

# Respiratory Disease in Chimpanzees of Gombe Stream National Park, Tanzania: Advancing Noninvasive Methods in Epidemiology

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# Dedication

I dedicate this work to my parents, Keith and Elaine. They passed along the genes and created the environment in which to raise strong, independent-minded, and driven children, embracing life and nature. They embody a level of generosity and love that I will always endeavor to replicate and reciprocate.

# Research Abstracts

**Chapter 2:** Growing concerns of emerging infectious diseases demand innovative approaches to disease surveillance. Disease surveillance in wildlife populations is rapidly expanding, and with it there is a strong need for systematic evaluations of surveillance system performance. Due to a large proportion of disease-associated mortality among chimpanzees in Gombe National Park, Tanzania, a syndromic health surveillance system was established in 2004 to collect data on several disease syndromes. In this study, an assessment of system performance was initiated, with analyses of data quality, baselines trends of disease, and statistical algorithms of outbreak detection. Given strong concerns for and need to understand the epidemiology and impacts of respiratory diseases in great ape populations, these analyses focused on respiratory syndrome. Overall, data quality was good, although identified problems in community coverage and data consistency can guide improvement in data collection methods and provide a framework for use and interpretation. Baselines trends of respiratory disease were low, which contributed to the development of low thresholds for outbreak detection. Two detection algorithms were used, resulting in the detection of 14 respiratory outbreaks from 2005-2012, 8 of which were previously unrecognized. This systematic evaluation of surveillance system performance offers key insights into the capacity of yet another tool for noninvasively studying a disease in primate and other wildlife populations.

**Chapter 3:** Respiratory diseases are increasingly recognized as having a significant impact on great ape populations. Unfortunately, our understanding of great ape respiratory disease has been based heavily on observations of large-scale outbreaks with high morbidity and mortality, which may not be representative of endemic respiratory diseases in these populations. To explore this issue further, outbreak data generated from the study in Chapter 2 was utilized to describe outbreak morbidity, demographics, and duration, and to evaluate patterns of infection associated with outbreak size. A total of 15 outbreaks in 2 chimpanzee communities in Gombe National Park, Tanzania were analyzed, which included 6 major outbreaks with 20% or more of a community affected

and 9 small outbreaks. Major outbreaks had a significantly higher morbidity and tended to be of shorter duration than smaller outbreaks, although the latter difference was not significant. In evaluating the role of demographics in the size and onset of outbreaks, males were significantly more likely to be associated with large outbreaks and the early onset of outbreaks. A significant positive association was also observed between an individual's case status in an outbreak and their matrilineal relationship to another case. Overall, respiratory outbreaks were an infrequent occurrence over 9-years of study, but these analyses provide further insight on the heterogeneity of disease transmission and the epidemiology of respiratory disease outbreaks in chimp populations.

**Chapter 4:** Syndromic surveillance is an emerging field in veterinary medicine and a novel approach in wildlife. As a result associated methodologies for outbreak detection and assessment of surveillance system performance are highly needed. Chapter 2 describes initial work to assess performance of a system in respiratory disease syndrome surveillance and outbreak detection among free-living chimpanzees in Gombe National Park, Tanzania. This chapter builds on that effort with a quantitative estimate of outbreak detection sensitivity. In this study, empirical demographic, behavioral and syndromic surveillance data were integrated with an agent-based, network model of the Kasekela chimpanzee community for outbreak and surveillance simulation. Out of 1064 outbreaks produced from 2000 simulations, 702 were detected using the weekly count threshold for outbreak detection described in Chapter 2 and 633 were detected using the weekly prevalence threshold. Thus, overall surveillance sensitivity for outbreak detection was estimated as 66% (95% Confidence Interval: 63.1, 68.8%) and 59.5% (95% Confidence Interval: 56.5%, 62.4%) for the weekly count and prevalence thresholds, respectively. Differences in sensitivity between quarters of the year were observed, with Quarter 1 (Count threshold: 81%; Prevalence threshold: 76%) having the highest outbreak detection sensitivity and Quarter 3 (Count threshold: 30%; Prevalence threshold: 25%) having the lowest. Difference between quarters in both outbreak detection sensitivity and outbreak characteristics provide important insight into the important role of the chimpanzee social network in disease transmission and detection.

**Chapter 5:** Epidemiology of tuberculosis in free-living primates has been limited when using traditional testing methods. PCR amplification of insertion element IS6110 of *Mycobacterium tuberculosis* from fecal samples was evaluated as a noninvasive screening test for tuberculosis in primates. Active tuberculosis was detected among inoculated macaques and naturally-exposed chimpanzees, demonstrating the utility of this test.

**Chapter 6:** Noninvasive disease detection methods in free-living primates are of critical need given significant emerging infectious disease concerns. A recently validated noninvasive tuberculosis test, fecal IS6110 PCR, was used to screen populations of chimpanzees (*Pan troglodytes schweinfurthii*) and baboons (*Papio anubis*) in Gombe National Park, Tanzania. Approximately 68% and 33% of chimpanzee and baboon populations were tested, respectively; no animals tested positive for tuberculosis. This study demonstrates the feasibility of large-scale, noninvasive screening of free-living primate populations for tuberculosis.

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# Chapter 1 | Literature Review

## *Section 1.1 Emerging Infectious Diseases and Primates*

In a world of increasing wildlife habitat loss, a growing human population, and expanding connectivity between human, domestic animal and wildlife populations, emerging infectious diseases are ever more a complex and disturbing issue. The public health threat is apparent, as evidenced by the global and regional epidemics of diseases like pandemic avian influenza, human immunodeficiency virus (HIV) and Ebola virus [Marí Saéz et al., 2015; Nelson et al., 2011; Jones et al., 2008; Keele et al., 2006]. In fact, approximately 60% of emerging infectious diseases of public health concern are zoonotic, and the majority of these are of wildlife origin [Jones et al., 2008; Woolhouse and Gowtage-Sequeria, 2005]. Of course, the negative impacts of emerging infectious disease are not unique to human populations, and there are numerous examples of disease spillover from humans and their domestic animals into wildlife populations, with long-term and sometimes devastating consequences [Cleaveland et al., 2005; Roelke-Parker et al., 1996; Nugent, 2011; Epstein and Price, 2009; Nituch et al., 2011; Kock et al., 1999; Michel et al., 2009].

Primate populations play a variety of roles in emerging disease events. Based on their close genetic relatedness to humans alone, the risks of infectious disease transmission between the two populations are quite high [Loomis, 2003]. In addition to host susceptibility, patterns of contact (among primates, humans, and domestic livestock) through habitat encroachment, bushmeat and wildlife pet trades, and human habituation for research and tourism already result in pathways for disease transmission [Wolfe et al., 2005; Pusey et al., 2008; Wilbur et al., 2012; Epstein and Price, 2009; Keele et al., 2006]. In some cases, primates are natural reservoir hosts that pose a risk to humans in the transmission of novel pathogens, such primate-specific viruses [Wolfe et al., 2005; Leendertz et al., 2009; Mugisha et al., 2010; Keele et al., 2006]. Unfortunately, these risks of transmission and the potential for disease development in humans are often

unknown. Primates may be non-maintenance, spillover hosts that serve as links for disease transmission between other wildlife reservoirs or the environment and humans. Examples of this include the transmission of Ebola virus and anthrax to humans through the consumption of dead primates [Leendertz et al., 2004; Cameroon: Primates Die From Anthrax, Causing Bush Meat Scare, 2005]. They may also be maintenance, spillover hosts, in which disease transmission is sustained at such a level within their own populations as to maintain endemic levels and pose a risk of spillback into human or domestic populations [Müller-Graf et al., 1997; Schaumburg et al., 2012b; Keet et al., 2000].

Most concerning to primate conservation, however, are the emerging infectious disease events among small and isolated primate populations in which the introduction of novel or reemerging pathogens causes catastrophic declines. The introduction of human respiratory viruses is a well-recognized example of this, where introduction into highly susceptible populations results in large-scale epidemics that tend to fizzle out after a short period of transmission [Köndgen et al., 2008; Hastings et al., 1991; Kaur et al., 2008]. Despite the recognized association between human habituation (e.g. the conditioning of primates to close encounters with human observers) and these disease outbreaks in great apes, among the benefits provided by ongoing, intense monitoring owing to research and tourism is the continued protection of these populations from other threats, such as poaching and further habitat loss [Pusey et al., 2007; Campbell et al., 2011]. Further, surveillance for these and other emerging infectious diseases among primate populations may provide key insights into the natural ecology of these diseases and risks to both primate and human populations [Wolfe et al., 2007; Jones et al., 2008; Woolhouse et al., 2001; Keele et al., 2009; Rudicell et al., 2010].

### *Infectious Respiratory Diseases of Great Apes*

Great apes are known to be susceptible to and suffer disease from a variety of respiratory pathogens (Table 1-1). Great apes are particularly susceptible to common human respiratory viruses (e.g. Influenza virus, Respiratory syncytial virus, human metapneumovirus) and are at high risk for exposure and infection under conditions of

close human contact, such as the captive environment or habituation for research or ecotourism [Sasseville et al., 2013; Slater et al., 2014; Szentiks et al., 2009]. Infection, disease, and mortality have been observed in all age groups, particularly among populations with no previous history of exposure [Köndgen et al., 2008; Kaur et al., 2008; Palacios et al., 2011; Williams et al., 2008]. In epidemics of wild apes, infants often suffer the greatest levels of mortality, not only from disease, but also due to orphaning [Kaur et al., 2008; Williams et al., 2008]. Respiratory illnesses can become more severe and prolonged when complicated by secondary bacterial infections such as *Streptococcus pneumoniae*, *Klebsiella pneumoniae* or *Pasteurella multocida* [Köndgen et al., 2008; Palacios et al., 2011; Murphy, 2015; Hastings et al., 1991; Szentiks et al., 2009]. Great apes are also susceptible to infection and disease caused by *Mycobacterium tuberculosis*, *M. bovis*, and *M. avium* [Murphy, 2015; Loomis, 2003]. Infections with these bacterial pathogens, specifically *M. tuberculosis* and *M. bovis* are rare in captivity as a result of strict testing and quarantine guidelines established in the 1970's and 1980's [Loomis, 2003]. Until a recent finding of infection by a novel organism of the Mycobacterium Tuberculosis Complex was made in a wild chimpanzee, tuberculosis was believed by many to be a disease of captive, but not wild, great apes [Coscolla et al., 2013]. More detailed discussion on mycobacterial pathogens in great apes can be found in Section 1.3 of this chapter.

Although much of our understanding of these infections and their associated pathology originates from observations of disease in captive animals, there are numerous reports of respiratory disease outbreaks and disease-induced mortalities among free-living populations. In 1988, several habituated mountain gorilla groups of the Virunga Volcanoes, Rwanda succumbed to a respiratory disease associated with measles virus and *Mycoplasma pneumoniae* infection, resulting in 81% morbidity and the death of six female gorillas [Sholley, 1989; Woodford et al., 2002]. The mountain gorillas of Virunga Volcanoes were affected again in 1991 by another respiratory disease epidemic; in this case the pathology of a dead silverback gorilla revealed severe bronchopneumonia associated with paramyxovirus infection [Homsy, 1999]. Eleven chimpanzees in Mahale Mountains National Park, Tanzania died during a respiratory disease outbreak in 1993

[Hosaka, 1995]. Although a pathogen was not identified, observations of flu-like illness among tourists during this period lead to the assumption that disease may have been influenza. In Gombe National Park, Tanzania, a review of 40 years of behavioral and health data of a community of chimpanzees revealed approximately 60% of known mortalities to be associated with illness, and almost half of those were respiratory in nature [Williams et al., 2008]. Most of the fatal respiratory illnesses in this study were associated with 3 major epidemics. Respiratory pathogens isolated in association with chimp mortalities in this population have been *S. pneumoniae* and *S. pyogenes* [Mlungeya, 2001]. In the past decade, there have been several outbreaks of respiratory disease among chimpanzees in multiple populations, resulting in high morbidity and mortality, which have been definitively linked through molecular evidence to human respiratory syncytial virus and metapneumovirus [Köndgen et al., 2008; Kaur et al., 2008; Palacios et al., 2011; Köndgen et al., 2010]. Despite a long history of such disease outbreaks among great ape populations, much remains unknown regarding endemic respiratory pathogens, cycles of disease, and routes of transmission.

Table 1-1 Well-recognized respiratory pathogens of great apes. Adapted from Murphy 2015.

| Pathogen                          | Disease                     | Epidemiology  | Diagnostic methods   | Documented in free-living species   |
|-----------------------------------|-----------------------------|---|--|---|
| Adenovirus                        | Adenovirus                  | Aerosol, fecal-oral transmission. Sporadic to epidemic outbreaks. | Serology, virus isolation, PCR                                       | Mountain gorillas, lowland gorillas, chimpanzees, bonobos [Wevers et al., 2011; Roy et al., 2009; Whittier, 2009]                         |
| Influenza virus (orthomyxovirus)  | Influenza                   | Aerosol transmission. Epidemic outbreaks.                         | Virus isolation, PCR, seroconversion                                 | Mountain gorillas [Whittier, 2009]  |
| Morbilivirus                      | Measles                     | Aerosol transmission. Sporadic to epidemic outbreaks.             | Virus isolation, PCR, seroconversion                                 | Mountain gorillas [Hastings et al., 1991]   |
| Human metapneumovirus             | Metapneumovirus             | Aerosol transmission. Sporadic outbreaks.                         | Virus isolation, PCR   | Mountain gorillas, chimpanzees [Palacios et al., 2011; Köndgen et al., 2008; Kaur et al., 2008; Kondgen et al., 2010]                     |
| Parainfluenza III (paramyxovirus) | Parainfluenza               | Aerosol or direct contact transmission. Sporadic outbreaks.       | Virus isolation, PCR, seroconversion                                 | Mountain gorillas [Whittier, 2009]  |
| Pneumovirus                       | Respiratory syncytial virus | Aerosol transmission. Sporadic outbreaks.                         | Virus isolation, PCR, seroconversion                                 | Mountain gorillas, chimpanzees [Whittier, 2009; Köndgen et al., 2008; Kondgen et al., 2010]   |
| <i>Streptococcus pneumonia</i>    | Pneumonia                   | Aerosol transmission  | Culture, PCR   | Mountain gorillas, chimpanzees [Chi et al., 2007; Köndgen et al., 2008; Palacios et al., 2011; Terio, unpublished; Williams et al., 2008] |
| <i>Mycobacterium tuberculosis</i> | Tuberculosis                | Aerosol transmission  | Intradermal tuberculin test, $\gamma$ -interferon test, culture, PCR |   |

## *Noninvasive Epidemiological Methods*

Noninvasive epidemiologic methods are approaches to studying disease in wildlife populations *in situ* without interruption or disturbance of normal behavior. Primarily, this refers to methods of sampling, screening for, or diagnosing disease without capturing animals for these purposes. This is a particularly important feature when studying disease among organisms that are also the subject of natural behavioral studies, for example primates. It is also advantageous in that the risk of capture and anesthesia of wildlife, whose true health status and suitability for anesthesia is inherently unknown, is eliminated. There is a long history of using fecal samples for direct testing of gastrointestinal pathogens or systemically circulating hormones, but use of noninvasively collected biological samples such as feces for agents affecting other systems is a more recent advancement in wildlife epidemiology. Work by Köndgen et al. (2010) is an excellent example of the use of noninvasively collected fecal samples to study the epidemiology of respiratory viruses both during and outside of epidemics in a population of free-living chimpanzees. It is this idea, the development and application of noninvasive epidemiological methods to understand the impact of respiratory disease in wild great ape populations, that is the basis of this dissertation. The following chapter sections include detailed discussions on noninvasive sampling opportunities for studying respiratory disease in great apes, specifically tuberculosis, an understudied disease of free-living great apes due to historical limitations in detection, as well as a broad discussion of noninvasive approaches to the systematic surveillance of wildlife disease.

## *Section 1.2 Wildlife Disease Surveillance and Applications for Great Ape Disease Research*

Disease surveillance is the routine collection, analysis, and dissemination of disease information of a population, coupled with the intent to respond or intervene to mitigate transmission and subsequent population effects [Thrusfield, 2007]. Disease

surveillance in wildlife is often implemented to identify changes in trends or geographic distributions of endemic diseases of public health or agricultural concern or to track emerging or reemerging disease events that directly threaten wildlife populations. In the former case, wildlife populations may serve as sentinels of disease of public concern, providing early indication of changing disease trends or signals of epidemics. Avian mortality events, which signaled the local and regional spread of West Nile virus (WNV) across North America, are an excellent example of this [Komar, 2001]. In fact, it was the unusual death of captive-managed avian species in a New York zoo that alerted veterinarians and public health officials of the emergence of this previously foreign disease in the United States [Lanciotti et al., 1999]. Now that WNV is endemic in the U.S., mortality caused by or seroprevalence of WNV in certain avian species has been recognized as potentially useful indicators of local changes in risk patterns and early warning signals of emergent human epidemics [Komar, 2001]. In other situations, wildlife populations harbor infectious agents as maintenance hosts, the transmission of which can result in profound economic losses or public health concerns. Thus disease surveillance in such species is an integral part of programs to control and mitigate direct transmission from infected wildlife to agriculture, domestic pets, or humans. Surveillance and control of raccoon rabies in the northeastern region of the U.S. and brucellosis in bison and elk in the Greater Yellowstone Area and Grand Teton National Park are examples [Peterson et al., 1991; Rhyan et al., 2009; Etter and Drew, 2006; USDA, 2010]. A variety of control programs such as vaccination and culling have been explored or implemented in response to changes in disease patterns identified by ongoing surveillance of these diseases [Peterson et al., 1991; Miller et al., 2004; Gordon et al., 2005; USDA, 2010]. Diseases of significant concern to the stability and persistence of wildlife populations have also been targeted in surveillance programs. North American bat populations have suffered massive mortalities and population declines as a result of White-nose syndrome, a devastating skin disease caused by *Psuedogymnoascus (Geomyces) destructans*, a fungus believed to have been introduced from Europe [Blehert et al., 2009; Zupal et al., 2014]. Intensive surveillance has been rapidly implemented in hibernacula and control measures explored in efforts to halt the geographic spread and

reduce the impact of the disease on bat populations and their ecosystems [Lorch et al., 2013; Hallam and Mccracken, 2011; Foley et al., 2011].

Different approaches have been utilized in these and other cases of wildlife disease surveillance. Passive surveillance, now also referred to as scanning surveillance, often involves the utilization of opportunistically collected data to monitor endemic disease or identify newly emerging diseases. For example, using cases diagnosed and treated by wildlife hospitals and rehabilitation centers to monitor infectious disease patterns or environmental toxins is a current topic in One Health research [Randall et al., 2012; Duncan et al., 2008; Stitt et al., 2007]. The investigation of mortality reports by state or federal agencies is another example. This type of surveillance is advantageous in that it is economical, it is often the first stage in identifying new or emerging disease processes in a system, and it can be implemented in a system or population without prior knowledge of disease levels [Thrusfield, 2007; Ryser-Degiorgis and Ryser - Degiorgis, 2013]. The disadvantage is that these types of surveillance data are likely to be biased, and won't accurately reflect true population trends of disease. Referring back to the example of using rehabilitated wildlife cases as indicators of population health, cases may be more casualties of anthropogenic disturbances and interactions than infectious disease events on the mere basis of being found and recovered in areas of higher human contact [Randall et al., 2012]. Further, these types of data often lack population-level denominator values, precluding the ability to generate population estimates of disease [Thrusfield, 2007; Ryser-Degiorgis and Ryser - Degiorgis, 2013]. Lastly, where wildlife species are reservoir hosts or healthy carriers of diseases of economic or public health concern, reliance on data from clinical cases or mortality events is unlikely to be informative [Ryser-Degiorgis and Ryser - Degiorgis, 2013].

In contrast to passive surveillance, active surveillance, also referred to as targeted surveillance, is a type of disease surveillance involving proactive sampling of select species for specific disease processes or agents [Thrusfield, 2007; Ryser-Degiorgis and Ryser - Degiorgis, 2013]. With this approach, a sampling scheme is designed to reflect the make-up of the population and would include healthy and diseased individuals in the

data collection. Thus, some a priori knowledge of the population and targeted disease is necessary for statistical sample size planning or to improve efficiency of detection (e.g. sampling high risk species or groups). The advantage to this approach is that unbiased population estimates of disease can be generated. The disadvantages of this approach are increased study complexity and cost. To maximize resources and improve efficiency, these approaches are often combined in efforts to understand trends and impacts of disease in wildlife populations. As an example, ongoing studies of moose mortality in a declining population in Minnesota, U.S. have employed both approaches, utilizing data from samples of radio-collared animals as well as publicly reported and hunter-harvested mortalities [Murray et al., 2006b; Wünschmann et al., 2015; Butler et al., 2008].

Wildlife capture for disease sampling is common, particularly when active surveillance methods are employed; however, there are several non-invasive approaches to wildlife disease surveillance that provide valuable information on disease. As mentioned previously, opportunistic sampling of mortality events can provide a wide breadth of health data in addition to cause-specific mortality data (e.g. seroprevalence of disease exposures from hunter-harvested or vehicle-killed individuals) [Butler et al., 2008; Wünschmann et al., 2015]. The same is true when standardized health screening or necropsy protocols are implemented for injured or ill wildlife submitted to rehabilitation facilities [Duncan et al., 2008; Randall et al., 2012]. Noninvasively collected fecal, urine, hair, or other biological samples have demonstrated utility in gathering information on a variety of health parameters such as nutritional status and stress, as well as pathogen detection [Kondgen et al., 2010; Macbeth et al., 2010; Smiley et al., 2010; DelGiudice, 1995]. Camera-trapping or aerial surveys may also be useful noninvasive approaches in gathering data on diseases that produce overt external lesions, such as sarcoptic mange or winter tick infestation of moose [Oleaga et al., 2011; McLaughlin and Addison, 1986]. Finally, surveys of wildlife agents, hunters, or other field workers on wildlife observations can provide useful information on disease trends [Ryser-Degiorgis and Ryser - Degiorgis, 2013]. The latter two surveillance examples, in which a causative disease agent is unknown or not confirmed, might also be considered syndromic surveillance. Each of these approaches has some limitations, but they may be

advantageous over capture methods in reducing cost and risk of injury or disturbance to the species studied and in increasing sampling opportunities.

### *Syndromic Surveillance*

Syndromic surveillance has been defined by the Centers for Disease Control as the collection of pre-diagnosis health data that can signal a case or outbreak warranting a public health response [Henning, 2004]. This type of surveillance targets general types of diseases, or “syndromes,” and utilizes clinical or laboratory submission data. Such data is less specific than confirmatory diagnostic data, but is sensitive to changes in the levels of disease within a population, providing an early signal of disease outbreak (Figure 1-1) [Dórea et al., 2011]. Syndromic surveillance is effective as a cost-efficient early disease detection system; however, it is not a replacement for traditional surveillance systems that utilize diagnostic data [Rodríguez-Prieto et al., 2014]. Advantages of syndromic health surveillance go beyond outbreak detection, but also improve understanding of disease trends, provide data for risk analysis, and facilitate infection control and prevention [Ward and Carpenter, 2000].

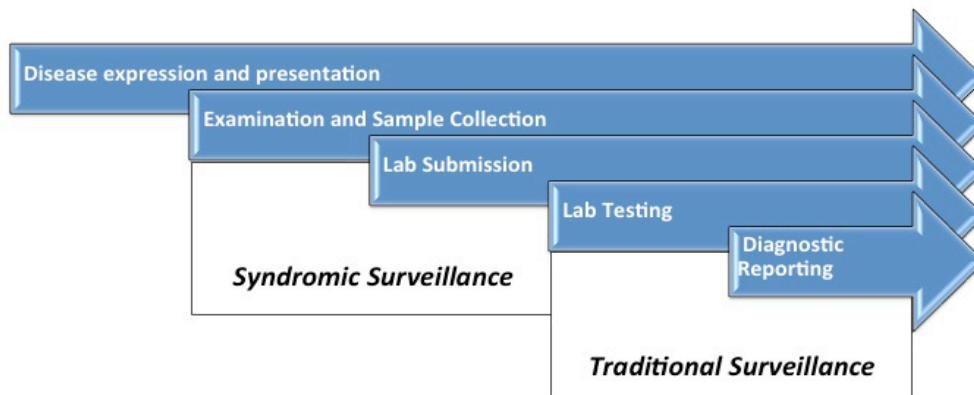


Figure 1-1 Relative time scale for outbreak detection by syndromic surveillance and traditional surveillance.

Syndromic surveillance in veterinary medicine is an emerging field. Reviews of syndromic surveillance in veterinary medicine in recent years reveal only a handful of

published initiatives on this front, the majority of which utilize data from livestock or companion animal medicine for surveillance, and all but two existing in developed countries [Dórea et al., 2011; Rodríguez-Prieto et al., 2014]. Evidence for the application of syndromic surveillance in wildlife populations is scant. Surveys for skin lesions typical of sarcoptic mange in mammalian wildlife using photographic data, telescopic observation, or infrared thermography have been investigated [Oleaga et al., 2011; Arenas et al., 2002]. The statistical classification of lesions identified on post-mortem examination into syndromes has also been examined retrospectively for wildlife mortalities in France, suggesting utility as a tool for the surveillance of preliminary mortality data [Warns-Petit et al., 2010]. However, review of the literature reveals no published reports of the systematic use of syndromic surveillance for endemic disease surveillance, early outbreak, or emerging disease detection in wildlife. Clearly, there is much room for further exploration of this type of surveillance and associated statistical methods in the areas of veterinary and wildlife health.

#### *Disease Surveillance in Great Apes*

Primates are recognized as important species in which to conduct disease surveillance, as they may serve as either sentinels or sources of zoonotic infections to humans [Jones et al., 2008; Woolhouse and Gowtage-Sequeria, 2005; Wolfe et al., 2007; Calvignac-Spencer et al., 2012]. Disease surveillance in great apes is critical also because of the recognized threat that infectious diseases pose to these populations and their conservation [Walsh et al., 2008; Fruth et al., 2008; Oates et al., 2008; Robbins and Williamson, 2008]. Because of their close genetic relatedness to humans as well as the increasing contacts between humans and great apes as a result of habitat encroachment and trade, great apes have been identified as a key taxon for targeted surveillance for novel pathogens in forecasting for emerging disease events.

As point sources of zoonotic disease, surveillance of bush meat and confiscated, rehabilitated primates and great apes have provided key insights into the pathogens to which hunters or animal care workers might be exposed [Wolfe et al., 2005; Mugisha et al., 2011; Whittier, 2009]. Disease surveillance in recently confiscated great apes and

those residing in rehabilitation facilities can provide valuable information on previous disease exposures as well as transmission pathways that exist between great apes and humans in their captive setting [Schaumburg et al., 2012a, 2012b; Whittier, 2009; Mugisha et al., 2011]. Considering cultural tendencies for bushmeat consumption, which includes consumption of animals found dead in the forest, surveillance of mortalities of free-living great apes may aid in protecting the public from exposure to fatal zoonotic pathogens [Leendertz et al., 2004; Cameroon: Primates Die From Anthrax, Causing Bush Meat Scare, 2005].

Great ape populations that are closely monitored for research and tourism present the greatest opportunity for disease surveillance. The mountain gorillas of Virunga Volcanoes and Bwindi Impenetrable Forest have been the focus of disease surveillance efforts on the part of Gorilla Doctors, previously known as the Mountain Gorilla Veterinary Program [Cranfield, 2008]. Established in 1986 to treat injuries to gorillas caused by poaching and the bushmeat trade, the Gorilla Doctors program leveraged opportunities to sample mountain gorillas in their veterinary work to conduct disease surveillance. Much of the surveillance has focused on disease risks to gorillas associated with high human density surrounding their habitat, including environmentally transmitted parasites and enteric bacterial pathogens as well as directly transmitted viral pathogens [Cranfield, 2008; Graczyk et al., 2002b, 2002a; Nizeyi et al., 2002; Whittier, 2009]. Similar surveillance for enteric pathogens has been conducted in other habituated great ape populations as a means to understand normal disease trends and risks of human pathogen transmission [Goldberg et al., 2008; Rwego et al., 2008; Gillespie et al., 2010]. Long term surveillance for SIV<sub>cpz</sub> infection through noninvasively collected fecal samples and systematic pathological examinations of chimpanzee mortalities in Gombe National Park has led to important revelations on the pathogenicity of the virus in this species [Keele et al., 2009; Rudicell et al., 2010; Terio et al., 2011]. SIV<sub>cpz</sub> surveillance continues today in combination with new streams of disease surveillance in Gombe chimpanzees, including ongoing surveillance of enteric pathogens and syndromic disease [Gillespie et al., 2010; Travis et al., 2008; Lonsdorf et al., 2006]. Certainly, the most common and informative source of data for disease surveillance among many of these

closely monitored and habituated populations is great ape mortalities, providing information on important and ongoing disease threats to great apes as well as discoveries of novel and emerging pathogens [Cranfield, 2008; Terio et al., 2011; Coscolla et al., 2013; Williams et al., 2008; Kaur et al., 2008; Köndgen et al., 2008; Leendertz et al., 2004].

#### *Validation of Diagnostic Tests Used in Wildlife Disease Surveillance*

Good surveillance requires the use of accurate diagnostic tests, of which there is a significant need in wildlife. Although diagnostic tests are available for a variety of diseases to which wildlife are susceptible, application is not always appropriate in species for which the tests were not developed. Due to the high cost of diagnostic test development and validation, most commercially available diagnostic tests have been developed for use in humans or domestic animals, for which use is high and funding more readily available. Unfortunately, because many tests utilize species-specific reagents, accurate test performance may be hindered even in closely related species.

Diagnostic test validation calls for assessment of sensitivity, the probability that a diseased animal will be positively identified by the test, and specificity, the probability that a disease-free animal will test negative [Dohoo et al., 2009]. In an ideal experiment of test sensitivity and specificity, true disease status would be known. As often is the case, however, an experimental group is unavailable and true disease status is largely unknown for test validation in wildlife species. Even so, experimental conditions of infection don't necessarily reflect natural infection, where infection dose and host immunologic response can impact detection. Further, differences between populations in prevalence of other diseases or conditions that may interfere or cross-react with a diagnostic test results can impact estimations of sensitivity and specificity, therefore test validation should ideally be performed in target populations [Szklo and Nieto, 2007]. Despite these challenges, methods such as Bayesian modeling have been developed and applied for evaluation of diagnostic test performance in wildlife, even in the absence of a gold standard test of comparison [Skerratt et al., 2011; Singer et al., 1998; Drewe et al., 2010]. These methods are advantageous in that they combine prior information (experimental data) on test

parameters, sensitivity and specificity, which may be imprecise yet informative, with field data (from wildlife studies) to generate posterior estimates of test performance in the target species or population. It is critical that such methods are employed in wildlife epidemiology for the validation of existing and newly developed diagnostic tests. For it is only with well-validated diagnostic tests that we can progress in our efforts of disease surveillance in wildlife populations.

### *Section 1.3 The Risk of Tuberculosis Transmission to Free-ranging Great Apes<sup>1</sup>*

In 2011, there were an estimated 8.7 million new cases of tuberculosis among humans worldwide, with a global prevalence of approximately 170 cases per 100,000 people [WHO, 2012]. This global pandemic is primarily caused by *Mycobacterium tuberculosis*, of which humans are the natural host, although other pathogenic mycobacteria of the Mycobacterium Tuberculosis Complex (MTC), such as *M. africanum* and *M. bovis*, also play a role in human infection [Cosivi et al., 1999; Gagneux, 2012; Kazwala et al., 2001]. Tuberculosis is predominantly a pulmonary disease, spread when bacteria are expelled from the lungs with the onset of active disease, but it may also present as extra-pulmonary disease involving other organs of the body [WHO, 2012]. Among humans infected with *M. tuberculosis*, only about 5-10% develop active disease and become infectious, while the remainder either eliminate infection or remain latently infected and do not transmit infection [WHO, 2012; Gagneux, 2012; Palomino et al., 2007]. However, those co-infected with human immunodeficiency virus (HIV) are much

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<sup>1</sup> **Publication:** Section 1.2 has been published in the form presented in this chapter. Permission for use has been obtained from the publisher, John Wiley and Sons. The citation for the manuscript is:

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more likely to develop active disease [WHO, 2012; Gagneux, 2012; Cosma et al., 2003; Palomino et al., 2007]. Advances in molecular research are revealing much more genomic heterogeneity of *M. tuberculosis* strains than previously recognized [Gagneux, 2012; Cosma et al., 2003; Sreevatsan et al., 1997; Hershberg et al., 2008]. This genomic diversity has been linked to function and may explain some of the observed differences in infection outcome, disease progression, and transmission among infected humans [Portevin et al., 2011; de Jong et al., 2008; Hershberg et al., 2008; Gagneux, 2012].

Until recently, infection with *M. tuberculosis* or any other MTC member has never been detected in free-ranging great ape populations, and many argue that contact between great apes and *M. tuberculosis* infected humans is insufficient for transmission to susceptible free-ranging great apes. However, as tuberculosis remains a major global human health threat and contact rates between humans and great apes increase with habitat encroachment, forest fragmentation, and conservation-driven research and ecotourism, the risk of tuberculosis transmission from humans to great apes must be continuously assessed. Moreover, transmission pathways from humans through other animal hosts whose contact with humans and great apes are high must be closely evaluated. Spillover of MTC infection from domestic animals and possibly humans into free-living monkey populations is well documented and may be an important source of transmission of human or domestic animal tuberculosis infection to great apes [Wilbur et al., 2012; Tarara et al., 1985; Sapolsky and Else, 1987; Keet et al., 2000]. A recent diagnosis of tuberculosis infection in a wild chimpanzee by a novel MTC strain underscores the knowledge gaps on the epidemiology and impact of tuberculosis to primate conservation [Coscolla et al., 2013]. The existence of great ape species in small, isolated populations requires that the long-term impact of tuberculosis transmission on population persistence be considered when characterizing this risk of disease caused by members of the MTC. Here we review reports on disease transmission, great ape conservation strategies, tuberculosis infection in non-human primates, and current methods of detection to demonstrate that tuberculosis transmission is a realistic threat for great ape conservation. Further, we identify specific areas where more research is needed to fully characterize this disease threat for great ape populations and demonstrate the

need for an ecosystem health-based approach to mitigate this transmission risk. This review focuses on African populations of great apes, although many of the arguments presented here have application in Asian populations as well.

### *Disease Transmission between Humans and Great Apes*

Most extant great ape populations live in fragmented populations distributed across equatorial Africa. These populations include Eastern (*Gorilla beringei*) and Lowland (*Gorilla gorilla*) gorillas, bonobos or pygmy chimpanzees (*Pan paniscus*), and common chimpanzees (*Pan troglodytes*) [Fruth et al., 2008; Walsh et al., 2008; Oates et al., 2008; Robbins and Williamson, 2008]. Eastern gorillas, of which there are two subspecies, mountain gorillas (*G. b. beringei*) and Eastern lowland gorillas (*G. b. graueri*) can be found in Uganda, Rwanda, and the Democratic Republic of Congo (DRC) [Robbins and Williamson, 2008]. Lowland gorilla (*G. gorilla*) populations, also consisting of two subspecies (*G. g. gorilla* and *G. g. diehli*), exist in forest fragments of several western African countries, such as Angola, Nigeria, Cameroon, Congo, and Gabon [Walsh et al., 2008]. While bonobo populations are limited to DRC, common chimpanzee populations, consisting of four subspecies (*Pan troglodytes verus*, *P. t. ellioti*, *P. t. troglodytes*, and *P. t. schweinfurthii*), are the most widely distributed of the great apes, stretching discontinuously across equatorial Africa from southern Senegal to western Tanzania and Uganda [Fruth et al., 2008; Oates et al., 2008]. All of these great ape populations are declining and are currently listed by the International Union for Conservation of Nature as endangered or critically endangered [Fruth et al., 2008; Oates et al., 2008; Walsh et al., 2008; Robbins and Williamson, 2008]. Each of these species is threatened by infectious diseases such as Ebola and a range of human pathogens, although differences in species behavior and social organization may be influencing exposure to and population impacts associated with certain pathogens [Nunn et al., 2007, 2003].

There is accumulating evidence indicating that great apes are exposed to, and in some cases, suffer disease from human and domestic animal pathogens [Whittier, 2009; Williams et al., 2008; Köndgen et al., 2008; Kaur et al., 2008; Palacios et al., 2011;

Rwego et al., 2008]. There have been numerous independent reports of disease outbreaks among great ape populations across Africa in which pathogens have been linked to transmission from humans (Table 1-2). In many of these epidemics, a definitive diagnosis of the etiological agent was not conclusively determined. In these cases, transmission from humans is speculative, based on circumstantial evidence associating animal behavior, clinical disease signs, and contact with local infected humans. However, in recent years molecular epidemiological methods have significantly improved our ability to more definitively determine the role of human pathogen transmission in the occurrence of infectious disease outbreaks among great apes. For example, several outbreaks of respiratory disease in chimpanzees of Taï National Forest, Côte d'Ivoire were determined by molecular techniques to be caused by human metapneumovirus (HMPV) and respiratory syncytial virus (HRSV) [Köndgen et al., 2008; Köndgen et al., 2010]. Gene sequencing and phylogenetic analyses of HMPV and HRSV PCR products revealed virus strains to be closely related to those circulating in the human population, providing the first evidence for human disease transmission into a great ape population. Subsequently, HMPV infection has also been associated with separate respiratory outbreaks among chimpanzees of Mahale Mountains National Park, Tanzania and mountain gorillas of Virunga Massif, Rwanda using PCR and phylogenetic analyses [Kaur et al., 2008; Palacios et al., 2011]. These findings demonstrate that sufficient contact between humans and great apes exists which enables the transmission of certain human pathogens, but much remains to be learned about such contact, the dynamics of these transmission events, and if these coupling points between humans and great apes would facilitate the transmission of other human pathogens.

Microbial transmission from humans to free-living great apes and other primates has also been documented beyond the scope of outbreak investigation. Several studies of antimicrobial resistance and genetic relatedness of enteric bacteria have shown that bacterial isolates from primates living in close proximity to humans share similar antimicrobial resistance patterns and are more genetically related to isolates from humans, as opposed to isolates from primates not living in close proximity to humans [Goldberg et

al., 2008; Rwego et al., 2008]. These studies highlight the significance of environmental transmission of microorganisms and potential pathogens between humans and great apes.

Table 1-2 Infectious disease epidemics of free-ranging great ape populations linked to humans.

| Outbreak            | Date                       | Species           | Location                                  | Morbidity (%)/<br>Mortality* | Etiology  | Sources   |
|---------------------|----------------------------|-------------------|---|------------------------------|---|---|
| Paralytic disease   | 1966                       | Chimps            | Gombe National Park, Tanzania             | 20/6                         | Suspected polio   | [Williams et al., 2008; Goodall, 1986]              |
| Respiratory disease | 1968<br>1987<br>2000       | Chimps            | Gombe National Park, Tanzania             | 63/4<br>40/9<br>75/2         | Undiagnosed, <i>Streptococcus pneumoniae</i> and <i>S. pyogenes</i> (2000 outbreak) | [Williams et al., 2008; Mlengeya, 2001]             |
| Respiratory disease | 1988                       | Mountain gorillas | Virunga Volcanoes, Rwanda                 | 81/3                         | Suspected measles and <i>Mycoplasma pneumoniae</i>                                  | [Sholley, 1989; Hastings et al., 1991; Homsy, 1999] |
| Respiratory disease | 1990                       | Mountain gorillas | Virunga Volcanoes, Rwanda                 | 61/1                         | Suspected paramyxovirus   | [Homsy, 1999]                                       |
| Dermatitis          | 1996                       | Mountain gorillas | Bwindi Impenetrable National Park, Uganda | 100/1                        | Scabies   | [Kalema-Zikusoka et al., 2002]                      |
| Respiratory disease | 1999**<br>2004**<br>2006** | Chimps            | Tai National Forest, Cote d'Ivoire        | 100/6<br>100/8<br>92/1       | Human respiratory syncytial virus and metapneumovirus                               | [Köndgen et al., 2008]                              |

|                     |                        |                   |  |                       |                       |                         |
|---------------------|------------------------|-------------------|--|-----------------------|-----------------------|-------------------------|
| Respiratory disease | 2003<br>2005<br>2006** | Chimps            | Mahale Mountains National Park, Tanzania | 98/4<br>52/2<br>48/12 | Human metapneumovirus | [Kaur et al., 2008]     |
| Respiratory disease | 2009**                 | Mountain gorillas | Virunga Volcanoes, Rwanda                | 92/2                  | Human metapneumovirus | [Palacios et al., 2011] |

\*Morbidity is represented as the percentage of the total population that demonstrated clinical signs of disease, whereas mortality is the total number of deaths associated with the epidemic.

\*\*There is strong molecular evidence that the etiological agents associated with these outbreaks originated from humans.

Besides patterns of contact arising from anthropogenic impacts on the natural environment (e.g. habitat fragmentation and increased human densities surrounding great ape habitat), pathogen transmission has been associated with human habituation of great apes for research and ecotourism [Köndgen et al., 2008; Homsy, 1999]. Human habituation, a tool utilized in the conservation of endangered great apes, entails the conditioning of these animals to close encounters with human observers. The benefits of human habituation to great ape survival have been realized through the reduction of poaching and habitat loss in areas where research and ecotourism exist [Köndgen et al., 2008; Pusey et al., 2007; Campbell et al., 2011]. Thus, to maintain the benefits of habituation and mitigate the disease risks, managers must consider the health of the humans in contact with these animals: tourists, researchers, park workers, and local humans living in proximity or within the parks.

Tourists have been a primary focus in assessing disease risks to great apes given their potential for introducing new pathogens into an ecosystem [Homsy, 1999; Woodford et al., 2002; Sandbrook and Semple, 2007]. However, it is important to note that several disease outbreaks in great ape populations (Table 1) have been attributed to

transmission from researchers (e.g. HRSV and HMPV outbreaks in Tai National Forest) or the local human population, including park workers (scabies, measles, polio) [Kalema-Zikusoka et al., 2002; Köndgen et al., 2008; Sholley, 1989; Woodford et al., 2002; Williams et al., 2008]. It has been shown that human behaviors, such as defecating, urinating, poor waste disposal, and aerosol contamination through sneezing and coughing, within and in proximity to mountain gorilla habitat are a health risk to mountain gorilla populations, with local communities posing the greatest risk [Nizeyi et al., 2012]. Thus, as we consider endemic disease risks to habituated great apes, it becomes clear that contact between great apes and local humans may pose a risk for the transmission of *M. tuberculosis* and other pathogenic members of the MTC, pathogens which may have a high prevalence in local African human and domestic animal populations and which may have potentially devastating effects on great ape populations.

#### *The Risk of Tuberculosis Transmission to Great Apes*

With an initial assessment of the risk of tuberculosis transmission from humans to great apes, it may be hypothesized that the risk is fundamentally related to the incidence of active infection in the local human or animal populations with which great apes have contact. In the most basic Susceptible-Infectious-Recovered (SIR) transmission models, contact rate and increasing incidence of infectiousness drive transmission. Thus, in areas where human or domestic animal tuberculosis is higher and there is contact with great apes or other primates, higher transmission risk would be expected. Conversely, in areas where human/domestic animal tuberculosis and/or great ape contact is lower, the risk would inherently be lower. According to the 2012 WHO Global Tuberculosis Control report, among the 8.7 million global incident cases of human tuberculosis, 24% of these occurred in Africa [WHO, 2012]. Furthermore, the geographical distribution of African great ape habitat falls within countries that have some of the world's highest rates of human tuberculosis, ranging from 50 to over 300 incident cases per 100,000 people (Figure 1-1) [WHO, 2012]. These statistics as well as the high prevalence of HIV co-infection among humans in this region raises additional concern for transmission risk, as co-infection with HIV generally results in a higher likelihood of active tuberculosis.

Furthermore, recent evidence of MTC DNA among populations of free-ranging synanthropic macaques demonstrates that frequent human contact and high tuberculosis prevalence within the human population increases the risk of tuberculosis for non-human primate populations [Wilbur et al., 2012]. Unfortunately, the epidemiology of tuberculosis is not so simple as to be explained by basic SIR models. For instance, most human infections are latent and therefore not infectious, which complicates assessments of risk. Additionally, the contact needed for tuberculosis transmission among humans is typically close and sustained, which is generally not characteristic of the contact between humans and free-living great apes. Thus, increases in human tuberculosis incidence will not necessarily be linearly related to the tuberculosis risk for great apes, particularly if other hosts are involved in transmission of infection. Moreover, much remains to be understood about the observed variation in susceptibility and transmission of different *M. tuberculosis* strains among humans and the genetic drivers of these events before reasonable predictions can be made about risk to primates [Gagneux, 2012]. However, as basic science and epidemiological research enhances our understanding of this variability among humans, our ability to predict this risk for primate populations will also advance.

A survey conducted in 2000 of local inhabitants of Bwindi Impenetrable Forest National Park, Uganda found that despite a high level of respiratory symptoms in the region, many people were not tested for tuberculosis and infection status was largely unknown [Guerrera et al., 2003]. These data suggest that many cases of tuberculosis may go undetected and untreated. This situation is slowly changing as global efforts and funding for tuberculosis control are increasing, especially in areas of Africa with high HIV prevalence [WHO, 2012]. Since park workers employed to protect great apes originate from these local communities, updated information on the tuberculosis status and awareness among these communities would be valuable to both public health and great ape conservation. While population managers generally recognize concern for tuberculosis introduction and guidelines for tuberculosis testing among park employees have been developed, employee health and disease screening programs have not yet been widely adopted for park workers [Ali et al., 2004; WCS, 2005].

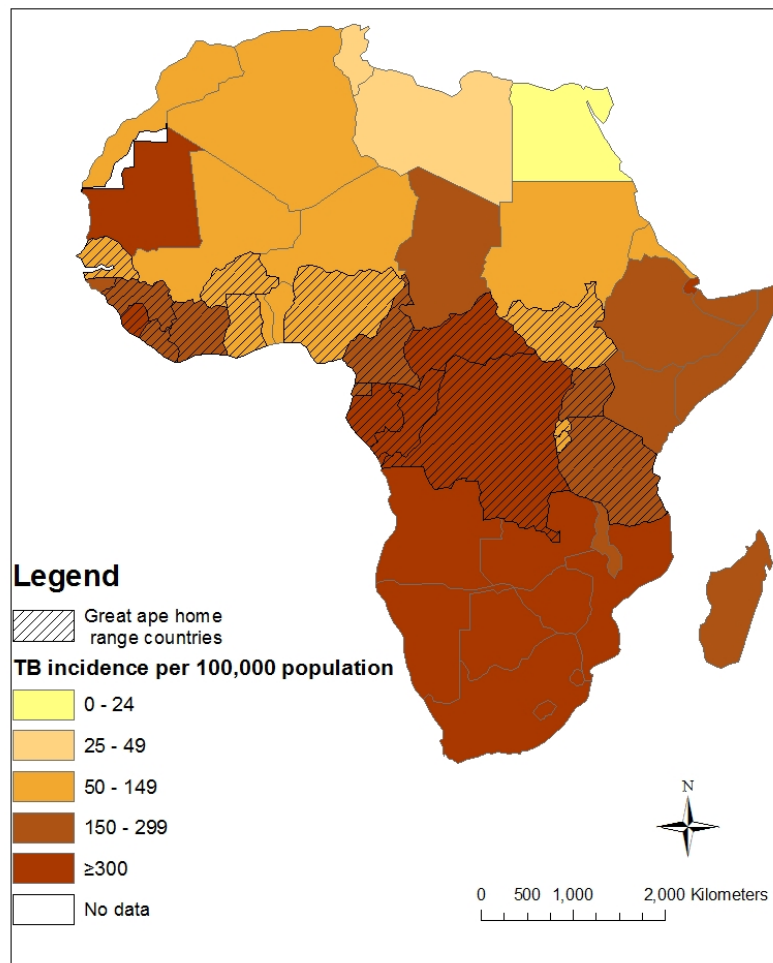


Figure 1-2 Geographic distribution of great ape home range countries compared to the incidence of human tuberculosis in Africa. Data contained in this map originated from Robbins and Williamson, 2008; Oates et al., 2008; Walsh et al., 2008; Fruth et al., 2008; WHO, 2012.

Many parks have established rules to reduce pathogen transmission from humans to great apes, such as restricting great ape visitation by people who are ill and coughing, or through vaccination [Homsy, 1999; Williamson and Macfie, 2010]. As *M. tuberculosis* is generally transmitted by the aerosolization of infectious particles (through coughing, talking, or sneezing) that can be suspended in the air for hours before being inhaled, such park rules should prevent the transmission of this pathogen to great apes from infectious people with pulmonary tuberculosis simply by eliminating contact [Baker, 1995].

Although this rule may not capture people infected with gastrointestinal tuberculosis, who may be shedding high numbers of organism in their stool, other rules restricting defecation within great ape habitat should reduce such a risk [Sharma and Bhatia, 2004; Rasheed et al., 2007]. However, as habitat use by non-research and non-tourist humans increases, the risks of disease transmission that are mitigated by these rules might be expected to increase. Additionally, in situations where park workers, researchers, or other local humans reside within the park and great apes enter areas of human habitation, restricting visitation by ill humans may not be enough to completely eliminate contact and transmission that may occur within these areas of human habitation. Furthermore, the use of vaccination in humans as a preventative measure may provide a false sense of security, as bacille Calmette-Guérin (BCG), the only vaccine available against tuberculosis, does not reliably protect against pulmonary tuberculosis [Russell et al., 2010].

Indirect routes of transmission such as contamination and pathogen persistence in the environment should also be considered as possible pathways for tuberculosis transmission. Great apes that frequent areas of human habitation, either within or outside of parks, may be at greatest risk for both direct and indirect transmission. For example, *M. tuberculosis* (as well as other respiratory pathogens) may be transmitted via interaction with contaminated objects (i.e. fomites) - such as tissues or handkerchiefs - that capture the attention of curious great apes, which often touch, smell, and potentially consume such novel objects [Wallis and Lee, 1999; Woodford et al., 2002]. In general, *Mycobacterium* species are well adapted to survival in harsh environments, with the lipid-rich, protective cell wall, slow growth rate, and long dormancy [Baker, 1995; Palomino et al., 2007; Chadwick, 1981]. Environmental contamination and fomites have been implicated in the transmission of MTC organisms (e.g. *M. bovis*, *M. mungi*) between wildlife, humans, and domestic animals [Tarara et al., 1985; Courtenay et al., 2006; Alexander et al., 2010]. Further, other primate or wildlife species may serve as a vector for transmission of tuberculosis (human, bovine or other) into great ape populations. The role of environmental, fomite, or vector species transmission in other human respiratory pathogen outbreaks among great apes has not yet been assessed, but should be explored

when weighing the risks of tuberculosis transmission into great ape and other primate populations.

Another potential source of human tuberculosis for free-living great ape populations is the reintroduction of rehabilitated great apes by primate sanctuaries. Great apes at these facilities originate from diverse locations throughout Africa in various states of health and have assorted histories of human contact [Mugisha et al., 2011; Schoene and Brend, 2002]. These sanctuaries are challenged with managing injuries and illnesses in the face of limited resources. Crowded conditions and animal stress contribute to efficient disease transmission, and cross-species transmission between animals and human caretakers is a significant concern. This concern was exemplified in a recent study of *Staphylococcus aureus* epidemiology in African sanctuaries where chimpanzees were found infected with a variety of human-associated, multi-drug resistant strains of *S. aureus*, indicating transmission from their human caretakers [Schaumburg et al., 2012b]. Tuberculosis outbreaks have also been diagnosed within primate sanctuaries and are particularly concerning given the challenges of early detection, diagnosis, and management of infected individuals with limited resources [Unwin et al., 2012]. The number of great apes turned over to sanctuaries for medical care and rehabilitation is increasing, as is interest in reintroduction of these animals into their natural habitat. Given the current challenges of disease screening in these settings, rehabilitated animals would pose a significant risk for the introduction of tuberculosis and other human pathogens into presumably naïve free-living populations.

Understanding pathogen transmission across host species within an ecosystem is a complex task, particularly when several closely related pathogens are circulating and causing disease. This is certainly an issue in human medicine, where closely related members of the mycobacterium genus have been responsible for disease in humans. For example, *Mycobacterium bovis*, the etiologic agent of bovine tuberculosis and close relative of *M. tuberculosis* in the MTC, has been documented in cases of extrapulmonary tuberculosis in rural Tanzania [Kazwala et al., 2006, 2001]. Unfortunately, it is not easily distinguished from *M. tuberculosis* when culture is unavailable, thus its contribution to

the tuberculosis epidemic in humans is not fully understood [Kazwala et al., 2001; Cleaveland et al., 2007]. Moreover, despite a growing body of evidence for the zoonotic potential of *M. bovis*, developing countries often lack regulations for control and prevention of infection in livestock, and general knowledge regarding risks of infection are lacking [Michel et al., 2010; Cosivi et al., 1999].

The distinction between *Mycobacterium* species is relevant with regard to the source of transmission and how these pathogens are transmitted between species. Although humans may be infected with and suffer disease from either *M. tuberculosis* or *M. bovis*, a much higher prevalence of *M. tuberculosis* has been documented in humans with tuberculosis [Kazwala et al., 2001, 2006]. Additionally, the transmission of *M. tuberculosis* among humans (e.g. via aerosolized infectious organisms) is generally different than the transmission of *M. bovis* to humans (e.g. via unpasteurized milk and exposure to infected animal tissues) [Baker, 1995; Cosivi et al., 1999]. On the contrary, livestock with tuberculosis are typically infected with *M. bovis* and not *M. tuberculosis*, and are generally infected by *M. bovis* through aerosolized infectious organisms from conspecifics or through exposure to infectious materials such as feces and urine from alternative hosts sharing their environment (as observed with wildlife hosts such as badgers in Britain) [Morris et al., 1994; Courtenay et al., 2006]. This distinction between *Mycobacterium* species becomes important when discussing transmission risk as these organisms are transmitted between species and through the environment by different mechanisms and pathways, which in turn impacts the risk of exposure to these pathogens for primates within their own environment. Therefore, to further consider strategies that might reduce the risk of disease in primate populations, it is important to evaluate mycobacterium species-specific differences (including infected source populations) in transmission that might impact primate exposure.

Given the phylogenetic similarity of humans and great apes, as well as evidence of *M. bovis* infection in free-living baboon populations, it may be presumed that great apes share a similar risk of infection by *M. bovis* [Keet et al., 2000; Tarara et al., 1985; Sapolsky and Else, 1987]. Species such as baboons, whose behavior brings them in

frequent contact with humans, livestock, and great apes, might be potential coupling points for disease transmission across some of these populations that might not otherwise come into direct contact [Müller-Graf et al., 1997; Murray et al., 2000; Keet et al., 2000]. Thus, to fully understand the risk of tuberculosis transmission to great apes, the prevalence of *M. bovis* in local livestock as well other wildlife species (e.g. baboons or other monkeys) must also be considered.

### *Tuberculosis Infection in Primates*

Much of our understanding of naturally acquired tuberculosis infection in great apes and monkeys originates from observations of captive animals [Michel and Huchzermeyer, 1998; Michel et al., 2003; Diniz et al., 1983; Loomis, 2003]. Clinical signs are absent in latent infection, but quite varied with active disease, ranging from nonspecific abnormalities, such as anorexia, lethargy, or weight loss to respiratory signs such as tachypnea or coughing [Michel et al., 2003; Diniz et al., 1983]. Extra-pulmonary infection results in changes in health associated with the tissue of infection (e.g. draining abscessation, hemorrhagic diarrhea) [Michel et al., 2003]. Pathologic lesions may be characterized by infiltrates or cavitations of the lungs or other infected tissues, including lymph nodes, bone, kidney, central nervous system, and others. Within the realm of captive management, there is much concern for the transmission of tuberculosis from humans to great apes, due to the recognized susceptibility of great apes to tuberculosis [Michel and Huchzermeyer, 1998; Loomis, 2003]. It is difficult, however, to predict how susceptibility, disease, and transmission of tuberculosis as observed among captive great apes might translate to free-ranging populations. Certainly stress, social interactions, human contact, and activity patterns can strongly influence susceptibility and disease; however, the difficulties in measuring these factors for direct comparison of captive and free-ranging populations challenges our ability to extrapolate from our knowledge of this disease in captivity to estimate the risk of infection and potential impacts on free-ranging populations.

A recent diagnosis of MTC infection in a wild chimpanzee is our first glimpse of tuberculosis infection in free-ranging great apes [Coscolla et al., 2013]. In this report,

researchers describe the identification of a genetically distinct MTC strain of tuberculosis, most closely related to Lineage 6 (i.e. *M. africanum* West-Africa type-2), on a routine necropsy of an aged female chimpanzee killed by a leopard in Tai National Forest. Aside from deteriorating body condition over a period of years, the report indicated no other clinical signs associated with the extra-pulmonary tuberculosis infection. The investigators further report that despite extensive necropsies and molecular screens of other chimpanzees in the region, this appears to be a unique finding, and it is yet unknown as to whether this novel strain is a chimpanzee-specific pathogen or one transmitted from another primate or animal host. Although most closely related to human-associated strains of tuberculosis, the results of this investigation do not suggest that infection originated from humans. Undoubtedly, this finding warrants more active investigations into the prevalence of this pathogen and the genetic diversity of tuberculosis infection among free-living primates to better understand the epidemiology of and impact of tuberculosis infection to the conservation of these populations.

There are inherent challenges in positively identifying tuberculosis in great apes. Multiple diagnostic modalities, typically relying on the demonstration of tissue lesions, host immune responses, or culture of the organism, are required for the diagnosis in great apes by standard methods [Miller, 2008; Lin et al., 2008]. Reliance on these traditional tuberculosis test methods makes tuberculosis surveillance impractical given the need for animal handling and anesthesia for collection of the necessary diagnostic specimens. Thus, the detection of tuberculosis in free-ranging species has been mostly limited to post-mortem diagnosis, at which time transmission of tuberculosis may be well advanced through a social primate group. Given these limitations, without systematic monitoring of population health accompanied by recovery and post-mortem examination of all carcasses, a low level of tuberculosis infection among a great ape population might go undetected. To overcome this potential problem, consideration must be given to the application of molecular methods of pathogenic organism detection in the development of non-invasive methods of tuberculosis diagnosis.

Non-invasive sampling refers to the collection of biological samples without the need for animal handling or anesthesia. Such methods have been useful in the screening of saliva, feces and urine for systemic, gastrointestinal, and respiratory pathogens of great ape populations [Kondgen et al., 2010; Kaur et al., 2008; Keele et al., 2009; Rudicell et al., 2010; Liu et al., 2008; Schaumburg et al., 2012a; Makuwa and Souquiere, 2003; Gillespie et al., 2010]. Readers are referred to excellent reviews of infectious diseases of free-living great apes and noninvasive sampling methods for the screening of a variety of pathogens [Leendertz et al., 2006; Gillespie et al., 2008; Calvignac-Spencer et al., 2012]. Accordingly, there are several molecular methods that may be applied to such samples and be useful in the detection of tuberculosis infection (Table 1-3).

Table 1-3 Non-invasive sampling and potential methods for tuberculosis detection.

| <b>Sample</b> | <b>Potential target or detection method</b>               | <b>Limitations</b>   |
|---------------|---|--|
| Saliva        | Culture and genotyping<br>Mycobacterial PCR<br>Antibodies | Infected individual must be infectious for the detection of organisms by culture or PCR, thus latent infection may go undetected. Possible low sensitivity associated with antibody detection.   |
| Urine         | LAM*  | Low sensitivity and specificity in humans.   |
| Feces         | Culture and genotyping<br>Mycobacterial PCR<br>Antibodies | Infected individual must be infectious for the detection of organisms by culture or PCR, thus latent infection may go undetected. Possible low sensitivity associated with antibody detection; antibodies present in swallowed sputum may be denatured in the stomach. |

\* LAM - Lipoarabinomannan

The collection of saliva samples of great apes from what is commonly referred to as “wadges”, or masticated clumps of forest food, has found use in genetic research of free-living great apes and has more recently been employed in noninvasive disease screening [Shimada et al., 2004; Inoue et al., 2007; Smiley et al., 2010; Schaumburg et al., 2012a]. Saliva samples from animals with clinical signs of disease could be utilized for the detection and genotyping of *M. tuberculosis* through culture and commonly employed techniques such as IS6110 PCR-RFLP, spoligotyping, or mycobacterial-interspersed-repetitive-unit-variable-number-tandem-repeat (MIRU-VNTR) genotyping [Wilbur et al., 2012; Sankar et al., 2011]. These techniques are useful in distinguishing *M. tuberculosis* from infection with other MTC strains. In human medicine, mannose-capped lipoarabinomannan (LAM), a cell wall component of pathogenic mycobacteria, has been utilized as a urine biomarker of tuberculosis infection [Hamasur et al., 2001]. The utility of this biomarker in the diagnosis of infection in humans has been limited by low sensitivity and specificity, although it has shown greater accuracy in patients co-infected with HIV [Peter et al., 2010]. The usefulness of LAM in the detection of tuberculosis in non-human primates has yet to be determined. Urine collection is a realistic option for non-invasive sample collection, having been used in other disease surveys; thus, it is reasonable to consider LAM as a possible biomarker for non-invasive tuberculosis detection in great apes [Leendertz et al., 2006]. Fecal samples are the most readily available and easily attainable biological samples of free-ranging great apes. The detection of fecal antibodies against pathogenic organisms has not been widely utilized for disease screening in primates; however, methods for fecal antibody detection have proven successful for the non-invasive detection of Simian Immunodeficiency virus (SIV) and Simian Foamy virus in wild chimpanzees [Liu et al., 2008; Keele et al., 2009]. Given the development of a detectable humoral immune response to tuberculosis in primates, the detection of anti-tuberculosis antibodies in feces may be a feasible option for diagnosis [Lin et al., 2008; Lyashchenko et al., 2007]. Hence, exploration into fecal antibody detection may be warranted as another option for non-invasive tuberculosis screening in great apes. Alternatively, fecal culture or molecular detection of mycobacterial DNA in the feces of great apes offers another opportunity for the diagnosis

of disease. Recent studies among humans with active pulmonary tuberculosis reveal approximately 50% sensitivity and 100% specificity for the detection of *M. tuberculosis* by stool culture, and even higher sensitivity using molecular detection (e.g. IS6110 PCR-RFLP) [Cordova et al., 2010; El Khéchine et al., 2009]. Therefore, culture and/or PCR may be a useful approach to pathogen detection in the feces of great apes.

A major limitation to the detection of tuberculosis infection by any of these methods is the latent stage of disease, in which case animals are not infectious and detection of the organism and immune response is often more challenging [Lin et al., 2008]. Alternatively, given the utility of these non-invasively collected specimens for potential disease screening of other pathogens, it is advantageous to move toward the development and validation of such methods. Certainly, as these methods for non-invasive tuberculosis detection improve and become more widely available, a more comprehensive assessment of tuberculosis status among great ape populations (e.g. disease-free or not) can be undertaken through ante-mortem population surveillance or monitoring.

#### *Directions for Future Research and Mitigation of Tuberculosis Risk*

Understanding and/or mitigating the risk of tuberculosis for the conservation of great ape populations requires an ecosystem health approach. *M. tuberculosis* is a human pathogen, and there is evidence of high prevalence among humans residing in close proximity to great ape habitats across their home ranges. Better estimates and understanding of control measures for this disease in local human populations are needed for accurate estimation of risk to great ape populations with which they have contact. Thus, it is essential to develop partnerships among conservation managers and those involved in human health at local and non-governmental levels. Given the evidence of human respiratory diseases in great ape populations, it can be concluded that the necessary contacts already exist between humans and great apes for successful disease transmission. Whether these contacts are sufficient for tuberculosis transmission has yet to be determined. Furthermore, the role of the environment in the transmission of such pathogens remains unknown. Accordingly, epidemiological research into routes of

transmission of known human pathogens affecting great ape populations are needed not only for protecting against specific disease, but also in understanding and potentially predicting opportunities for *M. tuberculosis* transmission within these ecosystems. Certainly, the most promising means of protecting great apes from *M. tuberculosis* is by improving the healthcare infrastructure among local human communities, thereby reducing the burden of human tuberculosis in these regions.

*M. tuberculosis* is, unfortunately, not the only mycobacterial pathogen for which great apes may be at risk of infection. *M. bovis*, a known pathogen of domestic livestock and wildlife, not only causes disease in humans, but has also spilled over into free-ranging monkey populations. Thus, understanding of the risk and prevention of *M. bovis* infection in great apes also requires efforts in the area of bovine tuberculosis. There is a significant need for regulation, surveillance, and control of bovine tuberculosis in developing countries, as well as education on the zoonotic potential of this pathogen. Endeavors to meet such objectives could significantly reduce the impact of this disease for humans and their livestock, as has been observed in developed countries, as well as eliminate a disease risk to great ape populations. Until these needs are met, however, estimates of *M. bovis* levels in local livestock populations and potential routes of transmission are necessary to characterize this disease risk to great ape populations.

*M. tuberculosis* is an old pathogen, originating in Africa [Cosma et al., 2003; Gagneux, 2012]. This pathogen's co-evolution with its human host is complex and there is much we are still learning about variability of infection, host-response, distribution, and genetic and functional diversity [Cosma et al., 2003; Gagneux, 2012]. Likewise, similar observations of variations in infection and host response among primates have yet to be fully explored. Combined with historical limitations of diagnosing tuberculosis infection in free-ranging primate species, it cannot be known with certainty that this pathogen is not already present in these populations nor the full extent to which other MTC members (such as "Chimpanzee bacillus", reported by Coscolla et al.) infect these populations [Coscolla et al., 2013]. The impact of tuberculosis and the dynamics of co-infection with other diseases (e.g. SIV) on the persistence of free-ranging primate

populations cannot be fully assessed without the development and employment of sensitive and reliable means for detecting infection and characterizing the pathogen.

As long as tuberculosis continues as a significant human and livestock disease, there is inherent risk of transmission to remnant great ape populations with which there is human contact. Accordingly, just as protection of these populations against threats of further habitat loss and poaching is ensured through conservation and research activities, we must endeavor to enhance our understanding and mitigate the risks of tuberculosis and other human and domestic animal pathogens that equally threaten the persistence of these populations.

# Chapter 2 | Syndromic Surveillance in Free-Living Chimpanzees: Examination of The Performance of a Novel Disease Detection System for Wildlife

## *Background*

Growing concerns of emerging zoonotic infectious diseases demand innovative approaches to disease surveillance. As 60% of human emerging infectious diseases (EID) are zoonotic, the need for EID surveillance in animal populations is well recognized [Jones et al., 2008; Woolhouse et al., 2001]. In particular, approximately 70% of zoonotic EIDs originate from wildlife species, and these EID events have been associated with regions of the world with wildlife species richness [Jones et al., 2008]. Thus, to meet the demands for EID prediction and early warning, surveillance efforts should be implemented in these regions and target important wildlife species with which humans and their domestic animals have direct and indirect contact. As our growing human population continues to expand into wildlife habitat, understanding the risks of EID transmission through wildlife contact is of increasing importance.

Approaches to disease surveillance in wildlife are quite varied. In some cases, surveillance targets point sources of potential disease transmission between species. The screening of bushmeat, a source of zoonotic pathogens for humans, or hunters for infection or exposure to recognized and novel pathogens is an example [Weiss et al., 2012; Wolfe et al., 2005]. Targeted surveillance for specific zoonotic pathogens in species at the human-wildlife interface is another approach to better understand the role of wildlife species in disease transmission. For example, studies to screen small mammals or primates, whose habitat or behavior brings them in close proximity with humans, have been employed to identify disease risks associated with habitat overlap or direct interaction [Bublitz et al., 2014; Jobbins et al., 2014; Jones-Engel et al., 2006]. Wildlife have also served as sentinels in the passive surveillance of emerging or reemerging

diseases important to public health or agriculture. The sampling of hunter-harvested deer for bovine tuberculosis or the examination of avian mortality events for West Nile virus as early indicators of epidemics are examples of this approach [Schmitt et al., 1997; Komar, 2001].

In Gombe Stream National Park, Tanzania, researchers and managers have employed similar strategies in their ongoing efforts to understand disease dynamics in a well-studied population of free-living chimpanzees (*Pan troglodytes schweinfurthii*). Two of three chimpanzee communities comprising the population are habituated to human presence, which has facilitated chimpanzee behavioral research since 1960 and the 1980s, respectively, making this the longest studied great ape population in the world [Lonsdorf et al., 2006]. Ongoing study of habituated Gombe chimpanzees has offered insights on the impact of disease on this population; over 40 years, more than half of known mortalities were associated with disease [Williams et al., 2008]. As a result of these findings and growing interest in EIDs and the role primates play in EID events [Woolhouse and Gowtage-Sequeria, 2005], the Greater Gombe Ecosystem Health Program was born, and with it new strategies of disease surveillance. Ongoing since 2000, active surveillance for chimpanzee Simian Immunodeficiency virus (SIVcpz) has been conducted through noninvasive fecal sampling of all three chimpanzee communities [Keele et al., 2009; Rudicell et al., 2010]. This research has provided unique insights into the pathogenicity of the virus and population-level impacts of infection, such as increased adult and infant mortality. A passive system of surveillance was implemented in 2004 to screen for disease associated with mortality through rigorous and systematic necropsy and histopathology of recovered tissues [Terio et al., 2011]. In concert with this, three additional streams of surveillance were also initiated: noninvasive surveillance of feces for enteric pathogens, observational surveillance of syndromic disease, and opportunistic disease surveillance on the rare occasion where veterinary intervention is required for sick individuals [Gillespie et al., 2010; Lonsdorf et al., 2006; Travis et al., 2008]. All of these streams of surveillance provide a unique, longitudinal and long-term dataset for researchers to better understand disease dynamics in a scientifically important population of great apes.

The use of syndromic surveillance to study a range of diseases in a wildlife population is novel. Indeed, the ongoing behavioral research of habituated Gombe chimpanzees offers a unique opportunity for the integration of this type of surveillance for the collection of standardized health data in a free-living species. Syndromic surveillance is the collection of pre-diagnosis health data that can signal a case or outbreak triggering public health responses that might reduce morbidity and mortality [Henning, 2004]. This type of surveillance targets general types of diseases, or “syndromes.” In Gombe, specific clinical signs, which researchers have been trained to recognize, are targeted as indicators of syndromic diseases such as respiratory, dermatologic, gastrointestinal, traumatic, and wasting. This type of data is less specific than confirmatory diagnostic data, but is sensitive to changes in the levels of disease within a population, providing an early signal of disease outbreak [Dórea et al., 2011]. Advantages of syndromic health surveillance go beyond outbreak detection, but also improve understanding of disease trends, provide data for risk analysis, and facilitate infection control and prevention [Ward and Carpenter, 2000]. Accordingly, a key goal with the inception of this surveillance system in Gombe was to better understand baseline trends or endemic levels of disease. In this study, we evaluated the performance of the Gombe syndromic surveillance system and its utility in describing disease patterns and detecting outbreaks. Study objectives included 1) an assessment of data quality, 2) the generation of baseline trends of disease from syndromic data, and 3) an evaluation of statistical algorithms for outbreak detection. We focused analyses on respiratory disease surveillance based on the recognized importance of respiratory diseases as a cause of morbidity and mortality in great ape populations [Köndgen et al., 2008; Palacios et al., 2011; Lonsdorf et al., 2011; Williams et al., 2008; Terio et al., 2011].

## *Methods*

### *Study Site*

Gombe Stream National Park, Tanzania is the site of the syndromic disease surveillance system described in this study. It is a 35km<sup>2</sup> park in northwestern Tanzania,

where it is bordered by Lake Tanganyika to the west, and villages to the north and south. Within the park lives a population of approximately 100 chimpanzees (*Pan troglodytes shweinfurthii*), which comprises 3 communities: Mitumba (n=24-28) in the northern part of the park, Kasekela (n=60-70) centrally, and Kalande (n=10-15) in the southern part of the park [Gillespie et al., 2010]. Chimpanzees in the Mitumba and Kasekela communities are habituated to human observers, are individually known by Gombe researchers, and are the subjects of the syndromic surveillance system.

### *Syndromic Disease Surveillance*

In 2004, a prospective health monitoring system was established with the aim of collecting systematic, standardized health data on Kasekela and Mitumba chimpanzees to establish baseline trends of disease to more readily identify outbreak events and inform outbreak contingency plans [Lonsdorf et al., 2006; Travis et al., 2008]. Behavioral researchers collect observational data on the presence or absence of clinical signs associated with specific syndromes of disease: respiratory, gastrointestinal, dermatologic, trauma, and wasting. As previously described, this surveillance system was developed with two streams of standardized data and one of non-standardized, veterinary data [Lonsdorf et al., 2006]. The Daily Health Record captures standardized health data on individuals that are the subject of a focal, behavioral follow, whether healthy or unhealthy, using a health check sheet. [Lonsdorf et al., 2006] In conjunction, a fecal sample is collected from the individual during the follow and preserved in 10% neutral buffered formalin. If an individual other than the primary subject of the follow is observed ill, an additional health check sheet is generated for the ill individual and fecal sample collected opportunistically. The goal for this surveillance system was to capture focal health data (i.e. Daily health data) on 60% of each community monthly. In addition to the Daily health record, Weekly standardized health data is collected on all chimpanzees seen by researchers during the week, whether the subject of a focal follow or not. This stream of data was designed to capture health data on greater numbers of chimpanzees each week, although the level of detail is less than that contained within the Daily record. Lastly, detailed, non-standardized, health observations are recorded for

individual chimpanzees by the resident veterinarian in response to reports of illness. Daily and Weekly record data were analyzed for the period of March 2004 to December 2012 in this study. Given ongoing concerns of respiratory disease on this and other great ape populations, the surveillance of respiratory diseases was the focus of these analyses. Surveillance for syndromic respiratory disease was conducted through the systematic collection of observations of coughing, sneezing, and rhinorrhea.

### *Data Quality*

Several analyses were employed to evaluate the quality of the data collected by the Daily and Weekly syndromic surveillance systems. Community coverage was assessed as the proportion of each community on which health data was collected each month. Daily health check coverage was calculated as the number of unique animals that were observed as focal animals out of the total number of animals alive in the community each month. Coverage was calculated similarly for Weekly data as the number of unique animals for which health status was documented out of the total number of animals alive in the community each month. A crude mean estimate of monthly coverage was generated for each community for all years following the initial year, as well as mean estimates adjusted by month. The first year was excluded from the crude estimate as data quality in this first year might differ from subsequent years when data collection methods would be an established routine. Because time of year or season might influence variability in researcher ability to locate animals and collect health observations (thus coverage), temporal differences in coverage were examined. General linear regression models were generated for each data set to test for an association between month and community coverage. Regression analyses were performed using SAS software, Version 9.4 of the SAS System for Windows (Copyright 2002-2012, SAS Institute Inc., Cary, NC, USA).

Completeness of the data was evaluated by the completion of each data field for respiratory signs for both Daily and Weekly health check sheets. For Daily health data, the proportion of respiratory data missing from records was calculated for each day of observation. For example, if two animals were focally observed on a specific date, 3

fields of respiratory data (i.e. coughing, rhinorrhea, sneezing) should contain 6 total values of respiratory data for that date. Missing observations are summed and then divided over the total possible observations. So, if there is missing data about the presence of sneezing in one of the observed animals and all other observations are recorded, the proportion of incomplete data for that date is  $1/6$  or 0.167. An overall estimate of completeness was calculated for each community for all years following the first year of introduction of the surveillance system as  $1 - \text{the overall mean proportion incomplete} \times 100$ . For Weekly data, if an animal was seen during an observation week but normal health was not indicated in the relevant field and respiratory data was missing, the record for that animal was classified as incomplete. The number of animals documented as seen in the Weekly data each year was totaled, as was the number of missing respiratory records among those observations. The annual proportion incomplete was calculated as the number of missing respiratory records over the number of observations each year. Mean percentages of Weekly data completeness from 2005-2012 were calculated for each community. Lastly, we were interested to know if some observations were more easily observed than others. For example, due to limited visibility in the jungle environment, a researcher might more easily detect the presence and frequency of coughing or sneezing than visualize rhinorrhea. In this case, a researchers inability to confirm the presence or absence of a particular clinical sign might result in missing data. To address this question, we examined the Daily data for differences in completeness by clinical sign. Clinical sign-specific daily proportions of incomplete data were calculated as above, and annual means of missing data for each clinical sign were generated for comparison.

Finally, consistency between Daily and Weekly data was evaluated by comparing agreement between weekly counts of chimpanzees with respiratory signs. These analyses were performed only on weeks that contained both Weekly and Daily data; weeks containing only one set of data were excluded from the analyses. Crude estimates of the percentages of data agreement were generated for each community for all years following the initial year of study. However, since the Weekly record was created to capture data on all chimpanzees seen, including those that were not the subject of focal follows (and thus

not part of the Daily record), some disagreement in the weekly counts of sick chimpanzees between the two data sources would be expected. In fact, the Weekly data would be expected to have equal to or higher weekly counts of sick chimpanzees than the Daily data. Therefore, an additional analysis was conducted which focused only on weeks with counts of sick chimps in both Daily and Weekly data. These were compared and classified as consistent if Weekly data had greater than or equal to the weekly count of sick chimps in the Daily data. Community percentages were recalculated based on this type of agreement. Finally, the data were examined more closely to determine the level of agreement on the identities of sick chimps each week. Again, based on the design of this system, Weekly data would be expected to recapture data on focal animals that were observed ill during the week, as well as any other ill chimps not observed as focal animals in the Daily record. Weekly and Daily data were classified as consistent if the Weekly data documented at least the same sick chimpanzees as the Daily data each week. Estimates of consistency based on chimpanzee identity were also calculated as community percentages of agreement.

### *Trends of Respiratory Disease*

A primary goal in the establishment of the syndromic surveillance system in Gombe was the accrual of baseline health data that could be used to effectively identify changes in disease trends and signal the occurrence of disease outbreak events. In keeping with this goal, baseline levels of respiratory signs were estimated from the Daily record. These baseline estimates were generated using all years of data, excluding months when major outbreaks occurred. Major outbreaks have been previously described as epidemics of disease in which 20% or more of a community is affected [Williams et al., 2008]. Monthly counts of abnormal clinical signs were summed and mean counts were estimated for each community to determine the frequency of disease by clinical sign. Weekly counts of chimps with respiratory disease were then calculated as the total number of chimpanzees observed with any respiratory sign during the observation week. A crude mean weekly count of chimps affected by respiratory disease was estimated over all years of data. To account for variation in the number of chimpanzees observed weekly,

baseline levels of weekly case prevalence were also calculated by community, excluding data collected during major outbreak weeks. Prevalence was calculated as daily number of chimpanzees with respiratory signs out of the daily number of chimpanzees observed in the Daily data.

Data on the weekly and monthly number of respiratory cases reported were analyzed for temporal trends. These analyses were performed using all data, including weeks within major outbreaks. Initially, weekly counts of respiratory cases were aggregated as monthly means, compiling all years of surveillance, to examine for monthly trends. The amount of variation in weekly respiratory cases across months of the year was examined using a monthly index. The monthly index depicts how much the mean number of weekly cases for a particular month differs from the mean weekly case count for the entire year [Gallego et al., 2007]. Time series analyses were performed for each community using proc timeseries in SAS, and monthly case statistics over the years of surveillance were examined visually for secular trends. Data on the monthly number of cases was also modeled by linear regression in SAS to test for trends in disease and determine the rate of change in disease patterns over time. Each community was modeled separately, with time (expressed in study months) as the independent variable and number of respiratory cases as the dependent variable. If a disease trend was identified, the data were further evaluated for any changes in disease trends over the duration of the study. To do this, time periods were selected by visual examination of monthly case statistics generated from the time series analyses. Monthly case counts were modeled again by linear regression, but a term for time period and an interaction term for time period and study month was also included. A change in disease trend was assessed by significance of the interaction term in the new model.

### *Retrospective Outbreak Detection*

Using baseline measures of syndromic respiratory disease among the habituated chimpanzee communities for improved disease outbreak detection was a major goal in the inception of the surveillance system. A simple set of detection algorithms were utilized to explore the surveillance data for smaller outbreaks outside of the major

outbreaks previously recognized. For this objective, two baselines of weekly respiratory disease were generated using 2004 study data: weekly case counts and prevalence estimates of respiratory disease by community. Prevalence was estimated as the number of respiratory cases identified in a week out of the total number of chimps observed in the Daily data that week. This measure was included for evaluation as a detection algorithm to account for variation in the numbers of chimpanzees observed in the Daily data each week. A weekly time step was chosen to optimize the time lag in outbreak detection for future real-time application. Mean estimates of each measure were generated and the upper limit of the 95% confidence interval of the baseline measures was used as an outbreak threshold. Thus, monthly counts or prevalences of respiratory disease exceeding these thresholds would signal the presence of an outbreak. The remaining years of data (2005-2012) were screened for outbreak signals in each community using both algorithms. Daily and Weekly data were examined at each outbreak signal for evidence to support the presence of an outbreak. Specifically, an outbreak was only confirmed if more than one individual within a community was identified as ill, either within the same week or in consecutive weeks of the signal. Although a gold standard, diagnostic sampling data were not available to demonstrate pathogen transmission within the communities as outbreak confirmation. Chamberlain's percent positive agreement was included in the evaluation of these two approaches to outbreak detection [Szklo and Nieto, 2007]. This was calculated as:

$$\text{Chamberlain's PPA} = \frac{a}{a+b+c} * 100 \quad (\text{Equation 2.1})$$

where  $a$  represents the number of outbreaks for which a signal was triggered by both algorithms,  $b$  represents the number of outbreaks signaled only by the count threshold and  $c$ , the number of outbreaks signaled only by the prevalence threshold. As this is an index of reliability of measures, applicable in situations where prevalence is very low or high, and we expected the number of weeks where an outbreak would be signaled to be far lower than the number of weeks where there would be no signal, this was considered the best estimate of reliability between each algorithm of detection.

## Results

### Data Quality

Monthly community coverage by the Daily health record for 2005-2012 averaged 54% (s.d.  $\pm 12.5\%$ ) and 52% (s.d.  $\pm 15.2\%$ ) for the Mitumba and Kasekela communities, respectively (Figure 2-1). Weekly health record coverage for the same time period was much higher, averaging 95.3% (s.d.  $\pm 8.1\%$ ) and 86.8% (s.d.  $\pm 11.1\%$ ) for Mitumba and Kasekela, respectively. No differences were observed in community coverage by the Daily health record between months in either community (Figure 2-2). In Mitumba, there was no difference between months in community coverage by the Weekly data, but in Kasekela, although there was no overall difference in coverage by month ( $F = 0.99$ ,  $P = 0.4650$ ), March had significantly less coverage than other months ( $T = 2.47$ ,  $P = 0.0152$ ) (Figure 2-2). However, the amount of variation explained by the model was fairly small (R-square: 0.1034).

Data completeness was very near 100% in both communities, with 97.7% and 99.2% of the data completed on average in Kasekela and Mitumba, respectively. To evaluate completeness by clinical sign, data from both communities were combined, assuming that researchers would have similar experiences in observing clinical signs of chimpanzees across the park environment. There were no differences between clinical sign in the amount of data fields left incomplete (Figure 2-3).

There were 416 weeks of surveillance data from 2005-2012, and 378 and 379 of those contained Weekly and Daily data for analysis of consistency in Kasekela and Mitumba, respectively. Consistency between the Daily and Weekly data was initially evaluated by crude estimates of the frequency with which the two records agreed on the weekly number of respiratory cases. In Kasekela, the two records agreed 85.2% (s.d.  $\pm 1.8\%$ ) of the time, and in Mitumba the records agreed 90% (s.d.  $\pm 1.5\%$ ) of the time (Figure 2-4). This level of agreement was primarily driven by weeks when no respiratory illness was observed, which was 692 out of 757 total weeks (91.4%). Analysis of consistency using the frequency with which the Weekly data matched or exceeded the

numbers of cases in the Daily data revealed an agreement level of 62.5% (s.d.  $\pm$  5.7%) and 70% (s.d.  $\pm$  5.9%) in Kasekela and Mitumba, respectively. Further evaluation of the frequency of agreement on the identities of sick chimpanzees (i.e. Cases in Daily data also identified as sick in Weekly data) revealed 25% (s.d.  $\pm$  6.5%) and 55% (s.d.  $\pm$  7.7%) consistency between the two records in Kasekela and Mitumba respectively.

Figure 2-1 Mean monthly coverage of each community by Daily and Weekly data. The red line indicates the projected monthly coverage goal of 60%. Monthly coverage was averaged for the years 2005-2012. KK = Kasekela community; MT = Mitumba community.

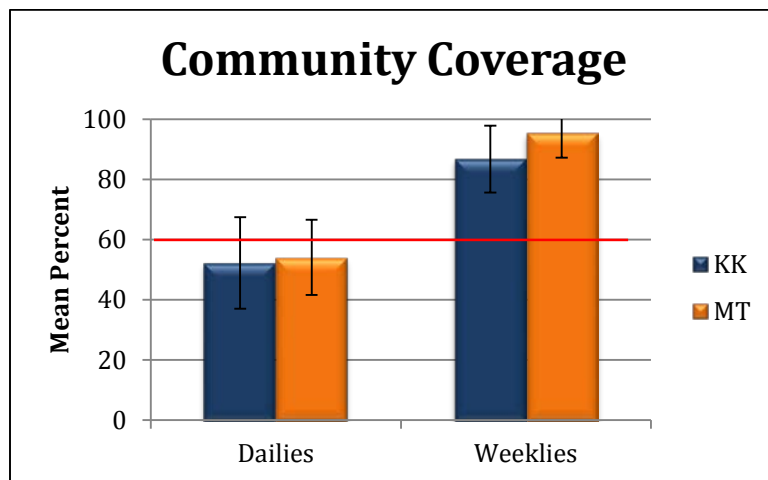


Figure 2-2 Mean community coverage by month. Panel A shows coverage of each community by the Daily data for each month, whereas Panel B shows mean coverage by the Weekly data by month. Monthly coverage was averaged for the years 2005-2012. KK = Kasekela community; MT = Mitumba community.

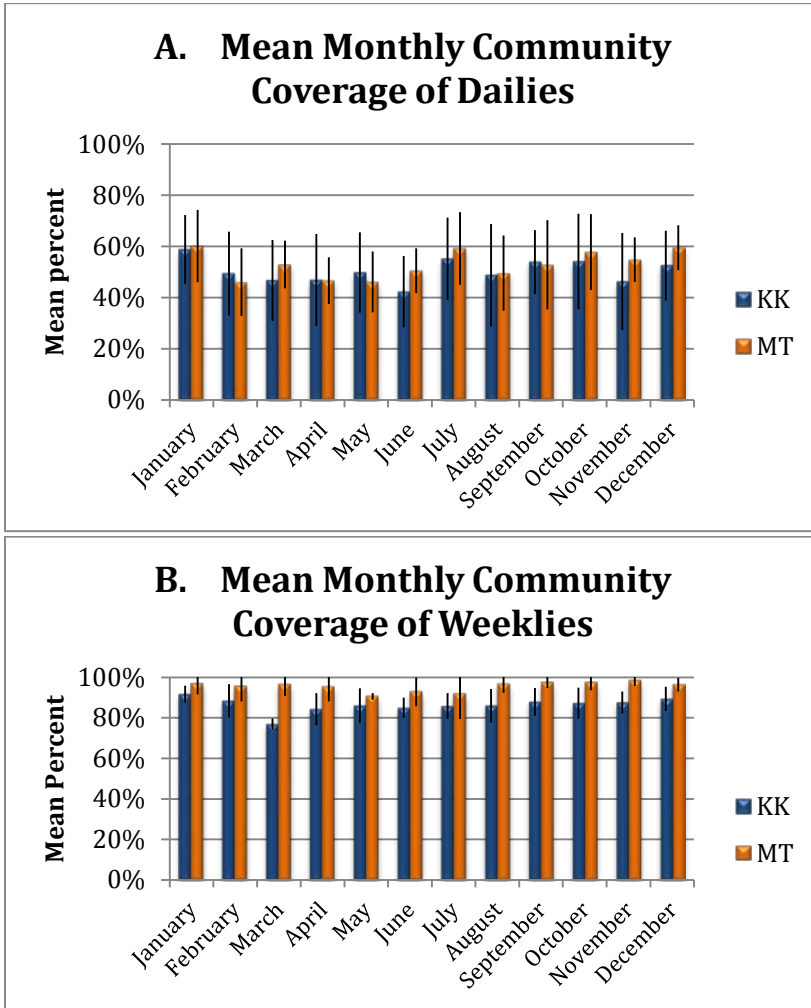


Figure 2-3 Proportion of the data associated with each clinical sign left incomplete. Mean annual proportions were calculated for each clinical sign. No significant differences between proportions of completeness between clinical signs were observed.

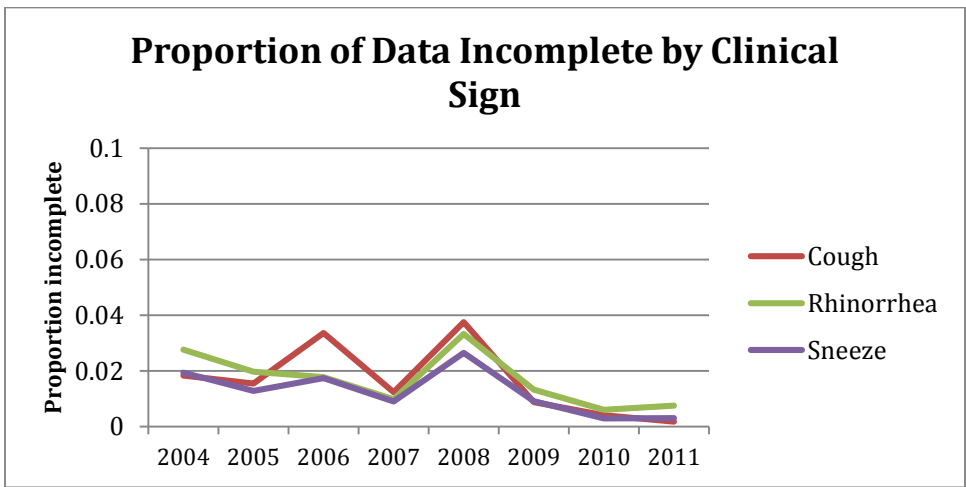
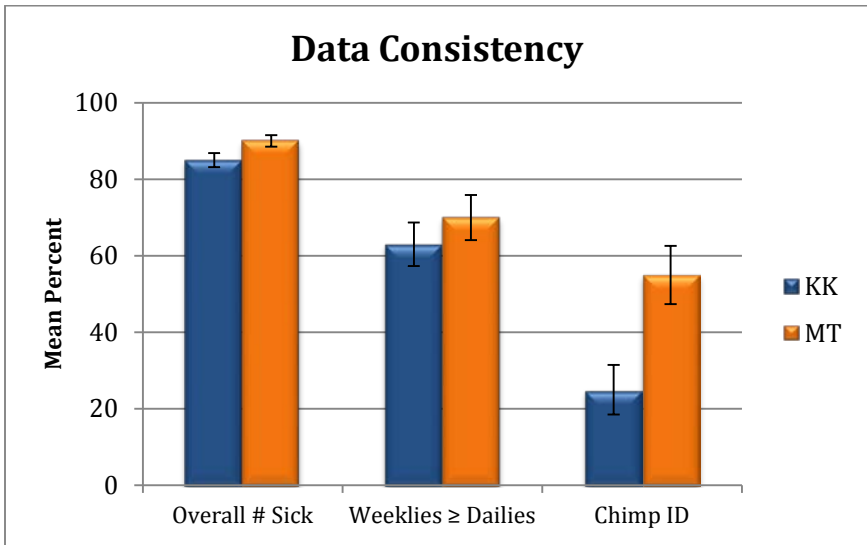


Figure 2-4 Mean agreement between Weekly and Daily data for each community. The first column set represents the mean percent of the Weekly and Daily data that is consistent on the number of weekly respiratory cases. The middle column set depicts the mean percent of the Weekly data which contains as many or more weekly respiratory cases than the Daily data. The last column set represents the mean percent of the time when Weekly data contains at least the same identities of cases as the Daily data. The second and third column sets are an evaluation of a subset of the data that includes only weeks where respiratory cases were identified, and takes into account that, by design, Weekly data should contain at least the same number and identities of cases as the Daily data. KK = Kasekela community; MT = Mitumba community.



### *Trends of Respiratory Disease*

Estimations of baseline trends of disease reveal low levels of respiratory disease from 2004-2012. Although cough was the most frequently observed sign of respiratory disease, all signs were observed at very low frequencies in non-epidemic months (Table 2-1). Similar results were found with the estimation of weekly baselines of respiratory disease. On average, the weekly number of chimps on which data was collected in the Daily record was 10 (s.d.  $\pm$  6) and 5 (s.d.  $\pm$  3) in Kasekela and Mitumba, respectively. Among these, the numbers of chimps that were observed with any combination of respiratory signs in non-epidemic weeks were very low (Table 2-2), with most weeks containing no observations of respiratory illness. Thus the weekly prevalence of respiratory disease was also low (Table 2-2), with an average of 2.1% (s.d.  $\pm$  7.4%) of the chimps observed each week in both communities reported with signs of respiratory disease.

Table 2-1 Mean monthly counts of respiratory signs observed in each habituated chimpanzee community. Counts of clinical signs were obtained from Daily data and exclude months with major outbreaks.

| <b>Clinical sign</b> | <b>Kasekela</b><br>(mean $\pm$ sd) | <b>Mitumba</b><br>(mean $\pm$ sd) |
|----------------------|------------------------------------|-----------------------------------|
| Cough                | 0.35 $\pm$ 0.79                    | 0.57 $\pm$ 1.21                   |
| Sneezing             | 0.22 $\pm$ 0.59                    | 0.15 $\pm$ 0.41                   |
| Rhinorrhea           | 0.27 $\pm$ 0.70                    | 0.17 $\pm$ 0.51                   |

Table 2-2 Mean weekly respiratory cases observed in each habituated chimpanzee community. Measures were obtained from Daily data and exclude major outbreak weeks. Prevalence accounts for the weekly variation in the number of chimps observed.

|            | <b>Kasekela</b><br>(mean $\pm$ sd) | <b>Mitumba</b><br>(mean $\pm$ sd) |
|------------|------------------------------------|-----------------------------------|
| Count      | 0.13 $\pm$ 0.49                    | 0.12 $\pm$ 0.37                   |
| Prevalence | 1.5% $\pm$ 5.9%                    | 2.6% $\pm$ 8.6%                   |

Trends of weekly case counts were first examined by month to explore for seasonal trends in respiratory disease. Visualization of weekly case counts aggregated as monthly means and plotted by month reveals fewer cases of respiratory disease in Mitumba from May to September, although the same trend is not observed in Kasekela (Figure 2-5). The lower case trend observed in Mitumba is only a difference of approximately one case, but the variation in weekly cases numbers across all study years during these months also appears to be low. Monthly indices were generated for each community to depict changes in the amount of variation in weekly case numbers across months. These analyses demonstrate that the average number of cases in July, August, September, and November generally fall below the annual monthly mean in Mitumba (Figure 2-6). In contrast, monthly averages generally fall below the annual average in May, October, November, and December in Kasekela (Figure 2-6). Monthly case statistics were also calculated and plotted across all surveillance years (Figure 2-7). Linear regression modeling to test for secular trend in case numbers over time through the years of the study revealed no evidence for trend in Kasekela community ( $t = -0.22$ ,  $P = 0.8262$ ); however, a negative trend in the monthly cases was observed in Mitumba ( $t = -2.83$ ,  $P = 0.0056$ ). Visualization of monthly case statistics (Figure 2-7), suggest that a change in trend may have occurred in 2010, when no cases were observed in Mitumba for the whole year. Therefore, trend in monthly cases was modeled again by linear regression, but the data was broken into two periods: 2004-2009 and 2010-2012. Trend was no longer significant ( $t = -0.88$ ,  $P = 0.3795$ ) and there was no significant difference in the monthly change in cases over time between the two periods ( $t = 0.89$ ,  $P = 0.3739$ ).

Figure 2-5 Seasonal trends of weekly respiratory cases observed in each habituated chimpanzee community. Each point represents a monthly mean of weekly cases for every year of the study, 2004-2012. KK = Kasekela community; MT = Mitumba community.

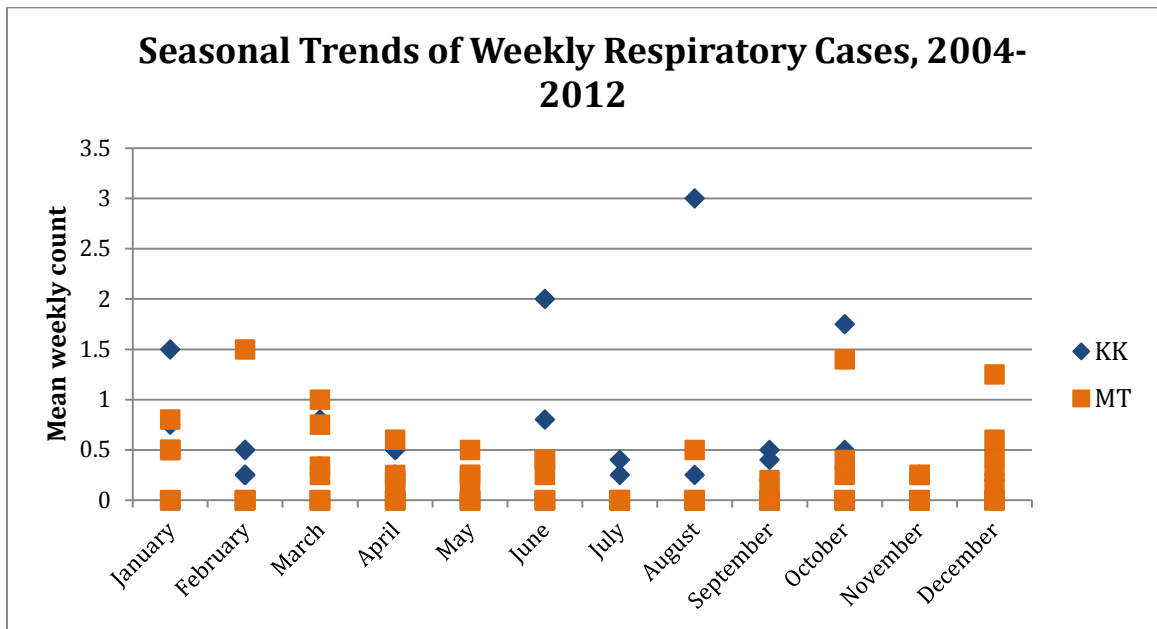


Figure 2-6 Monthly case index of the habituated chimpanzee communities. This index captures the amount of variation in weekly respiratory cases across months of the year. The monthly index is calculated as the difference between the mean number of weekly cases for a particular month and the mean weekly case count for the entire year. Panel A shows monthly case indices for Kasekela community and Panel B for Mitumba.

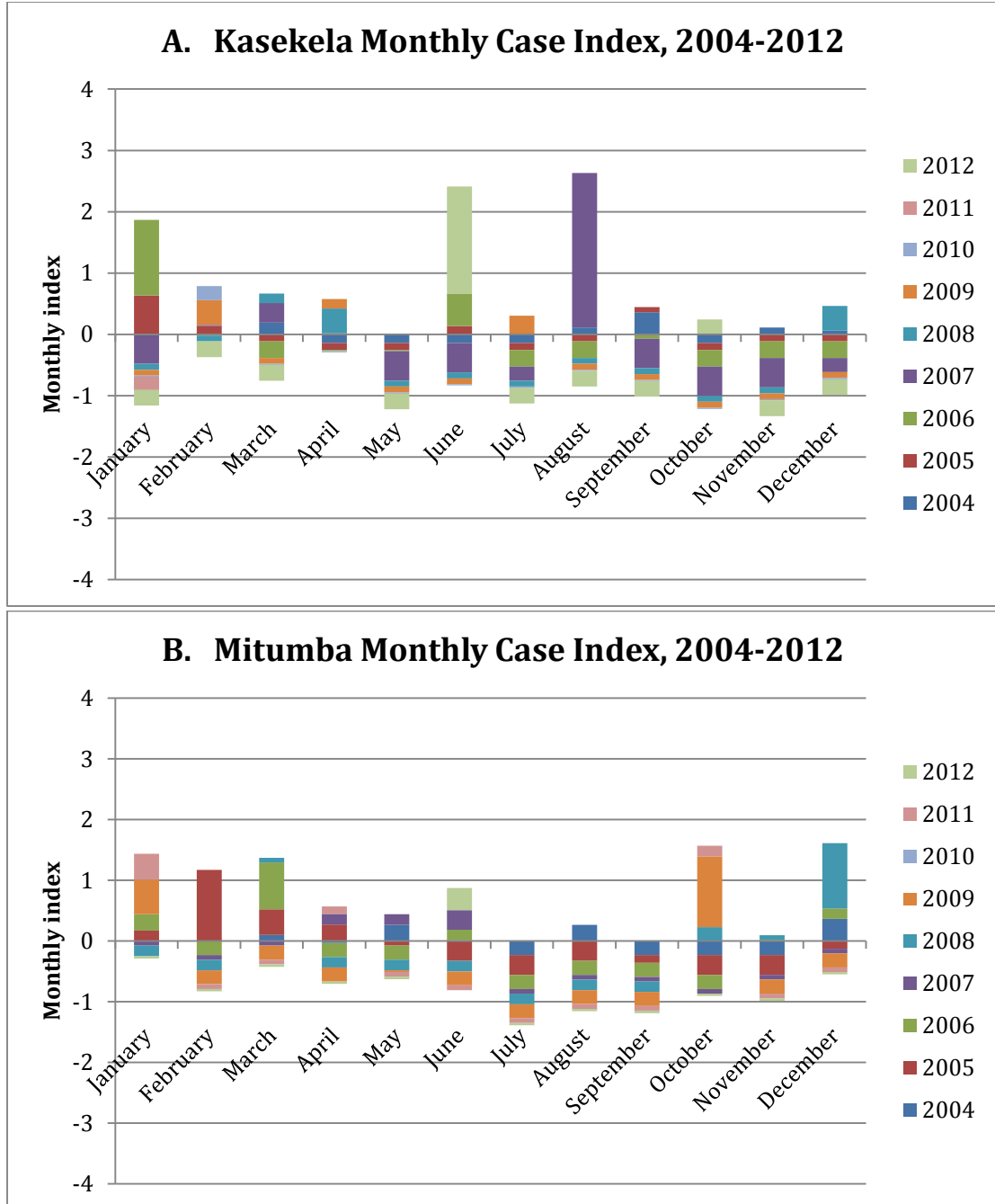
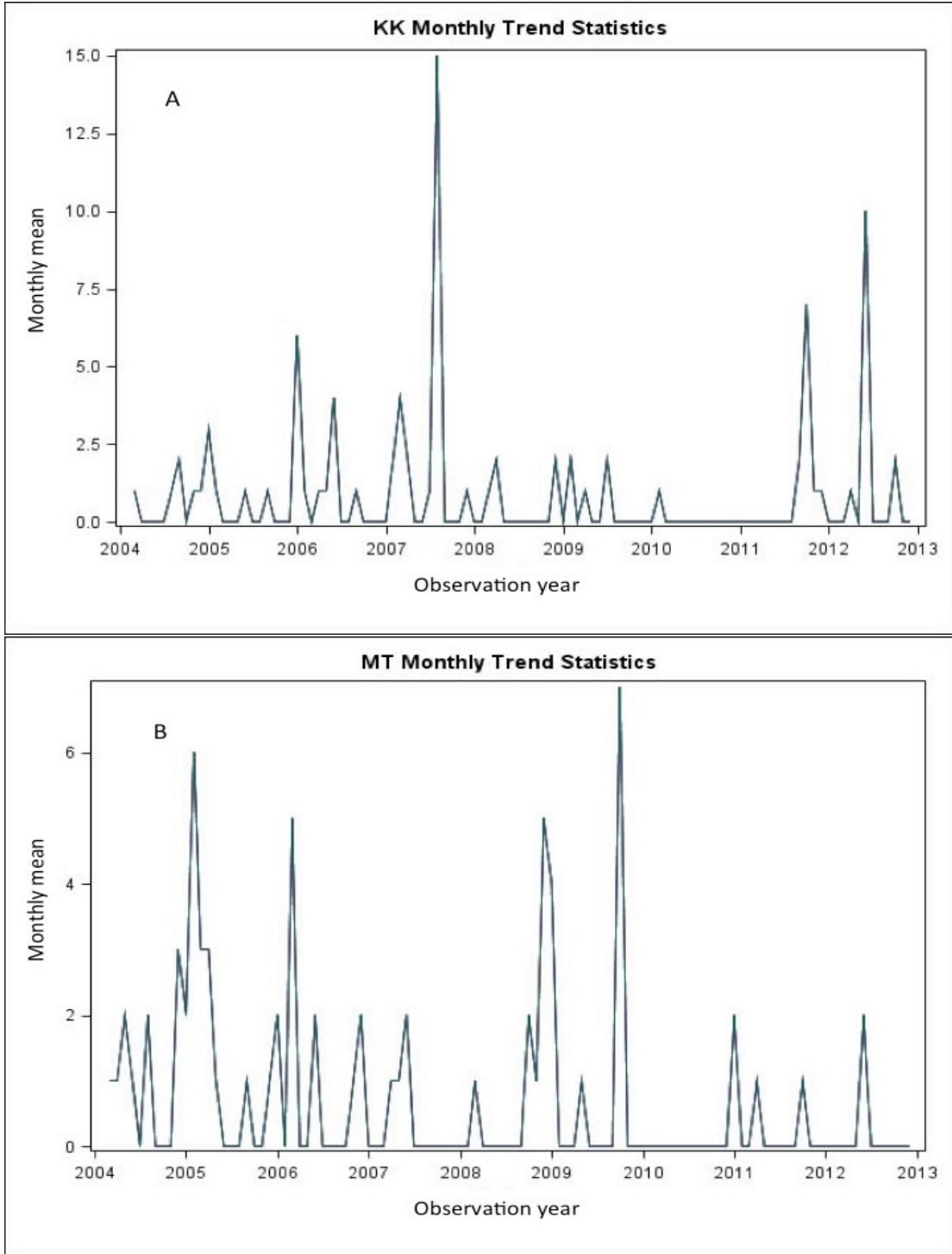


Figure 2-7 Mean monthly cases plotted across all study years (2004-2012) in Kasekela and Mitumba chimpanzee communities. A statistical trend in the change in cases each month was not observed in Kasekela (Panel A). In Mitumba (Panel B) the change in monthly cases was lower from 2010-2012, although this trend was not significantly different from 2004-2009. KK= Kasekela; MT= Mitumba.



*Retrospective Outbreak Detection*

Year 1 baseline weekly count and prevalence estimates of respiratory cases in the Daily data of each community are shown in Table 2-3. Using the upper limit of the 95% confidence interval of these estimates, the thresholds established for outbreak detection were 2 or more cases or greater than 15.6% prevalence in Kasekela and 35.8% in Mitumba. Screening the following years of data using the weekly case count threshold resulted in 12 weeks of outbreak signals in Kasekela and 10 weeks of outbreak signals in Mitumba, comprising a total of 8 and 6 outbreaks from 2005-2012 in Kasekela and Mitumba, respectively. Examination of Weekly and Daily data at each of these outbreaks signals revealed the number of chimps affected with respiratory signs ranged from 2-55 chimps in Kasekela and 2-20 chimps in Mitumba. Using the prevalence thresholds, 12 and 10 weeks of outbreak signals were generated in Kasekela and Mitumba, respectively, comprising 7 Kasekela outbreaks and 5 Mitumba outbreaks. However, in examining the Weekly and Daily data at each of these outbreak signals, two signals involved illness in only one chimp. Since this did not meet criteria for classification of an outbreak (i.e. two or more chimps observed ill), these signals were considered false alarms. After removing false alarms, there were 5 signals detected in each community using the prevalence threshold, with the number of affected chimps in each outbreak ranging from 6-55 in Kasekela and 3-20 in Mitumba. The percent positive agreement between the two detection algorithms was 71.4% (s.d.  $\pm 1.7\%$ ).

Table 2-3 Year 1 baseline mean estimates and outbreak detection thresholds for weekly respiratory cases in each chimpanzee community. Threshold levels were estimated using the upper limit of the 95% confidence interval of Year 1 baseline mean estimates.

|                                    | <b>Measures</b> | <b>Kasekela</b> | <b>Mitumba</b>   |
|------------------------------------|-----------------|-----------------|------------------|
| <b>Baseline</b><br>(mean $\pm$ sd) | Count           | 0.2 $\pm$ 0.45  | 0.35 $\pm$ 0.63  |
|                                    | Prevalence      | 2.7% $\pm$ 6.6% | 8.2% $\pm$ 14.1% |
| <b>Threshold</b>                   | Count           | 2               | 2                |
|                                    | Prevalence      | >15.6%          | >35.8%           |

## *Discussion*

Surveillance for disease in wildlife is challenging. Researchers and population managers are frequently working with some degree of population data, imperfect knowledge of disease transmission dynamics, and limited opportunities for disease sampling. The latter is particularly true when ante-mortem sampling requires animal handling and/or anesthesia, which are inherently risky enterprises. Thus, there is great interest in the advancement of noninvasive methods for disease surveillance in wildlife that will have minimal impact on the targeted populations, but serve as early warning systems for novel and emerging diseases. In this study, we examined the performance of the first syndromic disease surveillance system developed for noninvasive disease monitoring and detection in a wildlife population, chimpanzees in Gombe National Park, Tanzania. System performance analyses included data quality assessment, the generation of baseline trends of disease from syndromic data, and an evaluation of statistical algorithms for outbreak detection. In this study, analyses focused on respiratory disease surveillance, which is only one syndrome for which data is collected by this surveillance system. This was chosen based on the recognized importance of respiratory diseases as a cause of morbidity and mortality in great ape populations and the need for better understanding of the impacts of this disease syndrome on the Gombe chimpanzee population [Köndgen et al., 2008; Palacios et al., 2011; Lonsdorf et al., 2011; Williams et al., 2008; Terio et al., 2011].

The strength of the syndromic surveillance system for disease surveillance in primates and other wildlife is, first and foremost, the noninvasive collection of standardized health data. When such a system can be implemented into ongoing observational studies, large amounts of health data on different disease processes can be accrued with comparably little effort and expense. In Gombe, syndromic surveillance was incorporated into ongoing behavioral studies, which allowed the daily collection of health data when researchers were already working in the forest. The data generated from the syndromic surveillance system provides key information on background levels of disease, providing an early warning when disease exceeds levels beyond normal variation. This

type of surveillance generally identifies outbreaks in earlier stages than other types of surveillance that utilize diagnostic data. This is a key advantage in a remote setting such as Gombe, where veterinary or other diagnostic laboratories are extremely limited or non-existent. Diagnostic screening requires shipment of samples, often over several days, to specialized laboratories that can screen samples for disease agents. Thus, in comparison to a surveillance system utilizing diagnostic data, syndromic surveillance has a profoundly reduced lag time between data collection and outbreak detection in this type of setting. In this study, outbreak detection was conducted retrospectively, however, the same thresholds can be applied to real-time data, with an expected minimum time lag from observation to outbreak signaling of only a week.

A distinct disadvantage of this type of system is the lack of data on agents causing the observed disease. For example, a major assumption in this study was in the classification of a possible outbreak event: at least two chimps had to be observed with any combination of respiratory signs in a week. This classification was lenient in order to be inclusive, but without identification of a common disease agent, we cannot conclusively classify such events as true disease outbreaks. Ideally, this syndromic surveillance system will work in concert with a diagnostic detection system that will be enhanced by the syndromic surveillance data and utilize non-invasively collected samples from ill and contact animals for pathogen identification.

In our assessment of surveillance system performance, we found that data quality was good overall. Data completeness was very high, and there was no indication from the analysis that any one clinical sign was underrepresented in the data. Analysis of community coverage of the Daily record by both communities fell short of the projected goal of 60% each month. Community coverage did not vary significantly by month, suggesting that seasonal changes in chimp behavior and distribution in the park did not impact researchers' ability to acquire observations. The average number of chimps on which data was collected in the Daily record each week was 10 in Kasekela and 5 in Mitumba. So, to increase community coverage, researchers would either have to increase the weekly number of animals observed for the Daily health record or reduce the amount

of repeated sampling within the month. Specifically, with an average community size of 60 individuals in Kasekela, 9 unique individuals would have to be surveyed weekly over a 4-week interval in order to meet the projected goal. Considering that repeated sampling may be unavoidable to some extent, establishing a weekly goal exceeding this bottom-line estimate may better aid researchers in meeting the projected goal for community coverage. Kasekela researchers are currently achieving 52% community coverage, suggesting that 7-8 unique individuals are observed weekly in a 4-week interval; therefore, a small increase in the weekly number surveyed should improve coverage to the projected goal. In contrast, Mitumba's weekly average of 5 chimps surveyed in a community of approximately 25 individuals and a monthly coverage of 54% suggests that there is a large amount of repeated sampling. Alternatively, if two-thirds of that effort was put into surveying unique individuals, the projected goal could be met.

Community coverage of the Weekly data is much higher, as would be expected based on system design; however, assessment of the consistency between the two data sets suggests that the system is not functioning as it was intended. As previously described, the Weekly record was designed to capture data on all chimps observed by researchers throughout the week, those who were captured in the Daily data and those who were not. So, the Weekly record was created to capture less data on more individuals. This characteristic is definitely reflected by the higher community coverage. However, the low levels of consistency in the numbers and identities of respiratory cases each week raise concerns. Given that the Weekly record relies on researchers' recollection of the previous 7 days of observation, it is subject to recall bias. This inherent weakness combined with the findings of low consistency, suggest that a Weekly data record should not be used as a sole data source for the study of syndromic disease, but it may be useful as an adjunct to a Daily data collection system, as currently employed in Gombe.

Overall, respiratory disease was found to be at low baseline levels in both communities. An initial examination of the data for seasonal trends using mean weekly case counts plotted by month (Figure 2-5), suggests seasonal fluctuation in case numbers in Mitumba with higher numbers occurring from December through March, and fewer

case numbers from May to September. This trend is not as prevalent in Kasekela, although the occurrences of outbreaks in some years in Kasekela are easily identified as outliers. Further evaluation of the variation in monthly means from the annual mean using monthly index lends further support to possible underlying seasonal trend to respiratory disease in Mitumba, particularly with case numbers generally falling below the annual mean from July through September. In Kasekela, a seasonal trend in the monthly index is not as clear, and months with high variation appear to be largely driven by outbreaks in January 2005 and 2006, June 2012, and August 2007. There was no evidence of a secular trend in respiratory disease, although in this study the data were only tested for a linear increase or decrease in monthly cases over the duration of the study. Examination of the plots of monthly case statistics (Figure 2-7) clearly demonstrates fluctuations in case numbers over time. Interestingly, Mitumba had no cases of respiratory disease for a 14-month period beginning at the end of 2009, and Kasekela had an 18-month period with no respiratory cases, which lagged the period in Mitumba by 4 months. Consultation with Gombe researchers and local Jane Goodall Institute staff reveals no systematic changes in surveillance that might account for the drop in respiratory cases observed in the data. Therefore, we concluded that the absence of respiratory cases during this period is real, reflecting a time of good respiratory health for both communities.

The time series analyses for seasonal trends of disease in this study were primarily descriptive in nature, but suggest that additional analytical methods are needed. In particular, autoregressive integrated moving average (ARIMA) modeling is a statistical modeling approach for non-stationary, time series data that can help explain seasonal changes in disease or aid in forecasting by identifying significant trends in disease fluctuation [Box et al., 2008]. Additionally, significant seasonal trends identified from such a model would aid in the selection of an optimal outbreak detection algorithm that is specific for each season.

We developed a simple set of algorithms generated from Year 1 baseline data to screen the following 8 years of data for outbreaks. Using weekly case count and

prevalence thresholds developed for each community, we were able to detect 8 outbreaks that were previously unrecognized, in addition to 6 major outbreaks that were recognized in real-time. The weekly count algorithm appeared to be more sensitive, having detected 4 more outbreaks than the prevalence approach. However, the prevalence approach was clearly more vulnerable to false alarms, based on two signaling events that occurred when only a single animal was sick, hence not meeting our outbreak criteria. This occurred in weeks when the number of chimps observed in the Daily data was very few (3 and 6), thus raising the prevalence of illness above threshold with the identification of a single ill animal. The remaining disagreement in outbreak signals between the two algorithms occurred when few animals were sick in a single week. The majority of these outbreaks were of one-week duration, but one outbreak involved 7 animals over 5 weeks, and possibly 9 animals over a total of 10 weeks. The latter reveals an important distinction between the two algorithms. While both algorithms successfully detect sharp increases in respiratory disease, the weekly count algorithm appears to be better at detecting outbreaks with low-level, sustained disease transmission. If a seasonal trend to disease is confirmed in future studies, an additional detection algorithm to explore would be a temporal scan statistic, utilizing a moving average to create a dynamic threshold for disease detection.

As noted previously, all signals triggered by increases in respiratory disease above our established thresholds are referred to as outbreaks for the purposes of this study, but transmission of a disease agent was not confirmed in any of these events. However, the outbreak detection algorithms, when used in real-time surveillance, will be valuable in raising awareness of possible outbreak events and triggering targeted diagnostic sampling of ill animals and their contacts for pathogen detection.

In conclusion, this study demonstrates the performance and utility of syndromic surveillance in the detection of disease in a wildlife population. In a readily observed wildlife population, this type of system can provide valuable information on changing disease trends and early warning, ahead of diagnostic surveillance, of outbreak events. Its greatest limitation is the lack of pathogen detection, but, combined with diagnostic

surveillance, this can be a powerful system of detection of disease in wildlife. For primate populations, this study offers insights into the capacity of another tool for noninvasively studying a major risk factor in the persistence of extant populations. This is particularly true for habituated primate populations, where the risks and need to study zoonotic disease transmission are great.

# Chapter 3 | Understanding the Epidemiology of Respiratory Outbreaks among Free-Living Chimpanzees through Syndromic Surveillance

## *Background*

Respiratory diseases are increasingly recognized as having a significant impact on great ape populations. There is ample evidence showing that great apes are exposed to, and in some cases, suffer disease from human respiratory pathogens [Palacios et al., 2011; Köndgen et al., 2008; Kaur et al., 2008]. Increased pathogen transmission events between humans and great apes can be attributed to new patterns of contact arising from anthropogenic impacts on the natural environment combined with human habituation of great apes. However, the benefits of human habituation to great ape survival have also been realized through research and ecotourism [Köndgen et al., 2008; Pusey et al., 2008, 2007; Campbell et al., 2011]. The chimpanzee population of Gombe Stream National Park, Tanzania, the longest studied population of great apes, is an excellent example [Pusey et al., 2008, 2007]. Here, chimpanzee conservation has benefited not only from research specifically focused on chimpanzee ecology and behavior, but also from intense monitoring and continued protection of the population. Thus, in the continued effort to improve great ape survival and conservation, population managers strive to mitigate the disease risks associated with human habituation.

Unfortunately, our understanding of great ape respiratory disease has been based on observations of large-scale outbreaks with high morbidity and mortality. Such outbreaks and their associated impacts may not be representative of the epidemiology of endemic respiratory diseases in these populations, for which there is a paucity of information. In an effort to remediate this situation, Gombe researchers have utilized multiple data sources to better understand ongoing impacts of respiratory disease in the Kasekela (n ~55-70) and Mitumba (n ~24-30) chimpanzee communities. These

communities are habituated to human presence, which has facilitated behavioral research of these communities since 1960 and the 1980s, respectively [Lonsdorf et al., 2006]. Throughout the entire period of behavioral study, health data has been collected, but, prior to 2004, systematic health data collection occurred only from 1970-1987 and 2001-2003 [Lonsdorf et al., 2006]. A study of 40 years of this existing health data on the Kasekela community revealed disease as a leading cause of mortality, with respiratory illness associated with almost half of the disease-related mortalities [Williams et al., 2008]. Delving further into respiratory disease transmission risks, park practices and chimpanzee behavioral and standardized health data were examined from 1979-1987 to identify risk factors associated with respiratory disease rates in the Kasekela community [Lonsdorf et al., 2011]. Overall, respiratory disease rates were low, with a maximum monthly prevalence of respiratory disease being less than 3.5%; however, a positive association of illness with banana feeding that was influenced by season was revealed. In contrast to the earlier mortality study, comprehensive postmortem pathological examinations conducted from 2004-2010 revealed that respiratory disease was not a cause of morbidity or mortality among recovered carcasses [Terio et al., 2011].

Taken together, these studies demonstrate the value of the integration of health and behavioral data to understanding disease risks and impacts on a well-studied population of chimpanzees. However, they invite additional questions: are respiratory disease rates and associated mortality changing over time, perhaps in response to population management practices (e.g. elimination of banana provisioning), or are improved health data collection practices providing a better framework and context for understanding true disease impacts? To examine this further, we utilize standardized disease data collected by the Greater Gombe Ecosystem Health Program (GEHP) to describe the epidemiology of respiratory disease outbreaks over the same time period as the Terio et al. pathology study.

GEHP was established in 2004 to systematically collect observational data for syndromic disease surveillance. [Lonsdorf et al., 2006; Travis et al., 2008; Williams et al., 2008] This type of surveillance collects pre-diagnosis health data on general types of

diseases, or “syndromes.” In this context, researchers are trained to identify specific clinical signs as indicators of syndromic disease. This type of data is less specific than confirmatory diagnostic data, but is sensitive to changes in disease levels within a population, providing an early signal of disease outbreak. [Dórea et al., 2011] Advantages of syndromic health surveillance go beyond outbreak detection, by improving understanding of disease trends, providing data for risk analysis, and facilitating infection control and prevention [Ward and Carpenter, 2000]. In a setting such as Gombe, it also meets the need for noninvasive methods to study disease.

In advance of this study, respiratory syndromic data was used to describe baseline trends of respiratory disease and identify outbreaks (Chapter 2). In general, respiratory disease was an infrequent occurrence among the habituated chimp communities, with no observations of respiratory disease in most weeks, and an average of 2.1% (s.d.  $\pm$  7.4%) of weekly-observed chimps having some clinical sign of respiratory disease. In addition, 14 respiratory outbreaks were identified from 2005-2012 in which the numbers or prevalence of chimps with respiratory disease significantly exceeded baseline variation. In this study, we describe the epidemiology of the outbreaks detected by these methods from 2004-2012. The objectives of this study were to 1) utilize standardized health data to describe outbreak morbidity, demographics, and duration, and 2) evaluate patterns of infection associated with outbreak size.

## *Materials and Methods*

### *Syndromic Disease Surveillance*

From March 2004 through the present, the systematic collection of syndromic disease data has been a component of ongoing behavioral data collection on the Kasekela and Mitumba chimpanzee communities of Gombe National Park, Tanzania, and has been described previously [Lonsdorf et al., 2006] (Chapter 2). Briefly, through direct observation, behavioral researchers document the presence or absence and severity of specific clinical signs associated with syndromes of disease, including respiratory, gastrointestinal, dermatologic, traumatic, and wasting. Clinical signs of coughing,

sneezing, and rhinorrhea are specific to respiratory syndrome. As previously described, this health data is collected on individuals that are the focus of a behavioral follow, whether healthy or ill, using a Daily health check sheet. [Lonsdorf et al., 2006] In conjunction, a fecal sample is collected from the individual during the focal follow and preserved in 10% neutral buffered formalin. If an individual other than the primary subject of the follow is observed ill, an additional Daily health check sheet is generated for the ill individual and fecal sample collected opportunistically. In addition to the Daily health data, Weekly health data is collected on all individuals seen during the week, whether they were the subject of a focal follow or not. The Weekly health data is less detailed, documenting presence or absence of disease associated with any of the major syndromes. To supplement these data, more detailed, non-standardized health observations are collected by the resident veterinarian in response to reports of illness. These three data types: Daily, Weekly, and veterinary reports, from March 2004 to December 2012, were utilized in the analyses of respiratory disease for this study.

#### *Descriptive and Statistical Analyses of Respiratory Outbreaks*

A set of outbreak detection algorithms described in Chapter 2 were applied to the GEHP Daily syndromic data from 2004-2012 and identified a total of 15 outbreaks of respiratory disease. These outbreak events were weeks in which the number or prevalence of respiratory cases exceeded estimated thresholds under which normal disease variation was expected to occur (Chapter 2). Daily and Weekly data sets, and where available, veterinary reports were utilized to determine the cumulative case incidence and duration of each outbreak. A case is defined as any individual demonstrating any single or combination of respiratory signs during the time frame of the recognized outbreak. Cases that were identified within 2 weeks of an outbreak event were included in the outbreak incidence. Outbreak duration was calculated as the number of weeks over which new cases of respiratory disease were identified.

Major epidemics have been defined previously as 20% or more of a community demonstrating respiratory signs in a short duration of time (up to 3 months) and more than one chimpanzee death associated with respiratory illness [Lonsdorf et al., 2011;

Williams et al., 2008]. Outbreaks were classified as major in this study if the size of the outbreak at least met with this definition. Between March 2004 and December 2012, six major respiratory epidemics occurred in the habituated chimpanzee communities. Each of these epidemics was recognized in real-time due to the large proportion of the communities affected; as a result, a substantial amount of supplemental data in the form of non-standardized veterinary reports were available. Therefore, analyses of major epidemics utilized standardized data from Daily and Weekly health checks as well as non-standardized veterinary reports. Because of the substantial amount of daily-level data, epidemic curves of major outbreaks, depicting the daily case incidence, were generated by plotting the number of new cases observed each day of the epidemic.

All outbreaks were initially plotted by size and time of year to assess seasonal trends. Outbreaks were then classified as small or major and compared by duration, morbidity, and demographics. Morbidity was calculated as the percentage of the community identified with respiratory signs during the time of the outbreak. Because morbidity was not normally distributed, this variable was log transformed and compared by t-test. A 2-class age structure was utilized to separate the population by age demographics: subadult (< 12y) and adult (12y and older) [Markham et al., 2015; Murray et al., 2006a, 2009]. Differences in risk of being a case in a major outbreak versus a small outbreak between sex and age class were examined. To do this, outbreak size was modeled as a binomial dependent variable using Generalized estimating equations (GEE) with chimpanzee identity as a random effect and sex, age class, and an interaction term for sex and age class as fixed effects. Fixed effects were first examined in univariate models and then added in a forward stepwise manner to a multivariate model. The best covariance matrix and model was selected using the lowest quasilikelihood under the independence model criterion (QIC) [Cui, 2007; Hanley, 2003].

We wanted to determine if certain characteristics or demographics were drivers of epidemics. Specifically, we wanted to test the association between age class, sex, and dominance rank in the community with the onset of outbreaks, and determine if illness in chimps with these characteristics at the start of outbreaks predicted the scale of an

outbreak (i.e. small vs. major). To do this, we first modeled outbreaks of greater than one-week duration using GEE. For these analyses we modeled illness in the first week of an outbreak as a binomial response variable. Chimp identification was modeled as a random effect, and fixed effects included sex, a two-class age variable (i.e. adults  $\geq 12$ y and subadults  $< 12$ y), and a 3-class rank variable, added in a forward stepwise manner. Rank was a 3-level categorical variable that included high, medium, or low for adult females and males. Male and female rank were calculated over a 2-year window corresponding to the timing of the outbreak by the modified David's score method [de Vries et al., 2006], using directional male-male and female-female pant-grunts for male and female dominance rank, respectively [Feldblum et al., 2014; Markham et al., 2015]. Since dominance rank is a characteristic limited to adults, this analysis was restricted accordingly. Rank data were only available for Kasekela community, thus rank was analyzed for this community only. To determine if there were differences or interactions in significant demographics at the start of an outbreak with outbreak size (major vs. small), a final set of models were run with an additional binomial variable for outbreak size (i.e. small vs. major) as a fixed effect and interaction terms for outbreak size and the significant variables identified in the previous set of models.

Finally, we were interested in whether or not disease patterns were associated with familial relationships. To evaluate this question, all individuals in a community at the time of an outbreak were binomially classified as being related to a case or not in the specified outbreak (binomial variable = family member case status). Family member case status was assigned based on matrilineal relationships and assigned a true status if a mother, offspring or any immature siblings ( $< 12$ y of age) were also cases in the specified outbreak. In recognizing that behavioral associations between mothers and adult male offspring ( $\geq 12$ y) can be quite different from mothers and immature or adult female offspring, a separate set of analyses was performed using the same relationship assignments, except male offspring  $\geq 12$  y were never allowed a true family member case assignment based on relationships with mothers or immature siblings. These separate analyses were conducted to explore possible patterns of genetic and behavioral influences on disease. Case relationship analyses were performed on major outbreaks only. GEE

were used to evaluate the association of disease status in an outbreak to the status of being related to a case in the same outbreak. In each model, individual chimps were designated as a random effect. Fixed effects included community, age class, sex, and interaction terms for family member case status and age class and family member case status and sex; each fixed effect was added in a forward stepwise manner and QIC was used to select the best covariance matrix and model fit. All GEE models were performed using SAS software, Version 9.4 of the SAS System for Windows (Copyright 2002-2012, SAS Institute Inc., Cary, NC, USA).

## Results

A total of 15 outbreaks were identified from March 2004 to December 2012, using the set of detection algorithms described in Chapter 2. Six outbreaks were identified in Mitumba and nine in Kasekela (Table 3-1). The mean cumulative case incidence associated with these outbreaks was 13 (range: 2-55) and 7 (range: 2-20) cases in Kasekela and Mitumba, respectively. Mean duration of outbreaks was 3 weeks (range: 1-5). Outbreaks were fairly well distributed across months of the year, although larger outbreaks appeared to cluster in August-October (Figure 3-1). Six major outbreaks were observed in the habituated communities during the study period. These included two outbreaks in Kasekela (August 2007 and October 2011), two outbreaks in Mitumba (December 2008/January 2009 and October 2009), and two outbreaks that occurred simultaneously in the two communities (June 2012). Comparisons in duration, morbidity, and demographics between small and major outbreaks are summarized in Table 3-2. On average, major outbreaks were of shorter duration than small outbreaks, although this difference was not significant. The progression in the daily case incidence of major outbreaks over time is depicted in the epidemic curves of Figure 3-2. Log morbidity was significantly different between major and small outbreaks. Both sex (Chi square=4.77,  $p=0.0290$ ) and age class (Chi square=4.71,  $p=0.0300$ ) were significant predictors of outbreak size in univariate GEE models, with males and subadults having significantly higher incidences in major outbreaks than small outbreaks. However, when combined in the same model, significance was marginal (sex: Chi square=3.62,  $p=0.0572$ ; age class:

Chi square=3.68,  $p=0.0549$ ), and interaction was not significant. The best model was the univariate model containing sex as the predictor variable (QIC=195.6440).

Table 3-1 General characteristics of respiratory disease outbreaks detected in the Gombe habituated chimpanzee communities from 2004-2015. Incidence is the cumulative number of cases that developed during each outbreak. Outbreaks were detected by screening the Daily data by the methods described in Chapter 2. Weekly, Daily and veterinary report (available for major outbreaks) data were utilized to determine outbreak incidence.

| Community | Number of outbreaks | Mean incidence (range) | Mean duration, wks (range) |
|-----------|---------------------|------------------------|----------------------------|
| Kasekela  | 9                   | 14 (2-55)              | 3 (1-5)                    |
| Mitumba   | 6                   | 8 (2-24)               | 3 (1-5)                    |

Figure 3-1 Monthly distribution of respiratory outbreaks in Kasekela and Mitumba from 2004-2012. The vertical axis represents the cumulative incidence of respiratory disease of each outbreak, or the total number of chimpanzees that developed respiratory disease during the outbreak period. Incidence was calculated using data from Daily, Weekly, and veterinary records (the latter available for major outbreaks only). KK = Kasekela community; MT = Mitumba community.

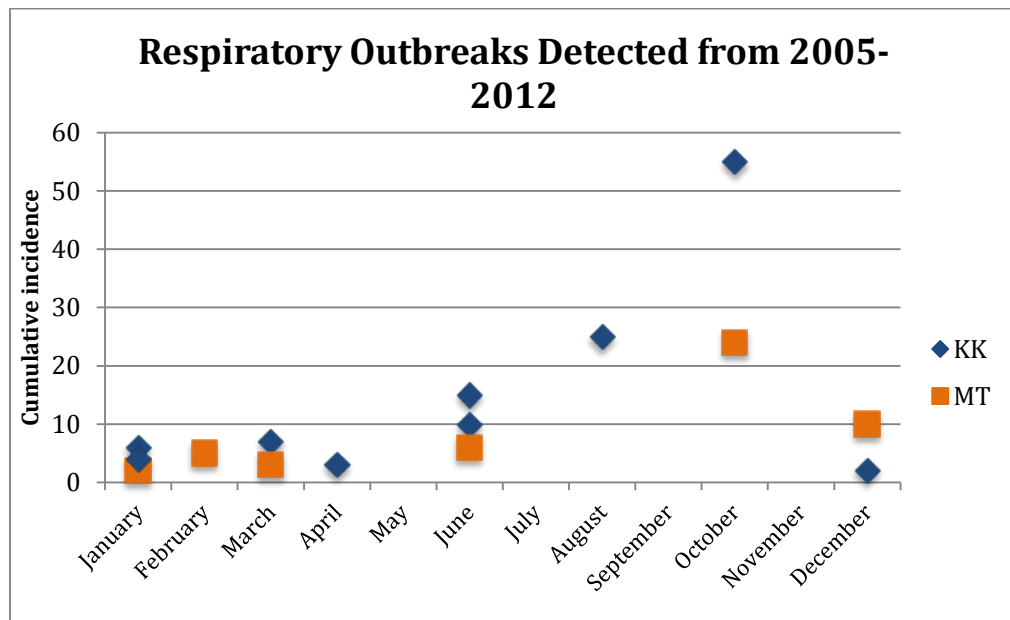


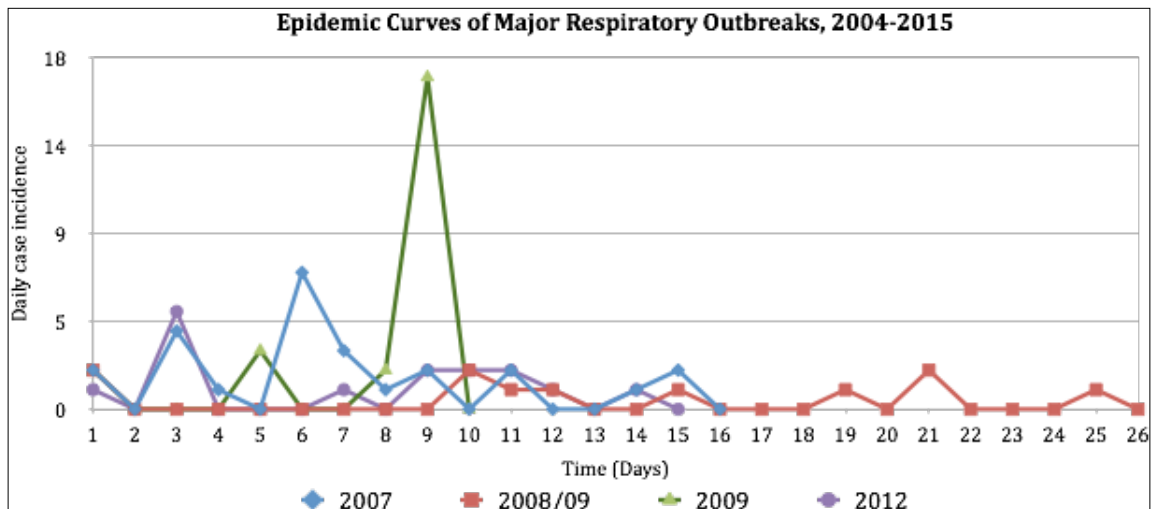
Table 3-2 Comparisons morbidity, duration, and demographics between small and large respiratory outbreaks in habituated chimpanzee communities from 2004-2012.

| <b>Outbreak size</b> | <b>Percent morbidity</b><br>(mean ± sd) | <b>Duration, wks</b><br>(mean ± sd) | <b>Adult:subadult case ratio</b><br>(mean ± sd) | <b>Male:female case ratio</b><br>(mean ± sd) |
|----------------------|---|-------------------------------------|---|--|
| Small                | 10.6 ± 6.6                              | 3.2 ± 1.8                           | 2.2 ± 0.8                                       | 0.6 ± 0.66                                   |
| Large                | 50.0 ± 30.3                             | 2.5 ± 1.2                           | 1.4 ± 0.5                                       | 0.8 ± 0.34                                   |

To evaluate key characteristics or demographics that might be important drivers of outbreaks early in the event, we analyzed a total of 10 outbreaks of duration >1 week. Of the outbreaks analyzed, 4 were classified as major outbreaks (Mitumba = 2, Kasekela = 2) and 6 were small outbreaks (Mitumba = 2, Kasekela = 4). Sex was the only variable significantly associated with the start of an outbreak (Chi square = 5.23,  $p=0.0222$ ). There were significantly more male cases at the start of an outbreak, and this finding was not different between the two age classes. No significant difference was observed when the model was adjusted for outbreak size (Chi square = 0.00,  $p=0.9545$ ), suggesting that the role of sex at the start of an outbreak is the same for all outbreak sizes.

In major outbreaks, a significant positive association was observed between being a case and having a family member also a case (Chi square= 35.92,  $p<0.0001$ ). The best models were those that did not allow the inclusion of a family member case for relationships between adult males and their mothers or siblings (QIC < 324.5). Of these, the best fit was a multivariate model (QIC = 315.3394) including family member case status (Chi square=46.93,  $p<0.0001$ ) and variables to account for confounding created by the exclusion of family member case status among adult males: age class (Chi square=8.27,  $p=0.0040$ ) and sex (Chi square=6.24,  $p=0.0125$ ). Interactions between family member case status and sex, and family member case status and age class, were not significant. Model fit was worse among models where adult males were allowed a true family member case status if siblings or mothers were cases (QIC >326). There was no significant difference observed by community in either modeling approach.

Figure 3-2 Epidemic curves of major respiratory outbreaks from 2004-2015. Line curves represent the daily case incidence, or daily number of new cases of respiratory disease, associated with each outbreak. The June 2012 outbreak in Mitumba and October 2011 outbreak in Kasekela are excluded due to missing daily incidence data.



## Discussion

In the 9 years of study, respiratory disease outbreaks were not found to occur with high frequency in Kasekela and Mitumba. Over this period, each community averaged 1 outbreak per year. The majority of the outbreaks that occurred were small events ( $n=9$ ), whereas 6 were major outbreaks, meeting the criteria of 20% or more of the community affected. Although high morbidity was observed in each of the major outbreaks, no mortalities were observed in association with disease. This is consistent with the findings of Terio et al. for the same time period [Terio et al., 2011]; combined, these studies demonstrate that respiratory disease outbreaks, even those of major scale, are not always a cause of chimp mortality. These findings are seemingly in contrast with those of Williams et al. in which 30% of illness-associated mortality of Kasekela chimps was attributed to epidemic respiratory disease [Williams et al., 2008]. It is possible that changes in management practices (e.g. the elimination of banana provisioning in 2000) were successful in reducing the incidence and mortality of respiratory disease; however, the lack of standardized health data for many of those years provides no information on

the annual frequency of respiratory disease outbreaks in the communities. Therefore, it cannot be known with certainty how the epidemiology of non-fatal respiratory outbreaks might have changed over time and between these studies.

In addition to morbidity levels, several differences were observed between small and major outbreaks. Generally, the respiratory disease outbreaks observed in this study were of short duration (5 weeks or less); however, although not significantly different, major outbreaks tended to have a shorter duration than smaller outbreaks, indicating that transmission moved quickly through the communities before stopping altogether. Although seasonality did not appear to be associated with the timing of outbreaks, there may be a seasonal trend to the size of the outbreaks, with larger outbreaks seeming to cluster in the August-October months of the year (not statistically tested). This time of the year coincides with the end of the long dry season in Tanzania. Interestingly, this is in contrast to the monthly baseline trends of respiratory disease described in Chapter 2, where respiratory cases generally fell below average in August and September in Mitumba and in October in Kasekela.

Differences in the demographics of cases between major and small outbreaks were also explored for heterogeneity in disease transmission. All age classes were affected in major outbreaks, but the univariate model of age class and outbreak size indicated a higher case incidence among subadults than adults, as compared to smaller outbreaks. This might suggest that acquired immunity is playing a role in the protection of older animals in these outbreaks. Alternatively, behavioral differences in contact among subadults may facilitate disease transmission. Research of Tai National Park chimpanzee infant mortality cycles provides support of the latter hypothesis, with respiratory outbreak cycles peaking with social connectivity derived by infant play behavior [Kuehl et al., 2008].

The best fitting model in these analyses, however, revealed a higher incidence of male cases in major outbreaks, suggesting a possible role of males in the transmission of disease through a community. Males were also significantly more likely to be a case in the first week of an outbreak of any size, indicating their importance as propagators of

disease leading to the development of outbreaks. This is consistent with recent research of a chimp community in Kibale National Park, Uganda, which suggested high-ranking males as important individuals in disease transmission through a social chimp network [Rushmore et al., 2013]. Experimental manipulation in birds and rodents have shown males to be important drivers of population-level disease rates as a result of increased testosterone, which both suppresses the immune system and increases the number of social contacts [Gear et al., 2009; Ferrari et al., 2003; Mougeot et al., 2005]. Additionally, chronic stress associated with the agonistic interactions of dominants and subordinates within the social rank structure of the community may suppress immune function and facilitate disease transmission [Abbott et al., 2003; Boonstra, 2013; Charmandari et al., 2005]. Unfortunately, rank data for both communities were not available to evaluate in these analyses to provide further support of this hypothesis. Overall, these findings illuminate a key subgroup that may play an important role in disease transmission, either through social behavior or host susceptibility and immune response that facilitates the propagation of outbreaks.

In addition to social behavior, host genetics can also impact disease transmission. Thus, to explore this further we evaluated patterns of infections in association with matrilineal relatedness. In our analyses we found that being related to another case in an outbreak was a significant predictor of being a case; however, this was not consistent for adult males. Excluding assignment of being related to a case among adult males resulted in the best fitting models, demonstrating that relatedness to other cases is not an important predictor of being a case among adult males. In general, this supports a hypothesis for social behavior as a stronger driver of disease transmission than host genetics, as adults of both sexes would share similar genetics to their family members and thus genetically-associated disease susceptibility, but adult females generally have stronger behavioral associations with their matrilineal family groups [Goodall, 1986]. Therefore, this difference in social contact may better explain the model performance observed in these analyses. Previous research on disease transmission through the social network of chimp communities has lacked real world outbreak data to validate models and hypotheses of transmission [Rushmore et al., 2013]. Thus, a clear next step would be

to combine these outbreak data and analyses with social network analyses and modeling to explore further the role of social behavior in disease transmission and outbreak epidemiology.

Understanding differences in disease incidence across age classes, sex, and family relatedness can provide important clues on the heterogeneity of disease transmission, and how these traits may contribute to the development of major disease epidemics in chimp populations. These analyses are limited by a lack of diagnostic data to confirm outbreak cases, and do not encompass all factors that may facilitate disease transmission in an outbreak (e.g. seasonal variables, SIV infection status). However, these analyses do provide key insights on respiratory disease outbreaks from 2004-2012, and combined with the pathology study of the same period [Terio et al., 2011], enhance our understanding of the population-level impacts of respiratory disease in Gombe chimpanzees.

# Chapter 4 | Agent-based Modeling of Respiratory Disease Transmission to Evaluate the Sensitivity of a Syndromic Surveillance System in Free-living Chimpanzees

## *Background*

In a world of increasing wildlife habitat loss, a growing human population, and expanding connectivity between human, domestic animal and wildlife populations, emerging infectious diseases are ever more a complex and disturbing issue. The public health threat is apparent, with approximately 60% of emerging infectious diseases a result of zoonotic transmission. Of course, the negative impacts of emerging infectious disease are not unique to human populations, and there are numerous examples of disease spillover from humans and their domestic animals into wildlife populations, with long-term and sometimes devastating consequences [Cleaveland et al., 2005; Roelke-Parker et al., 1996; Nugent, 2011; Epstein and Price, 2009; Nituch et al., 2011; Kock et al., 1999; Michel et al., 2009]. Primates are recognized as an important taxon in emerging disease events, as they may serve as sentinels, sources of zoonotic infections to humans, or cases of human-associated disease transmission [Jones et al., 2008; Woolhouse and Gowtage-Sequeria, 2005; Wolfe et al., 2007; Calvignac-Spencer et al., 2012; Epstein and Price, 2009]. Based on their close genetic relatedness to humans alone, the risks of infectious disease transmission between the two populations are quite high [Loomis, 2003]. Hence, from both public health and conservation perspectives, there is a critical need for disease surveillance in primate populations.

Disease surveillance in primates and wildlife is often implemented to identify changes in trends or geographic distributions of endemic diseases of public health or agricultural concern or to track emerging or reemerging disease events that directly

threaten wildlife populations. Since intervention to mitigate transmission and population impacts is a key component to disease surveillance [Thrusfield, 2007], early warning of an emergent event is an important feature of surveillance systems. With these concepts in mind, a syndromic surveillance system was implemented in a well-studied population of wild chimpanzees in Gombe Stream National Park, Tanzania to better understand endemic disease trends and improve recognition of outbreak events and disease risk assessment [Lonsdorf et al., 2006; Travis et al., 2008]. Syndromic surveillance is the collection of pre-diagnosis health data that can signal a case or outbreak [Henning, 2004]. This type of surveillance targets general types of diseases, or “syndromes”; in Gombe, specific clinical signs are targeted as indicators of syndromic diseases such as respiratory, dermatologic, gastrointestinal disease, trauma and wasting. These types of data are less specific than confirmatory diagnostic data, but they are sensitive to changes in disease trends, providing an avenue for early outbreak detection [Dórea et al., 2011].

Syndromic surveillance is an emerging field in veterinary medicine and a novel approach in wildlife, thus associated methodologies are developing [Oleaga et al., 2011; Arenas et al., 2002; Warns-Petit et al., 2010]. Unquestionably, formal evaluations of syndromic surveillance performance in wildlife populations are sparse. To help fill the gap, we have undertaken a systematic evaluation of the performance of the Gombe syndromic surveillance system to fully describe its utility and limitations in primate disease surveillance. The start of this evaluation was described in Chapter 2, with a thorough assessment of data quality and qualitative evaluation of methods for respiratory disease outbreak detection. However, an important component in this evaluation is the quantitative assessment of outbreak detection performance [Rodríguez-Prieto et al., 2014; Dórea et al., 2013, 2011].

Quantitative assessment is similar to that employed for diagnostic tests, with surveillance sensitivity being the probability that an outbreak is detected by the system employed and specificity measuring resistance of the system to false alarms [Rodríguez-Prieto et al., 2014; Buckeridge et al., 2008]. The quantitative evaluation of surveillance methods can be employed using either real, simulated data or both [Dórea et al., 2013;

Jackson et al., 2007; Rodríguez-Prieto et al., 2014]. In syndromic surveillance, accompanying diagnostic laboratory data is useful in confirming or refuting the presence of a signaled outbreak, thus contributing to the quantitative assessment of specificity. In the context of this study, the detection of respiratory pathogens from diagnostic specimens such as respiratory secretions, feces, or tissues recovered from mortalities would provide a platform for estimating the specificity of our outbreak detection algorithms (Chapter 2). Unfortunately, as veterinary interventions (e.g. capture) for diagnostic sampling or treatment are generally not undertaken in Gombe, methodologies for noninvasive diagnostic sampling are a relatively new approach to disease detection in primates, and mortalities were not associated with any of the outbreaks detected from 2004-2012, diagnostic respiratory data were unavailable for assessment of specificity. Since respiratory disease is not a large disease burden on the Gombe chimpanzee population, the disease thresholds established by our detection algorithms were very low, thus we expect sensitivity to be high at the cost of a high rate of false alarms. Up until now however, the detection sensitivity has not been formally quantified. What is also unclear is the robustness of the syndromic surveillance system under different behavioral and seasonal conditions. Understanding these dynamics will allow us to better understand the effectiveness of the data collection methods and provide insight and guidance in the optimization of our outbreak detection algorithms.

Theoretical disease models offer the opportunity to evaluate disease transmission in an ecosystem through a simplified representation of complex processes that are not easily observed or understood [Anderson and May, 1979]. When combined with empirical population data, theoretical disease models become powerful epidemiological tools, enabling us to answer the “what if” questions related to infectious disease transmission and to assess the effectiveness of strategies to mitigate transmission (e.g. vaccination, treatment) even before they are undertaken. The utility of this approach for predicting disease impacts and vaccination in primate populations has already been demonstrated [Rushmore et al., 2013; Nunn et al., 2007; Carne et al., 2013; Rushmore et al., 2014]. To date, primate disease models have relied heavily on demographic and behavioral data for parameterization, but have lacked empirical disease data derived from

the populations they are modeling. In contrast, the long-term and ongoing research of Gombe chimpanzees has resulted in both demographic, behavioral and disease data, offering the unique opportunity to create a fully informed disease transmission model. Thus, the objective of this study was to use theoretical disease modeling, informed by the collection of these empirical data, to couple the simulation of respiratory disease transmission with syndromic surveillance to estimate the sensitivity of the Gombe syndromic surveillance system to outbreak detection. Our study focused on the Kasekela chimpanzee community, for which exist the most robust empirical data sets, which we modeled through an agent-based, network modeling approach. Agent-based models combine infectious disease epidemiology with individual behavior, making them useful in describing disease spread through individual entities within a population, an approach well-suited to a population that is small and isolated such as the Gombe chimpanzee population [Perez and Dragicevic, 2009]. Social network modeling has become popular for studying disease transmission among highly social primate and wildlife populations for its ability to capture the contact heterogeneity associated with a population's social structure [Craft and Volz, 2011; Rushmore et al., 2013; Carne et al., 2013; Craft and Caillaud, 2011]. Given these advantages, we incorporated both of these modeling approaches in our disease transmission model. Through these efforts we provide a complete assessment of syndromic surveillance in Gombe chimpanzees, providing a framework for other primate research communities and the field of wildlife disease surveillance as a whole.

## *Methods*

### *Empirical Data Inputs*

Chimpanzee social networks were created from behavioral data that captured pairwise associations between individuals of the Kasekela community at a party and grooming level. A Dyadic Association Index (DAI) was estimated for each pair of chimpanzees based on the amount of time they spent in the same party relative to the total

amount of time each individual was observed, with 100% certainty. The DAI was calculated as:

$$DIA = \frac{AB}{A+B-AB} \quad (\text{Equation 4.1})$$

where  $A$  represents the total observation time for individual  $A$ ,  $B$  represents the total observation time for individual  $B$ , and  $AB$  represents the total amount of time in minutes that individual  $A$  spent in the same party as individual  $B$ . DAI matrices were generated by the Jane Goodall Institute Research Center at Duke University. Matrices were constructed by annual quarter for all adults and some immature individuals. Infants and immature individuals with missing data were assigned the same DAI values as their mother, assuming they would always be with the mother (infants) or would have similar social networks (immatures). Infants were assigned a DAI of 1 for the pairwise association with their mother. However, in recognizing that immature individuals would not always be in the same party as their mother and infant siblings, a DAI unique to each quarter was inferred from existing data for associations between immature individuals with missing data and their mothers and infant siblings. The DAI assigned in these cases was the mean of existing immature-mother DAIs for each quarter.

A grooming association index was also calculated from behavioral data to estimate the time a pair of chimpanzees spent grooming each other. The Grooming Association Index (GAI) was calculated as:

$$GAI = \frac{AB_{grooming}}{AB_{party}} \quad (\text{Equation 4.2})$$

where  $AB_{grooming}$  represents the time a pair spent grooming and  $AB_{party}$  represents the total amount of time that a pair spent in the same party. GAI matrices were generated by the Jane Goodall Institute Research Center at Duke University by annual quarter on adults only. Missing GAI values for infants and immature individuals were not inferred from existing GAI values, but instead assigned a value of 0 so that a grooming network was never established for those individuals.

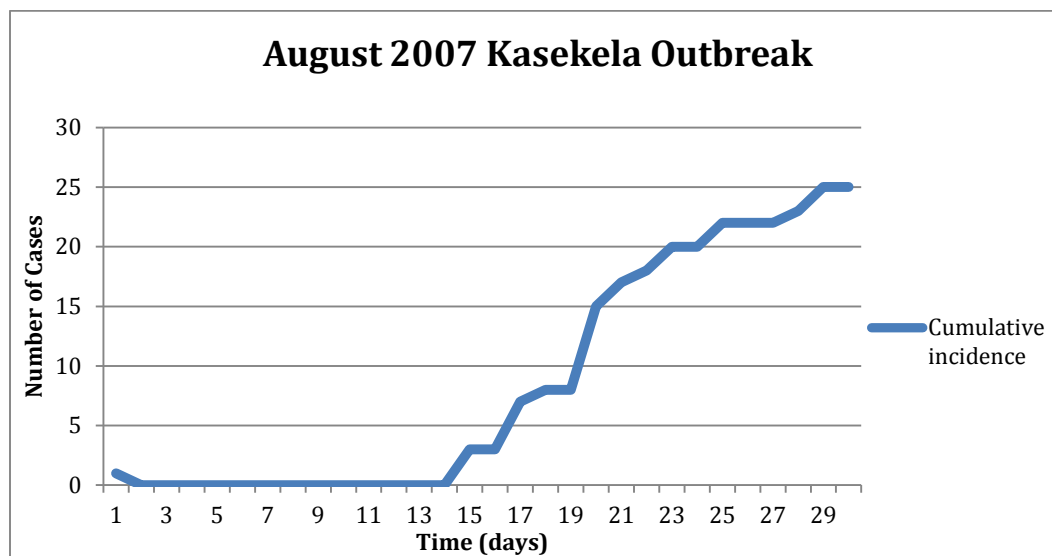
Syndromic surveillance data were used to generate individual probabilities of

detection, or probabilities of observation, as model inputs for simulation of the surveillance system. To do this a cumulative sum of observation records from the Daily data were generated for each chimpanzee for every quarter of each study year. Quarterly sums of observation were then divided by a total of 90 possible observation days, resulting in individual daily detection probabilities specific to each quarter of surveillance from 2004-2012. To determine the best approach to aggregating rates of detection for simulation model parameterization, generalized estimating equations (GEE) were used to model the longitudinal data to evaluate the influence of chimpanzee traits (e.g. age, sex, rank), quarter and year on probabilities of detection [Hanley, 2003]. In these statistical models, chimpanzee identity was included as a random effect, while age-class, sex, rank, quarter, year and an interaction term for quarter and year were modeled as fixed effects, and daily detection probabilities as the dependent variable. Quarter was a multinomial categorical variable representing the 4 calendar quarters of the year. A commonly applied 2-class age structure was used to separate the population by age demographics: subadult (< 12y) and adult (12y and older) [Markham et al., 2015; Murray et al., 2006a, 2009]. Rank was a 3-level categorical variable that included high, medium, or low for adult females and males. Male and female ranks were calculated by the Jane Goodall Institute Research Center at Duke University over a 2-year window by the modified David's score method [de Vries et al., 2006], using directional male-male and female-female pant-grunts for male and female dominance rank, respectively [Feldblum et al., 2014; Markham et al., 2015]. Since the dominance hierarchy applies only to adults, models that included rank as a covariate were performed on adult data only. Fixed effects were added in a forward stepwise manner to build a multivariate model with an identity link function. The best covariance matrix was selected using the lowest quasilielihood under the independence model criterion (QIC) [Cui, 2007]. GEE models were performed using SAS software, Version 9.4 of the SAS System for Windows (Copyright 2002-2012, SAS Institute Inc., Cary, NC, USA).

Finally, outbreak data from the Kasekela community was selected from previous work (Chapter 2) to calibrate the disease model. Outbreak selection criteria included the availability of daily incidence data for an outbreak of >1 week duration, which occurred

within the same period for which DAI and GAI data were available, 2005-2011. Further, the selection of a major outbreak was considered important to ensure enough data points (daily incidence values) to estimate a good fit of model data to empirical data. There were 3 major outbreaks in Kasekela between 2004 and 2012, two of which did not meet our selection criteria: an outbreak in October 2011 being only of 1-week duration and an outbreak in June 2012 being outside of the time period of accompanying empirical data. This left an outbreak in August 2007 for use in model calibration. This outbreak lasted 29 days and resulted in a cumulative incidence of 25 cases (Figure 4-1), with a morbidity of 38%.

Figure 4-1 Cumulative incidence of respiratory cases associated with the August 2007 major outbreak in Kasekela community. The total number of cases associated with the outbreak was 25, with a community morbidity of 38%.



### Model Overview

An agent-based, network model was constructed using AnyLogic software, version 7.1.2 of the Researcher/Educational edition (The AnyLogic Company, Illinois, USA), a tool for creating models in the Java language. A stochastic Susceptible-Exposed-

Infectious-Recovered (SEIR) disease transmission model was created to simulate disease through the Kasekela chimpanzee community, where individuals progressed through states of infection using contact parameters and transmission probabilities [Anderson and May, 1979]. The model was designed to simulate respiratory disease outbreaks described in Chapter 3: outbreaks of short duration (weeks) with a finite period of transmission. Two networks, a party-level network and a grooming network, were created to define connections of chimpanzees within the Kasekela community based on natural chimpanzee social behavior [Goodall, 1986]. Network connections between individuals were set by a connection probability, informed by the DAI and GAI of each pair of individuals. To mimic the fission-fusion social structure of chimpanzee communities [Goodall, 1986], network connections were reset every 6 hours. The transition of an individual from Susceptible to Exposed state was dependent on its connection with an Infectious individual within its networks, and defined by:

$$\Delta S \rightarrow I = \beta_I \gamma \quad (\text{Equation 4.3})$$

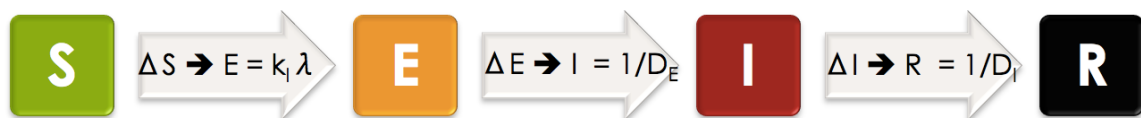
where  $\beta_I$  is a daily contact rate with an infectious connected individual and  $\gamma$  is a probability of disease transmission. The product of these two rates may also be thought of as an individual effective contact rate, or the rate at which contact between an Infectious and Susceptible individual results in a successful transmission event [Vynnycky and White, 2010]. Grooming and party-level networks were assigned unique  $\beta$  and  $\gamma$  parameters to capture the heterogeneity of contact and opportunity for disease transmission. For example, grooming animals will have extended periods of direct contact, whereas animals within a party may or may not come into direct contact or even be in proximity with each other. These parameters, party-level ( $\beta_p$ ) and grooming ( $\beta_g$ ) contact rates and party-level ( $\gamma_p$ ) and grooming ( $\gamma_g$ ) transmission probabilities, were calibrated using August 2007 outbreak data.

The remaining transitions between infection states were a function of the duration of time spent in the state. Transition from the Exposed state into the Infectious state was a rate set by the reciprocal of the number of days of latent infection or the incubation period. Transition from the Infectious state to the Recovered state was a rate set as the

reciprocal of the infectious period. All rates were Poisson distributed. Once recovered, individuals did not return to the susceptible state and were assumed to be immune for the remaining duration of the outbreak. This assumption was made based on the outbreaks analyzed in Chapter 3, where outbreaks lasted for a finite period and persistence of clinical signs or recurrence of clinical signs were not a regular occurrence. Since the outbreak periods modeled were of short duration, a closed population model was constructed which excluded birth and mortality events. Figure 4-2 depicts an overview of infection states and transitions.

The model was created so that at the start of each simulation a new population of agents (i.e. chimpanzees) would be created from an Excel file containing a list of all individuals, their associated demographic data, probabilities of detection by surveillance, and network matrices (DAI and GAI). This data was stratified by quarter so that prior to a simulation run, the quarter in which to run the simulation could be specified as a model parameter value. This allows flexibility in modeling different populations and network structures, offering the opportunity to test questions on the contribution of these characteristics to disease transmission and outbreak propagation and progression. The empirical population data used in this study were chosen for consistency with the outbreak data used for model calibration, thus all simulations were conducted using 2007 population data.

Figure 4-2 An overview of the Susceptible-Exposed-Infectious-Recovered model, depicting how an individual transitions through states of infection. Transition from the Susceptible (S) state to Exposed (E) state is a function of an individual's contact rate with an Infectious individual within its network ( $\beta I$ ) and a transmission probability ( $\gamma$ ). The rate of transition out of the Exposed and Infectious (I) states is a function of the duration of the incubation ( $D_E$ ) and infectious ( $D_I$ ) periods, respectively. Once an individual reaches the recovered state it does not transition further. Births and deaths are not included in this closed population model.



A final component of the model was the simulation of the Gombe syndromic surveillance system. At each time step of the simulation (i.e. each day), the model screens the entire population of agents, testing whether or not individuals are detected by the syndromic surveillance and testing whether or not they are infectious. Two Boolean values are logged for each individual at the time step, where a value of true is set if the individual is in the Infectious state and true if a randomly generated number falls within the individual's probability of detection. As the model progresses through a simulation, these values are tabulated on a weekly basis, tracking the number of individuals that were infectious, the number of individuals that were detected by surveillance, and the number of individuals that were infectious AND detected by surveillance. The probability of detection by surveillance used in the model is based on individual rates of observation from the Daily syndromic surveillance data, which includes observations in various states of health and illness. Detection by surveillance in the model is not a function of being in the Infectious state; individuals have the same probability of detection no matter their disease state. Additionally, the model was set so that only individuals in the Infectious state can be detected as "sick", thus detection while in the Infectious state is assumed to be equivalent to expression of clinical signs and observation of illness. Variations in the expression of clinical signs by disease states were not modeled.

### *Model Calibration*

In order to determine the best parameters for disease simulation through the Kasekela community, the model was fit to empirical data from the August 2007 outbreak. This was done using the Calibration Experiment tool in AnyLogic, which minimizes the difference between model generated data and empirical data through parameter variation. The cumulative incidence of the August 2007 outbreak was the value with which the model parameters were calibrated. All calibration experiments were performed over 1000 iterations of 5 replicate model runs. The parameters allowed to vary within each fitting process were network-specific contact rates and transmission probabilities, whereas incubation and infectious periods were varied between experiments. The best fitting parameters were selected from the experiment that produced the best feasible cumulative

incidence value and the smallest model-empirical data difference estimate. All calibration experiments were conducted for the third quarter of the year to match the timing of the empirical outbreak data. Parameter constraints were set to reflect the closeness of contact associated with grooming relative to the more transient contacts within the party network and infectious periods of known human pathogens with short durations (e.g. influenza) (Table 4-1) [Anderson and May, 1991].

Table 4-1 Constraints were set around model parameters for calibration using empirical data. Minimum and maximum values define the boundaries of uniform distributions and were set to reflect the closeness of contact associated with the type network within which contact would occur.

| <b>Parameter</b>                     | <b>Scale of variation</b> | <b>Minimum</b> | <b>Maximum</b> |
|--------------------------------------|---------------------------|----------------|----------------|
| Grooming contact rate                | continuous                | 0.3            | 0.6            |
| Party-level contact rate             | continuous                | 0.1            | 0.5            |
| Grooming transmission probability    | continuous                | 0.5            | 0.99           |
| Party-level transmission probability | continuous                | 0.01           | 0.3            |
| Incubation period                    | discrete                  | 1              | 2              |
| Infectious period                    | discrete                  | 3              | 4              |

### *Monte Carlo Simulation*

In order to obtain the relevant outbreak associated data for testing the sensitivity of the Gombe syndromic surveillance system, Monte Carlo simulation methods were employed. Monte Carlo experiments were performed for each annual quarter, with simulations parameterized by the parameter values generated from the calibration experiments. Each experiment was performed with 500 simulations of the introduction of infection by a single random individual. Each simulation was set to end when there were no additional Infectious agents or after 90 days of simulation. Final output from each simulation included outbreak duration in weeks and weekly aggregated numbers of

chimpanzees in the Infectious state, numbers of chimpanzees detected by surveillance (sick and healthy), cumulative observed incidence, and cumulative incidence (i.e. true cumulative incidence).

In addition to the Monte Carlo experiments performed for each quarter, two additional experiments were conducted. The first experiment was a sensitivity analysis of the probabilities of detection used in the experiments. The probabilities used to inform the model were chosen based on GEE analyses of associations between probability of observation and chimpanzee traits and time; however, it was anticipated that selection on this basis would reduce the amount of empirical data used to inform the model and also produce results that may be very specific to a certain period or population. Therefore, to evaluate the impact of the probability of detection inputs on the estimation of surveillance sensitivity, a Monte Carlo experiment was performed for the third quarter of the year using surveillance detection data aggregated as individual mean detection probabilities by age-class and quarter. All other parameters were maintained at calibrated levels. Comparison between the GEE-selected detection probability inputs and the aggregated inputs were made by qualitative assessment of the mean surveillance sensitivity estimates and 95% confidence intervals.

Finally, we were interested to know how an increase in surveillance effort might affect surveillance sensitivity. To evaluate this, we performed a final Monte-Carlo experiment, simulating outbreaks in the quarter with the lowest surveillance sensitivity estimate. For these simulations, the detection probability was doubled to simulate a doubling of researcher observation efforts. This would result in an expected increase from 10 (Chapter 2) to 20 chimpanzees observed weekly. All other parameters were maintained at calibrated levels. The resulting surveillance sensitivity estimate and 95% confidence interval were qualitatively compared to the original quarter estimate [Vynnycky and White, 2010]. Model and experiment documentation is provided in Appendix 1.

### *Descriptive and Statistical Analyses of Model Output*

Simulation results were reported by quarter, describing the number of simulations that resulted in an outbreak (where at least one infection transmission event occurred), mean cumulative incidence, mean number of chimpanzees infectious each week of an outbreak, and mean outbreak duration. Surveillance analyses included qualitative comparisons by quarter of the mean weekly number of chimpanzees observed by surveillance and the mean weekly proportion detected sick, which was calculated as the weekly number of sick chimpanzees detected by surveillance out of the weekly number of Infectious chimpanzees. The mean weekly proportion detected sick is a measure equivalent to diagnostic test sensitivity, where test positivity ( $T+$ ) is conditional on being diseased ( $D+$ ), or

$$Se = P\{T + | D +\} \quad (\text{Equation 4.4})$$

[Dohoo et al., 2009]. A weekly apparent prevalence was calculated as the number of detected sick chimpanzees out of the total number of chimpanzees detected by surveillance. This measure may also be compared to the estimation of apparent prevalence from diagnostic testing:

$$AP = \frac{T+}{T+ + T-} \quad (\text{Equation 4.5})$$

where, in this study,  $T+$  is the number of animals detected sick by surveillance while in the Infectious state and  $T-$  is the number of animals detected by surveillance without clinical signs of illness in any other disease state [Dohoo et al., 2009]. The maximum of this weekly value and the maximum weekly number of detected sick chimpanzees from each simulation were then used to screen outbreaks using the algorithms described in Chapter 2. So, if the maximum weekly apparent prevalence exceeded 15.6% or the maximum number of detected sick chimpanzees was 2 or more (Chapter 2), then an outbreak was classified as “detected.” An overall estimate of surveillance sensitivity was calculated for each quarter as the number of outbreaks detected out of the total number of outbreaks produced in the experiment.

Associations between outbreak size, quarter, and outbreak detection were examined by logistic regression modeling. For these analyses, a categorical value for outbreak size was generated, where outbreaks that included 20% or more of the community were classified as major and outbreaks less than that were classified as small. Outbreak detection was a binomial variable denoting outbreak detection by the detection algorithm. Univariate logistic regression models were performed to examine associations between quarter and outbreak size, quarter and outbreak detection, and outbreak size and detection. A final multivariable model was generated with outbreak detection as the dependent variable and quarter and outbreak size as predictor variables; odds of outbreak detection and 95% confidence intervals were estimated by outbreak size and quarter. Logistic regression models were performed using SAS software, Version 9.4 of the SAS System for Windows (Copyright 2002-2012, SAS Institute Inc., Cary, NC, USA).

## *Results*

Prior to model simulation, GEE statistical modeling and simulation model calibration were used to select the best inputs for model parameterization. GEE models revealed significant associations between rates of detection by syndromic surveillance and age-class, sex, quarter, year and the interaction of quarter and year. Thus, the best surveillance detection rates for model parameterization were determined to be individual chimpanzee rates specific to the year and quarter being modeled, Quarter 3 of 2007. Parameter calibration of the simulation model was carried out over 4 separate calibration experiments where parameters with continuous values, contact rates and transmission probabilities, were allowed to vary within experiments during the fitting process and parameters with discrete values, infection period and incubation period, were varied between experiments. The experiment from which the parameter values were selected (Table 4-2) produced the best feasible cumulative incidence (CI) from simulation (CI=26) and the lowest mean difference between model-generated and empirical data ( $|\overline{a - b}| = 5.8$ ).

Table 4-2 Parameters included in the respiratory disease transmission model. All values used as rates in the model are Poisson distributed.

| <b>Parameter</b>                     | <b>Value</b>   | <b>Data source</b>  |
|--------------------------------------|--|---|
| Agent                                | Chimpanzees, n=60  | 2007 Kasekela community data, Jane Goodall Institute Research Center at Duke University |
| Party network                        | Quarter-specific, 2007 pairwise Dyadic Association Indices   | Jane Goodall Institute Research Center at Duke University                               |
| Grooming network                     | Quarter-specific, 2007 pairwise Grooming Association Indices | Jane Goodall Institute Research Center at Duke University                               |
| Grooming contact rate                | 0.535  | Model calibrated  |
| Party-level contact rate             | 0.436  | Model calibrated  |
| Grooming transmission probability    | 0.529  | Model calibrated  |
| Party-level transmission probability | 0.085  | Model calibrated  |
| Incubation period                    | 2  | Model calibrated  |
| Infectious period                    | 4  | Model calibrated  |
| Surveillance detection probabilities | Quarter-specific, 2007 individual detection probabilities    | Gombe syndromic surveillance data, 2004-2012  |

Out of a total of 2000 simulations (500 per quarter), 1064 outbreaks were produced where at least one transmission event took place. Average duration of outbreaks was 5.1 wks (95% PI: 1, 9)) (Figure 4-3) with an average cumulative incidence of 36 cases (95% PI: 2, 55) (Figure 4-4). The mean weekly number of chimpanzees that were Infectious during an outbreak and assumed to be displaying clinical signs of illness was 9

(95% PI: 1, 18). The mean weekly number of chimpanzees detected by syndromic surveillance was 12 (95% PI: 9, 15) and an average of 8.2% (95% PI: 0, 27%) of Infectious chimpanzees were detected by surveillance on a weekly basis (Figure 4-5). Out of 1064 outbreaks, 702 were detected using the weekly count threshold for outbreak detection and 633 were detected using the weekly prevalence threshold, yielding a surveillance sensitivity for outbreak detection of 66% (95% Confidence Interval: 63.1, 68.8%) and 59.5% (95% Confidence Interval: 56.5%, 62.4%), respectively. Comparison of these results by quarter are displayed in Table 4-3.

Figure 4-3 Frequency histogram of outbreak duration over 2000 model simulations, including all quarters of the year.

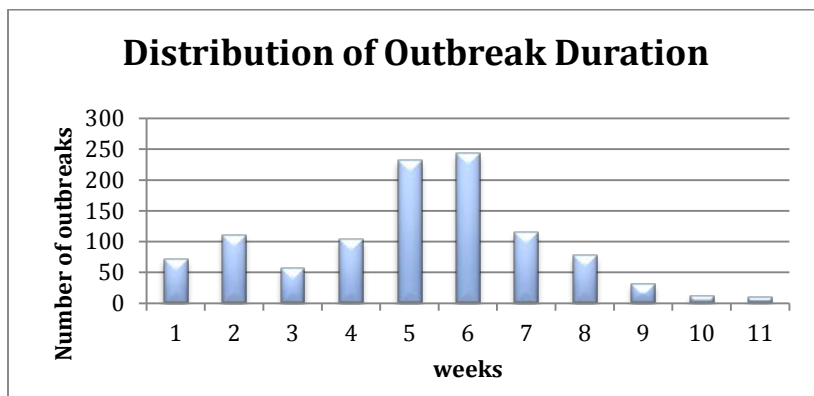


Figure 4-4 Frequency histogram of outbreak cumulative incidence over 2000 model simulations, including all quarters of the year.

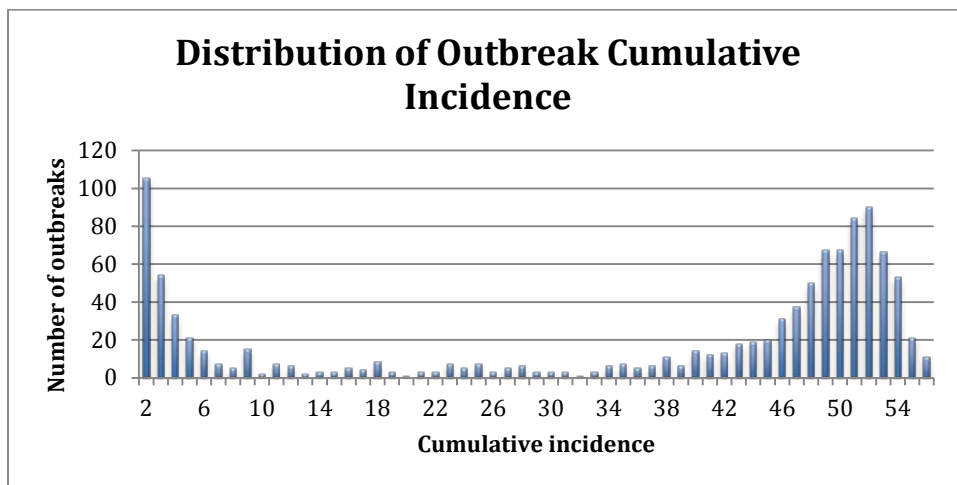
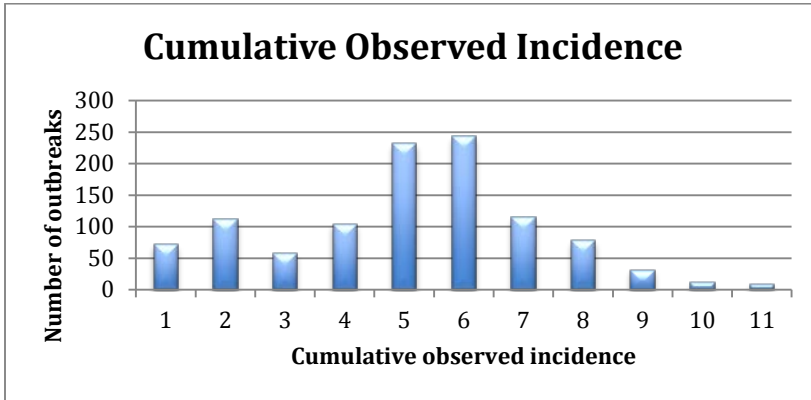


Figure 4-5 Frequency histogram of the cumulative observed incidence of 1064 outbreaks out of 2000 model simulations, including all quarters of the year.



Out of the 1064 outbreaks produced from the simulations, 801 were classified as major outbreaks based on a cumulative incidence of  $\geq 20\%$  of the community. Outbreak size was significantly associated with the quarter in which the simulation was run. With Quarter 4 as the reference, Quarter 1 had significantly higher odds of a major outbreak and Quarter 3 had significantly lower odds of a major outbreak (Table 4-4). Outbreak detection by the count method was examined for association with quarter and also found to be significantly associated, with Quarters 1 and 2 having significantly higher odds of an outbreak being detected than Quarter 4, and Quarter 3 having significantly lower odds of an outbreak being detected than Quarter 4. As would be expected, outbreak detection was significantly associated with outbreak size, with small outbreaks having significantly lower odds of detection than major outbreaks (OR: 0.003; 95% Confidence Interval: 0.001, 0.007). Since outbreak size would be considered a confounder of the outbreak detection-quarter association, and confirmed to be significantly associated with both, a final multivariate logistic regression model included outbreak size with quarter as independent variables. This resulted in  $>10\%$  change in the log odds estimates of outbreak detection for all quarters, providing further confirmation of outbreak size as a confounding variable. After controlling for confounding, all quarters were found to be significantly associated with outbreak detection, with both Quarters 1 and 2 having significantly higher odds of outbreak detection and Quarter 3 significantly lower odds of outbreak detection than Quarter 4.

Table 4-3 Summary of model results by quarter, including outbreak characteristics and surveillance sensitivity results. Displayed are model results for simulations of all quarters from the 2007 model, as well as results from the simulations of quarter 3 using age-class-aggregated detection probabilities. Age-class aggregated detection probabilities were used to assess the sensitivity of model results to the use of a larger amount of empirical syndromic surveillance data as model input.

| <b>Model output</b>  | <b>Quarter 1<br/>mean<br/>(95%PI)</b> | <b>Quarter 2<br/>mean<br/>(95%PI)</b> | <b>Quarter 3<br/>mean<br/>(95%PI)</b> | <b>Quarter 4<br/>mean<br/>(95%PI)</b> | <b>Quarter 3 aggregated<br/>mean<br/>(95%PI)</b> |
|--|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|--|
| Total outbreaks  | 278                                   | 287                                   | 221                                   | 278                                   | 232  |
| No. major outbreaks  | 246                                   | 245                                   | 90                                    | 220                                   | 113  |
| Outbreak duration, weeks   | 5<br>(1, 9)                           | 5<br>(1, 9)                           | 4<br>(1, 10)                          | 5<br>(1, 9)                           | 4<br>(1, 9)                                      |
| Cumulative incidence   | 46<br>(2, 56)                         | 42<br>(2, 54)                         | 13<br>(2, 40)                         | 37<br>(2, 54)                         | 16<br>(2, 41)                                    |
| Mean weekly Infectious   | 12<br>(1, 19)                         | 11<br>(2, 18)                         | 4<br>(1, 10)                          | 9<br>(2, 16)                          | 4<br>(1, 11)                                     |
| Mean weekly number observed by surveillance                            | 13<br>(10, 16)                        | 12<br>(9, 15)                         | 11<br>(7, 15)                         | 11<br>(9, 14)                         | 11<br>(8, 14)                                    |
| Mean weekly proportion detected sick                                   | 0.09<br>(0, 0.25)                     | 0.08<br>(0, 0.22)                     | 0.08<br>(0, 0.33)                     | 0.08<br>(0, 0.23)                     | 0.08<br>(0, 0.36)                                |
| No. outbreaks detected by weekly Count threshold                       | 226                                   | 227                                   | 66                                    | 183                                   | 67   |
| No. outbreaks detected by weekly Prevalence threshold                  | 211                                   | 206                                   | 55                                    | 161                                   | 68   |
| Sensitivity of outbreak detection using weekly Count threshold, %      | 81<br>(77, 86)*                       | 79<br>(74, 84)*                       | 30<br>(24, 36)*                       | 66<br>(60, 71)*                       | 29<br>(24, 36)*                                  |
| Sensitivity of outbreak detection using weekly Prevalence threshold, % | 76<br>(71, 81)*                       | 72<br>(67, 77)*                       | 25<br>(19, 31)*                       | 58<br>(52, 64)*                       | 25<br>(19, 31)*                                  |

\*95% Confidence Interval

Table 4-4 Odds ratios for the associations between quarter and outbreak detection and outbreak size. Quarter 4 was the reference for all models. The multivariate model included outbreak size as a predictor variable to account for confounding due to its association with quarter and outbreak detection.

| <b>Model response variable</b> | <b>Model structure</b> | <b>Quarter 1</b><br>(95% Confidence Interval) | <b>Quarter 2</b><br>(95% Confidence Interval) | <b>Quarter 3</b><br>(95% Confidence Interval) |
|--------------------------------|------------------------|---|---|---|
| Outbreak size                  | univariate             | 2.0 (1.3, 3.2)                                | 1.5 (0.99, 2.4)                               | 0.18 (0.1, 0.3)                               |
| Outbreak detection             | univariate             | 2.3 (1.5, 3.3)                                | 2.0 (1.4, 2.9)                                | 0.22 (0.2, 0.3)                               |
| Outbreak detection             | multivariate           | 2.2 (1.3, 3.9)                                | 2.4 (1.4, 4.2)                                | 0.54 (0.3, 0.9)                               |

GEE results guided the selection of surveillance detection probability inputs from empirical data using a single year of surveillance. Out of interest in making the model more generalizable, we evaluated how individual detection rates aggregated by quarter over all years of a chimpanzee's given age-class would impact our estimation of sensitivity. In general, detection probabilities aggregated over chimpanzees' age classes were lower on average than the detection probabilities of 2007, although the difference was not significant. Simulation of aggregated detection probabilities was done for Quarter 3 only. For comparison, the average detection probability for Quarter 3 in 2007 was 0.032 (s.e.  $\pm$  0.025), whereas the detection probability for the same quarter, but aggregated over chimpanzees' age classes averaged 0.029 (s.e.  $\pm$  0.015). The surveillance sensitivity resulting from the comparative simulation was almost identical to the 2007 model, with a sensitivity of outbreak detection by the count method of 29% (95% Confidence Interval: 24, 36%) and by the prevalence method of 25% (95% Confidence Interval: 19, 31%) (Table 4-3).

Finally, we were interested to know how a two-fold increase in surveillance effort might affect surveillance sensitivity. In doubling the detection probability of Quarter 3 to mimic a doubling of data collection efforts, the resulting average detection probability used in the simulations was 0.064 (s.e.  $\pm$  0.049). This resulted in an increase in the

average weekly number of animals detected by surveillance to 20 (95% PI: 16, 24), as expected. The resulting surveillance sensitivity by the count method of outbreak detection increased significantly to 47% (95% Confidence Interval: 41, 54%) for Quarter 3. However, there was no change in sensitivity using the prevalence method of outbreak detection, with a resulting sensitivity of 23% (95% Confidence Interval: 17, 28%). Notably, among outbreaks with a cumulative incidence of 5 or more cases, the sensitivity of outbreak detection by the count method increased from 53% (95% Confidence Interval: 44, 62%) to 74% (95% Confidence Interval: 67, 81%) with a doubling of surveillance efforts.

## *Discussion*

This study was the final component in an assessment of the performance of a syndromic surveillance system for disease and outbreak detection in free-living chimpanzees in Gombe National Park. In this study, an agent-based, network model of disease transmission was used to simulate disease transmission in different quarters of the year to estimate the sensitivity of syndromic surveillance for respiratory outbreak detection. Two methods for outbreak screening described in Chapter 2 were examined using the model: the count method, which signals an outbreak when 2 or more chimpanzees are detected with respiratory signs in a week, and the prevalence method, which signals an outbreak when  $\geq 15.6\%$  of the chimpanzees observed by surveillance are detected with respiratory signs. Overall, the count method demonstrated better sensitivity than the prevalence method. This held true for simulations performed using the doubled detection probabilities, representing a doubling of surveillance efforts. While the count method of outbreak detection demonstrated a markedly increased sensitivity with increased surveillance efforts, the prevalence method did not. This can be explained by the fact that the increased detection probability increased the overall number of animals observed by surveillance each week, thus diluting any increase in the number of sick animals detected by the increase in surveillance effort. If surveillance efforts were differentially increased, targeting “high risk” individuals, for example, there may be an associated increase in detection by prevalence. Males were identified as significantly

associated with the start of outbreaks and with large outbreaks (Chapter 3); therefore, focusing efforts on males may improve outbreak detection by either method. Based on the results of this research the count method is recommended for outbreak detection, given its higher sensitivity. An additional benefit of this algorithm for detection is its simplicity for prospective use. For example, researchers will readily be able to recognize the potential onset of an outbreak when 2 or more animals are observed sick within a week without further analysis of incoming data.

Outbreak detection sensitivity did vary by quarter, with the highest sensitivity being in the first and second quarters and the lowest sensitivity in the third quarter. Overall, fewer outbreaks were produced in the third quarter, and they were smaller in scale. This was the only quarter where the number of small outbreaks exceeded major outbreaks; however, the significance of the lower sensitivity of outbreak detection in the third quarter was consistent after controlling for confounding associated with the size of outbreaks. These findings call for a systematic review of surveillance practices and chimpanzee behavior that might be contributing to the lower disease detection sensitivity in Quarter 3, but should also raise awareness of the differences in outbreak epidemiology (i.e. smaller outbreaks, with fewer weekly illnesses) that make disease detection in Quarter 3 more challenging.

Overall, the validity of the model to simulate outbreaks like those observed in the Kasekela community was fairly good. Cumulative incidence fell within the range of observed outbreaks, as calibrated. Model stochasticity resulted in both failure of sustained transmission as well as the production of large and small outbreaks with a single random seed of infection, as would be expected under natural conditions. There was no situation, however, where more than eleven chimpanzees were detected sick (i.e. the cumulative observed incidence) in an outbreak, even when the cumulative incidence was very high, which diverges from empirical data. There are several possible explanations for this. First, although cumulative incidence reached high levels in many outbreaks generated by the model, the average outbreak duration was 2 weeks longer than the average duration of outbreaks described in Chapter 3. The longer duration would thus

spread the number of cases out over a longer time period, reducing the average weekly number of sick individuals. Although the average number of individuals detected by surveillance each week in the model aligned well with that estimated from empirical data (Chapter 3), the average weekly number sick may have been lower than what might actually occur in a large scale outbreak of short duration. Secondly, model calibration was performed by fitting the model-generated cumulative incidence, or true incidence, to the empirical cumulative observed incidence. Assuming that the empirical data will be an underestimate of the true cumulative outbreak incidence, our calibration process would be fitting model parameters to smaller outbreaks. Another approach might be to calibrate the model-generated cumulative observed incidence (i.e. the number detected ill by surveillance) to the empirical outbreak data, thus matching model surveillance data with empirical surveillance data. However, the alternative approach might result in a predominance of major outbreak simulations, which would restrict our ability to assess outbreak detection sensitivity across outbreaks of different sizes. Lastly, there was no function in the model that would adjust the detection probability after illness was initially detected. Since respiratory disease is an infrequent occurrence among Gombe chimpanzees, it is reasonable to expect that recognition of disease onset in several individuals might raise awareness among researchers of the presence of contagious disease, thus triggering increased efforts to collect data on sick individuals in the community. Indeed, established protocols direct researchers to collect data on individuals when illness or abnormalities are observed. Based on these directives, detection probabilities would be expected to increase during outbreak conditions. Therefore, to improve model validity, further exploration of surveillance data for differences in detection probabilities between epidemic and nonepidemic periods would be valuable for informing a function that would adjust the detection probability parameter in the model accordingly.

Findings from our work to describe the epidemiology of respiratory outbreaks (Chapter 3) demonstrate the occurrence of only one outbreak in the third quarter from 2004-2012, and the single outbreak being one of major size. That single outbreak was the one with which the disease model was calibrated. The findings of these combined studies

demonstrate two things. First, the disease model, at least for Quarter 3, appears to be valid based on the consistency in model results and empirical data (i.e. fewer outbreaks in Quarter 3). Second, outbreaks from Quarter 3 simulations (both the 2007 model and aggregated detection probability model) were not detected at all by our algorithms until 5 or more chimpanzees were sick and then only more consistently when 20 or more chimpanzees were sick. Although fewer in number, we would then expect major outbreaks to be the majority of outbreaks detected in the third quarter. Without demonstrating with our model that a substantial amount of small outbreaks may be occurring and going undetected in this quarter, the detection of major outbreaks alone would suggest that Quarter 3 is a risk factor for major outbreaks, when in fact the opposite is true.

In contrast, Quarter 1 demonstrated a similar number of outbreaks to Quarters 2 and 4, but the odds of major outbreak development were significantly higher in Quarter 1. Since all disease transmission parameters were held constant, the primary difference between quarters that would generate such significant differences in outbreak size is the network connections. This finding substantiates the importance of the inclusion of parameters that capture the heterogeneity of contact of highly social species in disease transmission models [Keeling and Eames, 2005; Craft and Caillaud, 2011; Godfrey, 2013]. Further, it points to characteristics of chimpanzee behavior or environmental conditions during these quarters that drives these patterns of contact, which may offer new insights into disease transmission within chimpanzee communities.

### *Limitations*

The model was developed in such a way as to allow the construction of a population of chimpanzees from empirical data, which provides results specific to the population under study, but may limit generalizability. In fact, the results from this study were derived from data originating from the Gombe Kasekela community in 2007. Since GEE results indicate that there are differences in detection probabilities between years of study, this would suggest that simulation results may only reflect the sensitivity of surveillance in 2007. However, our sensitivity estimates that resulted from simulations

with aggregated detection probabilities demonstrate that the year of study may not be important in deriving these estimates.

What was not tested in this study was how differences in population size, demographics or network structure might influence disease transmission and subsequent outbreak detection. Gombe has two communities of habituated chimpanzees that are under syndromic surveillance; the Mitumba community is much smaller, with different population demographics, and possibly a different network structure. The surveillance system may have a different level of sensitivity based on these differences, which were not examined in this study. However, the design of the model facilitates incorporation of new population data, permitting flexibility in answering these questions in the future.

Assessment of surveillance performance was also conducted with a focus on respiratory disease, although the system collects data on several other disease syndromes. The model developed in this study was based on assumptions of direct or aerosol transmission through network contacts. As constructed, it is not spatially explicit and does not account for environmental transmission, nor does it model sexually or vertically transmitted diseases. However, AnyLogic software offers the flexibility to build into the existing model a spatial platform or additional rules governing transmission within a reproductive network. Thus, the model, though currently limited to the simulation of directly or aerosol transmitted diseases, may be expanded for further disease and surveillance study.

### *Future Directions*

As detailed above, there is much room for further exploration of the syndromic surveillance system performance with regard to the other syndromes on which data is collected. Gombe is an important population for the study of the natural history of SIV<sub>cpz</sub> infection, and changes in the frequency or severity of coinfections (e.g. gastrointestinal, respiratory diseases) can be important markers of the development and progression of immunological disease caused by SIV<sub>cpz</sub>. As the data originating from syndromic surveillance contributes to these SIV<sub>cpz</sub> study efforts, it is important to understand the

capabilities and limitations of the surveillance system. Building on this study and contributing to the general study of disease among chimpanzees in Gombe would be the development or application of methods to infer true disease prevalence from the data collected through surveillance [Akanda and Alpizar-Jara, 2014; Dohoo et al., 2009]. Further questions to address include how illness might influence an individual's detection probability by surveillance and how this might impact the sensitivity of the system to outbreak detection. For example, if an individual isolates itself as a result of illness, how readily will it be detected by surveillance, and how frequently does such behavior limit the spread of disease? Some of these questions may be answered with further exploration of longitudinal changes in detection probabilities within the syndromic data.

The availability of empirical network and health data on the Gombe chimpanzee population makes it a unique system in which to ask questions about how disease transmission occurs through the chimpanzee network. This study did not address such questions, but the model created here may serve as a platform for future disease network studies [Keeling and Eames, 2005; Godfrey, 2013]. For example, in this study, infection was seeded by random individuals in the community, and out of 500 simulations per experiment, only a little over half of the seeded infections resulted in a transmission event. Part of this may be explained by model stochasticity, but the question of the role of individuals' network connectivity in disease transmission can readily be addressed by seeding infection among individuals with different levels of network centrality [Keeling and Eames, 2005]. As suggested above, the observed differences in outbreak frequency and size by quarter is best explained by differences in the network connections. Thus, network analyses that describe characteristics of the network that change between quarters and the contribution of those characteristics to the modeled and observed differences in disease patterns may provide greater insight on disease transmission in chimpanzee communities. Additionally, expansion of the model to allow simulation of disease by different transmission routes through the chimpanzee social network would also provide the opportunities to gain further insight on the importance of individuals in and key pathways of SIV<sub>cpz</sub> transmission at the community and population levels.

## *Conclusions*

In this study, the sensitivity of respiratory outbreak detection by syndromic surveillance in a free-living population of chimpanzees was quantitatively estimated through the integration of empirical data and theoretical disease modeling. The results of this work reveal important temporal differences in the sensitivity of respiratory outbreak detection by the existing syndromic surveillance system, demonstrating the importance of chimpanzee behavior in the propagation and detection of respiratory outbreaks as well as the need for new strategies to improve outbreak detection sensitivity in the third quarter of the year. The resulting simulation model is flexible for future use, easily allowing the incorporation of demographics, network structures, and surveillance data from other populations of great apes to assess disease transmission and surveillance sensitivity. Thus, as syndromic surveillance gains traction across primate populations as a valuable tool for the noninvasive collection of large amounts of health data and early outbreak detection, comparable assessments can be made across populations.

# Chapter 5 | Noninvasive Test for Tuberculosis Detection in Primates

## Background<sup>2</sup>

The susceptibility of non-human primates to tuberculosis is well known [Lerche et al., 2008; Loomis, 2003], although the extent of the disease among free-living primates remains unclear. Much of our understanding of primate tuberculosis is based on *M. tuberculosis* transmission in captive primates [Loomis, 2003; Lerche et al., 2008], while *M. bovis* spillover dominates among populations of free-living monkeys [Keet et al., 2000; Sapolsky and Else, 1987]. Research demonstrates increases in infections of the Mycobacterium Tuberculosis Complex (MTC) among free-ranging macaques in areas of frequent human contact and high human tuberculosis prevalence [Wilbur et al., 2012]. The first evidence of tuberculosis in a free-living ape was reported recently in west Africa; the infectious agent was identified upon routine necropsy of a chimpanzee as a novel MTC strain closely related to Lineage 6 (i.e., *M. africanum* West-Africa type-2) [Coscolla et al., 2013].

Unfortunately, epidemiological studies of tuberculosis among free-living primates have been limited by existing diagnostic technologies. Diagnosis of disease in primates traditionally relies upon procedures that identify tissue lesions, demonstrate host immune responses, or culture of the organism [Lerche et al., 2008], which is generally not feasible in free-living species given the need for handling and anesthesia. To overcome this challenge, we evaluated a novel approach to tuberculosis screening in free-living primates through molecular detection of MTC-specific DNA in non-invasively-collected

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<sup>2</sup> **Publication:** Chapter 2 has been published in the form presented in this chapter. Permission for use has been obtained from the publisher, Centers for Disease Control and Prevention. The citation for the manuscript is:

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fecal samples. This approach has shown excellent sensitivity among humans with active pulmonary tuberculosis [Cordova et al., 2010; El Khéchine et al., 2009]. Thus, our objective was to evaluate the performance of fecal IS6110 PCR for tuberculosis detection in experimentally infected and naturally exposed primates. We hypothesized that primates with active tuberculosis infection could be accurately identified using fecal IS6110 PCR as a non-invasive method of tuberculosis detection.

## The Study

Fecal IS6110 PCR was first evaluated using primates with known tuberculosis infection status. Fecal samples were collected from 41 adult (>4 years) cynomolgus macaques (*Macaca fascicularis*) included in experimental *M. tuberculosis* infection studies and 13 uninfected rhesus macaques (*Macaca mulatta*) included in diabetes studies. Uninfected animals were housed under BSL-2 conditions; infected animals were housed in BSL-3 level facilities. All experiments and protocols were approved by either the University of Pittsburgh School of Medicine or University of Minnesota Institutional Animal Care and Use Committees.

As part of other studies, 36 cynomolgus macaques were inoculated with a low or mid dose (~25 or 50-100 CFU, respectively) *M. tuberculosis* Erdman strain by bronchoscopic instillation, as described previously [Lin et al., 2009]; 5 animals were uninfected controls. Infection was confirmed by tuberculin skin test (TST) conversion, lymphocyte proliferation assay, and gamma interferon enzyme-linked immunosorbent spot of peripheral blood mononuclear cells (PBMC) [Lin et al., 2009]. In the cynomolgus macaque low dose model, half of the animals develop active tuberculosis, typically between 4-12 months post-infection, with substantial variability in timing and presentation of clinical signs. [Lin et al., 2009] The other half develop clinically latent infection and have no signs of disease. Included in this study were ten macaques that had developed active disease, as determined by clinical signs and disease on thoracic radiography in association with *M. tuberculosis* growth from gastric aspirate (GA) or bronchoalveolar lavage (BAL). *M. tuberculosis* culture methods have been described

previously. [Lin et al., 2009] Briefly, culture of GA samples were performed by the University of Pittsburgh Medical College clinical microbiology laboratory. The samples were subcultured onto LJ slants for *M. tuberculosis*. BAL samples were cultured on 7H11 plates. Twenty-three animals were characterized as latently infected based on absence of both clinical signs and *M. tuberculosis* growth with a positive TST reaction and peripheral responses to *M. tuberculosis* antigen [Lin et al., 2009]. Three infected animals were classified as subclinically diseased or “percolators” based on the absence of clinical disease but intermittent *M. tuberculosis* growth on GA or BAL [Lin et al., 2009]. Fecal samples were collected from all macaques on a single day, coinciding with varying durations of infection, ranging from 63 to 286 days (Table 5-1).

Fecal IS6110 PCR was also evaluated in primates under conditions of natural exposure and infection. Fecal samples were collected from 36 juvenile and adult (7-27yrs, mean=15yrs) chimpanzees (*Pan troglodytes*) managed in 2 sanctuaries and 1 zoo in East Africa. Many chimpanzees were raised from infant stages by the sanctuaries as a result of confiscation. All are managed in social groups in indoor/outdoor housing. Human contact includes direct, intimate contact up until age 5yrs, followed by protected, close contact at older ages with regular visitation by tourists and researchers. Contact with free-ranging primate species is variable.

All animals were considered clinically healthy during sampling. Fecal PCR results of sanctuary chimpanzees were compared to their most recent TST responses, as described previously [Bernacky et al., 2002]. TST is a routine tuberculosis screening test employed by the chimpanzee sanctuaries during routine examinations, offering a platform for comparison of the fecal IS6110 PCR. In general, any TST responders are followed up with additional tuberculosis diagnostic testing (e.g. culture of BAL or GA samples). TSTs were performed opportunistically during routine exams on the same day as fecal collection in 27 chimps. TST results from 9 months before fecal collection were available for 3 chimps and from two years before for 6 chimpanzees. In addition to TST, results from the PrimaTB STAT-PAK (Chembio Diagnostic Systems, Inc.), a field-based serological assay, were also available for 6 animals.

Fecal samples were stored frozen at -80°C for 1 week to 30 months until processing. DNA was extracted using the QIAamp DNA Stool Mini Kit (QIAGEN, Inc.) according to manufacturer's instructions, with a few exceptions. First, feces (180-220mg) was added to a 2.0ml microcentrifuge tube containing 0.1mm Zirconia/Silica beads (BioSpec Products, Inc.) in addition to 1.4ml ASL Buffer, which was vortexed for 3 minutes. Additionally, water bath temperatures were increased from 70°C to 95°C. These alterations were to optimize mycobacterial cell wall lysis. Feces-free negative controls were included in all extraction procedures. Following completion of the extraction protocol, samples were stored frozen at -20°C until PCR testing.

Conventional and realtime (rtPCR) PCR were utilized to amplify a portion of the *IS6110* insertion sequence. Primers, master mixes, and thermocycling conditions are included in Table 5-2. For conventional PCR, amplicons were visualized under UV illumination after electrophoresing through a 1% agarose gel containing ethidium bromide; amplicons of target size were confirmed as *IS6110* by Sanger sequencing (University of Minnesota Genomics Center, St. Paul, Minnesota, USA). Nuclease-free water (Qiagen) negative controls were included in all amplification reactions.

Table 5-1 Fecal IS6110 PCR results for tuberculosis among cynomolgus and rhesus macaques. Animals sampled include 36 cynomolgus macaques (*Macaca fascicularis*) inoculated with a low ( $\approx 25$  colony-forming units) or mid dose (50–100 colony-forming units) of the Erdman strain of *M. tuberculosis* and 5 maintained as uninoculated controls in ongoing tuberculosis infection studies, and 13 uninoculated rhesus macaques (*Macaca mulatta*) included in ongoing diabetes studies. Infection status at time of fecal sampling was classified as “active” based on the presence of clinical signs and disease on thoracic radiography in association with *M. tuberculosis* growth from gastric aspirate or bronchoalveolar lavage, “latent” based on the absence of both clinical signs and *M. tuberculosis* growth in the presence of a positive TST reaction and peripheral responses to *M. tuberculosis* antigen, and “subclinical” based on the absence of clinical disease but intermittent *M. tuberculosis* growth on gastric aspirate or gastric aspirate.

| Species and infection status | Inoculation dose | No. animals | Time postinoculation for sampling, mo | No. PCR positive |
|------------------------------|------------------|-------------|---------------------------------------|------------------|
| Cynomolgus                   |                  |             |                                       |                  |
| Active                       | Mid              | 4           | 2                                     | 2                |
|                              | Mid              | 1           | 5                                     | 1                |
|                              | Mid              | 1           | 6                                     | 0                |
|                              | Low              | 2           | 7                                     | 1                |
|                              | Low              | 1           | 8                                     | 1                |
|                              | Low              | 1           | 9                                     | 0                |
|                              | Latent           | Mid         | 4                                     | 2                |
| Mid                          |                  | 1           | 5                                     | 0                |
| Mid                          |                  | 4           | 6                                     | 0                |
| Low                          |                  | 3           | 7                                     | 0                |
| Low                          |                  | 4           | 8                                     | 0                |
| Low                          |                  | 4           | 9                                     | 1                |
| Low                          |                  | 3           | 10                                    | 1                |
| Subclinical                  | Low              | 2           | 7                                     | 1                |
|                              | Low              | 1           | 8                                     | 0                |
| Uninfected                   | N/A              | 5           | NA                                    | 0                |
| Rhesus                       |                  |             |                                       |                  |
| Uninfected                   | N/A              | 13          | NA                                    | 0                |

Table 5-2 Fecal IS6110 conventional and real-time PCR master mixes and reactions conditions.

| Master mix                                     | Reaction conditions   |
|--|---|
| Conventional PCR                               |   |
| Forward primer:<br>5'-TTCAGGTCGAGTACGCCTTC-3'  | 95°C for 15 min/DNA polymerase activation   |
| Reverse primer:<br>5'-CGAACTCAAGGAGCACATCA-3'  | 40 cycles:<br>94°C for 30s/denaturation<br>56°C for 30s/annealing<br>72°C for 1 min/extension |
| 12.5µL HotStarTaq Master Mix*                  | 72°C for 10 min   |
| 8µL RNase-free water*                          |   |
| 0.4µM of each primer                           |   |
| 1.25µL DMSO                                    |   |
| 0.25µL 1% BSA                                  |   |
| 1µL DNA template                               |   |
| 25µL total volume                              |   |
| Real-time PCR                                  |   |
| Forward primer:<br>5'- AGAAGGCGTACTCGACCTGA-3' | 95°C for 5min<br>45 cycles:   |
| Reverse primer:<br>5'- CCGGATCGATGTGTACTGAG-3' | 95°C for 10s denaturation<br>50°C for 30s annealing<br>72°C for 1s extension                  |
| LightCycler 480 Probes Master**                | 65 to 95°C at 2.2°C/s melting curve analysis  |
| 0.2mM of each primer                           |   |
| 0.2mM of the FAM-labeled IS6110 probe**        |   |
| 5µL DNA template                               |   |
| 25µL total volume                              |   |

\*QIAGEN, Inc. \*\*Roche

## Results and Discussion

Fecal IS6110 PCR was effective in identifying 5 of 10 inoculated macaques with active disease and 8 of 36 total infected macaques. No uninfected macaques were positive by IS6110 PCR. Conventional PCR identified 3 actively infected macaques and rtPCR

identified 2 additional. Two latently infected macaques and 1 that was subclinical were also positive by *IS6110* PCR. This resulted in an overall sensitivity of 22% (95% Wilson Confidence Interval: 12-38%) and a specificity of 100% (95% Wilson Confidence Interval: 82-100%). Sensitivity of detection of active infections was estimated at 50% (95% Wilson Confidence Interval: 24-76%). The latter sensitivity estimate is equivalent to that of gastric aspirate of children with radiographic evidence of pulmonary tuberculosis [Abadco and Steiner, 1992].

The observed sensitivity of fecal *IS6110* PCR is limited by several factors. Unlike immunological tests, the success of this approach relies on bacterial shedding in sputum with subsequent swallowing and excretion in feces, hence active infection. Thus, the majority of latently infected animals may go undetected, as observed in this study. Aside from outbreaks, identifying large numbers of actively infected primates for test validation is challenging. We sampled animals in experimental infection studies, but even so, active infections were few. Further, low numbers of organisms are likely shed intermittently in feces, thus serial testing of multiple fecal samples may improve diagnostic sensitivity. PCR may also be paired with mycobacterial culture of feces for further molecular characterization of infection. [El Khéchine et al., 2009] Overall, this study demonstrates that fecal detection of mycobacterial DNA is best suited for identifying actively infected primates, which are crucial in tuberculosis transmission.

TST conversion was not observed in any chimpanzees; however, *IS6110* DNA was detected in 3 chimpanzee fecal samples. TST was conducted the same day as fecal sampling in one of these animals, one 9 months prior, and one 2 years prior. TST is a common tuberculosis screening method in primate sanctuaries, but is not a gold standard test, also being limited by sensitivity and specificity [Lerche et al., 2008]. Although this limitation can be overcome with Bayesian methods to estimate sensitivity and specificity for test validation purposes, the challenge remains in effectively identifying populations of captive primates with tuberculosis. Unfortunately, confirmation of infection status by additional diagnostic testing modalities of the 3 fecal PCR-positive chimpanzees has been limited. One chimpanzee demonstrated an immunological response to *M. tuberculosis*

antigen using the Chembio PrimaTB STAT-PAK, but culture of a BAL sample was unsuccessful. Another chimpanzee positive by fecal PCR retested positive the following year by fecal IS6110 PCR. The body size of this 14-year old male that was historically TST negative was stunted (e.g., reduced growth) compared to other similarly aged male chimpanzees. These circumstances demonstrate the complexity of tuberculosis diagnosis and the challenges surrounding successful validation of tuberculosis tests in the natural setting. To reach a more complete understanding of diagnostic performance of fecal IS6110 PCR in a natural setting where disease prevalence is low, larger scale and long term testing across many captive primate populations is still needed.

Fecal IS6110 PCR is a novel approach to the noninvasive detection of tuberculosis infection in primates, offering a new opportunity to screen for tuberculosis in free-living primates. IS6110 detection is advantageous for its MTC specificity, which is optimal given the known susceptibility of primates to *M. bovis*, *M. tuberculosis*, and the as yet unnamed strain, “Chimpanzee bacillus”. This approach offers new direction for the epidemiological investigation of tuberculosis in free-living primate populations.

# Chapter 6 | Noninvasive Tuberculosis Screening in Free-Living Primate Populations in Gombe National Park, Tanzania

## *Background*

Anthropogenic impacts such as deforestation, agriculture, ecotourism and research have led to new patterns of contact among humans, domesticated animals and human-habituated primates (i.e. primates conditioned for close encounters with human observers), resulting in the emergence and spread of new diseases. For instance, there is accumulating evidence of *M. bovis* morbidity among wild monkey populations, and recent research demonstrates increases in Mycobacterium Tuberculosis Complex (MTC) infections among populations of free-ranging macaques in areas of frequent human contact and high human tuberculosis prevalence [Tarara et al., 1985; Sapolsky and Else, 1987; Keet et al., 2000; Wilbur et al., 2012]. Even more, a novel pathogenic mycobacterial strain of the MTC has been diagnosed in a free-living chimpanzee in Tai National Forest in western Africa. This novel finding introduces the possibility of a chimpanzee-associated tuberculosis strain, which is circulating at low, undetected levels within free-living populations [Coscolla et al., 2013].

Unfortunately, our understanding of the true extent of tuberculosis (TB) infection and its impacts on free-living primates has been hampered by our inability to non-invasively screen for tuberculosis infection. Traditionally, the diagnosis of tuberculosis in primates requires multiple diagnostic modalities such as demonstration of tissue lesions, host immune responses, or culture of the organism [Lin et al., 2008; Lerche et al., 2008]. These diagnostic approaches are not feasible in free-ranging species given the need for handling and anesthesia. Detection has been limited to post-mortem diagnosis, which is inherently challenged by the retrieval of carcasses in a timely manner. Thus, if disease is present at low prevalence, it could go undetected. Advances in molecular technology

have enabled the detection of tuberculosis infection among free-ranging species, although these technologies have not yet been combined with non-invasive methods of sampling for primate surveillance [Wilbur et al., 2012]. Our team validated a non-invasive approach to tuberculosis detection among experimentally infected macaques and naturally exposed chimpanzees in African sanctuaries through the detection of MTC DNA in feces (Wolf et al., accepted). This report describes the first ever application of this method to screen a free-living population of primates in Gombe National Park, Tanzania.

### *The Study*

The study was conducted in Gombe National Park, Tanzania. The 35km<sup>2</sup> park, located in western Tanzania, lies on the eastern edge of Lake Tanganyika and is bordered by villages to the north and south. The park is home to seven species of non-human primates [Wallis and Lee, 1999], and is the site of the longest continuous research of free-living chimpanzees in the world. Three chimpanzee (*Pan troglodytes schweinfurthii*) communities, consisting of approximately 100 individuals, live within the park. Two communities are habituated to human observers: Kasekela, which is centrally located and visited by researchers and tourists, and Mitumba, which ranges in the northern part of the park and is visited only by researchers (Table 6-1). In addition to the chimpanzee communities, there are six olive baboon (*Papio anubis*) troops centrally located within the park that are also habituated to human observers for *in situ* research, totaling 189 individuals (Table 6-2).

Noninvasive fecal sampling of habituated, individually identified chimpanzees and baboons was conducted from January to June 2014. Sampling goals were two fecal samples per individual of the two habituated chimpanzee communities, Kasekela and Mitumba (n= 162), and a single fecal sample from a representative number of individuals from each of the 6 habituated baboon troops (n=70). Chimpanzees were followed daily by researchers, from nest to nest, as part of ongoing behavioral studies. Habituated baboons were similarly followed and observed for defecation. When defecation was

directly observed, a sample ca. 2g was collected into a 15ml tube containing 4.5ml RNALater (Qiagen, Inc). Samples were stored frozen at -20C for up to 9 months until testing commenced.

Table 6-1 Demographics of the habituated chimpanzee communities in Gombe National Park, Tanzania during the study sampling period, January-June 2014. Immature animals include ages 0 to 11 years and 11 months; adult animals are aged 12 years and older.

| <b>Age-sex classes</b> | <b>Kasekela</b> | <b>Mitumba</b> | <b>Total</b> |
|------------------------|-----------------|----------------|--------------|
| Adult males            | 13              | 6              | 19           |
| Adult females          | 26              | 9              | 35           |
| Immature males         | 8               | 3              | 11           |
| Immature females       | 8               | 8              | 16           |
| Total                  | 55              | 26             | 81           |

Table 6-2 Demographics of the habituated baboon troops in Gombe National Park, Tanzania during the study sampling period, March-April 2014. The table contains the number of baboons in each age-sex class in each group as documented on 31 October 2013. Males are classified as adults at the age in which they have emigrated and joined a new troop as a breeding male; females are classified as adults at the age in which they have their first vaginal swelling cycle (Collins, unpublished data).

| <b>Age-sex classes</b> | <b>BB</b> | <b>DB</b> | <b>AC</b> | <b>DA</b> | <b>BA</b> | <b>DC</b> | <b>Total</b> |
|------------------------|-----------|-----------|-----------|-----------|-----------|-----------|--------------|
| Adult males            | 1         | 2         | 5         | 3         | 10        | 11        | 33           |
| Adult females          | 7         | 8         | 13        | 7         | 18        | 19        | 72           |
| Immature males         | 2         | 6         | 11        | 8         | 7         | 16        | 50           |
| Immature females       | 5         | 0         | 3         | 6         | 2         | 18        | 34           |
| Total                  | 15        | 16        | 32        | 24        | 38        | 64        | 189          |

All testing was conducted in a dedicated Mycobacterium research lab (Sreevatsan lab) at the University of Minnesota's College of Veterinary Medicine. For each sample, DNA was extracted using the QIAMP Fast DNA Stool Mini Kit (Qiagen, Inc) according to manufacturer's instructions, with some modifications to optimize mycobacterial cell wall lysis, as previously described in Chapter 2. Specifically, feces were added to a tube containing Zirconia/Silica beads in addition to the recommended InhibitX Buffer and vortexed at high intensity for 3 minutes. Additionally, water bath temperatures were increased from 70°C to 95°C. Realtime (rtPCR) PCR using LightCycler 480 II (Roche) was utilized to amplify a portion of the IS6110 insertion sequence, as described in Chapter 2. Duplicate aliquots of each sample were tested and every reaction included positive and negative controls. Positive or suspect samples were reamplified and assessed by Tm analysis with positive controls for confirmation.

Laboratory results were used to estimate community or troop and population prevalence of infection among chimpanzees and baboons. Wilson score confidence intervals were chosen as an exact method for small n and rare disease [Brown et al., 2001; Newcombe, 2012]. This method for estimating confidence intervals accounts for the limits of a proportion, being bound by 0 and 1, and also for interval asymmetry that occurs when estimating a low proportion, providing a more precise estimate for the upper limit.

As tuberculosis was expected to be a rare disease, if present, in these primate populations, advanced statistical methods for rare diseases, where prevalence is expected to be close to 0, were also used. An Agresti-Coull prevalence shrinkage estimators and respective confidence intervals were thus compared with the maximum likelihood estimator. For comparison, the maximum likelihood prevalence estimator ( $P$ ) is calculated as:

$$P = \frac{m}{n} \quad (\text{Equation 6.1})$$

where  $m$  is the number positive and  $n$  is the number sampled. In contrast, the prevalence shrinkage estimator ( $P_\psi$ ) for rare disease is estimated as:

$$P_{\psi} = \frac{(m+\psi)}{(n+2\psi)} \quad (\text{Equation 6.2})$$

where  $\psi$  is a pseudo-frequency greater than 0, commonly set as  $z^2/2$  [Newcombe, 2012]. When  $\alpha$  is set to 0.05,  $z=1.96$  and  $\psi=1.92$ . Thus, by setting  $\psi \approx 2$ , as done for the Agresti-Coull confidence interval [Newcombe, 2012], the equation is reduced to:

$$P_{AC} = \frac{(m+2)}{(n+4)} \quad (\text{Equation 6.3})$$

This method essentially adds 2 positive and 2 negative samples to the calculation of the prevalence estimate. The Agresti-Coull estimate is appropriate for situations where the true prevalence is expected to be close to 0, thus where disease may more easily be missed in surveillance [Tang, 2014]; however, the shrinkage estimator approaches 0.5 where  $n$  is small [Newcombe, 2012]. Therefore, this comparison was made for the population-level prevalence estimates, as the Agresti-Coull prevalence estimator is expected to perform better for  $n > 40$  [Newcombe, 2012].

Finally, true prevalence was estimated for each population. True prevalence ( $TP$ ) was calculated as:

$$TP = \frac{AP+Sp-1}{Se+Sp-1} \quad (\text{Equation 6.4})$$

where  $AP$  is the apparent or maximum likelihood prevalence,  $P$  [Dohoo et al., 2009; Rogan and Gladen, 1978]. Sensitivity ( $Se$ ) and specificity ( $Sp$ ) estimates from the test validation study described in Chapter 2 were used as inputs for the calculation. Ninety-five percent Wilson score confidence intervals were calculated using Epitools and were based on variance estimates that incorporate additional uncertainty associated with the sample sizes used in  $Se$  and  $Sp$  estimation (Chapter 2) [Sergeant, 2015; Rogan and Gladen, 1978].

## *Results and Discussion*

A total of 207 fecal samples were collected during this study, which included 144 chimpanzee (Kasekela: n =105, Mitumba: n= 39) and 62 baboon samples. In Kasekela, 84% of the chimpanzee community was sampled at least once, 60% was sampled twice, and 31% was sampled more frequently. Of the individuals sampled, 33 were adults and 12 were subadults, which accounted for 85% and 75% of adults and subadults in Kasekela, respectively. Twenty (95%) of the Kasekela males and 25 (74%) of the females were sampled. During the sampling period, 2 adult, male chimpanzees (ages: 42yr and 14yr) were known to be chronically ill, with clinical signs at time of sampling being severe weight loss and wasting in both. Before the end of the study, one individual died and the other disappeared and is presumed dead. One of these males was sampled once and the other three times. In Mitumba, 85% of the community was sampled at least once, 42% was sampled twice, and 23% was sampled more frequently. Of those sampled, 15 were adults and 7 subadults, accounting for 94% and 70% of adults and subadults in Mitumba, respectively. All Mitumba males and 12 females (71%) were sampled. The 62 baboon samples originated from individuals within 5 habituated troops, including 11 samples from troop AC, 17 from BA, 5 from DA, 4 from DB, and 25 from DC.

All chimpanzee and baboon samples tested negative by IS6110 rtPCR. Table 6-3 shows sample sizes, prevalences, and confidence intervals for each community and troop. The wider confidence intervals for the baboon troop prevalence estimates reflect the imprecision associated with low sample numbers, with between 21% and 45% of each troop sampled. In contrast, sample coverage was high in the two chimpanzee communities, improving the precision of the confidence interval estimation. The Agresti-Coull shrinkage estimates for prevalence were calculated for each population sample and are compared to the maximum likelihood estimates in Table 6-4. The adjusted prevalence estimates were 2.8% and 3% for the chimpanzee and baboon populations, respectively. While these prevalence estimates may be possible, the community coverage attained with sampling of the chimpanzee communities and the degree to which the health of the chimpanzee communities are monitored make them seem inflated [Terio et

al., 2011; Lonsdorf et al., 2006]. As noted previously, the estimator approaches 0.5 with smaller n [Newcombe, 2012]; therefore, it is likely that the small population size is impacting the precision of this method in estimating the population prevalence. Further, while the upper limits of the confidence intervals for each estimate were very similar, the lower limit of the Agresti-Coull intervals are unrealistic since proportions cannot be less than 0. The true population prevalence estimated by Equation 3.4 was 0 (95% Wilson CI: 0 – 0.11) for the chimpanzee populations and 0 (95% Wilson CI: 0 – 0.12) for the baboon population. While the confidence intervals for the true population prevalence are wider than the maximum likelihood estimators, they should be considered more precise as they take into account the uncertainty associated with the Se and Sp estimates.

Table 6-3 Results of tuberculosis testing of chimpanzee communities and baboon troops in Gombe National Park, TZ.

| <b>Species</b> | <b>Community or Troop</b> | <b>Sample size (Proportion of community)</b> | <b>Sample prevalence</b> | <b>Wilson score confidence interval</b> |
|----------------|---------------------------|--|--------------------------|---|
| Chimpanzees    | Kasekela                  | 46 (0.84)                                    | 0                        | 0 – 0.07                                |
|                | Mitumba                   | 22 (0.85)                                    | 0                        | 0 – 0.15                                |
| Baboons        | AC                        | 11 (0.34)                                    | 0                        | 0 – 0.26                                |
|                | BA                        | 17 (0.45)                                    | 0                        | 0 – 0.18                                |
|                | DA                        | 5 (0.21)                                     | 0                        | 0 – 0.43                                |
|                | DB                        | 4 (0.25)                                     | 0                        | 0 – 0.49                                |
|                | DC                        | 25 (0.39)                                    | 0                        | 0 – 0.13                                |

Table 6-4 Comparison of maximum likelihood and Agresti-Coull estimators of prevalence and respective confidence intervals.

| Species     | Sample size | Maximum likelihood estimate (P) | Agresti-Coull shrinkage estimate (P <sub>AC</sub> ) | Wilson Score Confidence Interval for P | Agresti-Coull Confidence Interval for P |
|-------------|-------------|---------------------------------|---|--|---|
| Chimpanzees | 68          | 0                               | 0.028   | 0 – 0.05                               | -0.01 – 0.06                            |
| Baboons     | 62          | 0                               | 0.030   | 0 – 0.06                               | -0.01 – 0.07                            |

Tuberculosis-infected animals in advanced stages of disease are expected to shed higher numbers of organisms, thus detection is more likely to be successful in animals that are very sick with tuberculosis. In this study, two chimpanzees with chronic, fatal disease were screened for tuberculosis by this method, both of which tested negative. Although, necropsies could not be performed to positively identify the underlying disease processes, one animal was screened at 3 time points during clinical disease with our fecal test. Thus, we would conclude that tuberculosis was unlikely to be associated with death in at least one of these cases.

The success of the noninvasive screening of fecal samples for *Mycobacteria* sp. to identify tuberculosis infection relies on the occurrence of bacterial shedding in sputum with subsequent swallowing and excretion in feces; this only occurs during active infection when animals are contagious. This approach does not detect all stages of disease by measuring host immunologic responses, as does the tuberculin skin test. Thus, detection of mycobacterial DNA in feces is best suited for identifying actively infected primates, which are most important in tuberculosis transmission. Animals that are latently infected and not shedding bacteria are expected to go undetected with this method. In this study, we did not identify any individuals with active tuberculosis infection. These results combined with the pathology study conducted by Terio et al., which also found no evidence of latent or active tuberculosis on post-mortem examination, reveal no evidence

of tuberculosis infection in the Gombe primate populations at this time [Terio et al., 2011].

In this study, we demonstrate the feasibility of large-scale, noninvasive screening of free-living primate populations for tuberculosis using fecal *IS6110* PCR. We also demonstrate the utility of this approach as a diagnostic tool in the investigation of disease in individuals. This approach will be invaluable to managers and researchers of primate populations where the epidemiology of tuberculosis, because of spillover events or endemic infection, requires further investigation.

# Chapter 7 Conclusions and Future Directions

In a world of increasing wildlife habitat loss, a growing human population, and expanding connectivity between human, domestic animal and wildlife populations, emerging infectious diseases (EIDs) are ever more a complex and disturbing issue. Primates are recognized as an important taxon in EID research, as they may be sentinels, reservoir hosts, or cases in spillover events [Jones et al., 2008; Woolhouse and Gowtage-Sequeria, 2005; Wolfe et al., 2007; Calvignac-Spencer et al., 2012; Epstein and Price, 2009]. Based on their close genetic relatedness to humans alone, the risks of infectious disease transmission between the two populations are quite high [Loomis, 2003]. Hence, from both public health and conservation perspectives, there is a critical need for disease surveillance in primate populations. The primary focus of my dissertation research was the validation of tools and methods for respiratory disease surveillance in free-living primate populations. In conjunction was the advancement of *noninvasive* methods of disease surveillance. This endeavor was undertaken to balance the need to better understand respiratory disease impacts with the goal of no disruption to the natural behavior of the study population for health data collection.

Chapters 2-4 provide a systematic evaluation of the performance of syndromic surveillance in the detection of respiratory outbreaks and an epidemiological study of those outbreaks detected from 2004-2012 in Gombe Stream National Park, Tanzania. Up to now, most of our understanding of respiratory disease in great ape populations originates from studies of major outbreaks, consisting of large-scale morbidity and mortality, which is likely not representative of endemic disease trends. The results of these efforts to retrospectively screen 9 years of syndromic surveillance data reveal the presence of 15 outbreaks, only 6 of which were considered major [Williams et al., 2008]. This presented a unique opportunity to explore differences in outbreak characteristics, season, and demographics that may be contributing to the propagation of large-scale outbreaks. The most interesting of these findings being the potential role of males and

immature animals in transmission during major outbreaks, demographics that should be given greater scrutiny in future epidemiologic studies of respiratory disease transmission.

In addition, a qualitative and quantitative analysis of surveillance sensitivity to respiratory outbreak detection was performed. Such analyses are highly useful to end-users as they provide a comprehensive assessment of data quality and effectiveness of the surveillance system to disease detection. This work meets an important need for the primate and wildlife community, in which syndromic surveillance is an incipient approach to disease surveillance and rigorous methods of system evaluation are greatly lacking. The results of this research revealed important temporal differences in surveillance sensitivity as well as the influence of the chimpanzee social network on disease transmission. These findings will assist Gombe managers in refining strategies of surveillance to improve outbreak detection as well as inform syndromic surveillance efforts in other primate populations. The simulation model built in this study is flexible for future use, easily allowing the incorporation of demographics, network structures, and surveillance data from other populations of great apes to assess disease transmission and surveillance sensitivity. Thus, as syndromic surveillance gains traction across primate populations as a valuable tool for the noninvasive collection of large amounts of health data and early outbreak detection, comparable assessments can be made across populations.

Chapters 5 and 6 describe my dissertation research to validate a noninvasive approach to tuberculosis detection in free-living primates. The work described in Chapter 5 demonstrates the utility of fecal *IS6110* PCR in the detection of primates with active tuberculosis infection through the screening of primates with known tuberculosis infection and alongside a traditional diagnostic screening test in a primate rehabilitation setting, while Chapter 6 demonstrates the feasibility of this noninvasive approach in the screening of a well-studied wild chimpanzee population. The sensitivity of this approach to the detection of tuberculosis infection in primates is limited; however, the high specificity of the test reduces the likelihood of falsely diagnosing infection, an event that could have dire consequences on the management of a wild primate population. The most

significant outcome of this work is a novel method for noninvasively screening free-living primate populations for tuberculosis, which opens new doors for understanding the epidemiology and risks of tuberculosis transmission in wild primates.

In conclusion, this research demonstrates syndromic surveillance as a valuable tool for early outbreak detection and an important method for the noninvasive collection of large amounts of health data on a primate population where capture and more invasive techniques are not an option. However, its greatest limitation is the absence of pathogen identification. Hence, this research also builds on the resources available to us for the noninvasive detection of respiratory pathogens in the form of a novel approach using feces to screen and study primate populations for tuberculosis, a globally important and impactful disease. Accordingly, this dissertation research exemplifies the direction that future work should take: building on syndromic surveillance with the incorporation of noninvasive diagnostic sampling. The coupling of syndromic surveillance with targeted noninvasive, diagnostic sampling during endemic or epidemic disease outbreaks, will generate a powerful system for studying respiratory disease transmission and population impacts. Indeed, as we enhance the data collected through this system of surveillance and noninvasive diagnostic sampling, we will advance our understanding of primate health while mitigating our impact as researchers on the natural behavior and ecology of these species. With growing concerns of emerging infectious disease, both human-introduced and zoonotic, future innovation on this front is imperative.

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# Appendix 1 | Gombe Chimp Respiratory Disease Model4

## *AnyLogic Model Documentation*

Description: Agent-based SEIR model simulating respiratory disease transmission among Gombe National Park chimpanzee population, Kasekela community. Model version specifies 2 contact networks (Party level or Grooming level) which are sampled from an annually or seasonally-derived weighted network.

| Name                             | Value   |
|----------------------------------|---|
| <b>General</b>                   |   |
| Model Time Units                 | days  |
| <b>Numerical methods</b>         |   |
| Differentiation Equations Method | Euler   |
| Algebraic Equations Method       | Modified Newton   |
| Mixed Equations Method           | RK45+Newton   |
| Absolute Accuracy                | 1.0E-5  |
| Time Accuracy                    | 1.0E-5  |
| Relative Accuracy                | 1.0E-5  |
| Fixed Time Step                  | 0.001   |
| <b>Advanced</b>                  |   |
| Java Package Name                | chimprespiratorydisease   |
| File Name                        | /Users/tiffanywolf/Dropbox/NewStuff/DiseaseModel/WorkingModel/Gombe Chimp Respiratory Disease Model_2015.1.25b/Gombe Chimp Respiratory Disease Model4.alp   |
| <b>Description</b>               |   |
| Description                      | Agent-based SEIR model simulating respiratory disease transmission among Gombe National Park chimpanzee population, Kasekela community. Model version specifies 2 contact networks (Party level or Grooming level) which are sampled from an annually or seasonally-derived weighted network. |

### Agent Type: Main

| Name                       | Value  |
|----------------------------|--|
| <b>Agent in flowcharts</b> |  |
| Use in flowcharts as       | Agent  |
| <b>Movement</b>            |  |
| Speed                      | 10 / getScale().pixelsPerUnit(METER) / 86400 meters per second |

|  |              |
|--|--------------|
| Rotate animation towards movement        | true         |
| Rotate vertically as well (along Z-axis) | false        |
| Space and network                        |              |
| Space Type                               | Continuous   |
| Dynamic: Width                           | 500          |
| Dynamic: Height                          | 500          |
| Dynamic: z Height                        | 0            |
| Layout Type                              | Random       |
| Layout Type Apply On Startup             | true         |
| Network Type                             | User-defined |
| Network Type Apply On Startup            | true         |
| Name                                     | Value        |
| Enable Steps                             | false        |
| Advanced Java                            |              |
| Generic                                  | false        |
| Advanced                                 |              |
| Auto-create Datasets                     | true         |
| Use model time                           | true         |
| Update time (absolute)                   | 0 days       |
| Recurrence time                          | 1 days       |
| Limit the number of data samples         | false        |

**Creating Population and Network Structure**

- populationList
- createPopulation
- readConnectionsInFile
- assignPbcConnectionsInPopulation
- setPopulationConnections
- resetIndividualPartyingConnections
- resetIndividualGroomingConnections
- createInitialPopulationAndNetwork
- exitFile
- weightGroomingConnections
- weightPartyingConnections
- testFile
- avgTDCOutbreak

**Initializing Infection**

- initInfection
- initInfectionTime

**Resetting Network Structure**

- resetResetConnections

**Collecting and Calculating Result**

- populationSicknessDuration
- sumInfectionCount
- week
- chompDetectedTracker
- chompDetectedSickTracker
- chompTruthSickTracker
- resetChompTrackers
- updateChompTrackers
- collectChompTrackersData
- writeOutputToFile
- writeWeeklyTrackerValuesToFile
- weekyDetected
- weekyDetectedSick
- weekyTruthSick
- currentCumulativeInfectionCount
- newInfectionCount
- eventTimeZero
- eventDaily
- eventWeekly
- checkPopulationSickness
- eventFinishSim

**Sliders and Buttons:**

- Display No...
- incubationPeriod
- durationOfInfection
- groomingContactRate
- partsContactRate
- groomingInfectionProbability
- partInfectionProbability
- season
- isShowingNames

**Graphs:**

- Daily Number Infectious (Red line graph)
- Daily New Infections (Blue line graph)

## Parameter: groomingInfectionProbability

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

## Parameter: groomingContactRate

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

## Parameter: incubationPeriod

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

## Parameter: durationOfInfection

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

### Parameter: partyContactRate

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

### Parameter: partyInfectionProbability

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

### Parameter: season

| Name    | Value |
|---------|-------|
| General |       |
| Array   | false |

|                       |            |
|-----------------------|------------|
| Default Value         | "Quarter3" |
| Type                  | String     |
| Show At Runtime       | true       |
| Show name             | true       |
| Value editor          |            |
| Editor Control        | Text       |
| Advanced              |            |
| System dynamics units | false      |
| Save In Snapshot      | true       |

## Dynamic Event: eventFinishSim

| Name            | Value  |
|-----------------|--|
| General         |  |
| Show At Runtime | true   |
| Show name       | true   |
| Action          |  |
| Action          | //writeOutputToExcel();<br>finishSimulation(); |

## Function: setPopulationConnections

| Name                  | Value   |
|-----------------------|---|
| General               |   |
| Return type:          | Just action (returns nothing)   |
| Show At Runtime       | true  |
| Show name             | true  |
| Function body         |   |
| Body                  | <pre>for (Chimp cp : chimpPopulation) {     resetIndividualPartyingConnections(cp);     resetIndividualGroomingConnections(cp); }</pre> |
| Advanced              |   |
| Static                | false   |
| Access Type           | default   |
| System dynamics units | false   |

## Function: resetIndividualPartyingConnections

| Name    | Value |
|---------|-------|
| General |       |

|                       |  |
|-----------------------|--|
| Return type:          | Just action (returns nothing)  |
| Show At Runtime       | true   |
| Show name             | true   |
| Function body         |  |
| Body                  | <pre> LinkToAgentCollection&lt;Chimp, Chimp&gt; link = indChimp.connectionsPartying; HashMap&lt;Chimp, Double&gt; candidatesProbabilities = indChimp.pConnectionPartying;  link.disconnectFromAll(); for (Map.Entry&lt;Chimp, Double&gt; entry : candidatesProbabilities.entrySet()) {     Chimp otherChimp = entry.getKey();     Double prob = entry.getValue();     if (randomTrue(prob)) {         link.connectTo(otherChimp);     } } </pre> |
| Advanced              |  |
| Static                | false  |
| Access Type           | default  |
| System dynamics units | false  |

### Arguments:

| Name     | Type  |
|----------|-------|
| indChimp | Chimp |

### Function: createPopulation

| Name            | Value                         |
|-----------------|-------------------------------|
| General         |                               |
| Return type:    | Just action (returns nothing) |
| Show At Runtime | true                          |
| Show name       | true                          |
| Function body   |                               |

|                       |   |
|-----------------------|---|
| Body                  | <pre>String sheetName = season+ "Pop"; int totalDataRows = excelFile.getLastRowNum(sheetName);  traceln("Total Population Data Rows is:" + totalDataRows);  int cName = 1; int cSex = 2; int cAge = 3; int cAgeClass = 4; int cRank = 5; int cDetectionProb =6;  for (int r = 2; r &lt;= totalDataRows ; r++) { //note starting at 2     String name = excelFile.getCellStringValue(sheetName,     r, cName);     String sex = excelFile.getCellStringValue(sheetName, r,     cSex);     double age = excelFile.getCellNumericValue(sheetName,     r, cAge);     String ageClass =     excelFile.getCellStringValue(sheetName, r, cAgeClass);     String rank = excelFile.getCellStringValue(sheetName, r,     cRank);     double detectionProb =     excelFile.getCellNumericValue(sheetName, r, cDetectionProb);     //    String xattribute =     excelFile.getCellStringValue(sheetName, i, indexnumber);     Chimp cp = this.add_chimpPopulation(name, sex, age,     ageClass, rank, detectionProb);     //need to add in attribute: detectionProbability to the</pre> |
| Advanced              |   |
| Static                | false   |
| Access Type           | default   |
| System dynamics units | false   |

## Function: readConnectionWeights

| Name            | Value                         |
|-----------------|-------------------------------|
| General         |                               |
| Return type:    | Just action (returns nothing) |
| Show At Runtime | true                          |
| Show name       | true                          |
| Function body   |                               |

|                       |  |
|-----------------------|--|
| Body                  | <pre>String sheetName = season + "Network"; int totalDataRows = excelFile.getLastRowNum(sheetName);  for (int i = 2; i &lt;= totalDataRows ; i++) { //note starting at 2     String nameX = excelFile.getCellStringValue(sheetName, i, 1);     String nameY = excelFile.getCellStringValue(sheetName, i, 2);     NamePair namePair = new NamePair(nameX, nameY);     double connectionWeightPartying = excelFile.getCellNumericValue(sheetName, i, 3);     double connectionWeightGrooming = excelFile.getCellNumericValue(sheetName, i, 4);     this.weightGroomingConnections.put(namePair, connectionWeightGrooming);     this.weightPartyingConnections.put(namePair, connectionWeightPartying); }</pre> |
| Advanced              |  |
| Static                | false  |
| Access Type           | default  |
| System dynamics units | false  |

## Function: assignPofConnectionsInPopulation

| Name                  | Value  |
|-----------------------|--|
| General               |  |
| Return type:          | Just action (returns nothing)  |
| Show At Runtime       | true   |
| Show name             | true   |
| Function body         |  |
| Body                  | <pre>for (Chimp cp : chimpPopulation) {     ArrayList&lt;Chimp&gt; others = (ArrayList&lt;Chimp&gt;)this.populationList.clone();     others.remove(cp);      for (Chimp o : others) {         NamePair namePair = new NamePair(cp.name, o.name);         cp.pConnectionGrooming.put(o, this.weightGroomingConnections.get(namePair));         cp.pConnectionPartying.put(o, this.weightPartyingConnections.get(namePair));     } }</pre> |
| Advanced              |  |
| Static                | false  |
| Access Type           | default  |
| System dynamics units | false  |

## Function: resetIndividualGroomingConnections

| Name            | Value                         |
|-----------------|-------------------------------|
| General         |                               |
| Return type:    | Just action (returns nothing) |
| Show At Runtime | true                          |

|                       |   |
|-----------------------|---|
| Show name             | true  |
| Function body         |   |
| Body                  | <pre> LinkToAgentCollection&lt;Chimp, Chimp&gt; linkPartying = indChimp.connectionsPartying; LinkToAgentCollection&lt;Chimp, Chimp&gt; linkGrooming = indChimp.connectionsGrooming; HashMap&lt;Chimp, Double&gt; candidatesProbabilities = indChimp.pConnectionGrooming;  linkGrooming.disconnectFromAll();  List&lt;Chimp&gt; candidates = linkPartying.getConnections();  for (Chimp cp : candidates) {     Double prob = candidatesProbabilities.get(cp);     if (randomTrue(prob)) {         linkGrooming.connectTo(cp);     } } </pre> |
| Advanced              |   |
| Static                | false   |
| Access Type           | default   |
| System dynamics units | false   |

#### Arguments:

| Name     | Type  |
|----------|-------|
| indChimp | Chimp |

### Function: checkPopulationSickness

| Name                  | Value  |
|-----------------------|--|
| General               |  |
| Return Type           | boolean  |
| Return type:          | Returns value  |
| Show At Runtime       | true   |
| Show name             | true   |
| Function body         |  |
| Body                  | <pre> boolean sick = true; if (time() &gt; initInfectionTime &amp;&amp; chimpPopulation.NumberofInfectious() == 0 &amp;&amp; chimpPopulation.NumberofLatent() == 0 ) {     sick = false;     populationSicknessDuration = time(); }  return sick; </pre> |
| Advanced              |  |
| Static                | false  |
| Access Type           | default  |
| System dynamics units | false  |

## Function: resetChimpTrackers

| Name                  | Value   |
|-----------------------|---|
| <b>General</b>        |   |
| Return type:          | Just action (returns nothing)   |
| Show At Runtime       | true  |
| Show name             | true  |
| <b>Function body</b>  |   |
| Body                  | <pre>chimpTruthSickTracker = new HashMap&lt;Chimp, Boolean&gt;(); chimpDetectedTracker = new HashMap&lt;Chimp, Boolean&gt;(); chimpDetectedSickTracker = new HashMap&lt;Chimp, Boolean&gt;();</pre> |
| <b>Advanced</b>       |   |
| Static                | false   |
| Access Type           | default   |
| System dynamics units | false   |

## Function: updateChimpTrackers

| Name                  | Value   |
|-----------------------|---|
| <b>General</b>        |   |
| Return type:          | Just action (returns nothing)   |
| Show At Runtime       | true  |
| Show name             | true  |
| <b>Function body</b>  |   |
| Body                  | <pre>for (Chimp cp : chimpPopulation) {     if (cp.SEIRStatechart.isStateActive(Chimp.Infectious)) {         chimpTruthSickTracker.put(cp, true);     }     if (randomTrue(cp.detectionProbability)) {         chimpDetectedTracker.put(cp, true);         if         (cp.SEIRStatechart.isStateActive(Chimp.Infectious)) {             chimpDetectedSickTracker.put(cp, true);         }     } }</pre> |
| <b>Advanced</b>       |   |
| Static                | false   |
| Access Type           | default   |
| System dynamics units | false   |

## Function: collectChimpTrackersData

| Name           | Value                         |
|----------------|-------------------------------|
| <b>General</b> |                               |
| Return type:   | Just action (returns nothing) |

|                       |  |
|-----------------------|--|
| Show At Runtime       | true   |
| Show name             | true   |
| Function body         |  |
| Body                  | <pre>double detectedCount = chimpDetectedTracker.size(); weeklyDetected.add(this.week, detectedCount); double detectedSickCount = chimpDetectedSickTracker.size(); weeklyDetectedSick.add(this.week, detectedSickCount); double truthSickCount = chimpTruthSickTracker.size(); weeklyTruthSick.add(this.week, truthSickCount);  writeWeeklyTrackerValuesToTextFile(week, detectedCount, detectedSickCount, truthSickCount, cumInfectionCount);</pre> |
| Advanced              |  |
| Static                | false  |
| Access Type           | default  |
| System dynamics units | false  |

## Function: writeWeeklyTrackerValuesToTextFile

| Name                  | Value  |
|-----------------------|--|
| General               |  |
| Return type:          | Just action (returns nothing)  |
| Show At Runtime       | true   |
| Show name             | true   |
| Function body         |  |
| Body                  | <pre>textFile.println(week + "\t" + detected + "\t" + detectedSick + "\t" + truthSick + "\t" + cumInfectionCount);</pre> |
| Advanced              |  |
| Static                | false  |
| Access Type           | default  |
| System dynamics units | false  |

### Arguments:

| Name              | Type   |
|-------------------|--------|
| week              | double |
| detected          | double |
| detectedSick      | double |
| truthSick         | double |
| cumInfectionCount | double |

## Table Function: aug2007Outbreak

| Name | Value |
|------|-------|
|------|-------|

| General                |         |
|------------------------|---------|
| Public                 | false   |
| Out Of Range Behaviour | Nearest |
| Interpolation          | Linear  |
| Show At Runtime        | true    |
| Show name              | true    |
| Advanced               |         |
| Static                 | true    |
| Access Type            | public  |
| System dynamics units  | false   |

### Table Data:

| Argument | Value |
|----------|-------|
| 0.0      | 0.0   |
| 1.0      | 1.0   |
| 2.0      | 3.0   |
| 3.0      | 3.0   |
| 4.0      | 7.0   |
| 5.0      | 8.0   |
| 6.0      | 8.0   |
| 7.0      | 15.0  |
| 8.0      | 18.0  |
| 9.0      | 19.0  |
| 10.0     | 21.0  |
| 11.0     | 21.0  |
| 12.0     | 23.0  |
| 13.0     | 23.0  |
| 14.0     | 23.0  |
| 15.0     | 24.0  |
| 16.0     | 26.0  |

### Event: initialInfection

| Name                   | Value                                       |
|------------------------|---|
| General                |   |
| Update time (absolute) | initInfectionTime days                      |
| Use model time         | true  |
| Mode                   | Occurs once                                 |
| Trigger Type           | Timeout                                     |
| Show At Runtime        | true  |
| Show name              | true  |
| Action                 |   |
| Action                 | this.deliverToRandomAgentInside("Infect!"); |

### Event: eventResetConnections

| Name                   | Value                       |
|------------------------|-----------------------------|
| General                |                             |
| Recurrence time        | 6 hours                     |
| Update time (absolute) | 0 hours                     |
| Use model time         | true                        |
| Mode                   | Cyclic                      |
| Trigger Type           | Timeout                     |
| Show At Runtime        | true                        |
| Show name              | true                        |
| Action                 |                             |
| Action                 | setPopulationConnections(); |

## Event: createInitialPopulationAndNetwork

| Name                   | Value   |
|------------------------|---|
| General                |   |
| Update time (absolute) | 0 days  |
| Use model time         | true  |
| Mode                   | Occurs once   |
| Trigger Type           | Timeout   |
| Show At Runtime        | true  |
| Show name              | true  |
| Action                 |   |
| Action                 | <pre> this.createPopulation(); this.applyLayout(); this.readConnectionWeights(); this.assignPofConnectionsInPopulation(); this.setPopulationConnections(); </pre> |

## Event: eventDaily

| Name                   | Value   |
|------------------------|---------|
| General                |         |
| Recurrence time        | 1 days  |
| Update time (absolute) | 1 days  |
| Use model time         | true    |
| Mode                   | Cyclic  |
| Trigger Type           | Timeout |
| Show At Runtime        | true    |
| Show name              | true    |
| Action                 |         |

|        |   |
|--------|---|
| Action | <pre> double value = cumInfectionCount - currentCumInfectionCount.getYMax(); newInfectionCount.add(value); //make sure the new infection count is calculated before cum count is recorded. currentCumInfectionCount.add(cumInfectionCount);  updateChimpTrackers();  if (!checkPopulationSickness()) {     double currentT = time();     double modRemainder = currentT % 7;     double dt = 7 - modRemainder + initInfectionTime; //initInfectionTime is just a very small increment     create_eventFinishSim(dt); } </pre> |
|--------|---|

## Event: eventTimeZero

| Name                   | Value  |
|------------------------|--|
| General                |  |
| Update time (absolute) | 0 days   |
| Use model time         | true   |
| Mode                   | Occurs once                                      |
| Trigger Type           | Timeout  |
| Show At Runtime        | true   |
| Show name              | true   |
| Action                 |  |
| Action                 | currentCumInfectionCount.add(cumInfectionCount); |

## Event: eventWeekly

| Name                   | Value   |
|------------------------|---|
| General                |   |
| Recurrence time        | 7 days  |
| Update time (absolute) | 7 days  |
| Use model time         | true  |
| Mode                   | Cyclic  |
| Trigger Type           | Timeout   |
| Show At Runtime        | true  |
| Show name              | true  |
| Action                 |   |
| Action                 | <pre> collectChimpTrackersData();  this.week++;  resetChimpTrackers(); </pre> |

## Variable: populationList

| Name                  | Value                  |
|-----------------------|------------------------|
| General               |                        |
| Initial Value         | new ArrayList<Chimp>() |
| Type                  | ArrayList<Chimp>       |
| Show At Runtime       | true                   |
| Show name             | true                   |
| Advanced              |                        |
| Access Type           | public                 |
| Static                | false                  |
| Constant              | false                  |
| Save In Snapshot      | true                   |
| System dynamics units | false                  |

### Variable: isShowingNames

| Name                  | Value   |
|-----------------------|---------|
| General               |         |
| Type                  | boolean |
| Show At Runtime       | true    |
| Show name             | true    |
| Advanced              |         |
| Access Type           | public  |
| Static                | false   |
| Constant              | false   |
| Save In Snapshot      | true    |
| System dynamics units | false   |

### Variable: cumInfectionCount

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Advanced              |        |
| Access Type           | public |
| Static                | false  |
| Constant              | false  |
| Save In Snapshot      | true   |
| System dynamics units | false  |

### Variable: initInfectionTime

| Name    | Value |
|---------|-------|
| General |       |

|                       |        |
|-----------------------|--------|
| Initial Value         | 0.001  |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Advanced              |        |
| Access Type           | public |
| Static                | false  |
| Constant              | false  |
| Save In Snapshot      | true   |
| System dynamics units | false  |

### Variable: populationSicknessDuration

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Advanced              |        |
| Access Type           | public |
| Static                | false  |
| Constant              | false  |
| Save In Snapshot      | true   |
| System dynamics units | false  |

### Variable: week

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Initial Value         | 1      |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Advanced              |        |
| Access Type           | public |
| Static                | false  |
| Constant              | false  |
| Save In Snapshot      | true   |
| System dynamics units | false  |

### Collection: weightGroomingConnections

| Name                | Value  |
|---------------------|--------|
| General             |        |
| Value Element Class | Double |

|                  |          |
|------------------|----------|
| Element Class    | NamePair |
| Collection Class | HashMap  |
| Show At Runtime  | true     |
| Show name        | true     |
| Advanced         |          |
| Access Type      | public   |
| Save In Snapshot | true     |
| Static           | false    |

## Collection: weightPartyingConnections

| Name                | Value    |
|---------------------|----------|
| General             |          |
| Value Element Class | Double   |
| Element Class       | NamePair |
| Collection Class    | HashMap  |
| Show At Runtime     | true     |
| Show name           | true     |
| Advanced            |          |
| Access Type         | public   |
| Save In Snapshot    | true     |
| Static              | false    |

## Collection: chimpDetectedTracker

| Name                | Value   |
|---------------------|---------|
| General             |         |
| Value Element Class | Boolean |
| Element Class       | Chimp   |
| Collection Class    | HashMap |
| Show At Runtime     | true    |
| Show name           | true    |
| Advanced            |         |
| Access Type         | public  |
| Save In Snapshot    | true    |
| Static              | false   |

## Collection: chimpDetectedSickTracker

| Name                | Value   |
|---------------------|---------|
| General             |         |
| Value Element Class | Boolean |
| Element Class       | Chimp   |
| Collection Class    | HashMap |
| Show At Runtime     | true    |

|                  |        |
|------------------|--------|
| Show name        | true   |
| Advanced         |        |
| Access Type      | public |
| Save In Snapshot | true   |
| Static           | false  |

## Collection: chimpTruthSickTracker

| Name                | Value   |
|---------------------|---------|
| General             |         |
| Value Element Class | Boolean |
| Element Class       | Chimp   |
| Collection Class    | HashMap |
| Show At Runtime     | true    |
| Show name           | true    |
| Advanced            |         |
| Access Type         | public  |
| Save In Snapshot    | true    |
| Static              | false   |

## Time Plot: plotNumberInfectious

| Name                       | Value            |
|----------------------------|------------------|
| General                    |                  |
| Public                     | true             |
| Data update                |                  |
| Analysis Auto Update       | true             |
| Use model time             | true             |
| Update time (absolute)     | 0 days           |
| Recurrence time            | 1 days           |
| Dataset Samples To Keep    | 30               |
| Scale                      |                  |
| Time Window                | 30               |
| Time                       | model time units |
| Vertical Scale             | Auto             |
| Appearance                 |                  |
| Labels Horizontal Position | DEFAULT          |
| Labels Vertical Position   | DEFAULT          |
| Label Format               | Model time units |
| Labels Text Color          | darkGray         |
| Chart Area Grid Color      | darkGray         |
| Draw Line                  | true             |
| Interpolation              | Linear           |
| Position and size          |                  |
| x                          | 500.0            |

|                              |              |
|------------------------------|--------------|
| Width                        | 420.0        |
| y                            | 30.0         |
| Height                       | 210.0        |
| <b>Legend</b>                |              |
| Show Legend                  | true         |
| Legend Size                  | 30.0         |
| Legend Text Color            | black        |
| <b>Chart area</b>            |              |
| Chart Area: X Offset         | 50.0         |
| Chart Area: Width            | 340.0        |
| Chart Area: Y Offset         | 30.0         |
| Chart Area: Height           | 120.0        |
| Chart Area: Background Color | white        |
| Chart Area Border Color      | black        |
| <b>Advanced</b>              |              |
| Time window moves            | Continuously |
| Show name                    | false        |

### Plot Items:

| Title                   | Type  | Dataset / Value | Point Style | Color   | Line | Width | Interpolatio |
|-------------------------|-------|-----------------|-------------|---------|------|-------|--------------|
| Daily Number Infectious | value |                 | CIRCLE      | crimson | true | 2.0   | LINEAR       |

### Time Plot: plotNewInfections

| Name                       | Value            |
|----------------------------|------------------|
| <b>General</b>             |                  |
| Public                     | true             |
| <b>Data update</b>         |                  |
| Analysis Auto Update       | false            |
| Dataset Samples To Keep    | 30               |
| <b>Scale</b>               |                  |
| Time Window                | 30               |
| Time                       | model time units |
| Vertical Scale             | Auto             |
| <b>Appearance</b>          |                  |
| Labels Horizontal Position | DEFAULT          |
| Labels Vertical Position   | DEFAULT          |
| Label Format               | Model time units |
| Labels Text Color          | darkGray         |
| Chart Area Grid Color      | darkGray         |
| Draw Line                  | true             |
| Interpolation              | Linear           |

| Position and size            |              |
|------------------------------|--------------|
| x                            | 500.0        |
| Width                        | 420.0        |
| y                            | 280.0        |
| Height                       | 210.0        |
| Legend                       |              |
| Show Legend                  | true         |
| Legend Size                  | 30.0         |
| Legend Text Color            | black        |
| Chart area                   |              |
| Chart Area: X Offset         | 50.0         |
| Chart Area: Width            | 340.0        |
| Chart Area: Y Offset         | 30.0         |
| Chart Area: Height           | 120.0        |
| Chart Area: Background Color | white        |
| Chart Area Border Color      | black        |
| Advanced                     |              |
| Time window moves            | Continuously |
| Show name                    | false        |

### Plot Items:

| Title                | Type    | Dataset / Value   | Point Style | Color | Line | Width | Interpolatio |
|----------------------|---------|-------------------|-------------|-------|------|-------|--------------|
| Daily New Infections | dataset | newInfectionCount | SQUARE      | blue  | true | 1.0   | LINEAR       |

### Data Set: currentCumInfectionCount

| Name                    | Value |
|-------------------------|-------|
| General                 |       |
| Dataset Samples To Keep | 10000 |
| Axis Data Freeze X Axis | true  |
| Show At Runtime         | true  |
| Show name               | true  |
| Data update             |       |
| Analysis Auto Update    | false |

### Data Set: newInfectionCount

| Name                    | Value |
|-------------------------|-------|
| General                 |       |
| Dataset Samples To Keep | 10000 |
| Axis Data Freeze X Axis | true  |
| Show At Runtime         | true  |

|                      |       |
|----------------------|-------|
| Show name            | true  |
| Data update          |       |
| Analysis Auto Update | false |

### Data Set: weeklyDetected

| Name                    | Value |
|-------------------------|-------|
| General                 |       |
| Dataset Samples To Keep | 10000 |
| Axis Data Freeze X Axis | false |
| Show At Runtime         | true  |
| Show name               | true  |
| Data update             |       |
| Analysis Auto Update    | false |

### Data Set: weeklyDetectedSick

| Name                    | Value |
|-------------------------|-------|
| General                 |       |
| Dataset Samples To Keep | 10000 |
| Axis Data Freeze X Axis | false |
| Show At Runtime         | true  |
| Show name               | true  |
| Data update             |       |
| Analysis Auto Update    | false |

### Data Set: weeklyTruthSick

| Name                    | Value |
|-------------------------|-------|
| General                 |       |
| Dataset Samples To Keep | 10000 |
| Axis Data Freeze X Axis | false |
| Show At Runtime         | true  |
| Show name               | true  |
| Data update             |       |
| Analysis Auto Update    | false |

### Rectangle: rectangle

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Embedded Icon   | false |
| Public          | true  |

| Appearance        |           |
|-------------------|-----------|
| Fill Color        | gainsboro |
| Line Color        | black     |
| Line Width        | 1.0       |
| Line Style        | SOLID     |
| Position and size |           |
| x                 | 0.0       |
| Width             | 500.0     |
| y                 | 0.0       |
| Height            | 500.0     |
| z                 | 0.0       |
| z Height          | 10.0      |
| Rotation          | 0.0       |
| Advanced          |           |
| Show in           | 2D and 3D |
| Show name         | false     |

## Agent Presentation: chimpPopulation\_presentation

| Name                                    | Value                    |
|---|--------------------------|
| General                                 |                          |
| Show At Runtime                         | true                     |
| Public                                  | true                     |
| Position and size                       |                          |
| x                                       | 0.0                      |
| y                                       | 0.0                      |
| z                                       | 0.0                      |
| Rotation                                | 0.0                      |
| Scale                                   | Automatically calculated |
| Advanced                                |                          |
| Show in                                 | 2D and 3D                |
| Draw agent with offset to this position | false                    |
| Show name                               | false                    |

## Text: text

| Name            | Value                                     |
|-----------------|---|
| General         |   |
| Show At Runtime | true                                      |
| Lock            | false                                     |
| Embedded Icon   | false                                     |
| Public          | true                                      |
| Text            |   |
| Text            | Creating Population and Network Structure |

| Appearance        |           |
|-------------------|-----------|
| Font Size         | 18        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | -580.0    |
| y                 | 40.0      |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show in           | 2D only   |
| Show name         | false     |

## Line: line

| Name              | Value             |
|-------------------|-------------------|
| General           |                   |
| Show At Runtime   | true              |
| Lock              | false             |
| Embedded Icon     | false             |
| Public            | true              |
| Appearance        |                   |
| Line Color        | black             |
| Line Width        | 3.0               |
| Line Style        | SOLID             |
| Position and size |                   |
| x                 | -580.0            |
| dX                | 240.0             |
| y                 | 94.01639344262296 |
| dY                | 0.0               |
| z                 | 0.0               |
| dZ                | 0.0               |
| z Height          | 10.0              |
| Advanced          |                   |
| Show in           | 2D and 3D         |
| Show name         | false             |

## Text: text1

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Embedded Icon   | false |

|                   |                        |
|-------------------|------------------------|
| Public            | true                   |
| Text              |                        |
| Text              | Initializing Infection |
| Appearance        |                        |
| Font Size         | 18                     |
| Font Name         | SansSerif              |
| Color             | black                  |
| Alignment         | LEFT                   |
| Position and size |                        |
| x                 | -300.0                 |
| y                 | 60.0                   |
| z                 | 0.0                    |
| Rotation          | 0.0                    |
| Advanced          |                        |
| Show in           | 2D only                |
| Show name         | false                  |

## Line: line1

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Embedded Icon     | false     |
| Public            | true      |
| Appearance        |           |
| Line Color        | black     |
| Line Width        | 3.0       |
| Line Style        | SOLID     |
| Position and size |           |
| x                 | -300.0    |
| dX                | 240.0     |
| y                 | 90.0      |
| dY                | 0.0       |
| z                 | 0.0       |
| dZ                | 0.0       |
| z Height          | 10.0      |
| Advanced          |           |
| Show in           | 2D and 3D |
| Show name         | false     |

## Text: text2

| Name    | Value |
|---------|-------|
| General |       |

|                   |                             |
|-------------------|-----------------------------|
| Show At Runtime   | true                        |
| Lock              | false                       |
| Embedded Icon     | false                       |
| Public            | true                        |
| Text              |                             |
| Text              | Resetting Network Structure |
| Appearance        |                             |
| Font Size         | 18                          |
| Font Name         | SansSerif                   |
| Color             | black                       |
| Alignment         | LEFT                        |
| Position and size |                             |
| x                 | -300.0                      |
| y                 | 170.0                       |
| z                 | 0.0                         |
| Rotation          | 0.0                         |
| Advanced          |                             |
| Show in           | 2D only                     |
| Show name         | false                       |

## Line: line2

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Embedded Icon     | false     |
| Public            | true      |
| Appearance        |           |
| Line Color        | black     |
| Line Width        | 3.0       |
| Line Style        | SOLID     |
| Position and size |           |
| x                 | -300.0    |
| dX                | 240.0     |
| y                 | 200.0     |
| dY                | 0.0       |
| z                 | 0.0       |
| dZ                | 0.0       |
| z Height          | 10.0      |
| Advanced          |           |
| Show in           | 2D and 3D |
| Show name         | false     |

## Text: text3

| Name              | Value                             |
|-------------------|-----------------------------------|
| General           |                                   |
| Show At Runtime   | true                              |
| Lock              | false                             |
| Embedded Icon     | false                             |
| Public            | true                              |
| Text              |                                   |
| Text              | Collecting and Calculating Result |
| Appearance        |                                   |
| Font Size         | 18                                |
| Font Name         | SansSerif                         |
| Color             | black                             |
| Alignment         | LEFT                              |
| Position and size |                                   |
| x                 | -300.0                            |
| y                 | 290.0                             |
| z                 | 0.0                               |
| Rotation          | 0.0                               |
| Advanced          |                                   |
| Show in           | 2D only                           |
| Show name         | false                             |

### Line: line3

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Embedded Icon     | false     |
| Public            | true      |
| Appearance        |           |
| Line Color        | black     |
| Line Width        | 3.0       |
| Line Style        | SOLID     |
| Position and size |           |
| x                 | -300.0    |
| dX                | 240.0     |
| y                 | 320.0     |
| dY                | 0.0       |
| z                 | 0.0       |
| dZ                | 0.0       |
| z Height          | 10.0      |
| Advanced          |           |
| Show in           | 2D and 3D |

|           |       |
|-----------|-------|
| Show name | false |
|-----------|-------|

## Check Box: displayNamesCheckbox

| Name                     | Value          |
|--------------------------|----------------|
| <b>General</b>           |                |
| Enabled                  | true           |
| Link                     | isShowingNames |
| Link                     | isShowingNames |
| Link To                  | true           |
| Label Text               | Display Names? |
| Public                   | true           |
| <b>Action</b>            |                |
| Action                   |                |
| <b>Position and size</b> |                |
| x                        | 10.0           |
| Width                    | 100.0          |
| y                        | 510.0          |
| Height                   | 30.0           |
| <b>Advanced</b>          |                |
| Font Size                | 11             |
| Font Name                | Dialog         |
| Show name                | false          |
| Embedded Icon            | false          |

## Text File: textFile

| Name            | Value        |
|-----------------|--------------|
| <b>General</b>  |              |
| File Mode       | Write/Append |
| Text File Name  | output.txt   |
| Text File Type  | File         |
| Show At Runtime | true         |
| Show name       | true         |

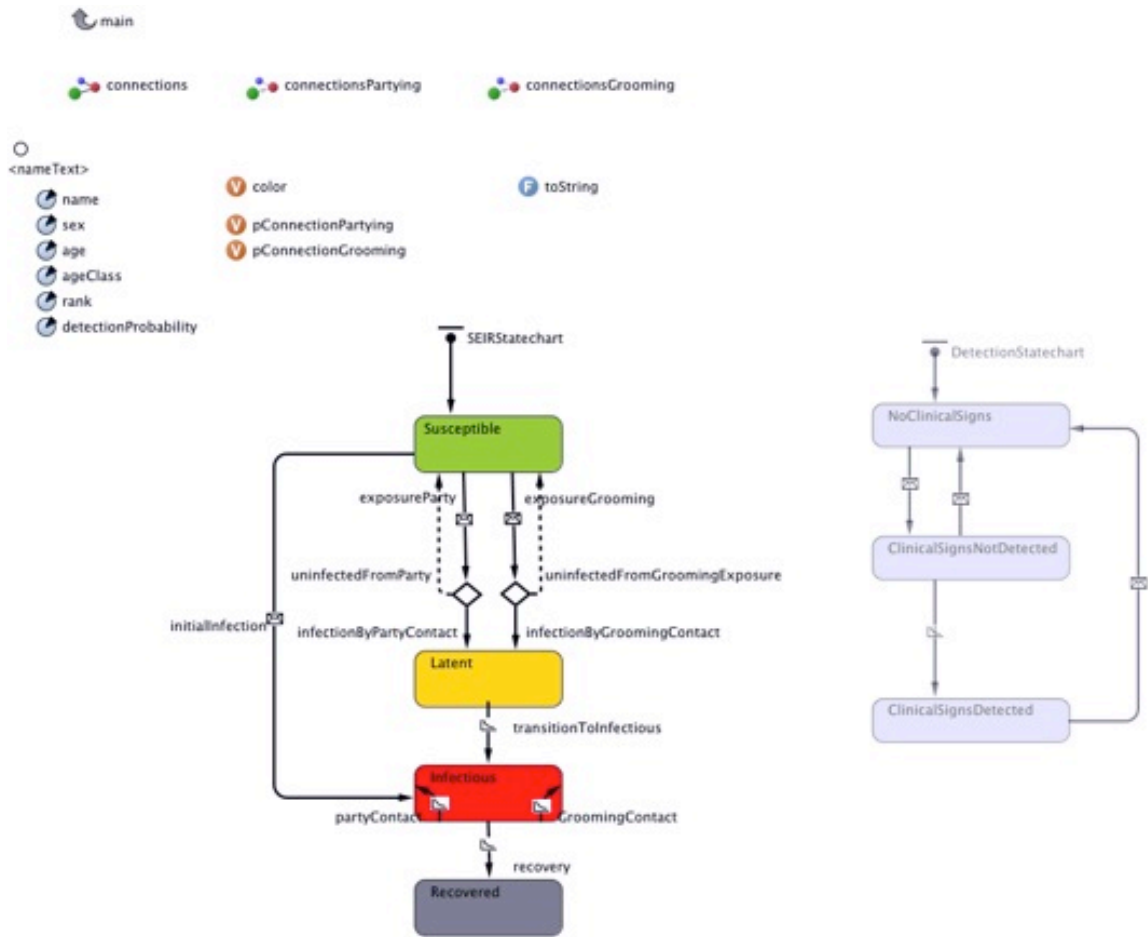
## Excel File: excelFile

| Name                      | Value     |
|---------------------------|-----------|
| <b>General</b>            |           |
| File name                 | Data.xlsx |
| Show At Runtime           | true      |
| Show name                 | true      |
| <b>Advanced</b>           |           |
| Load on model startup     | true      |
| Save on model termination | true      |

|                  |       |
|------------------|-------|
| Save In Snapshot | false |
|------------------|-------|

## Agent Type: Chimp

| Name                                | Value  |
|-------------------------------------|--|
| Agent in flowcharts                 |  |
| Use in flowcharts as                | Agent  |
| Movement                            |  |
| Speed                               | 10 / getScale().pixelsPerUnit(METER) / 86400 meters per second |
| Rotate animation towards movement   | true   |
| Rotate vertically as well (along Z- | false  |
| Space and network                   |  |
| Space Type                          | Continuous   |
| Advanced Java                       |  |
| Generic                             | false  |
| Advanced                            |  |
| Auto-create Datasets                | true   |
| Use model time                      | true   |
| Update time (absolute)              | 0 days   |
| Recurrence time                     | 1 days   |
| Limit the number of data samples    | false  |



## Parameter: name

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | String |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

## Parameter: sex

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | String |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

### Parameter: age

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | double |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

### Parameter: ageClass

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Array                 | false  |
| Type                  | String |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

### Parameter: rank

| Name    | Value |
|---------|-------|
| General |       |
| Array   | false |

|                       |        |
|-----------------------|--------|
| Type                  | String |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |        |
| Editor Control        | Text   |
| Advanced              |        |
| System dynamics units | false  |
| Save In Snapshot      | true   |

## Parameter: detectionProbability

| Name                  | Value  |
|-----------------------|--|
| General               |  |
| Array                 | false  |
| Type                  | double   |
| Show At Runtime       | true   |
| Show name             | true   |
| Value editor          |  |
| Editor Control        | Text   |
| Advanced              |  |
| System dynamics units | false  |
| Save In Snapshot      | true   |
| Description           |  |
| Description           | <p>Need to disable probabilityOfDetection in Main palette to incorporate chimp-specific probabilities.</p> <p>use probability of detection (probability of being seen by health system or probability of illness based on being seen?)</p> |

## Function: toString

| Name                  | Value         |
|-----------------------|---------------|
| General               |               |
| Return Type           | String        |
| Return type:          | Returns value |
| Show At Runtime       | true          |
| Show name             | true          |
| Function body         |               |
| Body                  | return name;  |
| Advanced              |               |
| Static                | false         |
| Access Type           | public        |
| System dynamics units | false         |

## Variable: color

| Name                  | Value  |
|-----------------------|--------|
| General               |        |
| Type                  | Color  |
| Show At Runtime       | true   |
| Show name             | true   |
| Advanced              |        |
| Access Type           | public |
| Static                | false  |
| Constant              | false  |
| Save In Snapshot      | true   |
| System dynamics units | false  |

### Variable: pConnectionPartying

| Name                  | Value                        |
|-----------------------|------------------------------|
| General               |                              |
| Initial Value         | new HashMap<Chimp, Double>() |
| Type                  | HashMap<Chimp, Double>       |
| Show At Runtime       | true                         |
| Show name             | true                         |
| Advanced              |                              |
| Access Type           | public                       |
| Static                | false                        |
| Constant              | false                        |
| Save In Snapshot      | true                         |
| System dynamics units | false                        |

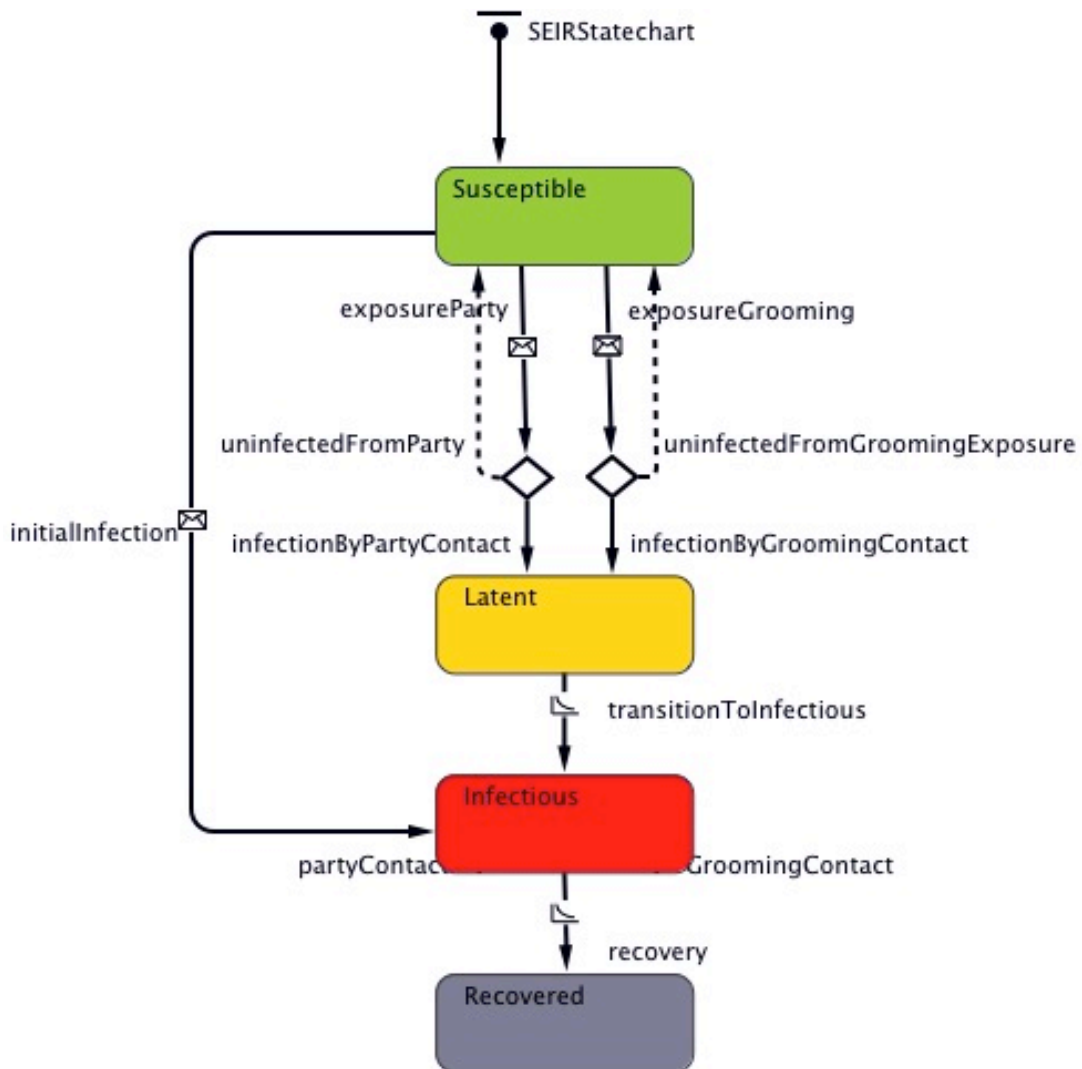
### Variable: pConnectionGrooming

| Name                  | Value                        |
|-----------------------|------------------------------|
| General               |                              |
| Initial Value         | new HashMap<Chimp, Double>() |
| Type                  | HashMap<Chimp, Double>       |
| Show At Runtime       | true                         |
| Show name             | true                         |
| Advanced              |                              |
| Access Type           | public                       |
| Static                | false                        |
| Constant              | false                        |
| Save In Snapshot      | true                         |
| System dynamics units | false                        |

### Statechart Entry Point: SEIRStatechart

| Name | Value |
|------|-------|
|------|-------|

| General         |      |
|-----------------|------|
| Show At Runtime | true |
| Show name       | true |



### Transition: exposureGrooming

| Name        | Value                  |
|-------------|------------------------|
| General     |                        |
| Equals      | "Exposed By Grooming!" |
| Filter Type | On particular message  |

|              |         |
|--------------|---------|
| Message Type | Object  |
| Trigger Type | Message |
| Show name    | true    |

### Transition: infectionByGroomingContact

| Name               | Value   |
|--------------------|---|
| General            |   |
| Condition          | randomTrue(main.groomingInfectionProbability) |
| Default Transition | false   |
| Show name          | true  |

### Transition: transitionToInfectious

| Name         | Value  |
|--------------|--|
| General      |  |
| Action       | this.main.cumInfectionCount++;<br>this.main.chimpTruthSickTracker.put(this, true); //flag this chimp as sick |
| Rate         | 1 / main.incubationPeriod per day  |
| Trigger Type | Rate   |
| Show name    | true   |

### Transition: recovery

| Name         | Value                                |
|--------------|--------------------------------------|
| General      |                                      |
| Action       | //traceln("infection subtracted");   |
| Rate         | 1 / main.durationOfInfection per day |
| Trigger Type | Rate                                 |
| Show name    | true                                 |

### Transition: partyContact

| Name         | Value   |
|--------------|---|
| General      |   |
| Action       | this.connectionsPartying.sendToAllConnected("Exposed By Partying!") |
| Rate         | main.partyContactRate per day                                       |
| Trigger Type | Rate  |
| Show name    | true  |

### Transition: GroomingContact

| Name         | Value   |
|--------------|---|
| General      |   |
| Action       | this.connectionsGrooming.sendToAllConnected("Exposed By Grooming!") |
| Rate         | main.groomingContactRate per day                                    |
| Trigger Type | Rate  |
| Show name    | true  |

## Transition: uninfectedFromGroomingExposure

| Name               | Value |
|--------------------|-------|
| General            |       |
| Default Transition | true  |
| Show name          | true  |

## Transition: initialInfection

| Name         | Value   |
|--------------|---|
| General      |   |
| Action       | this.main.cumInfectionCount++;<br>this.main.chimpTruthSickTracker.put(this, true);//flag this chimp as sick |
| Equals       | "Infect!"   |
| Filter Type  | On particular message   |
| Message Type | Object  |
| Trigger Type | Message   |
| Show name    | true  |

## Transition: exposureParty

| Name         | Value                  |
|--------------|------------------------|
| General      |                        |
| Equals       | "Exposed By Partying!" |
| Filter Type  | On particular message  |
| Message Type | Object                 |
| Trigger Type | Message                |
| Show name    | true                   |

## Transition: infectionByPartyContact

| Name               | Value                                      |
|--------------------|--|
| General            |  |
| Condition          | randomTrue(main.partyInfectionProbability) |
| Default Transition | false                                      |
| Show name          | true                                       |

## Transition: uninfectedFromParty

| Name               | Value |
|--------------------|-------|
| General            |       |
| Default Transition | true  |
| Show name          | true  |

## State: Susceptible

| Name         | Value          |
|--------------|----------------|
| General      |                |
| Entry Action | color = GREEN; |
| Fill Color   | yellowGreen    |
| Show name    | true           |

## State: Latent

| Name         | Value   |
|--------------|---|
| General      |   |
| Entry Action | color = ORANGE;<br>//traceIn("infection counted!"); |
| Fill Color   | gold  |
| Show name    | true  |

## State: Infectious

| Name         | Value        |
|--------------|--------------|
| General      |              |
| Entry Action | color = RED; |
| Fill Color   | red          |
| Show name    | true         |

## State: Recovered

| Name         | Value  |
|--------------|--|
| General      |  |
| Entry Action | color = BLACK;<br>this.receive("Feel better!") |
| Fill Color   | gray   |
| Show name    | true   |

## Branch: branch

| Name      | Value |
|-----------|-------|
| General   |       |
| Show name | false |

## Branch: branch1

| Name      | Value |
|-----------|-------|
| General   |       |
| Show name | false |

## Oval: oval

| Name                | Value     |
|---------------------|-----------|
| General             |           |
| Show At Runtime     | true      |
| Lock                | false     |
| Embedded Icon       | false     |
| Public              | true      |
| Appearance          |           |
| Fill Color          | white     |
| Dynamic: Fill Color | color     |
| Line Color          | black     |
| Dynamic: Line Color | color     |
| Line Width          | 1.0       |
| Line Style          | SOLID     |
| Position and size   |           |
| Circle              | true      |
| x                   | 0.0       |
| Radius X            | 5.0       |
| y                   | 0.0       |
| z                   | 0.0       |
| z Height            | 10.0      |
| Rotation            | 0.0       |
| Advanced            |           |
| Show in             | 2D and 3D |
| Show name           | false     |

## Text: nameText

| Name            | Value                                     |
|-----------------|---|
| General         |   |
| Show At Runtime | true                                      |
| Lock            | false                                     |
| Embedded Icon   | false                                     |
| Public          | true                                      |
| Text            |   |
| Dynamic: Text   | this.main.isShowingNames ? this.name : "" |
| Appearance      |   |

|                   |           |
|-------------------|-----------|
| Font Size         | 10        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | -10.0     |
| y                 | 10.0      |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show in           | 2D only   |
| Show name         | false     |

## Java Class: NamePair

| Name    | Value |
|---------|-------|
| General |       |

Text

```
/**
 * NamePair
 */
public class NamePair implements Serializable {

    String nameA;
    String nameB;

    /**
     * Constructor initializing the fields
     */
    public NamePair(String nameX, String nameY) {
        if (nameX.compareTo(nameY) <= 0) { //X first then Y
this.nameA = nameX;
            this.nameB = nameY;
        } else {
            this.nameA = nameY;
            this.nameB = nameX;
        }
    }

    @Override
    public int hashCode() {
        final int prime = 31;
        int result = 1;
        result = prime * result + ((nameA == null) ? 0 :
nameA.hashCode());
        result = prime * result + ((nameB == null) ? 0 :
nameB.hashCode());
        return result;
    }

    @Override
    public boolean equals(Object obj) {
        if (this == obj) {
            return true;
        }
        if (obj == null || this.getClass() != obj.getClass()){
            return false;
        }
        NamePair namePairObj = (NamePair)obj;
        return (this.nameA.equals(namePairObj.nameA)
            && this.nameB.equals(namePairObj.nameB));
    }

    @Override
    public String toString() {
        return
            "<" + nameA + "-" + nameB + ">";
    }

    /**
     * This number is here for model snapshot storing
purpose<br>
     * It needs to be changed when this class gets changed
     */
    private static final long serialVersionUID = 1L;
}
```

## Simulation Experiment: Simulation

| Name                                     | Value                                     |
|--|---|
| <b>General</b>                           |   |
| Maximum Available Memory                 | 256                                       |
| Agent Type                               | Main                                      |
| <b>Model time</b>                        |   |
| Execution Mode                           | Real time with scale                      |
| Real Time Scale                          | 1.0                                       |
| Use Calendar                             | false                                     |
| Stop Option                              | Stop at specified time                    |
| Initial Time                             | 0.0                                       |
| Final Time                               | 90.0                                      |
| <b>Randomness</b>                        |   |
| Random Number Generation Type            | Random seed (unique simulation runs)      |
| Selection Mode For Simultaneous Events   | LIFO (in the reverse order of scheduling) |
| <b>Window</b>                            |   |
| Real Time Of Simulation                  | false                                     |
| Model Date                               | true                                      |
| Title                                    | Gombe Chimp Respiratory Disease Model     |
| Width                                    | 1000.0                                    |
| Height                                   | 600.0                                     |
| Enable Panning                           | true                                      |
| Enable Zoom                              | true                                      |
| Maximized size                           | false                                     |
| Close confirmation                       | false                                     |
| <b>Advanced</b>                          |   |
| Enable Antialiasing                      | true                                      |
| Enable Enhanced Model Elements Animation | true                                      |
| Adaptive Frame Management                | true                                      |
| CPU Time Balance                         | 1 : 2                                     |
| Load Root From Snapshot                  | false                                     |

# Respiratory Disease Model

## Gombe National Park Chimpanzee Population

Run

Text: text

| Name              | Value                     |
|-------------------|---------------------------|
| General           |                           |
| Show At Runtime   | true                      |
| Lock              | false                     |
| Text              |                           |
| Text              | Respiratory Disease Model |
| Appearance        |                           |
| Bold Font Style   | true                      |
| Font Size         | 36                        |
| Font Name         | SansSerif                 |
| Color             | royalBlue                 |
| Alignment         | LEFT                      |
| Position and size |                           |
| x                 | 40.0                      |
| y                 | 30.0                      |
| z                 | 0.0                       |
| Rotation          | 0.0                       |

| Advanced  |       |
|-----------|-------|
| Show name | false |

## Text: text2

| Name              | Value                                     |
|-------------------|---|
| General           |   |
| Show At Runtime   | true                                      |
| Lock              | false                                     |
| Text              |   |
| Text              | Gombe National Park Chimpanzee Population |
| Appearance        |   |
| Font Size         | 24  |
| Font Name         | SansSerif                                 |
| Color             | black                                     |
| Alignment         | LEFT                                      |
| Position and size |   |
| x                 | 40.0                                      |
| y                 | 70.0                                      |
| z                 | 0.0                                       |
| Rotation          | 0.0                                       |
| Advanced          |   |
| Show name         | false                                     |

## Button: button

| Name              | Value   |
|-------------------|---|
| General           |   |
| Enabled           | true  |
| Dynamic: Label    | getState() == IDLE ?<br>"Run" :<br>"Top level agent"  |
| Label Text        | Run   |
| Action            |   |
| Action            | if ( getState() == IDLE )<br>run();<br>getPresentation().setPresentable( getEngine().getRoot() ); |
| Position and size |   |
| x                 | 60.0  |
| Width             | 100.0   |
| y                 | 380.0   |
| Height            | 30.0  |
| Advanced          |   |
| Font Size         | 11  |
| Font Name         | Dialog  |
| Show name         | false   |

## Optimization Experiment: Calibration\_dailyIncidence

| Name                                   | Value  |
|--|--|
| <b>General</b>                         |  |
| Maximum Available Memory               | 256  |
| Automatic Stop                         | false  |
| Iteration Count                        | 1000   |
| Stop After Iteration Count             | true   |
| Objective Function Code                | difference( root.currentCumInfectionCount, root.aug2007Outbreak )  |
| Objective                              | minimize   |
| Agent Type                             | Main   |
| <b>Model time</b>                      |  |
| Use Calendar                           | false  |
| Stop Option                            | Stop at specified time   |
| Initial Time                           | 0.0  |
| Final Time                             | 45.0   |
| <b>Randomness</b>                      |  |
| Random Number Generation Type          | Random seed (unique simulation runs)   |
| Selection Mode For Simultaneous Events | LIFO (in the reverse order of scheduling)  |
| <b>Replications</b>                    |  |
| Use Replications                       | true   |
| Fixed Replications Number              | true   |
| Replications Per Iteration             | 5  |
| <b>Window</b>                          |  |
| Experiment Progress                    | true   |
| Title                                  | Gombe Chimp Respiratory Disease Model1 : Calibration   |
| Width                                  | 1000.0   |
| Height                                 | 600.0  |
| Enable Panning                         | true   |
| Enable Zoom                            | true   |
| Maximized size                         | false  |
| Close confirmation                     | false  |
| <b>Java actions</b>                    |  |
| Before Each Experiment Run             | datasetCurrentObjective.reset();<br>datasetBestInfeasibleObjective.reset();<br>datasetBestFeasibleObjective.reset();   |
| After Simulation Run                   | dsCurrentFor_observable_1.reset();<br>observable_1.reset();<br>dsBestFeasibleFor_observable_1.reset();                 |
|  | observable_1.fillFrom( root.aug2007Outbreak );<br>dsCurrentFor_observable_1.fillFrom( root.currentCumInfectionCount ); |

```

After Iteration Code
if (isBestSolutionFeasible()) {
    datasetBestFeasibleObjective.update();
}
if (!isCurrentSolutionFeasible()) {
    bestInfeasibleObjective = min( bestInfeasibleObjective,
    getCurrentObjectiveValue() );
}
if (bestInfeasibleObjective != Double.POSITIVE_INFINITY) {
    datasetBestInfeasibleObjective.update();
}
if ( isBestSolutionFeasible() && isCurrentSolutionBest() ) {
    dsBestFeasibleFor_observable_1.fillFrom( dsCurrentFor
_observable_1 );
}

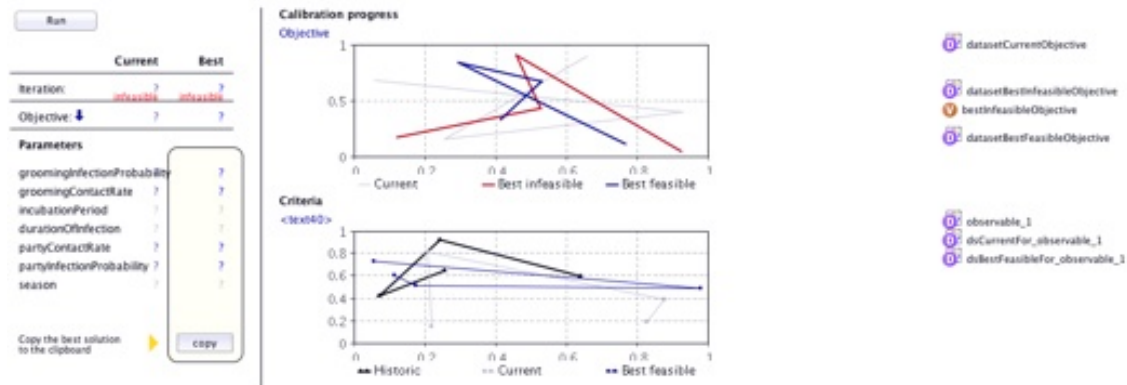
```

| Advanced                   |       |
|----------------------------|-------|
| Allow Parallel Evaluations | true  |
| Load Root From Snapshot    | false |

Optimization experiment parameters:

| Parameter                    | Type       | Value |      |      |         |
|------------------------------|------------|-------|------|------|---------|
|                              |            | Min   | Max  | Step | Initial |
| groomingInfectionProbability | CONTINUOUS | 0.3   | 0.6  |      |         |
| groomingContactRate          | CONTINUOUS | 0.5   | 0.99 |      |         |
| incubationPeriod             | FIXED      | 2     |      |      |         |
| durationOfInfection          | FIXED      | 3     |      |      |         |
| partyContactRate             | CONTINUOUS | 0.1   | 0.5  |      |         |
| partyInfectionProbability    | CONTINUOUS | 0.01  | 0.5  |      |         |
| season                       | FIXED      |       |      |      |         |

Gombe Chimp Respiratory Disease Model1 : Calibration



Variable: bestInfeasibleObjective

| Name                  | Value                    |
|-----------------------|--------------------------|
| General               |                          |
| Initial Value         | Double.POSITIVE_INFINITY |
| Type                  | double                   |
| Show At Runtime       | false                    |
| Show name             | true                     |
| Advanced              |                          |
| Access Type           | public                   |
| Static                | false                    |
| Constant              | false                    |
| Save In Snapshot      | true                     |
| System dynamics units | false                    |

## Plot: plot

| Name                         | Value    |
|------------------------------|----------|
| Data update                  |          |
| Analysis Auto Update         | false    |
| Dataset Samples To Keep      | 100      |
| Scale                        |          |
| Horizontal Scale             | Auto     |
| Vertical Scale               | Auto     |
| Appearance                   |          |
| Labels Horizontal Position   | DEFAULT  |
| Labels Vertical Position     | DEFAULT  |
| Labels Text Color            | darkGray |
| Chart Area Grid Color        | darkGray |
| Draw Line                    | true     |
| Interpolation                | Linear   |
| Position and size            |          |
| x                            | 330.0    |
| Width                        | 480.0    |
| y                            | 100.0    |
| Height                       | 180.0    |
| Legend                       |          |
| Show Legend                  | true     |
| Legend Size                  | 20.0     |
| Legend Text Color            | black    |
| Chart area                   |          |
| Chart Area: X Offset         | 80.0     |
| Chart Area: Width            | 380.0    |
| Chart Area: Y Offset         | 20.0     |
| Chart Area: Height           | 120.0    |
| Chart Area: Background Color | white    |
| Chart Area Border Color      | black    |

|           |       |
|-----------|-------|
| Advanced  |       |
| Show name | false |

### Plot Items:

| Title           | Type    | Dataset                        |              | Point | Color                | Line | Width | Interpolation |
|-----------------|---------|--------------------------------|--------------|-------|----------------------|------|-------|---------------|
|                 |         | X Axis Value                   | Y Axis Value |       |                      |      |       |               |
| Current         | dataset | datasetCurrentObjective        |              | NONE  | silver               | true | 1.0   | LINEAR        |
| Best infeasible | dataset | datasetBestInfeasibleObjective |              | NONE  | new Color(192, 0, 0) | true | 2.0   | LINEAR        |
| Best feasible   | dataset | datasetBestFeasibleObjective   |              | NONE  | navy                 | true | 2.0   | LINEAR        |

### Plot: plot1

| Name                       | Value    |
|----------------------------|----------|
| Data update                |          |
| Analysis Auto Update       | false    |
| Dataset Samples To Keep    | 100      |
| Scale                      |          |
| Horizontal Scale           | Auto     |
| Vertical Scale             | Auto     |
| Appearance                 |          |
| Labels Horizontal Position | DEFAULT  |
| Labels Vertical Position   | DEFAULT  |
| Labels Text Color          | darkGray |
| Chart Area Grid Color      | darkGray |
| Draw Line                  | true     |
| Interpolation              | Linear   |
| Position and size          |          |
| x                          | 330.0    |
| Width                      | 480.0    |
| y                          | 300.0    |
| Height                     | 180.0    |
| Legend                     |          |
| Show Legend                | true     |
| Legend Size                | 20.0     |
| Legend Text Color          | black    |

| Chart area                   |       |
|------------------------------|-------|
| Chart Area: X Offset         | 80.0  |
| Chart Area: Width            | 380.0 |
| Chart Area: Y Offset         | 20.0  |
| Chart Area: Height           | 120.0 |
| Chart Area: Background Color | white |
| Chart Area Border Color      | black |
| Advanced                     |       |
| Show name                    | false |

### Plot Items:

| Title         | Type    | Dataset                        |              | Point Style | Color  | Line | Width | Interpolation |
|---------------|---------|--------------------------------|--------------|-------------|--------|------|-------|---------------|
|               |         | X Axis Value                   | Y Axis Value |             |        |      |       |               |
| Historic      | dataset | observable_1                   |              | TRIANGLE    | black  | true | 2.0   | LINEAR        |
| Current       | dataset | dsCurrentFor_observable_1      |              | SQUARE      | silver | true | 1.0   | LINEAR        |
| Best feasible | dataset | dsBestFeasibleFor_observable_1 |              | CIRCLE      | navy   | true | 1.0   | LINEAR        |

### Data Set: datasetCurrentObjective

| Name                      | Value                      |
|---------------------------|----------------------------|
| General                   |                            |
| Dataset Samples To Keep   | 500                        |
| Axis Data Vertical Y Axis | getCurrentObjectiveValue() |
| Axis Data Freeze X Axis   | true                       |
| Show At Runtime           | false                      |
| Show name                 | true                       |
| Data update               |                            |
| Analysis Auto Update      | true                       |

### Data Set: datasetBestInfeasibleObjective

| Name                      | Value                   |
|---------------------------|-------------------------|
| General                   |                         |
| Dataset Samples To Keep   | 500                     |
| Axis Data Vertical Y Axis | bestInfeasibleObjective |
| Axis Data Freeze X Axis   | true                    |
| Show At Runtime           | false                   |
| Show name                 | true                    |
| Data update               |                         |
| Analysis Auto Update      | false                   |

### Data Set: datasetBestFeasibleObjective

| Name                      | Value                   |
|---------------------------|-------------------------|
| General                   |                         |
| Dataset Samples To Keep   | 500                     |
| Axis Data Vertical Y Axis | getBestObjectiveValue() |
| Axis Data Freeze X Axis   | true                    |
| Show At Runtime           | false                   |
| Show name                 | true                    |
| Data update               |                         |
| Analysis Auto Update      | false                   |

### Data Set: observable\_1

| Name                    | Value |
|-------------------------|-------|
| General                 |       |
| Dataset Samples To Keep | 1     |
| Axis Data Freeze X Axis | false |
| Show At Runtime         | false |
| Show name               | true  |
| Data update             |       |
| Analysis Auto Update    | false |

### Data Set: dsCurrentFor\_observable\_1

| Name                    | Value |
|-------------------------|-------|
| General                 |       |
| Dataset Samples To Keep | 1     |
| Axis Data Freeze X Axis | false |
| Show At Runtime         | false |
| Show name               | true  |
| Data update             |       |
| Analysis Auto Update    | false |

### Data Set: dsBestFeasibleFor\_observable\_1

| Name                    | Value |
|-------------------------|-------|
| General                 |       |
| Dataset Samples To Keep | 1     |
| Axis Data Freeze X Axis | false |
| Show At Runtime         | false |
| Show name               | true  |
| Data update             |       |
| Analysis Auto Update    | false |

Text: text

| Name              | Value  |
|-------------------|--|
| General           |  |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | Gombe Chimp Respiratory Disease Model1 : Calibration |
| Appearance        |  |
| Font Size         | 24   |
| Font Name         | SansSerif  |
| Color             | royalBlue  |
| Alignment         | LEFT   |
| Position and size |  |
| x                 | 40.0   |
| y                 | 30.0   |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text1

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Current   |
| Appearance        |           |
| Bold Font Style   | true      |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | RIGHT     |
| Position and size |           |
| x                 | 200.0     |
| y                 | 130.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text2

| Name    | Value |
|---------|-------|
| General |       |

|                   |           |
|-------------------|-----------|
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Best      |
| Appearance        |           |
| Bold Font Style   | true      |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | RIGHT     |
| Position and size |           |
| x                 | 270.0     |
| y                 | 130.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Line: line

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 40.0  |
| dX                | 240.0 |
| y                 | 150.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text3

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |

| Text              |            |
|-------------------|------------|
| Text              | Iteration: |
| Appearance        |            |
| Font Size         | 12         |
| Font Name         | SansSerif  |
| Color             | black      |
| Alignment         | LEFT       |
| Position and size |            |
| x                 | 50.0       |
| y                 | 160.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Text: text4

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format(getCurrentIteration())                        |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |
| y                 | 160.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text5

| Name             | Value   |
|------------------|---|
| General          |   |
| Dynamic: Visible | doesOptimizationExist() && getCurrentIteration() > 0<br>&& !isCurrentSolutionFeasible() |
| Show At Runtime  | true  |

|                   |            |
|-------------------|------------|
| Lock              | false      |
| Text              |            |
| Text              | infeasible |
| Appearance        |            |
| Font Size         | 10         |
| Font Name         | SansSerif  |
| Color             | red        |
| Alignment         | RIGHT      |
| Position and size |            |
| x                 | 200.0      |
| y                 | 170.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Text: text6

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | format(getBestIteration())                        |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | blue  |
| Alignment         | RIGHT   |
| Position and size |   |
| x                 | 270.0   |
| y                 | 160.0   |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text7

| Name             | Value   |
|------------------|---|
| General          |   |
| Dynamic: Visible | doesOptimizationExist() && getBestIteration() > 0<br>&& !isBestSolutionFeasible() |

|                   |            |
|-------------------|------------|
| Show At Runtime   | true       |
| Lock              | false      |
| Text              |            |
| Text              | infeasible |
| Appearance        |            |
| Font Size         | 10         |
| Font Name         | SansSerif  |
| Color             | red        |
| Alignment         | RIGHT      |
| Position and size |            |
| x                 | 270.0      |
| y                 | 170.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Line: line1

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 40.0  |
| dX                | 240.0 |
| y                 | 180.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text8

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Text            |       |

|                   |            |
|-------------------|------------|
| Text              | Objective: |
| Appearance        |            |
| Font Size         | 12         |
| Font Name         | SansSerif  |
| Color             | black      |
| Alignment         | LEFT       |
| Position and size |            |
| x                 | 50.0       |
| y                 | 190.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Text: text9

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format(getCurrentObjectiveValue())                   |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |
| y                 | 190.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text10

| Name             | Value   |
|------------------|---|
| General          |   |
| Dynamic: Visible | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime  | true  |
| Lock             | false   |
| Text             |   |

|                   |                                 |
|-------------------|---------------------------------|
| Text              | ?                               |
| Dynamic: Text     | format(getBestObjectiveValue()) |
| Appearance        |                                 |
| Font Size         | 12                              |
| Font Name         | SansSerif                       |
| Color             | blue                            |
| Alignment         | RIGHT                           |
| Position and size |                                 |
| x                 | 270.0                           |
| y                 | 190.0                           |
| z                 | 0.0                             |
| Rotation          | 0.0                             |
| Advanced          |                                 |
| Show name         | false                           |

## Line: line2

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 40.0  |
| dX                | 240.0 |
| y                 | 210.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Polyline: polyline

| Name            | Value    |
|-----------------|----------|
| General         |          |
| Polyline closed | true     |
| Show At Runtime | true     |
| Lock            | false    |
| Appearance      |          |
| Fill Color      | darkBlue |

|                   |       |
|-------------------|-------|
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 117.0 |
| y                 | 190.0 |
| z                 | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text11

| Name              | Value      |
|-------------------|------------|
| General           |            |
| Show At Runtime   | true       |
| Lock              | false      |
| Text              |            |
| Text              | Parameters |
| Appearance        |            |
| Bold Font Style   | true       |
| Font Size         | 12         |
| Font Name         | SansSerif  |
| Color             | black      |
| Alignment         | LEFT       |
| Position and size |            |
| x                 | 50.0       |
| y                 | 220.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Rounded Rectangle: roundRectangle

| Name              | Value       |
|-------------------|-------------|
| General           |             |
| Show At Runtime   | true        |
| Lock              | false       |
| Appearance        |             |
| Fill Color        | lightYellow |
| Line Color        | black       |
| Line Width        | 1.0         |
| Line Style        | SOLID       |
| Position and size |             |
| x                 | 210.0       |

|           |       |
|-----------|-------|
| Width     | 80.0  |
| y         | 230.0 |
| Height    | 230.0 |
| Rotation  | 0.0   |
| Radius    | 10.0  |
| Advanced  |       |
| Show name | false |

## Text: text12

| Name              | Value                        |
|-------------------|------------------------------|
| General           |                              |
| Show At Runtime   | true                         |
| Lock              | false                        |
| Text              |                              |
| Text              | groomingInfectionProbability |
| Appearance        |                              |
| Font Size         | 12                           |
| Font Name         | SansSerif                    |
| Color             | black                        |
| Alignment         | LEFT                         |
| Position and size |                              |
| x                 | 50.0                         |
| y                 | 250.0                        |
| z                 | 0.0                          |
| Rotation          | 0.0                          |
| Advanced          |                              |
| Show name         | false                        |

## Text: text13

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( groomingInfectionProbability )               |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |

|           |       |
|-----------|-------|
| x         | 200.0 |
| y         | 250.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text14

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0                  |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( getBestParamValue( _oqvar_groomingInfectionProbability ) ) |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | blue   |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 270.0  |
| y                 | 250.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text15

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | groomingContactRate |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |

|           |       |
|-----------|-------|
| x         | 50.0  |
| y         | 270.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text16

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( groomingContactRate )                        |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |
| y                 | 270.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text17

| Name             | Value   |
|------------------|---|
| General          |   |
| Dynamic: Visible | doesOptimizationExist() && getBestIteration() > 0         |
| Show At Runtime  | true  |
| Lock             | false   |
| Text             |   |
| Text             | ?   |
| Dynamic: Text    | format( getBestParamValue( _oqvar_groomingContactRate ) ) |
| Appearance       |   |
| Font Size        | 12  |
| Font Name        | SansSerif   |
| Color            | blue  |
| Alignment        | RIGHT   |

| Position and size |       |
|-------------------|-------|
| x                 | 270.0 |
| y                 | 270.0 |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |       |
| Show name         | false |

## Text: text18

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | incubationPeriod |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 50.0             |
| y                 | 290.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text19

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( incubationPeriod )                           |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | silver   |
| Alignment         | RIGHT  |
| Position and size |  |

|           |       |
|-----------|-------|
| x         | 200.0 |
| y         | 290.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text20

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | format( 0.0 )                                     |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | silver  |
| Alignment         | RIGHT   |
| Position and size |   |
| x                 | 270.0   |
| y                 | 290.0   |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text21

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | durationOfInfection |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 50.0                |

|           |       |
|-----------|-------|
| y         | 310.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text22

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( durationOfInfection )                        |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | silver   |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |
| y                 | 310.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text23

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | format( 0.0 )                                     |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | silver  |
| Alignment         | RIGHT   |
| Position and size |   |

|           |       |
|-----------|-------|
| x         | 270.0 |
| y         | 310.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text24

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | partyContactRate |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 50.0             |
| y                 | 330.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text25

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( partyContactRate )                           |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |

|           |       |
|-----------|-------|
| y         | 330.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text26

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0      |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( getBestParamValue( _oqvar_partyContactRate ) ) |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | blue   |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 270.0  |
| y                 | 330.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text27

| Name              | Value                     |
|-------------------|---------------------------|
| General           |                           |
| Show At Runtime   | true                      |
| Lock              | false                     |
| Text              |                           |
| Text              | partyInfectionProbability |
| Appearance        |                           |
| Font Size         | 12                        |
| Font Name         | SansSerif                 |
| Color             | black                     |
| Alignment         | LEFT                      |
| Position and size |                           |
| x                 | 50.0                      |
| y                 | 350.0                     |

|           |       |
|-----------|-------|
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text28

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( partyInfectionProbability )                  |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |
| y                 | 350.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text29

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0               |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | format( getBestParamValue( _oqvar_partyInfectionProbability ) ) |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | blue  |
| Alignment         | RIGHT   |
| Position and size |   |
| x                 | 270.0   |

|           |       |
|-----------|-------|
| y         | 350.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text30

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | season    |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 50.0      |
| y                 | 370.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text31

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | String.valueOf( season )                             |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | silver   |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |
| y                 | 370.0  |

|           |       |
|-----------|-------|
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text32

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | String.valueOf( "Quarter3" )                      |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | silver  |
| Alignment         | RIGHT   |
| Position and size |   |
| x                 | 270.0   |
| y                 | 370.0   |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text36

| Name              | Value                                      |
|-------------------|--|
| General           |  |
| Show At Runtime   | true                                       |
| Lock              | false                                      |
| Text              |  |
| Text              | Copy the best solution<br>to the clipboard |
| Appearance        |  |
| Font Size         | 10   |
| Font Name         | SansSerif                                  |
| Color             | black                                      |
| Alignment         | LEFT                                       |
| Position and size |  |
| x                 | 50.0                                       |
| y                 | 430.0                                      |

|           |       |
|-----------|-------|
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Polyline: polyline1

| Name              | Value |
|-------------------|-------|
| General           |       |
| Polyline closed   | true  |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Fill Color        | gold  |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 190.0 |
| y                 | 430.0 |
| z                 | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text37

| Name              | Value                |
|-------------------|----------------------|
| General           |                      |
| Show At Runtime   | true                 |
| Lock              | false                |
| Text              |                      |
| Text              | Calibration progress |
| Appearance        |                      |
| Bold Font Style   | true                 |
| Font Size         | 12                   |
| Font Name         | SansSerif            |
| Color             | black                |
| Alignment         | LEFT                 |
| Position and size |                      |
| x                 | 330.0                |
| y                 | 80.0                 |
| z                 | 0.0                  |
| Rotation          | 0.0                  |
| Advanced          |                      |
| Show name         | false                |

## Text: text38

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Objective |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | darkBlue  |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 330.0     |
| y                 | 100.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text39

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Criteria  |
| Appearance        |           |
| Bold Font Style   | true      |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 330.0     |
| y                 | 280.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text40

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | darkBlue  |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 330.0     |
| y                 | 300.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

### Line: line3

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 310.0 |
| dX                | 0.0   |
| y                 | 80.0  |
| dY                | 410.0 |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

### Button: button

| Name            | Value              |
|-----------------|--------------------|
| General         |                    |
| Dynamic: Enable | getState() == IDLE |
| Enabled         | true               |
| Label Text      | Run                |

| Action            |        |
|-------------------|--------|
| Action            | run(); |
| Position and size |        |
| x                 | 40.0   |
| Width             | 100.0  |
| y                 | 80.0   |
| Height            | 30.0   |
| Advanced          |        |
| Font Size         | 11     |
| Font Name         | Dialog |
| Show name         | false  |

## Button: button1

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Enable   | doesOptimizationExist() && getCurrentIteration() > 0  |
| Enabled           | true  |
| Label Text        | copy  |
| Action            |   |
| Action            | <pre>String s = ""; s += "groomingInfectionProbability\t" + format( getBestParamValue( _oqvar_groomingInfectionProbability ) ) + "\n"; s += "groomingContactRate\t" + format( getBestParamValue( _oqvar_groomingContactRate ) ) + "\n"; s += "incubationPeriod\t" + format( 0.0 ) + "\n"; s += "durationOfInfection\t" + format( 0.0 ) + "\n"; s += "partyContactRate\t" + format( getBestParamValue( _oqvar_partyContactRate ) ) + "\n"; s += "partyInfectionProbability\t" + format( getBestParamValue( _oqvar_partyInfectionProbability ) ) + "\n"; s += "season\t" + String.valueOf( "Quarter3" ) + "\n"; s += "probabilityOfDetection\t" + format( 0.0 ) + "\n";</pre> |
| Position and size |   |
| x                 | 220.0   |
| Width             | 60.0  |
| y                 | 430.0   |
| Height            | 20.0  |
| Advanced          |   |
| Font Size         | 11  |
| Font Name         | Dialog  |
| Show name         | false   |

## Optimization Experiment: Calibration\_cumIncidence

| Name    | Value |
|---------|-------|
| General |       |

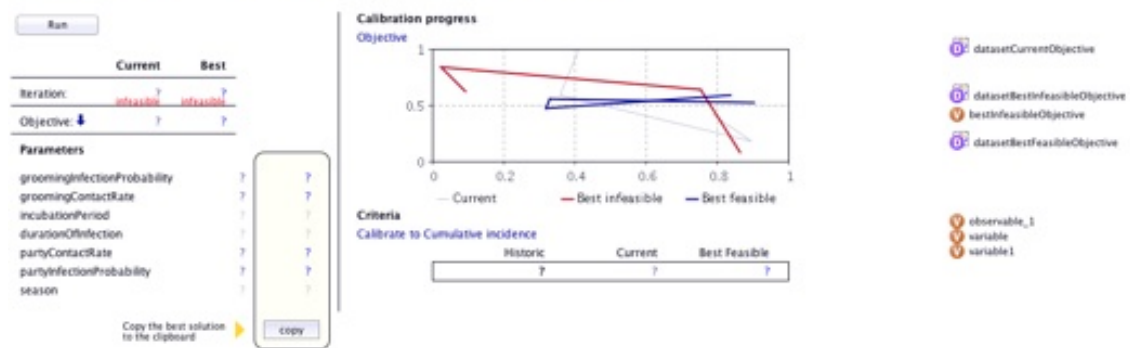
|  |   |
|--|---|
| Maximum Available Memory               | 256   |
| Automatic Stop                         | false   |
| Iteration Count                        | 1000  |
| Stop After Iteration Count             | true  |
| Objective Function Code                | abs( (root.cumInfectionCount) - (25) )  |
| Objective                              | minimize  |
| Agent Type                             | Main  |
| <b>Model time</b>                      |   |
| Use Calendar                           | false   |
| Stop Option                            | Stop at specified time  |
| Initial Time                           | 0.0   |
| Final Time                             | 45.0  |
| <b>Randomness</b>                      |   |
| Random Number Generation Type          | Random seed (unique simulation runs)  |
| Selection Mode For Simultaneous Events | LIFO (in the reverse order of scheduling)   |
| <b>Replications</b>                    |   |
| Use Replications                       | true  |
| Fixed Replications Number              | true  |
| Replications Per Iteration             | 5   |
| <b>Window</b>                          |   |
| Experiment Progress                    | true  |
| Title                                  | Gombe Chimp Respiratory Disease Model2 : Calibration2   |
| Width                                  | 1000.0  |
| Height                                 | 600.0   |
| Enable Panning                         | true  |
| Enable Zoom                            | true  |
| Maximized size                         | false   |
| Close confirmation                     | false   |
| <b>Java actions</b>                    |   |
| Before Each Experiment Run             | datasetCurrentObjective.reset();<br>datasetBestInfeasibleObjective.reset();<br>datasetBestFeasibleObjective.reset();  |
| After Simulation Run                   | observable_1 = 25;<br>variable = root.cumInfectionCount;  |
| After Iteration Code                   | if (isBestSolutionFeasible()) {<br>datasetBestFeasibleObjective.update();<br>}<br>if (!isCurrentSolutionFeasible()) {<br>bestInfeasibleObjective = min( bestInfeasibleObjective,<br>getCurrentObjectiveValue() );<br>}<br>if (bestInfeasibleObjective != Double.POSITIVE_INFINITY) {<br>datasetBestInfeasibleObjective.update();<br>}<br>if( isBestSolutionFeasible() && isCurrentSolutionBest() ) {<br>variable1 = variable;<br>}<br>} |
| <b>Advanced</b>                        |   |

|                            |       |
|----------------------------|-------|
| Allow Parallel Evaluations | true  |
| Load Root From Snapshot    | false |

### Optimization experiment parameters:

| Parameter                    | Type       | Value |      |      |         |
|------------------------------|------------|-------|------|------|---------|
|                              |            | Min   | Max  | Step | Initial |
| groomingInfectionProbability | CONTINUOUS | 0.3   | 0.6  |      |         |
| groomingContactRate          | CONTINUOUS | 0.5   | 0.99 |      |         |
| incubationPeriod             | FIXED      | 1     |      |      |         |
| durationOfInfection          | FIXED      | 4     |      |      |         |
| partyContactRate             | CONTINUOUS | 0.1   | 0.5  |      |         |
| partyInfectionProbability    | CONTINUOUS | 0.01  | 0.3  |      |         |
| season                       | FIXED      |       |      |      |         |

### Gombe Chimp Respiratory Disease Model2 : Calibration2



### Variable: bestInfeasibleObjective

| Name             | Value                    |
|------------------|--------------------------|
| General          |                          |
| Initial Value    | Double.POSITIVE_INFINITY |
| Type             | double                   |
| Show At Runtime  | false                    |
| Show name        | true                     |
| Advanced         |                          |
| Access Type      | public                   |
| Static           | false                    |
| Constant         | false                    |
| Save In Snapshot | true                     |

|                       |       |
|-----------------------|-------|
| System dynamics units | false |
|-----------------------|-------|

## Variable: observable\_1

| Name                  | Value      |
|-----------------------|------------|
| General               |            |
| Initial Value         | Double.NaN |
| Type                  | double     |
| Show At Runtime       | false      |
| Show name             | true       |
| Advanced              |            |
| Access Type           | public     |
| Static                | false      |
| Constant              | false      |
| Save In Snapshot      | true       |
| System dynamics units | false      |

## Variable: variable

| Name                  | Value      |
|-----------------------|------------|
| General               |            |
| Initial Value         | Double.NaN |
| Type                  | double     |
| Show At Runtime       | false      |
| Show name             | true       |
| Advanced              |            |
| Access Type           | public     |
| Static                | false      |
| Constant              | false      |
| Save In Snapshot      | true       |
| System dynamics units | false      |

## Variable: variable1

| Name             | Value      |
|------------------|------------|
| General          |            |
| Initial Value    | Double.NaN |
| Type             | double     |
| Show At Runtime  | false      |
| Show name        | true       |
| Advanced         |            |
| Access Type      | public     |
| Static           | false      |
| Constant         | false      |
| Save In Snapshot | true       |

|                       |       |
|-----------------------|-------|
| System dynamics units | false |
|-----------------------|-------|

## Plot: plot

| Name                         | Value    |
|------------------------------|----------|
| <b>Data update</b>           |          |
| Analysis Auto Update         | false    |
| Dataset Samples To Keep      | 100      |
| <b>Scale</b>                 |          |
| Horizontal Scale             | Auto     |
| Vertical Scale               | Auto     |
| <b>Appearance</b>            |          |
| Labels Horizontal Position   | DEFAULT  |
| Labels Vertical Position     | DEFAULT  |
| Labels Text Color            | darkGray |
| Chart Area Grid Color        | darkGray |
| Draw Line                    | true     |
| Interpolation                | Linear   |
| <b>Position and size</b>     |          |
| x                            | 410.0    |
| Width                        | 480.0    |
| y                            | 100.0    |
| Height                       | 190.0    |
| <b>Legend</b>                |          |
| Show Legend                  | true     |
| Legend Size                  | 20.0     |
| Legend Text Color            | black    |
| <b>Chart area</b>            |          |
| Chart Area: X Offset         | 80.0     |
| Chart Area: Width            | 380.0    |
| Chart Area: Y Offset         | 20.0     |
| Chart Area: Height           | 120.0    |
| Chart Area: Background Color | white    |
| Chart Area Border Color      | black    |
| <b>Advanced</b>              |          |
| Show name                    | false    |

Plot Items:

| Title   | Type    | Dataset                        |              | Point | Color          | Line | Width | Interpolation |
|---------|---------|--------------------------------|--------------|-------|----------------|------|-------|---------------|
|         |         | X Axis Value                   | Y Axis Value |       |                |      |       |               |
| Current | dataset | datasetCurrentObjective        |              | NONE  | silver         | true | 1.0   | LINEAR        |
| Best    | dataset | datasetBestInfeasibleObjective |              | NONE  | new Color(192, | true | 2.0   | LINEAR        |
| Best    | dataset | datasetBestFeasibleObjective   |              | NONE  | navy           | true | 2.0   | LINEAR        |

Data Set: datasetCurrentObjective

| Name                      | Value                      |
|---------------------------|----------------------------|
| General                   |                            |
| Dataset Samples To Keep   | 500                        |
| Axis Data Vertical Y Axis | getCurrentObjectiveValue() |
| Axis Data Freeze X Axis   | true                       |
| Show At Runtime           | false                      |
| Show name                 | true                       |
| Data update               |                            |
| Analysis Auto Update      | true                       |

Data Set: datasetBestInfeasibleObjective

| Name                      | Value                   |
|---------------------------|-------------------------|
| General                   |                         |
| Dataset Samples To Keep   | 500                     |
| Axis Data Vertical Y Axis | bestInfeasibleObjective |
| Axis Data Freeze X Axis   | true                    |
| Show At Runtime           | false                   |
| Show name                 | true                    |
| Data update               |                         |
| Analysis Auto Update      | false                   |

Data Set: datasetBestFeasibleObjective

| Name                      | Value                   |
|---------------------------|-------------------------|
| General                   |                         |
| Dataset Samples To Keep   | 500                     |
| Axis Data Vertical Y Axis | getBestObjectiveValue() |
| Axis Data Freeze X Axis   | true                    |
| Show At Runtime           | false                   |
| Show name                 | true                    |
| Data update               |                         |
| Analysis Auto Update      | false                   |

Text: text

| Name              | Value   |
|-------------------|---|
| General           |   |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | Gombe Chimp Respiratory Disease Model2 : Calibration2 |
| Appearance        |   |
| Font Size         | 24  |
| Font Name         | SansSerif   |
| Color             | royalBlue   |
| Alignment         | LEFT  |
| Position and size |   |
| x                 | 40.0  |
| y                 | 30.0  |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text1

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Current   |
| Appearance        |           |
| Bold Font Style   | true      |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | RIGHT     |
| Position and size |           |
| x                 | 200.0     |
| y                 | 130.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text2

| Name    | Value |
|---------|-------|
| General |       |

|                   |           |
|-------------------|-----------|
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Best      |
| Appearance        |           |
| Bold Font Style   | true      |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | RIGHT     |
| Position and size |           |
| x                 | 270.0     |
| y                 | 130.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Line: line

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 40.0  |
| dX                | 240.0 |
| y                 | 150.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text3

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |

| Text              |            |
|-------------------|------------|
| Text              | Iteration: |
| Appearance        |            |
| Font Size         | 12         |
| Font Name         | SansSerif  |
| Color             | black      |
| Alignment         | LEFT       |
| Position and size |            |
| x                 | 50.0       |
| y                 | 160.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Text: text4

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format(getCurrentIteration())                        |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |
| y                 | 160.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text5

| Name             | Value   |
|------------------|---|
| General          |   |
| Dynamic: Visible | doesOptimizationExist() && getCurrentIteration() > 0<br>&& !isCurrentSolutionFeasible() |
| Show At Runtime  | true  |

|                   |            |
|-------------------|------------|
| Lock              | false      |
| Text              |            |
| Text              | infeasible |
| Appearance        |            |
| Font Size         | 10         |
| Font Name         | SansSerif  |
| Color             | red        |
| Alignment         | RIGHT      |
| Position and size |            |
| x                 | 200.0      |
| y                 | 170.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Text: text6

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | format(getBestIteration())                        |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | blue  |
| Alignment         | RIGHT   |
| Position and size |   |
| x                 | 270.0   |
| y                 | 160.0   |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text7

| Name             | Value  |
|------------------|--|
| General          |  |
| Dynamic: Visible | doesOptimizationExist() && getBestIteration() > 0 && !isBestSolutionFeasible() |

|                   |            |
|-------------------|------------|
| Show At Runtime   | true       |
| Lock              | false      |
| Text              |            |
| Text              | infeasible |
| Appearance        |            |
| Font Size         | 10         |
| Font Name         | SansSerif  |
| Color             | red        |
| Alignment         | RIGHT      |
| Position and size |            |
| x                 | 270.0      |
| y                 | 170.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Line: line1

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 40.0  |
| dX                | 240.0 |
| y                 | 180.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text8

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Text            |       |

|                   |            |
|-------------------|------------|
| Text              | Objective: |
| Appearance        |            |
| Font Size         | 12         |
| Font Name         | SansSerif  |
| Color             | black      |
| Alignment         | LEFT       |
| Position and size |            |
| x                 | 50.0       |
| y                 | 190.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Text: text9

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format(getCurrentObjectiveValue())                   |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 200.0  |
| y                 | 190.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text10

| Name             | Value   |
|------------------|---|
| General          |   |
| Dynamic: Visible | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime  | true  |
| Lock             | false   |
| Text             |   |

|                   |                                 |
|-------------------|---------------------------------|
| Text              | ?                               |
| Dynamic: Text     | format(getBestObjectiveValue()) |
| Appearance        |                                 |
| Font Size         | 12                              |
| Font Name         | SansSerif                       |
| Color             | blue                            |
| Alignment         | RIGHT                           |
| Position and size |                                 |
| x                 | 270.0                           |
| y                 | 190.0                           |
| z                 | 0.0                             |
| Rotation          | 0.0                             |
| Advanced          |                                 |
| Show name         | false                           |

## Line: line2

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 40.0  |
| dX                | 240.0 |
| y                 | 210.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Polyline: polyline

| Name            | Value    |
|-----------------|----------|
| General         |          |
| Polyline closed | true     |
| Show At Runtime | true     |
| Lock            | false    |
| Appearance      |          |
| Fill Color      | darkBlue |

|                   |       |
|-------------------|-------|
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 117.0 |
| y                 | 190.0 |
| z                 | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text11

| Name              | Value      |
|-------------------|------------|
| General           |            |
| Show At Runtime   | true       |
| Lock              | false      |
| Text              |            |
| Text              | Parameters |
| Appearance        |            |
| Bold Font Style   | true       |
| Font Size         | 12         |
| Font Name         | SansSerif  |
| Color             | black      |
| Alignment         | LEFT       |
| Position and size |            |
| x                 | 50.0       |
| y                 | 220.0      |
| z                 | 0.0        |
| Rotation          | 0.0        |
| Advanced          |            |
| Show name         | false      |

## Rounded Rectangle: roundRectangle

| Name              | Value       |
|-------------------|-------------|
| General           |             |
| Show At Runtime   | true        |
| Lock              | false       |
| Appearance        |             |
| Fill Color        | lightYellow |
| Line Color        | black       |
| Line Width        | 1.0         |
| Line Style        | SOLID       |
| Position and size |             |
| x                 | 300.0       |

|           |       |
|-----------|-------|
| Width     | 80.0  |
| y         | 230.0 |
| Height    | 210.0 |
| Rotation  | 0.0   |
| Radius    | 10.0  |
| Advanced  |       |
| Show name | false |

## Text: text12

| Name              | Value                        |
|-------------------|------------------------------|
| General           |                              |
| Show At Runtime   | true                         |
| Lock              | false                        |
| Text              |                              |
| Text              | groomingInfectionProbability |
| Appearance        |                              |
| Font Size         | 12                           |
| Font Name         | SansSerif                    |
| Color             | black                        |
| Alignment         | LEFT                         |
| Position and size |                              |
| x                 | 50.0                         |
| y                 | 250.0                        |
| z                 | 0.0                          |
| Rotation          | 0.0                          |
| Advanced          |                              |
| Show name         | false                        |

## Text: text13

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( groomingInfectionProbability )               |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |

|           |       |
|-----------|-------|
| x         | 290.0 |
| y         | 250.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text14

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0                  |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( getBestParamValue( _oqvar_groomingInfectionProbability ) ) |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | blue   |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 360.0  |
| y                 | 250.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text15

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | groomingContactRate |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |

|           |       |
|-----------|-------|
| x         | 50.0  |
| y         | 270.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text16

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( groomingContactRate )                        |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 290.0  |
| y                 | 270.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text17

| Name             | Value   |
|------------------|---|
| General          |   |
| Dynamic: Visible | doesOptimizationExist() && getBestIteration() > 0         |
| Show At Runtime  | true  |
| Lock             | false   |
| Text             |   |
| Text             | ?   |
| Dynamic: Text    | format( getBestParamValue( _oqvar_groomingContactRate ) ) |
| Appearance       |   |
| Font Size        | 12  |
| Font Name        | SansSerif   |
| Color            | blue  |
| Alignment        | RIGHT   |

| Position and size |       |
|-------------------|-------|
| x                 | 360.0 |
| y                 | 270.0 |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |       |
| Show name         | false |

## Text: text18

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | incubationPeriod |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 50.0             |
| y                 | 290.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text19

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( incubationPeriod )                           |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | silver   |
| Alignment         | RIGHT  |
| Position and size |  |

|           |       |
|-----------|-------|
| x         | 290.0 |
| y         | 290.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text20

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | format( 0.0 )                                     |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | silver  |
| Alignment         | RIGHT   |
| Position and size |   |
| x                 | 360.0   |
| y                 | 290.0   |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text21

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | durationOfInfection |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 50.0                |

|           |       |
|-----------|-------|
| y         | 310.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text22

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( durationOfInfection )                        |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | silver   |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 290.0  |
| y                 | 310.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text23

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | format( 0.0 )                                     |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | silver  |
| Alignment         | RIGHT   |
| Position and size |   |

|           |       |
|-----------|-------|
| x         | 360.0 |
| y         | 310.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text24

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | partyContactRate |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 50.0             |
| y                 | 330.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text25

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( partyContactRate )                           |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 290.0  |

|           |       |
|-----------|-------|
| y         | 330.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text26

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0      |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( getBestParamValue( _oqvar_partyContactRate ) ) |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | blue   |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 360.0  |
| y                 | 330.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text27

| Name              | Value                     |
|-------------------|---------------------------|
| General           |                           |
| Show At Runtime   | true                      |
| Lock              | false                     |
| Text              |                           |
| Text              | partyInfectionProbability |
| Appearance        |                           |
| Font Size         | 12                        |
| Font Name         | SansSerif                 |
| Color             | black                     |
| Alignment         | LEFT                      |
| Position and size |                           |
| x                 | 50.0                      |
| y                 | 350.0                     |

|           |       |
|-----------|-------|
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text28

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | format( partyInfectionProbability )                  |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | darkSlateBlue  |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 290.0  |
| y                 | 350.0  |
| z                 | 0.0  |
| Rotation          | 0.0  |
| Advanced          |  |
| Show name         | false  |

## Text: text29

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0               |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | format( getBestParamValue( _oqvar_partyInfectionProbability ) ) |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | blue  |
| Alignment         | RIGHT   |
| Position and size |   |
| x                 | 360.0   |

|           |       |
|-----------|-------|
| y         | 350.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text30

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | season    |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 50.0      |
| y                 | 370.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text31

| Name              | Value  |
|-------------------|--|
| General           |  |
| Dynamic: Visible  | doesOptimizationExist() && getCurrentIteration() > 0 |
| Show At Runtime   | true   |
| Lock              | false  |
| Text              |  |
| Text              | ?  |
| Dynamic: Text     | String.valueOf( season )                             |
| Appearance        |  |
| Font Size         | 12   |
| Font Name         | SansSerif  |
| Color             | silver   |
| Alignment         | RIGHT  |
| Position and size |  |
| x                 | 290.0  |
| y                 | 370.0  |

|           |       |
|-----------|-------|
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text32

| Name              | Value   |
|-------------------|---|
| General           |   |
| Dynamic: Visible  | doesOptimizationExist() && getBestIteration() > 0 |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | ?   |
| Dynamic: Text     | String.valueOf( "Quarter3" )                      |
| Appearance        |   |
| Font Size         | 12  |
| Font Name         | SansSerif   |
| Color             | silver  |
| Alignment         | RIGHT   |
| Position and size |   |
| x                 | 360.0   |
| y                 | 370.0   |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text33

| Name              | Value                                      |
|-------------------|--|
| General           |  |
| Show At Runtime   | true                                       |
| Lock              | false                                      |
| Text              |  |
| Text              | Copy the best solution<br>to the clipboard |
| Appearance        |  |
| Font Size         | 10   |
| Font Name         | SansSerif                                  |
| Color             | black                                      |
| Alignment         | LEFT                                       |
| Position and size |  |
| x                 | 160.0                                      |
| y                 | 410.0                                      |

|           |       |
|-----------|-------|
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Polyline: polyline1

| Name              | Value |
|-------------------|-------|
| General           |       |
| Polyline closed   | true  |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Fill Color        | gold  |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 280.0 |
| y                 | 410.0 |
| z                 | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text34

| Name              | Value                |
|-------------------|----------------------|
| General           |                      |
| Show At Runtime   | true                 |
| Lock              | false                |
| Text              |                      |
| Text              | Calibration progress |
| Appearance        |                      |
| Bold Font Style   | true                 |
| Font Size         | 12                   |
| Font Name         | SansSerif            |
| Color             | black                |
| Alignment         | LEFT                 |
| Position and size |                      |
| x                 | 410.0                |
| y                 | 80.0                 |
| z                 | 0.0                  |
| Rotation          | 0.0                  |
| Advanced          |                      |
| Show name         | false                |

## Text: text35

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Objective |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | darkBlue  |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 410.0     |
| y                 | 100.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text36

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Criteria  |
| Appearance        |           |
| Bold Font Style   | true      |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 410.0     |
| y                 | 290.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text37

| Name              | Value                             |
|-------------------|-----------------------------------|
| General           |                                   |
| Show At Runtime   | true                              |
| Lock              | false                             |
| Text              |                                   |
| Text              | Calibrate to Cumulative incidence |
| Appearance        |                                   |
| Font Size         | 12                                |
| Font Name         | SansSerif                         |
| Color             | darkBlue                          |
| Alignment         | LEFT                              |
| Position and size |                                   |
| x                 | 410.0                             |
| y                 | 310.0                             |
| z                 | 0.0                               |
| Rotation          | 0.0                               |
| Advanced          |                                   |
| Show name         | false                             |

## Text: text38

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Historic  |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | RIGHT     |
| Position and size |           |
| x                 | 610.0     |
| y                 | 330.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text39

| Name    | Value |
|---------|-------|
| General |       |

|                   |           |
|-------------------|-----------|
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Current   |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | RIGHT     |
| Position and size |           |
| x                 | 730.0     |
| y                 | 330.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text40

| Name              | Value         |
|-------------------|---------------|
| General           |               |
| Show At Runtime   | true          |
| Lock              | false         |
| Text              |               |
| Text              | Best Feasible |
| Appearance        |               |
| Font Size         | 12            |
| Font Name         | SansSerif     |
| Color             | black         |
| Alignment         | RIGHT         |
| Position and size |               |
| x                 | 850.0         |
| y                 | 330.0         |
| z                 | 0.0           |
| Rotation          | 0.0           |
| Advanced          |               |
| Show name         | false         |

## Text: text41

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Text            |       |

|                   |                        |
|-------------------|------------------------|
| Text              | ?                      |
| Dynamic: Text     | format( observable_1 ) |
| Appearance        |                        |
| Bold Font Style   | true                   |
| Font Size         | 12                     |
| Font Name         | SansSerif              |
| Color             | black                  |
| Alignment         | RIGHT                  |
| Position and size |                        |
| x                 | 610.0                  |
| y                 | 350.0                  |
| z                 | 0.0                    |
| Rotation          | 0.0                    |
| Advanced          |                        |
| Show name         | false                  |

## Text: text42

| Name              | Value              |
|-------------------|--------------------|
| General           |                    |
| Show At Runtime   | true               |
| Lock              | false              |
| Text              |                    |
| Text              | ?                  |
| Dynamic: Text     | format( variable ) |
| Appearance        |                    |
| Font Size         | 12                 |
| Font Name         | SansSerif          |
| Color             | darkSlateBlue      |
| Alignment         | RIGHT              |
| Position and size |                    |
| x                 | 730.0              |
| y                 | 350.0              |
| z                 | 0.0                |
| Rotation          | 0.0                |
| Advanced          |                    |
| Show name         | false              |

## Text: text43

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Text            |       |

|                   |                     |
|-------------------|---------------------|
| Text              | ?                   |
| Dynamic: Text     | format( variable1 ) |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | blue                |
| Alignment         | RIGHT               |
| Position and size |                     |
| x                 | 850.0               |
| y                 | 350.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Rectangle: rectangle

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 490.0 |
| Width             | 380.0 |
| y                 | 347.0 |
| Height            | 20.0  |
| z                 | 0.0   |
| z Height          | 10.0  |
| Rotation          | 0.0   |
| Advanced          |       |
| Show name         | false |

## Line: line3

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Appearance      |       |
| Line Color      | black |
| Line Width      | 1.0   |

|                   |       |
|-------------------|-------|
| Line Style        | SOLID |
| Position and size |       |
| x                 | 390.0 |
| dX                | 0.0   |
| y                 | 80.0  |
| dY                | 320.0 |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Button: button

| Name              | Value              |
|-------------------|--------------------|
| General           |                    |
| Dynamic: Enable   | getState() == IDLE |
| Enabled           | true               |
| Label Text        | Run                |
| Action            |                    |
| Action            | run();             |
| Position and size |                    |
| x                 | 40.0               |
| Width             | 100.0              |
| y                 | 80.0               |
| Height            | 30.0               |
| Advanced          |                    |
| Font Size         | 11                 |
| Font Name         | Dialog             |
| Show name         | false              |

## Button: button1

| Name            | Value  |
|-----------------|--|
| General         |  |
| Dynamic: Enable | doesOptimizationExist() && getCurrentIteration() > 0 |
| Enabled         | true   |
| Label Text      | copy   |
| Action          |  |

|                          |   |
|--------------------------|---|
| Action                   | <pre>String s = ""; s += "groomingInfectionProbability\t" + format( getBestParamValue( _oqvar_groomingInfectionProbability ) ) + "\n"; s += "groomingContactRate\t" + format( getBestParamValue( _oqvar_groomingContactRate ) ) + "\n"; s += "incubationPeriod\t" + format( 0.0 ) + "\n"; s += "durationOfInfection\t" + format( 0.0 ) + "\n"; s += "partyContactRate\t" + format( getBestParamValue( _oqvar_partyContactRate ) ) + "\n"; s += "partyInfectionProbability\t" + format( getBestParamValue( _oqvar_partyInfectionProbability ) ) + "\n"; s += "season\t" + String.valueOf( "Quarter3" ) + "\n";</pre> |
| <b>Position and size</b> |   |
| x                        | 310.0   |
| Width                    | 60.0  |
| y                        | 410.0   |
| Height                   | 20.0  |
| <b>Advanced</b>          |   |
| Font Size                | 11  |
| Font Name                | Dialog  |
| Show name                | false   |

## Parameter Variation Experiment: MonteCarloQ3

| Name                                   | Value   |
|--|---|
| <b>General</b>                         |   |
| Number Of Runs                         | 500   |
| Use Freeform Parameters                | true  |
| Maximum Available Memory               | 256   |
| Agent Type                             | Main  |
| <b>Model time</b>                      |   |
| Use Calendar                           | false   |
| Stop Option                            | Stop at specified time                              |
| Initial Time                           | 0.0   |
| Final Time                             | 90.0  |
| <b>Randomness</b>                      |   |
| Random Number Generation Type          | Random seed (unique simulation runs)                |
| Selection Mode For Simultaneous Events | LIFO (in the reverse order of scheduling)           |
| <b>Replications</b>                    |   |
| Use Replications                       | false   |
| <b>Window</b>                          |   |
| Experiment Progress                    | true  |
| Title                                  | Gombe Chimp Respiratory Disease Model1 : MonteCarlo |
| Width                                  | 1000.0  |
| Height                                 | 640.0   |
| Enable Panning                         | true  |
| Enable Zoom                            | true  |

|                            |   |
|----------------------------|---|
| Maximized size             | false   |
| Close confirmation         | false   |
| Java actions               |   |
| After Simulation Run       | histogram0_data.add( root.populationSicknessDuration ); |
| Advanced                   |   |
| Allow Parallel Evaluations | true  |
| Load Root From Snapshot    | false   |

Parameter Variation Experiment Parameters:

| Parameter                    | Value |
|------------------------------|-------|
| groomingInfectionProbability | 0.529 |
| groomingContactRate          | 0.535 |
| incubationPeriod             | 2     |
| durationOfInfection          | 4     |
| partyContactRate             | 0.436 |
| partyInfectionProbability    | 0.085 |
| season                       |       |

Gombe Chimp Respiratory Disease Model1 : MonteCarlo

Run

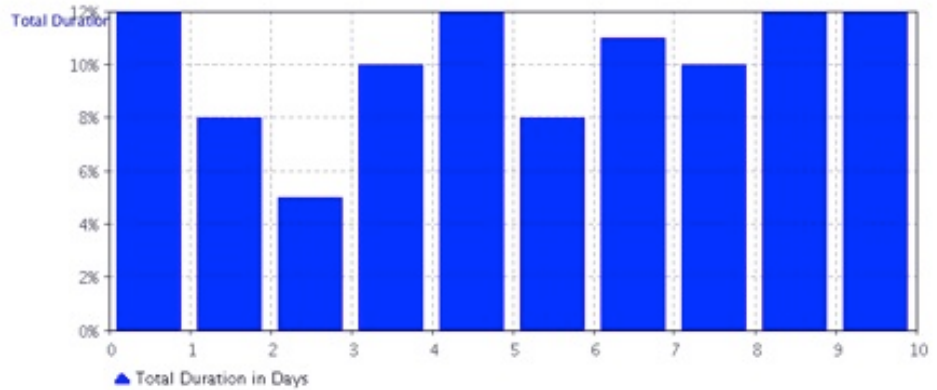
Number of runs: ?

Varied Parameters

|                              |   |
|------------------------------|---|
| groomingInfectionProbability | ? |
| groomingContactRate          | ? |
| incubationPeriod             | ? |
| durationOfInfection          | ? |
| partyContactRate             | ? |
| partyInfectionProbability    | ? |
| season                       | ? |

Charts

histogram0\_data



## Histogram: histogram0

| Name                         | Value    |
|------------------------------|----------|
| <b>General</b>               |          |
| Show Mean                    | false    |
| Show CDF                     | false    |
| Show PDF                     | true     |
| <b>Data update</b>           |          |
| Analysis Auto Update         | false    |
| <b>Appearance</b>            |          |
| Bars Relative Width          | 0.8      |
| Labels Vertical Position     | DEFAULT  |
| Labels Text Color            | darkGray |
| Chart Area Grid Color        | darkGray |
| <b>Position and size</b>     |          |
| x                            | 40.0     |
| Width                        | 760.0    |
| y                            | 300.0    |
| Height                       | 330.0    |
| <b>Legend</b>                |          |
| Show Legend                  | true     |
| Legend Size                  | 20.0     |
| Legend Text Color            | black    |
| <b>Chart area</b>            |          |
| Chart Area: X Offset         | 80.0     |
| Chart Area: Width            | 660.0    |
| Chart Area: Y Offset         | 20.0     |
| Chart Area: Height           | 260.0    |
| Chart Area: Background Color | white    |
| Chart Area Border Color      | black    |
| <b>Advanced</b>              |          |
| Show name                    | false    |

## Histogram Data Items:

| Title                  | Dataset         | PDF  | CDF   | Mean Color  | Width | Low % | High % |
|------------------------|-----------------|------|-------|-------------|-------|-------|--------|
| Total Duration in Days | histogram0_data | blue | black | saddleBrown | 1     | navy  | cyan   |

## Histogram Data: histogram0\_data

| Name                  | Value |
|-----------------------|-------|
| <b>General</b>        |       |
| Calculate Percentiles | false |

|                       |       |
|-----------------------|-------|
| Calculate CDF         | true  |
| Number Of Intervals   | 10    |
| Show At Runtime       | false |
| Show name             | true  |
| Values range          |       |
| Data range            | true  |
| Initial Interval Size | 1     |
| Data update           |       |
| Analysis Auto Update  | false |

## Text: text

| Name              | Value   |
|-------------------|---|
| General           |   |
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | Gombe Chimp Respiratory Disease Model1 : MonteCarlo |
| Appearance        |   |
| Font Size         | 24  |
| Font Name         | SansSerif   |
| Color             | royalBlue   |
| Alignment         | LEFT  |
| Position and size |   |
| x                 | 40.0  |
| y                 | 30.0  |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text1

| Name              | Value           |
|-------------------|-----------------|
| General           |                 |
| Show At Runtime   | true            |
| Lock              | false           |
| Text              |                 |
| Text              | Number of runs: |
| Appearance        |                 |
| Font Size         | 12              |
| Font Name         | SansSerif       |
| Color             | black           |
| Alignment         | LEFT            |
| Position and size |                 |

|           |       |
|-----------|-------|
| x         | 400.0 |
| y         | 70.0  |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text2

| Name              | Value                               |
|-------------------|-------------------------------------|
| General           |                                     |
| Show At Runtime   | true                                |
| Lock              | false                               |
| Text              |                                     |
| Text              | ?                                   |
| Dynamic: Text     | format( getEngine().getRunCount() ) |
| Appearance        |                                     |
| Font Size         | 12                                  |
| Font Name         | SansSerif                           |
| Color             | darkSlateBlue                       |
| Alignment         | RIGHT                               |
| Position and size |                                     |
| x                 | 620.0                               |
| y                 | 70.0                                |
| z                 | 0.0                                 |
| Rotation          | 0.0                                 |
| Advanced          |                                     |
| Show name         | false                               |

## Text: text3

| Name              | Value             |
|-------------------|-------------------|
| General           |                   |
| Show At Runtime   | true              |
| Lock              | false             |
| Text              |                   |
| Text              | Varied Parameters |
| Appearance        |                   |
| Bold Font Style   | true              |
| Font Size         | 12                |
| Font Name         | SansSerif         |
| Color             | black             |
| Alignment         | LEFT              |
| Position and size |                   |
| x                 | 40.0              |

|           |       |
|-----------|-------|
| y         | 100.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Line: line

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 150.0 |
| dX                | 650.0 |
| y                 | 110.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text4

| Name              | Value                        |
|-------------------|------------------------------|
| General           |                              |
| Show At Runtime   | true                         |
| Lock              | false                        |
| Text              |                              |
| Text              | groomingInfectionProbability |
| Appearance        |                              |
| Font Size         | 12                           |
| Font Name         | SansSerif                    |
| Color             | black                        |
| Alignment         | LEFT                         |
| Position and size |                              |
| x                 | 40.0                         |
| y                 | 120.0                        |
| z                 | 0.0                          |
| Rotation          | 0.0                          |

| Advanced  |       |
|-----------|-------|
| Show name | false |

## Text: text5

| Name              | Value                                  |
|-------------------|--|
| General           |  |
| Show At Runtime   | true                                   |
| Lock              | false                                  |
| Text              |  |
| Text              | ?                                      |
| Dynamic: Text     | format( groomingInfectionProbability ) |
| Appearance        |  |
| Font Size         | 12                                     |
| Font Name         | SansSerif                              |
| Color             | darkSlateBlue                          |
| Alignment         | RIGHT                                  |
| Position and size |  |
| x                 | 260.0                                  |
| y                 | 120.0                                  |
| z                 | 0.0                                    |
| Rotation          | 0.0                                    |
| Advanced          |  |
| Show name         | false                                  |

## Text: text6

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | groomingContactRate |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 40.0                |
| y                 | 140.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Text: text7

| Name              | Value                         |
|-------------------|-------------------------------|
| General           |                               |
| Show At Runtime   | true                          |
| Lock              | false                         |
| Text              |                               |
| Text              | ?                             |
| Dynamic: Text     | format( groomingContactRate ) |
| Appearance        |                               |
| Font Size         | 12                            |
| Font Name         | SansSerif                     |
| Color             | darkSlateBlue                 |
| Alignment         | RIGHT                         |
| Position and size |                               |
| x                 | 260.0                         |
| y                 | 140.0                         |
| z                 | 0.0                           |
| Rotation          | 0.0                           |
| Advanced          |                               |
| Show name         | false                         |

## Text: text8

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | incubationPeriod |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 40.0             |
| y                 | 160.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text9

| Name              | Value                      |
|-------------------|----------------------------|
| General           |                            |
| Show At Runtime   | true                       |
| Lock              | false                      |
| Text              |                            |
| Text              | ?                          |
| Dynamic: Text     | format( incubationPeriod ) |
| Appearance        |                            |
| Font Size         | 12                         |
| Font Name         | SansSerif                  |
| Color             | darkSlateBlue              |
| Alignment         | RIGHT                      |
| Position and size |                            |
| x                 | 260.0                      |
| y                 | 160.0                      |
| z                 | 0.0                        |
| Rotation          | 0.0                        |
| Advanced          |                            |
| Show name         | false                      |

## Text: text10

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | durationOfInfection |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 40.0                |
| y                 | 180.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Text: text11

| Name | Value |
|------|-------|
|------|-------|

| General           |                               |
|-------------------|-------------------------------|
| Show At Runtime   | true                          |
| Lock              | false                         |
| Text              |                               |
| Text              | ?                             |
| Dynamic: Text     | format( durationOfInfection ) |
| Appearance        |                               |
| Font Size         | 12                            |
| Font Name         | SansSerif                     |
| Color             | darkSlateBlue                 |
| Alignment         | RIGHT                         |
| Position and size |                               |
| x                 | 260.0                         |
| y                 | 180.0                         |
| z                 | 0.0                           |
| Rotation          | 0.0                           |
| Advanced          |                               |
| Show name         | false                         |

## Text: text12

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | partyContactRate |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 40.0             |
| y                 | 200.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text13

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |

|                   |                            |
|-------------------|----------------------------|
| Lock              | false                      |
| Text              |                            |
| Text              | ?                          |
| Dynamic: Text     | format( partyContactRate ) |
| Appearance        |                            |
| Font Size         | 12                         |
| Font Name         | SansSerif                  |
| Color             | darkSlateBlue              |
| Alignment         | RIGHT                      |
| Position and size |                            |
| x                 | 260.0                      |
| y                 | 200.0                      |
| z                 | 0.0                        |
| Rotation          | 0.0                        |
| Advanced          |                            |
| Show name         | false                      |

## Text: text14

| Name              | Value                     |
|-------------------|---------------------------|
| General           |                           |
| Show At Runtime   | true                      |
| Lock              | false                     |
| Text              |                           |
| Text              | partyInfectionProbability |
| Appearance        |                           |
| Font Size         | 12                        |
| Font Name         | SansSerif                 |
| Color             | black                     |
| Alignment         | LEFT                      |
| Position and size |                           |
| x                 | 40.0                      |
| y                 | 220.0                     |
| z                 | 0.0                       |
| Rotation          | 0.0                       |
| Advanced          |                           |
| Show name         | false                     |

## Text: text15

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Text            |       |

|                   |                                     |
|-------------------|-------------------------------------|
| Text              | ?                                   |
| Dynamic: Text     | format( partyInfectionProbability ) |
| Appearance        |                                     |
| Font Size         | 12                                  |
| Font Name         | SansSerif                           |
| Color             | darkSlateBlue                       |
| Alignment         | RIGHT                               |
| Position and size |                                     |
| x                 | 260.0                               |
| y                 | 220.0                               |
| z                 | 0.0                                 |
| Rotation          | 0.0                                 |
| Advanced          |                                     |
| Show name         | false                               |

## Text: text16

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | season    |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 40.0      |
| y                 | 240.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text17

| Name            | Value  |
|-----------------|--------|
| General         |        |
| Show At Runtime | true   |
| Lock            | false  |
| Text            |        |
| Text            | ?      |
| Dynamic: Text   | season |

| Appearance        |               |
|-------------------|---------------|
| Font Size         | 12            |
| Font Name         | SansSerif     |
| Color             | darkSlateBlue |
| Alignment         | RIGHT         |
| Position and size |               |
| x                 | 260.0         |
| y                 | 240.0         |
| z                 | 0.0           |
| Rotation          | 0.0           |
| Advanced          |               |
| Show name         | false         |

## Text: text20

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Charts    |
| Appearance        |           |
| Bold Font Style   | true      |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 40.0      |
| y                 | 280.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Line: line1

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Appearance      |       |
| Line Color      | black |
| Line Width      | 1.0   |
| Line Style      | SOLID |

| Position and size |       |
|-------------------|-------|
| x                 | 90.0  |
| dX                | 710.0 |
| y                 | 290.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text21

| Name              | Value          |
|-------------------|----------------|
| General           |                |
| Show At Runtime   | false          |
| Lock              | false          |
| Text              |                |
| Text              | Total Duration |
| Appearance        |                |
| Font Size         | 12             |
| Font Name         | SansSerif      |
| Color             | darkBlue       |
| Alignment         | LEFT           |
| Position and size |                |
| x                 | 40.0           |
| y                 | 320.0          |
| z                 | 0.0            |
| Rotation          | 0.0            |
| Advanced          |                |
| Show name         | false          |

## Button: button

| Name              | Value              |
|-------------------|--------------------|
| General           |                    |
| Dynamic: Enable   | getState() == IDLE |
| Enabled           | true               |
| Label Text        | Run                |
| Action            |                    |
| Action            | run();             |
| Position and size |                    |
| x                 | 40.0               |
| Width             | 100.0              |
| y                 | 60.0               |

|           |        |
|-----------|--------|
| Height    | 30.0   |
| Advanced  |        |
| Font Size | 11     |
| Font Name | Dialog |
| Show name | false  |

## Parameter Variation Experiment: MonteCarloQ2

| Name                                   | Value   |
|--|---|
| General                                |   |
| Number Of Runs                         | 500   |
| Use Freeform Parameters                | true  |
| Maximum Available Memory               | 256   |
| Agent Type                             | Main  |
| Model time                             |   |
| Use Calendar                           | false   |
| Stop Option                            | Stop at specified time                                  |
| Initial Time                           | 0.0   |
| Final Time                             | 90.0  |
| Randomness                             |   |
| Random Number Generation Type          | Random seed (unique simulation runs)                    |
| Selection Mode For Simultaneous Events | LIFO (in the reverse order of scheduling)               |
| Replications                           |   |
| Use Replications                       | false   |
| Window                                 |   |
| Experiment Progress                    | true  |
| Title                                  | Gombe Chimp Respiratory Disease Model1 : MonteCarlo     |
| Width                                  | 1000.0  |
| Height                                 | 640.0   |
| Enable Panning                         | true  |
| Enable Zoom                            | true  |
| Maximized size                         | false   |
| Close confirmation                     | false   |
| Java actions                           |   |
| After Simulation Run                   | histogram0_data.add( root.populationSicknessDuration ); |
| Advanced                               |   |
| Allow Parallel Evaluations             | true  |
| Load Root From Snapshot                | false   |

### Parameter Variation Experiment Parameters:

| Parameter                    | Value |
|------------------------------|-------|
| groomingInfectionProbability | 0.529 |
| groomingContactRate          | 0.535 |

|                               |            |
|-------------------------------|------------|
| incubationPeriod              | 2          |
| durationOfInfectio            | 4          |
| partyContactRate              | 0.436      |
| partyInfectionPro<br>bability | 0.085      |
| season                        | "Quarter2" |

## Gombe Chimp Respiratory Disease Model1 : MonteCarlo

Run

Number of runs:

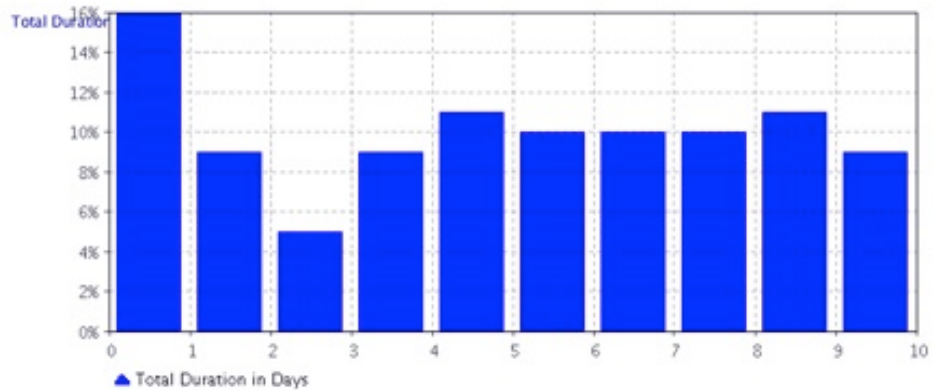
?

### Varied Parameters

|                              |   |
|------------------------------|---|
| groomingInfectionProbability | ? |
| groomingContactRate          | ? |
| incubationPeriod             | ? |
| durationOfInfection          | ? |
| partyContactRate             | ? |
| partyInfectionProbability    | ? |
| season                       | ? |

### Charts

histogram0\_data



## Histogram: histogram0

| Name                     | Value    |
|--------------------------|----------|
| General                  |          |
| Show Mean                | false    |
| Show CDF                 | false    |
| Show PDF                 | true     |
| Data update              |          |
| Analysis Auto Update     | false    |
| Appearance               |          |
| Bars Relative Width      | 0.8      |
| Labels Vertical Position | DEFAULT  |
| Labels Text Color        | darkGray |
| Chart Area Grid Color    | darkGray |

| Position and size            |       |
|------------------------------|-------|
| x                            | 40.0  |
| Width                        | 760.0 |
| y                            | 300.0 |
| Height                       | 330.0 |
| Legend                       |       |
| Show Legend                  | true  |
| Legend Size                  | 20.0  |
| Legend Text Color            | black |
| Chart area                   |       |
| Chart Area: X Offset         | 80.0  |
| Chart Area: Width            | 660.0 |
| Chart Area: Y Offset         | 20.0  |
| Chart Area: Height           | 260.0 |
| Chart Area: Background Color | white |
| Chart Area Border Color      | black |
| Advanced                     |       |
| Show name                    | false |

### Histogram Data Items:

| Title                  | Dataset         | PDF  | CDF   | Mean Color  | Width | Low % | High % |
|------------------------|-----------------|------|-------|-------------|-------|-------|--------|
| Total Duration in Days | histogram0_data | blue | black | saddleBrown | 1     | navy  | cyan   |

### Histogram Data: histogram0\_data

| Name                  | Value |
|-----------------------|-------|
| General               |       |
| Calculate Percentiles | false |
| Calculate CDF         | true  |
| Number Of Intervals   | 10    |
| Show At Runtime       | false |
| Show name             | true  |
| Values range          |       |
| Data range            | true  |
| Initial Interval Size | 1     |
| Data update           |       |
| Analysis Auto Update  | false |

### Text: text

| Name    | Value |
|---------|-------|
| General |       |

|                   |   |
|-------------------|---|
| Show At Runtime   | true  |
| Lock              | false   |
| Text              |   |
| Text              | Gombe Chimp Respiratory Disease Model1 : MonteCarlo |
| Appearance        |   |
| Font Size         | 24  |
| Font Name         | SansSerif   |
| Color             | royalBlue   |
| Alignment         | LEFT  |
| Position and size |   |
| x                 | 40.0  |
| y                 | 30.0  |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |   |
| Show name         | false   |

## Text: text1

| Name              | Value           |
|-------------------|-----------------|
| General           |                 |
| Show At Runtime   | true            |
| Lock              | false           |
| Text              |                 |
| Text              | Number of runs: |
| Appearance        |                 |
| Font Size         | 12              |
| Font Name         | SansSerif       |
| Color             | black           |
| Alignment         | LEFT            |
| Position and size |                 |
| x                 | 400.0           |
| y                 | 70.0            |
| z                 | 0.0             |
| Rotation          | 0.0             |
| Advanced          |                 |
| Show name         | false           |

## Text: text2

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Text            |       |

|                   |                                     |
|-------------------|-------------------------------------|
| Text              | ?                                   |
| Dynamic: Text     | format( getEngine().getRunCount() ) |
| Appearance        |                                     |
| Font Size         | 12                                  |
| Font Name         | SansSerif                           |
| Color             | darkSlateBlue                       |
| Alignment         | RIGHT                               |
| Position and size |                                     |
| x                 | 620.0                               |
| y                 | 70.0                                |
| z                 | 0.0                                 |
| Rotation          | 0.0                                 |
| Advanced          |                                     |
| Show name         | false                               |

### Text: text3

| Name              | Value             |
|-------------------|-------------------|
| General           |                   |
| Show At Runtime   | true              |
| Lock              | false             |
| Text              |                   |
| Text              | Varied Parameters |
| Appearance        |                   |
| Bold Font Style   | true              |
| Font Size         | 12                |
| Font Name         | SansSerif         |
| Color             | black             |
| Alignment         | LEFT              |
| Position and size |                   |
| x                 | 40.0              |
| y                 | 100.0             |
| z                 | 0.0               |
| Rotation          | 0.0               |
| Advanced          |                   |
| Show name         | false             |

### Line: line

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |
| Appearance      |       |
| Line Color      | black |

|                   |       |
|-------------------|-------|
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 150.0 |
| dX                | 650.0 |
| y                 | 110.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text4

| Name              | Value                        |
|-------------------|------------------------------|
| General           |                              |
| Show At Runtime   | true                         |
| Lock              | false                        |
| Text              |                              |
| Text              | groomingInfectionProbability |
| Appearance        |                              |
| Font Size         | 12                           |
| Font Name         | SansSerif                    |
| Color             | black                        |
| Alignment         | LEFT                         |
| Position and size |                              |
| x                 | 40.0                         |
| y                 | 120.0                        |
| z                 | 0.0                          |
| Rotation          | 0.0                          |
| Advanced          |                              |
| Show name         | false                        |

## Text: text5

| Name            | Value                                  |
|-----------------|--|
| General         |  |
| Show At Runtime | true                                   |
| Lock            | false                                  |
| Text            |  |
| Text            | ?                                      |
| Dynamic: Text   | format( groomingInfectionProbability ) |
| Appearance      |  |
| Font Size       | 12                                     |

|                   |               |
|-------------------|---------------|
| Font Name         | SansSerif     |
| Color             | darkSlateBlue |
| Alignment         | RIGHT         |
| Position and size |               |
| x                 | 260.0         |
| y                 | 120.0         |
| z                 | 0.0           |
| Rotation          | 0.0           |
| Advanced          |               |
| Show name         | false         |

## Text: text6

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | groomingContactRate |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 40.0                |
| y                 | 140.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Text: text7

| Name            | Value                         |
|-----------------|-------------------------------|
| General         |                               |
| Show At Runtime | true                          |
| Lock            | false                         |
| Text            |                               |
| Text            | ?                             |
| Dynamic: Text   | format( groomingContactRate ) |
| Appearance      |                               |
| Font Size       | 12                            |
| Font Name       | SansSerif                     |
| Color           | darkSlateBlue                 |

|                   |       |
|-------------------|-------|
| Alignment         | RIGHT |
| Position and size |       |
| x                 | 260.0 |
| y                 | 140.0 |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |       |
| Show name         | false |

## Text: text8

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | incubationPeriod |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 40.0             |
| y                 | 160.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text9

| Name              | Value                      |
|-------------------|----------------------------|
| General           |                            |
| Show At Runtime   | true                       |
| Lock              | false                      |
| Text              |                            |
| Text              | ?                          |
| Dynamic: Text     | format( incubationPeriod ) |
| Appearance        |                            |
| Font Size         | 12                         |
| Font Name         | SansSerif                  |
| Color             | darkSlateBlue              |
| Alignment         | RIGHT                      |
| Position and size |                            |
| x                 | 260.0                      |

|           |       |
|-----------|-------|
| y         | 160.0 |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text10

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | durationOfInfection |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 40.0                |
| y                 | 180.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Text: text11

| Name              | Value                         |
|-------------------|-------------------------------|
| General           |                               |
| Show At Runtime   | true                          |
| Lock              | false                         |
| Text              |                               |
| Text              | ?                             |
| Dynamic: Text     | format( durationOfInfection ) |
| Appearance        |                               |
| Font Size         | 12                            |
| Font Name         | SansSerif                     |
| Color             | darkSlateBlue                 |
| Alignment         | RIGHT                         |
| Position and size |                               |
| x                 | 260.0                         |
| y                 | 180.0                         |
| z                 | 0.0                           |

|           |       |
|-----------|-------|
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text12

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | partyContactRate |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 40.0             |
| y                 | 200.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text13

| Name              | Value                      |
|-------------------|----------------------------|
| General           |                            |
| Show At Runtime   | true                       |
| Lock              | false                      |
| Text              |                            |
| Text              | ?                          |
| Dynamic: Text     | format( partyContactRate ) |
| Appearance        |                            |
| Font Size         | 12                         |
| Font Name         | SansSerif                  |
| Color             | darkSlateBlue              |
| Alignment         | RIGHT                      |
| Position and size |                            |
| x                 | 260.0                      |
| y                 | 200.0                      |
| z                 | 0.0                        |
| Rotation          | 0.0                        |
| Advanced          |                            |

|           |       |
|-----------|-------|
| Show name | false |
|-----------|-------|

## Text: text14

| Name              | Value                     |
|-------------------|---------------------------|
| General           |                           |
| Show At Runtime   | true                      |
| Lock              | false                     |
| Text              |                           |
| Text              | partyInfectionProbability |
| Appearance        |                           |
| Font Size         | 12                        |
| Font Name         | SansSerif                 |
| Color             | black                     |
| Alignment         | LEFT                      |
| Position and size |                           |
| x                 | 40.0                      |
| y                 | 220.0                     |
| z                 | 0.0                       |
| Rotation          | 0.0                       |
| Advanced          |                           |
| Show name         | false                     |

## Text: text15

| Name              | Value                               |
|-------------------|-------------------------------------|
| General           |                                     |
| Show At Runtime   | true                                |
| Lock              | false                               |
| Text              |                                     |
| Text              | ?                                   |
| Dynamic: Text     | format( partyInfectionProbability ) |
| Appearance        |                                     |
| Font Size         | 12                                  |
| Font Name         | SansSerif                           |
| Color             | darkSlateBlue                       |
| Alignment         | RIGHT                               |
| Position and size |                                     |
| x                 | 260.0                               |
| y                 | 220.0                               |
| z                 | 0.0                                 |
| Rotation          | 0.0                                 |
| Advanced          |                                     |
| Show name         | false                               |

## Text: text16

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | season    |
| Appearance        |           |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 40.0      |
| y                 | 240.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text17

| Name              | Value         |
|-------------------|---------------|
| General           |               |
| Show At Runtime   | true          |
| Lock              | false         |
| Text              |               |
| Text              | ?             |
| Dynamic: Text     | season        |
| Appearance        |               |
| Font Size         | 12            |
| Font Name         | SansSerif     |
| Color             | darkSlateBlue |
| Alignment         | RIGHT         |
| Position and size |               |
| x                 | 260.0         |
| y                 | 240.0         |
| z                 | 0.0           |
| Rotation          | 0.0           |
| Advanced          |               |
| Show name         | false         |

## Text: text20

| Name              | Value     |
|-------------------|-----------|
| General           |           |
| Show At Runtime   | true      |
| Lock              | false     |
| Text              |           |
| Text              | Charts    |
| Appearance        |           |
| Bold Font Style   | true      |
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 40.0      |
| y                 | 280.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Line: line1

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 90.0  |
| dX                | 710.0 |
| y                 | 290.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text21

| Name    | Value |
|---------|-------|
| General |       |

|                   |                |
|-------------------|----------------|
| Show At Runtime   | false          |
| Lock              | false          |
| Text              |                |
| Text              | Total Duration |
| Appearance        |                |
| Font Size         | 12             |
| Font Name         | SansSerif      |
| Color             | darkBlue       |
| Alignment         | LEFT           |
| Position and size |                |
| x                 | 40.0           |
| y                 | 320.0          |
| z                 | 0.0            |
| Rotation          | 0.0            |
| Advanced          |                |
| Show name         | false          |

## Button: button

| Name              | Value              |
|-------------------|--------------------|
| General           |                    |
| Dynamic: Enable   | getState() == IDLE |
| Enabled           | true               |
| Label Text        | Run                |
| Action            |                    |
| Action            | run();             |
| Position and size |                    |
| x                 | 40.0               |
| Width             | 100.0              |
| y                 | 60.0               |
| Height            | 30.0               |
| Advanced          |                    |
| Font Size         | 11                 |
| Font Name         | Dialog             |
| Show name         | false              |

## Parameter Variation Experiment: MonteCarloQ1

| Name                     | Value |
|--------------------------|-------|
| General                  |       |
| Number Of Runs           | 500   |
| Use Freeform Parameters  | true  |
| Maximum Available Memory | 256   |
| Agent Type               | Main  |
| Model time               |       |

|  |   |
|--|---|
| Use Calendar                           | false   |
| Stop Option                            | Stop at specified time                                  |
| Initial Time                           | 0.0   |
| Final Time                             | 90.0  |
| <b>Randomness</b>                      |   |
| Random Number Generation Type          | Random seed (unique simulation runs)                    |
| Selection Mode For Simultaneous Events | LIFO (in the reverse order of scheduling)               |
| <b>Replications</b>                    |   |
| Use Replications                       | false   |
| <b>Window</b>                          |   |
| Experiment Progress                    | true  |
| Title                                  | Gombe Chimp Respiratory Disease Model1 : MonteCarlo     |
| Width                                  | 1000.0  |
| Height                                 | 640.0   |
| Enable Panning                         | true  |
| Enable Zoom                            | true  |
| Maximized size                         | false   |
| Close confirmation                     | false   |
| <b>Java actions</b>                    |   |
| After Simulation Run                   | histogram0_data.add( root.populationSicknessDuration ); |
| <b>Advanced</b>                        |   |
| Allow Parallel Evaluations             | true  |
| Load Root From Snapshot                | false   |

### Parameter Variation Experiment Parameters:

| Parameter                    | Value      |
|------------------------------|------------|
| groomingInfectionProbability | 0.529      |
| groomingContactRate          | 0.535      |
| incubationPeriod             | 2          |
| durationOfInfection          | 4          |
| partyContactRate             | 0.436      |
| partyInfectionProbability    | 0.085      |
| season                       | "Quarter1" |

## Gombe Chimp Respiratory Disease Model1 : MonteCarlo

Run

Number of runs:

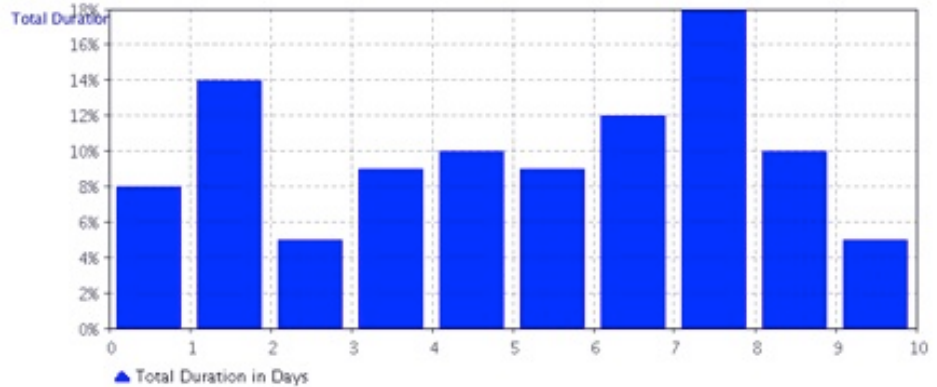
?

### Varied Parameters

groomingInfectionProbability ?  
 groomingContactRate ?  
 incubationPeriod ?  
 durationOfInfection ?  
 partyContactRate ?  
 partyInfectionProbability ?  
 season ?

### Charts

histogram0\_data



## Histogram: histogram0

| Name                     | Value    |
|--------------------------|----------|
| General                  |          |
| Show Mean                | false    |
| Show CDF                 | false    |
| Show PDF                 | true     |
| Data update              |          |
| Analysis Auto Update     | false    |
| Appearance               |          |
| Bars Relative Width      | 0.8      |
| Labels Vertical Position | DEFAULT  |
| Labels Text Color        | darkGray |
| Chart Area Grid Color    | darkGray |
| Position and size        |          |
| x                        | 40.0     |
| Width                    | 760.0    |
| y                        | 300.0    |
| Height                   | 330.0    |
| Legend                   |          |
| Show Legend              | true     |
| Legend Size              | 20.0     |
| Legend Text Color        | black    |

| Chart area                   |       |
|------------------------------|-------|
| Chart Area: X Offset         | 80.0  |
| Chart Area: Width            | 660.0 |
| Chart Area: Y Offset         | 20.0  |
| Chart Area: Height           | 260.0 |
| Chart Area: Background Color | white |
| Chart Area Border Color      | black |
| Advanced                     |       |
| Show name                    | false |

### Histogram Data Items:

| Title                  | Dataset         | PDF  | CDF   | Mean Color  | Width | Low % | High % |
|------------------------|-----------------|------|-------|-------------|-------|-------|--------|
| Total Duration in Days | histogram0_data | blue | black | saddleBrown | 1     | navy  | cyan   |

### Histogram Data: histogram0\_data

| Name                  | Value |
|-----------------------|-------|
| General               |       |
| Calculate Percentiles | false |
| Calculate CDF         | true  |
| Number Of Intervals   | 10    |
| Show At Runtime       | false |
| Show name             | true  |
| Values range          |       |
| Data range            | true  |
| Initial Interval Size | 1     |
| Data update           |       |
| Analysis Auto Update  | false |

### Text: text

| Name            | Value  |
|-----------------|--|
| General         |  |
| Show At Runtime | true   |
| Lock            | false  |
| Text            |  |
| Text            | Gombe Chimpanzee Respiratory Disease Model1 : MonteCarlo |
| Appearance      |  |
| Font Size       | 24   |
| Font Name       | SansSerif  |
| Color           | royalBlue  |
| Alignment       | LEFT   |

| Position and size |       |
|-------------------|-------|
| x                 | 40.0  |
| y                 | 30.0  |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |       |
| Show name         | false |

## Text: text1

| Name              | Value           |
|-------------------|-----------------|
| General           |                 |
| Show At Runtime   | true            |
| Lock              | false           |
| Text              |                 |
| Text              | Number of runs: |
| Appearance        |                 |
| Font Size         | 12              |
| Font Name         | SansSerif       |
| Color             | black           |
| Alignment         | LEFT            |
| Position and size |                 |
| x                 | 400.0           |
| y                 | 70.0            |
| z                 | 0.0             |
| Rotation          | 0.0             |
| Advanced          |                 |
| Show name         | false           |

## Text: text2

| Name              | Value                               |
|-------------------|-------------------------------------|
| General           |                                     |
| Show At Runtime   | true                                |
| Lock              | false                               |
| Text              |                                     |
| Text              | ?                                   |
| Dynamic: Text     | format( getEngine().getRunCount() ) |
| Appearance        |                                     |
| Font Size         | 12                                  |
| Font Name         | SansSerif                           |
| Color             | darkSlateBlue                       |
| Alignment         | RIGHT                               |
| Position and size |                                     |
| x                 | 620.0                               |

|           |       |
|-----------|-------|
| y         | 70.0  |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text3

| Name              | Value             |
|-------------------|-------------------|
| General           |                   |
| Show At Runtime   | true              |
| Lock              | false             |
| Text              |                   |
| Text              | Varied Parameters |
| Appearance        |                   |
| Bold Font Style   | true              |
| Font Size         | 12                |
| Font Name         | SansSerif         |
| Color             | black             |
| Alignment         | LEFT              |
| Position and size |                   |
| x                 | 40.0              |
| y                 | 100.0             |
| z                 | 0.0               |
| Rotation          | 0.0               |
| Advanced          |                   |
| Show name         | false             |

## Line: line

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 150.0 |
| dX                | 650.0 |
| y                 | 110.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |

|           |       |
|-----------|-------|
| z Height  | 10.0  |
| Advanced  |       |
| Show name | false |

## Text: text4

| Name              | Value                        |
|-------------------|------------------------------|
| General           |                              |
| Show At Runtime   | true                         |
| Lock              | false                        |
| Text              |                              |
| Text              | groomingInfectionProbability |
| Appearance        |                              |
| Font Size         | 12                           |
| Font Name         | SansSerif                    |
| Color             | black                        |
| Alignment         | LEFT                         |
| Position and size |                              |
| x                 | 40.0                         |
| y                 | 120.0                        |
| z                 | 0.0                          |
| Rotation          | 0.0                          |
| Advanced          |                              |
| Show name         | false                        |

## Text: text5

| Name              | Value                                  |
|-------------------|--|
| General           |  |
| Show At Runtime   | true                                   |
| Lock              | false                                  |
| Text              |  |
| Text              | ?                                      |
| Dynamic: Text     | format( groomingInfectionProbability ) |
| Appearance        |  |
| Font Size         | 12                                     |
| Font Name         | SansSerif                              |
| Color             | darkSlateBlue                          |
| Alignment         | RIGHT                                  |
| Position and size |  |
| x                 | 260.0                                  |
| y                 | 120.0                                  |
| z                 | 0.0                                    |
| Rotation          | 0.0                                    |
| Advanced          |  |

|           |       |
|-----------|-------|
| Show name | false |
|-----------|-------|

## Text: text6

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | groomingContactRate |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 40.0                |
| y                 | 140.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Text: text7

| Name              | Value                         |
|-------------------|-------------------------------|
| General           |                               |
| Show At Runtime   | true                          |
| Lock              | false                         |
| Text              |                               |
| Text              | ?                             |
| Dynamic: Text     | format( groomingContactRate ) |
| Appearance        |                               |
| Font Size         | 12                            |
| Font Name         | SansSerif                     |
| Color             | darkSlateBlue                 |
| Alignment         | RIGHT                         |
| Position and size |                               |
| x                 | 260.0                         |
| y                 | 140.0                         |
| z                 | 0.0                           |
| Rotation          | 0.0                           |
| Advanced          |                               |
| Show name         | false                         |

## Text: text8

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | incubationPeriod |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 40.0             |
| y                 | 160.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text9

| Name              | Value                      |
|-------------------|----------------------------|
| General           |                            |
| Show At Runtime   | true                       |
| Lock              | false                      |
| Text              |                            |
| Text              | ?                          |
| Dynamic: Text     | format( incubationPeriod ) |
| Appearance        |                            |
| Font Size         | 12                         |
| Font Name         | SansSerif                  |
| Color             | darkSlateBlue              |
| Alignment         | RIGHT                      |
| Position and size |                            |
| x                 | 260.0                      |
| y                 | 160.0                      |
| z                 | 0.0                        |
| Rotation          | 0.0                        |
| Advanced          |                            |
| Show name         | false                      |

## Text: text10

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | durationOfInfection |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 40.0                |
| y                 | 180.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Text: text11

| Name              | Value                         |
|-------------------|-------------------------------|
| General           |                               |
| Show At Runtime   | true                          |
| Lock              | false                         |
| Text              |                               |
| Text              | ?                             |
| Dynamic: Text     | format( durationOfInfection ) |
| Appearance        |                               |
| Font Size         | 12                            |
| Font Name         | SansSerif                     |
| Color             | darkSlateBlue                 |
| Alignment         | RIGHT                         |
| Position and size |                               |
| x                 | 260.0                         |
| y                 | 180.0                         |
| z                 | 0.0                           |
| Rotation          | 0.0                           |
| Advanced          |                               |
| Show name         | false                         |

## Text: text12

| Name    | Value |
|---------|-------|
| General |       |

|                   |                  |
|-------------------|------------------|
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | partyContactRate |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 40.0             |
| y                 | 200.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

### Text: text13

| Name              | Value                      |
|-------------------|----------------------------|
| General           |                            |
| Show At Runtime   | true                       |
| Lock              | false                      |
| Text              |                            |
| Text              | ?                          |
| Dynamic: Text     | format( partyContactRate ) |
| Appearance        |                            |
| Font Size         | 12                         |
| Font Name         | SansSerif                  |
| Color             | darkSlateBlue              |
| Alignment         | RIGHT                      |
| Position and size |                            |
| x                 | 260.0                      |
| y                 | 200.0                      |
| z                 | 0.0                        |
| Rotation          | 0.0                        |
| Advanced          |                            |
| Show name         | false                      |

### Text: text14

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |

| Text              |                           |
|-------------------|---------------------------|
| Text              | partyInfectionProbability |
| Appearance        |                           |
| Font Size         | 12                        |
| Font Name         | SansSerif                 |
| Color             | black                     |
| Alignment         | LEFT                      |
| Position and size |                           |
| x                 | 40.0                      |
| y                 | 220.0                     |
| z                 | 0.0                       |
| Rotation          | 0.0                       |
| Advanced          |                           |
| Show name         | false                     |

## Text: text15

| Name              | Value                               |
|-------------------|-------------------------------------|
| General           |                                     |
| Show At Runtime   | true                                |
| Lock              | false                               |
| Text              |                                     |
| Text              | ?                                   |
| Dynamic: Text     | format( partyInfectionProbability ) |
| Appearance        |                                     |
| Font Size         | 12                                  |
| Font Name         | SansSerif                           |
| Color             | darkSlateBlue                       |
| Alignment         | RIGHT                               |
| Position and size |                                     |
| x                 | 260.0                               |
| y                 | 220.0                               |
| z                 | 0.0                                 |
| Rotation          | 0.0                                 |
| Advanced          |                                     |
| Show name         | false                               |

## Text: text16

| Name            | Value  |
|-----------------|--------|
| General         |        |
| Show At Runtime | true   |
| Lock            | false  |
| Text            |        |
| Text            | season |

| Appearance        |           |
|-------------------|-----------|
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 40.0      |
| y                 | 240.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text17

| Name              | Value         |
|-------------------|---------------|
| General           |               |
| Show At Runtime   | true          |
| Lock              | false         |
| Text              |               |
| Text              | ?             |
| Dynamic: Text     | season        |
| Appearance        |               |
| Font Size         | 12            |
| Font Name         | SansSerif     |
| Color             | darkSlateBlue |
| Alignment         | RIGHT         |
| Position and size |               |
| x                 | 260.0         |
| y                 | 240.0         |
| z                 | 0.0           |
| Rotation          | 0.0           |
| Advanced          |               |
| Show name         | false         |

## Text: text20

| Name            | Value  |
|-----------------|--------|
| General         |        |
| Show At Runtime | true   |
| Lock            | false  |
| Text            |        |
| Text            | Charts |
| Appearance      |        |
| Bold Font Style | true   |

|                   |           |
|-------------------|-----------|
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 40.0      |
| y                 | 280.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Line: line1

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 90.0  |
| dX                | 710.0 |
| y                 | 290.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text21

| Name            | Value          |
|-----------------|----------------|
| General         |                |
| Show At Runtime | false          |
| Lock            | false          |
| Text            |                |
| Text            | Total Duration |
| Appearance      |                |
| Font Size       | 12             |
| Font Name       | SansSerif      |
| Color           | darkBlue       |

|                   |       |
|-------------------|-------|
| Alignment         | LEFT  |
| Position and size |       |
| x                 | 40.0  |
| y                 | 320.0 |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |       |
| Show name         | false |

## Button: button

| Name              | Value              |
|-------------------|--------------------|
| General           |                    |
| Dynamic: Enable   | getState() == IDLE |
| Enabled           | true               |
| Label Text        | Run                |
| Action            |                    |
| Action            | run();             |
| Position and size |                    |
| x                 | 40.0               |
| Width             | 100.0              |
| y                 | 60.0               |
| Height            | 30.0               |
| Advanced          |                    |
| Font Size         | 11                 |
| Font Name         | Dialog             |
| Show name         | false              |

## Parameter Variation Experiment: MonteCarloQ4

| Name                                   | Value                                     |
|--|---|
| General                                |   |
| Number Of Runs                         | 500                                       |
| Use Freeform Parameters                | true                                      |
| Maximum Available Memory               | 256                                       |
| Agent Type                             | Main                                      |
| Model time                             |   |
| Use Calendar                           | false                                     |
| Stop Option                            | Stop at specified time                    |
| Initial Time                           | 0.0                                       |
| Final Time                             | 90.0                                      |
| Randomness                             |   |
| Random Number Generation Type          | Random seed (unique simulation runs)      |
| Selection Mode For Simultaneous Events | LIFO (in the reverse order of scheduling) |

| Replications               |   |
|----------------------------|---|
| Use Replications           | false   |
| Window                     |   |
| Experiment Progress        | true  |
| Title                      | Gombe Chimp Respiratory Disease Model1 : MonteCarlo     |
| Width                      | 1000.0  |
| Height                     | 640.0   |
| Enable Panning             | true  |
| Enable Zoom                | true  |
| Maximized size             | false   |
| Close confirmation         | false   |
| Java actions               |   |
| After Simulation Run       | histogram0_data.add( root.populationSicknessDuration ); |
| Advanced                   |   |
| Allow Parallel Evaluations | true  |
| Load Root From Snapshot    | false   |

### Parameter Variation Experiment Parameters:

| Parameter                    | Value      |
|------------------------------|------------|
| groomingInfectionProbability | 0.529      |
| groomingContactRate          | 0.535      |
| incubationPeriod             | 2          |
| durationOfInfection          | 4          |
| partyContactRate             | 0.436      |
| partyInfectionProbability    | 0.085      |
| season                       | "Quarter4" |

## Gombe Chimp Respiratory Disease Model1 : MonteCarlo

Run

Number of runs:

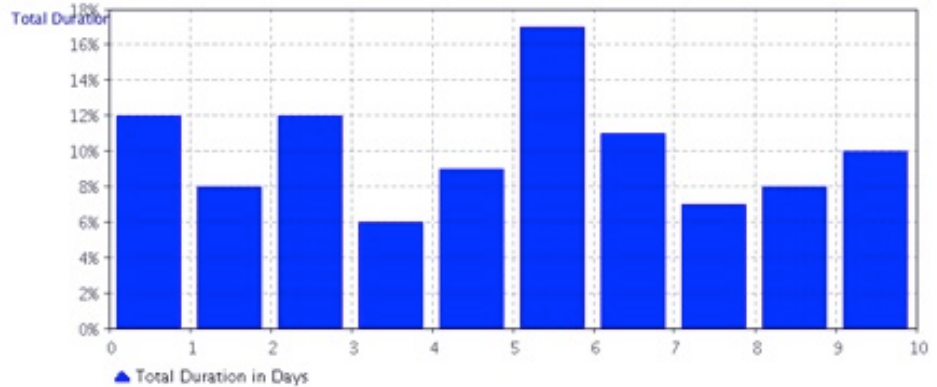
?

### Varied Parameters

groomingInfectionProbability ?  
groomingContactRate ?  
incubationPeriod ?  
durationOfInfection ?  
partyContactRate ?  
partyInfectionProbability ?  
season ?

### Charts

histogram0\_data



## Histogram: histogram0

| Name                     | Value    |
|--------------------------|----------|
| General                  |          |
| Show Mean                | false    |
| Show CDF                 | false    |
| Show PDF                 | true     |
| Data update              |          |
| Analysis Auto Update     | false    |
| Appearance               |          |
| Bars Relative Width      | 0.8      |
| Labels Vertical Position | DEFAULT  |
| Labels Text Color        | darkGray |
| Chart Area Grid Color    | darkGray |
| Position and size        |          |
| x                        | 40.0     |
| Width                    | 760.0    |
| y                        | 300.0    |
| Height                   | 330.0    |
| Legend                   |          |
| Show Legend              | true     |
| Legend Size              | 20.0     |
| Legend Text Color        | black    |

| Chart area                   |       |
|------------------------------|-------|
| Chart Area: X Offset         | 80.0  |
| Chart Area: Width            | 660.0 |
| Chart Area: Y Offset         | 20.0  |
| Chart Area: Height           | 260.0 |
| Chart Area: Background Color | white |
| Chart Area Border Color      | black |
| Advanced                     |       |
| Show name                    | false |

### Histogram Data Items:

| Title                  | Dataset         | PDF  | CDF   | Mean Color  | Width | Low % | High % |
|------------------------|-----------------|------|-------|-------------|-------|-------|--------|
| Total Duration in Days | histogram0_data | blue | black | saddleBrown | 1     | navy  | cyan   |

### Histogram Data: histogram0\_data

| Name                  | Value |
|-----------------------|-------|
| General               |       |
| Calculate Percentiles | false |
| Calculate CDF         | true  |
| Number Of Intervals   | 10    |
| Show At Runtime       | false |
| Show name             | true  |
| Values range          |       |
| Data range            | true  |
| Initial Interval Size | 1     |
| Data update           |       |
| Analysis Auto Update  | false |

### Text: text

| Name            | Value  |
|-----------------|--|
| General         |  |
| Show At Runtime | true   |
| Lock            | false  |
| Text            |  |
| Text            | Gombe Chimpanzee Respiratory Disease Model1 : MonteCarlo |
| Appearance      |  |
| Font Size       | 24   |
| Font Name       | SansSerif  |
| Color           | royalBlue  |
| Alignment       | LEFT   |

| Position and size |       |
|-------------------|-------|
| x                 | 40.0  |
| y                 | 30.0  |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |       |
| Show name         | false |

## Text: text1

| Name              | Value           |
|-------------------|-----------------|
| General           |                 |
| Show At Runtime   | true            |
| Lock              | false           |
| Text              |                 |
| Text              | Number of runs: |
| Appearance        |                 |
| Font Size         | 12              |
| Font Name         | SansSerif       |
| Color             | black           |
| Alignment         | LEFT            |
| Position and size |                 |
| x                 | 400.0           |
| y                 | 70.0            |
| z                 | 0.0             |
| Rotation          | 0.0             |
| Advanced          |                 |
| Show name         | false           |

## Text: text2

| Name              | Value                               |
|-------------------|-------------------------------------|
| General           |                                     |
| Show At Runtime   | true                                |
| Lock              | false                               |
| Text              |                                     |
| Text              | ?                                   |
| Dynamic: Text     | format( getEngine().getRunCount() ) |
| Appearance        |                                     |
| Font Size         | 12                                  |
| Font Name         | SansSerif                           |
| Color             | darkSlateBlue                       |
| Alignment         | RIGHT                               |
| Position and size |                                     |
| x                 | 620.0                               |

|           |       |
|-----------|-------|
| y         | 70.0  |
| z         | 0.0   |
| Rotation  | 0.0   |
| Advanced  |       |
| Show name | false |

## Text: text3

| Name              | Value             |
|-------------------|-------------------|
| General           |                   |
| Show At Runtime   | true              |
| Lock              | false             |
| Text              |                   |
| Text              | Varied Parameters |
| Appearance        |                   |
| Bold Font Style   | true              |
| Font Size         | 12                |
| Font Name         | SansSerif         |
| Color             | black             |
| Alignment         | LEFT              |
| Position and size |                   |
| x                 | 40.0              |
| y                 | 100.0             |
| z                 | 0.0               |
| Rotation          | 0.0               |
| Advanced          |                   |
| Show name         | false             |

## Line: line

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 150.0 |
| dX                | 650.0 |
| y                 | 110.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |

|           |       |
|-----------|-------|
| z Height  | 10.0  |
| Advanced  |       |
| Show name | false |

## Text: text4

| Name              | Value                        |
|-------------------|------------------------------|
| General           |                              |
| Show At Runtime   | true                         |
| Lock              | false                        |
| Text              |                              |
| Text              | groomingInfectionProbability |
| Appearance        |                              |
| Font Size         | 12                           |
| Font Name         | SansSerif                    |
| Color             | black                        |
| Alignment         | LEFT                         |
| Position and size |                              |
| x                 | 40.0                         |
| y                 | 120.0                        |
| z                 | 0.0                          |
| Rotation          | 0.0                          |
| Advanced          |                              |
| Show name         | false                        |

## Text: text5

| Name              | Value                                  |
|-------------------|--|
| General           |  |
| Show At Runtime   | true                                   |
| Lock              | false                                  |
| Text              |  |
| Text              | ?                                      |
| Dynamic: Text     | format( groomingInfectionProbability ) |
| Appearance        |  |
| Font Size         | 12                                     |
| Font Name         | SansSerif                              |
| Color             | darkSlateBlue                          |
| Alignment         | RIGHT                                  |
| Position and size |  |
| x                 | 260.0                                  |
| y                 | 120.0                                  |
| z                 | 0.0                                    |
| Rotation          | 0.0                                    |
| Advanced          |  |

|           |       |
|-----------|-------|
| Show name | false |
|-----------|-------|

## Text: text6

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | groomingContactRate |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 40.0                |
| y                 | 140.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Text: text7

| Name              | Value                         |
|-------------------|-------------------------------|
| General           |                               |
| Show At Runtime   | true                          |
| Lock              | false                         |
| Text              |                               |
| Text              | ?                             |
| Dynamic: Text     | format( groomingContactRate ) |
| Appearance        |                               |
| Font Size         | 12                            |
| Font Name         | SansSerif                     |
| Color             | darkSlateBlue                 |
| Alignment         | RIGHT                         |
| Position and size |                               |
| x                 | 260.0                         |
| y                 | 140.0                         |
| z                 | 0.0                           |
| Rotation          | 0.0                           |
| Advanced          |                               |
| Show name         | false                         |

## Text: text8

| Name              | Value            |
|-------------------|------------------|
| General           |                  |
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | incubationPeriod |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 40.0             |
| y                 | 160.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

## Text: text9

| Name              | Value                      |
|-------------------|----------------------------|
| General           |                            |
| Show At Runtime   | true                       |
| Lock              | false                      |
| Text              |                            |
| Text              | ?                          |
| Dynamic: Text     | format( incubationPeriod ) |
| Appearance        |                            |
| Font Size         | 12                         |
| Font Name         | SansSerif                  |
| Color             | darkSlateBlue              |
| Alignment         | RIGHT                      |
| Position and size |                            |
| x                 | 260.0                      |
| y                 | 160.0                      |
| z                 | 0.0                        |
| Rotation          | 0.0                        |
| Advanced          |                            |
| Show name         | false                      |

## Text: text10

| Name              | Value               |
|-------------------|---------------------|
| General           |                     |
| Show At Runtime   | true                |
| Lock              | false               |
| Text              |                     |
| Text              | durationOfInfection |
| Appearance        |                     |
| Font Size         | 12                  |
| Font Name         | SansSerif           |
| Color             | black               |
| Alignment         | LEFT                |
| Position and size |                     |
| x                 | 40.0                |
| y                 | 180.0               |
| z                 | 0.0                 |
| Rotation          | 0.0                 |
| Advanced          |                     |
| Show name         | false               |

## Text: text11

| Name              | Value                         |
|-------------------|-------------------------------|
| General           |                               |
| Show At Runtime   | true                          |
| Lock              | false                         |
| Text              |                               |
| Text              | ?                             |
| Dynamic: Text     | format( durationOfInfection ) |
| Appearance        |                               |
| Font Size         | 12                            |
| Font Name         | SansSerif                     |
| Color             | darkSlateBlue                 |
| Alignment         | RIGHT                         |
| Position and size |                               |
| x                 | 260.0                         |
| y                 | 180.0                         |
| z                 | 0.0                           |
| Rotation          | 0.0                           |
| Advanced          |                               |
| Show name         | false                         |

## Text: text12

| Name    | Value |
|---------|-------|
| General |       |

|                   |                  |
|-------------------|------------------|
| Show At Runtime   | true             |
| Lock              | false            |
| Text              |                  |
| Text              | partyContactRate |
| Appearance        |                  |
| Font Size         | 12               |
| Font Name         | SansSerif        |
| Color             | black            |
| Alignment         | LEFT             |
| Position and size |                  |
| x                 | 40.0             |
| y                 | 200.0            |
| z                 | 0.0              |
| Rotation          | 0.0              |
| Advanced          |                  |
| Show name         | false            |

### Text: text13

| Name              | Value                      |
|-------------------|----------------------------|
| General           |                            |
| Show At Runtime   | true                       |
| Lock              | false                      |
| Text              |                            |
| Text              | ?                          |
| Dynamic: Text     | format( partyContactRate ) |
| Appearance        |                            |
| Font Size         | 12                         |
| Font Name         | SansSerif                  |
| Color             | darkSlateBlue              |
| Alignment         | RIGHT                      |
| Position and size |                            |
| x                 | 260.0                      |
| y                 | 200.0                      |
| z                 | 0.0                        |
| Rotation          | 0.0                        |
| Advanced          |                            |
| Show name         | false                      |

### Text: text14

| Name            | Value |
|-----------------|-------|
| General         |       |
| Show At Runtime | true  |
| Lock            | false |

| Text              |                           |
|-------------------|---------------------------|
| Text              | partyInfectionProbability |
| Appearance        |                           |
| Font Size         | 12                        |
| Font Name         | SansSerif                 |
| Color             | black                     |
| Alignment         | LEFT                      |
| Position and size |                           |
| x                 | 40.0                      |
| y                 | 220.0                     |
| z                 | 0.0                       |
| Rotation          | 0.0                       |
| Advanced          |                           |
| Show name         | false                     |

## Text: text15

| Name              | Value                               |
|-------------------|-------------------------------------|
| General           |                                     |
| Show At Runtime   | true                                |
| Lock              | false                               |
| Text              |                                     |
| Text              | ?                                   |
| Dynamic: Text     | format( partyInfectionProbability ) |
| Appearance        |                                     |
| Font Size         | 12                                  |
| Font Name         | SansSerif                           |
| Color             | darkSlateBlue                       |
| Alignment         | RIGHT                               |
| Position and size |                                     |
| x                 | 260.0                               |
| y                 | 220.0                               |
| z                 | 0.0                                 |
| Rotation          | 0.0                                 |
| Advanced          |                                     |
| Show name         | false                               |

## Text: text16

| Name            | Value  |
|-----------------|--------|
| General         |        |
| Show At Runtime | true   |
| Lock            | false  |
| Text            |        |
| Text            | season |

| Appearance        |           |
|-------------------|-----------|
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 40.0      |
| y                 | 240.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Text: text17

| Name              | Value         |
|-------------------|---------------|
| General           |               |
| Show At Runtime   | true          |
| Lock              | false         |
| Text              |               |
| Text              | ?             |
| Dynamic: Text     | season        |
| Appearance        |               |
| Font Size         | 12            |
| Font Name         | SansSerif     |
| Color             | darkSlateBlue |
| Alignment         | RIGHT         |
| Position and size |               |
| x                 | 260.0         |
| y                 | 240.0         |
| z                 | 0.0           |
| Rotation          | 0.0           |
| Advanced          |               |
| Show name         | false         |

## Text: text20

| Name            | Value  |
|-----------------|--------|
| General         |        |
| Show At Runtime | true   |
| Lock            | false  |
| Text            |        |
| Text            | Charts |
| Appearance      |        |
| Bold Font Style | true   |

|                   |           |
|-------------------|-----------|
| Font Size         | 12        |
| Font Name         | SansSerif |
| Color             | black     |
| Alignment         | LEFT      |
| Position and size |           |
| x                 | 40.0      |
| y                 | 280.0     |
| z                 | 0.0       |
| Rotation          | 0.0       |
| Advanced          |           |
| Show name         | false     |

## Line: line1

| Name              | Value |
|-------------------|-------|
| General           |       |
| Show At Runtime   | true  |
| Lock              | false |
| Appearance        |       |
| Line Color        | black |
| Line Width        | 1.0   |
| Line Style        | SOLID |
| Position and size |       |
| x                 | 90.0  |
| dX                | 710.0 |
| y                 | 290.0 |
| dY                | 0.0   |
| z                 | 0.0   |
| dZ                | 0.0   |
| z Height          | 10.0  |
| Advanced          |       |
| Show name         | false |

## Text: text21

| Name            | Value          |
|-----------------|----------------|
| General         |                |
| Show At Runtime | false          |
| Lock            | false          |
| Text            |                |
| Text            | Total Duration |
| Appearance      |                |
| Font Size       | 12             |
| Font Name       | SansSerif      |
| Color           | darkBlue       |

|                   |       |
|-------------------|-------|
| Alignment         | LEFT  |
| Position and size |       |
| x                 | 40.0  |
| y                 | 320.0 |
| z                 | 0.0   |
| Rotation          | 0.0   |
| Advanced          |       |
| Show name         | false |

## Button: button

| Name              | Value              |
|-------------------|--------------------|
| General           |                    |
| Dynamic: Enable   | getState() == IDLE |
| Enabled           | true               |
| Label Text        | Run                |
| Action            |                    |
| Action            | run();             |
| Position and size |                    |
| x                 | 40.0               |
| Width             | 100.0              |
| y                 | 60.0               |
| Height            | 30.0               |
| Advanced          |                    |
| Font Size         | 11                 |
| Font Name         | Dialog             |
| Show name         | false              |