

## Estimation Of The Basic Reproduction Number To Assess The Impact Of Precipitation Change On The Risk Of An Anthrax Outbreak Among Livestock In Karnataka, India

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**Abstract:** The basic reproduction number ( $R_0$ ) is a measure of an infectious pathogen's infectiousness or transmissibility. It is the number of instances caused directly by an infected individual over the course of its infectious period.  $R_0$  is a statistic that is used to determine a disease's potential to spread within a population. It has been regarded as one of the most basic and widely used metrics for studying infectious disease dynamics. In the present study, we focused on the basic reproduction number ( $R_0$ ), that describes an epidemic's transmission potential. Data was obtained from the Dept. of animal husbandry, Bengaluru, Karnataka. For risk assessment and to explore the influence of changes in precipitation levels, disease incidence data was categorized into two groups, average annual precipitation above and below normal (1151mm).  $R_0$  package was used for the purpose of calculating the basic reproduction number. The variation in  $R_0$  ranged from 1.06 to 1.78 with average annual precipitation above normal and 0.76 to 2.08 with average annual

precipitation below normal. The objective was to evaluate the  $R_0$  of anthrax disease among livestock in Karnataka corresponding to changes in precipitation level and to describe the variation of  $R_0$ , to assess an infectious disease's ability to infect the population, and to determine the fraction of the population that should be vaccinated in order to prevent epidemic growth.

**Keywords:** Anthrax, Basic reproduction number, Livestock,  $R_0$ , Risk map

## 1. Introduction

Epidemiological models are commonly used to foresee the probability of infectious disease outbreaks. The basic reproduction number ( $R_0$ ), a threshold quantity, is commonly used by epidemiological models to indicate the risk (Joseph Sichone et al., 2020). These model outputs can be translated into spatial risk maps using various aggregation methods to provide an overall view of the risk (Yanchao Cheng et al., 2020). The basic reproduction number ( $R_0$ ) is a useful metric in epidemiological studies to assess infectious disease dynamics. The basic reproduction number refers to the total number of infections that one newly infected individual can produce in a completely susceptible community. At the population level, the basic reproduction ratio is the proportion of succeeding generations (Frank Van den Bosch, 2017) (Ying Liu et al., 2020). The  $R_0$ , determines whether or not an infection spreads within a population (Samath Dharmaratne et al., 2020). As a result,  $R_0$  is a dimensionless integer that indicates pathogen contagiousness.

The spread of disease and, as a result, the changes in  $R_0$  are influenced by environmental factors and animal interaction patterns. Number greater than, less than, or equal to one can be used as the fundamental reproduction number or threshold parameter for evaluating essential immunity coverage. When  $R_0 < 1$ , the disease will die out, if  $R_0 = 1$ , disease will be stable but not be spreading in turn indicating an endemic in the population and if  $R_0 > 1$  then disease will spread and will have an outbreak, indicating an epidemic in the population (Roya Nikbakht et al., Comparison of methods to Estimate Basic Reproduction Number ( $R_0$ ) of influenza, Using Canada 2009 and 2017-18 A (H1N1) Data, 2019).  $R_0$  can be a useful idea in the hands of professionals. The process of defining, calculating, interpreting, and applying  $R_0$ , on the other hand, is far from simple. The straightforward nature of a  $R_0$  number and its interpretation with respect to infectious disease dynamics hides the complexity of this metric (Najmul Haider et al., 2020). Despite the fact that  $R_0$  is a biological fact, it is frequently calculated using sophisticated mathematical models based on a variety of assumptions. Understanding the models' structures, inputs, and interactions is necessary for interpreting  $R_0$  estimations produced from various models (Paul L. Delamater et al., 2019).  $R_0$  is indeed equipped with a critical mission in the research of epidemic dynamics. Many studies used various ways to calculate the value of  $R_0$  (S. Blumberga, 2013). In general,  $R_0$  uses three factors such as the probability of infection per contact with a susceptible, the contact rate, and the infectious period (Nicolas Bacaer, 2011). Using these factors  $R_0$  is estimated by adopting three basic methods such as calculation of the spectral radius of the next generation operator, analysis of data on time series of cases, and analysis of local stability of the disease-free equilibrium

(Junyuan Yang, 2017). We have selected a zoonotic disease, “Anthrax” to estimate its basic reproduction number based on changes in precipitation level.

*Bacillus anthracis*, a gram-positive, spore-forming, rod-shaped bacteria, causes anthrax, which is an infectious ailment. The organism can be easily grown on normal nutritional media and thrives in aerobic conditions, but it can also replicate in anaerobic environments. (Suma A P et al., 2017). *Bacillus anthracis* contains three plasmid-encoded virulence factors: a poly D-glutamic acid capsule that inhibits phagocytosis, edema toxin (PA and EF), and lethal toxin (PA and LF). Both toxins bind to an analogous cell receptor via PA. (Sushma Bylaiah et al., 2021). Anthrax is endemic to various parts of South Europe, Africa, Asia, North and South America, and Australia (Bylaiah Sushma et al., 2021).

The aim of this research was to estimate  $R_0$  and layering of  $R_0$  on predicted risk maps for assessing the impact of precipitation change in the anthrax outbreak among livestock in Karnataka and to identify the fraction of the population that should be vaccinated in order to prevent the epidemic from spreading, and to analyze the potential of anthrax to infect the population as precipitation levels change.

## **2. Materials and methods**

### **2.1 Livestock and anthrax incidence data**

The data on livestock population in five major animal species, namely cattle, buffalo, sheep, goat, and pigs, was collected at the district level from India's 20th livestock census. The current study includes the incidence data of anthrax among livestock throughout Karnataka. The district level data on anthrax outbreaks in livestock over a 20-year period (2000–2019) was collected from the Department of Animal Husbandry in Bengaluru, Karnataka, India. Incidence data is divided into two data sets based on the average annual precipitation above and below normal in order to examine the impact of precipitation level change in the anthrax outbreak (M.N.Chakari, 2012).

### **2.2 Spatial and temporal endemicity**

The disease incidence pattern in relation to spatial and temporal endemicity was analyzed using year wise anthrax outbreak data from 2000 to 2019 (Sumiko Anno et al., 2019). To identify possible variations in disease reporting over time and space based on average annual precipitation, the cumulative outbreak of cases was represented at the district level using R statistical software version 3.1.3.

### **2.3 Risk maps with Basic Reproduction number $R_0$**

The risk factor data generated for the duration of 20 years (2000-2019) were aggregated to grid level. Anthrax severity was predicted by generating the risk map (2000-2019) for Karnataka state by performing climate-disease relationship modelling, which predicts the spatial occurrence of the disease. The data pertaining to risk variables was obtained, pre-processed and annotated with disease condition along with the respective latitude and longitude. The risk estimation was done by using machine learning models in order to produce an optimal prediction with improved

performance. Eleven machine learning models were used for disease modelling, namely Generalized Linear Models (GLM), Generalized Additive Models (GAM), Random Forest (RF), Gradient Boosting Machine (GBM), Artificial Neural Network (ANN), Multiple Adaptive Regression Splines (MARS), Flexible Discriminant Analysis (FDA), Classification Tree Analysis (CT), Support Vector Machine (SVM), Naive Bayes (NB) and Adaptive Boosting (ADA). Various modelling methods generated a variety of model artefacts, which were then used to make predictions for combinations of independent variables. To better understand and explore model predictions, response plots were developed.

Further, we aimed to estimate the basic reproduction number ( $R_0$ ) and mapping the estimated values on the predicted response plots.  $R_0$  is the average number of secondary infectious disease cases produced from the initial case in a fully susceptible population. If this number is less than one, small outbreaks with a high risk of extinction may be predicted in the population and disease may die out, while if it is greater than one, a major chance of an epidemic involving nearly the entire susceptible population is probable (Petter Holme et al., 2015). It is important to assess disease transmissibility and forecast outbreak sizes. Maximum Likelihood estimation (ML), Attack rate (AR), Exponential Growth rate (EG), Sequential Bayesian approach (SB), Time-Dependent method (TD), and other techniques are used to calculate  $R_0$  (Riaz Mahmud, 2020). In the present work  $R_0$  was estimated using EG, ML and AR approaches:

### 2.3.1 Exponential Growth rate (EG)

In the early phases of an epidemic, the number of cases grows exponentially. The exponential growth (EG) model is a simplified version. Exponential growth is defined as a rate of increase that remains constant over time (Sorana Froda, 2014). The exponential curve of epidemic growth can be used to infer the basic reproduction number  $R_0$ . In the early stages of an epidemic,  $R_0$  is linked to exponential growth as

$$R_0 = \frac{1}{M(-r)}$$

Where  $M$  is the generation time distribution's moment generating function, and  $r$  denotes the rate of exponential development. Integers make up the data for daily confirmed cases. To fit the value of the growth rate,  $r$ , poisson regression is employed (Riaz Mahmud, 2020).

### 2.3.2 Maximum Likelihood estimation (ML)

ML is proposed by White & Pagano's, and is based on the assumption that the number of secondary instances induced by an affected individual is poisson distributed with  $R$  being the expected value.  $R$  is determined by maximizing log-likelihood over a period of exponential growth. The deviance R-squared measure can be used to choose the ideal period. There is no assumption made about population mixing (Thomas Obadia et al., 2012).

### 2.3.3 Attack rate (AR)

The attack rate (AR) is the proportion of the population who becomes infected over time (Thomas Obadia et al., 2012). AR is linked to the basic reproduction number by:

$$R_0 = -\frac{\log((1 - AR)/s)}{AR - (1 - s)}$$

where  $s$  is the population's initial vulnerability percentage.

All the techniques intended to estimate the initial exponential growth rate from the cumulative rate of instances. We provided a visible and detailed perspective of disease impact in a given area by mapping the  $R_0$  on the predicted risk maps.

### 2.4 Vaccination coverage

During epidemic we need to keep a goal to stop the spread of the disease or to eradicate the disease. If  $R_0$  is zero, disease can be eradicated, and if  $R_0$  is one, disease can be prevented. Hence, we need to know the proportion of population needs to be vaccinated to at least to stop the spread. Calculating a minimum vaccination coverage to avoid an epidemic is made possible by determining a basic reproduction number (Mitsuo Uchida et al., 2018). A vaccination's minimum coverage is commonly determined as follows:

$$M = \frac{(R_0 - 1)}{R_0} \times 100$$

Where  $R_0$  is the basic reproduction number and  $M$  is the proportion of population need vaccine.

### 2.5 Statistical software

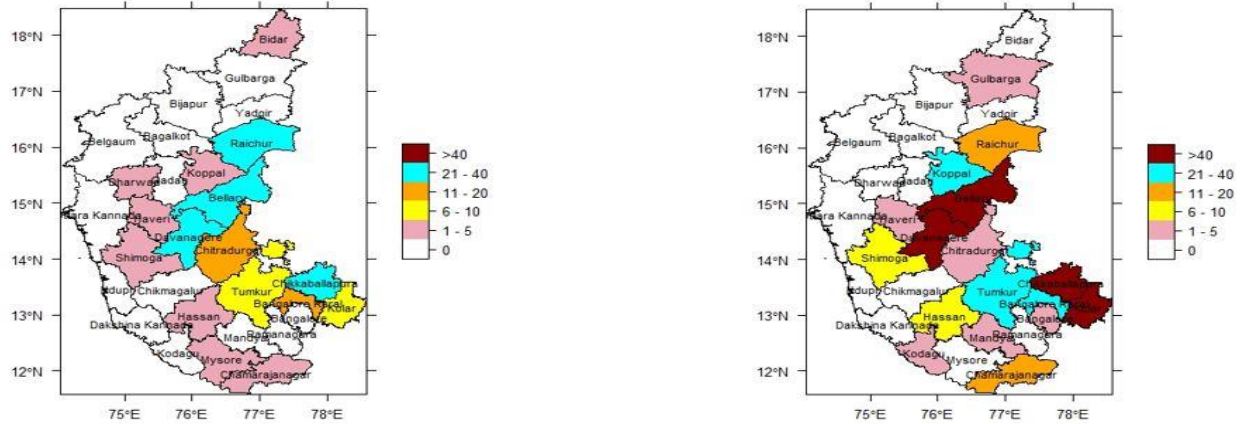
R statistical software version 3.1.3 (version 3.4.3, Vienna, Austria: R Foundation for Statistical Computing. <https://www.R-project.org/>) was used to conduct statistical analyses, risk maps, and predictions. R0 package, was used for the estimation of  $R_0$ .

## 3. Results

### 3.1 Spatial and temporal endemicity

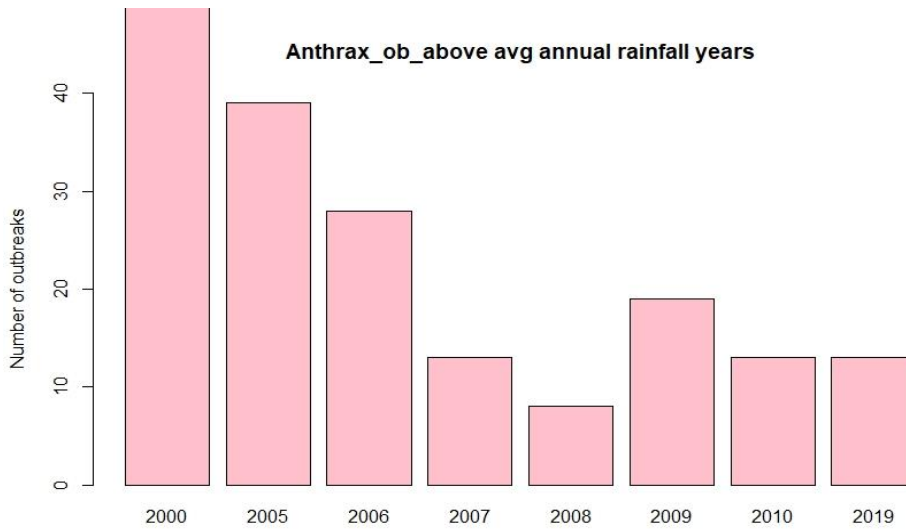
During the study period of 20 years from 2000-2019, the data on the incidence of anthrax in Karnataka, India is divided into two different sets based on annual precipitation. Incidence data of the years having annual precipitation above and below normal was analyzed to identify the distribution of disease and is represented in Figure 1(a) & (b). During the years with the average annual precipitation below normal, the highest incidence was observed in Bellary, Davanagere, Chikkaballapura and Kolar district (range >40) and moderately high incidence in Koppal, Tumkur and Bangalore rural districts (range 21-40). During the years with the average annual precipitation above normal, the highest incidence was not observed in any district (range >40) and moderately

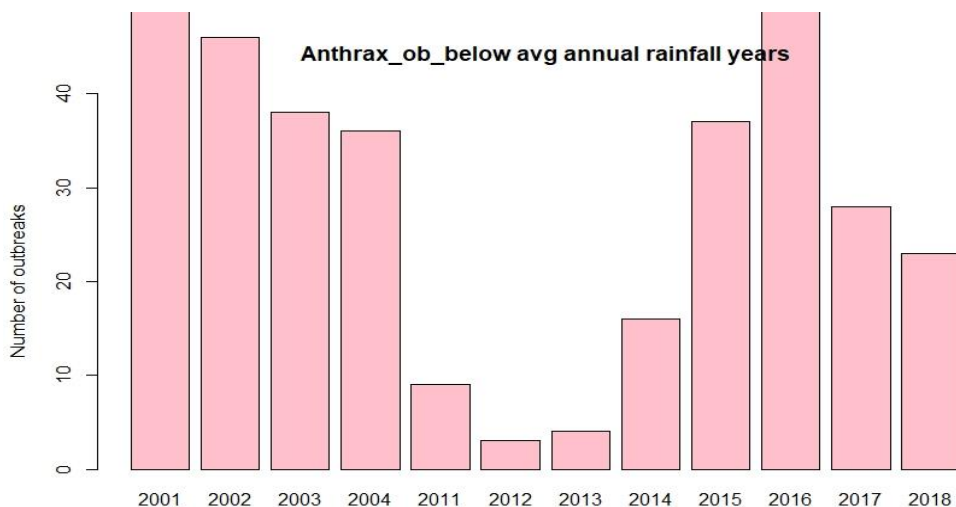
high incidence observed in Raichur, Bellary, Davanagere and Chikkaballapura, districts (range 21-40).



**Figure 1.** District wise cumulative incidence of anthrax in Karnataka (2000-2019), a) Average annual precipitation above normal years & (b) Average annual precipitation below normal years, respectively.

The temporal distribution of anthrax in Karnataka was analyzed based on the years having average annual precipitation above and below normal from 2000 to 2019 (Figure 2(a) & (b)).



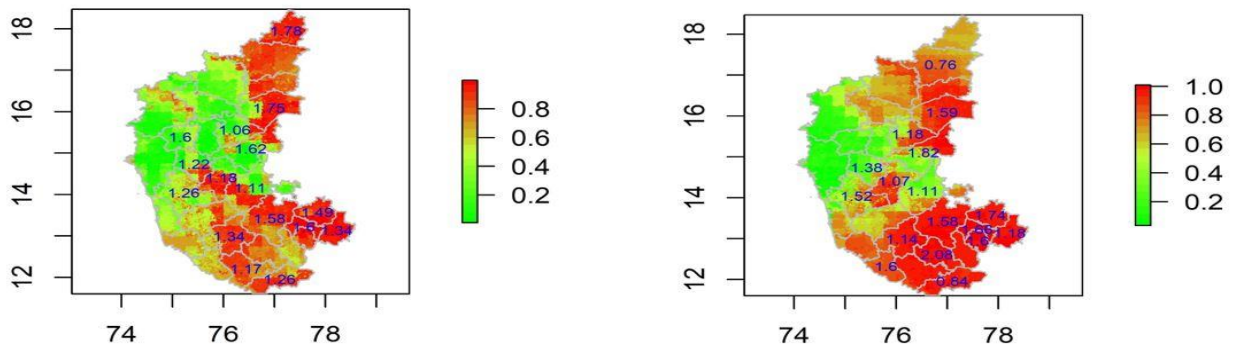


**Figure 2.** Year wise cumulative incidence of anthrax in Karnataka (2000-2019), a) Average annual precipitation above normal years & (b) Average annual precipitation below normal years, respectively.

### 3.2 Risk maps with Basic reproduction number ( $R_0$ )

The risk assessment involves the step to estimate the basic reproduction number ( $R_0$ ). The outcome obtained from this step is more projectable and interpretable for developing appropriate preventive measures. The daily incidence and the magnitude of outbreak are heavily reliant on the value of  $R_0$  suggesting more livestock population would be infected in future. help with disease management in the region. The risk maps were generated using the biomod2 package in R software.

According to the average annual precipitation above and below normal years in the study from 2000-2019,  $R_0$  was calculated for the districts falling in the significantly clustered region generated by SaTScan. The  $R_0$  values above 1.00 indicate the regions/districts with increased trend of disease occurrence, severity, high risk and vice-versa.  $R_0$  value ranged from 1.06 to 1.78 for the years with the average annual precipitation above normal, which revealed southern east and northern east regions are at high risk for anthrax (Figure 3(a)). The  $R_0$  value ranged from 0.76 to 2.08 for the years with the average annual precipitation below normal with southern, northern east and central regions has high disease severity (Figure 3(b)). Further, the regions having low  $R_0$  possibly might shift to high  $R_0$  values in near future due to migration of infected animals from one place to another.



**Figure 3.** Anthrax  $R_0$  Values on Risk Prediction Map District Wise (2000-2019) a) Average annual precipitation above normal years & (b) Average annual precipitation below normal years, respectively.

### 3.3 Vaccination coverage

Proportion of livestock population need vaccination coverage in order to avoid the anthrax disease outbreak in the predicted regions. Hence vaccination coverage was calculated (Table 1) for the years with the average annual precipitation above normal as well as for the years with the average annual precipitation below normal. When  $R_0$  is lesser than one disease will quickly die out and there may not be a vaccination requirement in those regions hence calculation of vaccination coverage for  $R_0 < 1$  was eliminated from the table.

**Table 1:** Proportion of livestock population vaccination coverage

Average annual precipitation above normal				Average annual precipitation below normal			
District	$R_0$	Minimum vaccination coverage	Previous outbreak	District	$R_0$	Minimum vaccination coverage	Previous outbreak
Koppal	1.06	5.44	2019	Davanagere	1.07	6.54	2018
Chitradurga	1.11	10.25	2009	Chitradurga	1.11	10.12	2018
Mysore	1.17	14.55	2019	Hassan	1.14	12.27	2003
Davanagere	1.18	15.55	2019	Kolar	1.18	15.22	2015
Haveri	1.22	18.31	2000	Koppal	1.18	15.40	2018
Chamarajanagara	1.26	20.39	2010	Haveri	1.38	27.66	2017
Shimoga	1.26	20.52	2000	Shimoga	1.52	34.05	2011
Kolar	1.34	25.28	2019	Tumkur	1.58	36.69	2018
Hassan	1.34	25.49	2009	Raichur	1.59	37.15	2016



Chikkaballapur a	1.49	32.69	2010	Bangalore	1.60	37.32	2003
Tumkur	1.58	36.69	2019	Kodagu	1.60	37.65	2003
Bangalore Rural	1.60	37.58	2009	Bangalore Rural	1.66	39.78	2016
Dharwad	1.60	37.65	2005	Chikkaballapur	1.74	42.47	2016
Bellary	1.62	38.43	2019	Bellary	1.82	45.00	2018
Raichur	1.75	42.93	2010	Mandya	2.08	52.04	2015
Bidar	1.78	43.89	2006	-	-	-	-

#### 4. Discussion

The  $R_0$  (Basic Reproduction Number) is the average number of secondary infections that an animal can produce in a totally susceptible population throughout its infectious period. As a result,  $R_0$  is a dimensionless integer that indicates a pathogen's contagiousness.  $R_0$  is directly related to epidemiological disease in turn epidemiological disease and environmental conditions has a positive association. Climate change is one of the most major challenges confronting life on this planet, and it will continue to be a major issue in the future, not only because of its complicated and widespread form, but also because of its long-term implications for sustainable development (Affairs). Henceforward, Climate action is designated as one of the 17 Sustainable Development Goals (SDGs). The United Nations established a 15-year plan ie., Sustainable Development Goals (SDGs) in 2015 to address some of the world's most important priorities. The 17 SDGs are the greatest plan in the world for making the world a better place for people and the environment by 2030. These objectives have the potential to improve the world by eradicating poverty, reducing inequality, and addressing the serious issue of climate change (Organization, 2015). This was the influential factor to conduct our research work based on changes in precipitation level and its impact on the disease occurrence. The spread of infectious disease and, as a result, the  $R_0$  are influenced by environmental factors and patterns of animal interactions. The general patterns of risk zones can be investigated using  $R_0$  maps. In the present, we have made an attempt to study the impact of environment conditions vis-à-vis changes in  $R_0$ . The disease's basic reproduction number is a critical parameter for estimating the probability of an outbreak and evaluating the efficiency of adopted measures (Clara Champagne et al., 2016). It's a popular tool in quantitative epidemiology for describing epidemic dynamics and evaluating control strategies (Zindoga Mukandavire et al., 2011) (F. I. Korennoy et al., 2016).  $R_0$  can be used to identify places where an outbreak is more likely to occur. Geographic maps showing the value of the basic reproduction number ( $R_0$ ), can be used to identify places at higher risk of an epidemic (N.A. Hartemink et al., 2009). The previous literatures brought up the fact that climate change and disease transmission

have strong relationship. If the temperature rises as a result of climate change, it is likely to have an impact on the disease's distribution and severity (Juan M. Cordovez et al., 2014).

Even anthrax outbreaks are most common during the hot, humid transition between the dry and wet seasons. Soil temperatures are greater than normal during this time, both during the day and at night. During the cultivation season, the soil is also greatly disturbed, which aids in the multiplication of bacteria, leading to an increase in animal diseases transmitted through the soil (Bylaiah Sushma et al., 2021).  $R_0$  has been a key idea in infectious disease epidemiology over the last two decades, but it has also become clear how difficult it is to implement in real-world circumstances (Dietz, 1993). Allowing for an exposed state is another natural expansion of the epidemic model. That is, imagine that when an individual is infected, they do not become infectious instantly, but instead enters an exposed phase during which the disease develops in the individual until the time arrives for the individual to become infectious (Peter Neal, 2019). Although there has been a lot of theoretical effort done to define the reproduction number in nonhomogeneous models, there is still no cohesive theory (Quan-Hui Liu et al., 2018).  $R_0$  can also be used to calculate the percentage of individuals who have been vaccinated. As a result, the reproduction number is used to calculate the critical vaccination coverage, or the proportion of individuals who receive vaccines (Roya Nikbakht et al., 2018). For most diseases, the reproduction number scenario, in which a single infectious case infects a completely susceptible population, is obviously impractical. Furthermore, because disease transmission is intrinsically stochastic, each realization of a disease introduction event is likely to take a different path (Warren Tennant, 2018) (N. Marquetoux et al., 2012).

Anthrax is known to change with time and space, which supports the current findings. In this study, the basic reproduction number ( $R_0$ ) for anthrax epidemics in livestock in Karnataka, India, was calculated. Because epidemiological data for the study outbreak was limited, models that predict  $R_0$  directly from epidemic incidence data were used to estimate  $R_0$ . The map may indicate the uncertainty of the estimates. On raster maps or maps with polygons where the  $R_0$  value is supplied by a color, the intensity (bright to dark) could be utilized to show the uncertainty in the estimation. The same is true for maps in which  $R_0$  is represented by the size of a circle or any other shape, and the degree of uncertainty is conveyed by the color intensity or even by using a box plot for each point. To examine the uncertainty in an estimate due to ambiguity in the input parameters, Latin Hypercube sampling or a similar technique can be employed.  $R_0$  maps are particularly useful for examining how the risk of developing infectious diseases changes as environmental conditions vary and can be used to alert public health officials about an infectious disease's risk level, vaccination strategy, and the possible consequences of control efforts. There are certain limitations in the study as the basic reproductive number is estimated using available data, and it may alter depending on the quality of the available data. The lack of complete datasets from the start of the outbreak in each province may have an impact on our findings.

## **5. Conclusion**

Geographical maps reflecting the value of the basic reproduction number ( $R_0$ ) could be used to identify regions in Karnataka with a higher risk of anthrax outbreaks. This is a first step toward developing an integrative method for predicting the risk of disease emergence based on mathematical modelling and a geographic information system that may include climate variables such as satellite data, landscape, host parameters, and other relevant factors in determining the risk of anthrax emergence. We found that northern east, central and southern areas are having higher  $R_0$  values and is estimated to be ranged from 1.06 to 1.78 and 0.76 to 2.08 respectively based on precipitation level. The study aimed to create risk maps layering with  $R_0$  and the vaccination coverage that will inform policymakers about the risk of emergent anthrax disease as well as the impact of environmental changes. And also, it is an effective input for surveillance programs. Overall, greater  $R_0$  values necessitate rapid epidemic detection and response, which can be difficult in both resource-constrained and well-resourced environments. This suggests that an epidemic or endemic prevention strategy based on collaboration between healthcare employees and policymakers is beneficial even in the countries that are developing. As a result, we believe that comparable methodologies can be used to predict anthrax transmission not only in Karnataka, but also in other states where anthrax is endemic or epidemic.

## **Acknowledgement**

We would like to thank the Spatial Epidemiology lab, Indian Council of Agricultural Research (ICAR) - National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI), Department of Veterinary Public Health and Epidemiology, Veterinary College and Outreach project on Zoonotic diseases, ICAR for providing necessary support to carry out this research work.

## **Ethical statement**

Authors declare that ethical statement is not applicable as we have not collected any animal samples for the study.

## **Author's contributions**

BS: Collected the data, conducted the research work and wrote the manuscript, SS: Performed review and supervision. KPS: Guided the research steps, LG: Performed writing review and editing. MK: Performed visualization. SSP: Performed writing review and editing. All authors read and approved the final manuscript.

## **Conflict of interest**

The authors declare no conflict of interest.

## **Funding statement**

No fund was received for this particular study.

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