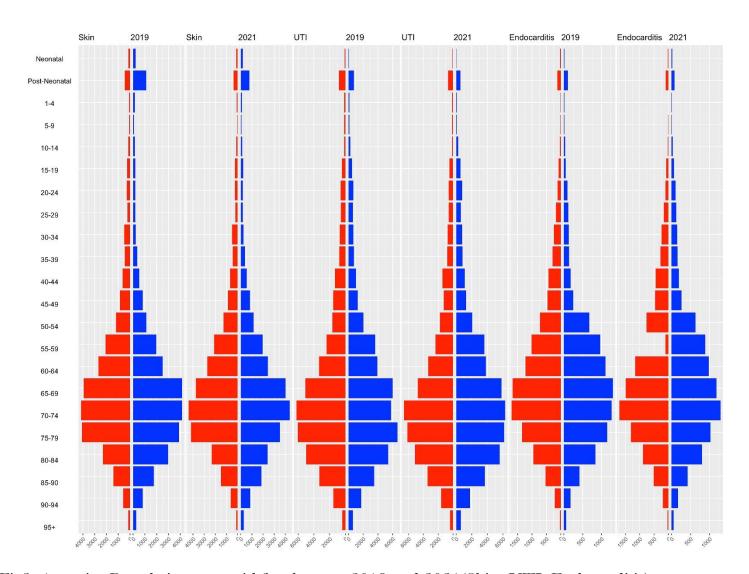


Fig2: Age-wise Population pyramid for the year 2019 and 2021 (Skin, UTI, Endocarditis)

### Interpretation: (60 to 95+):

For the 60–95+ age group, mortality due to Skin infections, Urinary Tract Infections (UTI), and Endocarditis shows clear age-related increases between 2019 and 2021. UTIs caused the highest death toll, particularly impacting females aged 65–94, with mortality rising by approximately 7% in 2021, likely linked to pandemic-related factors. Endocarditis mortality was moderate, peaking in the 70–84 age group, with a slight male predominance and stable death rates over the two years. Skin infections showed the lowest mortality, mostly balanced between genders and stable across the years, with deaths peaking at ages 65–79 and declining after 85+. Overall, UTIs represent the greatest risk for older adults, especially women, emphasizing the need for focused healthcare strategies to manage this vulnerability.

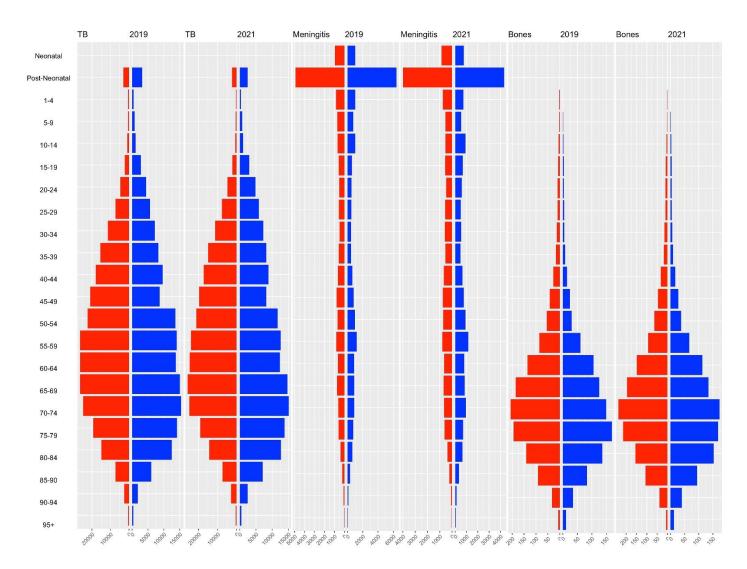


Fig3: Age-wise Population pyramid for the year 2019 and 2021(TB (Tuberculosis), Meningitis, and Bone infections)

## Interpretation:(60-95+):

Analysis of mortality by age and gender (60–95+) for Tuberculosis (TB), Meningitis, and Bone infections from 2019 to 2021 reveals distinct patterns. TB remains the most significant cause of death, with high mortality especially in males aged 60–80, showing little change over the two years. Deaths begin to decline after age 85 but persist among those aged 90 and above. Meningitis mortality is low across all older age groups, with slightly higher deaths in males aged 60–74 and almost negligible impact in those over 95, indicating it is not a major cause of death in this population. Bone infections show relatively low mortality but steadily increase from age 60, peaking between 70 and 84, with slightly more deaths in males; mortality drops sharply after age 85. Overall, TB poses the greatest threat to older adults, particularly men between 60 and 80, while meningitis has minimal impact, and bone infections represent a moderate risk. These findings highlight the need to prioritize TB screening and treatment efforts in elderly male populations.

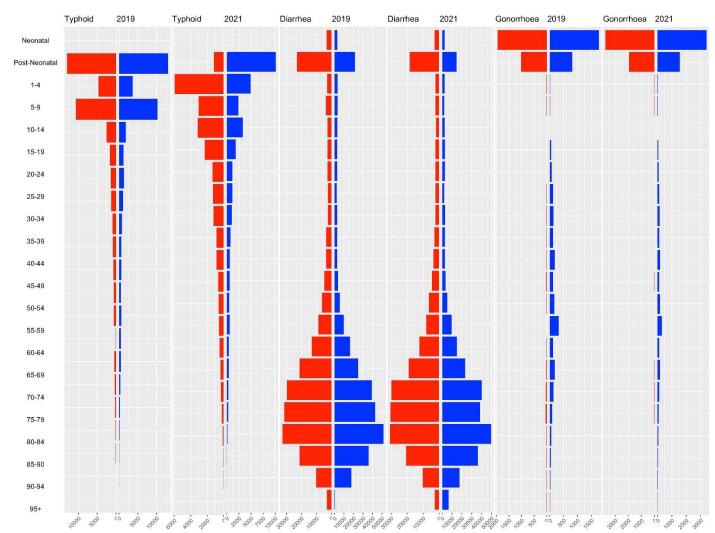


Fig4: Age-wise Population pyramid for the year 2019 and 2021(Typhoid, Diarrhoea, and Gonorrhoea)

## Interpretation:(60-95+):

Analysis of mortality for Typhoid, Diarrhoea, and Gonorrhoea in the 60–95+ age group during 2019 and 2021 shows distinct patterns. Typhoid and Gonorrhoea have negligible or no mortality among older adults, with deaths virtually absent across both genders, indicating these infections primarily affect younger populations. In contrast, Diarrhoea causes significant mortality in the elderly, especially males aged 70–84, with deaths slightly increasing or stable from 2019 to 2021. Mortality decreases after age 85 but remains notable, particularly in men. This highlights Diarrhoea as the main concern among these infections in older adults, suggesting that public health interventions should prioritize diarrhoea prevention and treatment for men over 70.

	Deaths 2019	Deaths 2021	Death Rate 2019	Death Rate 2021
	Number (95% UI)	Number (95% UI)	Rate, per 100,000 (95% UI)	Rate, per 100,000 (95% UI)
All infectious syndromes	2695589(2153009,3239047)	2551853(2003450,3101390)	194.1(155.0,233.3)	180.4(141.6,219.3)
male	1359735(1013614,1706304)	1305998(948156,1664405)	191.1(142.4,239.7)	180.3(130.9,229.8)
female	1335854(993616,1678613)	1245855(894111,1598236)	197.3(146.8,248.0)	180.5(129.5,231.5)
Infectious syndrome				
Bloodstream infections	558754 (499993, 617514)	542971 (492910, 593033)	40.2(36.0, 44.5)	38.4 (34.8, 41.9)
Lower respiratory infections and all		· ·		
related infections in the thorax	724219 (659971, 788466)	658708 (583164, 734260)	52.2 (47.5, 56.8)	46.6 (41.2, 51.9)
Peritoneal and intra-abdominal				
infections	78747 (65469, 92026)	79950 (65415, 94485)	5.7(4.7, 6.6)	5.7 (4.6, 6.7)
Bacterial infections of the skin and				
subcutaneous systems	53962(47531, 60394)	53913 (46170, 61655)	3.9 (3.4, 4.3)	3.8 (3.3, 4.4)
Urinary tract infections and				
pyelonephritis	88044(75352, 100737)	88911 (75677, 102144)	6.3(5.4, 7.3)	6.3 (5.4, 7.2)
Endocarditis and other cardiac				
infections	20428(17055, 23801)	19612 (16297, 22927)	1.5(1.2, 1.7)	1.4(1.2, 1.6)
Tuberculosis	413354(351869, 474838)	399571(325255, 473888)	29.8(25.3, 34.2)	28.3 (23.0, 33.5)
Meningitis and other bacterial central				
nervous system infections	36100 (30348, 41853)	32121 (27434, 36808)	2.6(2.2, 3.0)	2.3 (1.9, 2.6)
Infections of bones, joints, and				
related organs	2268 (1676, 2860)	2497 (1879, 3115)	0.2(0.1, 0.2)	0.2 (0.1, 0.2)
Typhoid fever, paratyphoid fever,				
and invasive non-typhoidal				
Salmonella	64648(31670, 97625)	55187 (26879, 83495)	4.7 (2.3, 7.0)	3.9 (1.9, 5.9)
Diarrhea	533980 (284916, 783044)	498401 (259182, 737621)	38.5 (20.5, 56.4)	35.2 (18.3, 52.1)
Gonorrhoea and chlamydia	7634(2702-12566)	12747(3480-22015)	0.6(0.2-0.9)	0.9(0.3-1.6)

<u>Table 1: Deaths burden of infectious syndrome in India, 2019&2021.</u>

**Interpretation:** For individuals aged 60 to 95 and older, the most affected infectious syndromes include bloodstream infections, lower respiratory infections, tuberculosis, and diarrhoea. These syndromes account for a significant proportion of infectious disease mortality in this age group. Therefore, we have analysed these four highlighted syndromes to understand trends in death counts and death rates between 2019 and 2021. 1.Bloodstream Infections:Between 2019 and 2021, deaths from bloodstream infections decreased slightly from 558,754 to 542,971 (a ~2.8%) decline). The death rate per 100,000 also fell from 40.2 to 38.4, indicating a modest improvement. This reduction could reflect better prevention, treatment efforts, or changes in healthcare access and reporting during the pandemic period. 2.Lower Respiratory Infections (and related thoracic infections): Deaths from lower respiratory infections dropped from 724,219 in 2019 to 658,708 in 2021, a decrease of about 9%. The death rate per 100,000 also declined from 52.2 to 46.6. This reduction may reflect improved respiratory disease management, the impact of public health measures like masking and distancing, or possible misclassification with COVID-19 cases during the pandemic. 3. Tuberculosis: Tuberculosis (TB) deaths decreased slightly from 413,354 in 2019 to 399,571 in 2021, with the death rate per 100,000 dropping from 29.8 to 28.3. However, the overlapping uncertainty intervals suggest this decline may not be statistically significant. COVID-19-related disruptions in TB services might have impacted case detection and reporting during this period. 4.Diarrhoea:Diarrhoea: related deaths decreased from 533,980 in 2019 to 498,401 in 2021, with the death rate per 100,000 falling from 38.5 to 35.2. Despite the decline, wide uncertainty intervals suggest caution in interpretation. Improved sanitation, healthcare access, and hygiene practices may have contributed to this reduction.

	DALYs 2019	DALYs 2021	DALY 2019	DALY 2021
	Number (95% UI)	Number (95% UI)	Rate, per 100,000 (95% UI)	Rate, per 100,000 (95% UI)
All infectious syndromes	110101839(85208205,135446756)	100195485(76182631,124675689)	7929(6136,9754)	7083.5(5385.9,8814.1)
male	56662619(40648908,72846073)	52903009(37002054,69029884)	7961.3(5711.3,10235.1)	7304.7(5109.1,9531.4)
female	53439220(39869049,67339972)	47292476(34047021,60811349)	7894.7(5890.0,9948.3)	6851.4(4932.4,8809.9)
Infectious syndrome				
Bloodstream infections	25119335(20720303, 29518367)	23345095(19371018, 27319173)	1808.9 (1492.1, 2125.7)	1650.4(1369.5, 1931.4)
Lower respiratory infections				
and all related infections in				
the thorax	27258713(24076419, 30441007)	22350511 (19623881, 25077141)	1963.0 (1733.8, 2192.2)	1580.1 (1387.3, 1772.9)
Peritoneal and intra-				
abdominal infections	2449734(2068428, 2831040)	2491417 (2067279, 291556)	176.4 (149.0, 203.9)	176.1 (146.1, 206.1)
Bacterial infections of the				
skin and subcutaneous				
systems	2068576 (1747957, 2389195)	2082079 (1745052, 2419106)	149.0 (125.9, 172.1)	147.2 (123.4, 171.0)
Urinary tract infections and				
pyelonephritis	2370448 (1997679, 2743217)	2371635(1994306, 2748964)	170.7(143.9, 197.5)	167.7(141.0, 194.3)
Endocarditis and other				
cardiac infections	573788 (486413, 661163)	554712 (463404, 646021)	41.3 (35.0, 47.6)	39.2 (32.8, 45.7)
Tuberculosis	15670007(13411874, 17928140)	15099053 (12380146, 17817960)	1128.5 (965.8, 1291.1)	1067.5 (875.2, 1259.7)
Meningitis and other				
bacterial central nervous				
system infections	2371249 (1924976, 2817522)	2025201 (1672848, 2377553)	170.8(138.6, 202.9)	143.2 (118.3, 168.1)
Infections of bones, joints,				
and related organs	447768(269907, 625629)	488024(286497, 689550)	32.2(19.4, 45.1)	34.5 (20.3, 48.7)
Typhoid fever, paratyphoid				
fever, and invasive non-				
typhoidal Salmonella	4811694 (2300341, 7323047)	4044984 (1908436, 6181533)	346.5(165.7, 527.4)	286.0 (134.9, 437.0)
Diarrhea	18487982(10705257, 26270707)	16853826 (9493284, 24214369)	1331.4 (770.9, 1891.9)	1191.5 (671.1, 1711.9)
Gonorrhoea and chlamydia	1177967(700789-1655145)	1660717(821238-2500196)	84.8(50.5-119.1)	117.4(58.1-176.8)

Table 2: DALYs burden of infectious syndrome in India, 2019&2021.

Interpretation: For individuals aged 60 to 95 and older, the syndromes with the highest disease burden in terms of Disability-Adjusted Life Years (DALYs) are bloodstream infections, lower respiratory infections, tuberculosis, and diarrhoea. These conditions reflect both premature mortality and years lived with disability, making them critical indicators of health impact in the elderly. Therefore, we analysed these four highlighted syndromes to understand trends between 2019 and 2021. 1.Bloodstream Infections: Bloodstream DALYs dropped from 25.1 million in 2019 to 23.3 million in 2021, with the DALY rate per 100,000 declining from 1808.9 to 1650.4. This reduction suggests progress in disease burden management—possibly due to better early diagnosis, more effective treatments, improved infection control, or adaptive health system responses during the COVID-19 pandemic. 2.Lower Respiratory Infections: Lower Respiratory Infections (LRI) DALYs decreased notably from 27.3 million in 2019 to 22.4 million in 2021, with the DALY rate dropping from 1963.0 to 1580.1 per 100,000.. Additionally, some LRI cases may have been misclassified or merged under COVID-19 in 2021, contributing to the observed reduction.

- 3.Tuberculosis: Tuberculosis (TB) DALYs showed a modest decline from 15.7 million in 2019 to 15.1 million in 2021, with the DALY rate decreasing from 1128.5 to 1067.5 per 100,000. The decrease may partly reflect underreporting or disruptions in TB diagnosis and treatment services during the COVID-19 pandemic—especially affecting older populations.
- 4. Diarrhoea: Diarrheal Diseases DALYs decreased slightly from 18.5 million in 2019 to 16.9 million in 2021, with the DALY rate falling from 1331.4 to 1191.5 per 100,000. This decline may suggest progress in public health measures such as sanitation, hygiene, and health education.

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			Death	Death			DALY	DALY			Death	Death	1001010111		DALY	DALY
	Deaths	Deaths	Rate	Rate	DALY	DALY	Rate	Rate	Deaths	Deaths	Rate	Rate			Rate	Rate
	2019	2021	2019	2021	2019	2021	2019	2021	2019	2021	2019	2021	DALY 201	DALY 202		2021
			Rate, per	Rate, per			Rate, per	Rate, per			Rate, per				Rate, per	
	Number	Number	100.000	100,000	Number		100,000	100,000	Number	Number	100,000		Number		100,000	
	(95% UI)	(95% UI)	(95% UI)	(95% UI)	(95% UI)		(95% UI)	(95% UI)	(95% UI)	(95% UI)	(95% UI)		(95% UI)		(95% UI)	
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	335586	326032	24.2	23.0	8,	6,	1029.5	939.9	97481	93953			(3435608	(3151706	299.6	271.4
	(299308,	(292118,	(21.6,	(20.7,	16775793	15601101	(850.8,	(776.8,	(85516,	(82464,	7.0 (6.2,	6.6 (5.8,	,	,	(247.4,	(222.8,
Bloodstream infections	371865)	359946)	26.8)	25.4)	)	)	1208.1)	1102.9)	85516)	105441)	7.9)	7.5)	4884171)	4526946)	351.7)	320.0)
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	394620	355498		25.1	4,	4,	1079.1	856.9(72	105838	95543			(3201255	(2584175	280.5	224.4
Lower respiratory infections and all related	(347168,	(303802,	28.4(25.0	(21.5,	17246362	14012427	(916.2,	3.2,	(89635,	(78645,	7.6 (6.5,	6.8 (5.6,		,	(230.5,	(182.7,
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Peritoneal and intra-abdominal infections	56299)	57409)	4.1)	4.1)	1766152)	1806343)	127.2)	127.7)	15628)	15715)	1.1)	1.1)	495219)	499406)	35.7)	35.3)
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subcutaneous systems	33627)	33872)	2.4)	2.4)	1414235)	1427199)	101.8)	100.9)	8578)	8459)	0.6)	0.6)	385170)	385386)	27.7)	27.2)
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	512,	660,	4.5 (3.9,	4.4 (3.7,	(1404100	(1370201	1.1,	(97.3,	(14125,	(13677,	1.2 (1.0,	1.2 (1.0,	(372936,	(359652,	(26.9,	31.2(25.4
Urinary tract infections and pyelonephritis	72154)	72607)	5.2)	5.1)	1944533)	1932664)	140.0)	136.6)	19746)	19663)	1.4)	1.4)	530125)	521984)	38.2)	, 36.9)
Officery tract infections and pyeloneprints	14337	13660	5.2)	5.1)	404097	387644	29.1	27.4	13740)	3717	1.4)	1.4)	111479	105820	30.2)	, 30.3)
	(11961,	(11154,	1.0 (0.9,	1.0 (0.8,	(342496,	(319554,	(24.7,	(22.6,	2042/224	(3002,	0.3 (0.2,	0.3 (0.2,	(93233,	(86381,	8.0 (6.7,	7.5 (6.1,
Endogarditis and other pardice infections	16714)	16166)	1.0 (0.9,	, ,	465698)	455734)	33.5)	32.2)	3942(324 3, 4642)	(3002, 4432)	0.3 (0.2,	0.3 (0.2,	(93233, 129725)	125258)	9.3)	7.5 (6.1, 8.9)
Endocarditis and other cardiac infections	56614(15	56223	1.2)	1.1)	2043470	2018972	147.2	142.7	3, 4042)	4432)	0.3)	0.3)	661325	654956	9.3)	0.9)
	053,	(14793,	4.1 (1.1,	4.0 (1.0,	(552160,	(539740,	(39.8,	(38.2,	19598 (0,	19584 (0,	1.4 (0,	1.4.0	(0,	(0,	47.6 (0,	46.3 (0,
Tubaraulasia	125580)	125532)	9.0)		4514167)	,	325.1)	317.1)	47431)	47203)	3.4)	1.4 (0,	1621868)	1596855)	116.8)	46.3 (0, 112.9)
Tuberculosis	,	,	9.0)	8.9)	- ,	4485012)	/	- /	- /	/	3.4)	3.3)	/	,	/	112.9)
Maningitic and other bacterial activity	12350(10	11184(92	00/07	0.0/0.7	759652	656065	54.7	46.4	3075	2787	00/00	00/00	188020	162998	13.5	44 5 (0.0
Meningitis and other bacterial central	163,	97,	0.9 (0.7,	0.8 (0.7,	(604370,	(530238,	(43.5,	(37.5,	(2480,	(2255,	0.2 (0.2,	0.2 (0.2,	(147995,	(129947,	(10.7,	11.5 (9.2,
nervous system infections	14538)	13072)	1.0)	0.9)	914934)	781892)	65.9)	55.3)	3671)	3318)	0.3)	0.2)	228045)	196049)	16.4)	13.9)
Interdess of boson St. C. C. C.	1683	1823	0.4 (0.4	0.4.(0.4	325519	350307	23.4	24.8	440 /00=	470 /056	0.0.00	0.00/0.0	96489	102511	00/10	70/10
Infections of bones, joints, and related	(1237,	(1358,	0.1 (0.1,	0.1 (0.1,	(197709,	(207843,	(14.2,	(14.7,	448 (327,		0.0 (0.0,	0.03(0.0,	(58195,	(59960,	6.9 (4.2,	7.2 (4.2,
organs	2128)	2288)	0.2)	0.2)	453329)	492772)	32.6)	34.8)	569)	603)	0.0)	0.0)	134783)	145061)	9.7)	10.3)
					3118939	2658356		l								
	41808	36178			(1289176	(1083893	224.6	187.9		4174	l		356738(9	304471		
Typhoid fever, paratyphoid fever, and	(17811,	(15294,	3.0 (1.3,	2.6 (1.1,	,	,	(92.8,	(76.6,	4814(130	(1142,	0.3 (0.1,	0.3 (0.1,	0542,	(76881,	25.7 (6.5,	, ,
invasive non-typhoidal Salmonella	65806)	57061)	4.7)	4.0)	4948702)	4232818)	356.4)	299.2)	6, 8322)	7205)	0.6)	0.5)	622934)	532060)	44.9)	37.6)
					2318542	1834376										
	52936	46364			(1381103	(1091147	167.0	129.7	10727(53	9440			443452	352277	31.9	24.9
	1.00000	104700	0 0 /0 4	22/40			/00 F	/77 A	04	/ AE AE	00/04	0 5 10 4	1055011	1000070	//0 /	(11 C
	(29222,	(24769,	3.8 (2.1,	3.3 (1.8,	,	,	(99.5,	(77.1,	31,	(4545,	0.8 (0.4,	0.5 (0.4,	(255311, 631594)	(206370,	(18.4,	(14.6,

Table 3: Deaths and DALYs associated with and attributable to bacterial antimicrobial resistance in India,2019 and 2021

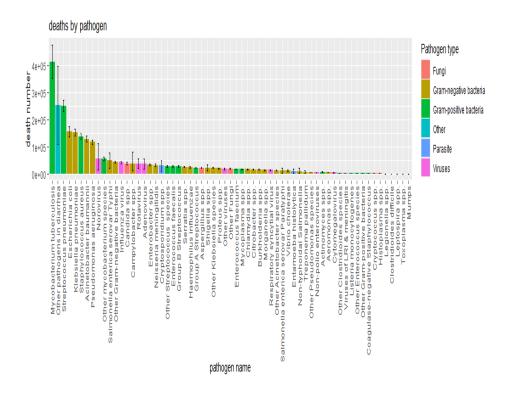
Interpretation: Burden of Infectious Syndromes Associated with and Attributable to Resistance (2019–2021) Among Older Adults (60–95+): Here is a concise Interpretation of your findings:

## Interpretation

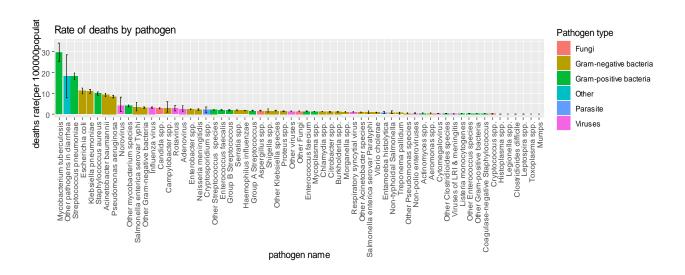
Between 2019 and 2021, infectious syndromes associated with antimicrobial resistance (AMR) showed a modest but encouraging decline in mortality and disease burden among older adults aged 60 and above in India. Notably, bloodstream and lower respiratory infections demonstrated reductions in both deaths and DALYs, with bloodstream infection deaths declining by 3.5% and DALYs by 7%, and lower respiratory infection deaths decreasing by 11.6%. Diarrheal diseases also saw a significant improvement, with a 13% reduction in deaths and a notable drop in DALYs.

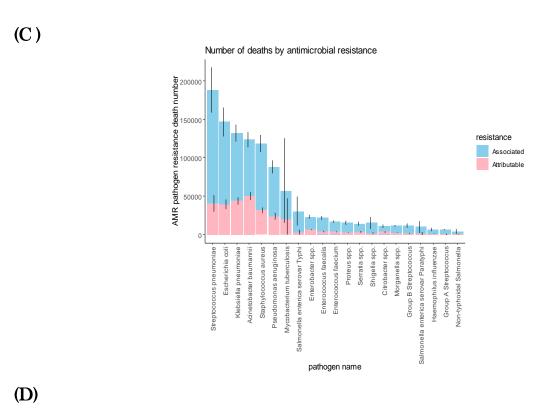
While tuberculosis mortality remained relatively stable, small improvements were observed. Infections directly attributable to AMR mirrored these trends, with lower respiratory and diarrheal diseases showing the most marked reductions in both deaths and DALYs. Despite these gains, AMR continues to pose a substantial health threat, especially among the elderly, underscoring the need for continued surveillance, prevention strategies, and antimicrobial stewardship.

A.



В.





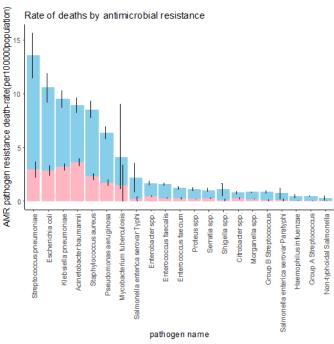


Fig 5: Number of deaths by pathogens and antimicrobial resistance in India,2019. (A)Number of deaths by pathogens; (B)Rate of deaths by pathogens; (C)Number of deaths by antimicrobial resistance; (D)Rate of deaths by antimicrobial resistance. The black vertical line represented 95%confidence interval.

#### Discussion:

Mycobacterium tuberculosis is the leading cause of death, contributing to over 400,000 deaths, confirming its persistent global health threat—especially in the context of drug resistance and impact on older or immunocompromised individuals. Streptococcus pneumoniae, Escherichia coli, and Klebsiella pneumoniae are also among the pathogens, mainly classified as Gram-positive and Gram-negative bacteria. These pathogens are commonly involved in pneumonia, bloodstream infections, and UTIs, with high antimicrobial resistance potential. The majority of high-burden pathogens are either **Gram-negative** or **Gram-positive** bacteria. This underscores that **bacterial infections**, not viral or fungal, account for the largest share of pathogen-attributable deaths, particularly those resistant to antibiotics. Viruses and parasites appear mostly in the mid-to-lower end of the death count . For example, pathogens like HIV, Mumps, or other parasitic protozoa show far fewer deaths than bacterial agents, possibly due to improved vaccines, treatments, or less prevalence in high-risk populations. Streptococcus pneumoniae tops the chart with over 200,000 deaths (combined attributable and associated), highlighting it as a critical AMR threat. Other highburden pathogens include: Escherichia coli, Klebsiella pneumoniae, A. baumannii, Staphylococcus aureus, Pseudomonas aeruginosa. These are known for hospital-acquired infections and resistance to multiple antibiotics, especially in ICUs and immunocompromised patients. Some pathogens like Streptococcus pneumoniae and E. coli show a high proportion of attributable deaths, meaning resistance itself is a direct cause of mortality. Others like Mycobacterium tuberculosis show a higher blue (associated) component, implying resistance complicates treatment significantly even if not the direct cause. Toward the right, pathogens like Haemophilus influenzae, Group A Streptococcus, and Non-typhoidal Salmonella have much lower death numbers, although still relevant in specific regions or populations. Drug-resistant bacterial infections cause a large number of direct and indirect deaths. Respiratory and bloodstream pathogens, especially those with multi-drug resistance, are the biggest contributors. AMR is not just an emerging issue—it is already a major global killer, with urgent implications for antibiotic stewardship, infection prevention, and development of new treatments.

# Here is the some comparison of Death between the years 2019 and 2021 for older age(85-95+): 85-89(Attributable, 2019, Death Number)

					An	tibiotic class			
	Aminog lycoside s	Carba pene ms	Fluoroq uinolon es	Meth icillin	Resistance to one or more antibiotics	Multi-drug resistance in Salmonella enterica	Penici llin	Trimethoprim- Sulfamethoxazo le	Third- generation cephalosporins
Pathogen	Categor y: Access		1			Category: Watch		1	
Acinetobacter baumannii	438.822 4017	1326.5 90981	727.084 885		2611.025805				
Escherichia coli		1097.8 42804	676.732 5968		3002.223135			338.7650458	485.3452411
Klebsiella pneumoniae	386.145 5851	1005.2 07069	484.235 7677		2230.168646				
Streptococcus pneumoniae		1204.8 05339			2238.052076		347.5 63647 3		
Staphylococc us aureus			367.574 4012	1166. 7009 8	1870.546325				
Pseudomona s aeruginosa		673.33 55219			1291.513579				
Mycobacteriu m tuberculosis					629.0834178	595.2177224			

#### 85-89(Attributable, 2021, Death Number)

					Antibiotic class			
	Aminogl ycosides	Carbap enems	Fluoroqu inolones	Meth icillin	Resistance to one or more antibiotics	Multi-drug resistance in Salmonella enterica	Trimethoprim- Sulfamethoxazol	Third-generation cephalosporins
Pathogen	Category : Access				C	ntegory: Watch	е	
Acinetobacter baumannii	430.851	1331.0 97	727.6604		2613.901			
Escherichia coli		1055.5 19	695.097		3075.074		384.7989	523.3307
Klebsiella pneumoniae	360.709 5	953.24 32	517.4631		2204.553			
Streptococcus pneumoniae		1262.3 06			2225.289			
Staphylococcu s aureus			420.7552	1295. 611	2056.45			
Pseudomonas aeruginosa		552.00 64			1269.064			
Mycobacteriu m tuberculosis					711.2144	671.9936		
Enterobacter spp.					331.0039			

#### Antibiotic ResistanceComparison (2019 vs 2021) - Age Group 85-89:

In the 85–89 age group, Escherichia coli deaths related to antibiotic resistance increased by about 2.4% overall, with fluoroquinolones (+2.7%) and Trimethoprim-Sulfamethoxazole (+13.6%) showing notable rises. Streptococcus pneumoniae also saw a slight increase in carbapenem-related deaths (+4.8%). In contrast, Acinetobacter baumannii showed a minimal overall increase of 0.1%, with aminoglycosides and carbapenems roughly stable. Klebsiella pneumoniae deaths decreased slightly by 1.2%, despite a small increase in fluoroquinolone resistance (+6.9%). New pathogen data reported in 2021 for Staphylococcus aureus (2056 deaths), Pseudomonas aeruginosa (1269 deaths), and Mycobacterium tuberculosis highlight

emerging resistance challenges. Overall, while some decreases occurred, antibiotic resistance remains a significant burden in this age group.

#### 90-94(Attributable, 2019, Death Number)

					Antibiotic cl	ass			
	Aminog lycoside s	Carba penem s	Fluoroq uinolone s	Meth icillin	Resistance to one or more antibiotics	Multi-drug resistance in Salmonella enterica	Peni cilli n	Trimethoprim- Sulfamethoxazol e	Third- generation cephalosporins
Pathogen	Categor y: Access		-	I		Category: Watch	1	-	Transfer   Transfer
Acinetobacter baumannii	183.650 2	555.18 74	304 <b>.</b> 293		1092.735				
Escherichia coli	_	536.89 61	332.884		1465.399			166.0407	232.1745
Klebsiella pneumoniae	168.776 8	439.35 66	211.655 6		974.7691				
Streptococcus pneumoniae		545.88 02			1014.031		157. 476 2		
Staphylococc us aureus				499. 2092	800.3713				
Pseudomonas aeruginosa		289.96 48			556.1792				
Mycobacteriu m tuberculosis					208.2259	197.0164			

#### 90-94(Attributable, 2021, Death Number)

					Antibiotic class			
	Aminogl ycosides	Carbap enems	Fluoroqu inolones	Meth icillin	Resistance to one or more antibiotics	Multi-drug resistance in Salmonella enterica	Trimethoprim- Sulfamethoxazol	Third-generation cephalosporins
Pathogen	Category : Access				C	ategory: Watch	e	
Acinetobacter baumannii	178.687 4	552.04 71	301.786		1084.069			
Escherichia coli		509.69 05	336.4228		1477.674		186.3265	244.4507
Klebsiella pneumoniae	156.022 2	412.31 84	223.8302		953.5686			
Streptococcus pneumoniae		564.75 47			995.5943			
Staphylococcu s aureus		235.46 01	178.6411	550.0 806	873.1121			
Pseudomonas aeruginosa					541.3261			
Mycobacteriu m tuberculosis					264.1052	249.5408		

Comparison of attributable deaths between 2019 and 2021 for the 90-94 age group due to antibiotic resistance: From 2019 to 2021, antibiotic resistance-attributable deaths in the 90-94 age group showed varied trends by pathogen and drug class. *Acinetobacter baumannii* demonstrated slight declines, with deaths due to aminoglycoside resistance down by 2.7%, carbapenem resistance by 0.6%, and overall resistance-related deaths by 0.8%. *Klebsiella pneumoniae* showed a 6.2% drop in carbapenem-related deaths and a 2.2% decrease overall, though fluoroquinolone resistance-related deaths increased by 5.7%. In contrast, *Escherichia coli* had a 0.8% rise in total resistance-related mortality, driven by increases of 12.2% in trimethoprim-sulfamethoxazole resistance and 5.3% in third-generation cephalosporin resistance, despite a 5.1% decline in carbapenem-related deaths. *Streptococcus pneumoniae* saw a 1.8% overall decline, but carbapenem resistance deaths increased by 3.5%. *Staphylococcus aureus* presented a concerning 10.2% rise in methicillin resistance-attributable

deaths and a 9.1% increase in total resistance-related deaths. *Pseudomonas aeruginosa* showed improvement with a 2.7% decline overall. Most notably, *Mycobacterium tuberculosis* showed sharp increases: 26.8% in multi-drug resistance deaths and 26.6% in deaths linked to trimethoprim-sulfamethoxazole resistance.

95+(Attributable,2019,Death Number)

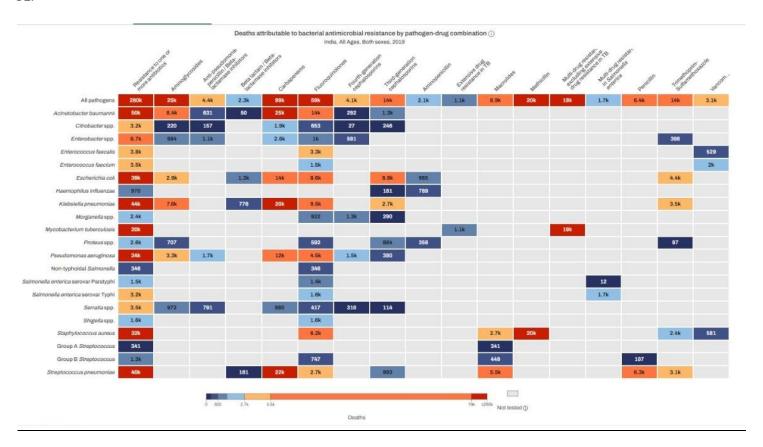
					Antibio	otic class			
	Aminogly cosides	Carbap enems	Fluoroqui nolones	Macr olides	Methi cillin	Resistance to one or more antibiotics	Peni cillin	Trimethoprim- Sulfamethoxazole	Third-generation cephalosporins
Pathogen	Category: Access					Category: Watch	h		
Acinetobacter baumannii	54.57106	164.972 1	90.42117			324.7043			
Escherichia coli		190.261 0451	118.8043			518.0645		59.00089	80.01891
Klebsiella pneumoniae	52.90546	137.722 5	66.34862			305.5573			
Streptococcus pneumoniae		182.515 8		45.80 695		339.0433	52.6 5237		
Staphylococcus aureus			48.24975		153.1 473	245.5377			
Pseudomonas aeruginosa		89.2172 8				171.1281			
Mycobacterium tuberculosis									
Enterobacter spp.						42.473			

## 95+(Attributable,2021,Death Number)

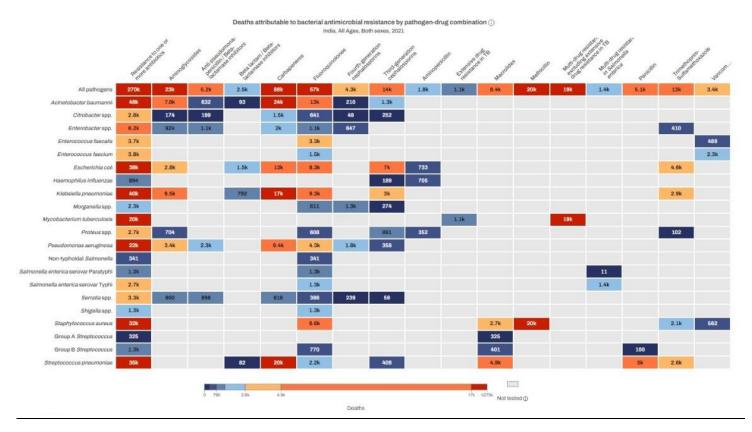
				Antibio	tic class			
	Amin	Carb	Fluoro	Resistance to	Multi-drug	Pe	Trimethopri	Third-
	oglyco	apen	quinol	one or more	resistance in	nici	m-	generation
	sides	ems	ones	antibiotics	Salmonella	llin	Sulfamethox	cephalospori
					enterica		azole	ns
Pathogen	Categ				Category: Watch			
	ory:							
	Access							
Acinetobac	48.716	150.5	82.278	295.5539				
ter		06	13					
baumannii								
Escherichi		166.7	110.34	480.7251			61.14847	76.89156
a coli		45	86					
Klebsiella	45.147	119.3	64.771	275.9356				
pneumonia	99	122	85					
e								
Streptococ		174.0		306.759		43.		
cus		099				490		
pneumonia						28		
e								
Staphyloco			50.495	246.7995				
ccus			83					
aureus								
Pseudomo		66.68		153.305				
nas		24						
aeruginosa								
Mycobacte				47.94514	45.30114			
rium								
tuberculosi								
S								

Comparison of attributable deaths between 2019 and 2021 in the 95+ age group due to antibiotic resistance: Between 2019 and 2021, there was an overall decline in antibiotic resistanceattributable deaths among the 95+ age group across most major bacterial pathogens and drug classes. Acinetobacter baumannii showed a consistent decrease, with deaths due to aminoglycoside resistance dropping by 10.7%, carbapenem resistance by 8.8%, fluoroquinolone resistance by 9%, and overall resistance to one or more antibiotics decreasing by 9%. Similarly, Escherichia coli exhibited a notable reduction, with carbapenem-related deaths falling by 12.3%, and resistance to one or more antibiotics decreasing by 7.2%, while deaths linked to trimethoprim-sulfamethoxazole showed a slight increase of 3.6%. Klebsiella pneumoniae followed the downward trend, with aminoglycoside and carbapenem resistance-attributable deaths declining by 14.7% and 13.4%, respectively. Streptococcus pneumoniae also showed encouraging declines, with a 9.3% decrease in carbapenem resistance-attributable deaths and a 9.5% reduction in overall resistance. However, Staphylococcus aureus was a key exception: deaths due to methicillin resistance surged by 61.2%, and fluoroquinolone resistance increased by 4.7%, highlighting an emerging concern. Pseudomonas aeruginosa saw improvements, with carbapenem-related deaths down by 25.3%. Notably, Mycobacterium tuberculosis appeared in 2021 data for the first time, reporting significant resistance burdens, including 47.95 deaths from multidrug resistance.

## A.



## B.



<u>Fig6:</u> Heatmap of\_deaths attributed with antimicrobial resistance by pathogen-drug combination.(2019)(A) and 2021(B).

<u>Discussion:</u> Heatmap of deaths attributed with antimicrobial resistance by pathogen-drug combination for 2019 and 2021:

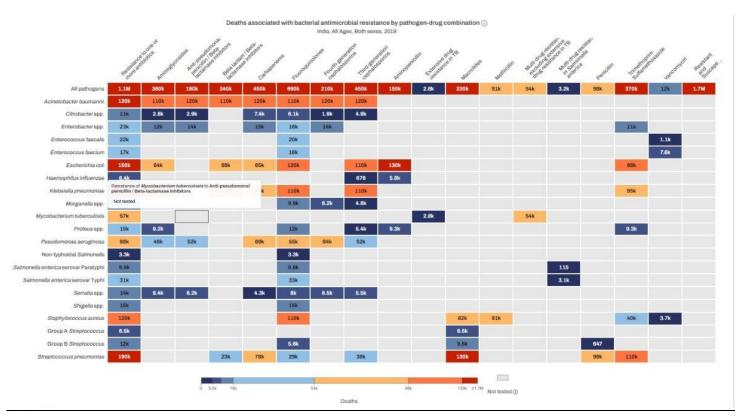
The heatmaps display deaths attributable to bacterial antimicrobial resistance (AMR) in India for the years 2019 and 2021, across all ages and sexes. The total number of deaths due to AMR declined slightly from 280,000 in 2019 to 270,000 in 2021. Among the pathogens, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Streptococcus pneumoniae* remained consistently among the top contributors to AMR-related deaths in both years, although each showed a modest decline. Notably, *Escherichia coli* was the only major pathogen for which deaths due to AMR increased—from 30,000 in 2019 to 36,000 in 2021—highlighting a growing concern.

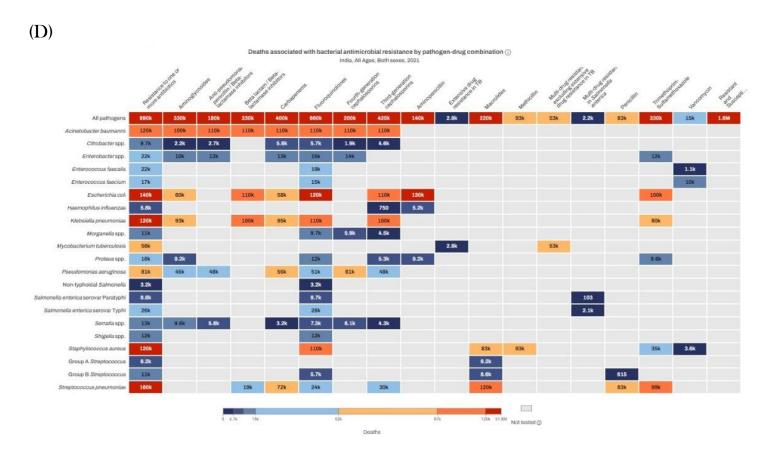
In terms of drug classes, resistance to cephalosporins continued to account for the highest number of deaths, though it declined from 99,000 in 2019 to 88,000 in 2021. Resistance to fluoroquinolones remained relatively stable (59,000 to 57,000), while carbapenem resistance saw a slight decrease (25,000 to 24,000). Deaths related to multidrug-resistant tuberculosis (MDR-TB) and methicillin-resistant *Staphylococcus aureus* (MRSA) remained unchanged at 19,000 and 20,000 respectively, suggesting persistent treatment challenges.

Among specific pathogen-drug combinations, *E. coli* resistant to fluoroquinolones and cephalosporins remained especially deadly, with little change in their high fatality numbers. Some minor increases were observed in resistance-related deaths involving less prominent pathogens like Group B *Streptococcus* and *Morganella* spp., though these changes were relatively small. Conversely, deaths linked to resistance in *Streptococcus pneumoniae* and *Klebsiella pneumoniae* against cephalosporins showed meaningful reductions.

Despite the modest overall improvement, the high number of deaths associated with common first-line antibiotics such as cephalosporins and fluoroquinolones indicates ongoing misuse and overuse. The consistently large "not tested" data segments in several pathogen-drug combinations highlight diagnostic gaps that hinder effective treatment. These trends underscore the urgent need for stronger antimicrobial stewardship, better surveillance systems, and expanded diagnostic capacities to combat AMR in India.

(C)





<u>Fig7:</u> Heatmap of\_deaths associated with antimicrobial resistance by pathogen-drug combination.(2019)(C) and 2021(D).

#### Discussion:

The heatmaps for the years 2019 and 2021 present a detailed overview of deaths associated with bacterial antimicrobial resistance (AMR) across various pathogen-drug combinations in India. In both years, the burden of AMR-related deaths remains alarmingly high, with 1.7 million deaths in 2019 and 1.6 million in 2021 linked to resistant infections. The most significant contributors across both years are resistance to fluoroquinolones, beta-lactam/beta-lactamase inhibitors, and third-generation cephalosporins. These drug classes consistently appear in deep red shades, indicating high mortality.

Among pathogens, *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Streptococcus pneumoniae* are responsible for the largest number of AMR-associated deaths. For example, in both years, *A. baumannii* shows consistently high resistance-associated mortality (around 120k deaths), particularly with carbapenems and beta-lactams. Similarly, *E. coli* and *K. pneumoniae* show high deaths across multiple drug classes, reflecting their widespread resistance and clinical importance. Notably, *Pseudomonas aeruginosa* and *Mycobacterium tuberculosis* also contribute significantly to the resistance burden, particularly with resistance to fluoroquinolones and rifampicin, respectively.

Comparing the two years, the overall trends remain similar, though there is a slight reduction in total deaths from 1.7 million in 2019 to 1.6 million in 2021. However, certain drug-pathogen combinations such as resistance of *K. pneumoniae* to cephalosporins and *S. aureus* to methicillin and beta-lactams remain persistently high. Additionally, some pathogens like *Group B Streptococcus* and *Shigella spp.* exhibit relatively low but consistent resistance-associated mortality, while a few like *Salmonella enterica serovar Typhi* show an increase in deaths due to resistance to fluoroquinolones and cephalosporins from 2019 to 2021.

In summary, both heatmaps underscore the sustained and broad impact of antimicrobial resistance across a range of pathogens and drug classes in India. The data highlight the urgent need for targeted antimicrobial stewardship, improved surveillance, and development of novel treatment options to address high-mortality resistance patterns, particularly involving beta-lactams, fluoroquinolones, and carbapenems.

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## Appendix:

```
blood_19 <- read.csv("bloodstream_raw_19.csv")
head(blood_19)
blood_19 \leftarrow blood_19[,c(1:3)]
names(blood_19)
library(stringr)
blood_19$agegroup <- str_replace_all(blood_19$agegroup, c("neonatal"="Neonatal","post-neonetal"="Post-Neonatal"))
#blood_19$agegroup
# to get an age wise order
blood_19$agegroup <- factor(blood_19$agegroup, levels=c("95+","90-94","85-90","80-84","75-79","70-74","65-69","60-64","55-
59","50-54","45-49","40-44","35-39","30-34","25-29","20-24","15-19","10-14","5-9","1-4","Post-Neonatal","Neonatal"))
library(ggplot2)
g1 <- ggplot(data=blood_19, aes(x=agegroup, y=Male)) +
 geom_bar(stat = "identity",fill="red") + ggtitle("Bloodstream") +
 theme(axis.title.x = element_blank(),
     axis.title.y = element_blank(),
     axis.text.y = element_blank(),
     axis.ticks.y = element_blank(),
     plot.margin = unit(c(1,-1,1,0), "mm")) +
 scale_y_reverse() + coord_flip() +
 theme(axis.text.x = element_text(angle = 45, hjust = 1)) # to rotate the label
g2 <- ggplot(data=blood_19, aes(x=agegroup, y=Female)) +
 geom_bar(stat = "identity",fill="blue") + ggtitle("2019") +
 xlab(NULL)+
 geom bar(stat = "identity",fill="blue") +
 theme(axis.title.x = element_blank(), axis.title.y = element_blank(),
     axis.text.y = element_blank(), axis.ticks.y = element_blank(),
     plot.margin = unit(c(1,0,1,-1), "mm")) +
```

```
coord_flip() +
 theme(axis.text.x = element_text(angle = 45, hjust = 1)) # to rotate the label
#g2 <- ggplot(amr.death.all.attr_21) + geom_bar( aes(x=Pathogen, y=Value), stat="identity", fill="skyblue", alpha=0.7) +
# geom_errorbar(aes(x=Pathogen, ymin=Upper, ymax=Lower), width=0.4, colour="orange", alpha=0.9, linewidth = 1.3) +
# theme(axis.text.x = element_text(angle = 90, vjust = 0.5, hjust=1)) +
# ggtitle("Deaths attributable to AMR in 2021") + scale y continuous(labels = scales::comma
blood 21 <- read.csv("bloodstream raw 21.csv")
head(blood_21)
blood 21 \leftarrow blood 21[,c(2:4)]
names(blood_21)
#library(stringr)
#blood_19$agegroup <- str_replace_all(blood_19$agegroup, c("95+"="95+","90-94"="90 to 94","85-90"="85 to 89","80-84"="80 to
84","75-79"="75 to 79","70-74"="70 to 74","65-69"="65 to 69","60-64"="60 to 64","55-59"="55 to 59","50-54"="50 to 54","45-49"="45
to 49","40-44"="40 to 44","35-39"="35 to 39","30-34"="30 to 34","25-29"="25 to 29","20-24"="20 to 24","15-19"="15 to 19","90-
94"="10 to 14","90-94"="5 to 9","90-94"="1 to 4","post-neonetal"="Post Neonetal", "neonatal"="Neonatal"))
#blood_19$agegroup
# to get an age wise order
blood 21$age group <- factor(blood 21$age group, levels=c("95+","90-94","85-89","80-84","75-79","70-74","65-69","60-64","55-
59", "50-54", "45-49", "40-44", "35-39", "30-34", "25-29", "20-24", "15-19", "10-14", "5-9", "1-4", "Post-Neonetal", "Neonetal"))
library(readxl)
library(pheatmap)
# Read reshaped data
data <- read_excel("reshaped_heatmap_data.xlsx")
# Set pathogen names as rownames
data_matrix <- as.data.frame(data)
rownames(data_matrix) <- data_matrix$Pathogen
data_matrix$Pathogen <- NULL
# Convert to numeric matrix
data matrix <- as.matrix(data matrix)
```

```
# Log10 transform (+1 to avoid log(0))
log_data_matrix <- log10(data_matrix + 1)
# Create display matrix (only show values where original is not 0)
display_matrix <- ifelse(data_matrix == 0, round(data_matrix, 0)) # show original values, blank if 0
# Define color palette
color_palette <- colorRampPalette(c("navy", "skyblue", "yellow", "orange", "red", "darkred"))(100)
# Generate heatmap
pheatmap(log_data_matrix,
     scale = "none",
     display_numbers = display_matrix, # show real values, blank where 0
     number_format = "%.0f",
     cellwidth = 40,
     cellheight = 20,
     fontsize_row = 10,
     fontsize_col = 10,
     fontsize_number = 8,
     color = color_palette,
     main = "Deaths by Pathogen and Drug Class (0s Hidden)")
```