OPTIMIZATION MODELS FOR LEISHMANIASIS CONTROL:

A CASE FOR BIHAR, INDIA

by

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To my parents, Savita and Kalyan, my sister Chandan and my bother Sujeet

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## ABSTRACT

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Leishmaniasis, is a family of infectious diseases, which mostly affects poor and developing countries. The highest prevalence and mortality rate of Visceral Leishmaniasis (VL) the world over occurs in Bihar state of India. Many disease control methods are available; however, procedures aimed at reducing sandfly population by spraying insecticide have been the most effective for controlling VL in Bihar. In this dissertation, optimization models for the control of Leishmaniasis are developed and analyzed. Novel optimization models are built and analyzed to identify the optimal amount of insecticide allocated for controlling the spread of VL in Bihar. Since the vector (disease transmitting insects) *Phlebotomus Argentipes*, responsible for the spread of this disease, are zoophilic in nature, the implication from this research study recommends schematic allocation of insecticide based on both human and cattle populations. Six models were developed for analyzing insecticide intervention to control the spread of VL in Bihar. All model formulations were calibrated using estimates of entomological, insecticide toxicity, demographical and budget related parameters from appropriate literature sources. A mathematical model for comparing the options of spraying insecticide in preplanned number of sites (houses and cattle sheds) was developed. An existing model of VL transmission dynamics in Bihar state was revised to include the effects of insecticide intervention. The two main optimization models developed were: linear and nonlinear. The linear optimization model recommends optimal insecticide allocation amount between the two types of sites. This model optimizes sandfly mortality using limited financial resources available to the public health department. The nonlinear optimization model optimizes the number of humans saved from infection. Results from the optimization models were analyzed to study the impact of considering state and district level demographic data on number of human infections saved. A qualitative analysis of the comparison of the four optimization models was performed to recommend best insecticide spray campaign policy.

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# CHAPTER 1

# INTRODUCTION

## 1.1 Visceral Leishmanisis as a Public Health Concern

*Visceral Leishmaniasis* (VL) is an infectious disease spread by the bite of an infected sandfly, which is fatal if not treated. Also called *Kala-Azar* in India, it is transmitted to the human population when a susceptible human is bitten by an infected female sandfly. Although Silva and Grunewald [1] reported that male sandflies are known to feed on blood, blood is also a source of protein and iron to develop eggs for female sand flies. When infected sand flies bite susceptible humans and susceptible sand flies bite infected humans, the parasite (*Leishmania Donovani*) is transmitted between the sandfly and human populations. In epidemiology, the disease carrying agent (sandflies in case of *Visceral Leishmaniasis*) are called vectors and humans who get infected by the disease are called hosts. In southern Asia, (sandfly) species *Phlebotomus Argentipes* is the primary vector of *Leishmania donovani* as shown by Ilango [2]. Since India's economy depends on agriculture, it has a sizable cattle population which is often visited by sandflies for feeding and mating purposes.

Bora [3] reported that untreated cases of this disease have up to 90% death rate. Jamison [4] estimated that in 1990, the global burden of Leishmaniasis was 0.86 million and 1.2 million disability-adjusted life years lost, for women and men respectively and in India the figures were estimated as 0.5 million and 0.68 million for women and men, respectively. The Indian state of Bihar is the epicenter of the VL endemic area of South Asia, it unfolds into neighboring states of Jharkhand, West Bengal, and Uttar Pradesh and also extends to some regions of Bangladesh and Nepal as mentioned by Das et al. [5] . As per a W.H.O. training module [6], an initiative was jointly launched in 2005, by the governments of India, Bangladesh, and Nepal to reduce the annual incidences of VL at district level to lower than one per 10000 persons by 2015. Vector control procedures have been very effective for controlling the spread of VL in Bihar. As an intervention measure, the Bihar government undertakes insecticide residual spraying (IRS) two times every year. The first round is carried out in February-March, and the second round in May-June, each round spanning a 60-day period as described in the W.H.O. report [7]. The Public health department of Bihar, India, considers only the human population size of each district for computing the amount (weight) of insecticide (presently dichlorodiphenyltrichloroethane or DDT) to be allocated to each district for each round of spray campaign. As per the present “National programmes of insecticide residual spray for VL vector control” in India, 0.0375 kilograms DDT is allocated per capita per round of spray as mentioned in the W.H.O. report [7]. The present insecticide allocation of 0.0375 kilograms DDT per individual may be sub optimal. Additionally, the host preference of sandfly species needs to be considered in computing insecticide allocation. Since the vectors responsible for the spread of this disease are known to feed on both humans and cattle, it is imperative that both human dwellings as well as cattle sheds are targeted in the insecticide spray campaign. The cattle population in a district, which is also a host for sandflies, is presently not included in insecticide allocation calculations. If separate insecticide quantity is allocated to reduce the sandfly density present in cattle shelters, it might help in reducing the vector population effectively .This might help to reduce disease incidences in humans better.

Spraying only at cattle sheds in brazil, had caused increased sandfly density in unprotected human dwellings and if only cattle sheds are sprayed with insecticide then this might cause increased transmission of Leishmania Donovani to humans as reported by Bern et al. [8]. Bongiorno et al. [9] mentioned that each sandfly species is known to have a different preference for the blood of different animals. The blood feeding preference of different sandfly species for the blood of various hosts, are available in literature. Mukhopadhyay and Chakravarty [10] found that female sandflies (*P. Argentipes*) in Bihar had a preference for bovine blood (68%), followed by human blood (18%), and avian blood (4%), hence showing them to be zoopholic. Sharma and Singh [11] concluded from examined soil samples of Bihar that *P. Argentipes* showed a higher tendency to breed in the alkaline soil of cattle sheds in contrast to *P. Papatasi*, which are more likely to breed in the soil with neutral pH found in human houses. Sharma [12] reported that cattle sheds, where the soil might have high content of moisture and organic matter such as cow dung, provide a breeding site for *P. Argentipes*. It is imperative that the insecticide residual spraying efforts target cattle sheds (sites) in addition to houses (sites).

## 1.2. Research Motivation

The public health department runs programs in order to reduce the disease burden of prevalent diseases like Malaria and Kala Azar. Amongst them are insecticide intervention, public awareness campaigning, testing and treatment of diseases in government run hospitals. Insecticide residual spraying is an important operation undertaken by the public health department and insecticide material cost is a major cost component accounting for up to 45% of the total cost of insecticide intervention activities as shown by Conteh et al. [13]. Simulating the outcomes of such an expensive operation by employing a mathematical model can aid better decision making. Each year limited financial resources are available to the public health department to run various programs. Optimal allocation of available resources can help to achieve highest possible reduction of the disease burden on the population. Planned fund allocation for different activities each year, can help receive optimum benefits from the investment. It would be better to plan the spray campaign, to account for differences in sandflies blood preference towards humans and cattle as described by Palit et al. [14]. The benefit can be in terms of: increased mortality in sandflies or reduced number of human infections in a year. Mathematical models to systematically analyze levels of different intervention activities carried out by the public health department would be valuable. A mathematical framework to identify an optimal allocation of insecticide based on local human as well as cattle populations might be useful.

Motivated by the above problem background, six models were developed to analyze the benefits received by schematically allocating insecticide sprayed at human as well as cattle dwellings, both at state level and district level. A mathematical function aimed at comparing preplanned options of spraying insecticide at different number of sites was formulated. Two optimization models aimed at recommending optimal insecticide allocation for achieving highest possible sandfly mortality and number of human infections saved were formulated. A system of coupled differential equations from literature was revised to include the effect of spraying insecticide at a given number of sites. This system of ordinary differential equations was calibrated such that it modeled the existing transmission dynamics of VL in Bihar as closely as possible. An expression for the basic reproduction number was derived. Since the disease prevails in Bihar, the value of the basic reproduction number was expected to be greater than one. The value of the basic reproduction number was verified to be greater than one using the parameter estimates chosen from literature. On simulating the model, the infected human and sandfly populations stabilized at non-zero steady state values. Finally, all optimization models were compared to recommend best insecticide spray campaign policy.

# CHAPTER 2

# REVIEW OF LITERATURE

This chapter presents a review of literature that helped to formulate the research criteria, build the models and perform this dissertation research.

## 2.1 Literature Sources for Model Formulation

Literature was studied for finding the best way to model insecticide intervention, chose parameters for the model and the metric to be optimized. Parameter estimates were searched from literature to model the vector and host populations, the budget allocation and VL transmission dynamics in Bihar, India. Only when parameter estimates specific to VL transmission in Bihar were unavailable, estimates of a similar infectious disease were used.

### Metric chosen for optimizing in the linear model:

Stauch et al. [15] have built and analyzed a mathematical model that includes VL transmission and intervention parameters to study the effects of different intervention strategies (treatment regimes, early case detection and vector-related intervention). Their model predicts that if the vector density is reduced by 80%, then VL infections might be eliminated. The highest possible reduction in vector density might be possible by increasing their death rate. Death rate might be maximized (using available money), if optimal insecticide amount is allocated per person and per cattle. Hence, insecticide induced death rate has been chosen as a metric to be optimized in the linear optimization model.

Metric chosen for optimizing in the nonlinear model:

Mathematical models in literature describe incorporating disease control strategies and measuring their impact using a metric. Lichiello and Turnock [16] have presented performance measures used by public health and social service agencies. Caetano and Yoneyama [17] have modeled an optimal control problem for Dengue epidemics that minimizes the “cost functional” comprising of insecticide application costs, educational campaign costs, and indirect costs of lost working days, low morale and treatment. The Health Metrics Network [18] have defined “improved health” and “reduced mortality” as the two health outcomes in their basic framework of health system monitoring. Stoto and Cosler [19] recommend using an appropriate “time horizon” and “incremental cost-effectiveness ratio” to compare two or more interventions for policy makers. Stringer et al. [20] have proposed “HIV free survival” for lower income countries as it captures the essential purpose of the programme to prevent mother-to-child HIV transmission. The 2010-2011 UNAIDS Performance Monitoring Report [21] proposed “number of infections averted” as an outcome measure for HIV prevention programs. The nonlinear optimization model in this dissertation also uses “number of human infections averted” as a performance metric of the insecticide spray campaign.

Review of blood preference of sandflies:

Gebre-Michael et al. [22] have studied the natural blood meal sources of different phlebotomine sand flies species in the VL endemic regions of north-west Ethiopia. Based on a dissection of a sample of 281 freshly engorged female *P.orientalis* they reported that a majority (91.6%) of them fed on bovine blood, 2.2% on human blood, 2.6% on both blood source (bovine and human) and 3.7% on unidentified blood sources. The authors recommended that the penchant of *P. orientalis* for cattle blood might be of epidemiological significance for controlling the disease. Palit et al. [14] and Mukhopadhyay and Chakravarty [10] have studied the blood meal preference of two main prevalent sandfly species (*P. Argentipes* and *P. Papatasi*) in West

Bengal and North Bihar respectively. They concluded that sandfly species *P. Argentipes* are zoopholic by nature.

Kawaguchi et al. [23] had introduced a parameter called "*human visitation rate*" of mosquitoes to model malaria transmission dynamics. A similar parameter (*human visitation proportion*) is used in our models, which quantifies the proportion of sandfly population that visits human and cattle sites based on their attraction rate towards human and cattle blood. This feeding behavior of the sandfy species has been directly incorporated in all optimization models developed in this dissertation. This parameter is a constant (fraction) in the linear optimization model and is expressed as a function of time in the differential equations model.

Literature review of insecticide decay rate:

Reithinger et al. [24] compared four different insecticides for reducing transmission of sandfly borne-diseases to dogs in Brazil. They presented the anti-feeding and survival rates of female sandflies exposed to dogs treated with different insecticides. In general, there was a reduction in the anti-feeding effect (except diazinon treated dogs) and death rates of exposed sandflies. Literature was searched to find a function to represent the decay of repellent and lethal effects of an insecticide. Molina et al. [25] and Miró et al. [26] examined the repellent and lethal effect of topical Permethrin solution and imidacloprid-permethrin combination, respectively, to protect dogs from sandfly bites. Courtenay et al. [27] have studied the effect of topical deltamethrin pour-on insecticide to protect dogs from VL in Brazil. They have used an exponential decay function to fit the data of decay of insecticide effects. This dissertation research also uses an exponential function to model the decay of insecticide's lethal and repellent effects.

Literature review on transmission term:

The rate of contact between vector and host individuals in vector-host disease models is captured by the disease-transmission term. Wonham et al. [28] analyzed the differences in predictions from vector-host models due to the form of disease-transmission term assumed. The three different forms of disease-transmission terms are: reservoir frequency dependence, mass action, and susceptible frequency dependence.

The reservoir frequency dependence assumes that biting rate of vectors (sandflies) is saturated and is not limited by reservoir (human) density. As per this biological assumption, the biting rate (per unit time) by sandflies is the maximum possible number of bites per day made by a single sandfly and depends on the sandflies' gonotrophic cycle. The biting rate of vector's on reservoirs increases with the population density of vectors. At disease free equilibrium, the reservoir to vector transmission rate is a function of both biting rate and ratio of vector and reservoir densities, whereas the vector to reservoir transmission rate is a function of only biting rate. Reservoir frequency dependence assumption was used by: Favier et al. [29] to derive a method to compute the reproduction number for Dengue in Brazil; Cruz-Pacheco et al. [30] to model the transmission dynamics of West Nile virus between the avian and vector populations. Nishiura et al. [31] modeled reciprocal infection between human and mosquito populations under reservoir frequency dependence assumption. Their Dengue transmission dynamics also considers an alternate blood source, similar to our differential equations model with a cattle population which deflects bites that would have come on humans.

Mass action assumes that biting rate is a function of both reservoir and vector population densities. At disease free equilibrium the reservoir to vector transmission rate is a function vector population density, whereas the vector to reservoir transmission rate is a function of reservoir population density. The assumption of mass action is valid only up to a threshold value of reservoir population density.

Under susceptible frequency dependence assumption, the vector-to-reservoir disease-transmission term is the same as that for the reservoir frequency dependence assumption, however the reservoir-to-host term is different. Susceptible frequency dependence assumes that the vector biting rate is not a function of either the reservoir population density or the vector population density and hence is not limited by them. The vector biting rate by one vector is the same as that for reservoir frequency dependence. The vector biting rate on one reservoir reaches a maximum value when the vector density reaches a threshold value beyond which the vector biting rate remains constant, even if the vector density increases. Many researchers have modeled infectious disease transmission using susceptible frequency dependence. Chowell et al. [32] modeled the transmission dynamics of dengue fever in the Mexican state of Colima, under the susceptible frequency dependence assumption. The disease transmission term in this dissertation research was formulated under “reservoir frequency dependence” assumption described by Wonham et al. [28] versus “susceptible frequency dependence” assumption used by Mubayi et al. [33].

Literature review on average herd size per cattle shed:

Khan and Usmani [34] have surveyed the rural areas of North West Frontier Province of Pakistan and found a high variability in the number of animals per household (4.2 ± 13.5 Buffalo per household and 1.7 ± 1.3 cattle per household). Boukary et al. [35] have collected data from the rural area of Torodi, Niger in sub-Saharan Africa and found that on an average, number of cattle owned per household is 18 ± 17. Barrett [36] presented average number of cattle per household across 8 communal lands in Zimbabwe as 7. Gupta [37] has quoted the average number of cattle owned by a family as 4.3 for a village studied in the state of Uttar Pradesh. Erenstein [38] surveyed 18 villages spread across 3 clusters in the Trans-Gangetic Plains of India and found that the average livestock herd size per household is almost universal (Mean(s.d.,n, p)=4.6(2.6,18,ns)). Average herd size per cattle shed estimate from Erenstein [38] is used in our modeling study, since this estimate is from India and does not have high variability.

VL incidence rate and underreporting estimation in literature:

Singh et al. [39] used stratified sampling to select houses in the East Champaran district, to provide "population based estimates" of the number of VL cases in that district, which can used as a guide for resource allocation for VL elimination campaigns. They have estimated the annual VL incidence rate for the high and medium-incidence stratums combined as 21.9 cases per 10000 per year, (90% CI: 14.0–34.2). Singh et al. [40] have used population stratified by age and sex variables to obtain better estimation of underreporting of VL cases in Vaishali district in Bihar.

Singh et al. [40] computed the underreporting factor, by comparing the "number of VL cases" from house to house survey with those recorded by passive case detection. Our models use the underreporting percentage estimated by Mubayi et al. [33].

## 2.2 Contributions to Literature

The novel ideas which this dissertation contributes to literature are tabulated in Table 2.1.

Table 2.1. Literature review versus contributions made by this research.

| Serial number | Literature review | Contribution to literature |
|---|---|---|
| 1 | Presently in Bihar the insecticide allocation (amount) for each spray round is 0.0375 kilograms per person as recommended by a W.H.O. report [7]. | The models proposed in this dissertation recommend optimal insecticide allocation (amount in kilogram) per person as well as per cattle. |
| 2 | Susceptible-Infected-Recovered models generally have only 3 mutually exclusive compartments | Both government and private hospitals are included in the differential equations model presented in this dissertation. The under-reporting percentage is included, accounting for infected individuals not reporting to government clinics. |
| 3 | Natural birth and death rate of humans are generally used in vector-host models. | Instead of birth rate for humans, recruitment rate is used, thus incorporating the immigration rate of humans. Different disease-induced death rates for infected and treatment compartments are included. |
| 4 | Only biological parameter distribution is generally considered in uncertainty and sensitivity analysis. | Spray campaign budget's distribution was estimated from literature. Thus, the impact of uncertainty in financial parameter is also studied in the uncertainty and sensitivity analysis. |

Table 2.1—*Continued*

| | | |
|---|---|---|
| 5 | Kawaguchi et al. [23] have introduced the parameter: “human visitation rate” to quantify the proportion of sand flies visiting human and cattle sites. | The attraction rate of the main vector (*P. Argentipes*) has been used to compute the “human visitation proportion” of sandflies in Bihar. This parameter is modeled as a function of time in the differential equations model to incorporate the dynamic human population. |
| 6 | Deterioration of insecticide’s intervention is usually not incorporated in vector-host models. | The deterioration of insecticide’s repellent and lethal effects with time is incorporated in both linear and nonlinear models. The insecticide sprayed in houses has a different decay rate than the insecticide sprayed in cattle sheds. The decay rate for repellent effect has been estimated from Molina et al. [25]. The initial efficacy for lethal effect and repellent effects has been taken from appropriate literature sources. |
| 7 | A model for optimizing insecticide induced death rate or human infections averted, was not found in present literature review. | The metric optimized by the linear model is: Insecticide induced death rate. |
| | | The metric optimized by the nonlinear model is: Cumulative human infections averted. |
| 8 | A model that can be simulated by choosing any day, on which insecticide effect becomes active, was not found in present literature review. | In the differential equations model, any day of the simulation run can be chosen as the day on which insecticide is sprayed. |

Only 31 districts in Bihar have been classified as VL affected districts. Table 2.2 provides a summary of the different modeling approaches developed and the data sets (Bihar state or 31 VL affected districts) for which they can be simulated. Model numbers 3, 4, and 5 account for dynamically varying human and sandfly populations. Model numbers 3 and 6 do not provide optimal insecticide allocations and can be simulated by using either the data set of Bihar state or the 31 VL affected districts of Bihar state. Models 3 and 6 can be simulated by providing a (preplanned) number of sites to be sprayed with insecticide.

Table 2.2. Summary of Models Developed

| Model no. | *Model name* | Dynamic | Optimization model | Data set | Described in section |
|---|---|---|---|---|---|
| 1 | *Two-dimensional linear optimization* | No | Yes | State level | 3.2.1 |
| 2 | *Multi-dimensional linear optimization* | No | Yes | District level | 3.2.2 |

Table 2.2—*Continued*

| | | | | | |
|---|---|---|---|---|---|
| 3 | *Differential equations model with insecticide intervention* | Yes | No | Both state and district level | 3.2.3 |
| 4 | *Two-dimensional nonlinear optimization* | Yes | Yes | State level | 3.2.4 |
| 5 | *Multi-dimensional nonlinear optimization* | Yes | Yes | District level | 3.2.5 |
| 6 | *BMCR function* | No | No | Both state and district level | 3.3.2 |

All four optimization models are solved to obtain the optimal number of sites to be sprayed to optimize either sandfly mortality or cumulative number of human infections at the time the second round of spray starts in Bihar (after a ninety day gap). The two-dimensional linear model recommends spraying only in houses using the 2012 VL budget of Bihar [41] (which is also the present policy of allocating insecticide based on human population only). However, the two-dimensional linear model's recommendation saves the least number of human infections, ninety days after spray. As compared to the two-dimensional linear model's recommendation, the two-dimensional nonlinear model's recommendation, (which considers human as well as cattle populations) saves 22 % more human infections, ninety days after spray. The multi-dimensional nonlinear model's recommendation, which considers both human and cattle populations (including other demographic data) at district level, saves 64 % more human infections, ninety days after spray. The model which computes the insecticide allocation amount by considering: first the (state level) cattle population and second the (district level) demographic data including human and cattle populations; saves increasing number of human infections.

# CHAPTER 3

# METHODOLOGY

The sources for data, assumptions made before model formulation, and derivation of the model equations are presented in this chapter. The linear model is analyzed to derive a closed form solution.

## 3.1 Data Sources

The sources of data for the models developed in this dissertation are presented below.

### 3.1.1 Data Sources for the Linear Optimization Model

The estimates of human and cattle population sizes for the 31 VL affected districts of Bihar have been taken from the 2010-2011 budget allocation document from the public health department of Bihar [42] and 1982 Cattle Census [43], respectively. The average livestock herd size (number of cow equivalents per household) was assumed to be the average number of cattle per cattle shed in Bihar state, in line with previous studies from Erenstein [38]. The insecticide spray campaign cost equation was formulated using data from the 2010-2011 budget document [42]. The insecticide spray campaign's total cost was calculated by collating the costs related to materials and implementation (including salaries, spray equipment, and miscellaneous expenses). The cost equation (derived in section 3.2.1) included both the direct and the indirect costs associated with implementation of insecticide spray campaign. The cost data included a total of 10,686 villages cared for by 354 public health centers (PHCs) from the 2010-2011 budget document [42]. The number of occupied residential houses was estimated from the 1991 Census of India [44] for the VL affected districts (excluding Arwal district's data).

Due to financial constraints it is not possible to spray insecticide at all houses and cattle sheds in a district. The two decision variables were defined as: “kilograms of insecticide allocated per person” and “kilograms of insecticide allocated per cattle.” The optimization models proposed in this dissertation aim to optimize the amount of insecticide allocated per person and per cattle (per capita hereafter). When available financial resources are not enough to procure insecticide to cover all sites in the district or state, it is referred to as a “resource limited case”, and it is used to formulate some of the constraints in the optimization models.

The natural sandfly death rate was estimated using 2 years monthly data of the daily probability of survival of *P. Papatasi* from Srinivasan and Panicker [45]. The mortality of *P. Argentipes’s* 24 hours after spraying with DDT and Deltamethrin were estimated from Huda et al. [46] and Dinesh et al. [47], respectively. The lethal effect of insecticide in the linear optimization model is assumed to decay exponentially over time as presented by Courtenay et al. [27]. Dinesh et al. [47] and Jacusiel [48] were referred for estimating the insecticide’s lethal effect decay rates, inside houses and cattle sheds (Chapter 4). The decay rates are assumed: to have the same value on each day after insecticide application (are not functions of time) and are assumed to be equal for both DDT and Deltamethrin. A parameter (*human visitation proportion, Q*), similar to “*human visitation rate*” of mosquitoes presented by Kawaguchi et al. [23], is used to quantify the proportion of sandfly population visiting human and cattle sites. The epidemiological and demographical parameters of the host and vector populations were estimated by consulting previous studies (Table 3.1 and Table 3.2). The demographic parameters used in the objective function as well as in the constraints are described in Table 3.1.

Table 3.1. Bihar's demographic parameters for linear optimization model.

| **Symbol** | **Definition** | **Units** | **Estimates : Mean (SD)** |
|---|---|---|---|
| $g$ | Number of PHCs in Bihar | Number of government clinics | 354 (2010 VL budget of Bihar [41]) |
| $N_h$ | Size of the affected human population of the 31 VL affected districts in Bihar | Number of humans | 33,898,857 (2010 VL budget of Bihar [41]) |
| $N_c$ | Size of the cattle population in the 31 VL affected districts in Bihar | Number of cattle | 21,571,585 (Cattle Census, 1982 [43]) |
| $N_v$ | Size of the sandfly population in Bihar | Number of sandflies | Assumed constant in the model |
| $H$ | Total number of houses in Bihar | Number of houses | 7,933,615 (Census of India, 1991 [44]) |
| $\beta$ | Average herd size per cattle shed | Number of cattle equivalents | 4.6 (2.6) (Erenstein [38]) |
| $Z = \frac{N_c}{\beta}$ | Number of cattle sheds | Number of cattle sheds | 4,689,475 (Cattle Census, 1982 [43]) |

SD: standard deviation

Table 3.2 defines the insecticide toxicity and entomological parameters used in the linear optimization model's objective function and constraints.

Table 3.2. Insecticide toxicity and entomological parameters in the linear optimization model.

| Symbol | Definition | Units | Estimates Mean (SD) (95% CI) (Reference) |
|---|---|---|---|
| $a_h$ | Female sandflies' feeding preference for human blood | Dimensionless | $179.2 \times 10^{-03}$ (95% CI, 15.14--20.72) (Mukhopadhyay and Chakravarty [10]) |
| $a_c = 1 - a_h$ | Female sandflies' feeding preference for cattle blood | Dimensionless | $820.8 \times 10^{-03}$ (Mukhopadhyay and Chakravarty [10]) |
| Q | Human visitation proportion of *P. Argentipes* based on blood preference | A proportion between 0 and 1 | 0.2554 (Estimated in section 4.1.1) |
| $\tau$ | Time elapsed after the spray of insecticide | Days | User-defined value |
| $\mu_v$ | Per capita death rate of sandflies | sandfly deaths/day/sandfly | 0.0759 (0.0162) (Srinivasan and Panicker [45]) |
| $I_h$ | Amount of DDT consumed per 200 $m^2$ house | kg/house | $533 \times 10^{-03}$ (Walker [49]) |
| $I_h$ | Amount of Deltamethrin consumed per 200 $m^2$ house | kg/house | $400 \times 10^{-03}$ (Walker [49]) |
| $I_k$ | Amount of DDT consumed per cattle shed | kg/cattle shed | $533 \times 10^{-03} /2 = 266.5 \times 10^{-03}$ (Walker [49]) |
| $I_k$ | Amount of Deltamethrin consumed per cattle shed | kg/cattle shed | $400 \times 10^{-03} /2 = 200 \times 10^{-03}$ (Walker [49]) |
| $C_{t0}$ | Initial efficacy of DDT (in houses and cattle sheds) | Dimensionless | 0.54 (95% CI, 48.7--59.3) (Huda et al. [46]) |
| $C_{t0}$ | Initial efficacy of Deltamethrin (in houses and cattle sheds) | Dimensionless | $9.75 \times 10^{-01}$ (Dinesh et al. [47]) |
| $b_1$ | Decay rate of both insecticides' lethal effect inside houses | Per day | 0.012 (0.009) ( Estimated in section 4.1.1 ) |
| $b_2$ | Decay rate of both insecticides' lethal effect inside cattle sheds | Per day | 0.081 (0.055) ( Estimated in section 4.1.1) |

CI: confidence interval , kg : kilogram

### 3.1.2 Data Sources for the Nonlinear Optimization Model

The nonlinear optimization model uses the same parameter symbols and estimates as those used in the linear optimization model. However, the following parameter symbols and estimates (Table 3.3) are different and are used specifically to obtain numerical results for the nonlinear model and for comparison of the models.

Table 3.3. Parameter symbols and estimates specific to the differential equations model.

| Symbol | Definition | Units | Estimates Mean (SD) | References |
|---|---|---|---|---|
| $H$ | Total number of residential houses in Bihar state | Number of houses | 16316527 | Census of India 2001 [50] |
| $H_i$ | Estimated number of residential houses in VL affected district *i* | Number of houses | Refer Table 4.6 | Estimated in section 4.3.1 |
| $N_c$ | Total number of cattle in Bihar state | Number of cattle | 19249457 | 18th Livestock census 2007 [51] (assumed as 23 million with 20% growth) |
| $N_{ci}$ | Estimated number of cattle in VL affected district *i* | Number of cattle | Refer Table 4.6 | Estimated in section 4.3.1 (assumed 20% growth in each district) |
| $K_i = \frac{N_{ci}}{\beta}$ | Number of cattle sheds in district *i* | Number of cattle sheds | Refer table in appendix A | Sharma and Singh [11] |
| $N_{hAct}$ | Total actual human population of 31 VL affected districts in Bihar | Number of persons | 87716860 | 2011 census of India [52] |
| $N_{hActi}$ | Actual number of humans in VL affected district *i* | Number of persons | Table A.1 | Appendix A |

Table 3.3—*Continued*

| | | | | |
|---|---|---|---|---|
| $N_{hAff}$ | Total VL affected persons in 31 VL affected districts of Bihar | Number of VL affected persons | 32393812 | State Health Society report [53] |
| $N_{hAffi}$ | VL affected human population in district *i* | Number of VL affected persons | Table A.1 | Appendix A |
| $g$ | Total number of government clinics in VL affected districts of Bihar | Number of clinics | 310 | State Health Society report [53] |
| $g_i$ | Number of government clinics in VL affected district *i* | Number of clinics | Table A.1 | Appendix A |
| $\Lambda$ | Human recruitment rate | persons added per day per person | 3194.41 | Estimated in section 4.3.1 |
| $b_3$ | decay rate of insecticide's repellent effect | per day | 0.0936 (0.0506) | Estimated in section 4.3.1 (Table 4.5) |
| $\widetilde{C_{Im}}$ | Spray campaign implementation cost | Rupees | 96.80 million | Bihar's budget 2012-2013 [41] |
| $\widetilde{C_{UB}}$ | Upper limit of available budget for spray campaign | Rupees | 220.48 million | Bihar's budget 2012-2013 [41] (Table 4.7) |
| $t$ | Simulation time starting at $t_0$ and ending at $t_{final}$. | Days | | |
| $d_{ODE}(t)$ | Insecticide induced death rate of sandflies | Number of sandflies killed per day per sandfly | Computed from equation 3.29 | Derived in section 3.2.3 |

Note: subscript "*i*" is used to denote the district number of one of the 31 districts

## 3.2 Assumptions and Model Formulation

The assumptions made to formulate the different models in this dissertation are described in this section.

### 3.2.1 Two-dimensional Linear Optimization Model

The two dimensional linear optimization model proposed has three main components. The objective function (equation 3.4) is the first component, which captures the insecticide-induced death rate. The model aims to maximize the objective function. The insecticide-induced death rate is assumed as an addition of death rates achieved by spraying insecticide in houses and cattle sheds. The decision variables (output from the model) in the objective function are the amount of insecticide allocated per person and per cattle.

Table 3.4 defines the notations representing the objective function, material and spray campaign implementation cost, available amount of state budget and per capita allocated amount (weight) used in the linear optimization models.

Table 3.4. Linear model's objective function, budget constraint & decision variables.

| **Symbol** | **Definition** | **Units** | **Description** |
|---|---|---|---|
| $d_v$ | Insecticide-induced death rate of sandflies | sandfly deaths/day/sandfly | Objective function value obtained from the model (Equation 3.4) |
| $\tilde{C}(x,y)$ | Total cost of insecticide materials and spray campaign implementation | Rs. | Budget constraint in the model (Equation 3.5) |
| $\widetilde{C_{UB}}$ | Upper bound on the budget available for the spray campaign | Rs. | User-defined (budget) value in the model |
| $x$ | Insecticide allocated per capita for a 60-day spray period | kg/person | Decision variable value obtained from the model |
| $y$ | Insecticide allocated per cattle for a 60-day spray period | kg/cattle | Decision variable value obtained from the model |

Table 3.4—*Continued*

| | | | |
|---|---|---|---|
| $H_s$ | Number of houses sprayed with insecticide | Number of houses | Decision variable value obtained from the model |
| $K_s$ | Number of cattle sheds sprayed with insecticide | Number of cattle sheds | Decision variable value obtained from the model |

Rs: Rupees

The deteriorating lethal effect of the insecticide is captured by temporal exponential functions ( $i(\tau)$, equation 3.1 and $o(\tau)$, equation 3.2) which include parameters, decay rate*(* $b_1$ and $b_2$*)* and initial efficacy *(*$C_{t0}$*)*. The estimates of $b_1$ and $b_2$ are assumed equal for both DDT and Deltamethrin and have the same value on each day after insecticide application. The sandfly population proportions that are killed on the $\tau^{\text{th}}$ day after insecticide application inside houses and cattle sheds, respectively, are given by

$$i(\tau) = C_{t0}e^{-b_1\tau} \ , \qquad \forall \ \tau \tag{3.1}$$

and

$$o(\tau) = C_{t0}e^{-b_2\tau} \ , \qquad \forall \ \tau. \tag{3.2}$$

The units of both $i(\tau)$ and $o(\tau)$ are the number of sandflies killed/(sandfly·day).

The value of initial efficacy ($C_{t0}$*)* for insecticide (both DDT and Deltamethrin) is assumed equal in both houses and cattle sheds. The assumed daily distribution of the sandfly population at sprayed and unsprayed sites is shown in Figure 3.1, which depends on *blood meal preference* parameter, *Q*. The objective function (equation 3.4) is formulated using this distribution of sandfly populations. Below the (objective function) insecticide-induced death rate at sprayed sites on the $\tau^{th}$ day post spray, is derived. Each day, a sandfly is assumed to die, either a natural death or due to the insecticide's lethal effect. The linear optimization models ignore the repellent effect of the insecticide. It is assumed that all sandflies that visit an insecticide-treated cattle shed or house, get exposed to the insecticide and a proportion of them die based on the insecticide's lethal effect on that day. The term “spray coverage” is used in this dissertation to refer to the number of houses ($H_s$) and cattle sheds ($K_s$) where insecticide is applied.

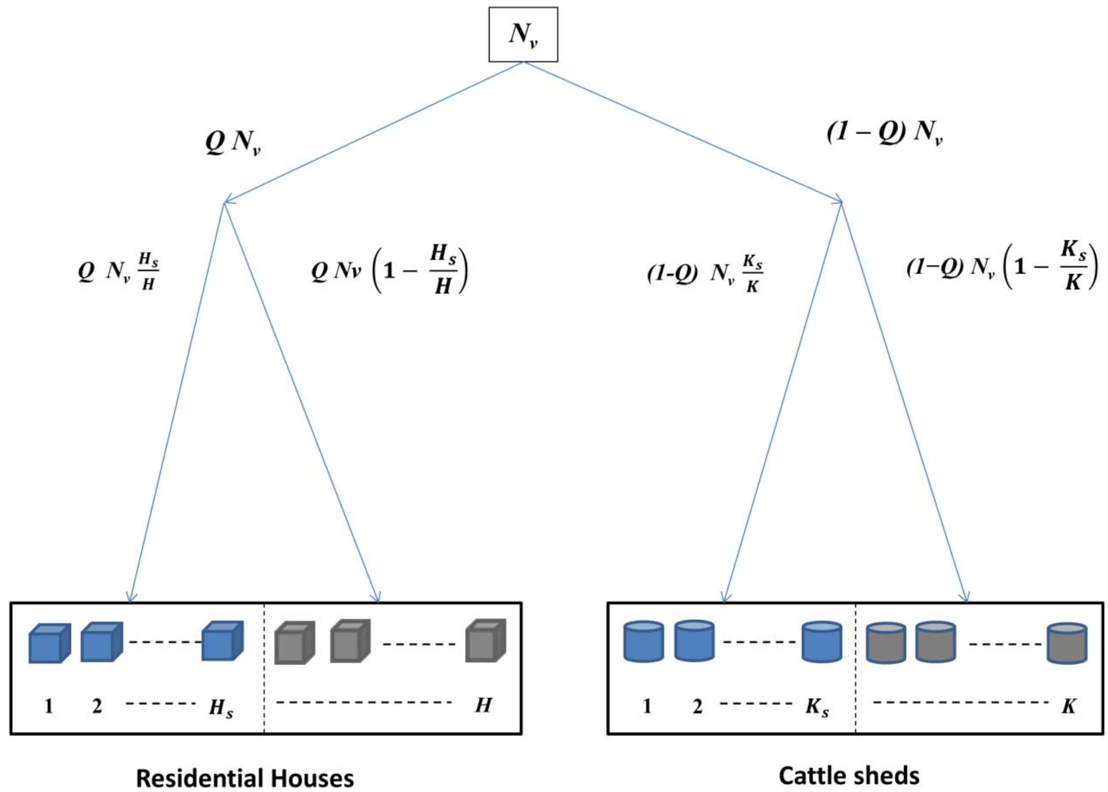


Figure 3.1. Daily distribution of the sandfly population based on their blood feeding behavior.

Total sandfly death rate can be computed by adding the natural death rate ($\mu_v$) and the insecticide induced death rate ($d_v$) at sprayed sites. The objective function equation (insecticide-induced death rate) is derived below. The daily sandfly deaths at different locations are enumerated in Table 3.5.

Table 3.5. Sandfly deaths at different sites.

| Serial no. | Number of sandfly deaths on any day after spraying | Formula |
|---|---|---|
| 1 | Natural deaths in sprayed houses | $N_v\, Q\, \left(\frac{H_s}{H}\right)\, \mu_v$ |
| 2 | Insecticide-induced deaths in sprayed houses | $N_v\, Q\, \left(\frac{H_s}{H}\right)\, i(\tau)$ |
| 3 | Natural deaths in unsprayed houses | $N_v\, Q\, \left(1 - \frac{H_s}{H}\right)\, \mu_v$ |
| 4 | Natural deaths in sprayed cattle sheds | $N_v\, (1 - Q) \left(\frac{K_s}{K}\right) \mu_v$ |
| 5 | Insecticide-induced deaths in sprayed cattle sheds | $N_v\, (1 - Q) \left(\frac{K_s}{K}\right) o(\tau)$ |
| 6 | Natural deaths in unsprayed cattle sheds | $N_v\, (1 - Q) \left(1 - \frac{K_s}{K}\right) \mu_v$ |

The total death rate, obtained by adding all six components (Table 3.5), is expressed as

$$Q\, \left(\frac{H_s}{H}\right) i(\tau) + \left(1 - Q\right) \left(\frac{K_s}{K}\right) o(\tau) + \mu_v \;=\; (1 + q)\mu_v \tag{3.3}$$

Where, $q$ - the percentage increase in the natural sandfly death rate. The objective function of the linear optimization model (insecticide induced death rate) is

$$d_v \;= Q\, [i(\tau)] \left(\frac{H_s}{H}\right) + (1 - Q)[o(\tau)] \left(\frac{K_s}{K}\right) \tag{3.4}$$

The third term on the left hand side of equation 3.3 (natural death rate) is not multiplied by a weight, as sandfly natural deaths occur equally at every site (sprayed and unsprayed). The first and second terms of the objective function (equation 3.4) can be interpreted as the insecticide-induced death rates in houses and cattle sheds, respectively.

The budget constraint (equation 3.6) is the second component of the model. It ensures that the total spray campaign cost (materials and implementation) is always less than or equal to the state budget available for the insecticide spray campaign. Table 3.6 enumerates the costs related to material and implementation of spray campaign.

Table 3.6. Costs related to insecticide spray campaign.

| Symbol | Material cost | Unit | Estimates |
|---|---|---|---|
| $N_1$ | Cost per kg of insecticide (DDT) | Rs./kg of DDT | 90 (Walker [49]) |
| $N_1$ | Cost per kg of insecticide (Deltamethrin) | Rs./kg of Deltamethrin | 810 (Walker [49]) |
| | **Implementation cost: Personnel and maintenance** | **Unit** | **Estimates** |
| $N_2$ | Number of spraying teams or squads allocated per 10 lakh population of a district | Squads/person | $55/10^6$ (2010 VL budget of Bihar [42]) |
| $N_3$ | Number of supervisors per squad | Number of supervisors/squad | 1 (2010 VL budget of Bihar [42]) |
| $N_4$ | Number of field workers per squad | Number of workers/squad | 5 (2010 VL budget of Bihar [42]) |
| $N_5$ | Salary paid to each supervisor/day of the 60-day spray period | Rs./day/supervisor | 145 (2010 VL budget of Bihar [42]) |
| $N_6$ | Salary paid to each field worker/day of the 60-day spray period | Rs./day/worker | 118 (2010 VL budget of Bihar [42]) |
| $N_7$ | Number of days allocated for spraying activity each time spraying is carried out | Number of days | 60 (2010 VL budget of Bihar [42]) |
| $N_8$ | Funds allocated per squad for the repair and purchase of spray equipment per 60-day spray period | Rs./squad/60-day spray period | 950 (2010 VL budget of Bihar [42]) |
| | **Implementation cost: Operational expenses** | **Unit** | **Estimates** |
| $N_9$ | Funds allocated to the district for the transportation of DDT/PHC in the district (assumed per 60-day spray period) | Rs./ PHC | 3500 (2010 VL budget of Bihar [42]) |
| $N_{10}$ | Funds allocated to the district as office expense per squad in the district (assumed per 60-day spray period) | Rs./squad | 250 (2010 VL budget of Bihar [42]) |
| $N_{11}$ | Funds allocated as contingency/squad (assumed per 60-day spray period) | Rs./ squad | 250 (2010 VL budget of Bihar [42]) |
| $N_{12}$ | Total funds allocated per district for general vehicle mobility/month of spray period | Rs./ month | 20000 (2010 VL budget of Bihar [42]) |
| $N_{13}$ | Funds allocated per district for PHC vehicle mobility/day/PHC for the 60-day spray period | Rs./day/PHC | 650 (2010 VL budget of Bihar [42]) |
| $N_{14}$ | Funds allocated for supervision/affected PHC (assumed per 60-day spray period) | Rs./affected PHC | 2000 (2010 VL budget of Bihar [42]) |
| $N_{15}$ | Funds allocated for education and communication activities per affected PHC (assumed per 60-day spray period) | Rs./affected PHC | 2000 (2010 VL budget of Bihar [42]) |

Exchange rate in the year 2000 for table 3.6 was assumed as: 1 USD = INR 45. [54]

The spray campaign cost equation is derived below, assuming that insecticide is sprayed only once per year rather than the existing policy of spraying twice per year in Bihar.

The total cost of executing the insecticide intervention program is a sum of the material (for a given insecticide) and implementation costs from Table 3.6, and is expressed as

$$\tilde{C}(x,y) = N_h[N_1 x + N_2N_3N_5N_7 + N_2N_4N_6N_7 + N_8N_2 + N_{10}N_2 + N_{11}N_2] + N_1N_c y + g[N_9 + 60N_{13} + N_{14} + N_{15}] + [2N_{12}] \quad (3.5)$$

The decision variable $y$ was introduced to obtain the amount of insecticide allocated to the cattle population. Total spray campaign cost can be simplified to

$$\widetilde{C}(x,y) = N_hN_1x + N_cN_1y + \widetilde{C_{Im}} \quad (3.6)$$

The first two terms of equation 3.6 can be interpreted as: the material cost of the insecticide allocated to houses ($N_hN_1x$), to cattle sheds ($N_1N_cy$) respectively. The third term is the spray campaign's implementation cost ($\widetilde{C_{Im}}$), which comprises field supervisors and spray worker's wages, the repair and purchase of spray equipment, office expenses, a contingency, insecticide transportation and storage, supervisors' travel allowances, and public awareness activities (Table 3.6).

The third component of the linear optimization model comprise of the remaining constraints (inequalities 3.7, 3.8, 3.9, 3.10 and 3.13), which are related to insecticide consumption and sites sprayed at, under the insecticide intervention program. It is assumed that the available budget is not enough to spray all houses and cattle sheds (resource-limited cases). The number of houses (cattle sheds) sprayed at, can vary between 0 and H (K), so the constraints for $H_s$ and $K_s$ can be written as

$$0 \leq H_s \leq H \tag{3.7}$$

and

$$0 \leq K_s \leq K \tag{3.8}$$

respectively.

The number of houses and cattle sheds that can be covered during the spray campaign are expressed as

$$H_s = \left(\frac{N_h x}{I_h}\right) \tag{3.9}$$

and

$$K_s = \left(\frac{N_c y}{I_k}\right) \tag{3.10}$$

respectively.

When all sites are sprayed with insecticide, equations 3.11 and 3.12 give the maximum values for the decision variables $x$ and $y$ in terms of demographic parameters:

$$x_{max} = \frac{I_h H}{N_h} \tag{3.11}$$

and

$$y_{max} = \frac{I_k K}{N_c} \tag{3.12}$$

The non-negativity constraints for the two decision variables give

$$x, y \geq 0 \tag{3.13}$$

All optimization models assume that there are only two types of sites to be sprayed at: human dwellings and cattle sheds (mixed dwellings do not exist). The other assumptions made are: the insecticide necessary to spray one cattle shed is assumed to be half of that required to cover one house; cattle are the only non-human hosts that sandflies bite; all houses are assumed to have an average area of 200 m$^2$ based on a previous estimate from Walker [49]. Based on the assumptions made and the three above-described components, the 2 dimensional linear optimization model formulation can be described as:

Maximize,

$$d_v = Q\,[i(\tau)]\left(\frac{H_S}{H}\right) + (1 - Q)[o(\tau)]\left(\frac{K_S}{K}\right) \tag{3.4}$$

Subject to,

$$\widetilde{C}(x, y) = N_h N_1 x + N_c N_1 y + \widetilde{C_{Im}} \leq \widetilde{C_{UB}} \tag{3.6}$$

$$0 \leq H_s \leq H \tag{3.7}$$

$$0 \leq K_s \leq K \tag{3.8}$$

$$H_s = \left(\frac{N_h x}{I_h}\right) \tag{3.9}$$

$$K_s = \left(\frac{N_c y}{I_k}\right) \quad (3.10)$$

$$x, y \geq 0 \quad (3.13)$$

The linear optimization model formulation in terms of $x$ and $y$ only (by substituting equations 3.9 and 3.10 in 3.4) is described below.

Maximize,

$$d_v(x, y) = \frac{Q\ i(\tau) N_h}{H\ I_h}\ x + \frac{(1-Q)[o(\tau)]\ N_c}{K I_k}\ y \quad (3.14)$$

Subject to,

$$\widetilde{C}(x, y) = N_h N_1 x\ +\ N_1 N_c y\ +\ \widetilde{C_{Im}} \leq\ \widetilde{C_{UB}} \quad (3.6)$$

$$0 \leq x \leq \frac{I_h\, H}{N_h} \quad (3.15)$$

$$0 \leq y \leq \frac{I_k\, K}{N_c} \quad (3.16)$$

### 3.2.2 Multi-dimensional Linear Optimization Model

Considering separate decision variables ($x$ and $y$) for each of the 31 VL affected districts in Bihar state, the above linear optimization problem can be re-formulated as a 62 dimensional linear optimization problem. (Note: The single budget constraint for entire Bihar state is $\widetilde{C_{UB}}$, same as the above 2 dimensional linear optimization model). To ensure that each district is allocated a minimum insecticide amount as per the present allocation policy as mentioned in the

W.H.O. report [7], the lower bound on all decision variables $H_{si}$ *(,∀ i = 1,..,31)* has been taken as $\frac{0.0375\, N_{hAffi}}{I_h}$. The spray campaign implementation cost for district $i$, in terms of number of affected humans and government clinics from 2010 VL budget of Bihar [42], is expressed as

$$\widetilde{C_{Imi}}\,(N_{hAffi}, g_i) = 2.50525\, N_{hAffi} + 46500\, g_i + 40000 \tag{3.17}$$

As per the 2010 VL budget of Bihar [42], the implementation cost is an addition of three components. The first component is the money allocated per affected person in the population for: spray team supervisor's salary, spray worker's salary, repair and purchase of spray equipment, office expenses and contingency allowance. The second component is the money allocated per government clinic for: insecticide transportation, mobility of vehicles for supervision, and activities related to information, education and communication. The third component is a constant amount of money allocated for mobility of vehicles to conduct miscellaneous activities.

The 62 dimensional linear optimization model formulation can be presented as

Maximize

$$\left(\frac{i(\tau)}{I_h}\right)\sum_{i=1}^{31} Q_i \left(\frac{N_{hActi}}{H_i}\right) x_i \;+ \left(\frac{o(\tau)}{I_k}\right)\sum_{i=1}^{31} (1 - Q_i)\left(\frac{N_{ci}}{K_i}\right) y_i \tag{3.18}$$

Subject to

$$N_1 \sum_{i=1}^{31} N_{hActi}\; x_i \;+\; N_1 \sum_{i=1}^{31} N_{ci}\; y_i \;+ \widetilde{C_{Imi}}\left(N_{hAffi}, g_i\right) \le\; \widetilde{C_{UB}} \qquad ,\forall\, i = 1,\ldots,31 \tag{3.19}$$

$$\frac{0.0375\, N_{hAffi}}{I_h} \le H_{si} \le\; H_i \qquad ,\forall\, i = 1,\ldots,31 \tag{3.20}$$

$$0 \le K_{si} \le\; K_i \qquad ,\forall\, i = 1,\ldots,31 \tag{3.21}$$

$$H_{si} = \left(\frac{N_{hActi}\, x_i}{I_h}\right) \qquad , \forall i = 1, \ldots, 31 \tag{3.22}$$

$$K_{si} = \left(\frac{N_{ci}\, y_i}{I_k}\right) \qquad , \forall i = 1, \ldots, 31 \tag{3.23}$$

$$x_i, y_i \geq 0 \qquad , \forall i = 1, \ldots, 31 \tag{3.24}$$

### 3.2.3 Differential Equations Model with Insecticide Intervention

Some assumptions were made to simplify the original transmission dynamics model developed by Mubayi et al. [33]. The insecticide's lethal and repellent effects were incorporated in the simplified transmission dynamics model. Table 3.7 describes the state variables in the simplified transmission dynamics model (Figure 3.2).

Table 3.7. State variables in the simplified model.

| **State variables** | **Definition** |
|---|---|
| S(t) | Number of susceptible humans |
| I(t) | Number of infected humans |
| G(t) | Number of infected humans undergoing treatment at public health facilities |
| T(t) | Number of infected humans undergoing treatment at private health facilities |
| R(t) | Number of recovered humans |
| $N_h$(t) | Total human population size = S(t) + I(t) + G(t) + T(t) + R(t) |
| X(t) | Number of susceptible sandflies |
| Z(t) | Number of infected sandflies |
| $N_v$(t) | Total sandfly population size = X(t) + Z(t) |

"$t$" denotes the $t^{th}$ day of the simulation run

The simplified model consists of 5 humans (host) compartments and 2 sandfly (vector) compartments. The simplified transmission dynamics model uses parameters defined in Table 3.2, Table 3.4 and Table 3.8 below.

Table 3.8. Transmission dynamics model parameter symbols, definitions, estimates, and their corresponding references.

| **Parameter** | **Definition** | **Estimate: Mean (S.D.) (C.I. range)** | **Reference** |
|---|---|---|---|
| $p$ | Proportion of infected humans choosing to seek treatment in public health clinics | $7.37\ \mathrm{e}-01$ | Mubayi et al. [33] |
| $\eta$ | Treatment seeking rate per capita | $8.77\ \mathrm{e}-03$/day (s.d.=$9.38\ e-03$/day) | Sud et al. [55] |
| $\alpha_1$ | Per capita recovery rate for G class individuals | $4.39\ e-02$/day | Mubayi et al. [33] |
| $\alpha_2$ | Per capita recovery rate for T class individuals | $3.27\ e-02$/day | Mubayi et al. [33] |
| $\delta_1$ | Disease related mortality in I class | $1.33\ \mathrm{e}-03$/day | Zerpa et al. [56] |
| $\delta_2$ | Disease related mortality in treatment (G and T) classes | $9.48\ \mathrm{e}-05$/day | Bora [3] |
| $\mu_h$ | Natural mortality rate per capita in humans | $4.6\ e-05/\mathrm{day}$ | Mubayi et al. [33] |
| $\beta_{hv}$ | Transmission probability per bite from infected vector to susceptible human | 0.74 (0.27–1.00) | Wonham et al. [28] |
| $\beta_{vh}$ | Transmission probability per bite from infected human to susceptible vector | 0.69(0.23–1.00) | Wonham et al. [28] |
| $C$ | Mean bite rate per sandfly | 0.09 (0.03–0.16) | Wonham et al. [57] |
| $C_{t0r}$ | Initial efficacy of DDT's repellent effect (both in houses and cattle sheds) | 0.81 (95% CI: 0.763-0.858) | Courtenay et al. [27] |
| $\widetilde{C_{Im}}$ | Spray campaign implementation cost | Rs. 96.80 million | Bihar's budget 2012-2013 [41] |

Figure 3.2 presents the simplified vector-host model, which shows the transmission of VL between the vector and host populations**.**

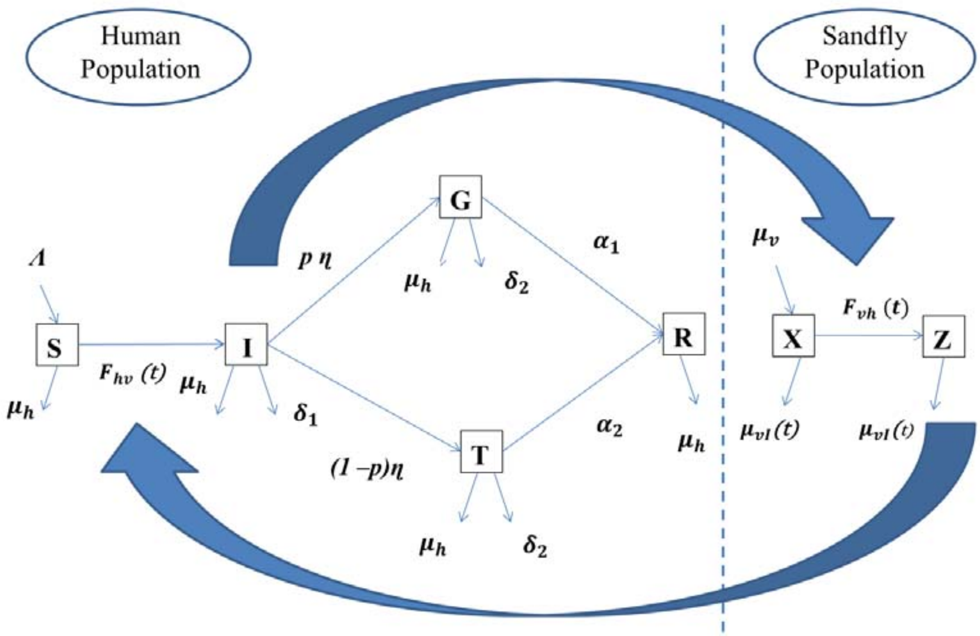


Figure 3.2. Simplified VL transmission dynamics model.

Criss-cross (reciprocal) infection takes place between the sandfly and human populations, when infected sandflies bite susceptible humans and susceptible sandflies bite infected humans. The main difference between the simplified model developed in this dissertation and the model developed by Mubayi et al. [33] is that, their model does not include any insecticide effects whereas our model incorporates both lethal and repellent effects of the insecticide. There are separate compartments for humans and sandflies in (latent) development stages of VL, in the model developed by Mubayi et al. [33]. These latent stages are excluded in our simplified model. Unlike the original model, our simplified model includes the insecticide-induced death rate of sandflies. The original model had a constant sandfly population. Unlike the original model which included only the natural birth and death rates in humans (assumption of constant human population), our simplified model includes the human recruitment rate and VL-induced deaths.

Assumptions in formulating the simplified vector-host model:

Some general assumptions include: mixed dwellings do not exist; only houses and cattle sheds need to be sprayed with insecticide, as sandflies are assumed to feed only on human and cattle blood. As some sandfly bites are deflected to the cattle populations, a constant cattle population is also incorporated in the model. The decay of insecticide's lethal effect is modeled using the same exponential decay function, as in the linear optimization model. Every morning sandflies are assumed to disperse from a common resting place, travelling towards human or cattle dwellings in search of blood (Figure 3.3).

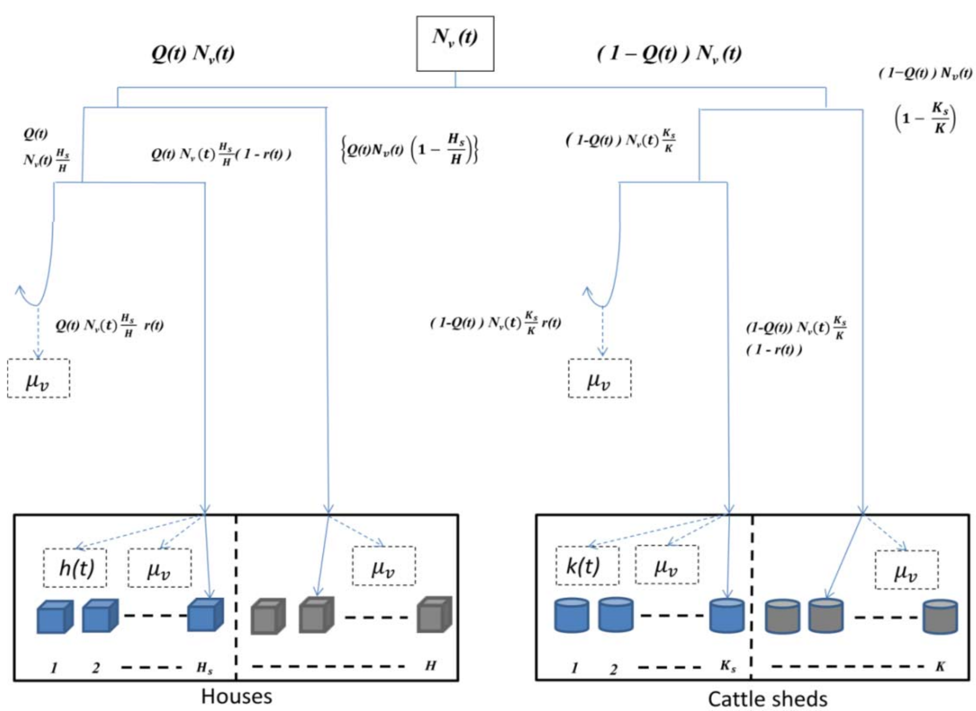


Figure 3.3. Assumed daily sandfly population break down.

In Figure 3.3 the dotted lines denote the cause of death for a given proportion of the population. The dotted arrows & rectangles indicate the death rate for a proportion of sandfly population. Each vector population either visits a sprayed or unsprayed site. Some sandflies do not land and fly back (Figure 3.3: curved arrow) to the common resting place because of the insecticide's repellent effect. As these flies are not exposed to insecticide's lethal effect, they die at a natural death rate (Figure 3.3: death rates in dotted boxes). Out of the sandfly population proportions that visit sprayed sites, some die due to insecticide exposure, whilst others die due to natural causes. The sandflies that land on unsprayed sites die at a natural death rate. At the end of each day, the sandflies that remain alive or get repelled, fly back to the same common resting place. On each day of the simulation run, this process repeats.

Although the public health department of Bihar sprays twice yearly as per 2010 VL budget of Bihar [42], only one spray round (on day $\gamma$) is assumed in the simplified transmission dynamics model. A female sandfly might bite only after reaching sexual maturity and a sandfly reaches sexual maturity, one day after emerging from an egg as quoted by Young and Duncan [58]. Our simplified model assumes that (all) sandflies bite on each day of their life. Since natural sandfly birth and death rates do not differ statistically depending on the blood source (human or bovine) they feed on as reported by Harre et al. [59]; cattle are assumed as being equivalent to humans in this regard. The simplified transmission dynamics model is mathematically represented as a set of coupled differential equations (referred to as differential equations model hereafter). In the differential equations model, the human visitation proportion is a function of time and is expressed as

$$Q(t) = \frac{a_h \; N_h(t)}{a_h \, N_h(t) + a_c \, N_c} \tag{3.25}$$

If no human or cattle are present at a site visited by sandflies, then they do not get a blood meal on that day and fly back to their common resting place. The probability of a sandfly biting a human from any compartment is directly proportional to the proportion of the human population present in that compartment. The human and sandfly populations are assumed to be homogeneously mixed. Each sandfly landing on a human or cattle is assumed to results in a bite. Either a natural death or a VL-induced death can occur to a human. Under these assumptions, the lethal and repellent effects are incorporated in the simplified model.

<u>Incorporating insecticide's lethal effect:</u> Equations 3.26 and 3.27 model the insecticide's lethal effect decay (same as the linear model).

$$i(t) = \begin{cases} 0, \ 0 \leq t < \gamma \\ C_{t0}\, e^{-b_1 (t-\gamma)}, \ \gamma \leq t \leq t_{final} \end{cases} \tag{3.26}$$

and

$$o(t) = \begin{cases} 0, \ 0 \leq t < \gamma \\ C_{t0}\, e^{-b_2 (t-\gamma)}, \ \gamma \leq t \leq t_{final} \end{cases} \tag{3.27}$$

respectively. The units of both $i(t)$ and $o(t)$ are the number of sandflies killed/(sandfly·day).

Before insecticide is applied, the sandfly population is given by the instantaneous value from the solution of the system of coupled differential equations. After insecticide application, the sandfly population reduces as more sandflies are born only to those that survived until the end of the previous day. Table 3.9 tabulates the various possible causes of sandfly deaths on any day.

Table 3.9. Causes of sandfly deaths in houses and cattle sheds.

| | **Cause of death after spraying** | **Formula** |
|---|---|---|
| 1 | Natural deaths of sandflies repelled from sprayed houses | $Q(t)N_v(t)\left(\frac{H_s}{H}\right) r(t)\,(\mu_v)$ |
| 2 | Insecticide induced and natural deaths of sandflies visiting sprayed houses | $Q(t)\,N_v(t)\left(\frac{H_s}{H}\right)[1-r(t)]\,[i(t)+\mu_v]$ |
| 3 | Natural deaths of sandflies visiting unsprayed houses | $Q(t)\,N_v(t)\left(1-\frac{H_s}{H}\right)(\mu_v)$ |
| 4 | Natural deaths of sandflies repelled from sprayed cattle sheds | $(1-Q(t))N_v(t)\left(\frac{K_s}{K}\right) r(t)(\mu_v)$ |
| 5 | Insecticide induced and natural deaths of sandflies visiting sprayed cattle sheds | $(1-Q(t))N_v(t)\left(\frac{K_s}{K}\right)[1-r(t)][o(t)+\mu_v]$ |
| 6 | Natural deaths of sandflies visiting unsprayed cattle sheds | $(1-Q(t))N_v(t)\left(1-\frac{K_s}{K}\right)[\mu_v]$ |

The total sandfly death rate at different (sprayed and unsprayed) sites can be derived by adding all sandfly deaths listed in Table 3.2, and is expressed as

$$\mu_{vI}(t) = [1-r(t)]\left[Q(t)\frac{H_s}{H}\; i(t) + \left(1-Q(t)\right)\frac{K_s}{K} o(t)\right] + \mu_v \tag{3.28}$$

The total sandfly death rate can be expressed as a sum of insecticide induced death rate ($d_{ODE}$) and natural death rate ($\mu_v$).

$$d_{ODE} = [1-r(t)]\left[Q(t)\frac{H_s}{H}\; i(t) + \left(1-Q(t)\right)\frac{K_s}{K} o(t)\right] \tag{3.29}$$

Incorporating insecticide's repellent effect: The insecticide's repellent effect is also assumed to decay exponentially with time as modeled by Courtenay et al. [27]. After insecticide application, the proportion of sandflies repelled at time *t*, is expressed as

$$r(t) = \begin{cases} 0, \ 0 \le t < \gamma \\ C_{t0r}\, e^{-b_3\,(t-\gamma)}, \ \gamma \le t \le t_{final} \end{cases} \tag{3.30}$$

where the unit of $r(t)$ is: reduced number of sandfly landings/(sandfly·day).

Both susceptible and infected sandfly populations follow the daily distribution shown in Figure 3.3. Therefore, the total number of susceptible and infected sandflies visiting houses sum to

$$Q(t)X(t)\ \left(1 - \frac{H_s}{H} r(t)\right) \tag{3.31}$$

and

$$Q(t)\, Z(t) \left[1 - \frac{H_s}{H} r(t)\right] \tag{3.32}$$

respectively.

The disease transmission terms under reservoir frequency dependent assumption as described by Wonham et al. [28], are the rates at which infected humans and infected sandflies are generated and can be expressed as

$$C\, \beta_{hv}\, Q(t)Z(t) \left[1 - \frac{H_s}{H} r(t)\right] \frac{S(t)}{N_h(t)} = F_{hv}(t)\, S(t) \tag{3.33}$$

and

$$C\,\beta_{vh}\,Q(t)X(t)\left[1-\frac{H_s}{H}r(t)\right]\frac{I(t)}{N_h(t)} = F_{vh}(t)\,X(t) \qquad (3.34)$$

respectively.

Where, $F_{hv}(t)$ and $F_{vh}(t)$ denote the forces of infection on susceptible humans and susceptible sandflies, respectively. The set of coupled ordinary differential equations representing the simplified transmission model including both insecticide effects is:

$$\frac{dS}{dt} = \Lambda - F_{hv}(t)\,S(t) - \mu_h S(t) \qquad (3.35)$$

$$\frac{dI}{dt} = F_{hv}(t)\,S(t) - (\delta_1 + \eta + \mu_h)\,I(t) \qquad (3.36)$$

$$\frac{dG}{dt} = p\,\eta\,I(t) - (\delta_2 + \alpha_1 + \mu_h)\,G(t) \qquad (3.37)$$

$$\frac{dT}{dt} = (1-p)\,\eta\,I(t) - (\delta_2 + \alpha_2 + \mu_h)\,T(t) \qquad (3.38)$$

$$\frac{dR}{dt} = \alpha_1\,G(t) + \alpha_2\,T(t) - \mu_h R(t) \qquad (3.39)$$

$$\frac{dN_h}{dt} = \Lambda - \delta_1 I(t) - \delta_2(G(t) + T(t)) - \mu_h\,N_h(t) \qquad (3.40)$$

$$\frac{dX}{dt} = \mu_v N_v(t) - F_{vh}(t)\,X(t) - \mu_{vI}(t)X(t) \qquad (3.41)$$

$$\frac{dZ}{dt} = F_{vh}(t)\,X(t) - \mu_{vI}(t)\,Z(t) \qquad (3.42)$$

$$\frac{d\,N_v(t)}{dt} = [r(t)-1]\left[Q\,\frac{H_s}{H}\;i(t) + (1-Q)\frac{K_s}{K}o(t)\right](N_v(t)) \tag{3.43}$$

Assumed initial conditions for humans: $N_h(0) = N_{hh} = 87716860$ (from 2011 census of India [52]), S(0) = 0.9 $N_{hh}$ ; I(0) = 0.07 $N_{hh}$ ; G(0) = 0.0005 $N_{hh}$ ; T(0) = 0.0015 $N_{hh}$ ; R(0) = 0.178 $N_{hh}$

Assumed initial conditions for sandflies: $N_v(0) = N_{vv} = 4\,N_{hh}$ ; X(0) = 0.7 $N_{vv}$ ; Z(0) = 0.3 $N_{vv}$

The above differential equations model can be simulated to obtain the number of human VL infections, over a time horizon. The difference between the number of human infections when the model is simulated without insecticide spray and with a certain level of spray is the cumulative number of prevented infections (Unit: person-days averted). Mathematically, it can be expressed as $a(H_s, K_s, t)$

= cumulative infection cases without intervention – cumulative infection cases with intervention

$$= \int_{t_0}^{t_{final}} C\beta_{hv}Q(t)Z(t)\,\frac{S(t)}{N_h(t)}\,dt - \int_{t_0}^{t_{final}} C\beta_{hv}Q(t)\,Z(t)\left[1-\frac{H_s}{H}r(t)\right]\frac{S(t)}{N_h(t)}dt$$

$$= \int_{t_0}^{t_{final}} \phi_0(0,0,t)\,dt - \int_{t_0}^{t_{final}} \phi(H_s, K_s, t)\,dt \tag{3.44}$$

### 3.2.4 Two-dimensional Nonlinear Optimization Model

The function $a(H_s, K_s) : \mathbb{Z}_+^2 \to \mathbb{R}_+^1$ (plotted in 0, for a given $t_{final}$) is the objective function the nonlinear optimization model aims to maximize.

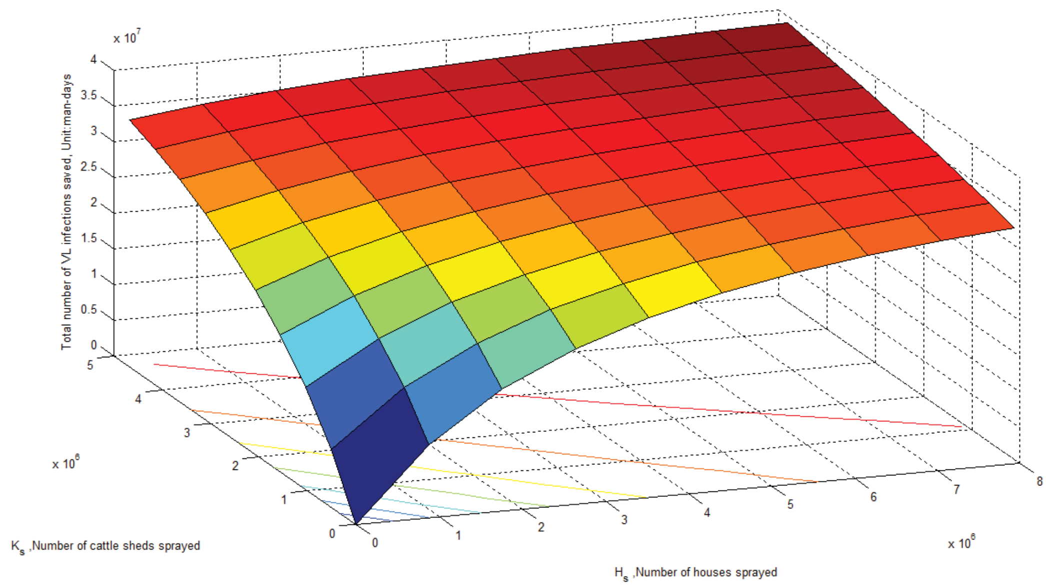


Figure 3.4. $\mathrm{a}(\mathrm{H}_s, \mathrm{K}_s)$ versus levels of spray coverage.

The graph in Figure 3.4 is generated for a 90-day time horizon, using the data of Bihar state. Levels of spray coverage denote the different number of houses ($H_s$) and cattle sheds ($K_s$) sprayed with insecticide. The insecticide material cost to spray in $H_s$ houses and $K_s$ cattle sheds, can be expressed as $N_1\, I_h\, H_s$ (Rs.) and $N_1\, I_k\, K_s$ (Rs.), respectively. The total insecticide spray campaign cost ($\widetilde{C}(H_s, K_s)$) is obtained by adding the insecticide material cost and implementation cost ($\widetilde{C_{Im}}$). The budget constraint of the nonlinear optimization model is obtained by taking $\tilde{C}(H_s, K_s)$ less than or equal to the available state budget ($\widetilde{C_{UB}}$). Using the objective function ($a(H_s, K_s)$ obtained from the differential equations model, the nonlinear optimization model formulation can be described as:

$$\underset{H_s,\, K_s}{\text{Max}} \quad a(H_s, K_s) \tag{3.45}$$

Subject to

$$\widetilde{C}(H_s, K_s) = N_1 I_h\ H_s + \ N_1 I_k\ K_s \ + \ \widetilde{C_{Im}} \leq \ \widetilde{C_{UB}} \tag{3.46}$$

$$0 \leq H_s \leq H \tag{3.7}$$

$$0 \leq K_s \leq K \tag{3.8}$$

In terms of the decision variables $x$ and $y$, the above model can be re-formulated as

$$\underset{H_S,\, K_S}{\text{Max}} \quad \alpha(H_s, K_s) \tag{3.47}$$

Subject to,

$$\widetilde{C}(x, y) = N_h N_1 x \ + \ N_c N_1 y \ + \ \widetilde{C_{Im}} \leq \ \widetilde{C_{UB}} \tag{3.46}$$

$$0 \leq H_s \leq H \tag{3.7}$$

$$H_s(\gamma) = \left(\frac{N_h(\gamma)x}{I_h}\right) \tag{3.48}$$

$$0 \leq K_s \leq K \tag{3.8}$$

$$K_s = \left(\frac{N_c y}{I_k}\right) \tag{3.10}$$

$$x, y \geq 0 \tag{3.13}$$

The optimal number of houses recommended for spraying is a function of time ($\gamma$). To obtain kilogram per person $x$ the actual human population at the time of spray ($\gamma$) can be used.

### 3.2.5 Multi-dimensional Nonlinear Optimization Model

The two-dimensional nonlinear optimization model has only two decision variables: number of houses ( $H_s$) and cattle sheds ( $K_s$), respectively, to be sprayed with insecticide in Bihar state. The upper bound on the budget constraint ($\widetilde{C_{UB}}$) is the amount of money available to conduct the spray campaign in all 31 VL affected districts of Bihar state. If the number of houses and cattle sheds to be sprayed, in individual districts are considered as the decision variables of the model, a 62 dimensional optimization model is obtained. The lower bound on $H_{si}$ for each district is chosen as $\left(\frac{0.0375\ N_{hAffi}}{I_h}\right)$; so each district is allocated a minimum amount of insecticide as per present allocation policy from 2010-2011 budget document [42].

To avoid any political fallback, the minimum number of houses that will be sprayed with insecticide is computed using the present insecticide allocation policy in Bihar. We assume the available budget as: Rs. 220.48 million (from Bihar's budget 2012-2013 [41]). This research study models an expansionary policy. It assumes that the all the money left after subtracting the implementation cost (equation 3.17 from 2010-2011 budget document [42]) from the available budget is used for buying insecticide material. This insecticide material is first consumed for spraying in minimum number of houses (lower bound of $H_s$) and the surplus money is used for optimizing. In effect, a lower implementation cost was assumed, so the surplus money can be used for buying extra insecticide material for optimizing. The 62 dimensional nonlinear model formulation is described below:

$$\underset{H_s,\,K_s}{Max} \sum_{\boldsymbol{i=1}}^{\boldsymbol{31}} \left( \int_{t_0}^{t_{final}} \phi_0(N_{hi}, N_{ci}, H_i, t)\, dt \ - \int_{t_0}^{t_{final}} \phi\, (H_{si}, K_{si}, N_{hi}, N_{ci}, H_i, t)\, dt \right) \tag{3.49}$$

Subject to

$$N_1 I_h \sum_{i=1}^{31} H_{si} + N_1 I_k \sum_{i=1}^{31} K_{si} + \widetilde{C_{Imi}}\left(N_{hAffi}, g_i\right) \leq \widetilde{C_{UB}} \quad , \forall\, i = 1, \dots, 31 \tag{3.50}$$

$$\frac{0.0375\, N_{hAffi}}{I_h} \leq H_{si} \leq H_i \quad , \ \forall\, i = 1, \dots, 31 \tag{3.51}$$

$$H_{si}(\gamma) = \left(\frac{N_{hi}(\gamma) x_i}{I_h}\right) \quad , \quad \forall\, i = 1, \dots, 31 \tag{3.52}$$

$$0 \leq K_{si} \leq K_i \quad , \ \forall\, i = 1, \dots, 31 \tag{3.53}$$

$$K_{si} = \left(\frac{N_{ci}\, y_i}{I_k}\right) \quad , \ \forall\, i = 1, \dots, 31 \tag{3.54}$$

$$x_i, y_i \geq 0 \quad , \ \forall\, i = 1, \dots, 31 \tag{3.55}$$

Where, $\widetilde{C_{UB}}$ is the single budget constraint for Bihar state. Here, Rs. 96.8 million is the cost of implementing the spray campaign in all 31 districts. To compute kilogram per person in each district ($x_i$) use actual human population of that district at the time of spray ($N_{hi}(\gamma)$).

## 3.3 Analysis of Linear Optimization Model

The closed form solution for the 2 dimensional optimization model is presented in this section.

### 3.3.1 Optimal Solution for Two-dimensional Linear Model

The steps towards finding possible solutions of the model are described in this section. The optimal values of per-capita insecticide allocated at the two sites (decision variables $x^*$ and $y^*$) are the optimal solution of the model at which the maximum insecticide-induced death rate is achieved. Depending on the conditions based on the model parameters (Table 3.10), an optimal solution can occur at one of the four distinct points in the feasible domain of the model. The feasible domain of the insecticide-induced death rate (objective function) $d_v(x, y)$ is a 2-D region defined by constraints 3.6, 3.7, 3.8, 3.9, 3.10 and 3.13. $d_{vA}$ represents the value of the function at point A in the domain. The vertical axis of the feasible domain represents the per-capita amount of insecticide allocated at cattle sites ($y$), and the horizontal axis represents the per-capita amount of insecticide allocated at house sites ($x$).

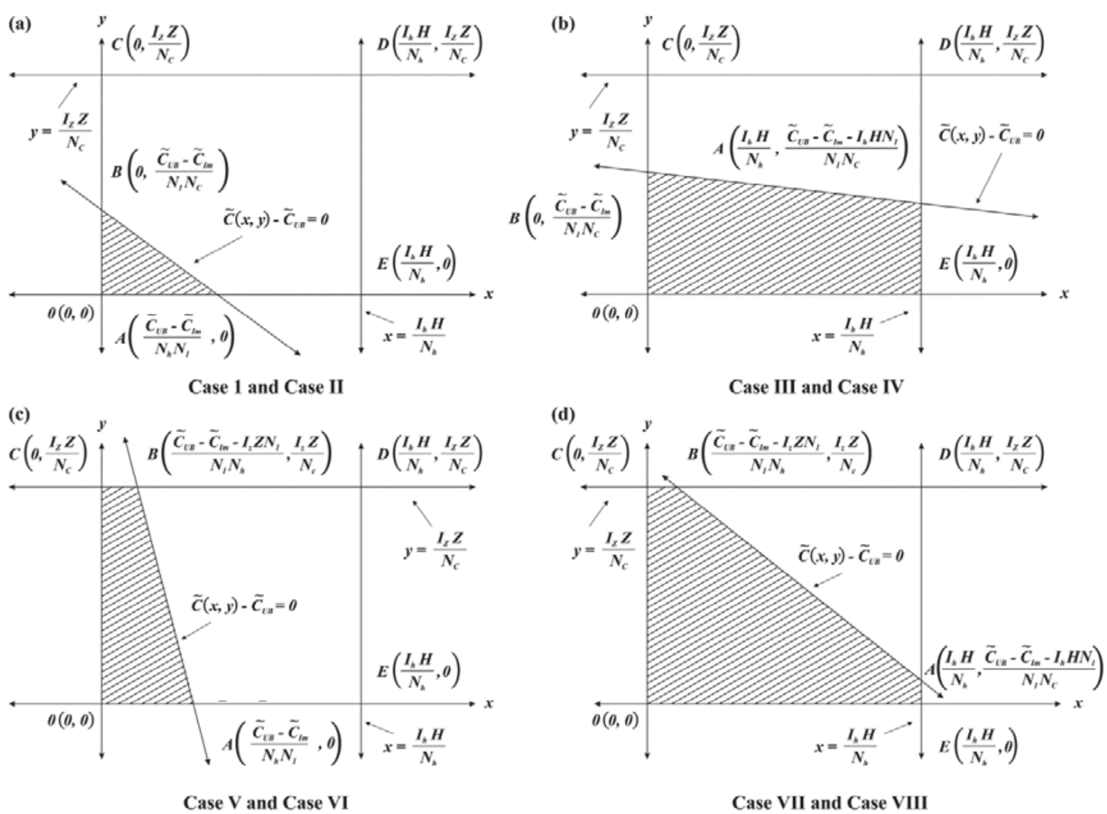


Figure 3.5. The feasible domain of the optimization model

The various possible cases in Figure 3.5 are described as: (a) Case I (Case II) arises when constraint 3.6 intersects with constraint 3.13 (between OC and OE) resulting in point A (point B) as an optimal solution. (b) Case III (Case IV) arises when constraint 3.6 intersects with constraint 3.13 and constraint 3.7 (between OC and DE) resulting in point A (point B) as an optimal solution. (c) Case V (Case VI) arises when constraint 3.6 intersects with constraint 3.13 and constraint 3.8 (between OE and CD) resulting in point A (point B) as an optimal solution. (d) Case VII (Case VIII) arises when constraint 3.6 intersects with constraint 3.7 and constraint 3.8 (between DE and CD) resulting in point A (point B) an optimal solution.

Corner points O, A, and B form the feasible domain in Figure 3.5 (a) which illustrates Cases I and II (details in Figure 3.5 (a) caption). In cases I and II, the optimal solution can exist at either point A or point B. It can be seen that the total insecticide-induced death rate at point A is always less than or equal to the corresponding value at point E, implying, $d_{vA} \leq d_{vE}$ (substituting the points A and E into equation 3.4) or

$$\widetilde{C_{UB}} - \widetilde{C_{Im}} \leq I_h H N_1 \tag{3.56}$$

Similarly, the total insecticide-induced death rate at point B is always less than or equal to that at point C, implying, $d_{vB} \leq d_{vC}$, which simplifies to

$$\widetilde{C_{UB}} - \widetilde{C_{Im}} \leq I_k \, K \, N_1 \tag{3.57}$$

<u>Case I (if the optimal solution occurs at point A, Figure 3.5 (a)):</u> Since $d_{vB} < d_{vA}$, which simplifies to

$$\frac{(1-Q)\ o(\tau)}{I_k\ K} < \frac{Q\ i(\tau)}{I_h H} \tag{3.58}$$

Note: the interpretation of the left-hand side of inequality 3.57 can be written as the ratio of insecticide-induced death rate achieved ($(1 - Q)\ i(\tau)$) to insecticide amount consumed in cattle sheds ($I_k K$). Similarly, the right-hand side of inequality 3.57 can be understood as the same ratio for house sites. Hence, inequality 3.57 shows that if the optimal solution occurs at point A, then the insecticide-induced death rate per kilogram of insecticide consumed for cattle sheds is smaller than the corresponding ratio for houses. Inequality 3.57 simplifies to

$$(1 - Q)\ o(\tau)\ I_h H\ <\ Q\ i(\tau)\ I_k K \tag{3.59}$$

In Case I, the optimal solution occurs at point A ($d_{vB} < d_{vA} \leq\ d_{vE}$).

<u>Case II (if the optimal solution occurs at point B, Figure 3.5 (a)):</u> This implies $d_{vA} < d_{vB}$, which gives

$$Q\ i(\tau) I_k K < (1 - Q) o(\tau) I_h H \tag{3.60}$$

In Case II, the optimal solution occurs at point B ($d_{vA} < d_{vB} \leq d_{vC}$).

Figure 3.5 (b) shows Cases III and IV (details in Figure 3.5 (b) caption). The optimal solution in these cases can occur at either point A or point B, and it is simple to see $d_{vE} < d_{vA} \leq d_{vD}$ , implying,

$$I_h H N_1 < \widetilde{C_{UB}} -\ \widetilde{C_{Im}} \leq\ I_h\ H\ N_1 + I_k\ K\ N_1 \tag{3.61}$$

In cases III and IV, $d_{vB} \leq d_{vC}$ satisfies obviously, and it simplifies to inequality 3.56.

Case III (if the optimal solution occurs at point A, Figure 3.5 (b)): In Case III, $d_{vB} < d_{vA}$ (inequality 3.58) and $d_{vE} < d_{vA} \leq d_{vD}$ (inequality 3.60) are easy to see. Hence, the optimal solution will occur at point A, as illustrated in Figure 3.5 (b).

Case IV (if the optimal solution occurs at point B, Figure 3.5 (b)): In Case IV, $d_{vA} < d_{vB}$ (inequality 3.59) and $d_{vB} \leq d_{vC}$ (inequality 3.56) both hold true. Hence, the optimal solution can occur at point B, as illustrated in Figure 3.5 (b).

Figure 3.5 (c) shows Cases V and VI (details in Figure 3.5 (c) caption). For both these cases, the optimal solution can occur only at point A or at point B. $d_{vA} \leq d_{vE}$ and $d_{vC} < d_{vB} \leq d_{vD}$ follows obviously, which simplifies, respectively, to inequality 3.55 and

$$I_k\ K\ N_1 < \widetilde{C_{UB}} - \widetilde{C_{Im}} \leq I_h\ H\ N_1 + I_k\ K\ N_1 \tag{3.62}$$

Case V (if the optimal solution occurs at point A, Figure 3.5 (c)): In Case V, $d_{vB} < d_{vA}$ (inequality 3.58) and $d_{vA} \leq d_{vE}$ (inequality 3.55) both hold true. Hence, the optimal solution exists at point A.

Case VI (if the optimal solution occurs at point B, Figure 3.5 (c)): In Case VI, $d_{vC} < d_{vB} \leq d_{vD}$ (inequality 3.16) and $d_{vA} < d_{vB}$ (inequality 3.59) hold true. Hence, the optimal solution exists at point B.

Figure 3.5 (d) shows Cases VII and VIII (details in Figure 3.5 (d) caption). The optimal solution in these cases can occur only at point A or at point B. It is obvious that $d_{vC} < d_{vB} \leq d_{vD}$ (inequality 3.61). The total insecticide-induced death rate ($d_v$) at points A, E, and D certainly satisfy the inequality: $d_{vE} < d_{vA} \leq d_{vD}$ (inequality 3.60)

Case VII (if the optimal solution occurs at point A, Figure 3.5 (d)): In Case VII, $d_{vE} < d_{vA} \leq d_{vD}$ (inequality 3.60) and $d_{vB} < d_{vA}$ (inequality 3.58) hold true and hence the optimal solution exists at point A.

Case VIII (if the optimal solution occurs at point B, Figure 3.5 (d)): In Case VIII, $d_{vC} < d_{vB} \leq d_{vD}$ (inequality 3.58) and $d_{vA} < d_{vB}$ (inequality 3.61) hold true. Hence, the optimal solution exists at point B.

Because some of the cases described above give the same optimal points, the results can be summarized as four distinct points (Table 3.10). Each row in Table 3.10 represents one distinct optimal solution, whose existence depends on two conditions (I and II). The optimal solution is a function of user defined inputs: $\tau$ and $\widetilde{C_{UB}}$.

Table 3.10. Optimal solution for the 2 dimensional linear model.

| **Existence** | | **Solution symbol** | $\left(x^*(\tau,\widetilde{C_{UB}}), y^*(\tau,\widetilde{C_{UB}})\right)$ |
|---|---|---|---|
| **Condition I** | **Condition II** | | |
| $\widetilde{C_{UB}} - \widetilde{C_{Im}} \leq Ʞ_1 N_1$ | $\frac{L_2}{Ʞ_2} < \frac{L_1}{Ʞ_1}$ | *FS 1* | $\left(\frac{\widetilde{C_{UB}} - \widetilde{C_{Im}}}{N_1 N_h}, 0\right)$ |
| $K_1 N_1 < \widetilde{C_{UB}} - \widetilde{C_{Im}} \leq N_1(Ʞ_1 + Ʞ_2)$ | $\frac{L_2}{Ʞ_2} < \frac{L_1}{Ʞ_1}$ | *FS 2* | $\left(\frac{Ʞ_1}{N_h}, \frac{\widetilde{C_{UB}} - \widetilde{C_{Im}} - Ʞ_1 N_1}{N_1 N_c}\right)$ |
| $\widetilde{C_{UB}} - \widetilde{C_{Im}} \leq Ʞ_2 N_1$ | $\frac{L_1}{Ʞ_1} < \frac{L_2}{Ʞ_2}$ | *FS 3* | $\left(0, \frac{\widetilde{C_{UB}} - \widetilde{C_{Im}}}{N_1 N_c}\right)$ |
| $K_2 N_1 < \widetilde{C_{UB}} - \widetilde{C_{Im}} \leq N_1(Ʞ_1 + Ʞ_2)$ | $\frac{L_1}{Ʞ_1} < \frac{L_2}{Ʞ_2}$ | *FS 4* | $\left(\frac{\widetilde{C_{UB}} - \widetilde{C_{Im}} - Ʞ_2 N_1}{N_1 N_h}, \frac{Ʞ_2}{N_c}\right)$ |
| $\widetilde{C_{UB}} - \widetilde{C_{Im}} > N_1(Ʞ_1 + Ʞ_2)$ | | *FS 5* | $\left(\frac{Ʞ_1}{N_h}, \frac{Ʞ_2}{N_c}\right)$ |
| $\widetilde{C_{UB}} < \widetilde{C_{Im}}$ | | *INFS* | *Infeasible* |

$L_1 = Q\, i(\tau)$, $L_2 = (1 - Q)\, o(\tau)$, $Ʞ_1 = I_h H$, $Ʞ_2 = I_k K$ ; The solution is valid only when both existence conditions are satisfied. A feasible solution (*FS*) does not exist (*INFS*) if $\widetilde{C_{UB}} < \widetilde{C_{Im}}$.

*FS* 5 (Table 3.10) can be interpreted as: surplus money left over ($\mathrm{Rs.}(\widetilde{C_{UB}} - \widetilde{C_{Im}} - \mathrm{N}_1(\text{ɥ}_1 + \text{ɥ}_2))$) after spraying 100% of both sites (point D in Figure 3.5). Table 3.11 collects the notation used for the optimal solution.

Table 3.11. Notations of the linear model's optimal solution.

| Notation | Explanation |
|---|---|
| FS 1 | Spray the maximum possible number of houses with the given budget |
| FS 2 | Spray 100% of houses and then maximum possible number of cattle sheds with the remaining budget |
| FS 3 | Spray the maximum possible number of cattle sheds with the given budget |
| FS 4 | Spray 100% of cattle sheds and then maximum possible number of houses with the remaining budget |
| FS 5 | Spray 100% of houses and cattle sheds |

### 3.3.2 Benefit to Material Cost Ratio (*BMCR*) Comparison

In this subsection, the simple *BMCR* function is developed, independent of the linear optimization model and is used to analyze preplanned spray coverage options. The linear optimization model maximizes the instantaneous (on the $\tau^{th}$ day after spray) insecticide-induced sandfly death rate using the available budget. Whereas using the *BMCR* approach helps identify the cumulative number of sandflies killed ("benefit") per unit material cost, until the $\tau^{th}$ day post spray. The optimization model assumes a constant sandfly populaiton $N_v$, in contrast the *BMCR* assumes exponentially decaying sandfly population.

The benefit in houses and cattle sheds $\tau$ days after spraying depends on $Q, H_s, K_s, i(\tau),$ and $o(\tau)$. The amount of insecticide consumed for spraying $H_s$ houses and $K_s$ cattle sheds is Rs. $I_h H_s$ and Rs. $I_k\, K_s$, respectively. The cost of insecticide material consumed to spray in $H_s$ houses and $K_s$ cattle sheds can be expressed as (Rs.) $N_1\, I_h\, H_s$ and (Rs.) $N_1\, I_k\, K_s$, respectively. Two contrasting extreme spray coverage options ($O_h$ and $O_k$) are compared with each other using *BMCR* function. $O_k$ and $O_h$ denote the options of spraying insecticide only in

100% cattle sheds ($O_k: H_{s2} = 0, K_{s2} = K$) and only in 100% houses ($O_h: H_{s1} = H, K_{s1} = 0$), respectively.

If $H_{s1}$ houses are sprayed, (using equation 3.4)

$$\text{Insecticide induced death rate per sandfly on the } \tau^{\text{th}} \text{ day } = Q\, C_{t0}\, e^{-b_1 \tau}\, \frac{H_{s1}}{H} \tag{3.63}$$

For option $O_h$, substituting $\frac{H_{s1}}{H} = 1$ in equation 3.63. The solution of continuous form of equation 3.63, which gives the number of sandflies alive on the $\tau^{th}$ day can be expressed as

$$N(\tau) = \frac{N_0}{e^{\frac{Q\, C_{t0}}{b_1}}}\; e^{Q\, C_{t0} \frac{e^{-b_1 \tau}}{b_1}} \tag{3.64}$$

Where, $\tau = 0, N(0) = N_0$.

*BMCR* for option $O_h$ can be expressed as:

$$BMCR_h(\tau) = \frac{N_0 \left(1 - \frac{e^{Q\, C_{t0} \frac{e^{-b_1 \tau}}{b_1}}}{e^{\frac{Q\, C_{t0}}{b_1}}}\right) sandflies\ killed}{N_1\, I_h\, H \quad Rupees\ spent} \tag{3.65}$$

Similarly, *BMCR* for $O_k$ can be expressed as:

$$BMCR_k(\tau) = \frac{N_0 \left(1 - \frac{e^{(1-Q)\, C_{t0} \frac{e^{-b_2 \tau}}{b_2}}}{e^{\frac{(1-Q)\, C_{t0}}{b_2}}}\right) sandflies\ killed}{N_1\, I_k\, K \quad Rupees\ spent} \tag{3.66}$$

Four different scenarios (Table 3.12) can be derived from the two *BMCR*'s (equations 3.65 and 3.66) corresponding to two extreme options, $O_h$ and $O_k$. For a given parameter set only one of the four scenarios can occur. The *BMCR*'s for the two options become equal at a particular $\tau$ ($=\tau^*$) value for scenarios III and IV only. The last two columns in Table 3.12 recommend the values of time post spray ($\tau$) until which, the *BMCR* is higher for a particular option. When the *BMCR* is equal for both spray coverage options, the default policy of spraying houses for all values of $\tau$ has been recommended.

Table 3.12. A particular scenario exists if its corresponding pair of parameter conditions is satisfied.

| **Scenario** | **Pair of conditions satisfied** | **Existence of $\tau^*$ (when $\mathbf{BMCR_h}(\tau) = \mathbf{BMCR_k}(\tau)$ )** | **The *BMCR* is higher in** | |
|---|---|---|---|---|
| | | | **houses for** | **cattle sheds for** |
| I | $\Theta_1\text{Ӽ}_2 \leq \text{Ӽ}_1$ , $\Theta_2\, e^{\psi}\text{Ӽ}_2 < \text{Ӽ}_1$ | *No* | $\forall\, \tau$ | |
| II | $\text{Ӽ}_1 \leq \Theta_1\text{Ӽ}_2$ , $\text{Ӽ}_1 \leq \Theta_2\, e^{\psi}\, \text{Ӽ}_2$ | *No* | | $\forall\, \tau$ |
| III | $\Theta_1\text{Ӽ}_2 < \text{Ӽ}_1$ , $\text{Ӽ}_1 < \Theta_2\, e^{\psi}\text{Ӽ}_2$ | *Yes* | $0 \leq \tau \leq \tau^*$ | $\tau^* < \tau$ |
| IV | $\text{Ӽ}_1 < \Theta_1\text{Ӽ}_2$ , $\Theta_2\, e^{\psi}\text{Ӽ}_2 < \text{Ӽ}_1$ | *Yes* | $\tau^* \leq \tau$ | $0 \leq \tau < \tau^*$ |

Note: For an existing scenario, one of the two spray options can be selected (knowing that a high *BMCR* is desirable $\tau$ days after spraying).

Where, $V = \frac{Q\, C_{t0}}{b_1}$ and $W = \frac{(1-Q)\, C_{t0}}{b_2}$; $\Theta_1 = \frac{e^W}{e^V}\left(\frac{e^V-1}{e^W-1}\right)$ and $\Theta_2 = \frac{V b_1\, e^W}{W\, b_2\, e^V}$; $\psi = (b_2 - b_1)\tau + V e^{-b_1\tau} - W e^{-b_2\tau}$; $O_h$-spray coverage of 100%houses; $O_k$-spray coverage of 100% cattle sheds

Although the following discussion is based on assumed spray coverage options: $O_h$ and $O_k$, it can be applied for any values of preplanned spray coverage's: $O_1(H_{s1}, K_{s1})$ and $O_2(H_{s2}, K_{s2})$ with nonzero values of houses and cattle sheds sprayed at. The expression for *BMCR*'s for both spray coverage options will need to be derived. Additionally, if the two preplanned options are being tested for 31 VL affected districts, then we will have 62 expressions: $BMCR_{1i}(\tau), \forall\, i =$

$1,..,31$ and $BMCR_{2i}(\tau), \forall\, i = 1,..,31$. A pseudo code similar to that described in section 3.3.3 (for the 62 dimensional linear model) can be used to rank the 62 *BMCR* values, $\tau$ days after spray.

Remark 1: In summary, after the first round of insecticide spray (at $\tau$ = *0*), if the objective is to always maintain a higher *BMCR* in houses, then scenarios I and II might be helpful. If scenario I (II) occurs, implementing $O_h$ ($O_k$) is recommended.

Remark 2: If it is known that the sandfly density might peak $\tau_1$ days after the first round of spraying (e.g., due to the start of the rainy season) and a second round of spraying is not possible at time $\tau_1$ due to financial constraints, then it is advisable to implement the spray option which maintains a higher *BMCR* at time $\tau_1$.

Scenario III (IV) suggests that, when $\tau < \tau^*$, the *BMCR* will be higher for option $O_h(O_k)$ and that, when $\tau^* < \tau$, the *BMCR* will be higher for option $O_k(O_h)$. Thus:

i) If scenario III exists and $\tau_1 < \tau^*$ days, then implementing $O_h$ is recommended, because after $\tau_1$ days, the *BMCR* is higher for $O_h$ ($BMCR_k(\tau_1) < BMCR_h(\tau_1)$, (implying that by implementing option $O_h$, a higher reduction in sandfly density per rupee invested will have been achieved in $\tau_1$ days). However, if $\tau > \tau^*$ days, then implementing $O_k$ is recommended, as $BMCR_h(\tau_1) < BMCR_k(\tau_1)$ .

ii) If scenario IV exists and $\tau_1 < \tau^*$ days, implementing $O_k$ is recommended, as $BMCR_h(\tau_1) < BMCR_k(\tau_1)$ . However, if $\tau_1 > \tau^*$ days, then implementing $O_h$ is recommended, as $BMCR_k(\tau_1) < BMCR_h(\tau_1)$ .

### 3.3.3 Pseudo Code for Multi-dimensional Linear Model

For solving the 62 dimensional linear model, unlike section 3.3.2, benefit from spray campaign is defined as the “insecticide induced death rate” on day $\tau$. For decision variable of the

$i^{th}$ district ($x_i$ and $y_i$), compute the value of the functions : $f^1{}_i$ (equation 3.67) for $x_i$ and $f^2{}_i$ (equation 3.68) for $y_i$ , where $f^1{}_i$ and $f^2{}_i$ are defined as:

$$f^1{}_i(N_{hi},\ N_{ci},\ H_i, b_1,\ I_h, \tau) = \left(\frac{a_h\ N_{hi}}{a_h\ N_{hi}+(1-a_h)N_{ci}}\right)\ \ \frac{e^{-b_1\tau}}{I_h\ H_i}\ \ ,\quad \forall\ i\ =\ 1,..,31 \tag{3.67}$$

and

$$f^2{}_i(N_{hi},\ N_{ci},\ K_i, b_2,\ I_k, \tau) = \left(1\ -\ \frac{a_h\ N_{hi}}{a_h\ N_{hi}+(1-a_h)N_{ci}}\right)\ \frac{e^{-b_2\tau}}{I_k\ K_i}\ \ ,\quad \forall\ i\ =\ 1,..,31 \tag{3.68}$$

respectively. Then sort (rank) all 62 variables in descending order, based on their respective function values ($f^1{}_i$and $f^2{}_i$).

The pseudo code for the 62 dimensional linear model is presented in this section. Let $H_{s\_lbi}$ and $K_{s\_lbi}$ denote the lower bound on decision variables $H_s$ and $K_s$ respectively, for the $i^{th}$ district.

1. Compute the function values: $f^1{}_i$ & $f^2{}_i$ , $\forall\ i\ =\ 1,..,31$.
2. Rank the 62 variables in descending order of their respective function values.
3. Initialize $b \leftarrow \left(\widetilde{C_{UB}} - \widetilde{C_{Im}}\right)$ ; as the total money available to buy insecticide material.
4. Compute money required to buy insecticide as per lower bound for all districts using : $N_1\left(I_h\ \sum_{i=1}^{31} H_{s\_lbi} +\ I_k\ \sum_{i=1}^{31} K_{s\_lbi}\ \right)$
5. Compute $b_{ava} \leftarrow b - N_1\left(I_h\ \sum_{i=1}^{31} H_{s\_lbi} +\ I_k\ \sum_{i=1}^{31} K_{s\_lbi}\ \right)$ ;
6. Use $b_{ava}$ to increase the highest ranking variable till its upper bound or until $b_{ava} = 0$.
7. While ($b_{ava} > 0$)
8. Do “consider the next highest ranked variable”
9. If $b_{ava} \geq money\ required\ to\ increase\ this\ variable\ to\ its\ upperbound$

Then “spend $b_{ava}$ to increase this variable to its upper bound”

Update $b_{ava}$ by subtracting money spent

Elseif $b_{ava} < money\ required\ to\ increase\ this\ variable\ to\ its\ upperbound$

Then “increase this variable as much as possible”

Update $b_{ava} \leftarrow 0$

End if loop

End while loop

Table 3.13 lists the 62 variables after sorting them in descending order of their *BMCR* values, using the parameter estimates from Table 3.1 and Table 3.2.

Table 3.13. Ranking of the 62 decision variables.

| Rank | Decision variable | *BMCR* value | Rank | Decision variable | *BMCR* value | Rank | Decision variable | *BMCR* value | Rank | Decision variable | *BMCR* value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $x_{13}$ | 6.18 E-09 | 17 | $x_8$ | 3.16 E-09 | 33 | $y_{26}$ | 1.73 E-11 | 49 | $y_1$ | 1.13 E-11 |
| 2 | $x_{26}$ | 5.63 E-09 | 18 | $x_1$ | 3.04 E-09 | 34 | $y_2$ | 1.71 E-11 | 50 | $y_6$ | 1.13 E-11 |
| 3 | $x_7$ | 4.96 E-09 | 19 | $x_{12}$ | 3.03 E-09 | 35 | $y_{16}$ | 1.71 E-11 | 51 | $y_{23}$ | 1.11 E-11 |
| 4 | $x_{10}$ | 4.80 E-09 | 20 | $x_{11}$ | 2.96 E-09 | 36 | $y_{15}$ | 1.59 E-11 | 52 | $y_{25}$ | 1.09 E-11 |
| 5 | $x_4$ | 4.79 E-09 | 21 | $x_{23}$ | 2.86 E-09 | 37 | $y_{11}$ | 1.55 E-11 | 53 | $y_{27}$ | 1.06 E-11 |
| 6 | $x_{28}$ | 4.78 E-09 | 22 | $x_{24}$ | 2.86 E-09 | 38 | $y_4$ | 1.50 E-11 | 54 | $y_{18}$ | 1.04 E-11 |
| 7 | $x_{16}$ | 4.70 E-09 | 23 | $x_{19}$ | 2.58 E-09 | 39 | $y_{10}$ | 1.46 E-11 | 55 | $y_{24}$ | 9.19 E-12 |
| 8 | $x_{30}$ | 4.32 E-09 | 24 | $x_{21}$ | 2.58 E-09 | 40 | $y_{14}$ | 1.38 E-11 | 56 | $y_{17}$ | 8.76 E-12 |
| 9 | $x_{15}$ | 4.31 E-09 | 25 | $x_{18}$ | 2.57 E-09 | 41 | $y_7$ | 1.37 E-11 | 57 | $y_{31}$ | 8.58 E-12 |
| 10 | $x_{25}$ | 4.12 E-09 | 26 | $x_{31}$ | 2.50 E-09 | 42 | $y_{20}$ | 1.34 E-11 | 58 | $y_{19}$ | 8.55 E-12 |
| 11 | $x_{20}$ | 3.99 E-09 | 27 | $x_{17}$ | 2.37 E-09 | 43 | $y_{28}$ | 1.29 E-11 | 59 | $y_{21}$ | 7.85 E-12 |
| 12 | $x_6$ | 3.93 E-09 | 28 | $x_9$ | 2.32 E-09 | 44 | $y_3$ | 1.29 E-11 | 60 | $y_5$ | 7.81 E-12 |
| 13 | $x_3$ | 3.56 E-09 | 29 | $x_5$ | 2.20 E-09 | 45 | $y_{29}$ | 1.25 E-11 | 61 | $y_9$ | 7.59 E-12 |
| 14 | $x_{27}$ | 3.41 E-09 | 30 | $x_{22}$ | 1.58 E-09 | 46 | $y_{30}$ | 1.21 E-11 | 62 | $y_{22}$ | 6.03 E-12 |
| 15 | $x_{14}$ | 3.38 E-09 | 31 | $x_2$ | 1.22 E-09 | 47 | $y_8$ | 1.15 E-11 | | | |
| 16 | $x_{29}$ | 3.29 E-09 | 32 | $y_{13}$ | 2.34 E-11 | 48 | $y_{12}$ | 1.14 E-11 | | | |

Note: Subscript denotes district number from Table 4.6 ; Unit: of *BMCR* is “sandflies killed per day per sandfly per rupee”.

From Table 3.13 above, $x_{13}$ has the highest *BMCR* value. $b_{ava}$ is first used to allocate to $x_{13}$ because it has the highest rank. Figure 3.6 shows the BMCR values of each of the 62 decision variables.

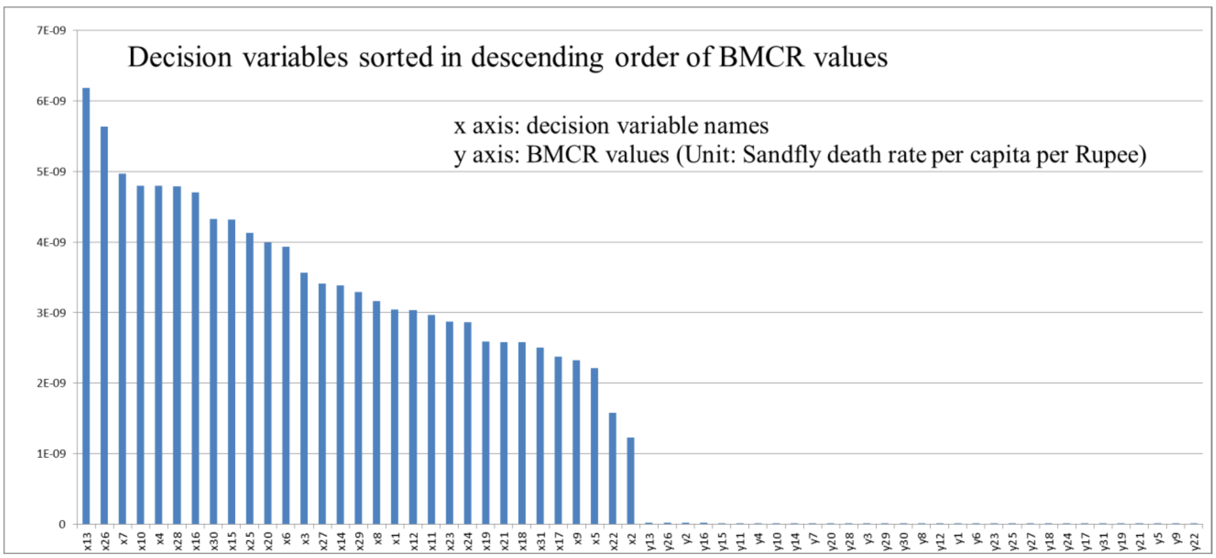


Figure 3.6. 62 decision variables sorted using *BMCR* values.

The following values were used to generate the above graph: $\widetilde{C_{UB}} = Rs. 220.48\, million$ ; $\widetilde{C_{Im}} = Rs. 96.80\, million$.

Money available after subtracting the implementation cost from the available budget is $b (= \widetilde{C_{UB}} - \widetilde{C_{Im}} = Rs. 123.67\, million)$. For allocating insecticide material as per the lower bound on all $x$ and $y$ variables, money spent $= N_1 \left( I_h \sum_{i=1}^{31} H_{s\_lbi} + I_k \sum_{i=1}^{31} K_{s\_lbi} \right) = 90(2279114 \times 0.533 + 0) = 109.32\, million$ . Money available for optimizing is $b_{ava} = b - N_1 \left( I_h \sum_{i=1}^{31} H_{s\_lbi} + I_k \sum_{i=1}^{31} K_{s\_lbi} \right) = Rs. 14.34\, million$ , which is first used to increase

If after $x_{13}$ reaches its upper bound and money was still available ($b_{ava} > 0$) then it would have been used to raise $x_{26}$. $b_{ava}$ was exhausted by increasing $x_{13}$ by a value of 9.62 e-02 (0.0962 Kg/person × 1657599 actual persons in the district 13 × 90 Rs./kg. = Rs. 1.4351 e+007 = $b_{ava}$). If each of the 31 districts was assigned two arbitrary preplanned spray coverage options each, a similar pseudo code could be used to choose from preplanned spray coverage options, based on values of $BMCR_{1i}(\tau), \forall\, i = 1,..,31$ and $BMCR_{2i}(\tau), \forall\, i = 1,..,31$ .

CHAPTER 4

# COMPUTATIONAL RESULTS

In this chapter, the numerical results, the uncertainty and sensitivity analysis results for the linear optimization model have been discussed. The optimal solutions from the 2 dimensional and 62 dimensional linear models are compared with those from the 2 dimensional and 62 dimensional nonlinear models, respectively.

## 4.1 Linear Optimization Model

The computational results from the linear model are presented in this section.

### 4.1.1. Numerical Results

Parameter estimates of the 2 dimensional linear model are collected in Table 3.1 and Table 3.2. The estimation process for *human visitation proportion* (*Q),* the decay rates in houses ($b_1$) (from Dinesh et al. [47]) and cattle sheds ($b_2$) (from Jacusiel [48]), are described below.

Parameter estimates: The *human visitation proportion* is defined as the sandfly population proportion that visits human dwellings based on their feeding preference ($a_h$) towards human blood:

$$Q = \frac{a_h N_h}{(a_h N_h + a_c N_c)} = 255.4 \times 10^{-3} \tag{4.1}$$

In words, only 25.5% of total sandflies ($N_v$) visit houses each day in the linear model. The percentage mortality of sandflies in sprayed houses (from Dinesh et al. [47]) and sprayed cattle sheds (from Jacusiel [48]), on different days after DDT was sprayed, is presented in Table 4.1. The estimate of $b_2$ are computed using the numerical results from control group C in Jacusiel [48]. The average number of sandflies that visited the control group houses on each day even after DDT was sprayed was taken as the average number of live sandflies counted on six consecutive days prior to DDT application. The difference between the average number of sandflies present prior to spraying and the sandfly count on particular day is taken as the proportion of sandflies killed on that particular day.

Table 4.1. Estimating $b_1$ and $b_2$ using percentage mortality values from literature.

| **Serial number** | **$b_1$ estimates for districts: Muzaffarpur, Vaishali, Samastipur, in Bihar state, India** | | **$b_2$ estimates from group C: two-storied house, having a cattle shed on the ground floor and living quarters on the first floor** | |
|---|---|---|---|---|
| | $\tau$ | **Percentage mortality** | $\tau$ | **Percentage mortality** |
| 1 | 1 | 0.54 | 2 | 0.855 |
| 2 | 14 | 0.4796 | 3 | 0.711 |
| 3 | 28 | 0.3228 | 6 | 0.653 |
| 4 | 140 | 0.2156 | 7 | 0.596 |

To all possible pairs of values in Table 4.1, a function was fitted (using Excel 2010) to obtain six estimates of $b_1$and $b_2$ (Table 4.2). The six values were averaged (column 2 and 4) to obtain the final, respective estimates of $b_1$and $b_2$.

Table 4.2. Estimating $b_1$ and $b_2$ using all possible data combinations.

| Serial number | $b_1$ | | $b_2$ | |
|---|---|---|---|---|
| | **Combination of days post-treatment** | **Fitted $b_1$ value** | **Combination of days post-treatment** | **Fitted $b_2$ value** |
| 1 | 1 and 14 | 0.009 | 2 and 3 | 0.184 |
| 2 | 1 and 28 | 0.019 | 2 and 6 | 0.067 |
| 3 | 1 and 140 | 0.007 | 2 and 7 | 0.072 |
| 4 | 14 and 28 | 0.028 | 3 and 6 | 0.028 |
| 5 | 14 and 140 | 0.006 | 3 and 7 | 0.044 |
| 6 | 28 and 140 | 0.004 | 6 and 7 | 0.091 |
| | Average = 0.012 per day, SD = 0.009 per day | | Average = 0.081 per day, SD = 0.055 per day | |

Using the estimates of *Q*, $b_1$ and $b_2$, the lethal effect's decay functions ( $i(\tau)$: equation 3.1 and $o(\tau)$: equation 3.2) are plotted in Figure 4.1.

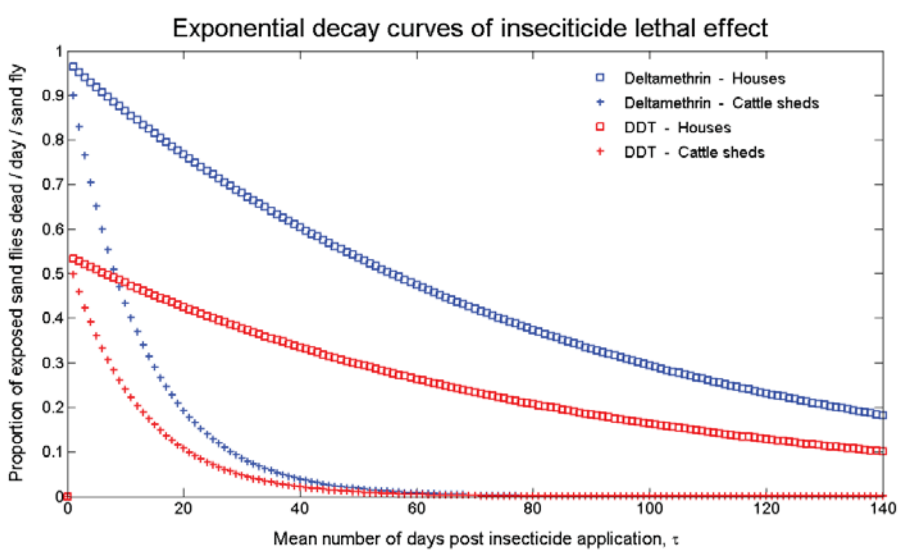


Figure 4.1. Decay functions of the insecticide's lethal effect over time.

The models developed in this dissertation are deterministic, and their parameter values can be found from the field apriori. Test instance (values) of input parameters were generated using assumed probability distributions, to study the distribution of model outputs. Two insecticides (DDT and Deltamethrin) are compared as well as uncertainty and sensitivity analysis of model output using distributions assigned to the uncertain parameters are presented next.

Estimation of $\tau^{\dagger}$: Here a different definition of *BMCR* is used, unlike the one defined in section 3.3.2. Using the linear optimization model's objective function (equation 3.4), the benefit from the spray campaign is defined as the insecticide induced sandfly death rate on the $\tau^{th}$ day after spray. We compute $\tau^{\dagger}$ of 2 dimensional LP model as the time at which $BMCR_h(\tau^{\dagger}) = BMCR_z(\tau^{\dagger})$ and is given by:

$$\tau^{\dagger} = \left|\frac{ln\big(I_h\, H(1-Q)\big) - ln\,(I_z\, Z\, Q)}{b_2 - b_1}\right| \qquad (4.2)$$

Using parameter values from Table 3.1 and Table 3.2, $\tau^{\dagger} = 29.88$ days.

Uncertain parameter estimates: Only $a_h$, $C_{t0}$, $b_1$, $b_2$, and $\widetilde{C_{UB}}$ were assumed to be uncertain parameters for performing uncertainty and sensitivity analysis. The female sandfly's feeding preference for human hosts ($a_h$) was assumed to follow a normal approximation to the binomial proportion distribution. Normal distribution was assumed for sandfly lifespan based on the data collected on female sandflies fed on mouse blood as reported by Srinivasan and Panicker [60]. $a_h$, $\mu_v$ and $C_{t0}$ were assumed to follow a truncated (at zero) normal distribution. The six estimates of $b_1$ and $b_2$ were assumed to follow a discrete uniform distribution, since no priori information was available on their distribution as presented in Marino et al. [61], with each of the six estimates having an equal probability of occurrence. As the budget amount that might be available for each future year's spray campaign is unknown, we arbitrarily assume a uniform distribution for $\widetilde{C_{UB}}$. The estimation of the minimum and maximum values of $\widetilde{C_{UB}}$ is presented next.

Estimation of minimum and maximum insecticide spray campaign costs: The maximum insecticide spray campaign cost (incurred when 100% of both sites are sprayed): $\tilde{C}_{max}(x,y) = N_1K_1 + N_1K_2 + \widetilde{C_{Im}} = Rs. 594.4\, million$ (using estimates from Table 3.1, Table 3.2 and Table 3.6). *FS 5* occurs if $\tilde{C}_{max}(x,y) \geq \widetilde{C_{UB}}$: surplus money is left after the spray campaign. If a small amount of money is allocated to the purchase of insecticide material, the minimum cost of the insecticide spray campaign is $\tilde{C}_{min}(x,y) \approx \widetilde{C_{Im}} = Rs. 101.4\, million$ (using 2010-2011 budget document [42]). *INFS* occurs if $\widetilde{C_{UB}} \leq \tilde{C}_{min}(x,y)$: the model cannot find a feasible solution. The possible range of $\widetilde{C_{UB}}$ values are shown in Figure 4.2.

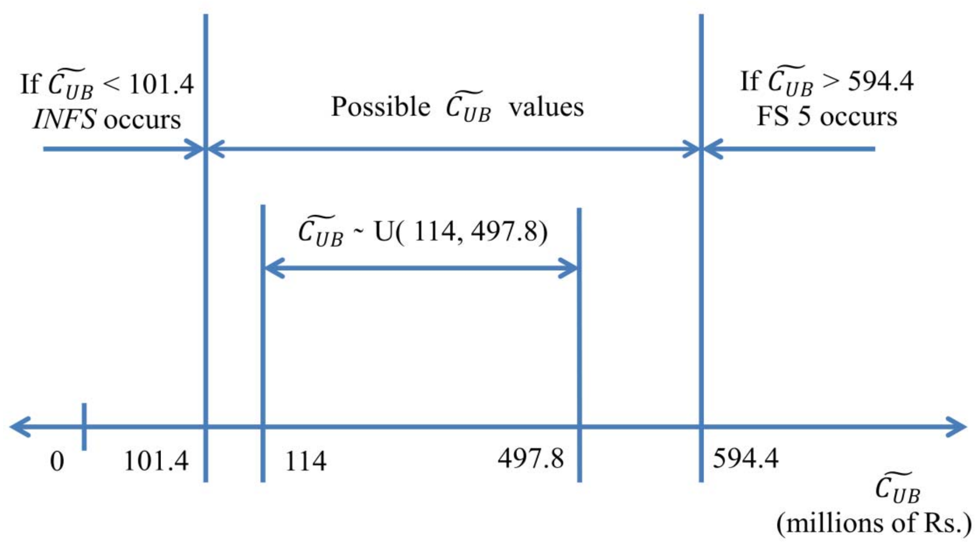


Figure 4.2. Range and distribution assumed for $\widetilde{C_{UB}}$ . Figure not drawn to scale.

A uniform distribution is assumed for $\widetilde{C_{UB}}$ : A minimum value is estimated using the material cost from 2010-2011 budget document [42] (Rs. 114 million) whereas the maximum value is assumed as 10% more (considering inflation) than the total fund allocation of Bihar's budget 2012-2013 [41] (Rs. 497.8 million). The 2012-2013 VL budget of Bihar state included funds allocated to: spray pumps and accessories, case search, operational costs for the spray campaigns assuming two rounds of spraying per year, monitoring and evaluation, supervisor travel expenses, training for field workers, information, education & communication activities for Kala-Azar and loss of wages.

<u>Comparison of insecticides:</u> The results from the model are: (kilograms per capita) (decision variables: $(x^{*}, y^{*})$), over the maximum insecticide-induced death rate (objective function) for an available amount of state budget. In order to yield these results, the model requires two inputs, the decay time ($\tau$) and available budget ($\widetilde{C_{UB}}$). The model checks for the pair of conditions satisfied in Table 3.10 and uses the corresponding feasible solution. The comparison of optimal insecticide-induced death rate for different scenarios $\tau$ days after spraying is presented in Table 4.3. The results for scenario IV is derived from estimates in Table 3.1, Table 3.2 and Table 3.6 whereas those for scenarios I, II, and III are obtained using hypothetical values.

Table 4.3. Optimal insecticide allocation $(x^{*}, y^{*})$ for different scenarios

| $\tau$ | $d_v^*(\mathbf{x}^*, \mathbf{y}^*)$ | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Scenario I** | | **Scenario II** | | **Scenario III** | | **Scenario IV** | |
| | **DDT** | **Deltamethrin** | **DDT** | **Deltamethrin** | **DDT** | **Deltamethrin** | **DDT** | **Deltamethrin** |
| 30 | 0.41 e-02 (0.41 e-02, 0) | 0.83 e-03 (0.45 e-03, 0) | 0.23 e-01 (0, 0.64 e-02) | 0.47 e-03 (0, 0.71 e-03) | 0.97 e-03 (0.41 e-02, 0) | 0.19 e-03 (0.45 e-03, 0) | 0.39 e-02 (0, 0.64 e-02) | 0.10 e-02 (0, 0.71 e-03) |
| 90 | 0.87 e-03 (0.41 e-02, 0) | 0.17 e-03 (0.45 e-03, 0) | 0.50 e-02 (0, 0.64 e-02) | 0.1 e-03 (0, 0.71 e-03 ) | 0.50 e-04 (0, 0.64 e-02) | 0.1 e-04 (0, 0.71 e-03 ) | 0.15 e-02 (0.41 e-02, 0) | 0.41 e-03 (0.45 e-03, 0) |

Note: ($\widetilde{C_{UB}} = Rs. 114\, million$, $\tau$ varied). Unit: $x^{*}$ is kilograms / person, $y^{*}$ is kilograms / cattle.

As per the 2 dimensional linear model, the maximum possible insecticide-induced death rate achieved by DDT (0.15 e-02 sandflies killed/day/sandfly) in Bihar remains about three (3.72) times that achieved by Deltamethrin (0.41 e-03 sandflies killed/day/sandfly) up to 90 days after spray. For scenario IV, taking the upper bound on cost ($\widetilde{C_{UB}}$) to be Rs. 114 million and $\tau = 90$ days, the model recommends 0.41 e-02 kilograms per person of DDT or 0.45 e-03 kilograms per person of Deltamethrin (Table 4.3). Comparing with present allocation policy in Bihar as presented in the W.H.O. report [7]: 0.375 e-01 kilograms of DDT per person and 0 kilograms of DDT per cattle and spray of insecticide twice a year with a 90-day gap between sprays. Using values: $\tau$ = 90 days, $(x, y)$ = (0.0375,0) and parameter values from Table 3.1 and Table 3.2 into equation 3.3, the maximum achievable increase in the natural sandfly death rate is $q$ = 18 %. This is an estimate of percentage increase in the natural sandfly death rate effective in Bihar when the second round of spray starts. Substituting $(x, y)$ = (0.0375,0) in equation 3.4, the number of residential houses that can be sprayed with DDT is estimated as 2,385,004 (i.e., 30% of all residential houses). Also, if the number of houses and cattle sheds that can be covered within the available budget, is substituted in the left-hand side of equation 3.3, the percentage increase in the death rate that can be achieved a certain number of days after spraying insecticide can be estimated.

Optimal insecticide-induced death rate versus budget constraints: Although the models developed in this dissertation can be used for qualitative analysis, the example in Figure 4.3 shows how the percentage increase in the death rate increases when more money is available for executing the insecticide spray campaign.

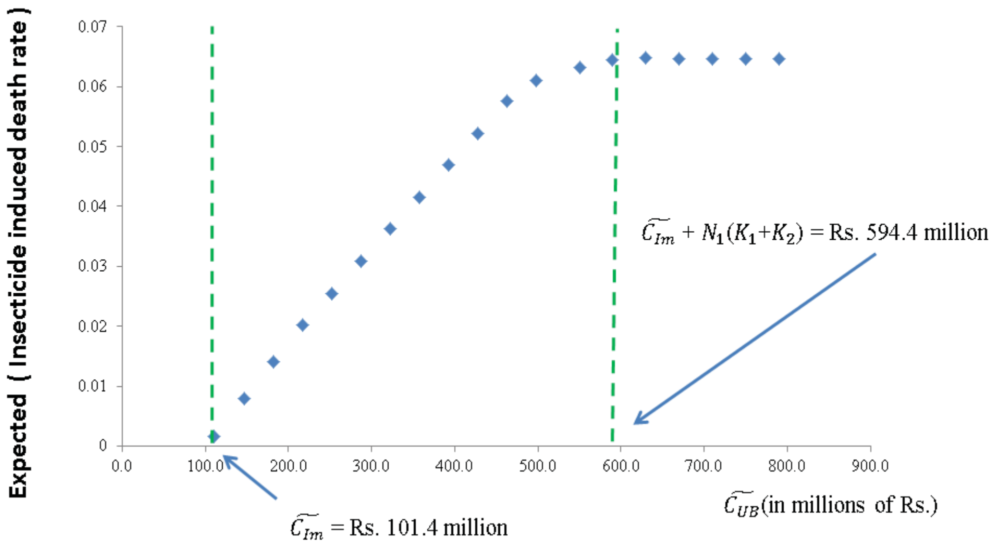


Figure 4.3. Expected optimal value of the insecticide induced death rate.

In Figure 4.3 the expected optimal values of insecticide-induced death rate is obtained by averaging the results from $10^5$ Monte-Carlo samples. $\tau$ was assumed as 90 days. The four uncertain parameters ($a_h, C_{t0}, b_1,$ and $b_2$) were assigned assumed distributions. The value of $\widetilde{C_{UB}}$ was varied. The insecticide-induced death rate rises almost linearly with an increase in the available budget. It reaches a maximum value of 0.064 sandflies dead/day/sandfly when 100% of both sites can be sprayed at using available budget. Even if more money were to become available (i.e., above Rs. 594.4 million), the insecticide-induced death rate does not exceed its maximum value, and surplus money would be left after completing the spray campaign. The insecticide-induced death rate increases very little, beyond $\widetilde{C_{UB}}$ = Rs. 500 million.

### 4.1.2 Uncertainty and Sensitivity Analysis

As all parameter estimates used in the linear model do not relate to the transmission dynamics of VL in Bihar, the resulting variations in the input parameter estimates are modeled by treating them as random variables as described by Sanchez and Blower [62]. Models used for recommending optimal intervention strategies must account for parameter uncertainty as presented by Luz et al. [63]. Uncertainty analyses was performed to investigate the uncertainty in the model outputs due to assumed distributions in the input parameters. The model outputs considered for uncertainty analysis were the occurrences of the feasible solutions (*FS 1, FS 2, FS 3*, and *FS 4*) and the distribution of the objective function value (insecticide-induced death rate). Multivariate sensitivity analysis is performed by sampling repeatedly from uncertain parameter distributions and simulating the model with each parameter value set, to identify input parameters that are most statistically influential the magnitude of the output parameters. Partial rank correlation coefficient (*PRCC*) was used as a sensitivity index for estimating the linear association strength between the input ($a_h$, $\mu_v$, $C_{t0}$, $b_1$, and $b_2$) and output parameter ($d_v$) as presented by Marino et al. [61].

Parameter distributions: $10^5$ independent samples were drawn from the probability distributions assigned to the five uncertain parameters ($a_h$, $\mu_v$, $C_{t0}$, $b_1$, $b_2$, and $\widetilde{C_{UB}}$) using a Monte-Carlo simulation. The decision variable statistics and the percentage occurrences of each of the five possible solutions, are plotted in Figure 4.4. Percentage distributions of all feasible solutions were computed by averaging 10 Monte-Carlo samples each with a size of $10^5$ sampled parameter values. Figure 4.4, Figure 4.5 and Figure 4.6 are generated using $\tau$ = 90 days and DDT as insecticide.

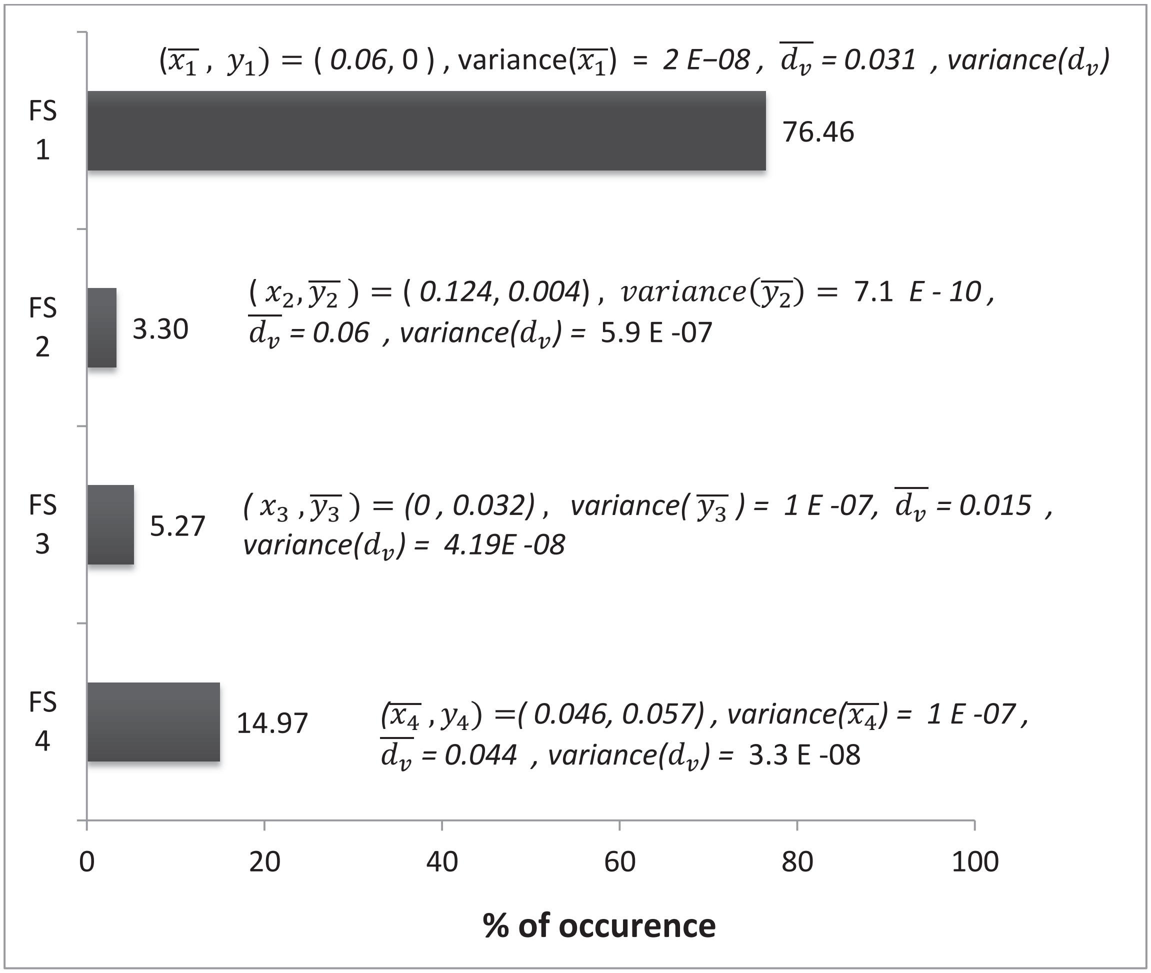


Figure 4.4. Percentage occurrences of the four feasible solutions of the model.

In Figure 4.4 , $d_v$ stands for insecticide- induced death rate. Variance is calculated only when the decision variable or insecticide induced death rate varies with the uncertain parameters. For the distribution assigned to $\widetilde{C_{UB}}$, INFS and FS 5 cannot occur. Using the input parameter distributions, *FS 1* occurs most often (76.46%), followed by *FS 4* (14.97%), *FS 3* (5.27%), and *FS 2* (3.3%). Hence, spraying the required percentage of houses only is recommended the most number of times (in conjunction with the model solution presented in Table 3.11).

Distribution of model outputs: The occurrences of the six possible model solutions is plotted (Figure 4.5), using $\widetilde{C_{UB}}$ values in the range: $(\widetilde{C}_{min}(x,y) < \widetilde{C_{UB}} < \widetilde{C}_{max}(x,y))$.

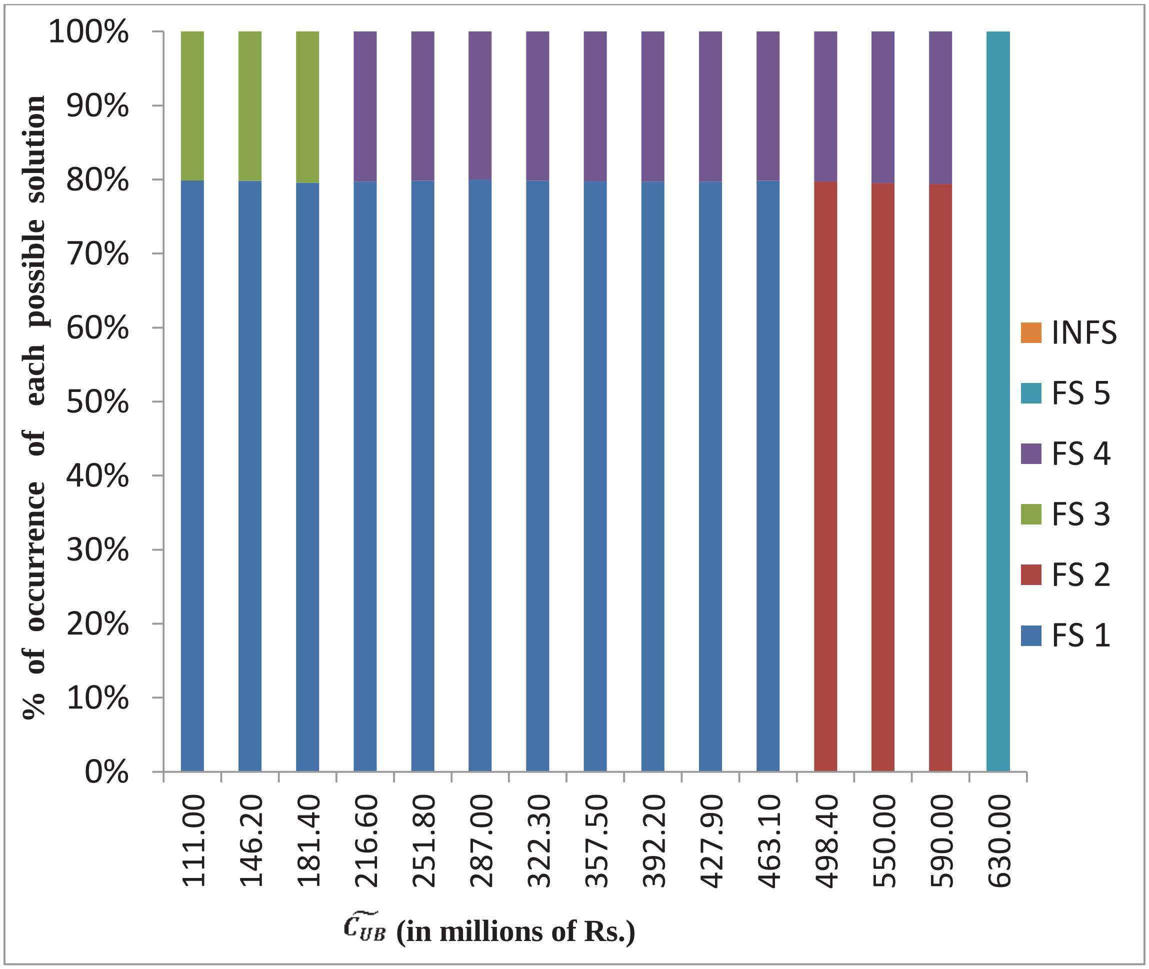


Figure 4.5. Occurrences of the six possible solutions versus $\widetilde{C_{UB}}$.

When $\widetilde{C_{UB}}$ is between Rs. 111.0 million and Rs. 181.4 million, the optimal solution is either spraying the maximum possible number of houses only (80%) or spraying the maximum possible number of cattle sheds only (20%). The optimal solution recommended the highest number of times (80%), when $\widetilde{C_{UB}}$ ranges: from Rs. 181.4 million to Rs. 463.1 million, is "spraying only the maximum possible number of houses" ; between Rs. 463.1 million and Rs. 590.0 million, is “spraying 100% of houses and then spraying the maximum possible number of cattle sheds”. When $\widetilde{C_{UB}}$ is Rs. 630.0 million, the optimal solution is spraying 100% of houses and 100% of cattle sheds. For $\tau$ = 30 days and $\tau$ = 90 days, the distributions of the optimal insecticide induced death rates are plotted in Figure 4.6.

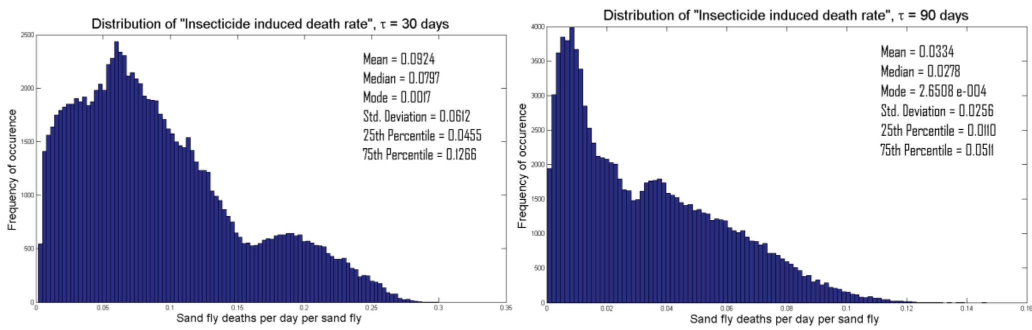


Figure 4.6. Distributions of the optimal insecticide induced death rate.

Figure 4.6 shows the distributions of the optimal insecticide induced death rate when $\tau$ = 30 days and $\tau$ = 90 days. Both distributions are generated by using a Monte-Carlo sample size of $10^5$ from input parameter distributions and DDT as the insecticide. The mean death rate is observed to reduce from 0.0924 sandflies killed per day per sandfly to 0.0334 sandflies killed per day per sandfly for the same budget distribution. If the second round of spraying were carried out after a 30-day gap (instead of the current 90-day gap), then fewer sites might need to be covered, because the optimal insecticide induced death rate is 2.7 times that after 90 days.

Sensitivity analysis: The sensitivity of the model outcome to the uncertainty in input parameter estimates is examined in this section. Uncertain parameters only affect the pair of conditions (Table 3.10) which make one of the five distinct solutions to be optimal. As the decision variables are not directly dependent on any of the four uncertain parameters chosen, the objective function value (the insecticide induced death rate) was chosen as an output parameter in the sensitivity analysis.

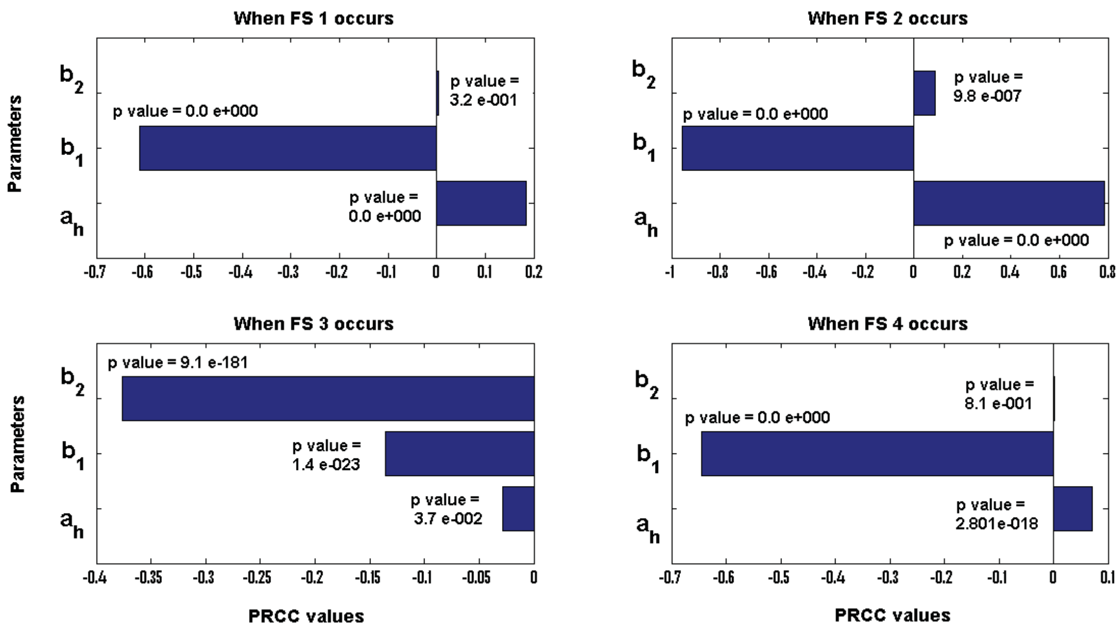


Figure 4.7. PRCC values of insecticide-induced death rate.

Figure 4.7 shows the PRCC values of insecticide-induced death rate, when a particular feasible solution (FS) from Table 3.10 occurs. A Monte-Carlo sample size of $10^5$ was used. *PRCC* values of insecticide induced death rate with respect to its corresponding uncertain input parameters are shown in Figure 4.7. For *FS 1*, the *PRCC*s associated with sandfly's feeding preference for human blood and insecticide's decay rate in houses are statistically significant at 5 % level. The input parameter: decay rate of the insecticide's lethal effect in houses (negatively correlated) has the most statistical influence ($|PRCC| > 0.5$) on the magnitude of the insecticide induced death rate because of its estimation uncertainty. *PRCC*s associated with all three input parameters are statistically insignificant for *FS 2* and *FS 3*. The sandfly's feeding preference for human blood (positively correlated) and decay rate of the insecticide's lethal effect in houses (negatively correlated) have the most statistical influences ($|PRCC| > 0.5$) in determining the magnitude of the insecticide induced death rate, for *FS 2*. None of the input parameters are influential in determining the magnitude of the insecticide induced death rate, for *FS 3*. The decay rate in cattle sheds is statistically insignificant for *FS 4*. Also, the decay rate of the insecticide's lethal effect in houses (negatively correlated) has the most statistical influence ($|PRCC| > 0.5$) on the magnitude of the insecticide induced death rate.

## 4.2 Simulation Results of Differential Equations Model

We have a system of first order, non-autonomous, nonhomogeneous and nonlinear coupled differential equations. The above system was simulated in Matlab 2009. Since ode45, a variable-step solver did not produce accurate solutions; ode 5, an explicit fixed step continuous solver was used for solving the above system. ode5 produced accurate results with the default step size in reasonable computational time.

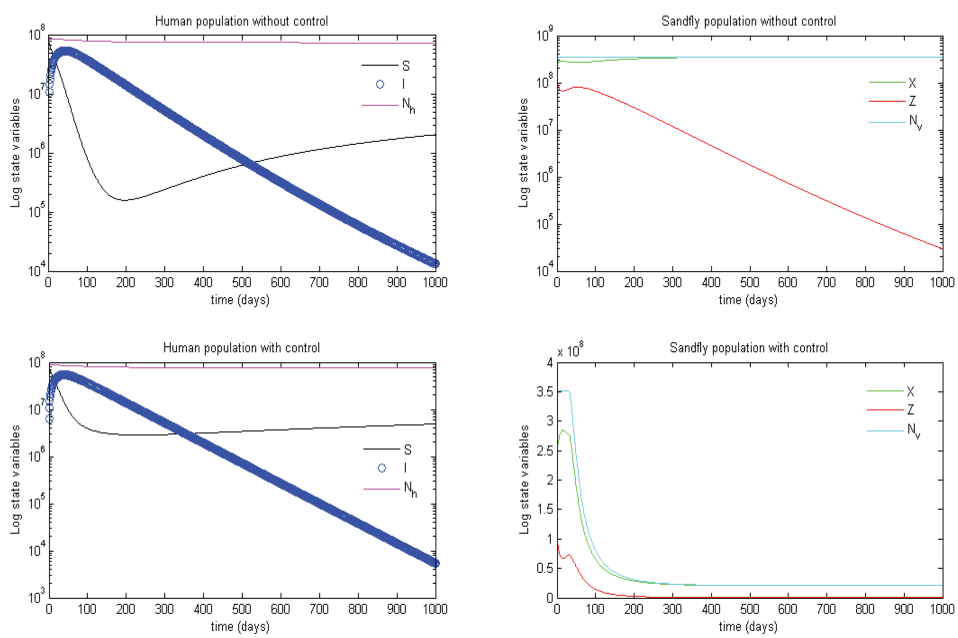


Figure 4.8 Human and sandfly populations with and without control.

Figure 4.8 is plotted by assuming that spray is done on the $32^{nd}$ day (1st February). (Spray coverage is assumed as: $H_s = 2578176, K_s = 0$). For the system of differential equations without any intervention, the basic reproduction number's expression (equation 4.3) was derived as

$$R_0 = \frac{C\, a_h}{a_h\, N_h + a_c\, N_c} \sqrt{\frac{N_h\, N_v\;\beta_{hv}\;\beta_{vh}}{\mu_v\,(\delta_1 + \eta + \mu_h)}} \tag{4.3}$$

Using parameter estimates from Table 3.3 and Table 3.8 and initial conditions for the set of equations 3.37 to 3.43, $\mathrm{R}_0 = 3.1865$. Since $\mathrm{R}_0 > 1$, the infected humans and infected sandflies reach a non-zero steady state vale and the disease persists in the population, without intervention (Figure 4.8).

## 4.3 Nonlinear Optimization Model

The estimation process for parameters used in the nonlinear optimization model are presented in this section.

### 4.3.1 Parameter Estimates

Estimation of human recruitment rate (Λ): Using the crude birth rate from the Profile of Bihar state [64] as 28.9 per 1000 persons and the total population of Bihar state from the Census of India, 2011 [52] as 103804637, the annual birth rate is computed as 2999954 ( = 103804637 × 28.9 / 1000) persons born per year. The difference between annual birth rate (2999954) and out-migration rate of Bihar (1833994) from the migration tables in the Census of India, 2001 [65] (1833994 persons migrating out of Bihar per year) is estimated as the human recruitment rate (2999954 persons born per year - 1833994 persons migrating out per year = 1165960 persons added to Bihar per year = 3194.41 persons added to Bihar per day).

Estimation of decay rate of DDT's repellent effect ($b_3$): The percent reduction of *Phlebotomus perniciosus* landings on dogs treated with 65% Permethrin solution was used to estimate the decay rate of repellent effect of DDT on humans from Molina et al. [25]. (Note: Value for day 14 was excluded as it was not consistent with the decreasing trend of other data values).

Table 4.4. Estimating $b_3$ using percentage reduction of landings.

| **Serial number** | **$b_3$ estimates** | |
|---|---|---|
| | **Post treatment days, $\tau$** | **% reduction of landings** |
| 1 | 7 | 78.5 |
| 2 | 21 | 42.1 |
| 3 | 28 | 33.1 |
| 4 | 35 | 14.6 |
| 5 | 49 | 1.2 |

To all possible pairs of values in Table 4.4 above, a function was fitted (using Excel 2010) to obtain ten estimates of $b_3$. The ten values were averaged (Table 4.5) to obtain the final estimate of $b_3$.

Table 4.5. Estimating $b_3$ using all possible data combinations.

| **Serial number** | **$b_3$** | |
|---|---|---|
| | **Combination of days post-treatment** | **Fitted $b_3$ value** |
| 1 | 7 and 21 | 0.045 |
| 2 | 7 and 28 | 0.041 |
| 3 | 7 and 35 | 0.06 |
| 4 | 7 and 49 | 0.1 |
| 5 | 21 and 28 | 0.034 |
| 6 | 21 and 35 | 0.076 |
| 7 | 21 and 49 | 0.127 |
| 8 | 28 and 35 | 0.117 |
| 9 | 28 and 49 | 0.158 |
| 10 | 35 and 49 | 0.178 |
| | Average = 0.0936 per day, SD = 0.0506 per day | |

Estimated cattle population and number of residential houses for 31 VL affected districts: First, using cattle population data of 21 VL affected districts from 1982 cattle census of Bihar, the cattle population was estimated for the remaining 10 VL affected districts* (Table 4.6). Next, total cattle population from the 18th Livestock census [51] was distributed in the same proportion as the 1982 cattle census [43] for each district. Number of residential houses for Arwal district^ (Table 4.6) was estimated by using data for 30 VL affected districts of Bihar using 1991 census of India [44]. The total of houses from 2001 census of India [50] was distributed in the same proportion as the 1991 census.

Table 4.6. Estimated district-wise number of cattle and residential houses.

| Serial no. | District name | Total cattle population (1982 census) [43] | Distributing the total 18th livestock 2007 census population in the same proportion as the 1982 cattle population | District-wise number of occupied residential houses and households in reorganized Bihar, according to 1991 census [44] | Distributing the total no. of houses in 2001 census in the same proportion as the 1991 census |
|---|---|---|---|---|---|
| 1 | Araria* | 803617.52 | 620950.22 | 282665 | 562585.07 |
| 2 | Arwal* | 803617.52 | 620950.22 | 264453.8333^ | 526339.58 |
| 3 | Banka* | 803617.52 | 620950.22 | 199407 | 396877.58 |
| 4 | Begusarai | 410004 | 316807.52 | 250058 | 497687.71 |
| 5 | Bhagalpur | 1413411 | 1092133.83 | 290086 | 577355.00 |
| 6 | Bhojpur | 827051 | 639057.13 | 211766 | 421475.56 |
| 7 | Buxar* | 803617.52 | 620950.22 | 128113 | 254981.91 |
| 8 | Darbhanga | 511578 | 395293.12 | 388108 | 772447.12 |
| 9 | E. Champaran | 988608 | 763891.21 | 449794 | 895220.09 |
| 10 | Gopalganj | 528199 | 408136.06 | 211637 | 421218.81 |
| 11 | Jehanabad* | 803617.52 | 620950.22 | 159491 | 317433.20 |
| 12 | Katihar | 725337 | 560463.36 | 313858 | 624668.15 |
| 13 | Khagaria | 317622 | 245424.53 | 170065 | 338478.51 |
| 14 | Kishanganj* | 803617.52 | 620950.22 | 186858 | 371901.44 |
| 15 | Lakhlsarai* | 803617.52 | 620950.22 | 100323 | 199671.77 |
| 16 | Madhepura | 497505 | 384419.00 | 196894 | 391875.98 |
| 17 | Madhubani | 839201 | 648445.36 | 446881 | 889422.38 |
| 18 | Munger | 1271079 | 982154.78 | 148913 | 296379.92 |
| 19 | Muzaffarpur | 815846 | 630399.09 | 427110 | 850072.38 |

Table 4.6—*Continued*

| | | | | | |
|---|---|---|---|---|---|
| 20 | Nalanda | 555818 | 429477.09 | 262322 | 522096.62 |
| 21 | Patna | 752078 | 581125.96 | 474943 | 945273.87 |
| 22 | Purnea | 1985029 | 1533819.47 | 337407 | 671537.47 |
| 23 | Saharsa | 1050076 | 811387.15 | 198611 | 395293.31 |
| 24 | Samastipur* | 803617.52 | 620950.22 | 369199 | 734812.74 |
| 25 | Saran | 586035 | 452825.57 | 283296 | 563840.94 |
| 26 | Sheohar* | 803617.52 | 620950.22 | 54745 | 108958.38 |
| 27 | Sitamarhi | 753938 | 582563.17 | 288622 | 574441.22 |
| 28 | Siwan | 495337 | 382743.80 | 243724 | 485081.22 |
| 29 | Supaul* | 803617.52 | 620950.22 | 229095 | 455965.28 |
| 30 | Vaishali | 541988 | 418790.73 | 265543 | 528507.34 |
| 31 | W. Champaran | 1010228 | 780596.85 | 364081 | 724626.44 |
| | Total | 24912143.20 | 19249457 [50] | 8198068.833 | 16316527 [49] |

Note: *For 10 districts marked with (*), the values were missing in the 1982 cattle population [43] and were estimated using the average of 21 VL affected districts of Bihar.

^ For Arwal district, the number of residential houses was estimated using the average of the 30 district's value from 1991 census of India [44] .

Assumed 20% growth in cattle population of each district for obtaining numerical results

<u>Estimation of upper bound spray campaign budget ($\widetilde{C_{UB}}$):</u> The various budget heads enumerated in Bihar's budget 2012-2013 [41] are:

Table 4.7 Budget allocation as per Bihar's budget 2012-2013 [41]

| **Serial no.** | **Budget head** | **Total money allocated** |
|---|---|---|
| 1 | Spray pump & accessories | 4000000 |
| 2 | Operational cost for spray including spray wages (KA DDT spray, May-June, Part I) | 211484715 |
| 3 | Monitoring and evaluation | 1500000 |
| 4 | Mobility & supervision | 500000 |
| 5 | Specific IEC and Advocacy for Kala-azar (VL) | 3000000 |
| | Total | 220,484,715 |

Note: IEC stands for Information, education and communications

Estimation of $\tau^{\dagger}$ : Since the analytic expression of the objective function for the 2 dimensional nonlinear model is unknown, the value of $\tau^{\dagger}$ was estimated by conducting simulation runs using parameter set in Table 3.1, Table 3.2 and Table 3.3, $\tau^{\dagger} \simeq 4.5 \text{ days}$ .

### 4.3.2 Check for Concavity of Objective Function

Although the number of houses and cattle sheds sprayed at can be only integers, we relax the integrality constraint on the decision variables. By definition, the function $a(H_s, K_s) : \mathbb{Z}_+^2 \to \mathbb{R}_+^1$ (equation 3.44) defined on the (real numbered) feasible domain, is concave, if for every $x^{(1)} \epsilon R_+^2$, $x^{(2)} \epsilon R_+^2$ in its domain and every step, $\lambda \epsilon [0,1]$, the below inequality is satisfied.

$$a\left(x^{(1)} + \lambda\left(x^{(2)} - x^{(1)}\right)\right) \geq a\left(x^{(1)}\right) + \lambda\left(a\left(x^{(2)}\right) - a\left(x^{(1)}\right)\right) \tag{4.4}$$

In words, the interpolation of the function values along the line segment from $x^{(1)}$ to $x^{(2)}$ should not overestimate for a concave function. Monte Carlo simulations were carried out with a sample size of 50000 randomly selected grid points in the feasible domain of the function (equation 3.44). Since each objective function value is computed by using ode5 function twice and simpsons function once, the concavity was violated for 880 times out of 50000 simulations (0.0176% of the total simulations). Out of the 880 violated grid points, the right-hand side of inequality 4.3 was larger than the left-hand side by a maximum percentage of 0.0099127 %. These violations are within the numerical errors (in Matlab) introduced due to 6 function calls to compute the right-hand side and 3 function calls to compute the left-hand side. Consequently, we would assume that the function presented in equation 3.44 is concave over the region being considered. Sequential quadratic programming algorithm from Matlab toolbox was used to solve both the 2 dimensional and 62 dimensional nonlinear optimization models. Since sequential quadratic programming is a gradient based method, it requires the objective function equation to evaluate the gradient. Matlab function “interp2” was used to generate an approximate equation of the response surface by using cubic spline interpolation.

## 4.4 Comparison of Optimization Models

The optimal solution of 4 optimization models formulated in section 3.2 are compared and analyzed in this section.

Comparison between the Linear and Nonlinear model: The optimal number of sites to be sprayed at recommended by the two models will be compared in this section. There are some differences between the two models.

1) The most important difference is: the nonlinear model is dynamic whereas the linear model is static with respect to time. The output from the nonlinear model is an accumulation of all days till the end of simulation. In the nonlinear model only the cattle population is static. In the linear model, the insecticide induced death rate on the final day, is an instantaneous value and not a function of time.
2) The repellent effect is ignored in the linear model.
3) The objective function in the linear model is insecticide induced death rate whereas in the nonlinear model it is the cumulative number of human infections averted. Apart from the objective functions all constraints are identical in both models.

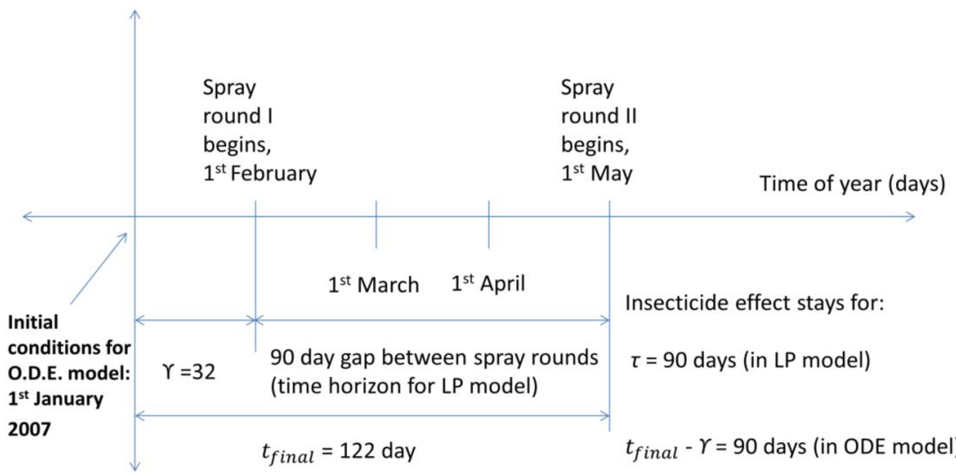


Figure 4.9 Simulation time horizons. Figure not drawn to scale

Figure 4.9 shows the simulation time horizons for linear and nonlinear models. When comparing the two models, the value of $\tau$ was taken as 90 days for the linear model and 122 for the nonlinear model. Figure 4.9 above shows that the insecticide effect stays for 90 days in both models, as the spray takes place on the 32$^{nd}$ day in the nonlinear model. Even though the time horizon is different for both models, the results from both optimization models is comparable because, the insecticide effect stays in both models for a 90 day period. The time between the two rounds of spray as per the present policy in Bihar is also 90 days.

The comparison of numerical results from the 4 models are presented next. The two-dimensional linear and nonlinear models are compared in Table 4.8.

Table 4.8. Comparing optimal values from two-dimensional optimization models.

| | Two-dimensional optimization model | |
|---|---|---|
| **Function value compared** | **2 dimensional linear** | **2 dimensional nonlinear** |
| $\left(x^* \frac{Kg.}{person}, y^* \frac{Kg.}{cattle}\right)$ | (0.0156, 0) | (0.0138, 0.0069) |
| $(H_s^* houses, K_s^* cattle\ sheds)$ | (2578176 , 0) | (2279100 , 598100) |
| Total DDT allocated (Unit: metric tons) | 1374.16 | 1374.15 |
| Maximum insecticide induced sandfly death rate, $d_v(H_s^*, K_s^*, t_{final})$^ | $d_v^*(2578176\ ,\ 0\ ,90) = 12454\ .\ 38\ \mathrm{e} - 06$ | $d_v(2279100\ ,\ 598100\ ,90) = 11038\ .\ 06\ e - 06$ |
| Maximum insecticide induced sandfly death rate, $d_{ODE}(H_s, K_s, t_{final})$^ | $d_{ODE}(2578176\ ,\ 0\ ,122) = 12452\ .\ 16\ e - 06$ | $d_{ODE}^*(2279100\ ,\ 598100\ ,122) = 11036\ .\ 09\ e - 06$ |
| Maximum human infections averted, $a(H_s, K_s, t_{final})^3$ | $a(2578176,\ 0,\ 122) = 224\ .39\ million$ | $a^*(2279100\ ,\ 598100\ ,122) = 274\ .\ 78\ \mathrm{million}$ |

The 62 dimensional linear and nonlinear models are compared in Table 4.9.

Table 4.9. Comparing optimal values from multi-dimensional optimization models

| | Multi-dimensional optimization model | |
|---|---|---|
| **Function value compared** | **62 dimensional linear** | **62 dimensional nonlinear** |
| $(\sum_{i=1}^{31} H_{si}^* houses, \sum_{i=1}^{31} K_{si}^* cattle\ sheds)$, $\forall\ i = 1,..,31$ | (2578176, 0) | ( 2279130 , 598120 ) |
| Total DDT allocated (Unit: metric tons) | 1374.16 | 1374.17 |
| Maximum insecticide induced sand fly death rate: $\sum_{i=1}^{31} d_v\left(H_s^*, K_s^*, t_{final}\right)$^ , $\forall\ i = 1,..,31$ | $d_v^*(2578176\ ,\ 0,\ 90) = 466124\ .\ 9\ e - 06$ | $d_v(2279130\ ,\ 598120{,}122) = 366285\ .\ 5\ e - 06$ |
| Maximum insecticide induced sand fly death rate: $\sum_{i=1}^{31} d_{ODE}\ \left(H_s^*, K_s^*, t_{final}\right)$^ , $\forall\ i = 1,..,31$ | $d_{ODE}(2578176\ ,\ 0\ ,122) = 466042\ .\ 9\ e - 06$ | $d_{ODE}^*(2279130\ ,\ 598120{,}122) = 366220\ .\ 4\ e - 06$ |
| Maximum human infections averted: $\sum_{i=1}^{31} a_i(H_s, K_s, t_{final})^3$ , $\forall\ i = 1,..,31$ | $a = 262\ .\ 64\ \mathrm{million}$ | $a^* = 368\ .\ 34\ \mathrm{million}$ |

Note: ^ Unit of Insecticide induced death rate: Sandflies dead per day per sandfly. [3]Unit of human infections averted: Person days. Insecticide effect stays for 90 days in both models. $\widetilde{C_{UB}}$= Rs. 220.48 million. Assuming 1st January as the first simulation day and insecticide is sprayed on 1st February. $(x^*,\ y^*)$ have been computed using actual human and cattle population, respectively. $x^*$ is not computed using affected human population. $(H_s^*\ \text{houses}\ , K_s^*\ \text{cattle sheds})$ for the 62 dimensional model are obtained by adding the optimal $(H_{si}^*\ , K_{si}^*\ ), \forall\ i\ =\ 1,..,31$ for each of the 31 VL affected districts.

The insecticide induced death rate achieved by the 2 dimensional linear model's solution (on the last day of the simulation) is 12 % higher than that achieved by the 2 dimensional nonlinear model's solution. The insecticide induced death rate achieved by the 62 dimensional linear model's solution (on the last day of the simulation) is 27 % higher than that achieved by the 62 dimensional nonlinear model's solution. The number of human infections averted by the 2 dimensional nonlinear model's solution is 22 % higher than that achieved by the 2 dimensional linear model's solution. The number of human infections averted by the 62 dimensional nonlinear model's solution is 40% higher than that achieved by the 62 dimensional linear model's solution.

As shown in Figure 4.10, the linear model aims to maximize the instantaneous value of insecticide induced death rate on the final day. The nonlinear model aims to maximize the difference between the cumulative number of human infections without and with intervention. Henceforth, the abbreviation 'LP' and 'NLP' will be used to denote "linear optimization model" and "nonlinear optimization model", respectively.

$$d_{ODE}\left(H_s, K_s, t_{final}\right) = (1\text{-r(t)}) \ \left( \ Q\ [i(\tau)] \left(\frac{H_s}{H}\right) + (1-Q)[o(\tau)] \left(\frac{K_s}{K}\right) \right)$$

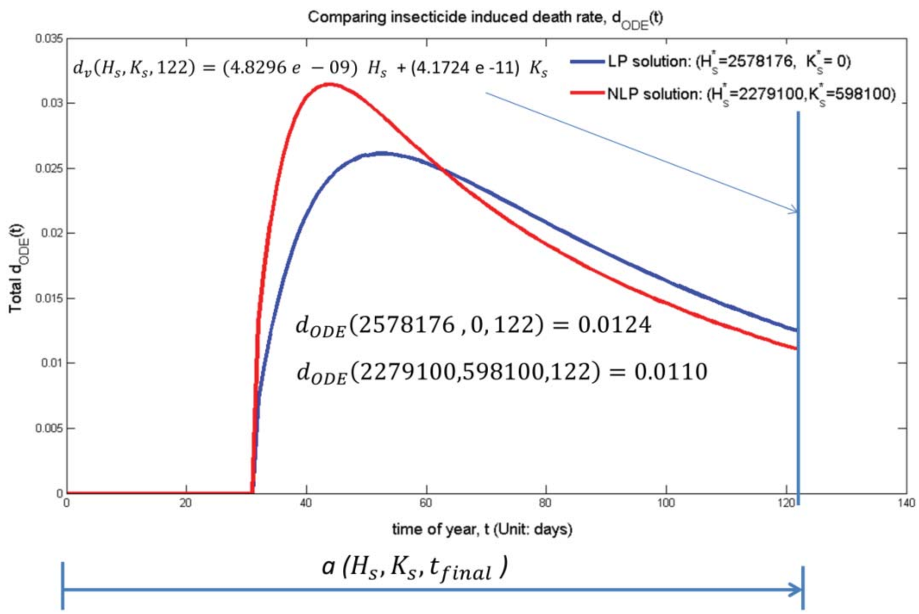


Figure 4.10. Comparing the insecticide induced death rates

Figure 4.10 plots the values of insecticide induced death rate, when the optimal solutions from the linear and nonlinear models are implemented. The NLP aims to find optimal spray coverage $(H^*{}_s, K^*{}_s)$ such that the area between the no spray curve: ($\phi_0$ (0 , 0 , 122)) and with spray curve: $\phi_{NLP}$ $(H^*{}_s, K^*{}_s, t_{final})$ is maximized (Figure 4.11).

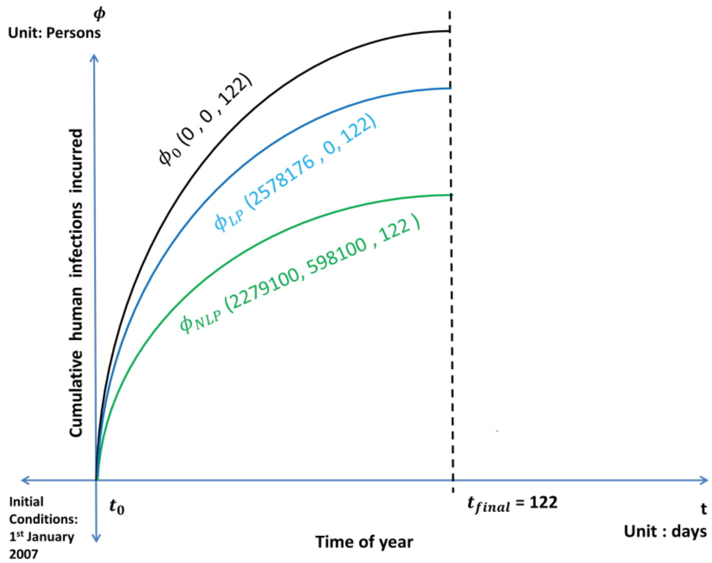


Figure 4.11 Area between curves $\phi(H_s, K_s, t_{final})$. Figure not to scale, drawn only for explanatory purpose.

Figure 4.11 shows the area between curves $\phi_0$ (0 , 0 , 122) and $\phi_{LP}$ (2578176, 0, 122) = 224 million person days averted. Area between curves $\phi_0$ (0, 0, 122) and $\phi_{NLP}$ (2279100, 598100, 122 ) = 274 million person days averted. The initial conditions at $t_0$ are from 1$^{st}$ January, 2007 data and spray is assumed to take place on 1$^{st}$ February.

<u>Comparison between the 2 dimensional LP and NLP model results:</u> Both optimal solutions result in approximately equal metric tons of insecticide required as they have the same available budget. The time taken for the infected human and infected sandfly populations to become less than one (effectively extinct), is almost the same (Figure 4.12).

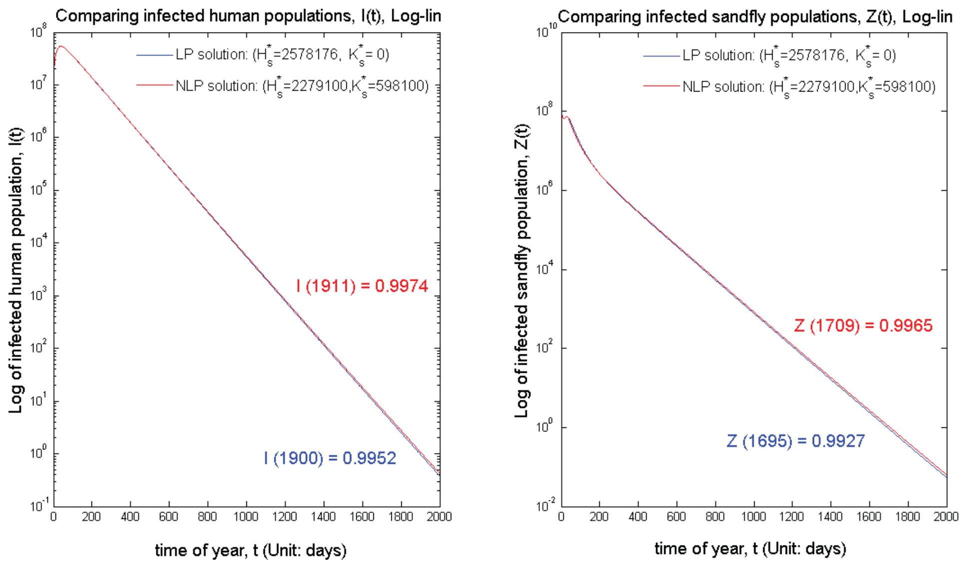


Figure 4.12 Time taken by the infected populations to become less than one.

Figure 4.12 shows the time (days) taken by the infected human and infected sandfly populations to become less than one. With LP model's solution, the infected human and infected sandfly population becomes less than one earlier, as compared to the NLP model's implementation (Figure 4.12). The fundamental difference between the two dimensional LP and NLP models is that, (for a finite time horizon) the LP model recommends spraying in maximum possible number of houses first with the available money, whereas the NLP model recommends spraying in maximum possible number of cattle sheds first for the available money. If enough money is available to spray in all houses then the LP model would recommend spraying in all houses and maximum possible number of cattle sheds. Similarly if enough money is available to spray in all cattle sheds in Bihar state, then the NLP model will recommend to spray in all cattle sheds and maximum possible number of houses.

The reason for these differences is explained next. The cumulative area under the function: $d_{ODE}(H_s, K_s, t)$ is larger with the implementation of the LP model's optimal solution (Figure 4.13). This implies that more sandflies are killed by implementing the LP model's optimal solution. The cumulative area under the $d_{ODE}(H_s, K_s, t)$ curve is a metric similar to the *BMCR* function developed in section 3.3.2, the difference being that the cumulative area has the unit: "cumulative number of sandflies killed per sandfly" versus *BMCR* function's unit: "cumulative sandflies killed per unit cost of insecticide material."

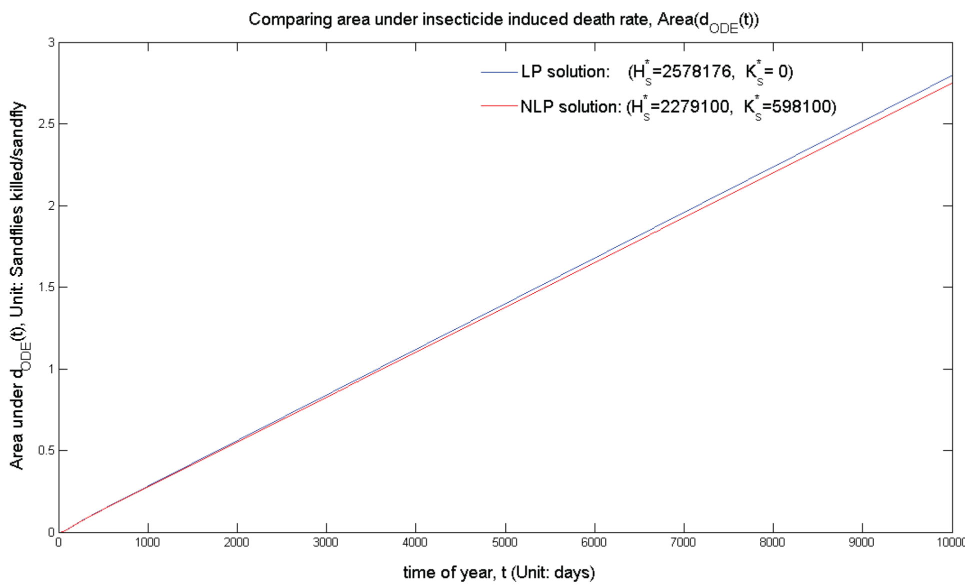


Figure 4.13. Cumulative area covered by $d_{ODE}(H_s, K_s, t)$ for the two model's solutions.

Since $d_{ODE}(2578176{,}0{,}10000) > d_{ODE}(2279100{,}598100{,}10000)$, more sandflies are killed by implementing the optimal solution from the LP model, in the long term future. So, the LP model's optimal solution should also have less number of human infections incurred ($\phi(t)$ in figure 4.14). However, the "cumulative number of human infections incurred" (blue curve in the below graph) is higher at the end of 10000 days. This can be explained by comparing the values of $a(H_s, K_s, t_{final})$ by the time ($t_{final} = 1710$ days) the number of infected sandflies become less than one.

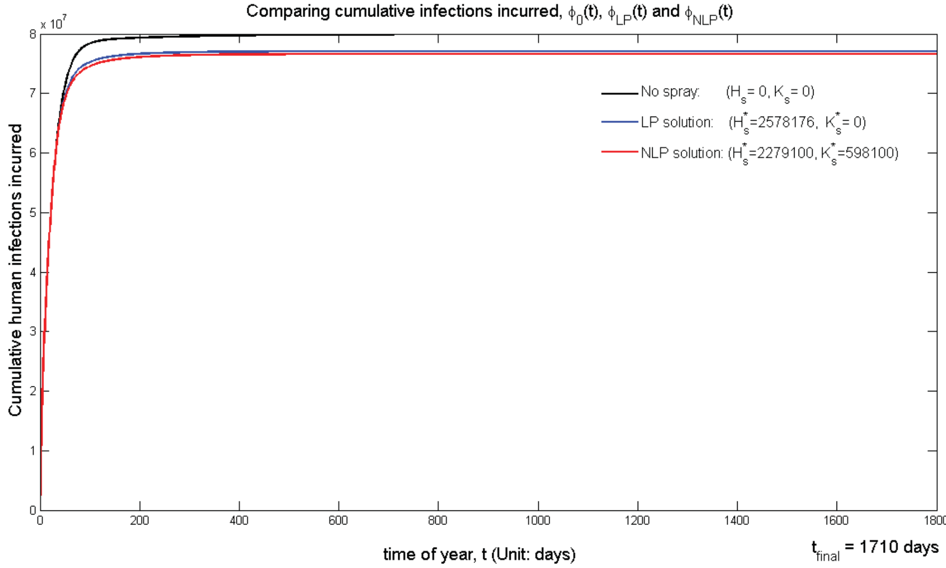


Figure 4.14. Comparison of cumulative number of human infections incurred.

The cumulative number of human infections incurred without spray ($\Phi_o(0,0,t)$) ; implementing LP model's optimal solution ($\Phi_{LP}(2578176,0,t)$) ; implementing the NLP model's optimal solution ($\Phi_{NLP}(2279100,598100,t)$) are compared in Figure 4.14. Spray is done for both models on 1st February ($\gamma = 32$). By the time the infected sandfly population becomes less than one ( t = 1710 days ), the NLP model's optimal solution ($H_s = 2279100, K_s = 598100$) has already saved 5537.2 million person days (area between $\Phi_o(0,0,1710)$ and $\Phi_{NLP}(2279100,598100,1710)$ in Figure 4.14), whereas the LP model's optimal solution has saved 4818.4 million person days (area between $\Phi_o(0,0,1710)$ and ($\Phi_{LP}(2578176,0,1710)$) in figure 4.14). These figures are obtained by computing the cumulative area between the curves, $a(H_s, K_s, t_{final})$ (Figure 4.15).

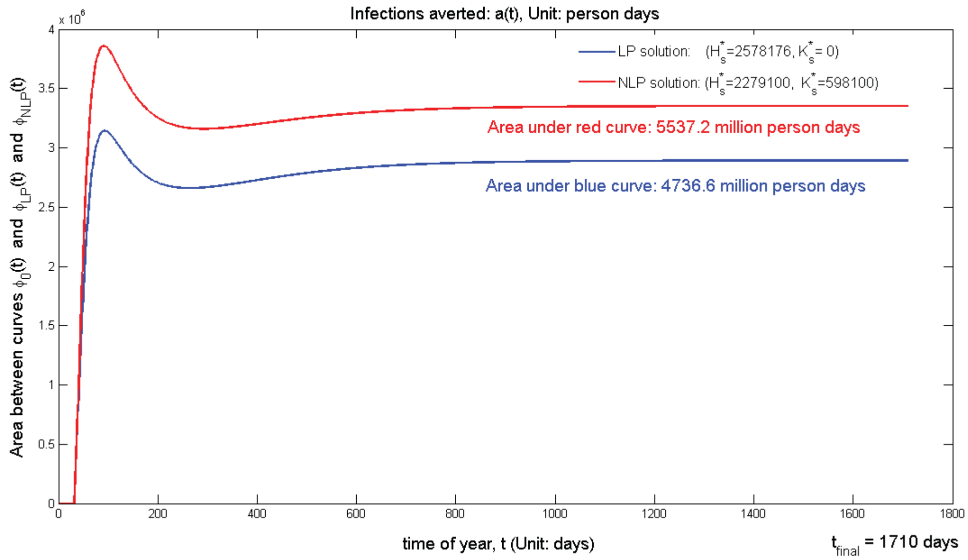


Figure 4.15. Cumulative number of person days averted by the two model's solutions.

In 1710 days, the implementation of NLP solution has gained 718.8 million person days over the implementation of the LP model. After 1710 days, the number of infected sandflies for both systems shown above (blue and red curves) will continue to approach zero. Figure 4.16 shows the "number of humans that get infected" on different days when the two optimal solutions are implemented.

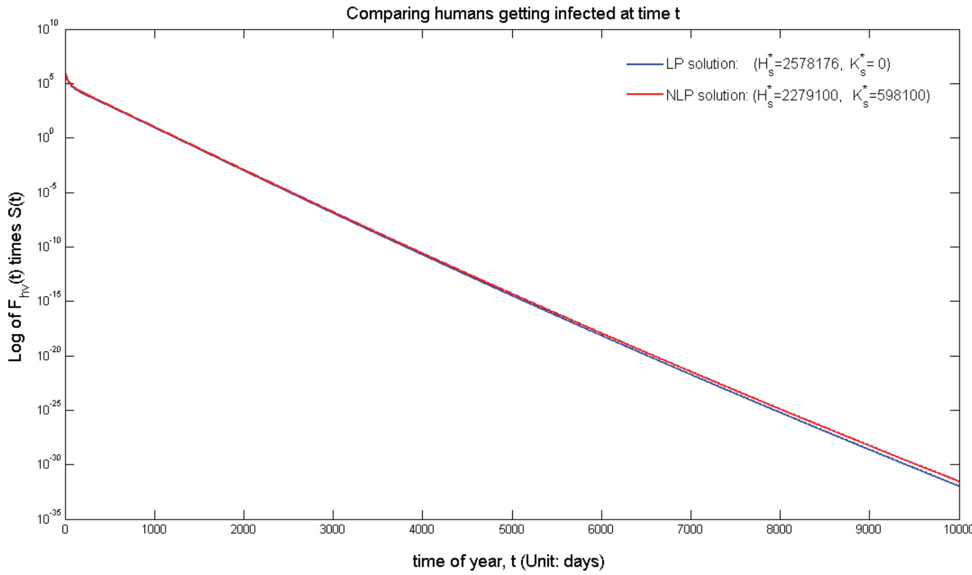


Figure 4.16 . Comparing the number of humans getting infected at time $t$ : $F_{hv}(t)S(t)$.

Since the number of human infections at time t (given by the disease transmission term : $F_{hv}(t)S(t)$), for the NLP model's solution is increasing by extremely small amounts (of the order of $10^{-30}$), theoretically in the long term future (as $t_{final} \to \infty$), the area under the NLP solution's curve $\left(\int_{t_0}^{t_{final}} F_{hv}\,(t)S(t)\ \ dt = \Phi_{NLP}\left(H_s, K_s, t_{final}\right)\right)$ will become larger than that under the LP solution's curve $\Phi_{LP}\left(H_s, K_s, t_{final}\right)$. Therefore, after an extremely long time, the number of infections averted by the LP model's solution will be larger than those averted by the NLP model's solution: $\left(a_{LP}(2578176, 0, t_{final}) < \ a_{NLP}(2279100, 598100,\ t_{final})\right)$ as the blue and red curves will intersect in figure 4.15 above. The curves $a\left(H_s, K_s, t_{final}\right)$ intersect after an extremely long time, because after 1710 days, the number of sandflies is between 0 and 1, so the LP model's solution takes a long time to make up for the difference of 718.8 million person days. Hence, the LP model's solution kills more sandflies (Figure 4.13) and in the long term future also saves more humans from getting infected.

Figure 4.17 shows the time taken for the infected sandfly population to become less than one, as more money is available to conduct the spray campaign.

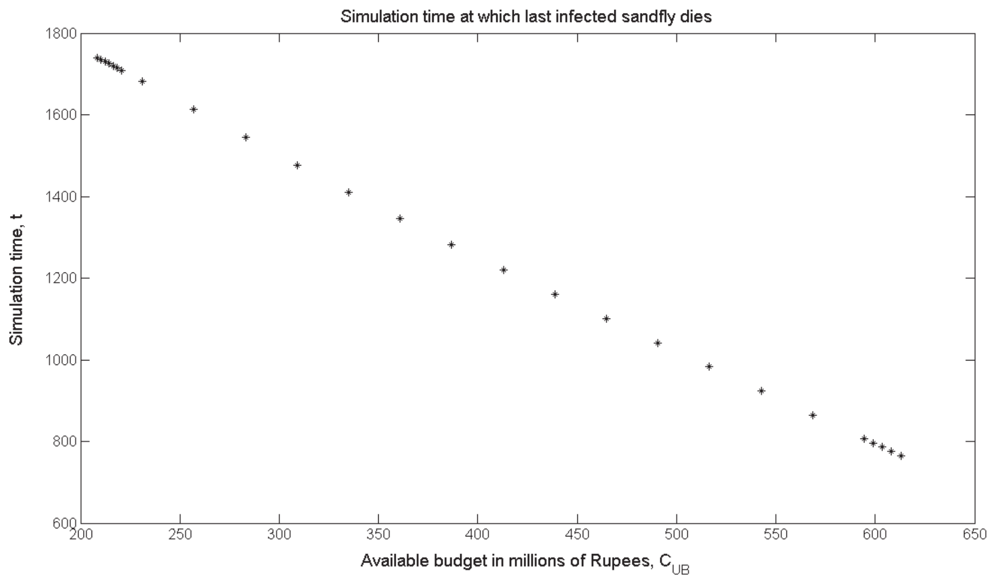


Figure 4.17 Time taken by infected sandflies to become less than one versus budget.

Figure 4.17 shows the time taken for the infected sandflies to become less than one versus available budget, using the 2 dimensional nonlinear model. Since the time taken by the infected sandfly population to become less than one should reach a non-zero value, after which it is not expected to reduce even if more budget is available, an exponential function might be a good fit for the above data. However, due to uncertainty in parameter estimates and approximation errors, the trend in data (Figure 4.17) does not seem to be exponential for the range of budget considered.

Comparing the 62 dimensional linear and nonlinear models: A graph similar to Figure 3.4 can be drawn for each of the 31 VL-affected districts. For each of the 31 graphs the slope (*BMCR*) of the objective function is variable in the $H_s$ and $K_s$ directions. The first reason for this is a difference in the number of sites available for spraying in each district. The ratio of houses to cattle sheds is minimum for district Sheohar (0.8) and maximum for district Darbhanga (8.9). The second reason being: there is a difference in insecticide material cost for spraying in each house ($I_h N_1 = Rs. 47.97$) and each cattle shed ($I_k N_1 = Rs. 23.98$). This model considers each district separately, and recommends spraying the most efficient districts ($x$ or $y$ variables with highest *BMCR* values) first, and thus achieves a 37 times higher insecticide induced death rate on the last day as compared to the 2 dimensional linear model. Since the 62 dimensional nonlinear model allocates insecticide cost-effectively across 62 variables, the number of human infections averted is 34% higher than those averted by the 2 dimensional nonlinear model. Table 4.10 compares the optimal allocation $(H_s^*, K_s^*)$ recommended by the 62 dimensional LP and NLP models, respectively.

Table 4.10. Optimal allocation from the multi-dimensional models.

| District number | District name | Lower bound of $H_s$ for each district | Linear model | | Nonlinear model | | Upper bound on $K_s$ for each district |
|---|---|---|---|---|---|---|---|
| | | | $H_s^*$ | $K_s^*$ | $H_s^*$ | $K_s^*$ | |
| 1 | Araria | 151519.137 | 151519.1 | 0 | 151520 | 0 | 134989.2 |
| 2 | Arwal | 2894.746717 | 2894.747 | 0 | 2890 | 0 | 134989.2 |
| 3 | Banka | 894.8639775 | 894.864 | 0 | 890 | 99950 | 134989.2 |
| 4 | Begusarai | 70305.394 | 70305.39 | 0 | 70310 | 0 | 68871.2 |
| 5 | Bhagalpur | 10257.76266 | 10257.76 | 0 | 10260 | 127530 | 237420.4 |
| 6 | Bhojpur | 14782.31707 | 14782.32 | 0 | 14780 | 93140 | 138925.5 |
| 7 | Buxar | 7320.731707 | 7320.732 | 0 | 7320 | 78570 | 134989.2 |
| 8 | Darbhanga | 112754.4794 | 112754.5 | 0 | 112750 | 0 | 85933.29 |
| 9 | E. Champaran | 184353.8696 | 184353.9 | 0 | 184350 | 0 | 166063.3 |
| 10 | Gopalganj | 48796.57598 | 48796.58 | 0 | 48800 | 0 | 88725.23 |
| 11 | Jehanabad | 2621.271107 | 2621.271 | 0 | 2620 | 38840 | 134989.2 |
| 12 | Katihar | 79787.68762 | 79787.69 | 0 | 79790 | 0 | 121839.9 |
| 13 | Khagaria | 24503.11914 | 229583.3 | 0 | 24500 | 24410 | 53353.16 |
| 14 | Kishanganj | 50135.45966 | 50135.46 | 0 | 50140 | 48400 | 134989.2 |
| 15 | Lakhlsarai | 7136.749531 | 7136.75 | 0 | 7140 | 18370 | 134989.2 |

Table 4.10—*Continued*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **16** | Madhepura | 100696.9981 | 100697 | 0 | 100700 | 0 | 83569.35 |
| **17** | Madhubani | 96855.67542 | 96855.68 | 0 | 96860 | 0 | 140966.4 |
| **18** | Munger | 6827.040338 | 6827.04 | 0 | 6830 | 0 | 213511.9 |
| **19** | Muzaffarpur | 190185.5769 | 190185.6 | 0 | 190190 | 0 | 137043.3 |
| **20** | Nalanda | 22191.90901 | 22191.91 | 0 | 22190 | 0 | 93364.58 |
| **21** | Patna | 74597.91276 | 74597.91 | 0 | 74600 | 0 | 126331.7 |
| **22** | Purnea | 158880.394 | 158880.4 | 0 | 158880 | 0 | 333439 |
| **23** | Saharsa | 97171.01313 | 97171.01 | 0 | 97170 | 6360 | 176388.5 |
| **24** | Samastipur | 133988.6961 | 133988.7 | 0 | 133990 | 0 | 134989.2 |
| **25** | Saran | 101103.7992 | 101103.8 | 0 | 101100 | 0 | 98440.34 |
| **26** | Sheohar | 14976.64165 | 108958.4 | 0 | 14980 | 0 | 134989.2 |
| **27** | Sitamarhi | 127137.3827 | 127137.4 | 0 | 127140 | 0 | 126644.2 |
| **28** | Siwan | 104219.1839 | 104219.2 | 0 | 104220 | 0 | 83205.17 |
| **29** | Supaul | 56946.03659 | 56946.04 | 0 | 56950 | 62550 | 134989.2 |
| **30** | Vaishali | 144571.4353 | 144571.4 | 0 | 144570 | 0 | 91041.46 |
| **31** | W. Champaran | 80700.4925 | 80700.49 | 0 | 80700 | 0 | 169695 |
| | **Total** | **2279114** | **2578176** | **0** | **2279130** | **598120** | **4184665** |
| | | Kg. required | **1374176.8** | **0** | **1214776.3** | **159398.98** | |
| | | Metric tonnes required | **1374.17** | **0** | **1214.7** | **159.4** | |
| | | **Grand total (Metric tonnes)** | **1374.17** | | **1374.1** | | |

Note: The difference between total $H_s^*$ (2279130) in column 6 and the lower bound of $H_s$ (2279114) in column 3, is due to approximation errors introduced by Matlab functions: ode5 and simpsons. In the 62 dimensional LP model, only district 13 (Khagaria), is allocated insecticide above its lower bound for houses. All other districts have an allocation equal to the lower bound based on their affected human population. Simulation time horizon, $t_{final} = 122\ days$.

After allocating as per the lower bound, the 62 dimensional NLP model invests every additional dollar of the remaining money, in one of the 62 decision variables ($H_{si}$ , $K_{si}$ , $\forall\, i = 1,..,31$) which increases the total number of infections averted (objective function). As the slope of the objective function for each district (Figure 3.4) is variable over the feasible domain, the model chooses to increase one of the decision variable’s value as long as there is no other decision variable that provides a higher increase in the objective function’s value per dollar invested.

CHAPTER 5

# DISCUSSION AND FUTURE RESEARCH

In this dissertation mathematical models were built and analyzed to identify the optimal insecticide allocation and number of sites to be covered during an insecticide spray campaign. The models developed provide different perspectives on optimizing insecticide allocation. The results can be better predicted if data is collected to find a good estimate and distribution of uncertain parameters. Experts from Veterinary and toxicology area need to be consulted to provide precautions and guidelines to be followed when spraying insecticide in cattle sheds, such that the quality of products obtained from cattle are not adversely affected. The minimum number of houses that should be sprayed with insecticide has been computed using the present policy of insecticide allocation in Bihar (to avoid any political fallback). This research study proposes an expansionary policy, since only the money left after spraying in minimum number of houses is available for optimizing.

## 5.1 Linear Optimization Model

The discussion and future work of the linear optimization model are presented in this section.

### 5.1.1 Discussion on the Linear Model

Leishmaniasis is a vector borne disease which is in urgent need of public health policy because of its impact on the economy and health of the populations of affected developing countries. Effective and optimal insecticide intervention might be able to achieve the maximum possible death rate in the vector population and thus help in reducing the risk of disease transmission to humans. The linear model provides a novel mathematical framework to obtain three types of results, where the first result may help in choosing a cost effective (optimal) insecticide spraying strategy and the second result may help to visualize the increase in optimal value of insecticide induced death rate with varying levels of available budget. The third result might provide a better understanding of the scenarios in which a particular preplanned spray coverage option could be selected for achieving highest possible reduction in sandfly population per unit material cost. The first result helps to perform comparisons of insecticides for achieving maximum insecticide induced sandfly death rate with the same available budget. The public health department might find this information helpful in deciding between potential insecticides to be used for the next spray campaign. This model might be particularly helpful to Bihar's public health department for deciding the next insecticide to be used considering the reduced initial efficacy of DDT due to the resistance developed by sandflies as reported by Dinesh et al. [47].

### 5.1.2 Future Work on the Linear Model

For simplicity, the model treats the spraying activity at human and cattle sites as two separate (mutually exclusive) projects, and recommends spraying at one of the two site types, based on a higher insecticide induced death rate to material cost ratio. Only insecticide's lethal effect is incorporated in the model and the repellent effect is ignored. One of the limitations of this simple model is that the distribution of the sandfly population visiting the two types of sites is assumed deterministic and the same sandfly population distribution is assumed to be effective daily.

In the proposed model, only the insecticide material cost is a function of the two decision variables. A better way of formulating the cost function might be to express the storage, transportation, spray equipment and personnel costs also as functions of decision variables. Impact of number of insecticide applications on sandfly population size and development of resistance in vectors can be incorporated to suggest the optimal combination of insecticide based control strategy at both larval and adult stages of the vector as discussed by Luz et al. [66].

Optimal insecticide amount allocated per chicken can also be obtained from the model by incorporating the sandfly's attraction towards avian blood and poultry population in the state.

The average number of cattle per cattle shed (presently assumed constant), is unknown and can be treated as a random variable. Hence, the number of cattle sheds also becomes a random variable. Since, the upper bound on one constraint would be known probabilistically, the model can be formulated as a stochastic linear program. The problem formulation would include assumptions on the recourse policy. After the uncertainty in the constraint's upper bound is realized, the actual insecticide induced death rate can be calculated by solving the second stage problem.

The *BMCR* function (presented in section 3.3.2) can be derived for comparing two preplanned spray coverage options in each of the 31 VL affected districts of Bihar state. A simplistic pseudo code similar to that developed in section 3.3.3 can be used to rank the 62 different *BMCR*'s and choosing to spray in districts which yield the highest reduction in sandfly population per rupee invested in insecticide material.

## 5.2 Discussion and Future Work on the Differential Equations Model

A stability analysis will be carried out on the system of coupled ordinary differential equations, by assuming a fixed number of sites sprayed at and a constant value for insecticide effects. Since many parameters are uncertain and only known as a range, an uncertainty and sensitivity analysis will be performed to estimate the distribution of the number of human infections averted and the basic reproduction number. Features will be added to the differential equations system to model the situation in Bihar state more closely. The daily migration of humans between districts of Bihar will be incorporated in the system. The present model accounts for, only the number of bites deflected from humans due to the presence of the cattle population. The effects of seasonal variation and a dynamic cattle population on the sandlfy population will be studied.

Bonds et al. [67] has modeled natural death rate, transmission rate and recovery rate as functions of per capita income. In future work, the vector-host model will be modified to include the death rate, transmission rate and recovery rate as functions of per capita income. This might help in analyzing the effect of economy and the role of poverty trap on the dynamics of VL transmission. An alternate formulation of the disease transmission term will be derived considering the possibility of all sandfly bites going on only a subset of the susceptible human population. This formulation might be helpful to compute the expected number of humans getting infected at a given time.

## 5.3 Nonlinear Optimization Model

The discussion and future work on the nonlinear optimization model are presented in this section.

### 5.3.1 Discussion on the Nonlinear Model

In this research study a coupled differential equations model accounting for the sprayed insecticide's lethal and repellent effects has been developed. The output from this differential equations model forms the objective function of a nonlinear optimization model. The numerical results from the nonlinear model are compared with the linear model which aims to maximize the insecticide induced death rate. This provides the public health policy makers with a comparison of insecticide allocation, when the criterion is increasing sandfly mortality versus increasing human infections. Attempting to achieve highest possible mortality in the sandfly population does not necessarily result in saving highest number of people from getting infected (over a short time horizon). Comparing the numerical results from the two-dimensional models with multi-dimensional models provides an opportunity to study the impact of using state level and district level demographic data on optimal insecticide allocation.

All four optimization models are solved to obtain the optimal number of sites to be sprayed for optimizing a metric at the time the second round of spray starts in Bihar (after a ninety day gap). The two-dimensional linear model recommends spraying only in houses, when the 2012 VL budget of Bihar [41] was used as available budget (in line with the present policy of allocating insecticide based on human population only). However, the two-dimensional linear model's recommendation also saves the least number of human infections, ninety days after spray. The two-dimensional nonlinear model's recommendation, computed by considering human and cattle populations, saves 22 % more human infections, ninety days after spray. The multi-dimensional nonlinear model considers both human and cattle populations (including other demographic data) at district level, and can save 64 % more human infections, ninety days after spray. As more details are considered in the insecticide allocation calculations: first the (state level) cattle population and second the (district level) demographic data including human and cattle populations; the recommendation from the models can save increasing number of human infections.

Another important insight obtained by qualitatively analyzing the results from the two-dimensional linear and nonlinear optimization models is on the choice of the best spray campaign policy. If the goal is to save a maximum number of humans from infection in the short term or a second round of spray is feasible soon, then spraying in the minimum number of houses and the maximum possible number of cattle sheds is a better policy. In the near future, this spray campaign policy will help to save maximum number of humans from getting infected. If the goal is to save a maximum number of humans from getting infected in the long term or a second round of spray is not feasible in the near future, then spraying in the maximum possible number of houses is a better spray campaign policy. A long time after such a spray campaign policy has been implemented; maximum number of humans would have been saved from infection.

### 5.3.2 Future Work on the Nonlinear Model

Since insecticide is sprayed twice annually in Bihar state, multiple spray rounds will be incorporated in the model. Depending on whether the goal is to save humans from getting infected in the short or long term and annual frequency of spray, the best “spray campaign policy” will be studied using dynamic program or an optimal control method. The sandfly map, when completed, can be incorporated to represent the spatial and temporal distribution of sandfly population in different VL affected districts of Bihar.

APPENDIX A

DATA SET FOR DISTRICTS

## Appendix A

The number of government clinics, affected human population and actual human population in each of the 31 VL affected districts of Bihar state are tabulated below.

Table A.1. Demographic data for VL affected districts.

| Serial no. | District name | No. of government clinics, $g$ (State Health Society report [53]) | VL affected human population, $N_{hAff}$ (State Health Society report [53]) | Human population, $N_{hAct}$ (2011 census of India [52]) |
|---|---|---|---|---|
| 1 | Araria* | 9 | 2,153,592 | 2806200 |
| 2 | Arwal* | 3 | 41,144 | 699563 |
| 3 | Banka* | 1 | 12,719 | 2029339 |
| 4 | Begusarai | 11 | 999,274 | 2954367 |
| 5 | Bhagalpur | 7 | 145,797 | 3032226 |
| 6 | Bhojpur | 9 | 210,106 | 2720155 |
| 7 | Buxar* | 4 | 104,052 | 1707643 |
| 8 | Darbhanga | 14 | 1,602,617 | 3921971 |
| 9 | E. Champaran | 20 | 2,620,283 | 5082868 |
| 10 | Gopalganj | 10 | 693,562 | 2558037 |
| 11 | Jehanabad* | 5 | 37,257 | 1124176 |
| 12 | Katihar | 18 | 1,134,049 | 3068149 |
| 13 | Khagaria | 6 | 348,271 | 1657599 |
| 14 | Kishanganj* | 6 | 712,592 | 1690948 |
| 15 | Lakhlsarai* | 2 | 101,437 | 1000717 |
| 16 | Madhepura | 7 | 1,431,240 | 1994618 |
| 17 | Madhubani | 18 | 1,376,642 | 4476044 |
| 18 | Munger | 6 | 97,035 | 1359054 |
| 19 | Muzaffarpur | 14 | 2,703,171 | 4778610 |
| 20 | Nalanda | 11 | 315,421 | 2872523 |
| 21 | Patna | 16 | 1,060,285 | 5772804 |
| 22 | Purnea | 13 | 2,258,220 | 3273127 |
| 23 | Saharsa | 7 | 1,381,124 | 1897102 |
| 24 | Samastipur* | 14 | 1,904,426 | 4254782 |
| 25 | Saran | 15 | 1,437,022 | 3943098 |
| 26 | Sheohar* | 2 | 212,868 | 656916 |
| 27 | Sitamarhi | 13 | 1,807,046 | 3419622 |
| 28 | Siwan | 14 | 1,481,302 | 3318176 |
| 29 | Supaul* | 11 | 809,393 | 2228397 |
| 30 | Vaishali | 11 | 2,054,842 | 3495249 |
| 31 | W. Champaran | 13 | 1,147,023 | 3922780 |
|  | Total | 310 | 32393812 | 87716860 |

# APPENDIX B

# NATURAL SANDFLY DEATH RATE ESTIMATION

Table B. 1. Daily survival probability of *P. Papatasi* (Srinivasan and Panicker [45])

| Month Number | Month | Daily survival probability ($s_p$) | Sandflies dead/day/sandfly ( - ln $s_p$ ) |
|---|---|---|---|
| 1 | Mar-88 | 0.93 | 0.072571 |
| 2 | Apr-88 | 0.921 | 0.082295 |
| 3 | May-88 | 0.919 | 0.084469 |
| 4 | Jun-88 | 0.912 | 0.092115 |
| 5 | Jul-88 | 0.893 | 0.113169 |
| 6 | Aug-88 | 0.922 | 0.08121 |
| 7 | Sep-88 | 0.926 | 0.076881 |
| 8 | Oct-88 | 0.942 | 0.05975 |
| 9 | Nov-88 | 0.932 | 0.070422 |
| 10 | Dec-88 | 0.944 | 0.057629 |
| 11 | Jan-89 | 0.93 | 0.072571 |
| 12 | Feb-89 | 0.931 | 0.071496 |
| 13 | Mar-89 | 0.935 | 0.067209 |
| 14 | Apr-89 | 0.917 | 0.086648 |
| 15 | May-89 | 0.921 | 0.082295 |
| 16 | Jun-89 | 0.902 | 0.103141 |
| 17 | Jul-89 | 0.9 | 0.105361 |
| 18 | Aug-89 | 0.932 | 0.070422 |
| 19 | Sep-89 | 0.949 | 0.052346 |
| 20 | Oct-89 | 0.927 | 0.075802 |
| 21 | Nov-89 | 0.928 | 0.074724 |
| 22 | Dec-89 | 0.948 | 0.053401 |
| 23 | Jan-90 | 0.945 | 0.05657 |
| 24 | Feb-90 | 0.943 | 0.058689 |
| | | | Mean = 0.075882, s.d.= 0.016239 |

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