Forecasting the new case detection rate of leprosy in four states of Brazil: a comparison of modelling approaches

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S3: SIMCOLEP

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Contents

SIMCOLEP is a stochastic individual-based model, which models leprosy transmission in a population structured by household. It simulates the life histories of individuals and the natural history of infection with M. leprae. The model is divided into two modules: a population module and a leprosy module. A full description of the model is provided by Fischer et al. [1].

1 Population

The population module describes processes that are not related to leprosy, including birth, death and household processes. Input data used to quantify the model are presented in table 1.

Table S3.1: Population data used as input for the model.

Data	Level	Years	Source
Population size/growth	State-specific	1872-2010	[2]
Age distribution	State-specific	1980, 1991, 2000, 2010	[2]
Fraction married	State-specific	1980, 1991, 2000, 2010	[2]
Fertility rates	State-specific	1980, 1991, 2000, 2010	[2]
Lifetables	Countrywide	1960, 1975, 1990, 2000, 2013	[3, 4]

1.1 Population growth

Changes in population size are determined by birth and death rates. The population grows with a time-dependent growth rate, assuming an exponential growth. It is kept at required size by replacing deaths by births or additional births. The model assumed a close population. Population growth rates were based on state-specific data. Table 2 presents the growth rates used in SIMCOLEP. Figure 1 illustrates how exponential growth curve used as input for the model is compared to the observed population size. The modelled population was scaled down to a population size of 4500 individuals in 1990.

Table S3.2: Population growth rates used as input for the model.

Year	Rio Grande do Norte	Amazonas	Ceará	Tocantins[1]
1872	0.018204	0.028061	0.016894	0.025959
1950	0.022332	0.034421	0.022465	0.038534
1980	0.022332	0.034421	0.016876	0.020203
1990	0.016064	0.032258	0.017133	0.024897
2000	0.013182	0.021408	0.012883	0.017866

[1]Part of Goias unitl 1980. Growth rates prior to 1980 are based on Goias.

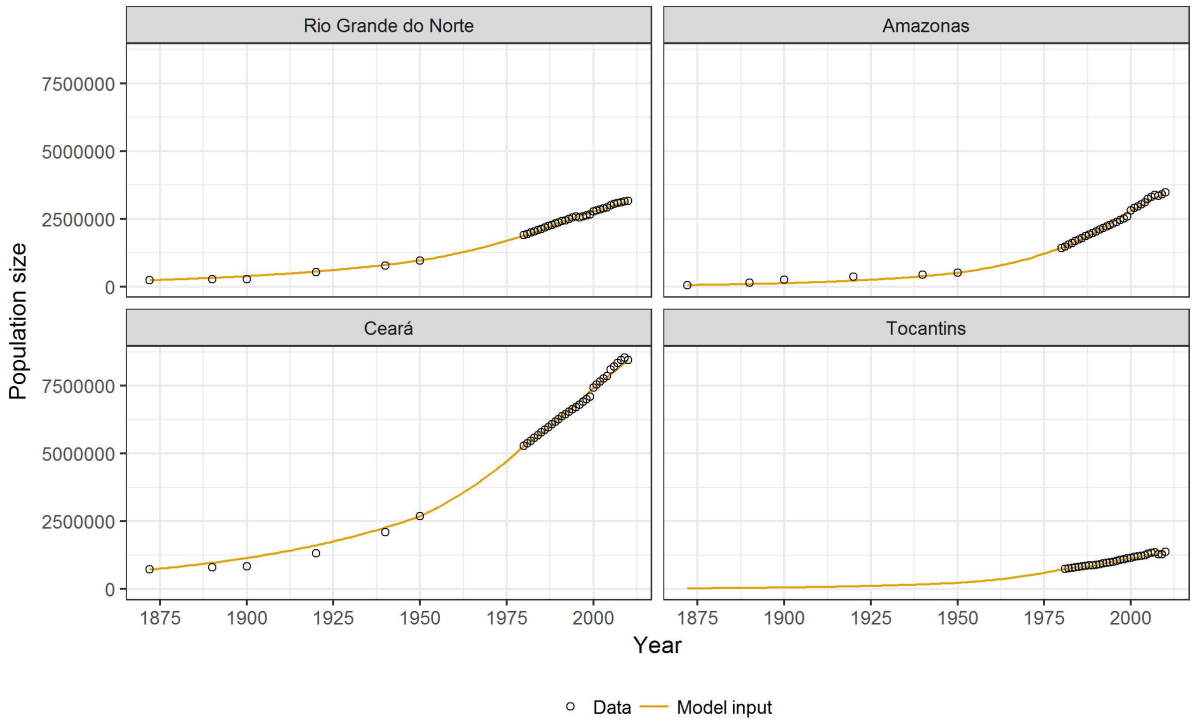

Figure S3.1: Observed population size and exponential growth curve used as input for the model of four states in Brazil from 1872-2010.

1.2 Household structure

Household processes were fitted to the household size distribution in each state separately. Data were obtained from the IBGE website of Brazil. All parameters were based on previous studies, except for fraction of random moving males, and the fraction of moving males that create a single household. Table 3 provides a full overview of all household parameters.

Table S3.3: Overview of household parameters.

Parameter	Value	Source
Fraction random moving males	RN1: 0.1 AM2: 0.0 CE3: 0.1 TO4: 0.0	Calibrated
Age of first movements of individuals	12-22years	[1]
Household size to move to	Triangular distribution (0,4,2)	[5, 6]
Rate of splitting household after marriage	Exponential(12)	[1]
Fraction of widow(er) moving to children	Widow(er): 1.0	[5, 6]
Fraction females moving to partner after marriage	0.75	[5, 6]
Fraction of males creating a single household	RN1: 0.1 AM2: 0.1 CE3: 0.1 TO4: 0.2	Calibrated

Fitting of household sizes was conducted in in iterative process. All combination of the parameters fraction of random moving males, and the fraction of males create a single household were evaluated in discrete steps of 0.05. Goodness of fit of the distribution of household size was evaluated by a Chi-square test. The household size distribution did not significantly differ from the data (figure 2). The fitted

values are presented in table 3.

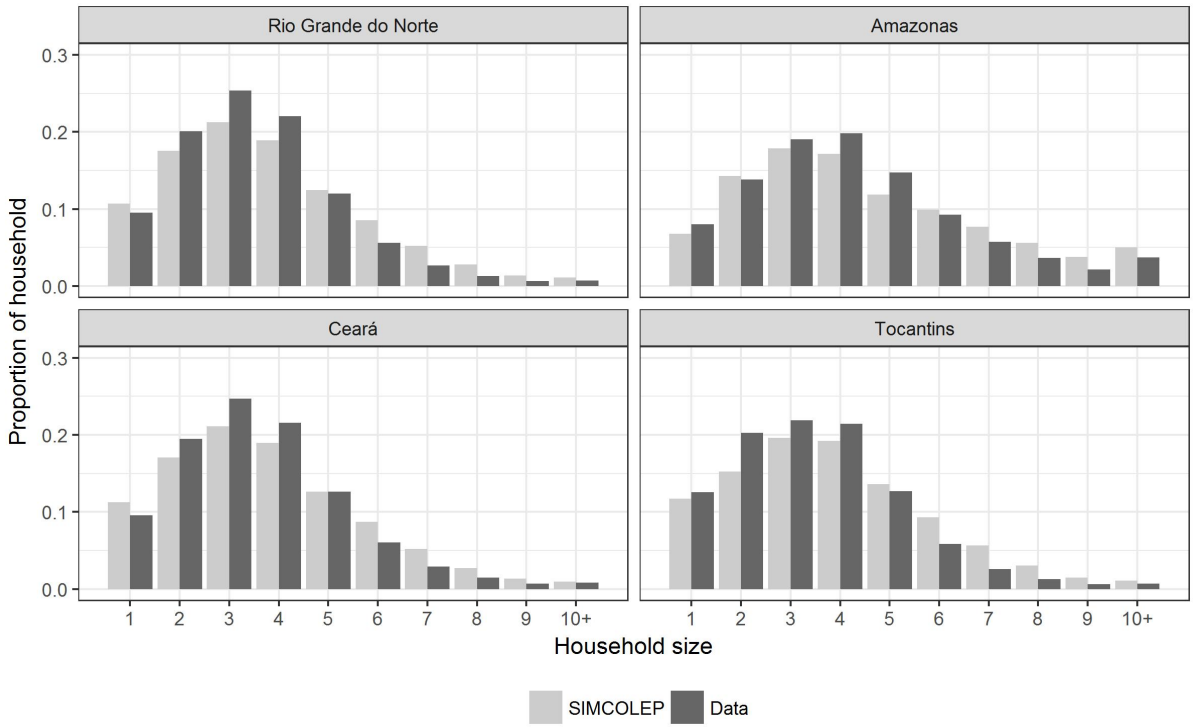

Figure S3.2: Observed and modelled distribution of household size in four states of Brazil in 2010. There is no significant difference between data and simulated distribution (Rio Grande do Norte: $p = 0.80$; Amazonas: $p = 0.93$; Ceará: $p = 0.89$; Tocantins: $p = 0.65$, 2-test).

2 Leprosy

2.1 Natural history of infection

The natural history of leprosy is modelled following Meima et al. The model distinguishes susceptible and non-susceptible (i.e. who will never develop the disease) individuals. An infected individual will either develop paucibacillary (PB) or multibacillary (MB) leprosy (See figure 3. Table 4 gives an overview of the main parameters and characteristics of the natural history of disease.

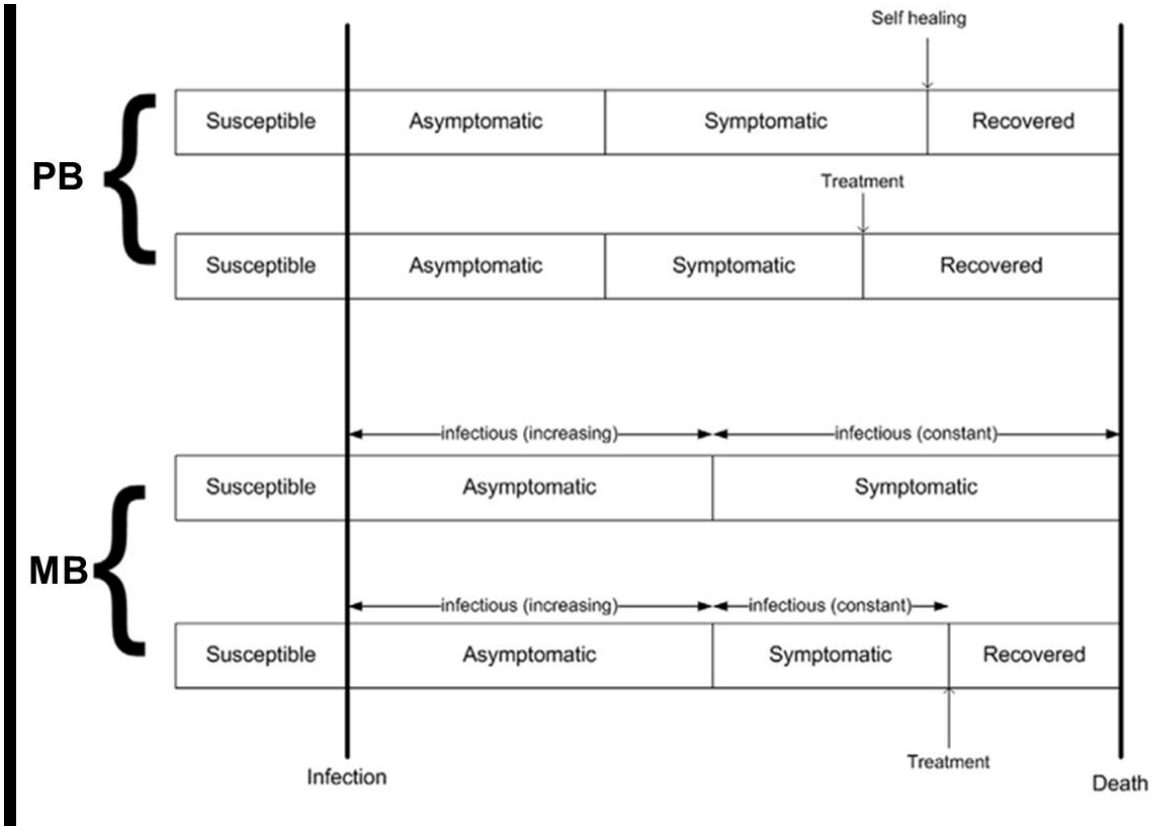

Figure S3.3: Natural history of infection with M.leprae. Paucibacillary (PB) leprosy enters an asymptomatic state, progresses to the symptomatic state, is followed the recovered state upon self-healing or treatment. Multibacillary (MB) leprosy enters an asymptomatic state, progresses to the symptomatic state, and remains in that state until death unless treatment is provided.

2.2 Transmission

Transmission occurs when an infectious individual has contact with a susceptible individual SIMCOLEP models two transmission processes: (1) transmission in the general population, and (2) an additional within-household transmission. Contacts in the general population are made with both people within and outside the household. Infectivity is determined by the product of the contact rate and the infectivity function. A detailed description can be found elsewhere (1). Since no data are available on the number of new cases by household size, contact rates within households was fixed to 0.98, based on previous work [1]. In this study, we only fitted the contact rate in the general population to match the level of leprosy incidence in the data.

Table S3.4: Fixed input parameters of leprosy natural history of infection, treatment and control.

Parameter	Value	Source
Natural history of infection		
Susceptible	20%; Allocation randomly determined	[1, 7, 8]
PB asymptomatic	Mean duration: 4.2yrs (SD: 1.9); Gamma distributed	[1]
PB symptomatic	Mean duration: 5yrs; Exponentially distributed	[1]
MB asymptomatic	Mean duration: 11.1yrs (SD: 5.0); Gamma distributed	[1]
Infectivity	PB: not infectious	[8]
	MB: Asymptomatic: 0-1 (linear increase);Symptomatic: 1	
Treatment		
Dapsone	1970-1990; relapse rate: 0.015 y-1	[9]
MDT	after 1990; relapse rate: 0.001y-1	[10]
Relapse to MB	90%	
Relapse to PB	10%	
Control		
Active case detection (coverage)	After 2003: 43% in all states	[11, 12]
	After 2014: 56% in Rio Grande do Norte;	
	76% in Amazonas	
	70% in Ceará	
	85% in Tocantins	
BCG coverage in infants	Protective effect of 60%	[13, 14]
	Annual coverage rates 1980-2010	

2.3 Leprosy control

SIMCOLEP models past and current leprosy control, including treatment with MDT, passive case detection, and active case finding. The model assumes that after 1990 MDT treatment is provided to all detected cases of leprosy. Prior to 1990, we assume that all cases are treated with dapsone. Each detected case will receive treatment. After treatment the patient is not infectious anymore. Passive case detection is reflected by detection delays that are Gamma distributed. Since true detection delays are unknown, detection delays will be estimated. Active case finding or household contact tracing is specified by year and coverage rate based on the available data. Table 4 gives an overview of the fixed input parameters of leprosy control used in SIMCOLEP.

2.4 Model fitting

Contact rates in the general population and detection delays were fitted to match the observed level of new case detection rate in each state. We only fitted the most recent detection delay, and assumed that historic detection delays have improved at years of operational changes. Detection delays are expressed in average years, and we assumed improvement of a 0.5 year in Rio Grande do Norte, Amazonas and Ceará, and 0.25 year in Tocantins at the assumed years of changes. Since reported detection rate reflects operational variation in time, some known other unknown [15], these years were identified based on the trend of the NCDR in the data and literature for each state separately (See table 5).

Table S3.5: Assumed years of changes in passive detection delays.

State	Years	Source
Rio Grande do Norte	1993-1994, 1997, 2003-2005, 2007, 2009	[15]
Amazonas	1992-1994, 1996, 1997, 2001	[16, 17]
Ceará	1995-1998, 2001, 2003-2004	[18]
Tocantins	1994-2001 and 2003-2008	[19]

Fitting the new case detection was done in an iterative process, where we varied the contact rate (range 0.8-8.0) and detection delays (range 0-20). Detection delays above 20 years were considered not realistic. The simulated new case detection rates were compared to the data by a log-likelihood function assuming a Poisson distribution. The likelihood ratios were fitted to a polynomial regression model to obtain the optimum value of the contact rate and average detection delay (See also Fischer et al. [1]).

First, the ability of the models to forecast was evaluated by omitting data from 2012 to 2014 and SIMCOLEP was fitted to the data from 1990-2011. Afterwards, all of the data were included in the second analyses and forecasts of NCDR for total diagnoses and MB diagnoses were generated for each year from 2015 to 2040. To obtain the number of new leprosy cases in each state, we multiplied the scaled number of new cases as predicted by the model with the scalings factor of the population. The calibrated values of the first and second analysis can be found in table 6. Results of simulations are presented in figure 4 and 5.

Table S3.6: Calibrated values of contact rate in the general population and the average detection delays.

Parameter	Rio Grande do Norte	Amazonas	Ceará	Tocantins
Analysis 1: 1990-2011				
Contact rate in the general population	2.309 (95%CI 2.235-2.383)	1.096 (95%CI 1.072-1.120)	1.720 (95%CI: 1.658-1.782)	6.080 (95%CI 5.450-6.710)
Average detection delays	20.483 (95%CI 16.830-24.136)	3.020 (95%CI 2.079-3.961)	15.623 (95%CI: 13.255-17.991)	10.347 (95%CI 9.088-11.606)
Analysis 2: 1990-2014				
Contact rate in the general population	2.28 (95%CI 2.211-2.349)	1.097 (95%CI 1.074-1.120)	1.726 (95%CI: 1.668-1.784)	6.596 (95%CI 6.015-7.177)
Average detection delays	18.72 (95%CI 15.208-22.232)	3.126 (95%CI 2.246-4.006)	15.181 (95%CI: 13.164-17.198)	11.426 (95%CI 10.169-12.683)

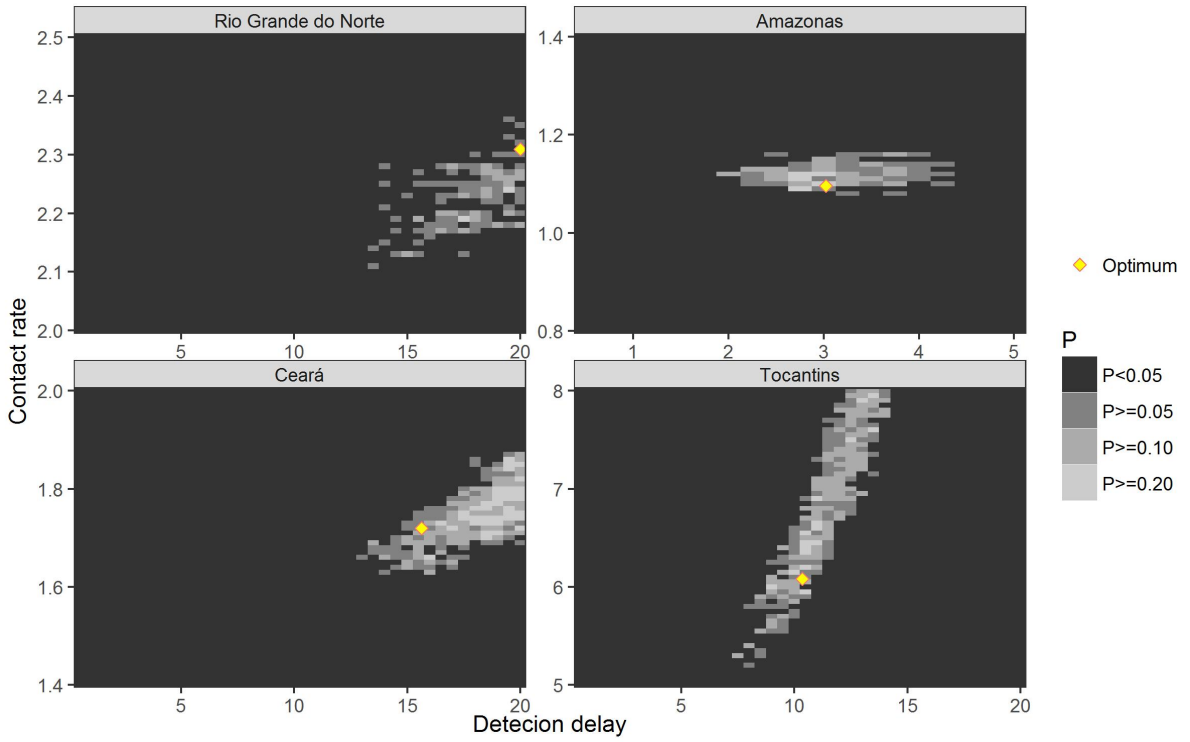

Figure S3.4: Fit to data 1990-2011. Simulated values and optimum derived from a meta-model for each state. The color indicates the difference with the log-likelihood of the data.

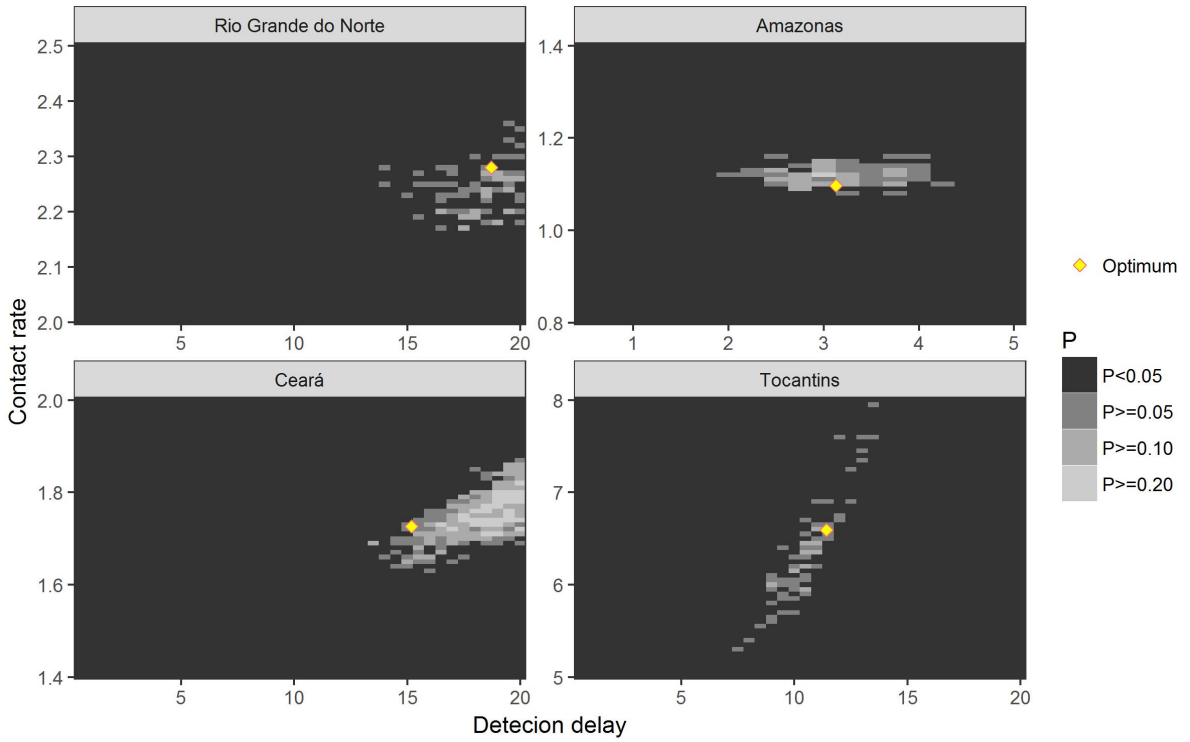

Figure S3.5: Fit to data 1990-2014. Simulated values and optimum derived from a meta-model for each state. The color indicates the difference with the log-likelihood of the data.

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