Quantifying the mortality, health outcomes, and disability due to snakebite envenoming in India

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Abstract

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Venomous snakebites cause substantial mortality and morbidity in India, despite the existence of antivenom treatment for the most common Indian venomous snakes. There have been few efforts to quantify the disease burden at a population level, primarily due to scarce data. By incorporating data on snakebite habitat, nonfatal health outcomes, and mortality, this study measured the morbidity and mortality from venomous snakebites in India from 2000 to 2019 by sex, age, and state. This study expanded on estimates from the Global Burden of Disease (GBD) 2019 study, which modeled mortality in India due to “venomous animal contact”, an umbrella category that includes all venomous animals. The proportion of all venomous animal contact deaths due only to snakes was modeled and applied to GBD estimates of death and years of life lost (YLLs). Information on the relative occurrence of hemotoxic and neurotoxic snakes in India and each snake type’s case fatality rate and common health outcomes were analyzed to produce estimates of incidence, years lived with disability (YLDs), and disability-adjusted life years (DALYs). In 2019, 827,000 (95% CI: 411,000 to 1.6 million) venomous snakebites occurred in India and resulted in 51,000 (30,000 to 64,000) deaths and 3.0 million (1.8 to 3.7) DALYs. The disease burden was greatest in the central and eastern region of the country. Amputation was the greatest cause of nonfatal disability. Venomous snakebites are a large cause of preventable morbidity and mortality in India. By better understanding the epidemiology of venomous snakebites and its

amenable nature, prevention initiatives, healthcare resource investment, and rural antivenom distribution interventions can be more effectively implemented.

Introduction

Venomous snakebites are estimated to affect millions globally, especially in impoverished and rural areas.[1] In South Asia, specifically India, snake envenoming kills more people than any other neglected tropical disease (NTD).[2] In 2017, snakebite envenoming was re-recognized as a category A NTD, and the WHO established a target to halve the number of deaths and cases of snakebite envenoming by 2030. Recently there has been renewed interest in understanding disease burden so that progress towards Sustainable Development Goal 3.3, which is to end the epidemic of NTDs, can be quantified.[3]

While venomous snakebites are a growing concern worldwide, they are a particularly large source of burden in India, and estimated to kill over 50,000 people per year.[4] In the Indian state of Bihar, snakebites accounted for 7.6% of all unintentional injury deaths and 33.3% of deaths in the 10-14 years age group.[5] While there are many types of snakes, the Big Four, which includes the spectacled cobra (*Naja naja)*, common krait (*Bungarus caerelus)*, Russell's viper *(Dabroia russeli),* and saw-scaled viper (*Echis carinatus*), account for 90% of all venomous snakebite deaths in India.[6] Within the Big Four, there are two main categories of snake: hemotoxic vipers (Russell's and saw-scaled viper) and neurotoxic elapids (cobra and krait), whose bites cause substantially different sequelae.[7] Because of their prominence, the venom of these four snakes has been studied extensively and packaged into a single polyvalent antivenom capable of treating the poison from all four species, although its efficacy has been criticized.[1,8] Recently, efforts to systematically identify the prevalence of these snakes have been conducted, whether through literature reviews or crowd-sourced reports of snake sightings or bites.[7,9] Understanding the incidence and type of envenoming at a local level has been done elsewhere using geostatistics,[10] and could allow greater capacity building of a health system that currently lacks the necessary resources for proper treatment.[11,12] Previous modeling studies of venomous snakebite burden have faced a lack of high-quality data as a major limitation, especially because of the rural and low-resource nature of where venomous snakebites are concentrated.[6]

This study aims to incorporate various data sources on mortality, morbidity, and snake habitat to quantify the disease burden of venomous snakebites in India over time and by age, sex, and Indian state. It specifically analyzes the epidemiology of the Big Four snakes and their unique health outcomes, which enabled deconstruction of nonfatal morbidity into the attributable sequela. With this more detailed level of understanding of state-level disease burden, policies and interventions can be more efficiently implemented and their efficacy can be better understood.

Methods

Snakebite disability was estimated in three overarching steps. First, the number of deaths due to venomous snakes was derived from Global Burden of Disease 2019 (GBD) estimates of venomous animal contact. Second, occurrences of the Big Four snake genera were extracted from the Global Biodiversity Information Facility database and the relative density of hemotoxic versus neurotoxic snakes was mapped to Indian states according to borders used in the GBD. Third, a literature review of incidence, case fatality rate, and disease sequelae allowed estimation of incidence and non-fatal disability. These steps resulted in the quantification of the disability-adjusted life years (DALYs) due to venomous snakebites in India. DALYs are equal to the sum of years of life lost (YLLs) and years lived with disability (YLDs). YLLs are equal to the cause-specific mortality rate at a specific age multiplied by the residual life expectancy at that age, which is based on the observed maximum global life expectancy. YLDs are equal to the product of the prevalence of disease times the disease's disability weight, which is an estimate of the magnitude of health loss associated with a non-fatal outcome, measured on a scale of 0 to 1 where 0 is the equivalent of full health and 1 is equivalent to death.[13] The methodology to calculate disability weights has been discussed elsewhere.[13,14]

Mortality

GBD 2019 estimated the mortality due to venomous animal contact, which is an umbrella category that includes deaths from snakes, bees, spiders, scorpions, and other venomous animals. This study derived the proportion of GBD 2019 deaths due specifically to venomous snakes using verbal autopsy and vital registration data that could be attributed specifically to snakes. Venomous snakebite mortality was modeled around the world, and included 10,637 location-years of data. Prior to modeling, data underwent noise reduction (NR) and garbage code redistribution (GCR), which are two data processing steps used in the GBD.[15] NR utilizes a Poisson regression model and Bayesian averaging process to reduce stochastic variation in the data. For venomous animal contact, GCR redistributes deaths due to ICD codes E905, E905.9, and X29, which code for deaths due to unspecified venomous animals. GCR leverages region, age, and sex patterns from correctly coded deaths to redistribute the unspecified codes.

Spatiotemporal Gaussian Process Regression (ST-GPR), a modeling approach that captures trends over space, time, and age, was run with the input data described above to estimate the rate of death due to snakes, bees, scorpions, spiders, and the residual "other venomous animal" category for every country, age, sex, and year from 1990 to 2019.[16] See Appendix pp 1-7 for further details on ST-GPR parameters and covariates. The total mortality from all five animal models was aggregated to derive the proportion of overall venomous animal deaths due to snakebites alone. The snakebite-specific proportion was applied to GBD 2019 estimates of the number of deaths and YLLs due to venomous animal contact.

Snake type mapping

To estimate the proportion of bites attributable to hemotoxic or neurotoxic snakes, occurrences of each of the Big Four snake genera were extracted from the Global Biodiversity Information Facility database (GBIF), which is an international network and research infrastructure aimed at providing open access to biodiversity data.[17] The genus of each of the Big Four Indian species were queried using the *rgbif* R statistical package.[18] Every snake occurrence with listed latitude and longitude coordinates or identifiable location was extracted and mapped to Indian state lines according to GBD borders. Within each state, the proportion of venomous snake occurrences that were hemotoxic (genus *Daboia* and *Echis*) and neurotoxic (genus *Bungarus* and *Naja*) was calculated. There were no occurrence data in five states –Jammu & Kashmir and Ladakh, Arunachal Pradesh, Manipur, Mizoram, and Nagaland. For Jammu and Kashmir, the proportion of the neighboring state of Himachal Pradesh was applied. For the other four missing states, the proportion from neighboring Assam was applied. For every state, the standard error of the proportion was calculated and 1,000 draws were taken from a binomial distribution around the proportion.

Non-fatal disability

The process to determine the non-fatal disability of snakebites in India is shown in Appendix Figure 6, and includes estimating the age and sex pattern of incident venomous snakebites, mapping the primary and secondary clinical manifestations resulting from hemotoxic and neurotoxic snakebites to GBD health states, and calculating the respective case-fatality rate of the two types of snakes.

Data sources

A literature review using a snowball search on epidemiological studies of venomous snakebite in India was conducted. PubMed and Semantic Scholar were queried for combinations of the terms "venomous snakebite", "viper", "cobra", "krait", "epidemiology", "mortality", and "case fatality". Any study that analyzed venomous snakebites specifically due to hemotoxic and/or neurotoxic snakes in an Indian state was considered. Studies from Bangladesh and Nepal were also included if snake species information was provided. Information on case-fatality rate and symptoms were only extracted if it could be specifically attributable to a hemotoxic or neurotoxic snake. Information on the age and sex distribution of venomous snakebite incidence was aggregated over all species. Appendix pp 8-10 contains information for each extracted literature source.

A single ICD10 coded clinical source from the Indian state of Karnataka that had admissions by age and sex was used to estimate the GBD 5-year age group distribution of venomous snakebites, because the most precise age groups in the literature were 10-year windows. (Appendix pp 11).

Incidence estimation from case-fatality rates

Case fatality rate (CFR) was used to translate the mortality calculated above to incidence. CFR information was extracted from any source that provided mortality and incidence estimates due specifically to hemotoxic or neurotoxic snakes. These proportions were input into Meta-Regression: Bayesian, Regularized, Trimmed (MR-BRT), a meta-regression model that incorporates the uncertainty of the input data and weights data according to a likelihood estimator meant to detect outliers (Appendix pp 15).[19] 1,000 estimates were taken from the posterior distribution around the CFR estimate.

For each state, a weighted CFR was calculated based on the proportion of bites expected to be from hemotoxic or neurotoxic snakes, which was calculated from GBIF queries above, and shown in Eq. 1 below.

$$\text{Eq. 1: } CFR_{hem,neuro} = CFR_{hem} * P_{hem} + CFR_{neuro} * P_{neuro}$$

Where CFR is the case fatality rate due to either hemotoxic or neurotoxic snakes, and P is the proportion of bites due to hemotoxic or neurotoxic snakes.

Applying this weighted CFR to the number of deaths in each state gave an estimate of the number of incident cases across all ages due specifically to neurotoxic and hemotoxic snakes.

Estimates of incidence across all ages and both sexes were then split using the age and sex distribution extracted from epidemiological literature. Appendix pp 11-14 describes the process of age and sex-weighting incidence.

Non-fatal health outcome mapping

To calculate DALYs due to snake envenoming, the different clinical presentations that result from venomous snakebite were extracted from the literature review above. The most common snakebite sequelae in the literature were each mapped to one of 235 GBD health states, each of which has a lay description of the functional effects and symptoms associated with a condition. Mapping was done by matching the most common symptoms of a sequela to a health state description, or using health states that already align with a GBD cause. See Table 1 for the mapping of clinical presentation to health state and disability weight. An outcome had to appear in six or more studies to be included.

For each clinical presentation in Table 1, the proportion of bites resulting in that sequela was calculated based on literature inputs and modeled using MR-BRT (Appendix pp 16-20).[19] 1,000 draws were taken from the posterior distribution of each MR-BRT model.

Combined disability weight estimation

A combined disability weight that takes into account the multitude of non-fatal health outcomes caused by venomous snakebites was created through a simulation of 20,000 snakebites, similar to processes in the GBD study accounting for comorbid outcomes.[20] MR-BRT estimates described above of the proportion of bites resulting in each outcome were used to independently predict the occurrence of each outcome across 20,000 simulations. The combined disability weight was estimated for each simulant using Eq. 2 below, and the attributable disability weight across all 20,000 simulants for each outcome could then be calculated using Eq. 3.

$$\text{Eq. 2: } DW_{combined} = 1 - \prod_{k=i}^{j}(1 - DW_k)$$

Where DW_{combined} is the total disability weight of a simulant across all of the k diseases, which each have a disability weight of DW_k.

$$\text{Eq. 3: } DW_{a,k} = \frac{DW_k}{\sum_{k=i}^{k=j} DW_k} * DW_{combined}$$

Where $DW_{a,k}$ is the attributable disability weight due only to disease *k* among all disease sequelae that simulant *l* has acquired, from *j* to *i*, which are combined into $DW_{combined}$ in Eq. 1.

These simulations involve an underlying assumption that each sequelae occurs independently, and no conditional probabilities of sequelae were used because little data exists on the conditional probabilities of the presenting symptoms of venomous snakebites. Each individual disability weight reported in the GBD has uncertainty, and 1,000 draws were derived from a Gaussian distribution around the mean and standard deviation of every disability weight. The 20,000 snakebite simulation was run for each draw, to estimate the uncertainty of the combined disability weight.

Long-term disability

The most common long-term complications from venomous snakebites, which were chronic kidney disease (CKD), hypopituitarism, skin necrosis scarring without amputation, and amputation, were all mapped to each snake type and their preceding short-term sequelae. Appendix Table 5 outlines this mapping along with the proportion of short-term bites resulting in long-term complications. Other long-term complications due to venomous snakebites, such as blindness and chronic pain, have been reported in the literature, but were not included due to insufficient information on the rate of their occurrence and evidence that they may subside over time.[21] Proportions were based on literature studies and expert opinion, because conditional probabilities of long-term outcomes were rare in the literature. Of acute kidney failure cases, 10% were assumed to manifest to hypopituitarism and 15% were assumed to manifest to chronic kidney disease stage IV, based on the studies by Golay et al.[22] and Waikhom et al.[23], respectively. Amputations and skin necrosis were described more often in the literature review in Appendix pp 8-10.

Proportions were applied to the incidence estimates of short-term acute kidney failure and skin infections to calculate the probability of having a long-term complication. These long-term incidence estimates were input into DisMod-MR 2.1, which is a Bayesian mixed-effects meta-regression tool developed specifically for the GBD by the Institute for Health Metrics and Evaluation (Settle, WA, USA), that determines the relationship between incidence, mortality, remission, and prevalence.[20] The sex-, state-, year-, and age-specific ratio of CKD stage 5 incidence over CKD stage 4 prevalence, based on GBD estimates, was input as remission to model the number of cases over age who leave the pool of people with CKD stage 4 to become a prevalent case of CKD stage 5. In India, approximately 10% of patients who need renal replacement therapy receive it.[24,25] This proportion was applied to those who progress to CKD stage five and require dialysis to survive in order to separate the incidence of short-term ESRD cases who die and the incidence of long-term ESRD cases with dialysis, which is converted to prevalence using DisMod-MR 2.1. YLDs were then calculated from prevalence estimates of CKD stage 4, CKD stage 5 with dialysis, and CKD stage 5 without dialysis.

Results

Snake type density

The relative occurrence of the Big Four snake genera differed geographically across India, with hemotoxic vipers occurring more frequently in the western regions of the country and neurotoxic cobras and kraits occurring more frequently in the central and eastern states. Three states had over 100 occurrences of the Big Four snake genera reported in GBIF, including Maharashtra, Tamil Nadu, and West Bengal. 13 states in GBIF had fewer than 5 recorded occurrences in GBIF. The states with the greatest proportion of hemotoxic snakes were Kerala (77%; 33/44) and Gujarat (69%; 9/13). Delhi, Meghalaya, Odisha, Telangana, and Tripura only had reported occurrences of cobras and kraits, and zero reported occurrences of Russell's or Saw-scaled vipers.

Non-fatal health outcomes

Mapping of non-fatal health outcomes from epidemiological literature yielded different results for hemotoxic and neurotoxic snakes (Table 1). MR-BRT meta-regressions showed that open wound and coagulopathy were the most frequent manifestations in hemotoxic snakes, occurring in 89% (95% UI: 76 to 96) and 63% (31 to 86) of venomous bites, respectively. In neurotoxic snakes, open wound and generalized bulbar weakness were the most common sequelae, occurring in 58% (26 to 86) and 54% (40 to 69) of bites, respectively. See Appendix pp 16-20 for inputs and results of each sequela's MR-BRT model.

Incidence and Mortality

In 2019, venomous snakebites caused 827,000 (95% UI: 411,000 to 1.6 million) poisonous envenomings, which resulted in 51,000 (30,000 to 64,000) deaths (Table 2). This was equivalent to an age-standardized rate of 59 (29 to 115) venomous bites per 100,000 and 4.0 (2.4 to 5.1) deaths per 100,000. Venomous snakebites were more common in men, with an age-standardized incidence rate of 69 (31 to 136) bites per 100,000, compared to 48 (22 to 100) bites per 100,000 in females. Since 2000, the age-standardized rate of deaths from snakebites in India has decreased 39% (-51 to -18). The greatest number of deaths occurred in Uttar Pradesh, where 12,000 (5,000 to 16,000) died from venomous snakebites. Chhattisgarh had the greatest age-standardized death rate at 6.5 (3.5 to 8.4) deaths per 100,000.

YLDs, YLLs, and DALYs

In India, venomous snakebite resulted in 237,000 (220,000 to 272,000) YLDs, 2.7 million (1.6 to 3.5) YLLs, and 3.0 million (1.8 to 3.8) DALYs in 2019. This was equivalent to an age-standardized rate of 218 (130 to 277) DALYs per 100,000, and was a decrease of 43% (-54 to -22) since 2000. Uttar Pradesh, Rajasthan, and Chhatisgharh had the greatest age-standardized DALY rates, with over 300 DALYs per 100,000 (Figure 2). Tripura and Mizoram had the lowest age-standardized rate of DALYs, with 40 (28 to 99) per 100,000 and 48 (31 to 119) per 100,000, respectively. There was considerable regional variation across India, with the greatest rates occurring in Central India (Figure 3). Previously, the eastern region also had a high rate of DALYs relative to other regions, but significantly decreased 57% (-67 to -38) since 2000, primarily due to a steep decline in Bihar (Table 2).

The majority of the disease burden due to venomous snakebites in India came from YLLs. However, YLDs due to long-term causes made up over 10% of DALYs for all ages above the 30-year-old age group (Figure 4). YLDs due to non-fatal short-term outcomes made up less than two percent of DALYS in every age group.

Attributable long-term sequela of long-term YLDs

Amputations accounted for the largest number of YLDs in both males and females (Figure 5), accounting for 44% of total YLDs (104,640 out of 235,694). Hypopituitarism, a disorder caused by necrosis of the pituitary gland due to kidney damage and venom-induced coagulopathy[21], was the only other sequela to cause over 50,000 YLDs in 2019. CKD stage 4, stage 5 without dialysis, and stage 5 with dialysis caused 6.7% of YLDs (15,925/235,694). Acute injury caused 14% (14,303/100,147) of YLDs in females and 11% (15,269/136,447) of YLDs in males.

Discussion

This study estimates 827,000 (95% UI 411,000 to 1.6 million) envenomings occurred in India in 2019, causing over 51,000 (30,000 to 64,000) deaths and 2.9 million (1.8 million to 3.8 million) DALYs. Although the age-standardized rate of DALYs has decreased 43% (-54 to -22) since 2000, the 2019 burden estimates would make venomous snakebites the 5th greatest source of burden among injuries, behind road injuries, self-harm, falls, and drowning, according to GBD 2017.[20] The age-standardized rate of 218 (130 to 277) DALYs per 100,000 is almost two times greater than the rate of dengue, the NTD with the greatest burden in India, which is estimated to cause 113 (59-159) age-standardized DALYs per 100,000.[20]

There was marked geographical variation across India, with the greatest age-standardized rates of DALYs occurring in the states of Bihar, Rajasthan, and Chhattisgarh (Table 1). Venomous snakebite has previously been studied in Bihar using verbal autopsy, which is a method to use interviews to ascertain the cause of death and has been shown to have high sensitivity and specificity when assessing snakebites.[4,5] Dandona et al.'s findings of 4.4 deaths per 100,000 closely aligned with our estimates for 2014, the final year of their survey, which was an age-standardized rate of 4.0 (1.8 to 4.9) deaths per 100,000.[5]

This study is the first to estimate the disease burden due to snakebites in India in terms of DALYs, and is the first to incorporate the health loss from a range of non-fatal sequelae that result from snake envenoming. Previous estimates of DALYs due to snakebites have either used a single disability weight for all snakebites or only considered the disability due to amputations.[26,27] While the Global Burden of Disease study includes multiple disability weights for all injuries through the use of its matrix of E-to-N ICD codes, disability due to conditions such as kidney disease or respiratory failure are not included.[13,28] While these DALY estimates take into account a large range of physical complications of snakebites, they still have shortcomings, such as not including the potential effect of snakebites on psychological morbidities like depression.[29] They also do not take into account the socioeconomic effect of snakebites, which may cause extensive economic cost due to antivenom and hospital treatment, loss of employment, and death of livestock.[26,30]

The extent of death and secondary disability due to snakebites demonstrates that much of the disease burden is preventable, and there is a need for interventions that can ensure more rapid access to antivenom across India. Previous studies have shown the probability of death especially increases if antivenom has not been administered within six hours after the bite, yet in South Asia only half of patients reach a clinic in this amount of time and 70-80% die before reaching a clinic.[6] Interventions such as adapting motorcycles that provide rapid emergency transport of snakebite victims has been shown to prevent deaths in rural Nepal[31], however, have not had success in India due to not being coupled with antivenom delivery and training of the emergency responders.[6] Drones could provide another viable option for efficient antivenom delivery to rural areas.[32] By quantifying the disease burden of snakebites, the cost-effectiveness of these interventions can be better understood, especially in addition to interventions such as training primary health care workers, increasing education around snakebites, and distributing mosquito nets.[1,11,33]

Beyond antivenom, strengthening of the health system in rural areas so that ventilators, dialysis, blood transfusions, and other resources are available will also be important to decreasing the amount of death and chronic disability due to venomous snakebites. Snakebites are a sizable cause of kidney failure in India.[34,35] Without emergency dialysis, each case of acute kidney failure faces a high probability of complications and death, but in India it is estimated that less than 10% of people that require dialysis receive it, and this proportion is likely less in the more rural areas where snakebite is common.[24,25] Blood transfusions are also commonly necessary, yet the blood supply has been estimated to be inadequate in the country.[36–38] Mechanical ventilation may be required to treat the respiratory distress that results from neurotoxic snakebites, which requires an advanced clinical setting at greater cost to the victim.[30] Hypopituitarism has been reported in the literature as a result of venomous snakebite and associated with acute kidney failure, however, is not commonly looked for at the time of envenoming despite its magnitude of morbidity.[21,39] Understanding which snakes are the most common to bite on a local scale can help guide infrastructure strengthening and treatment, for example, to provide dialysis where vipers are most common and ventilators where neurotoxic elapid bites are most common.

This analysis calculated non-fatal disability through mapping the relative frequency of the Big Four snake genera based on occurrences in the GBIF. Up to this point, the density of different venomous snake species has not been mapped in India. Ecological mapping of the habitat of specific species at a geospatial scale has been done elsewhere[40], and should be replicated in India, where only four species cause the majority of burden.[6] Longbottom et al. previously mapped 216 venomous snake species globally, but focused on snake species that do not have effective antivenom treatment in order to estimate the vulnerability to snakebite.[41] The case of India demonstrates that a large burden persists despite the existence of polyvalent antivenom for the Big Four species. Dissemination of antivenom as well as preventive measures such as education need to be expanded.[42,43]

Several limitations apply to this analysis. First, estimates of non-fatal incidence and CFR depended on many studies based in hospitals or clinics instead of community-based surveys. This is problematic because a large proportion of cases do not go to a clinic or hospital, with estimates widely ranging from 23% to 71%.[30,44] Similarly, Mohapatra et al. estimated from their representative survey that only 23% of deaths make it to a hospital.[4] Also, the settings of the clinic and their proximity to snakebite victims likely differed, and this was not controlled for in the CFR meta-regressions.

Second, mapping health outcomes from the literature review to sequelae used in the GBD was inexact due to variable case descriptions across studies. For example, some studies defined blood coagulopathy based on the result of the 20-minute whole blood clotting test (WBCT20), which is specifically recommended by the WHO to test for spontaneous hemorrhage due to hemotoxic snakebite.[45] Other studies just listed the number of patients with blood clotting disorders without evidence of a WBCT20. Similarly, only a percentage of cases had a confirmation of the species of snake responsible for the bite through sight or capture. In one review, snakebite victims in India were found to have spotted the culpable snake 77% of the time and captured it 24% of the time.[46] Some hemotoxic and neurotoxic snake classifications were defined by the symptoms of the victim, which can overlap and cause mis-classification.[47,48] Snakebites from venomous species other than the Big Four also occur, which may have been present in epidemiological studies that identified the snake type by pathology and not a concrete sighting.[7] The trimming function of MR-BRT likely eliminated the most important misclassification issues (See Appendix pp 16-20), but some could have persisted and accounted for the wide uncertainty intervals in the incidence estimates of Table 1.

Third, it is well-known that snakebite envenoming causes long-term complications, however, the exact probability of having chronic issues like hypopituitarism from pituitary gland necrosis or chronic kidney disease is not well understood.[21,35] In two different studies, the proportions of patients who had suffered chronic kidney disease after an initial acute kidney injury due to a venomous snakebite were 17% and 8%, respectively.[23,49] This study assumed 15% of acute kidney failure cases resulted in CKD stage 4, and applied the ratio of CKD stage 5 incidence over CKD stage 4 prevalence to estimate the number of cases of CKD stage 4 who progress to stage 5. In India, 10% of new end-stage renal disease patients have been shown to receive dialysis, and this proportion was used uniformly to split ESRD patients into those with and without long-term dialysis. 10% is the proportion across all of India, and may mask local differences. Because snakebites tend to occur in more rural and poor areas and private dialysis centers make up 85% of hemodialysis stations in India, 10% is likely an overestimate for snakebite victims.[25]

Fourth, GBIF is not exhaustive of all snake occurrences in India and is an approximation of the relative proportion of incidence by snake type. GBIF has been shown to have spatial biases, such as containing fewer records in the tropical regions that have the greatest snake populations.[50] However, bias has not been shown to occur when comparing the volume of records between species. Crowd-sourced biodiversity technology has been successful in previous surveillance initiatives on the intersection of wildlife and public health, and could be scaled up in areas where venomous snakebite is common.[51]

Publicly available apps could also be coupled with public health education information, increasing the abundance of snakebite biodiversity data while facilitating educational communication.

While venomous snakebites are securing increased attention in the global health field, population-level estimates of disease burden do not exist. This study produces the first estimate of DALYs at the national and state level in India from 1990 to 2019 and by age, time, and sex. Understanding the burden at the state level will provide important policy implications. Building on this, studying the burden with geospatial analysis has been successful elsewhere for snakebites,[10] and should be replicated in future studies. To achieve more robust data-driven estimates of the burden of venomous snakebites and a greater understanding of health-seeking behavior, large national household surveys in India should incorporate questions on snakebites. These results suggest that snakebite envenoming needs to be targeted at multiple levels to decrease the incidence, long-term disability, and death, especially to reach the WHO's goal of halving the number of deaths due to venomous snakes by 2030.

Tables and Figures

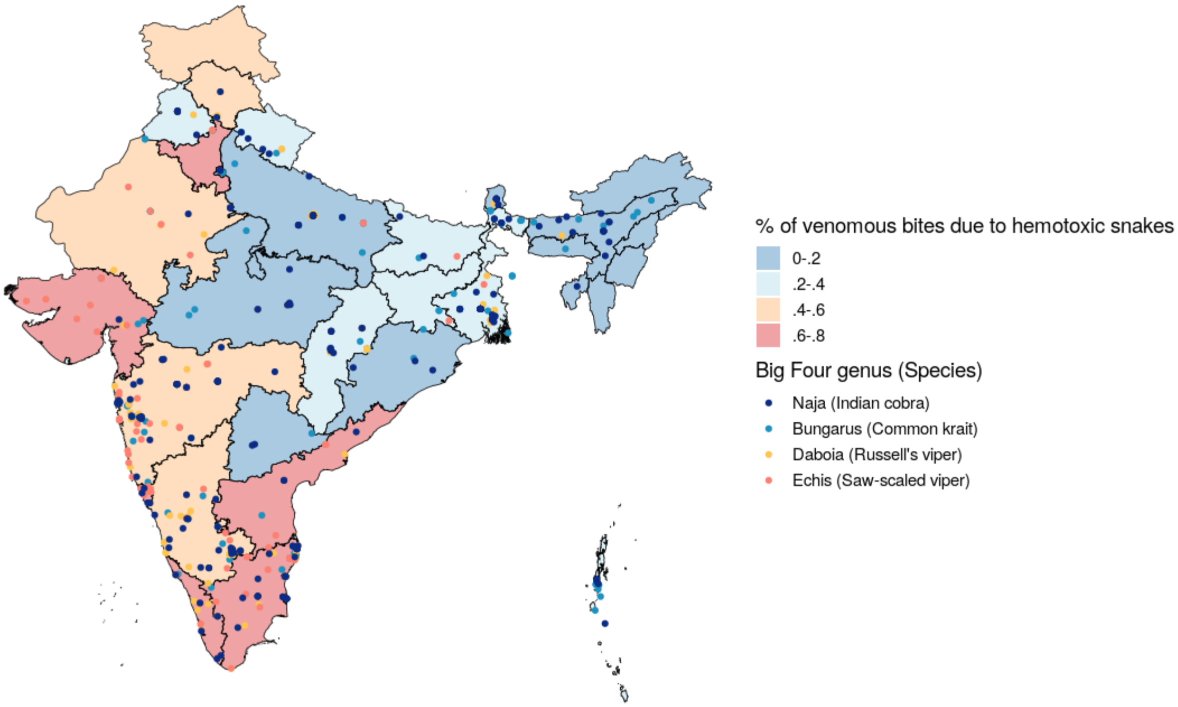

Figure 1. Mapping of occurrence of the Big Four venomous snake genera in India from the Global Biodiversity Information Facility to states in India. Each point represents an occurrence in the database, with the color of the point representing the snake species. The background color of the state represents the proportion of those occurrences due to hemotoxic snakes, aggregated across all of the occurrences within the state.

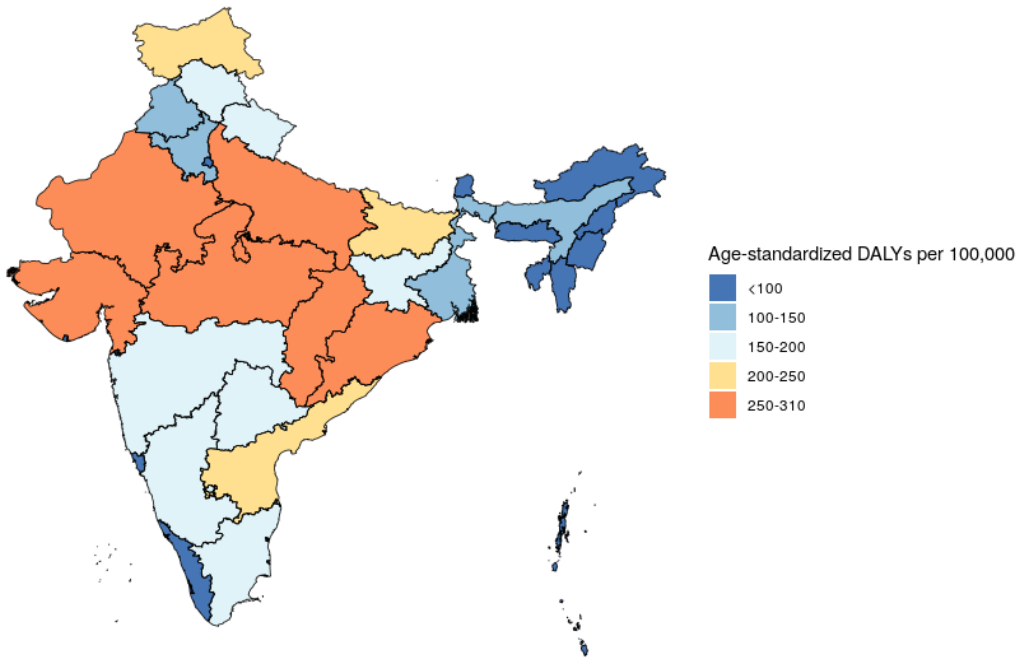

Figure 2. Age-standardized DALYs per 100,000 estimates in 2019 across both sexes, by state in India.

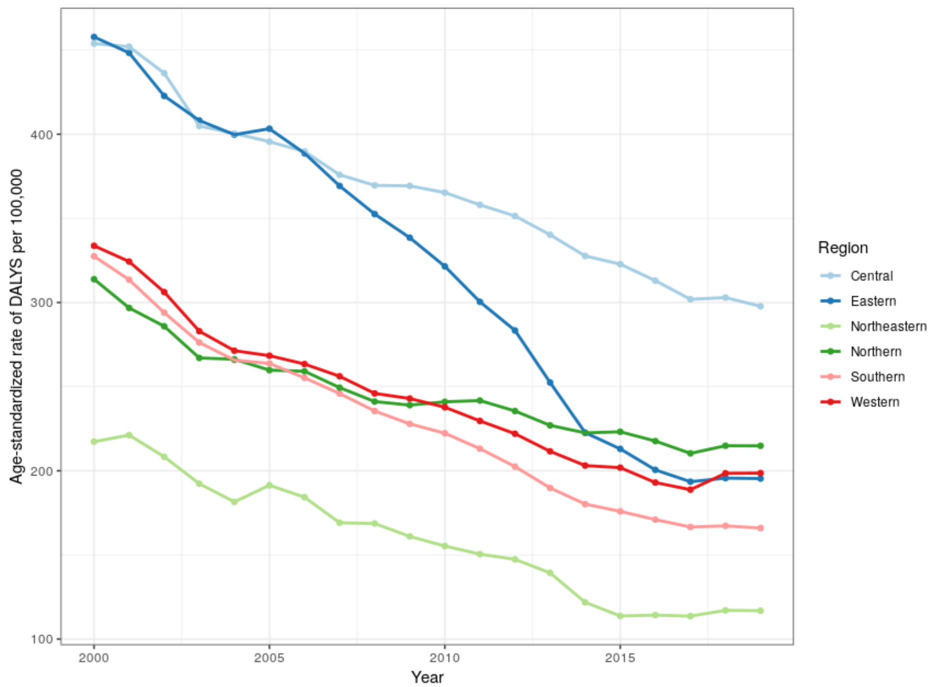

Figure 3. Age-standardized DALYs per 100,00 over time for six different regions of India. The central region includes Madhya Pradesh, Chhattisgarh, Uttar Pradesh, and Uttarakhand. The eastern region includes Odisha, Jharkhand, Bihar, and West Bengal. The northeastern region includes Sikkim, Assam, Meghalaya, Tripura, Mizoram, Manipur, Nagaland, and Arunachal Pradesh. The northern region includes Jammu and Kashmir, Himachal Pradesh, Punjab, Haryana, Rajasthan, and Delhi. The southern region includes Karnataka, Kerala, Tamil Nadu, Andhra Pradesh, Telangana, and the Union Territories other than Delhi. The western region includes Gujarat, Maharashtra, and Goa.

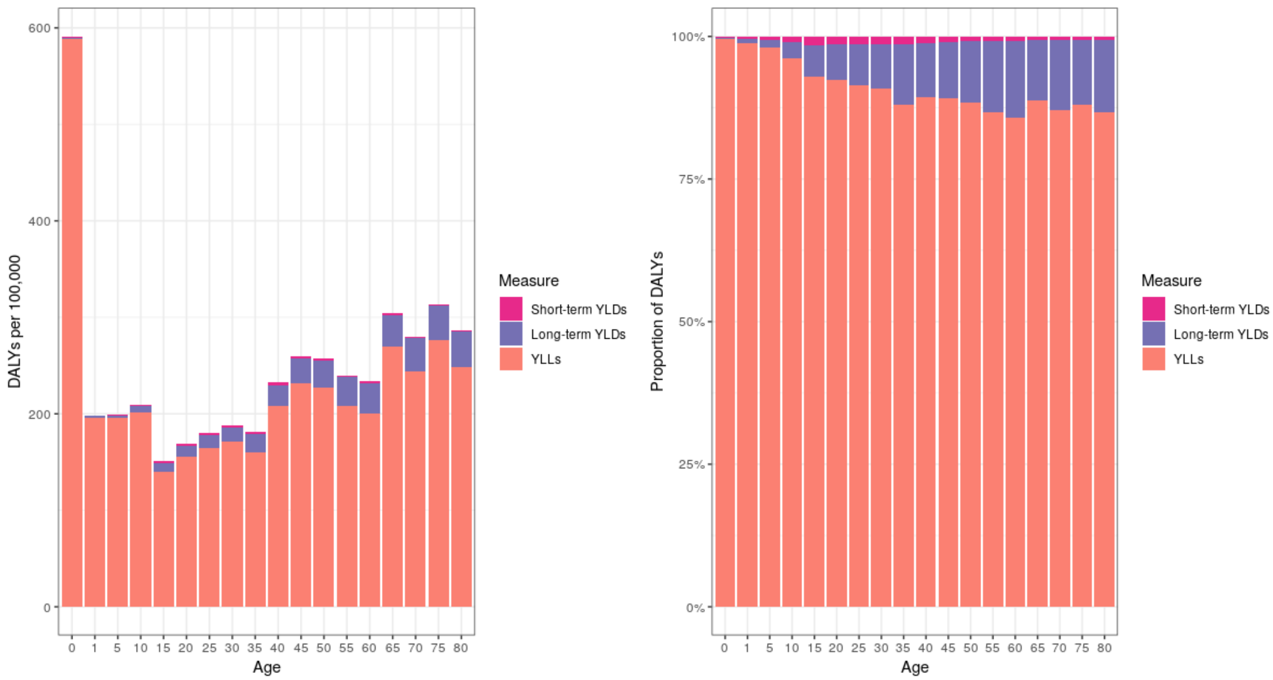

Figure 4. Age-standardized DALY rates in 2019 across both sexes and all of India, broken down by age and the composition of short-term YLDs, long-term YLDs, and YLLs.

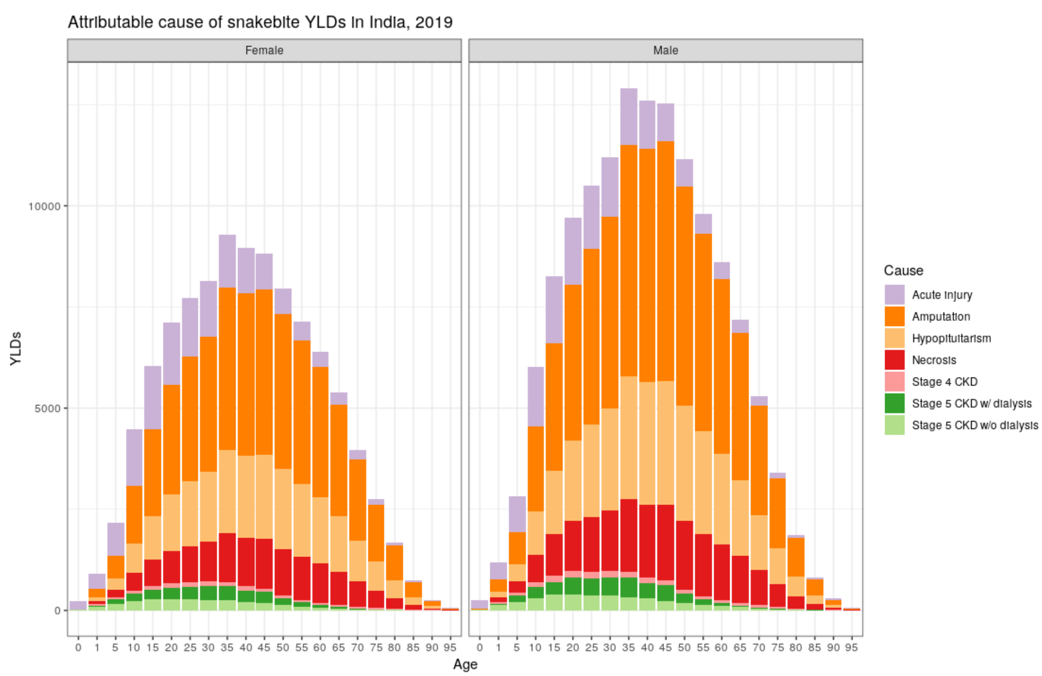

Figure 5. YLDs estimated in the year 2019 in India, broken down by sex, age, and the attributable cause of disability. Acute injury is the result of the initial complication of snakebite envenoming and includes all causes listed in Table 1, while the rest are secondary complications.

Table 1. Short-term health outcomes and their respective simulated incidence and mapped disability weight and health state.

Snake type	Sequelae	Proportional incidence of acute bites (95% UI)	Health state lay description (Health state name)	Disability weight (95% UI)
Hemotoxic	Acute kidney failure	0.17 (0.05-0.43)	Is tired and has itching, cramps, headache, joint pains and shortness of breath. The person needs intensive medical care every other day lasting about half a day (End-stage renal disease: with kidney transplant).	0.569 (0.389-0.727)
Hemotoxic	Coagulopathy (excessive bleeding disorders)	0.63 (0.31-0.86)	Easily bruises and sometimes bleeds from the gums and nose; feels weak and has some difficulty with daily activities (Thrombocytopenic purpura)	0.159 (0.106-0.226)
Hemotoxic	Local skin blister/infection	0.53 (0.16-0.85)	Has a blistering skin rash that causes pain, with some burning and itching (Herpes zoster)	0.058 (0.035-0.090)
Hemotoxic	Open wound, including pain and swelling	0.89 (0.76-0.96)	Has a cut in the skin, which causes pain and numbness around the cut (Open wound: short term, with or without treatment)	0.006 (0.002-0.012)
Neurotoxic	Paralysis	0.40 (0.07-0.86)	Is paralyzed from the waist down, cannot feel or move the legs and has difficulties with urine and bowle control. The person uses a wheelchair to move around (Spinal cord lesion below neck: treated)	0.296 (0.198-0.414)
Neurotoxic	Respiratory failure	0.44 (0.18-0.72)	Has cough, wheezing and shortness of breath all the time. The person has great difficulty walking even short distances or climbing any stairs, feels tired when at rest, and is anxious (COPD and other chronic respiratory diseases: severe)	0.408 (0.273-0.556)
Neurotoxic	Neurological bulbar weakness/Ptosis /Dysphagia	0.54 (0.40-0.69)	Has some difficulty in moving around, and difficulty in lifting and holding objects, dressing and sitting upright, but is able to walk without help (Motor impairment: moderate)	0.061 (0.040-0.089)
Neurotoxic	Local skin blister/infection	0.43 (0.24-0.65)	Has a blistering skin rash that causes pain, with some burning and itching (Herpes zoster)	0.058 (0.035-0.090)
Neurotoxic	Blurry and double vision	0.53 (0.30-0.74)	Has vision problems that make it difficult to recognize faces or objects across a room (Distance vision: moderate impairment)	0.031 (0.019-0.049)
Neurotoxic	Open wound, including pain and swelling	0.58 (0.26-0.86)	Has a cut in the skin, which causes pain and numbness around the cut (Open wound: short term, with or without treatment)	0.006 (0.002-0.012)

Table 2. Results of incidence, mortality, and DALYs for every state within India as well as the country. Estimates are for 2019 and across both sexes.

Location	Incidence			Deaths			DALYs		
	Absolute number	Age-standardized rate per 100,000	Change since 2000	Absolute number	Age-standardized rate per 100,000	Change since 2000	Absolute number	Age-standardized rate per 100,000	Change since 2000
Andhra Pradesh	44,453 (19,438 to 95,657)	80.90 (35.37 to 174.14)	-40% (-59% to -12%)	2,313 (1,186 to 3,108)	4.19 (2.15 to 5.63)	-46% (-64% to -23%)	117,139 (69,221 to 154,070)	215.95 (127.11 to 283.97)	-53% (-68% to -33%)
Arunachal Pradesh	294 (133 to 772)	18.36 (8.29 to 48.28)	-41% (-62% to -10%)	21 (15 to 42)	1.68 (1.22 to 3.27)	-34% (-55% to -3%)	1,174 (839 to 2,343)	74.74 (54.35 to 145.96)	-37% (-58% to -4%)
Assam	10,880 (5,431 to 24,797)	30.97 (15.45 to 70.60)	-48% (-61% to -27%)	768 (605 to 1,000)	2.44 (1.92 to 3.14)	-42% (-55% to -20%)	50,871 (40,264 to 67,870)	144.76 (115.60 to 191.76)	-46% (-59% to -23%)
Bihar	56,209 (20,809 to 114,773)	48.59 (17.97 to 99.28)	-62% (-75% to -42%)	3,761 (1,571 to 5,286)	3.63 (1.53 to 5.05)	-58% (-72% to -36%)	273,783 (116,113 to 390,514)	226.60 (97.84 to 317.05)	-62% (-74% to -42%)
Chhattisgarh	27,729 (12,935 to 54,606)	88.43 (41.21 to 174.48)	-39% (-55% to -13%)	1,814 (962 to 2,370)	6.50 (3.52 to 8.42)	-33% (-50% to -7%)	92,666 (53,802 to 122,184)	302.55 (173.02 to 397.74)	-40% (-55% to -13%)
Delhi	2,949 (1,469 to 6,689)	15.03 (7.49 to 34.09)	-51% (-64% to -32%)	211 (148 to 275)	1.22 (0.86 to 1.58)	-48% (-61% to -29%)	11,634 (8,567 to 15,302)	62.02 (45.57 to 81.22)	-52% (-65% to -32%)
Goa	375 (179 to 881)	25.14 (12.00 to 58.86)	-23% (-49% to 14%)	19 (14 to 25)	1.11 (0.81 to 1.48)	-42% (-61% to -16%)	1,037 (804 to 1,316)	65.37 (51.14 to 84.06)	-44% (-59% to -21%)
Gujarat	58,378 (22,845 to 141,844)	84.83 (33.13 to 206.41)	-34% (-50% to -14%)	2,727 (1,489 to 3,443)	4.23 (2.29 to 5.34)	-32% (-48% to -11%)	173,384 (102,829 to 216,022)	253.88 (149.54 to 316.00)	-40% (-53% to -22%)
Haryana	15,167 (6,342 to 41,027)	50.85 (21.26 to 137.54)	-43% (-57% to -22%)	710 (535 to 891)	2.62 (1.99 to 3.30)	-41% (-55% to -20%)	42,140 (32,831 to 52,372)	146.55 (113.81 to 183.09)	-44% (-57% to -22%)
Himachal Pradesh	4,843 (2,043 to 11,291)	62.93 (26.55 to 146.75)	-22% (-44% to 6%)	268 (157 to 339)	3.52 (2.04 to 4.44)	-30% (-50% to -6%)	13,332 (8,434 to 16,503)	174.81 (109.65 to 216.32)	-34% (-49% to -11%)
Jammu & Kashmir and Ladakh	8,617 (2,717 to 20,711)	61.40 (19.36 to 147.67)	-28% (-48% to 0%)	478 (172 to 623)	3.97 (1.41 to 5.15)	-27% (-47% to -1%)	28,407 (11,966 to 36,370)	212.63 (89.24 to 271.29)	-32% (-49% to -8%)
Jharkhand	15,711 (7,354 to 32,214)	41.64 (19.50 to 85.36)	-63% (-74% to -42%)	1,044 (580 to 1,477)	3.20 (1.78 to 4.44)	-57% (-69% to -35%)	55,216 (32,433 to 78,575)	153.39 (90.52 to 217.09)	-62% (-73% to -41%)
Karnataka	37,993 (20,254 to 75,579)	54.75 (29.19 to 108.92)	-30% (-48% to -7%)	2,098 (1,585 to 2,597)	3.19 (2.40 to 3.94)	-34% (-50% to -13%)	111,985 (89,161 to 135,396)	164.01 (131.27 to 199.47)	-38% (-51% to -18%)
Kerala	6,973 (3,261 to 17,073)	20.83 (9.77 to 50.96)	-42% (-57% to -22%)	307 (238 to 453)	0.74 (0.58 to 1.13)	-57% (-68% to -42%)	16,506 (13,546 to 24,404)	43.46 (35.62 to 66.17)	-58% (-67% to -46%)
Madhya Pradesh	63,622 (28,644 to 129,580)	72.61 (32.78 to 147.96)	-39% (-56% to -15%)	4,391 (2,473 to 5,791)	5.68 (3.08 to 7.39)	-32% (-50% to -7%)	247,513 (148,103 to 333,511)	287.22 (169.24 to 381.88)	-38% (-55% to -11%)
Maharashtra	68,778 (34,862 to 129,108)	53.88 (27.32 to 101.08)	-38% (-52% to -17%)	4,010 (2,391 to 5,066)	3.25 (1.95 to 4.08)	-40% (-54% to -21%)	211,980 (139,084 to 258,814)	169.50 (110.70 to 205.83)	-40% (-53% to -22%)
Manipur	502 (233 to 1,293)	14.21 (6.60 to 36.63)	-34% (-56% to -3%)	35 (25 to 59)	1.19 (0.85 to 2.00)	-33% (-55% to -4%)	1,891 (1,368 to 3,036)	56.44 (41.14 to 90.62)	-37% (-56% to -9%)
Meghalaya	458 (209 to 1,158)	14.34 (6.55 to 36.35)	-49% (-66% to -24%)	33 (22 to 63)	1.29 (0.92 to 2.50)	-38% (-58% to -8%)	1,888 (1,309 to 3,582)	59.81 (42.32 to 112.66)	-46% (-64% to -19%)
Mizoram	151 (61 to 496)	11.96 (4.84 to 39.26)	-39% (-63% to -4%)	11 (6 to 29)	1.05 (0.63 to 2.86)	-38% (-63% to -3%)	585 (372 to 1,447)	48.14 (30.90 to 118.76)	-36% (-59% to -3%)
Nagaland	317 (155 to 748)	16.64 (8.16 to 39.28)	-48% (-65% to -24%)	22 (17 to 31)	1.49 (1.12 to 2.06)	-41% (-60% to -17%)	1,258 (922 to 1,775)	69.74 (52.10 to 97.41)	-44% (-62% to -20%)

Odisha	31,710 (14,757 to 72,932)	67.44 (31.37 to 155.09)	-47% (-61% to -22%)	2,249 (1,357 to 3,025)	5.00 (3.01 to 6.69)	-44% (-58% to -19%)	126,499 (77,272 to 169,617)	275.09 (167.41 to 373.88)	-46% (-61% to -21%)
Punjab	13,512 (7,062 to 27,370)	42.68 (22.34 to 86.40)	-28% (-47% to -4%)	881 (633 to 1,113)	2.78 (2.00 to 3.51)	-33% (-51% to -12%)	44,416 (33,517 to 55,017)	140.25 (105.46 to 171.40)	-34% (-49% to -14%)
Rajasthan	72,828 (34,997 to 145,813)	91.99 (44.14 to 184.37)	-31% (-48% to -6%)	4,072 (2,444 to 5,234)	5.80 (3.48 to 7.44)	-22% (-41% to 4%)	242,908 (151,084 to 308,416)	308.70 (192.13 to 392.08)	-26% (-42% to 2%)
Sikkim	92 (44 to 219)	13.86 (6.65 to 32.79)	-58% (-76% to -34%)	7 (4 to 10)	1.18 (0.77 to 1.71)	-54% (-73% to -28%)	331 (228 to 490)	53.71 (37.28 to 77.08)	-59% (-74% to -36%)
Tamil Nadu	54,021 (26,536 to 116,492)	69.43 (34.10 to 149.25)	-52% (-65% to -34%)	2,784 (1,721 to 3,528)	3.40 (2.13 to 4.30)	-47% (-61% to -27%)	146,272 (105,007 to 179,485)	179.33 (127.78 to 220.37)	-49% (-61% to -32%)
Telangana	21,736 (9,257 to 48,627)	56.48 (24.05 to 126.34)	-48% (-65% to -21%)	1,545 (780 to 2,181)	4.38 (2.19 to 6.05)	-48% (-65% to -20%)	74,801 (41,483 to 102,564)	197.80 (109.31 to 270.24)	-52% (-67% to -28%)
Tripura	361 (155 to 1,093)	8.81 (3.77 to 26.63)	-42% (-62% to -14%)	26 (17 to 68)	0.69 (0.46 to 1.77)	-44% (-62% to -19%)	1,576 (1,090 to 4,008)	39.89 (27.75 to 98.72)	-51% (-66% to -30%)
Uttar Pradesh	170,990 (68,978 to 367,964)	74.62 (30.01 to 160.90)	-31% (-49% to 3%)	11,954 (5,230 to 16,147)	6.02 (2.60 to 7.99)	-21% (-41% to 13%)	708,783 (330,068 to 978,073)	306.86 (142.75 to 422.21)	-31% (-48% to 5%)
Uttarakhand	6,363 (2,943 to 13,973)	55.11 (25.50 to 121.20)	-44% (-62% to -7%)	423 (231 to 591)	3.91 (2.16 to 5.46)	-43% (-62% to -6%)	21,408 (12,537 to 29,673)	186.61 (108.98 to 258.74)	-45% (-62% to -11%)
West Bengal	30,375 (14,317 to 64,778)	29.99 (14.14 to 63.97)	-49% (-62% to -29%)	2,092 (1,220 to 2,727)	2.16 (1.23 to 2.81)	-48% (-61% to -28%)	129,654 (80,923 to 167,834)	133.79 (82.68 to 174.78)	-51% (-63% to -31%)
Other Union Territories	481 (235 to 1,066)	12.61 (6.18 to 27.93)	-49% (-68% to -18%)	33 (22 to 49)	0.94 (0.65 to 1.38)	-54% (-71% to -28%)	1,828 (1,301 to 2,702)	50.51 (36.68 to 74.43)	-56% (-71% to -34%)
India	**826,869 (410,793 to 1,613,364)**	**58.71 (29.13 to 114.53)**	**-41% (-52% to -20%)**	**51,108 (29,567 to 64,118)**	**4.11 (2.35 to 5.13)**	**-39% (-51% to -18%)**	**2,952,863 (1,782,184 to 3,748,589)**	**217.72 (130.25 to 277.09)**	**-43% (-54% to -22%)**

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