Eco-epidemiology of tuberculosis in Maasai Mara Kenya: Conceptualizing sociocultural practices for One Health

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Abstract

The control of tuberculosis has proven an ongoing challenge for public health. For pastoralists, those defined by their fundamental cultural relationship with livestock and migration in search of pasture and water, the complexity of tuberculosis control intersects with social and cultural practices that should be considered when designing interventions not as binary attributes of the community, but as a continuum within which the community lives and operates. The goal of the work contained within this thesis is to characterize *Mycobacterium tuberculosis* complex species (MTBC) in a high-exposure human-animal interface; explore the relevance of social and cultural factors; and evaluate the potential role of livestock movement in the transmission and control of zoonotic tuberculosis in the Mara ecosystem. In this dissertation, I document the co-circulation of multiple MTBC species in this ecosystem, with zoonotic tuberculosis substantially contributing to the overall burden, especially in villages adjacent to the Maasai Mara National Reserve, a protected wildlife area. Further, this work demonstrates that livestock movements not only mediate connectivity between villages within this ecosystem, but also interact with other factors to shape household tuberculosis patterns. Specifically, consumption of raw animal products, and movement of livestock for grazing or trade influence household tuberculosis occurrence, and reinforce the importance of zoonotic tuberculosis. Using data on livestock movement, this study demonstrates that dry season grazing patterns are important for enhancing the embeddedness of households’ in their community social networks, with villages adjacent to the Maasai Mara National Reserve as the most common destination for grazing. Overall, the work presented here reinforce the complexity of this issue within this ecosystem, and demonstrates that network-based

control measures aimed at highly connected villages, have the potential to enhance the proactive development of targeted disease control programs as traditional and/or narrowly focused approaches for tuberculosis control are unlikely to work. Thus, in accordance with the current global wave of thinking, One Health approaches are also necessary and even required in this system. However, the operationalization of One Health approaches need to be culturally appropriate and tailored specifically to the characteristics of a locality and contextualized to its practices and structures.

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Chapter 1 | Introduction: Social determinants of health and tuberculosis: Gaps for One Health approaches in pastoralist populations

Pastoralism, marginalization and determinants of health

Pastoralism as a socio-cultural system is characterized by raising livestock on rangelands. It is classified into nomadic, semi-sedentary, sedentary and agro-pastoralists based on distance of movement (Schwartz, 1993). Unlike the agro-pastoralist or sedentary pastoralists whose practices include potential settlement and the raising of crops, nomadic and semi-sedentary pastoralist societies are inherently dynamic, characterized by livestock and human movement in search of water and forage (Galaty, 2015). Nomadic pastoralism involves movement of livestock, people and homesteads following the temporal distribution of forage and water, while semi-sedentary pastoralism denotes the long-distance movement of animals, mostly by young men, for forage during the dry season while maintaining a permanent homestead in a single location (Schwartz, 1993). In both nomadic and semi-sedentary pastoralism, long-standing traditional management strategies have been progressively undermined by socioecological, economic and political factors. For instance, the lack of permanent locations and constant migration has led to their exclusion from education (Dyer, 2013; Krätli et al., 2013), economic and national development policies (Thompson and Homewood, 2002; Markakis, 2004), as well as access to health services (Duba et al., 2001; Caulfield et al., 2016; Wild et al., 2020b). This continued marginalization, coupled with the continued lack of national and local supportive policies enhances a negative feedback loop between the coupled natural-human system, reinforcing cycles of poverty and poor health outcomes (Grace et al., 2017).

The myriad of challenges posed to the sustainability and resilience of the pastoral way of life have both direct and indirect repercussions for health at the population level (Ekaya, 2005; Little, 2013; Serbessa et al., 2016). For instance, a closer look at local biodiversity hotspots in East Africa, such as the Maasai Mara Ecosystem in Southwestern Kenya, show that increased fencing (due to individuation of communal lands) threatens the contiguity of both human and animal migration patterns (Løvschal et al., 2017; Mwiu et al., 2019; Weldemichel and Lein, 2019). The resulting conversion of communal lands to individual holdings has led to increased human settlements in protected areas (Lamprey and Reid, 2004; Nyariki et al., 2017), with concomitant disturbance and destruction of habitat, and decrease in some wildlife species and ecosystem services (Ogutu et al., 2009). With subsequent increased contact between livestock and wildlife, there have been reported increases in the prevalence of livestock diseases (Lekolool, 2011; Nthiwa et al., 2019a; Nthiwa et al., 2020) with presumed correlation in human health in these livestock-human coupled systems. Although direct empirical evidence linking livestock and human health is still formative, recent work in western Kenya has shown that poor livestock health leads to poorer health outcomes in dependent households, including child stunting (Mosites et al., 2015). This complex relationship, coupled with poor investment in veterinary health, livestock insurance and drought mitigation measures, is a form of re-marginalization perpetuated by national and donor policies (Oxby, 1999; Markakis, 2004; Elias and Abdi, 2010; Nyanjom, 2014).

That pastoralists occupy habitats with an intensive human-livestock-wildlife interface is common knowledge. However, social and cultural practices of different groups are relatively unique, differing in areas such as spatial habitat use (range and frequency) in order to efficiently utilize resource-scarce ecosystems, and are based on community tradition and values, leadership, cultural identity and resilience (Smith, 1992; Anderson, 1993; Straight, 1998; Leslie et al., 2013; Carabine, 2014; Jandreau and Berkes, 2016). Unfortunately, these same practices may also put these communities at increased risk for the acquisition and transmission of zoonotic diseases (Miller and Olea-Popelka, 2013a; Olea-Popelka et al., 2017; Amulyoto et al., 2018; Kemunto et al., 2018; Onono et al., 2019). This is extremely concerning when combined with the fact that there is a paucity of information available to support culturally appropriate disease control strategies for these communities (Onesmo, 2013; Grace, 2015; Halliday et al., 2015; Mangesho et al., 2017). It has been proposed that as a precursor to alleviating poverty and enhancing wellbeing, one must disentangle the complex interactions between social and environmental determinants of health (Perry and Grace, 2009; Grace et al., 2012; Jones et al., 2013; Travis et al., 2014a; Travis et al., 2014b; Grace, 2015; Grace et al., 2017).

Social determinants of health and tuberculosis in pastoralist communities

Health is a complex phenomenon (Donev, 2000). It is a continuum between the individual and the community with diverse determinants including genetic, behavioral, social and environmental factors that need to be incorporated for effective disease control (Frieden, 2015). The recognition that the biomedical approach to medicine does not holistically address health challenges (Feinstein, 1999), has brought to the fore the concept of health as an equilibrium between the individual and their environment. On this front, it is acknowledged that settings in which individuals grow, live, work and age are shaped by interactions among social, economic and political exigencies, which in turn influence health and health outcomes both at the individual and population level. These are collectively known as the social determinants of health (CDSH, 2008).

Social determinants of health as a concept is important for the control of socially driven diseases such as tuberculosis, which in 2019 alone affected ~10 million people, and caused 1.4 million deaths (WHO, 2020). The current approaches to tuberculosis control focus on reducing transmission through timely case detection and treatment (Volmink and Garner, 2007; Lonnroth and Raviglione, 2008; WHO, 2013, 2019, 2020). However, there has been a shift to a social model of health to bridge inequity and address broader causes of exposure, infection, lack of access and adherence to therapy for tuberculosis patients (Lonnroth et al., 2009; Rasanathan et al., 2011). This follows epidemiological studies showing that infections are higher in communities ranking low on socioeconomic indicators such as overcrowding in households, unemployment rates, education level, general poverty, and among marginalized groups (Cantwell et al., 1998; Stout et al., 2006; Muniyandi et al., 2007; Baker et al., 2008; Dye et al., 2009; Lonnroth et al., 2009; Baussano et al., 2013). These determinants influence all aspects of tuberculosis epidemiology including baseline prevalence in the population, exposure type and transmission rates between infected and susceptible individuals, potential pathogenesis of the infection, access to care and treatment outcomes. The determinants are further shaped by gender, nutritional status, syndemics, lack of ventilation within households and human movement across environments including urban areas (Hargreaves et al., 2011).

Focus on social determinants of health as a model for tuberculosis surveillance and control is especially lacking in marginalized populations (Meleis and Im, 1999; Venkatapuram et al., 2010; Baah et al., 2019) such as pastoralist communities who are marginalized on multiple fronts (Mkutu, 2007; Pavanello, 2009; Elhadary, 2010; Pike et al., 2010; Heathcote, 2012; Ahearn, 2016; Wild et al., 2020a). Among these communities, unique sociocultural practices increasing the risk of tuberculosis include housing with minimal ventilation, overcrowding in households, consumption of raw or undercooked animal products, and close interaction with animals. These parallel the social determinants of tuberculosis (Lonnroth et al., 2009; Rasanathan et al., 2011). It has been shown that in high burden settings, there is need for more health personnel, diagnostic and contact tracing resources to stem the transmission of tuberculosis (Bonadonna et al., 2017). However, in pastoralist communities, barriers to tuberculosis care, diagnosis and treatment stem from lack of access to healthcare and knowledge on control, and in some communities, adherence to traditional beliefs and healers (Gele et al., 2009; Gele et al., 2010). These factors, in addition, are complicated by socioeconomic status, gender, and mobility (Getnet et al., 2019; Nooh et al., 2019; Megerso et al., 2020). The challenge of tuberculosis in pastoralist communities is further complicated by the reliance on microscopy - which has a low sensitivity (<60%) (Siddiqi et al., 2003; Ganoza et al., 2008) - for the diagnosis of tuberculosis. Furthermore, microscopy cannot differentiate between competing causative agents of tuberculosis in humans; an important consideration in such communities with potential exposure to a variety of mycobacterium species of humans, animals and the environment (Kankya et al., 2011; Gumi et al., 2012; Gumi, 2013; Mnyambwa et al., 2018a). Thus, there is need for a more holistic approach incorporating structural interventions that target proximate levels of disease determinants, in addition to diagnostics and treatment for the effective control of tuberculosis (Blankenship et al., 2000; Sumartojo et al., 2000; Blankenship et al., 2006).

Disentangling determinants of human tuberculosis in pastoralist communities

The social determinants of tuberculosis as a concept have been acknowledged since before the identification of the actual causative agent - *Mycobacterium tuberculosis* - in humans in 1882 (Dubos and Dubos, 1987). *Mycobacterium tuberculosis* is part of a group of mycobacterial organisms capable of infecting human beings and other animals, known as *Mycobacterium tuberculosis* complex (MTBC). In addition to *Mycobacterium tuberculosis*, these include *Mycobacterium africanum*, *Mycobacterium bovis*, *Mycobacterium canettii*, *Mycobacterium caprae*, *Mycobacterium microti*, *Mycobacterium* pinnipedii, *Mycobacterium suricattae*, *Mycobacterium dassie*, *Mycobacterium oryx*, and *Mycobacterium mungi* (Velayati and Farnia, 2016; Gagneux, 2018). Of these, *M. tuberculosis* and *M. africanum* are human pathogens while *M. bovis* is a zoonotic pathogen with the greatest host range, including domestic and wild animals (Wayne, 1986; Palmer et al., 2012; Muller et al., 2013). *Mycobacterium canettii* has been isolated from human beings but is thought to be an opportunistic environmental pathogen (Pfyffer et al., 1998; Koeck et al., 2011; Supply and Brosch, 2017).

The complexity of the epidemiology of tuberculosis among pastoralists mimics the challenge of understanding the general ecology of infectious diseases at the human-livestock-wildlife interface where various infectious diseases occurrence and patterns are amplified by the community's social and cultural practices (MacGregor and Waldman, 2017). The ecology of *M. tuberculosis* in marginalized pastoralist populations is in parallel with the occurrence of zoonotic tuberculosis caused by *M. bovis* (Mfinanga et al., 2003; Cleaveland et al., 2007). *M. bovis* is not endemic in much of the world but represents a risk for spillback to humans in intensive livestock interfaces, and through foodborne transmission (Miller and Olea-Popelka, 2013a; Müller et al., 2013; Olea-Popelka et al., 2017). In 2019 the World health Organization estimated the occurrence of ~140,000 (Range: 69,800-235,000) *M. bovis* cases worldwide, of which 49% occurred in Africa (WHO, 2020). Thus the risk is real and coupled with diagnostic approaches with low sensitivity and discriminatory power, there are significant demerits to instituting only healthcare-based interventions (Marmot, 2005; Hargreaves et al., 2011). On the other hand, similarities in social and structural drivers of *M. tuberculosis* and *M. bovis* ecologies make it difficult to tease them apart and identify appropriate points for public health interventions. For example, tuberculosis occurrence is influenced by socioeconomic status, co-morbidities, age, geographical location and housing status (Hargreaves et al., 2011). In the case of zoonotic tuberculosis, the risk is influenced by number of people in a household, income, co-morbidities, consumption of raw milk or meat, proximity to wildlife areas and close interaction with domestic animals (Mfinanga et al., 2003; Caron et al., 2013; Brooks-Pollock et al., 2014; Anderson et al., 2015; Cowie et al., 2015; Olea-Popelka et al., 2017). These are practically the same determinants being seminal to different diseases in the same communities and/or ecosystems. Thus, there is need to understand nuances around transmission for effective control.

Studies investigating the association between household tuberculosis, livestock *M. bovis* status, and socio-cultural practices have had varying results (Koech, 2001; Mfinanga et al., 2003; Meisner et al., 2019). Many socio-cultural factors were commonly associated with increased risk of both *M. tuberculosis* and *M. bovis* (Mfinanga et al., 2003; Fetene et al., 2011; Meisner et al., 2019). Furthermore, while *M. tuberculosis* is primarily considered a pulmonary disease, its occurrence has also been associated with cases of extrapulmonary forms of tuberculosis (Berg et al., 2015b). A review of tuberculous adenitis cases in Africa show association with livestock exposure (52%), and consumption of raw animal products (46%) (Mekonnen et al., 2019a). Thus, the often assumed association between extrapulmonary tuberculosis with *M. bovis* (Koech, 2001), may be a misdiagnosis as it has been shown that certain lineages of *M. tuberculosis* may have extrapulmonary involvement (Kong et al., 2006, 2007). The intricacies surrounding risk factors extend to their association with *M. bovis* in human populations. In some studies, presence of reactors in a household's cattle herd was protective against human tuberculosis (Meisner et al., 2019), and in other studies, consumption of raw milk was also protective (Koech, 2001). However, consumption of raw milk led to elevated risk in several other studies (Tschopp et al., 2009; Fetene et al., 2011; Berg et al., 2015b; Mengistu A et al., 2015). Thus, despite numerous studies on human tuberculosis in high-risk populations, there are still gaps in our understanding of risk factors and, consequently, the appropriateness of interventions in the face of imperfect diagnostic techniques. Thus, obfuscating the control and management of tuberculosis in general in these communities.

Future directions and opportunities for integrating social determinants to tuberculosis surveillance

There is no question that traditional approaches to tuberculosis control in pastoralist populations have not been effective. This is due to the obvious diagnostic challenges, but is also a result of the complex eco-epidemiology of disease in these communities. Managing this complexity necessitates an integrated approach to control in an interconnected human, animal, environmental system - in a culturally acceptable manner - which is often ignored or beyond the scope of traditional thinking and funding.

The confluence between *M. tuberculosis* and *M. bovis* in pastoralist populations is worrisome, as *M. bovis* has been shown to be resistant to first line antituberculosis drugs (Sreevatsan et al., 1997). In addition, it has been suggested that the complex relationship between livestock, wildlife and sociocultural factors in the ecologies of both *M. tuberculosis* and *M. bovis*, and their management necessitates a “One Health” approach (De Garine-Wichatitsky et al., 2013; Miller and Olea-Popelka, 2013b; Travis et al., 2014b; Olea-Popelka et al., 2017). This is in recognition of the limitations traditional approaches to tuberculosis control including dependence on patient initiated hospital visitation, imperfect diagnostics and lack of culturally appropriate and surveillance approaches.

Implementation of the “One Health” paradigm implicitly advocates for the harnessing of collaborative and multi-disciplinary methodologies - integrating human, animal and socioecological knowledge to control diseases (Travis et al., 2014b; Binot et al., 2015; Cardona et al., 2015; Munyua et al., 2019) – towards risk-based stratification of surveillance efforts for maladies such as tuberculosis (Gebreyes et al., 2014; Roug et al., 2014; Meisner et al., 2019). However, with competing determinants, this approach needs more evidence on several fronts, and explicit efforts to understand transmission patterns and the effect of heterogeneity within populations. Accordingly, there is need to expound on both risk factors, and their synergistic or antagonistic interactions, to identify areas that may allow population or area specific interventions (Koplan et al., 2009; Conrad et al., 2013). This may be further supported by cheap and easy to implement or portable molecular methods for characterizing mycobacterial species in suspected tuberculosis patients. This is especially critical in high exposure interfaces where the frequency of different *Mycobacterium tuberculosis* complex species and nontuberculous mycobacteria, may complicate diagnosis and management of tuberculosis in patients as recently shown (Mnyambwa et al., 2018b). In combination with advanced quantitative methods, triaging risk factors and diagnostic results allows for the resolution of competing determinants (Koech, 2001; Meisner et al., 2019) or teasing apart risk factors in cases where multiple population-based predictors seem to be interacting (Berg et al., 2015b).

A new area for exploration in disease transmission and management is network analysis. Network analysis has been used to elucidate transmission and control strategies in livestock (Christley et al., 2005; Dube et al., 2009; Kao and Kiss, 2010; Poolkhet et al., 2013; VanderWaal et al., 2016; VanderWaal et al., 2017; Kinsley et al., 2019; Mekonnen et al., 2019b) and wildlife systems (Bohm et al., 2008; Godfrey, 2013; Craft, 2015; Silk et al., 2017). It has also been employed in human disease to understand epidemic structure (De et al., 2004), and potential transmission nodes (Yaganehdoost et al., 1999; Klovdahl et al., 2001). In pastoralist communities, network analysis has been used to characterize seasonal distribution of grazing patterns and effect of mobility on livestock disease transmission (VanderWaal et al., 2017; Pomeroy et al., 2019a), and on the role of movement of personnel on disease transmission between farms (Rossi et al., 2017). Pastoralists move across the ecosystem in search of forage and water for their livestock. The role of such movements in increasing human and animal congregation, and specifically their effect on occurrence of human diseases, is an important area for research. These can also be applied in developing contact tracing methodologies in mobile populations. In conclusion, it is important to note that pastoralists have intricate biocultural calendars that drive different types of livestock movements, human and animal congregations across their ecosystems. Transmission of tuberculosis has been shown to occur in areas where humans cluster (Yaganehdoost et al., 1999; Klovdahl et al., 2001), thus social and cultural factors that promote human congregation, including festivities, market and grazing coalitions are important avenues for the potential control of tuberculosis in these populations. Thus, we must endeavor to develop a deeper understanding of sociocultural practices, human and animal movement and landscape utilization, in order to develop targeted and effective interventions for tuberculosis.

Goal of this dissertation

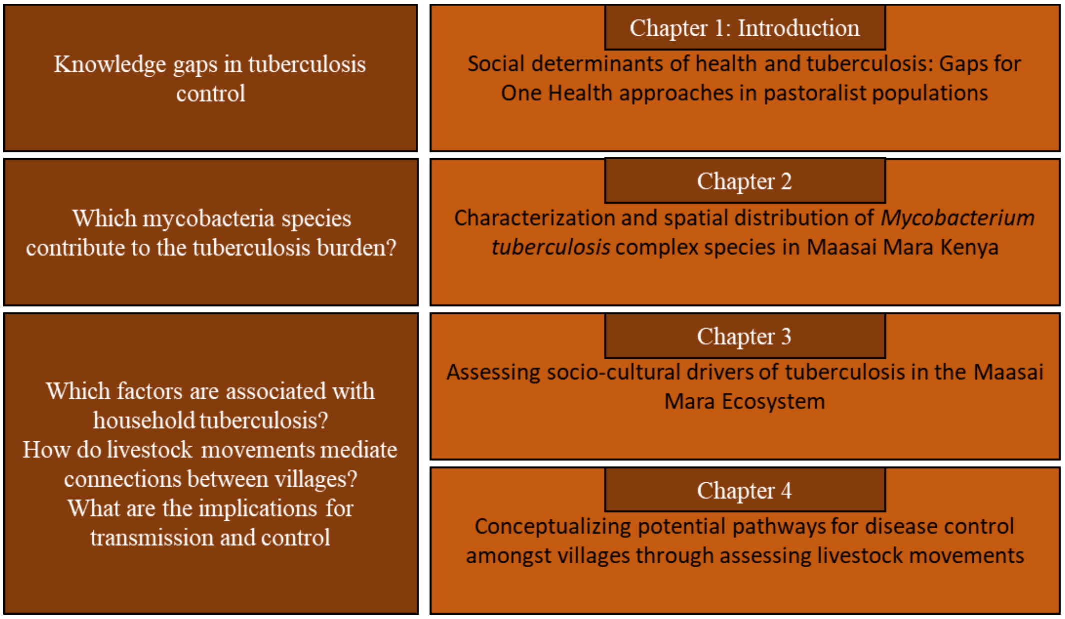
In an attempt to fill the knowledge gaps identified above, the overarching objective of this dissertation was to investigate the role of social and cultural factors in shaping tuberculosis patterns in a pastoralist population in Maasai Mara Ecosystem, Kenya with an eye toward developing more comprehensive disease control strategies. The Maasai Mara Ecosystem is part of Narok County, Kenya characterized by the presence of the Maasai Mara National Reserve, which through availability of forage during the dry season drives human, livestock and wildlife movement across the ecosystem. There have been reports of *Mycobacterium tuberculosis* within this population but not of *Mycobacterium bovis* despite the community's continued observation of sociocultural practices, including consumption of raw milk and other animal products (Koech, 2001; Kirui, 2014). To accomplish this objective, the specific aims of this dissertation were as follows (Figure 1.1):

Aim 1. Characterization and spatial distribution of *Mycobacterium tuberculosis* complex species in Maasai Mara Kenya. In this aim, sputum collected from tuberculosis suspected patients was analyzed using polymerase chain reaction and classification of the mycobacterial species based upon molecular analysis (**Chapter 2**).

Aim 2. Assessing socio-cultural drivers of tuberculosis in the Maasai Mara Ecosystem. Here, using survey data from households in the ecosystem, in this aim a machine-learning algorithm as developed to characterize drivers and their interaction patterns associated with household tuberculosis (**Chapter 3**).

Aim 3. Conceptualizing potential pathways for disease control amongst villages through assessing livestock movements. This aim defined and characterized livestock-associated cultural movements and evaluated their potential role in network-based disease control within the ecosystem (**Chapter 4**).

Figure 1.1. Schematic diagram of the dissertation chapters and questions they are addressing



Knowledge gaps in tuberculosis control	Chapter 1: Introduction Social determinants of health and tuberculosis: Gaps for One Health approaches in pastoralist populations
Which mycobacteria species contribute to the tuberculosis burden?	Chapter 2 Characterization and spatial distribution of *Mycobacterium tuberculosis* complex species in Maasai Mara Kenya
Which factors are associated with household tuberculosis? How do livestock movements mediate connections between villages? What are the implications for transmission and control	Chapter 3 Assessing socio-cultural drivers of tuberculosis in the Maasai Mara Ecosystem
	Chapter 4 Conceptualizing potential pathways for disease control amongst villages through assessing livestock movements

Chapter 2 | Characterization and spatial distribution of *Mycobacterium tuberculosis* complex species in Maasai Mara, Kenya

Background

The *Mycobacterium tuberculosis* complex (MTBC) is a group of mycobacterial organisms capable of infecting humans and other animals (Brosch et al., 2002; Comas et al., 2013; Velayati and Farnia, 2016; Gagneux, 2018). In addition to *Mycobacterium tuberculosis* (*M. tuberculosis*), the most common agent of human tuberculosis (TB) infections, MTBC includes *M. africanum* (humans), *M. canettii* (humans), *M. bovis* (animals and humans), *M. caprae* (animals and humans), *M. microti* (voles), *M. pinnipedii* (seals), *M. suricattae* (meerkats), *M. dassie* (hyrax), *M. oryx* (oryx), *M. mungi* (mongoose) (Velayati and Farnia, 2016; Gagneux, 2018), and the newly recognized chimpanzee bacillus (Coscolla et al., 2013). Pastoralist communities are at a higher risk of different MTBC due to their lived experiences – social determinants of TB (Hargreaves et al., 2011; Olea-Popelka et al., 2017). Among the MTBC species, *M. bovis* is a re-emergent zoonosis with the greatest host range, including domestic and wild animals (Wayne, 1986; Palmer et al., 2012; Muller et al., 2013), and is a pathogen of concern in pastoralist communities due to their sociocultural practices (Etter et al., 2006; De Garine-Wichatitsky et al., 2013).

The challenge of TB control in pastoralist communities is further complicated by reliance on smear microscopy for diagnosis. This has low sensitivity and cannot differentiate among MTBC (Siddiqi et al., 2003; Ganoza et al., 2008). Ideally, smear microscopy needs to be confirmed by culture, followed by MTBC speciation and antibiotic susceptibility testing. However, this would take weeks, and require specialized facilities and personnel, which are significant barriers, especially in Africa (Parsons et al., 2011; Harries and Kumar, 2018), leading to the continued lack of MTBC speciation, and potentially limiting the efficacy of TB control programs. Other diagnostic techniques including portable molecular techniques such as Xpert® MTB/RIF – an onsite molecular based test that simultaneously detects MTBC and rifampicin resistance - are available but require high infrastructure and maintenance needs (Lawn and Nicol, 2011; Parsons et al., 2011; Zeka et al., 2011). On the other hand, *IS*6110, a mobile genetic element found in MTBC has been an important diagnostic marker for differentiating MTBC from other mycobacteria (Thierry et al., 1990; Gonzalo-Asensio et al., 2018). Although *IS*6110 does not provide high resolution as whole genome sequencing (Kohl et al., 2014), it is standardized and reliable as an epidemiological marker for MTBC (Van Embden et al., 1993). Comparative genomic analyses have also identified several regions of difference (RD) resulting from loss of genetic material in the genomes of MTBC following their evolution (Behr et al., 1999; Gordon et al., 1999). Analysis of these RD have revealed differences in their occurrence among MTBC subspecies hence allowing for the establishment of their genetic lineages (Brosch et al., 2002; Warren et al., 2006). This provides an alternative approach for speciation of MTBC in at-risk communities such as pastoralists.

Kenya is a high TB burden country (WHO, 2019, 2020), where microscopy, and occasionally, culture and Xpert MTB/RIF are routinely used for TB diagnosis (Enos et al., 2018). A recent survey showed a TB prevalence of 558 (95% CI: 455–662) per

100,000 adults (Enos et al., 2018), which was higher than previous estimates of 233 per 100,000 (95% CI: 188-266) (WHO, 2016). In this survey, however, Xpert MTB/RIF identified 78% of the cases compared to only 46% identified by smear microscopy – highlighting the limitations of smear microscopy. This survey and many other studies spotlight deficiencies in currently employed diagnostic testing, which among others, the lack of differentiation among MTBC precludes epidemiological consideration for the role played by other mycobacterial species in the TB incidence and control in at-risk communities.

This study was conducted in the Maasai Mara Ecosystem, which is primarily occupied by a rural Maasai pastoralist community, and consists of Maasai Mara National Reserve (MMNR) and adjacent villages. This region saw an increase in cases of extrapulmonary TB in the 1990s which were attributed to *M. bovis* (Koech, 2001). The Maasai continue to observe their cultural practices, including consumption of raw animal products, close interaction between humans and animals, and congregation of humans and livestock around the MMNR during the dry season (Omondi et al., 2021), which provides further support that *M. bovis* may play an important role in TB incidence in this ecosystem. Surprisingly, one study in this region found that practices such as consumption of raw milk were protective against TB infections (Koech, 2001). These reports, which conflict with well-recognized risk factors for specific MTBC species, necessitate further investigation for effective TB control. Thus, the objective of this study was to characterize *Mycobacterium tuberculosis* complex species and their spatial distribution in the Maasai Mara Ecosystem in Kenya. We hypothesized that zoonotic TB would account for the highest proportion among MTBC species in suspected TB patients, with spatial clustering of MTBC cases influenced by Maasai Mara National Reserve possibly due to human congregation during dry season grazing of cattle in the protected area.

Methods

Study site and sample collection

Sampling for this study was conducted in three local hospitals in the Maasai Mara Ecosystem. Sputum samples were collected, by convenience sampling, from all patients referred for a TB test at Sekenani, Aitong, and Talek health centers, which are three of the four local hospitals with capacity to diagnose and manage TB. All persons attending TB clinic in any of the three hospitals between November 2017 and June 2018, and were residents of the study area met the inclusion criteria. From all patients, sputum samples were collected in a sterile cup by laboratory technicians, decontaminated using 5% NaOH or phenol (Giacomelli et al., 2005), and evaluated by smear microscopy following acid-fast staining. All samples, both smear microscopy positive and negative, were aliquoted into cryovials, labeled with a unique sample number, hospital name, and village of origin, and stored in liquid nitrogen until analyzed.

Identification of *Mycobacterium tuberculosis* complex species

DNA Extraction

The extraction of DNA from sputum samples followed the manufacturer's Quick-DNA™ Fungal/Bacterial Miniprep Kit (Zymo Research). Briefly, 100µl of the solubilized sputum sample was transferred into a ZR BashingBead™ lysis tube and 750µl BashingBead™ Buffer added. This mixture was vortexed for 15 minutes and the ZR

BashingBead™ lysis tube centrifuged at 10,000x *g* for three minutes. Following centrifugation, 400µl of the supernatant was transferred into a Zymo-Spin™ III-F Filter in a Collection Tube, and centrifuged again at 8,000x g for one minute. Genomic lysis buffer (1,200µl) was then added into the filtrate in the collection tube and transferred into Zymo-Spin™ IICR column followed by centrifugation at 10,000 x g for one minute. This was then followed by addition of DNA pre-wash buffer (200µl) to the column and centrifuged at 10,000x g for one minute. Five hundred microliter g-DNA wash buffer was then added and this mixture centrifuged at 10,000x g for an additional minute. For DNA elution, the column was transferred into clean 1.5ml micro tube, and 100µl of elution buffer was added followed by centrifugation at 10,000x g for one minute. The eluted DNA was stored at -20°C until required for further analysis.

Classification of MTBC species

This study employed a two-step approach where following DNA extraction, all samples were analyzed using *IS*6110 primer, an insertion element exclusive to MTBC (Hellyer et al., 1996; Kamerbeek et al., 1997; Thorne et al., 2011). *IS*6110 positive samples were then speciated through the analysis of regions of difference (Huard et al., 2003; Huard et al., 2006) using polymerase chain reaction. These are regions deleted from different MTBC genomes during evolution allowing for the establishment of their genetic lineages (De Jong et al., 2010; Brites and Gagneux, 2017; Gagneux, 2018).

The amplification reactions were done in a 25µl final reaction volume using HotStarTaq Master Mix kit (Qiagen, Heidelberg, Germany). The IS6110 PCR reaction mix included 12.5µl of 2x HotStarTaq mastermix, 0.5µl of each primer (10pmol/ul forward [5'- TCA GCC GCG TCC ACG CCG CCA - 3'] and reverse [5'- CCG ACC GCT

CCG ACC GAC GGT - 3'] primers, respectively), 2µl of template DNA and the reaction was topped up with molecular grade PCR water. The DNA was amplified in a Veriti® thermal cycler (Applied Biosystems) using the following conditions. Initial denaturation at 95 °C for 15 min followed by 35 cycles at 94 °C for 30 seconds, 55 °C for 30 seconds, and 72 °C for 45 seconds. Final extension was performed at 72 °C for 5 minutes. The success of the PCR was evaluated by visualizing size separation of the products on 1.5% agarose gel by electrophoresis, and illuminated by ethidium bromide stain under UV light.

To determine the species of MTBC, all samples were further subjected to PCR using primers targeting the regions of differentiation (RD) 1, 4, 9 and 12 (Huard et al., 2003; Huard et al., 2006). These primers included RD1 - Rv3877/8 (forward [5' - CGA CGG GTC TGA CGG CCA AAC TCA TC - 3'], and reverse [5' - CTT GCT CGG TGG CCG GTT TTT CAG C- 3']); RD 4 – Rv1510 (forward 5' - GTG CGC TCC ACC CAA ATA GTT GC- 3'], and reverse [5' - TGT CGA CCT GGG GCA CAA ATC AGT C- 3']); RD9 – Rv2073c (forward [5' - TCG CCG CTG CCA GAT GAG TC – 3'] and reverse [5' - TTT GGG AGC CGC CGG TGG TGA TGA - 3']); and RD12 – Rv3120 (forward [5' - GTC GGC GAT AGA CCA TGA GTC CGT CTC CAT – 3'] and reverse [5' - GCG AAA AGT GGG CGG ATG CCA GAA TAG T - 3']). The amplification reactions were done in a 25µl final reaction volume using HotStarTaq Master Mix kit (Qiagen, Heidelberg, Germany), using a PCR reaction mix comprised of 12.5µl of 2x HotStarTaq mastermix, 0.5ul of each primer (10pmol/µl), 2µl of template DNA and topped up with molecular grade PCR water. The DNA was amplified in a Veriti® thermal cycler (Applied Biosystems), and success visually evaluated as aforementioned, using gel electrophoresis and ethidium bromide. Classification of the MTBC based on the results of the RD PCR was done following the schema shown in Table 2.1. Samples that did not meet the criteria were classified as indeterminate. These were positive on *IS*6110 but did not match to any known RD presence/absence pattern (Warren et al., 2006).

Table 2.1. Classification of *Mycobacterium tuberculosis* complex species based on presence or absence of RD1, RD4, RD9 and RD12. Schema modified from (Warren et al., 2006).

Pathogen	**RD1**	**RD4**	**RD9**	**RD12**
Mycobacterium canettii	Present	Present	Present	Absent
Mycobacterium tuberculosis	Present	Present	Present	Present
Mycobacterium africanum	Present	Present	Absent	Present
Mycobacterium microti	Present	Present	Absent	Present
Mycobacterium pinnipedii	Present	Present	Absent	Present
Mycobacterium caprae	Present	Present	Absent	Absent
Mycobacterium bovis	Present	Absent	Absent	Absent
Mycobacterium bovis BCG	Absent	Absent	Absent	Absent

Local cluster analysis for MTBC species in the Maasai Mara Ecosystem

Following classification of the MTBC, data were geocoded to their villages of origin. To identify local clustering and evaluate their significance, a purely spatial multinomial model of the spatial scan statistics was performed using SaTScan software v9.4.4 (Kulldorff, 1997; Jung et al., 2010). The units of analysis were villages with five nominal attributes based on MTBC classification: category 1 (*Mycobacterium canettii*), category 2 (*Mycobacterium bovis*), category 3 (*Mycobacterium caprae*), category 4 (*Mycobacterium bovis BCG*) and category 5 (*Indeterminate*).

Using a likelihood ratio test, the purely spatial multinomial cluster analysis compares cases using a circular scanning window moving across the geocoded samples space (Kulldorff and Nagarwalla, 1995). The windows are variable in size, and when a cluster is identified, a test statistic comparing the potential cluster with the remaining area is calculated based on a permutation approach, thus, testing the hypothesis that cases caused by the same MTBC species are more likely to occur within the clusters than expected by chance (Kulldorff and Nagarwalla, 1995; Kulldorff, 1997). The windows that maximize the likelihood ratios, a ratio of observed to the expected number of cases, are identified as potential clusters. The maximum radius of the spatial window was set at 50% with a Monte Carlo based p-value <0.05 indicative of statistically significant clusters (Jung et al., 2010).

Results

Molecular analysis and identification of MTBC species

This study analyzed 227 sputum samples (57% females and 43% males) from TB suspect patients at three local hospitals in the Maasai Mara Ecosystem that met the inclusion criteria. Sample distribution from the local hospitals was 71%, 4% and 25% from Sekenani Health Centre, CMF Aitong Health Centre and Talek Community Health Centre, respectively. Out of the 227 samples analyzed, 13% (29/227) were positive on smear microscopy while 40.5% (92/227) were positive on *IS*6110 PCR. Five percent of the samples (12/227) were positive on smear microscopy but negative on *IS*6110 PCR, thus, potentially indicative of the presence of nontuberculous mycobacteria or an MTBC species with a low copy number. Surprisingly, only 8% (17/227) of samples were positive on both smear microscopy and *IS*6110 PCR analysis. For the classification of the ninety two samples that were *IS*6110 PCR positive into MTBC species, an initial binary grouping was made using RD9. Its presence (positive RD9 PCR) is indicative of *M. tuberculosis* or *M. canettii* while its absence (negative RD9 PCR) denotes either *M. africanum*, *M. caprae*, *M. pinnipedii*, *M. microti*, *M. bovis* or *M. bovis BCG* (Huard et al., 2003; Warren et al., 2006). From these two broad classifications (RD9 positive or negative), samples were then sequentially differentiated using RD4, RD1 and RD12, with 8% (n=7), 48% (n=44), 9% (n=8), 3% (n=3) and 32% (n=30) being classified as *M. bovis, M. bovis* BCG, *M. canettii*, *M. caprae* and indeterminate (did not match any known RD pattern for speciation), respectively**.** Surprisingly, RD-based classification did not yield any *M. tuberculosis*. Distribution of the MTBC species in different villages across the ecosystem and among different age groups are shown in Figure 2.1 and Table 2.2, respectively.

Figure 2.1. Distribution of the different *Mycobacterium tuberculosis* complex species (n=62) in different villages across the Maasai Mara Ecosystem. Indeterminate samples are not shown.

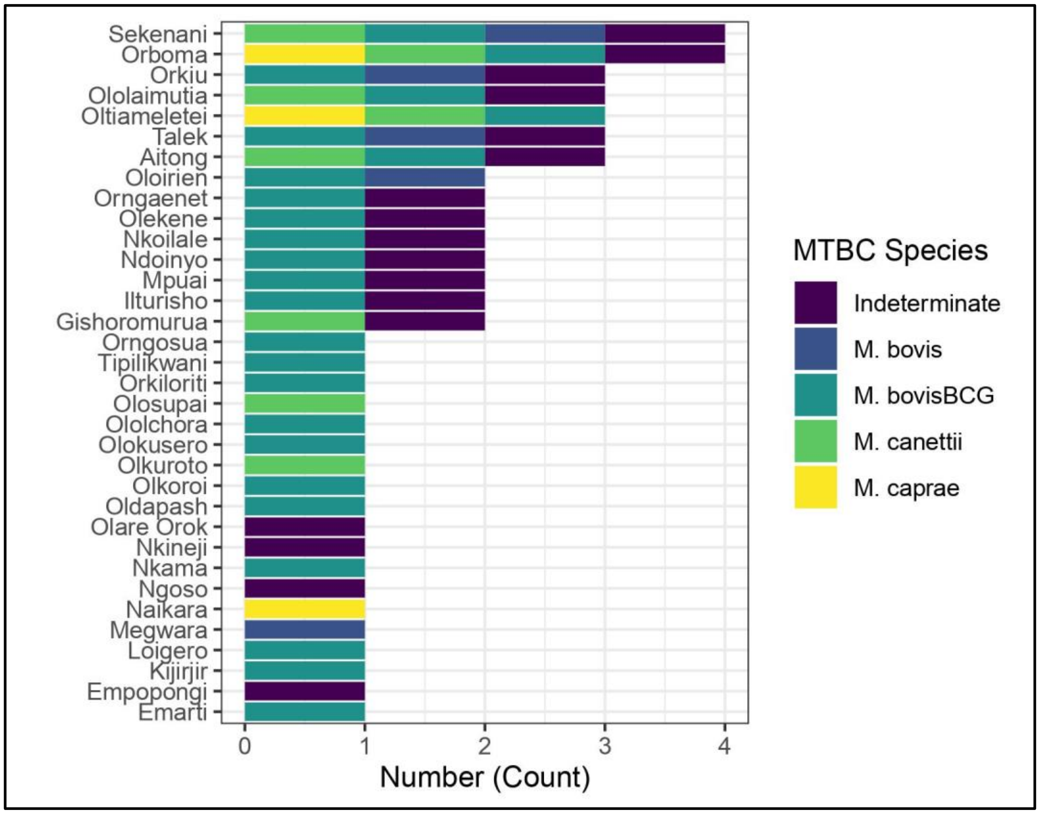


Table 2.2. Distribution of Mycobacterium tuberculosis complex species from the Maasai Mara Ecosystem by age groups. Three individuals did not have their age indicated.

	0-9 years	10-19 years	20-29 years	30-39 years	40-49 years	50-59 years	>60 years	Total
Indeterminate	0	7	6	4	2	4	6	29
Mycobacterium bovis	0	2	0	1	2	0	0	5
Mycobacterium bovis BCG	1	7	3	10	7	4	12	44
Mycobacterium canettii	0	1	1	0	3	2	1	8
Mycobacterium caprae	0	0	0	0	0	1	2	3

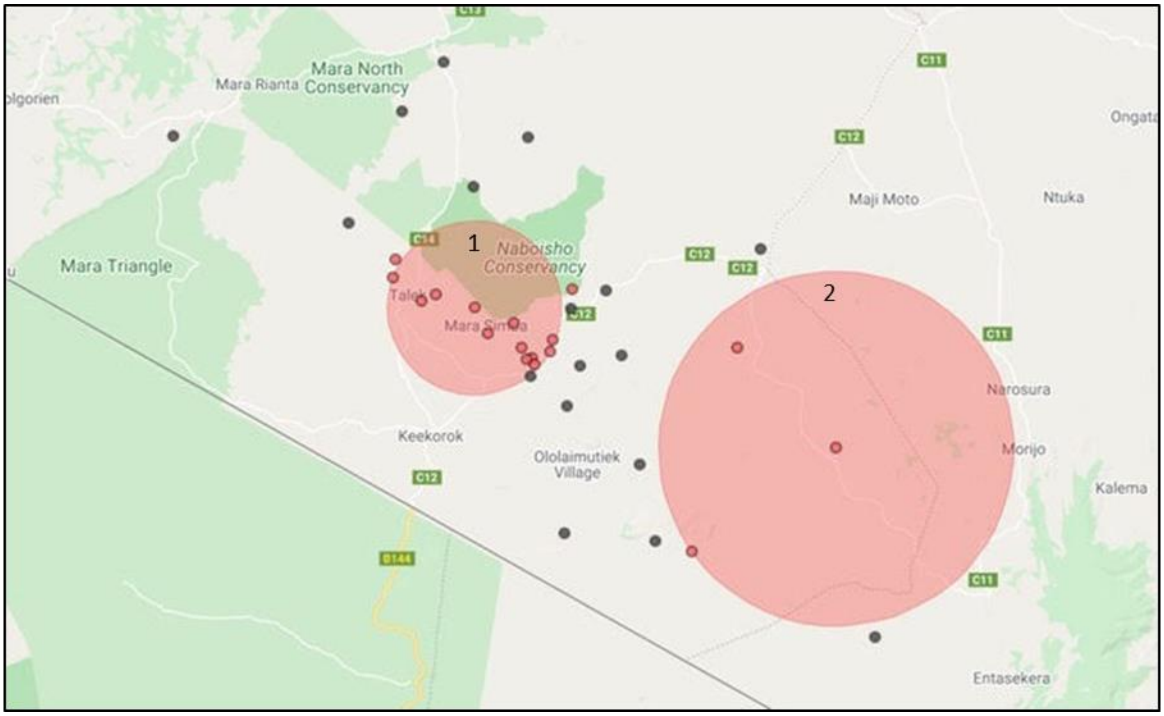
Spatial cluster analysis

The multinomial model of the spatial scan statistic revealed four clusters, though these were not statistically significant (p-value>0.05). Cluster 1 included twelve villages situated in a belt around the Maasai Mara National Reserve. A patient from any of these villages had a 7.14x greater risk of testing positive for *M. bovis* compared to being from any other village in the ecosystem. Cluster 2 involved three villages located towards the southern side of the ecosystem along the Tanzania border (Figure 2.2). A patient from any of these villages had a 14.8x greater risk of testing positive for *M. caprae* compared to the other remaining villages. Cluster 3 and 4 included one village each with the predominant category being *M. caprae* in each cluster (Table 2.3). The distribution of the different MTBC species across different villages is shown in Table 2.2.

Table 2.3. Spatial clustering results from the multinomial spatial scan statistics of Mycobacterium tuberculosis complex species distribution in the Maasai Mara Ecosystem (filtered to those with a relative risk>1). Cluster 1 was comprised of villages adjacent to the Maasai Mara National Reserve, while villages located along the Tanzania border dominated cluster 2. No clusters were statistically significant (p-value >0.05).

Cluster	Radius	Villages	Category	Relative Risk
1	10.24km	Tipilikwani, Ololchora, Ndoinyo, Emarti, Talek, Oldapash, Sekenani, Orkiu, Oloirien, Ngoso, Loigero, Olekene	*M. bovis*	7.14
			M. bovis BCG	1.09
			Indeterminate	1.04
2	20.85km	Naikara, Nkineji, Olosupai	*M. canettii*	4.24
			M. caprae	14.83
			Indeterminate	1.02
3	0km	Gishoromurua	*M. canettii*	3.14
			Indeterminate	2.44
4	0km	Oltiameletei	*M. canettii*	4.24
			M. caprae	14.83

Figure 2.2. Clusters 1 and 2 from the multinomial spatial scan statistics of Mycobacterium tuberculosis complex distribution in the Maasai Mara Ecosystem. Cluster 1 was comprised of twelve villages located adjacent to the Maasai Mara National Reserve. Cluster 2 had three villages located along the Tanzania border. All clusters were not statistically significant (p-value >0.05).



Discussion

The overall goal of this study was to evaluate the occurrence of MTBC species and their patterns of spatial clustering in the Maasai Mara Ecosystem in Kenya. The molecular analysis revealed the possibility of at least four different MTBC species co-circulating in the ecosystem (Figure 2.1). Although cases of *M. bovis* were expected, their frequency in this population (8%) was high in comparison to other populations at high-risk human-livestock-wildlife interfaces in which the prevalence is between 0.2-3% (Gumi et al., 2012; Ibrahim et al., 2016; Katale et al., 2017; Getahun et al., 2020). However, this is not entirely surprising as this study focused on a high-risk community with widespread consumption of raw meat, milk and other animal products, and congregation of humans in villages around the Maasai Mara National Reserve during dry season grazing of livestock (Omondi et al., 2021). Although, *M. bovis* has been isolated from various livestock species in Kenya, especially those from pastoralist areas (Gathogo et al., 2012; Kuria and Gathogo, 2013; Kuria et al., 2018), there is paucity of data from human populations, and especially from at-risk marginalized populations. These populations mix livestock herds from different households during dry season grazing, with increased contact with wildlife, through forage patches and at watering points, a factor shown to influence seropositivity rates in such livestock populations (Lekolool, 2011). Consequently, the potential for infected livestock spreading disease to humans in the face of close contact and consumption of raw animal products exists (Ayele et al., 2004; Mfinanga et al., 2004a).

The presence of *M. caprae* in addition to *M. bovis* is profound as these two pathogens are the main causes of zoonotic TB. *M. caprae* infects many wild and domestic ungulates, and is considered a pathogen of public health concern even though its contribution to the overall human TB burden is low (Hansen et al., 2012). In this study, *M. caprae* cases represented 3% of the overall TB burden in this population; a higher proportion when compared to that in Spain (Rodríguez et al., 2009). This is usually associated with exposure to animals, consumption of raw animal products or reactivation following changes to the immune system with age or disease (Prodinger et al., 2014). However, these results need to be interpreted with caution, as this was a small sample, and only from three local hospitals serving the ecosystem. Thus, not representative of the whole population.

Based on the results of the regions of difference analysis, the majority of the cases in this sample were due to *M. bovis* BCG (48%). This is a surprising finding given that *M. bov*is BCG is a rare disease, and typically associated with local or disseminated infections following BCG (bacillus Calmette-Guérin) immunization (Grange, 1998; Liberek et al., 2006; Furuichi et al., 2020), as nosocomial infections (Wansaula et al., 2019) or following intravesical infusion for treatment of bladder cancer (Abu-Nader and Terrell, 2002; Nadasy et al., 2008). BCG immunization rates in Kenya are high at 96.7% (95% CI: 95.9-97.5%) (KNBS, 2015; Allan et al., 2021), although with high levels of concomitant syndemics (Vos et al., 2020), the potential role of BCG vaccination and development of infection is unknown, and warrants further research. *M. bovis* BCG has also been reported as a pulmonary infection in a healthy individual (Jiang et al., 2015). Kenya has conducted two national TB surveys in 1956 and 2016 (MOH, 2016; Enos et al., 2018); in both surveys, there was no data on MTBC other than *M. tuberculosis*. Although these results warrant further investigation, they may reflect local transmission with concurrent influences of other syndemics in the region (NACC, 2016; Achoki et al., 2019). On the other hand, however, RD-based classification of *M. bovis BCG* is based on the absence of these regions of differences, which implies potential misclassification when using RD-based methods without culture. This may be challenging since RD exists in low copy numbers across the mycobacterial genome, and may lead to non-detection using PCR in the absence of culture.

The presence of *M. canettii* in this part of the world is not surprising given most cases have been associated with the Horn of Africa (Pfyffer et al., 1998; Miltgen et al., 2002; Boyer-Cazajous et al., 2014; Aboubaker Osman et al., 2016; Supply and Brosch, 2017). The proportion of cases attributable to *M. canettii* in this study is similar to that in Djibouti, a region associated with most of the global isolates of this pathogen (Boyer-Cazajous et al., 2014). *M. canettii* is thought to be an opportunistic environmental pathogen (Koeck et al., 2011) with minimal capability for human-to-human transmission, and potentially part of an ancestral clade of MTBC organisms (Veyrier et al., 2011; Supply et al., 2013). In this study, the findings may reflect the opportunistic nature of the pathogen.

The multinomial model of the spatial scan statistics revealed four clusters with the primary cluster comprising twelve villages (Table 2.3). Although the clusters were not statistically significant, they provide some insights to explore the epidemiology of MTBC, in communities in this ecosystem against the backdrop of sociocultural practices. First, the twelve villages are located within <2 kilometers from the border of the Maasai Mara National Reserve. These villages have also been shown to be important for dry season grazing where animals and people from across the ecosystem congregate to access the forage-rich protected area (Omondi et al., 2021). Pastoralist migration has been known to follow familial social networks (Grandin, 1991), and these gatherings involve overcrowding in manyattas, pastoralist households, and survival based upon meat and milk. Thus, the high relative risk for *M. bovis* (7.14) may be indicative of localized transmission, more likely associated with spatiotemporal-linked risk factors. The higher relative risk for *M. caprae* in cluster 2, which consists of villages in remote areas of the ecosystem, warrants further investigation. These villages are situated on the southwestern part of the ecosystem towards the Tanzania border, and the spatial patterns may be capturing either increased consumption of sheep and goat products or the influence of the international border considering that movement of livestock and people is common for business and to access forage and water for livestock (Omondi et al., 2021). Cluster 3 and 4 villages are found in areas that relatively sandwiched between community conservancies. The role such conservancies play in delineating human and animal movement, and interaction patterns, and hence potential exposures needs to be investigated further. In addition, though speculative, this finding may reflect the change in species kept at households from cattle to sheep and goats, in response to reduced forage areas for cattle. Interestingly, Oltiameletei village in cluster 4 is located close to several villages in cluster 1. Thus, the high relative risks for *M. caprae* and *M. canettii* may point to nuances in exposure and transmission at a local level (Lonnroth et al., 2009; Hargreaves et al., 2011; Shelby et al., 2018).

While there were many indeterminate cases, which need to be investigated further, a sample negative on *IS*6110 but positive on microscopy may be indicative of nontuberculous mycobacteria which have been associated with significant human infections and treatment challenges (Mnyambwa et al., 2018a). Alternatively, these may reflect limitations of using RD PCR for differentiation of MTBC.

This study has several potential limitations. The gold standard for TB diagnosis is the culturing of the causative organism from sputum, bronchial washings and other samples. This provides pure isolates that allows for the interpretation of tests including RD-based classification less challenging. MTBC are phylogenetically very close and notoriously difficult to tease apart using common protocols. Secondly, the use of convenience sampling limits the generalizability of the results as the persons attending TB clinic in the three local hospitals may not be representative of the target population in the ecosystem. In addition, the lack of concurrent animal data hampers our understanding of sources of zoonotic tuberculosis in the ecosystem. Further, the study was conducted in a relatively small geographical region, and was hospital-based without concurrent information on exposures, risks or presence of concomitant infections from the patients, further limiting the generalizability of the findings. However, the study provides a useful initial step in understanding the occurrence of MTBC in a high-risk population as a precursor to designing appropriate One Health based studies and interventions.

Conclusions

Although the study was conducted in a small geographical region with samples collected conveniently, this study has shown that there are several different MTBC members co-circulating in this ecosystem. Specifically, this study has shown higher levels of zoonotic TB due to *M. bovis* and *M. caprae* as hypothesized – although these results warrant further investigation. Although the potential role of sociocultural practices, including consumption of raw animal products, movement patterns and interactions within the ecosystem are difficult to quantify, the findings from this study point to their possible influence in MTBC occurrence and spatial patterns. Specifically, this study shows that villages adjacent to the Maasai Mara National Reserve have a relatively higher risk of *M. bovis* and *M. caprae*, which may be attributed to human congregation patterns during the dry season grazing of livestock (Omondi et al., 2021). Finally, the fact that *IS*6110 PCR had a higher rate of test positivity when compared to smear microscopy shows it utility in identifying potentially infected individuals – an important component for TB control (WHO, 2019, 2020).

Chapter 3 | Assessing socio-cultural drivers of tuberculosis infections in the Maasai Mara Ecosystem

Background

Tuberculosis (TB), is a concern in pastoralist communities who have traditionally been excluded from public health infrastructure (Gele et al., 2009; Gele et al., 2010; Adlo et al., 2020). The primary agent of human TB, *Mycobacterium tuberculosis* (*M. tuberculosis*), is part of the *Mycobacterium tuberculosis* complex (MTBC), which comprises several species of mycobacteria capable of infecting humans and animals (Brites and Gagneux, 2017; Malone and Gordon, 2017). Pastoralist communities are at a higher risk of different MTBC (Olea-Popelka et al., 2017), with TB control confounded by zoonotic TB, caused by *Mycobacterium bovis* (*M. bovis*), and whose epidemiology is influenced by prevalent social and cultural practices (Mfinanga et al., 2003; Brooks-Pollock et al., 2014; Olea-Popelka et al., 2017). TB management in these communities is further complicated by the use of smear microscopy for diagnosis as it does not allow for the speciation of MTBC (Siddiqi et al., 2003; Ganoza et al., 2008), especially between *M. tuberculosis* and *M. bovis*, which have overlapping social determinants.

TB is a social disease with communities ranking low on socioeconomic indicators having higher incidences of infection (Baker et al., 2008; Lonnroth et al., 2009; Baussano et al., 2013). Social determinants of TB, which take account of socioeconomic inequalities, overcrowding within households, and urbanization, among other social determinants of health (CDSH, 2008), influence TB epidemiology including baseline prevalence in the population, exposure and transmission, pathogenesis of the infection, access to care and treatment outcomes (Hargreaves et al., 2011).

Although the sociocultural practices are diverse, migration in search of forage and water for livestock, is key to pastoralist resilience (Galaty, 2015). However, livestock movements are associated with increased risk of infections to domestic herds, which in turn pose a threat to humans due to accompanying sociocultural factors, such as consumption of raw animal products (Cleaveland et al., 2007). Seldom explored is the impact of livestock-mediated human migration on the occurrence of human diseases such as TB. For instance, farms with high number of inward contacts have been shown to have a higher risk of infection with *M. bovis* (Sintayehu et al., 2017). However, there is paucity of data on how these livestock-mediated community movements influence human health. In addition, there is contradictory evidence on the role of sociocultural mediated exposures on the occurrence of TB in pastoralist communities. For example, although one would expect increased risk of zoonotic TB against the backdrop of sociocultural practices (Gumi et al., 2012; Muller et al., 2013; Olea-Popelka et al., 2017), cattle-associated risk factors are not always linked with TB in humans (Meisner et al., 2019). In this study (Meisner et al., 2019), presence of a tuberculin skin test positive livestock in a household was associated with lower risk of TB in men. Further, while household consumption of raw milk has been shown to be risk factor for zoonotic TB (Ayele et al., 2004; Mfinanga et al., 2004a), some studies found the practice protective (Koech, 2001). These findings, although contrarian, point to a need to understand local drivers of TB infections as a precursor to designing control programs and localizing One Health approaches.

Amongst tools for evaluating risk factors, machine learning models are increasingly used in epidemiology to tease apart the relative influences of risk factors to disease outcomes (Friedman and Meulman, 2003; Mansiaux and Carrat, 2014; Machado et al., 2015; Fountain-Jones et al., 2019; Lu et al., 2019; Machado et al., 2019), as they offer a flexible approach to analyzing nonlinear responses and modeling high dimensional interactions with better predictive performances (Tu, 1996; Elith et al., 2008; Fountain-Jones et al., 2019). In this study, we compared three popular machine leaning models; Random Forest (Breiman, 2001), Gradient Boosting Machine (Friedman, 2001), and Support Vector Machine (Noble, 2006) to classify household TB events based on a set of risk factors in the Maasai Mara Ecosystem. Household TB exposure is a complex process involving several risk factors and their interactions (Cleaveland et al., 2007; Shelby et al., 2018; Meisner et al., 2019). Although machine learning models focus more on the predictive rather than causal modeling, it is recognized that heterogeneity in outcomes can be explained by both causal and non-causal factors (VanderWeele, 2009). This insight allows for the utilization of predictive modeling as a guide for areas to consider when designing interventions (Lynch and Moore, 2016; Flaxman and Vos, 2018; Wager and Athey, 2018; Bi et al., 2019).

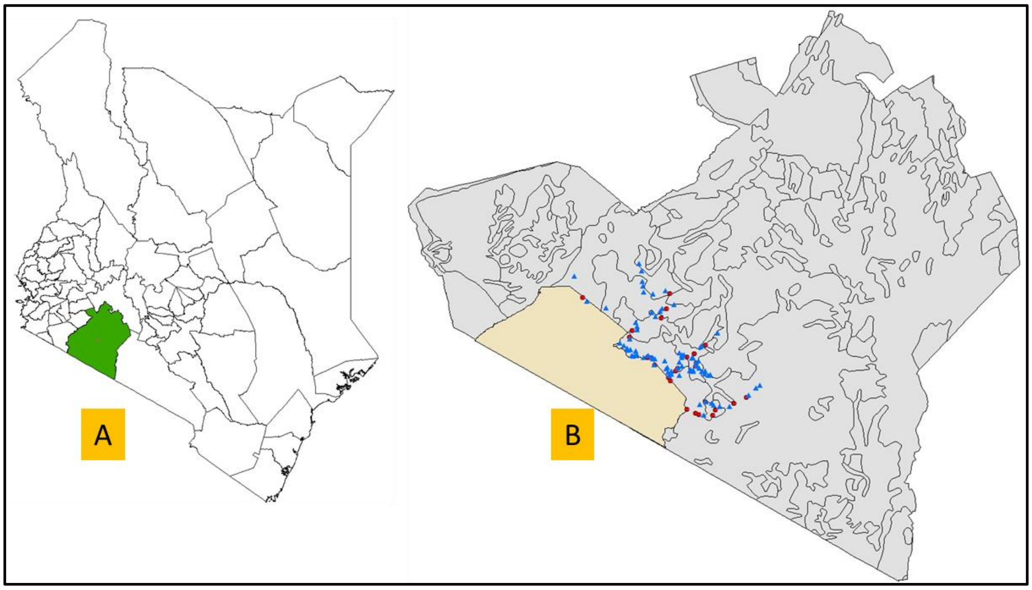
This study was conducted in the Maasai Mara Ecosystem in Kenya, an area occupied by Maasai pastoralist community, and characterized by human and animal migration during the dry season for livestock grazing, and other socioeconomic activities, with implications for disease transmission and control (Omondi et al., 2021). Kenya is a high TB burden country (WHO, 2020), with TB case notification data showing higher rates in pastoral areas (Oliwa et al., 2018) where communities have low levels of knowledge on TB control, and unique sociocultural practices that heighten its risk (Koech, 2001; Mfinanga et al., 2003; Haasnoot et al., 2010). Thus, these communities may greatly benefit from an integrated approach that goes beyond the traditional human health sector if risk factors are identified (Lonnroth et al., 2009; Lönnroth et al., 2010; Rasanathan et al., 2011). The goal of this study was to understand the epidemiology of human TB in the ecological context of sociocultural mediated risk factors in a pastoralist community in Kenya. We hypothesized that livestock-mediated human movements expose households to infection, and drive TB occurrence patterns in pastoral households in this ecosystem.

Methods

Study design

Sampling was conducted using a heterogeneous purposive sampling scheme in households within 20 kilometers of the Maasai Mara National Reserve (Figure 3.1) (Patton, 1990; Suri, 2011; Palinkas et al., 2015). This distance cutoff was selected as it represented the daily average distance covered by pastoralists when grazing livestock (Coppolillo, 2000; Coppolillo, 2001; Turner and Schlecht, 2019). Questionnaires were administered to 164 households who identified as pastoralists, had at least one species of livestock, and consented to participating in the study. Households were defined as all persons living within a *manyatta*, for a period of one month prior to the interview, and were identified by the respondent at the time of the interview.

Figure 3.1. Map of the study area, with (A) showing map of Kenya with Narok County shaded, while (B) a zoomed in map of Narok County showing the Maasai Mara National Reserve, with households in circles and diamonds denoting tuberculosis positive and negative households, respectively.



Household TB was defined as the presence of at least one case of hospital diagnosed human TB in the household in the last year prior to the interview. The definition was highly influenced by the fact that local health facilities predominantly used smear microscopy for the diagnosis of TB. However, this may be an underrepresentation of the true number of TB positive cases in the area (Enos et al., 2018). Data was collected on sociodemography of the households: location, sex, number of males and females, education (none, primary, secondary, college and university), duration of residence and occupation. In addition, data was collected on consumption of raw animal products (milk, blood and meat), and their frequencies, and sharing housing with animals (always, never, and sometimes). Consumption of raw animal products was defined as always, sometimes, rarely and never. Variables associated with animals included numbers of different species in the household, grazing patterns (categorized as <5 km, 5-10 km, and >10 km from home), livestock utilization of the MMNR (categorized as always, sometimes, rarely and never), and season of MMNR use (long wet, dry, short wet or others). Transboundary movement was recorded as livestock movement into Tanzania, while wildlife-livestock interaction was recorded as always, sometimes, rarely, and never. Livestock movement included gifting (respondent receiving livestock as a gift), bride price (respondent receiving livestock when a female household member is married), in addition to buying and selling, denoting the trading of household livestock in formal or informal markets. A final category of livestock movement recorded was agistment, which denoted the respondents' temporary transfer of livestock to another location (village) for purposes of accessing forage and water during the dry season. The definitions of all variables are provided in the Appendix (Table 6).

Data analysis

Bipartite network construction and metrics

For the household livestock movement data (gifting, bride price, agistment, buying and selling), household-village bipartite networks were constructed. In graph theory, nodes can be divided into *k* independent groups. Networks with two groups are termed *bipartite* networks (Jacoby and Freeman, 2016). Five household-village bipartite networks were constructed to represent each type of livestock movement in the ecosystem, with linkages denoting villages to which households sent to and/or received animals from. This network representation is appropriate as data collected on households' livestock movements to and/or from different villages in the Maasai Mara Ecosystem. These bipartite graphs were then reprojected as one-mode networks, using an overlap counting method (Wasserman and Faust, 1999), leading to a household-household network with an edge (connection) existing between households if they had sent to and/or received animals from a common village.

Degree and betweenness centrality values were then calculated for each household. These values were extracted and used in the subsequent analysis. Degree was defined as the number of contacts a household engages via a movement type, while betweenness denoted a measure of the proportion of times a household lies on the path between other households in the network, thus, creating indirect connections between other households in the network (Freeman, 1978; Wasserman and Faust, 1994).

Construction of predictive models

Prior to analyses, we divided into tertiles (low, medium and high) the number of cattle, goats and sheep in a household; the length of time a respondent has lived in the village (residence); and number of males and females within a household (Kotsiantis and Kanellopoulos, 2006; Webb, 2014). Due to the low number of respondents indicating "university" as a level of education, "university" and "college" were combined to form one level, "college". For all questions relating to frequencies, sometimes and rarely categories were collapsed into a single "sometimes" category. For each household, a GPS location was recorded and used to calculate distance to the MMNR border using ArcGIS 10.5 (ESRI, 2011). The distance, and extracted centrality metrics were also used in the construction of predictive models.

Variable selection

In machine learning, variable selection is important as it allows for the improvement of model accuracy, and reduction in training time by eliminating irrelevant variables (Khalid et al., 2014). In this study, we examined the cross tabulations between each set of variables and the outcome, household TB status, for significance using a chi-square test of independence (Zibran, 2007). Variables that had p-value <0.15 were included in the subsequent machine learning models.

Machine learning models

For classification, we developed three machine learning models; Random Forest (RF), Gradient Boosting Machine (GBM) and Support Vector Machine (SVM). RF is a classification and regression algorithm where a set of data from the original dataset is generated without replacement, and used to create an ensemble of decision trees by repeatedly bootstrapping samples from the training set and fitting trees to each replicate (Breiman, 2001). In a single tree, the leaves represented the TB status of the household (positive or negative), and the branches represented combinations of risk factors. RF construct hundreds of trees using bootstrap samples, using set criteria for the number of trees (n_{tree}), and number of risk factors (m_{try}) to be used to split each node. These trees are then aggregated, by majority vote, to obtain estimates (Breiman, 2001). Briefly, one draws n_{tree} bootstrap samples from the original dataset (training set: 80% of the data), then for each bootstrap sample a classification tree is grown based on selected number predictors (m_{try}) at each node, and finally to validate the model, the performance of the model is evaluated against new data (testing set: 20% of the data) and predictions aggregated (Breiman, 2001; Liaw and Wiener, 2002). In essence, each tree predicts the positive or negative classification of an observation by majority vote, and this 'voting' is aggregated as the overall RF prediction (Breiman, 2001).

GBM is a non-parametric algorithm for supervised machine learning technique where boosting refers to the sequential iterative addition of an ensemble of models fitted from a base learner, thus improving the accuracy of the model (Friedman, 2001; Natekin and Knoll, 2013). Unlike RF where the trees are grown in parallel from the original dataset, and a voting by majority of all trees to give prediction, GBM grows each decision tree in series, where each decision tree predicts the error of the previous one, hence, improving/reducing (boosting) the residuals/error (gradient). In summary, GBM optimizes the prediction accuracy based on iterations of weaker classification tree models. To illustrate GBM, if we take dataset $\mathrm{x}, \mathrm{y}_{\mathrm{i}=1}^{N}$, where $x = (x_{1 \ldots}\, \mathrm{x}_{\mathrm{n}})$ is a set risk factors and y is the outcome. We aim to develop a function approximating the data and its error term *e;*

$$y_i = \mathrm{F}_1\,(\mathrm{X}_\mathrm{i}) + e_{1i} \qquad \text{[Equation 1]}$$

$\mathrm{F}_1\,(\mathrm{X}_\mathrm{i})$ has poor accuracy. Thus, we train a second model on the error term, weighting it to account for the poor accuracy in the previous model (a weak learner):

$$y_i - \mathrm{F}_1\,(\mathrm{X}_\mathrm{i}) = e_{1i} = \mathrm{h}_1\,(\mathrm{X}_i) + e_{2i} \qquad \text{[Equation 2]}$$

Thus, the new model is:

$$F_2 (X_i) = F_1 (X_i) + h_1 (X_i) + e_{2i} \qquad \text{[Equation 3]}$$

Thus, at the end, we have iteratively trained new models *M* times, with the final model (Equation 4), containing a series of h_M (X_i) weak learners, with a minimized residual error, expressed as the loss of function L [Y, F_M (X)].

$$F_M (X_i) = F_{M-1} (X_i) + h_{M-1} (X_i) \qquad \text{[Equation 4]}$$

SVM is an algorithm for binary classification problems based on the Vapnik–Chervonenkis and dimension theory, a statistical learning theory, and structural risk minimization principle, aimed at enhancing the separation of the two classes using a multidimensional hyperplane, thus, improving generalization of the model (Cortes and Vapnik, 1995; Noble, 2006). Briefly, SVM finds an optimal classification hyperplane which fulfills the conditions of classification based on the data. It then tries to achieve the widest separation of the two classes by maximizing the distance between the data and the hyperplane. The largest achievable maximal margin of separation is considered optimal (Fradkin and Muchnik, 2006).

For each machine learning model, 80% of the data was used as training dataset, with the remaining 20% used for model evaluation as independent dataset, and model performance evaluated. Across all models, we used 10 repetitions of 10-fold crossvalidation to estimate model performance and prevent overfitting as the same dataset was used for both training and testing the models.

Model performance

Model performance was assessed by calculating accuracy (ACC), specificity (Sp) and sensitivity (Se) of the model through a confusion matrix. A confusion matrix comprised the total number of TB positive households that were correctly (true positive; TP) or incorrectly predicted by the model (false positive; FP). It also included the number of TB negative households correctly (true negative; TN) or incorrectly (false negatives; FN) predicted. ACC was defined as (TP + TN)/(TP +TN + FP + FN); Sp = (TN)/(TN + FP)*100; while Se = TP/(TP + FN)*100. The Receiver Operating Characteristics (ROC) curve was also plotted and the area under the curve calculated to evaluate model performance.

The best model was assessed by comparing the AUC score, sensitivity and specificity from the three models, from which we visualized and explored the results using variable importance and partial dependency plots. The variable importance plot was calculated using classification loss error, which computes the pairwise expected loss in predictive performance in classification of TB positive versus TB negative households in comparison to the full model (Goldstein et al., 2015). Partial dependency plots visualize the marginal effect of a risk factor, while controlling for other risk factors, on the likelihood of a positive household TB status, and are reported on the logit scale, with higher values signifying high risk of a household being TB positive (Friedman, 2001).

Results

Overall, 164 households from sixty seven villages in the Maasai Mara Ecosystem were represented in this study, with 18% of households (29/164) reporting at least one TB case in the year prior to the interview. Thirty six percent of respondents reported consuming raw milk from cattle, and 15% each, from goat and sheep. Consumption of raw milk from cattle was associated with higher odds of household TB infections (4.5, 95% CI 1.9-10.8), with households who reported to 'always' consuming raw milk from livestock having higher odds of infection when compared to those who reported 'never'. Households that reported consuming raw milk from goats had lower odds (0.2, 95% CI 0.01-1) when compared to those who did not. For the bride price degree and betweenness, and selling degree, households that had high centrality metrics had higher odds of household tuberculosis infection (Table 3.1). Descriptive summaries for all variables in this study are presented in the appendix (Table 6).

Variable selection and performance of machine learning models

Using a chi-square test of independence, and a cutoff of p-value<0.15 for inclusion, 11 out of 54 variables were selected for inclusion in the machine learning models (Table 3.1). None of the wildlife related variables met the inclusion criteria, while nine of the variables selected were associated with food consumption practices, and movement of livestock within the Maasai Mara ecosystem.

The best model was chosen by comparing the accuracy, area-under-the-curve (AUC) scores, specificity, and sensitivity generated from the confusion matrix averaged over 10 repetitions of 10-fold crossvalidation. The model accuracies for RF, GBM and

SVM were 71.5% ±4.5, 84.4% ±0.9, and 81% ±1.7, respectively. Specificities for the three models were 71.6% ±4.8 for RF, 94.6% ±0.7 for GBM, and 96.9% ±1.7 for SVM. Model sensitivities were 69.2% ±11, 38.3% ±4.1, 9.6% ±4.8, for RF, GBM and SVM, respectively, with a corresponding AUC scores of 92.6%, 91.8% and 90.4%. RF was the best performing model as it had a good AUC score with a better sensitivity, when compared to the GBM and SVM.

Table 3.1. Variables included in the machine leaning models. All variables with a chi-square test of independence p-value<0.15 were included. Household tuberculosis status is categorized as positive or negative, with their associated proportions based on the number of respondents, odds ratios and p-value.

Variable (code)	Levels	Number (% Positive)	Number (% Negative)	Odds Ratio (95% CI)	p-value
Business person	Yes	4 (2.4)	5 (3.1)	4.2 (0.9-17.3)	0.09
	No	25 (15.2)	130 (79.3)		
Consumption of raw cattle milk	Yes	19 (11.6)	40 (24.4)	4.5 (1.9-10.8)	0.0006
	No	10 (6.1)	95 (57.9)		
Consumption of raw goat milk	Yes	1 (0.6)	24 (14.6)	0.2 (0.01-1)	0.096
	No	28 (17.1)	111 (67.7)		
Consumption of raw sheep kidney	Yes	20 (12.2)	70 (42.7)	2.1 (0.9-5.1)	0.140
	No	9 (5.5)	65 (39.6)		
Frequency of consumption of raw milk	Never	10 (6.1)	95 (57.9)	Ref	0.0001
	Sometimes	1 (0.6)	10 (6.1)	0.95 (0.2-25)	
	Always	18 (11)	30 (18.3)	5.7 (2.4-14)	
Household resident coughing for >1 month	Yes	10 (6)	17 (10.4)	3.6 (1.4-9.1)	0.009
	No	19 (11.6)	118 (72)		
Bride price network degree	Low	16 (9.8)	102 (62.2)	2.5 (1.1-5.8)	0.047
	High	13 (7.9)	33 (20.1)		
Bride price network betweenness	Low	24 (14.6)	126 (76.8)	2.9 (0.8-9.4)	0.138
	High	5 (3.1)	9 (5.5)		
Buying network betweenness	Low	14 (8.5)	41 (25)	Ref	0.071
	Medium	10 (6.1)	43 (26.2)	0.7 (0.3-1.7)	
	High	5 (3.1)	51 (31.1)	0.3 (0.1-0.9)	
Selling degree	Low	14 (8.54)	40 (24.39)	Ref	0.007
	Medium	3 (1.83)	55 (33.53)	0.2 (0.03-0.6)	
	High	12 (7.32)	40 (24.39)	0.9 (0.35-2.1)	
Selling betweenness	Low	14 (8.5)	40 (24.4)	Ref	0.140
	Medium	9 (5.5)	51 (31.1)	0.5 (0.2-1.3)	
	High	6 (3.7)	44 (26.8)	0.4 (0.1-1.1)	

Variable importance

The most important predictors based on the RF model, for a positive household tuberculosis status were selling degree, consumption of raw milk from goats, frequency of consumption of raw milk in the household, bride price degree, and household's buying betweenness (Figure 3.2). To further elucidate the functional relationships between variables and the outcome, we used partial dependence plots to graphically visualize the marginal effects of variables in our model on household's tuberculosis risk (Hastie et al., 2009). Essentially, we hold a variable value constant, and average the effect of combinations of all the other variables in predicting the occurrence of household tuberculosis (Friedman, 2001). We present the partial dependence plot for all the eleven predictors in the RF model (Figure 3.3), with higher values on the y-axis indicating a higher probability of having a positive case of tuberculosis in the household. There was an increased risk of household tuberculosis with increased frequency of consumption of raw milk, being a merchant, and consumption of raw milk from cattle. In addition, household tuberculosis risk increased with the presence of a household member coughing for more than a month, having a high bride price degree and betweenness (Figure 3.3). The risk for household tuberculosis was low among those who consumed raw milk from goats.

Figure 3.2. Variable importance plot. Variables in the random forest model are ordered based on expected loss of predictive performance following permutation. The more a variable alters model performance during permutation, the more important it is considered to be in predicting household tuberculosis status.

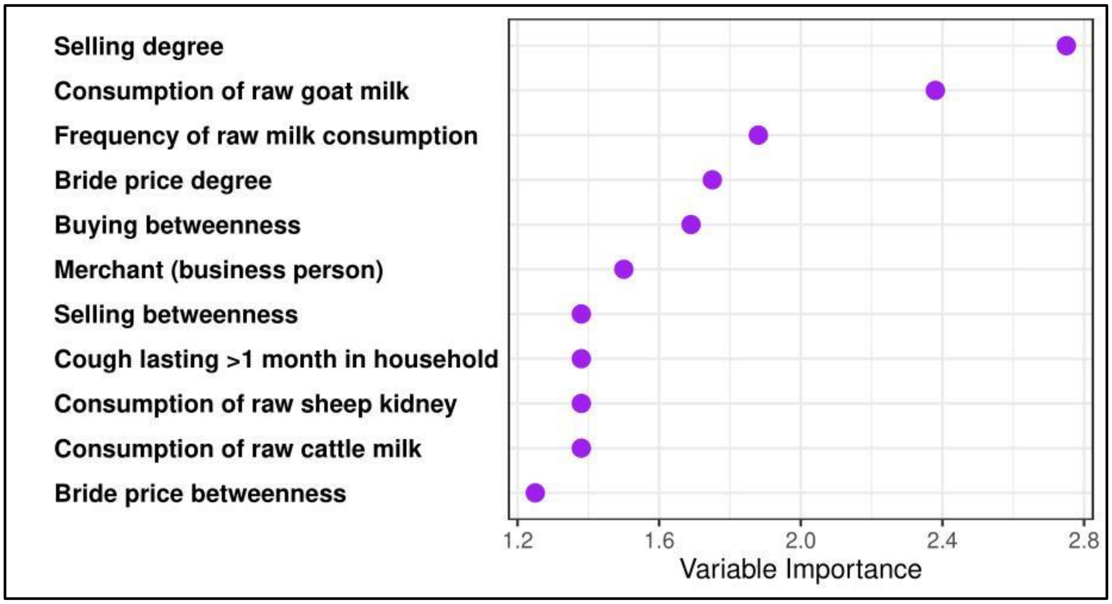
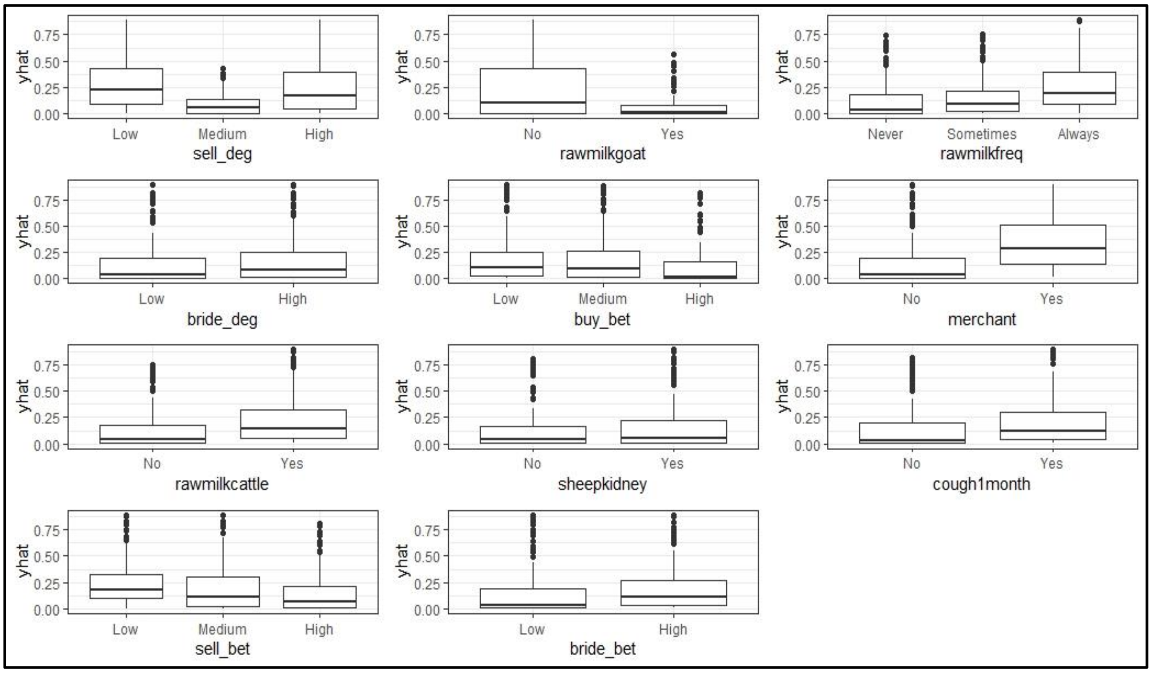


Figure 3.3. Partial dependence plots of the marginal effect of all eleven variables on the risk of tuberculosis in a household in the random forest model. The predictor names are: sell_deg = a household's selling degree; rawmilkgoat = consumption of raw milk from goats; rawmilkfreq = frequency of consumption of raw milk; bride_deg = a household's bride price degree; buy_bet = a household's buying degree; merchant = a businessperson; sell_bet = a household's selling degree; rawmilkcattle = consumption of raw milk from cattle; bride_deg = a household's bride price degree; cough1month = presence of a household member coughing for more than 1 month; and bride_bet = a household's bride price betweenness.



Discussion

The goal of this study was to investigate the epidemiology of human tuberculosis in the context of sociocultural mediated risk factors in the Maasai Mara Ecosystem in Kenya. Our analysis revealed several key findings. First, all wildlife-associated variables were not selected as important variables. However, we did identify eleven variables spanning food practices, livestock-mediated movements, and individual household characteristics that were associated with household tuberculosis status. Of these, selling degree, consumption of raw milk from goats, frequency of consumption of raw milk, bride price degree and a household's buying betweenness were the most important. Those households reporting to 'always' consuming raw milk had a higher risk of TB. On the contrary, consumption of raw milk from goats was associated with a lower risk of household tuberculosis. The inference here though speculative may be related to immunological modulators in goat milk (Jirillo and Magrone, 2014) which are known to influence the pathogenesis of tuberculosis (Redford et al., 2011; Jamaati et al., 2017). Alternatively, this may confounding, relating to the differing consumption patterns of raw milk where community members are more likely to drink raw cattle milk, while goat milk is mixed with boiling tea (Amenu et al., 2019). Nevertheless, this warrants further research to tease out the mechanisms. Overall, these results taken together confirm that focusing on livestock-associated sociocultural practices, especially consumption of raw animal products, may help unravel areas for tuberculosis control and potential management in this community (Roug et al., 2014).

Patterns of tuberculosis occurrence in the larger Narok County area have previously been linked to sociocultural practices (Koech, 2001; Kirui, 2014). However, such sociocultural practices are often over-simplified, focusing on the household level (i.e., consuming raw animal products), while the role of livestock in maintaining and amplifying infection via their role in social connectivity of communities is over-looked. It has been demonstrated that livestock are central to the social networks of pastoralist communities (Omondi et al., 2021). For example, livestock mobility can be viewed through the lens of social and family bonds among households, even among those living some distance apart. Thus, livestock movement can be used as a correlate for human interconnectedness, with implications for surveillance and health programs (Schelling et al., 2016). That said, all eleven variables associated with household tuberculosis in the Maasai Mara Ecosystem (Table 3.1) are related to kinship and social bonds (Radcliffe-Brown and Forde, 2015). However, how each variable relates to the sociocultural fabric of the community is not clear cut. When taken against the backdrop of how pastoralists utilize marginal rangelands, the interplay between social, economic, political and ecological constructs (Western, 1982; Bekure, 1991; Oyugi, 2014; Tyrrell et al., 2017) may explain the synergy between these seemingly disparate but connected variables. For instance, consumption of raw animal products has been shown to be a codification of the Maasai culture in which certain activities such as communal meat feasts are used to enhance the bonds within the community, especially within an age-set (Århem, 1989). A group of men within an age-set (a cohort of persons within an age range) will usually go to the bush for weeks and celebrate while learning about culture, kinship and strengthening their bonds (Århem, 1989). Thus, even though cultural consumption of raw and/or undercooked products is usually associated with increased risk of zoonotic diseases (Onesmo, 2013; Asiimwe et al., 2015; Barnes et al., 2017), contextualization of exposure and transmission of diseases such as tuberculosis may be better explained by events associated with feasts or other social congregations (Zinsstag et al., 2006; Kirui, 2014), and not necessarily the consumption of raw animal products.

Livestock serve as both long-term assets and short-term daily currency in pastoralists communities (Glass, 2019). Livestock trade and market access in pastoralist communities follow a constitutive organizational configuration originating from cultural and social values convergence outside of markets (Igoe, 2006; Allegretti, 2017). Livestock trading can be conducted by individual households and merchants (Allegretti, 2017), both of which involve familial networks, decision making and interactions among community members with most of the ties existing prior to the process of buying or selling (Allegretti, 2017). In this study, a high selling degree denoted households that sold animals in more markets, potentially due to a household seeking higher prices (Motta et al., 2018). Markets form multiple and potentially overlapping communities, in the social network sense (Salathé and Jones, 2010). Network analysis has been used to reveal finer details about tuberculosis transmission. For instance, in the Houston Tuberculosis Initiative, a network analysis of tuberculosis cases showed that common places such as restaurants or bars were potential areas of high exposure, and these locations were identified as playing a role even tying in cases from outside the ‘Greater Houston’ area (Yaganehdoost et al., 1999; Klovdahl et al., 2001). In this Houston Tuberculosis Initiative study, one patient was shown to have had contacts with at least nine other patients at common places. In a different study, homeless shelters and extra-household locations were observed to be central in predicting tuberculosis infections within a cluster (Barnes et al., 1997), underscoring the fact that surveillance for tuberculosis should consider both areas of congregation and the persons involved. These considerations should also be driven by characteristics of the population and/or the outbreak, and could be aptly applied to evaluating the role of different types of movements in pastoral communities which tend to follow familial social networks (Grandin, 1991), which are strengthened by marriage and gifting of different livestock species. Households involved in buying or selling of livestock in many markets also have a higher probability of tuberculosis due to the Maasai community organization, and sociocultural practices, values and relationships existing prior to the market structure (Allegretti, 2017).

This study has several limitations. First, this study reflects the experiences of a limited number of pastoralists in an intensely utilized human-wildlife-livestock interface, as data was collected by a maximum variation sampling scheme, thus the results may not be generalizable to all pastoralists (Maxwell, 1961). In addition, although the interviews were geared towards understanding drivers of tuberculosis in a community with potential exposures to multiple MTBCs, the risk and exposures differ among the species. Thus, although both *M. bovis* and *M. tuberculosis* may have overlapping determinants (Cosivi et al., 1998; Hargreaves et al., 2011; Olea-Popelka et al., 2017), they have distinct eco-epidemiologies for which questions may need to be appropriately framed to capture their distinct drivers. Further, while the use of structured questionnaires allows for the comparability of answers and quantitative analysis, they can also limit the depth of information received and insights drawn from the data in comparison to other methods such as focus group discussions (De Jong and Van Ommeren, 2002; Leung and Savithiri, 2009). However, the strength of this study are two pronged; first, this is the first time that household-level information have been collected from this population, and secondly, the insights are partly corroborated by hospital-based studies that have given consistent results, with respect to association between food consumption practices and the occurrence of tuberculosis, albeit without a holistic community lens (Koech, 2001; Kirui, 2014; Enos et al., 2018).

Conclusions

Evidence from the analysis of risk factors associated with tuberculosis in the Maasai Mara ecosystem suggest that livestock-mediated movements may play an important role in shaping households' tuberculosis risk. Thus, livestock-associated movement can be interpreted as one of the potential proxies for the embeddedness of a household within community, and should be considered in designing tuberculosis surveillance schemes in this community. This however, warrants further investigation to gain an understanding on areas or villages in which the community congregates and their activities. Secondly, we have shown that sociocultural consumption of raw animal products, especially consumption of raw milk, may explain household tuberculosis infections. However, the association between consumption of raw animal products and household tuberculosis may also be construed to represent the presence of *Mycobacterium bovis* in this community, and this deserves further exploration especially molecular analysis of suspected cases in the ecosystem. Thus, this study advances knowledge on the social determinants of tuberculosis in pastoralists communities, and highlights the role of sociocultural mediated livestock mobility in the ecoepidemiology of tuberculosis infections in Narok County, southwestern Kenya.

Chapter 4 | Conceptualizing potential pathways for disease control amongst villages through assessing livestock movements.

Background

Rangeland ecosystems in Africa, defined as areas of natural or semi-natural vegetation in arid or semi-arid climates, host large numbers of wildlife, livestock, and marginalized pastoralist populations (Homewood, 2004). These areas are characterized by low rainfall and seasonally heterogeneous resources such as forage and water, necessitating human and livestock movement to utilize these spatiotemporally distributed resources (Swallow, 1994; Butt, 2010; Goldman and Riosmena, 2013; Turner and Schlecht, 2019). Animal movements have been shown to impact disease patterns (Fevre et al., 2006; Altizer et al., 2011), especially among pastoral livestock with high inter-herd interactions or contact with wildlife (Rajeev et al., 2017; Sintayehu et al., 2017; VanderWaal et al., 2017). Losses emanating from livestock diseases affect livelihoods, and their control has the potential to enhance household productivity and health outcomes (Marsh et al., 2016). Rangeland systems are especially at high risk for pathogen introduction and spread because grazing livestock interact with both wildlife and other livestock directly and indirectly through shared forage and water resources (Rajeev et al., 2017). Herds with high rates of between-herd contacts have a higher risk of acquiring and spreading infections (VanderWaal et al., 2017). In addition, it has been shown that infections often propagate from a small number of actors (Woolhouse et al., 1997; Volkova et al., 2010), with so-called “super-spreaders” disproportionately contributing to transmission events (Lloyd-Smith et al., 2005). Targeted control measures aimed at these important nodes in the network have been shown to be more effective than random measures. Thus, characterizing the underlying architecture of contact networks within a population can help elucidate important drivers and pathways for disease transmission, which can inform critical control points and approaches for surveillance and control (Kiss et al., 2005; Kao et al., 2006; Kiss et al., 2006; Bajardi et al., 2012; VanderWaal et al., 2016; Chaters et al., 2019).

In pastoralist communities, livestock movement data is seldom available, and thus contact is difficult to characterize. Several studies have attempted to model livestock movement by analyzing sales records (Chaters et al., 2019), animal transaction records combined with questionnaire surveys (Motta et al., 2017), census of migrating pastoralists (Pomeroy et al., 2019b), Global Positioning System data loggers (VanderWaal et al., 2017), and ego-based approaches (Bronsvoort et al., 2004). However, none of the methods above capture the diversity of social drivers behind movements within rangeland pastoral communities. For instance, in addition to buying and selling, Maasai pastoralists move animals, with or without the transfer of ownership, through lending animals between friends and families, conferring animal gifts to neighbors, friends and relations, and seasonally moving animals to pasture and water (Perlov, 1987 in (Aktipis et al., 2016)). Thus, in pastoralist populations, moving or sharing animals is a survival strategy, a relationship building exercise, and often a method of risk pooling (Aktipis et al., 2011; Aktipis et al., 2016). The role that such livestock movements play in disease dissemination is seldom evaluated, but may be key to maximizing productivity of this management system through effective targeted disease control (Sintayehu et al., 2017).

Designing disease control strategies is complex, and traditional epidemiological approaches often fail to capture the dynamic, non-linear, and interconnected nature of pastoral systems (Benham-Hutchins and Clancy, 2010). To further understanding of animal movements, graph theory can be used to quantify village movements such that household actions (for instance buying/selling) connect different villages. In graph theory, networks are used to characterize interacting systems in which nodes (here defined as villages) are inter-connected through edges (here defined as movement of animals between villages (Craft and Caillaud, 2011; Danon et al., 2011; Silk et al., 2017; Sintayehu et al., 2017; Balasubramaniam et al., 2018; Ogola et al., 2018)).

There are several approaches to using network analyses to evaluate network properties and connectedness. Using network analysis, we can calculate centrality metrics, evaluate the importance of a node in the network, and investigate the propagation of a disease. Further, we can assess the network structure to estimate the epidemic sizes (Kao et al., 2006) and evaluate the potential for targeted surveillance or control if a node is removed. Node removal can be interpreted as the impact of vaccination or depopulation in removing nodes from potential transmission pathways in the network (Christley et al., 2005; Martinez-Lopez et al., 2009; Marquetoux et al., 2016; Motta et al., 2017; Kinsley et al., 2019; Yang et al., 2019). Risk-based interventions targeted at high-risk nodes significantly reduce the explosiveness of rapidly spreading acute infections like foot-and-mouth disease virus or diminish the prevalence of chronic endemic infections such as bovine tuberculosis (Kao et al., 2006).

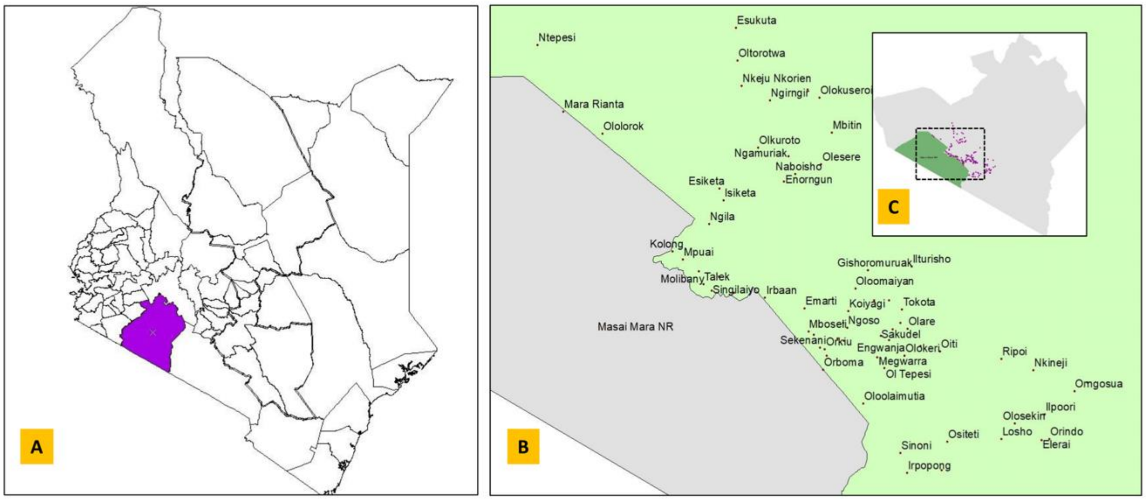
In this study, our objective was to use network analysis to characterize the network patterns associated with different types of animal movements, and evaluate their potential role in disease transmission and control in pastoralist communities in the Maasai Mara Ecosystem (MME) in Kenya. Due to the abundance of dry-season forage available in the Maasai Mara National Reserve (MMNR), we hypothesized that villages proximal to MMNR will play an important role in maintaining the connectivity of villages in the ecosystem, as measured by their centrality metrics. Further, targeted control measures aimed at villages with the most connections will be more efficient at fragmenting the network and reducing the number of potential secondary infections than a non-targeted approach. This study advances our understanding of the movement patterns of livestock within a rangeland pastoralist community and their role in network-based interventions for livestock disease surveillance and control.

Methods

Study site

This study examined the dynamics of livestock movement in pastoralist communities living within the Maasai Mara Ecosystem (MME) (Figure 4.1). MME is located in southwestern Kenya, and encompasses the 1,530-km^2 Maasai Mara National Reserve (MMNR), within which illegal livestock grazing occurs. Communal settlements and legal livestock grazing occur in pastoral ranches adjacent to MMNR (Bhola et al., 2012). Rainfall in this ecosystem is largely bimodal, varying from 500 mm in the southeast to 1300 mm in the northwest (Bartzke et al., 2018) creating spatiotemporal heterogeneity in water and forage distribution, which influences wild herbivores and domestic stock movement. This ecosystem is located within the larger Narok County, which is a 17,953 km^2 area with more than one million cattle, 2.3 million sheep and goats, and a human population that is largely rural (KNBS, 2010).

Figure 4.1. Map of the Maasai Mara Ecosystem. (A). Map of Kenya with Narok County. (B). Unique villages from which households were sampled in this study. (C). Map of Narok County with households sampled, dotted square represents the study area (equivalent to B).



Study design

Sampling for this study was conducted between November 2017 and June 2019. We defined households as persons living within an abode for a period of one month prior to the sampling, and herds as groups of cattle, sheep and goats, and any other domestic stock owned by the respondent. We purposively sampled 165 households in 67 villages, targeting villages within 20 kilometers of the Maasai Mara National Reserve. Pastoral cattle tend to move longer daily distances than small stock, with an average of 2-9 kilometers being the norm for grazing (Turner and Schlecht, 2019). We focused on longer-term migration in pastoralist systems, the average distance moved ranges from 47-170 kilometers (Turner and Schlecht, 2019), with the wide variation indicative of an individual household's cost-benefit valuation of the move.

For this study, we recorded two broad categories of animal movements, temporary and permanent. For the temporary movement, we defined agistment as re-location of animals to access forage and water in other locations during the dry season, usually lasting 2-3 months, while maintaining a household in a single village. We recorded four types of permanent animal movements: gifting (receiving livestock as a gift), bride price (receiving livestock when a female member is married), buying, and selling, denoting the trading of household livestock. We defined buying origin and selling destination as any village from/to which the respondent buys or sells animals, respectively, in order to capture both formal markets and local non-market-based transactions. Respondents were asked to identify villages (by common name) to which or from which they sent or received cattle, sheep or goats through any of the aforementioned movement types over the last five years. This period was chosen to capture multiple seasons and is a timeframe most appropriate for chronic slowly spreading diseases, such a bovine tuberculosis. The MMNR and neighboring Tanzania were also included as locations for agistment movements following the initial pretesting of the questionnaire that identified these as important locations utilized for grazing in the dry season. The respondents were requested to name villages rather than specific households due to the logistical constraints of collecting locational data on households named by respondents. For each household interviewed and village named, locational data was recorded using a handheld Global Positioning System. In villages where multiple households were sampled, we calculated a centroid using ArcGIS to generate representative coordinates (ESRI, 2011).

Data analysis

Network construction and metrics

In our study, a node represented a village while an edge the movement of livestock from or to a village. Livestock movements have long been associated with livestock disease transmission both for acute and chronic conditions (Fevre et al., 2006; Sintayehu et al., 2017; VanderWaal et al., 2017; Machado et al., 2019). Agistment constituted the temporary transfer of animals to another village, while selling was the permanent moving of animals to another village. Gifting, bride price and buying represented the introduction of animals into the respondent’s village. We constructed five separate between-village networks for each of the five classes of movement. At the node-level, we calculated two centrality metrics: in and out-degree and betweenness, while at the network level, we calculated the density, clustering coefficient, giant strongly and weakly connected components, and the fragmentation index. Further, we constructed a combined network of all the movements to gain an understanding of the high-ranking villages by degree and betweenness. Definitions for node and network level metrics and their significance for disease spread are provided in Table 4.1. All analysis were conducted using the *igraph* package (Csardi and Csardi, 2007).

Table 4.1. Definition of node and network metrics and their epidemiological significance as used in this analysis.

Parameter	Definition	Epidemiological significance
Betweenness	Number of times a village is located on the shortest path between any two pairs within the observed network.	Villages with high betweenness are more central to the network and are likely to be infected earlier. Thus, may serve as good targets for interventions (Freeman, 1978; Bell et al., 1999).
In and out-degree	Total number of other villages to which a village received or sent livestock, respectively.	A village with a higher in-degree is considered a sink (higher probability of disease introduction) in the network whereas one with a higher out-degree is considered influential (higher probability of spreading disease) (Wasserman and Faust, 1994; Martínez-López et al., 2009).
Density	Proportion of observed contacts relative to the total number contacts possible in the network.	Networks with higher densities have more connections between pairs of villages, thus potential for large epidemics (Wasserman and Faust, 1994; Martínez-López et al., 2009).
Clustering coefficient	Probability of any two villages, connected to a third village in common, to themselves be connected, forming a triangle in the network	This identifies the spatial structuring of a network, with high clustering hypothesized to reduce transmission (Wasserman and Faust, 1994).
Giant strongly/weakly connected component (GSCC/GWCC)	A strongly connected component in a network is a group of villages in which every village can be reached from every other village when following existing directed edges. On the other hand, a weakly connected component denotes that part of the network where all villages are linked to each other but not all the villages can be reached from every other village in the network.	Given that any villages can be reached from all other villages within the GSCC, the size of the GSCC is a metric of the potential size of an epidemic in the network. The GWCC relaxes the assumption that all villages can be reached from any other village by directed paths in the connected component, and the size of the GWCC often is interpreted as the maximum size for an epidemic within the system (Wasserman and Faust, 1994; Christley et al., 2005).
Fragmentation index	Proportion of pairs of villages not connected in the network relative to all the existing pairs in the network.	Based on the strategy adopted for identification of key villages (high degree or high betweenness), the best strategy for node removal (immunization or surveillance) identifies the minimum number of villages to be removed to prevent the spread of an epidemic in the resulting network. The index (ranging from 0-1) gives us a measure of how the network is disconnected (Webb, 2005; Borgatti, 2006; Chen et al., 2007; Chami et al., 2017).

Scale-free topology of the networks

Many real-world networks are deemed scale free since node degree *k* follows a power-law distribution $k^{-\alpha}$, where $\alpha>1$ implies that a small number of nodes have many connections while the majority of the nodes have few connections (Barabási and Albert, 1999; Albert and Barabási, 2002). This has profound implications in disease dynamics at the population level (Bansal et al., 2007), and suggests the existence of super-spreaders in the network. We analyzed the distribution of contacts per village by fitting a power-law distribution using Maximum Likelihood Estimation and used the Kolmogorov-Smirnov test to evaluate the goodness of fit as described by (Clauset et al., 2009). This was done using the *poweRlaw* package (Gillespie, 2015).

Implication of node removal on network topology and basic reproduction number

In network epidemiology, the giant strongly (GSCC) and weakly (GWCC) connected component estimate the lower and upper bounds of the size of an epidemic in the network, respectively (Christley et al., 2005; Kao et al., 2006; Volkova et al., 2010; Dorogovtsev and Mendes, 2013). Indeed, the GSCC provides a metric of the proportion of nodes that are mutually inter-connected by a directed path in the network, and thus disease introduction in one node could reach the other. However, no transmission paths exist between nodes that belong to disconnected components. Thus, control measures that fragment potential transmission paths in the network and increase the number of network components can stymie pathogen spread (Christley et al., 2005; Volkova et al., 2010). This can be achieved by removing nodes with high betweenness (many paths passing through them) or degree (number of neighbors to which a node is connected) (Christley et al., 2005;

Kao et al., 2006; Dube et al., 2009; Volkova et al., 2010). Fragmentation of the network can be quantified using a fragmentation index, *F*, where *F* = 0 would represent a fully-connected, non-fragmented network in which all pairs of nodes are connected through paths in the network, and *F* = 1 would represent a fully fragmented network where every node is isolated (Borgatti, 2006; Chen et al., 2007; Martínez-López et al., 2009). We used two criteria to remove villages from the network; first, random removal, where we sequentially selected any 2, 5, or 10 villages at random, calculated fragmentation index, and repeated this process for 1,000 iterations to generate an expected distribution. Secondly, targeted removal, where we sequentially selected top 2, 5, and 10 villages based on degree or betweenness, and recalculated the fragmentation index (Albert et al., 2000; Holme et al., 2002; Chen et al., 2007).

Networks can also be evaluated by assessing the potential of a pathogen to spread using the basic reproduction number, R_0, which estimates the number of secondary infected nodes from a single introduction into a susceptible population (Diekmann et al., 1990). A population's R_0 is a function of a pathogen's duration of infectiousness, mean contact rate between-villages, and probability of transmission (Woolhouse et al., 1997). Heterogeneity in contact patterns leads to variation in transmission such that the majority of the infections are attributable to a small proportion of the population (Woolhouse et al., 1997; Lloyd-Smith et al., 2005). Thus, the network's contribution to R_0 can be separated into two components: the mean contact rate (i.e., mean degree), and the variances in contact rates across villages (Woolhouse et al., 1997). In a population with a homogeneous contact rate, R_0 will only be a factor of the mean contact rate alone, but the addition of heterogeneity has a multiplicative effect on R_0. We calculated the multiplicative effect of network heterogeneity on R_0 (hereafter referred to as $R_{0\ (heterogeneous)}$) using the method developed by (Volkova et al., 2010) where;

$$R_{0(heterogeneous)} \propto \sqrt{\beta_{in} * \beta_{out} + \sigma(\beta_{in}) * \sigma(\beta_{out}) * r(\beta_{in}\beta_{out})} \qquad \text{Equation 1}$$

β_{in} and β_{out} denote the mean village in-degree and out-degree, respectively, while σ denotes the village standard deviation for in- and out-degree, and *r* is the Pearson's product correlation coefficient. In the absence of contact heterogeneity,

$$R_{0\ (homogeneous)} \propto \sqrt{\beta_{in} * \beta_{out}} \qquad \text{Equation 2}$$

Thus, the relative effect of contact heterogeneity on R_0 was defined as $R_{0\ (heterogeneous)}$/ $R_{0\ (homogeneous)}$ (Volkova et al., 2010).

Effectiveness of disease control and potential targets

A village's importance for disease transmission is determined by its degree or betweenness. A village with high degree has more incoming or outgoing connections to other villages, thus, a higher risk of disease introduction or dissemination. Villages with high betweenness can be interpreted as either having connections to many other villages (this leads to high correlation with degree) or lie on the paths that are breakpoints for information flow between villages (important for disease control as their removal fragments the network) (VanderWaal et al., 2014). We calculated the Spearman's rank correlation coefficient between the total degree and betweenness for all the five networks. Then, to assess the effectiveness of targeted versus random interventions, we quantified the relative change, $R_{0\ (removed)}$/ $R_{0\ (heterogeneous)}$. $R_{0\ (removed)}$ denoted the R_0 of the network with village *i* removed without replacement. This quantification was done in three scenarios a) sequential removal of villages based on degree, b) sequential removal of villages based on betweenness, and c) random removal of villages. For random village removal, we recalculated equation 1 for each network and averaged the reduction in R_0 over 1000 iterations.

Results

Network metrics

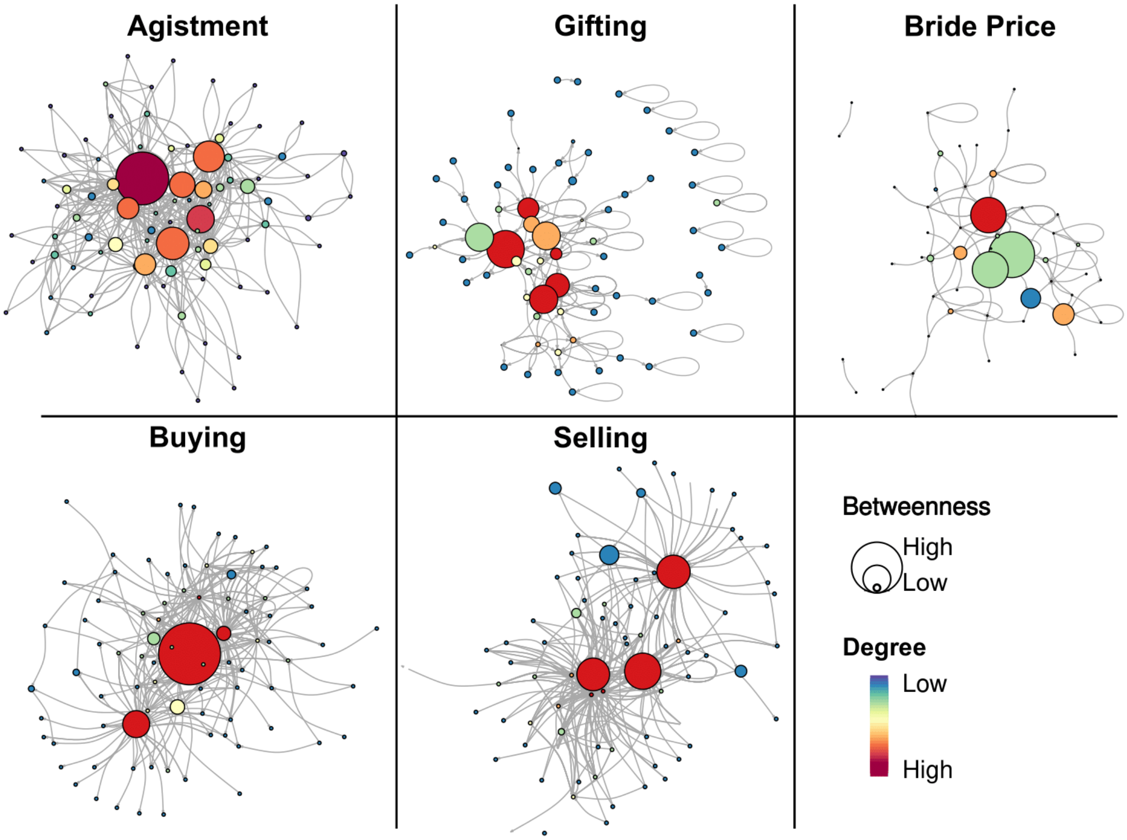
We sampled 165 households in 67 unique villages (Figure 1 B) across the Maasai Mara Ecosystem. The median livestock movement distance for agistment was 39.49 kilometers (22.03-63.49 km), while that for gifting, bride price, buying, and selling were 13.97 km (0-40.30 km), 30.75 km (10.02-66.03 km), 31.14 km (17.56-59.08 km), and 33.21 km (17.78-58.49 km), respectively. Network metrics are summarized in Table 4.2. For agistment, gifting, bride price, buying and selling movements, the respective network densities were 0.065, 0.034, 0.036, 0.054, and 0.054. The median village total degrees for agistment, gifting, bride price, buying and selling were 6 (interquartile range: 2-12), 2 (1-5.5), 2.5 (1-5), 3 (2-9), and 4 (2-7), respectively (Table 4.2). This means that on average, the villages in the agistment network contacted more villages than in gifting, bride price, buying, and selling networks. In all networks apart from the selling network, there was a positive correlation between the in- and out-degree, with agistment and gifting networks having the highest correlations (Table 4.2). The giant strongly connected components comprised of 78.8%, 5.3% and 1.8% of all villages in the agistment, gifting and bride price networks, with no GSCC found in the buying and selling networks.

In the combined network, villages with the highest degree also had the highest betweenness with a few exceptions (Appendix, Table 6). For disease control, villages with high betweenness and high degree tend to lie on paths that control information flow in the network thus could be considered potential breakpoints in that if they are removed, the number of components in the network increases (VanderWaal et al., 2014). These villages included Ololaimutia, Aitong, Olesere, Megwara, Ingoso, Gishoromuruak, Olesheke, Oldapash, Enkoika, Molibany, Esukuta, Nkoiroro, Irbaan and Oltorotwa. Interestingly, over half of these villages are within 3 kilometers of the MMNR, with the others being on the outer periphery of the study area.

Table 4.2. Descriptive measures of the agistment, gifting, bride price, buying and selling networks of the Maasai Mara Ecosystem.

Network metric	Agistment	Gifting	Bride Price	Buying	Selling
Nodes	89	67	50	84	83
Edges	506	150	88	376	370
Density	0.065	0.034	0.036	0.054	0.054
Clustering coefficient	0.124	0.136	0.114	0.106	0.107
Giant Strongly Connected component (% of villages)	78.8%	5.3%	1.8%	0%	0%
Giant Weakly Connected component (% of villages)	78.8%	47.8%	39.8%	74.3%	73.5%
Mean in-degree (Standard deviation)	5.69 (8.3)	2.24 (2.61)	1.76 (1.92)	4.48 (5.69)	4.46 (15.13)
Mean out-degree (Standard deviation)	5.69 (8.3)	2.24 (3.03)	1.76 (2.02)	4.48 (13.60)	4.46 (5.7)
Pearson's correlation in ~ out-degree (95% CI)	1 (1-1)	0.53 (0.33-0.68)	0.006 (-0.27 – 0.28)	0.013 (-0.20 – 0.23)	-0.06 (-0.27 – 0.16)
Relative effect of network heterogeneity on R_0	1.77	1.35	1.00	1.02	0.86

Figure 4.2. Plot of the agistment, gifting, bride price, buying, and selling animal movement networks with sizes scaled by betweenness. Larger circles also had a higher total degree.

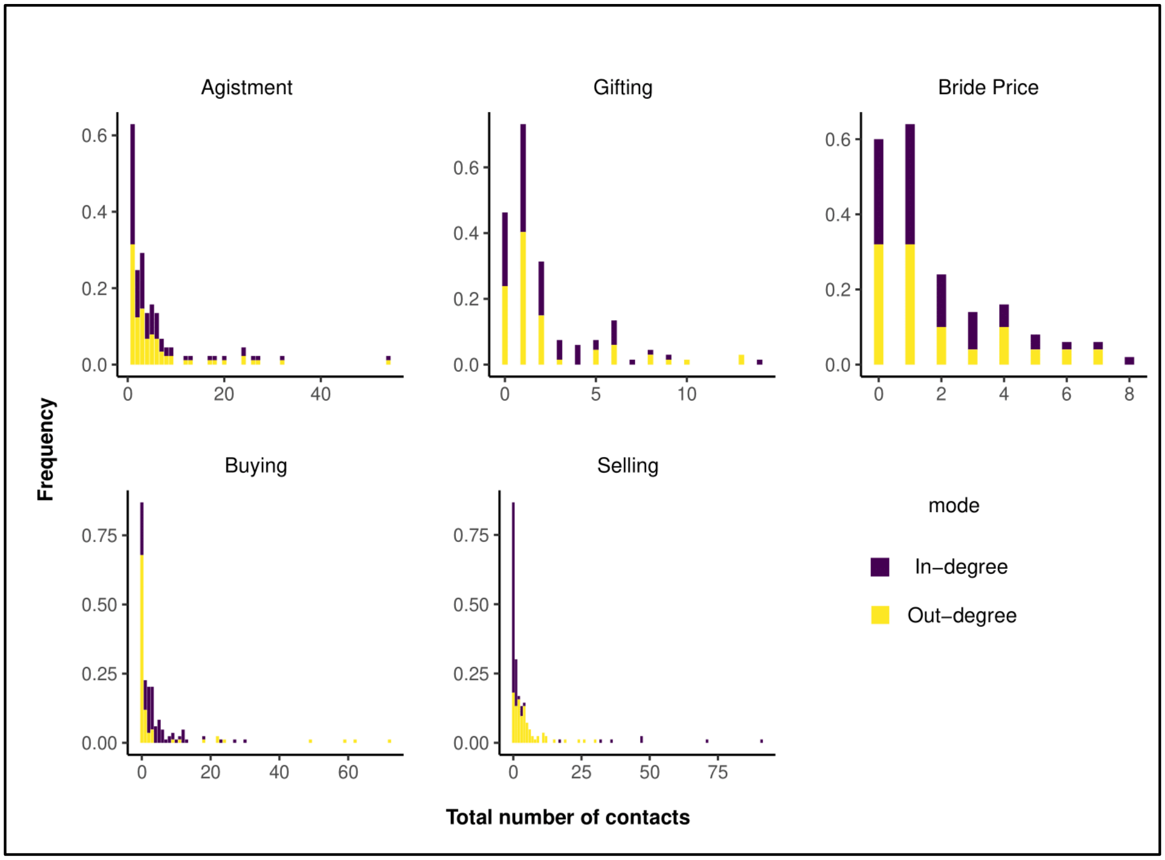


Scale free topology of the networks

For the agistment network, the best cutoff for a power law tail was >37 observations, an exponent, $\alpha = 2.23$, $x_{min} = 8$, and p-value = 0.989. In all the networks, the high p-value indicated that there was no evidence to reject the null hypothesis and most probably, the degree distribution follows a power law distribution. For the gifting, bride price, buying and selling networks, the best cutoff for a power law tail were 49, 2, 56, and

42 observations, respectively, with corresponding α of 2.03 (p-value =0.912), 5.88 (p-value = 0.906), 1.92 (p-value = 0.987) and 2 (p-value =0.836) (Figure 4.3).

Figure 4.3. Plot of the distribution of contacts of the agistment, gifting, bride price, buying and selling movement networks.



Implication of node removal on network topology and basic reproduction number

The results for the top ten-villages ranked by degree and their respective betweenness are given in Table 4.3. Three villages were present among the top ten villages in all the networks. These included Olesere, Empopongi and Nkoilale. Ololaimutia was present among the top ten villages in four of the five evaluated networks. Of the villages evaluated, Maasai Mara National Reserve (though technically not a village) had the highest degree and betweenness for agistment. In this network, Tanzania, a country neighboring MME on the southwest, was also highly ranked by degree. In the buying and selling networks, other than formal livestock markets (Nkoilale, Ololaimutia, Ngoswani, Aitong, Ol Pusimoru, Trans Mara, Naikara and Lolgorien), the top ten villages included local non-market villages such as Empopongi, Olesere and Ilpoori.

Table 4.3. Degree and betweenness of the top 10 villages in the five movement networks evaluated in this study. [*] Not a village but serves as an important hub in the network. [Ψ] Villages that appear in the top ten across all networks. VILL = Village; DG = degree; BET = betweenness.

Agistment			Gifting			Bride Price			Buying			Selling		
VILL	**DG**	**BET**	**VILL**	**DG**	**BET**	**VILL**	**DG**	**BET**	**VILL**	**DG**	**BET**	**VILL**	**DG**	**BET**
MMNR [*]	108	0.32	Empopongi [Ψ]	22	0.03	Nkoilale [Ψ]	13	0.01	Nkoilale [Ψ]	76	0.02	Ngoswani	91	0.00
Talek	64	0.15	Nkoilale [Ψ]	19	0.04	Ololchora	9	0.00	Ololaimutia	75	0.00	Aitong	72	0.01
Olesere [Ψ]	54	0.19	Olesere [Ψ]	19	0.03	Empopongi [Ψ]	8	0.00	Ngoswani	62	0.00	Nkoilale [Ψ]	60	0.01
Nkoilale [Ψ]	52	0.14	Nkineji	17	0.03	Sekenani	8	0.00	Aitong	60	0.00	Ololaimutia	51	0.01
Sekenani	48	0.18	Talek	15	0.01	Losho	8	0.00	Empopongi [Ψ]	30	0.00	Ewaso Ngiro	47	0.00
Trans Mara	48	0.12	Ololchora	12	0.03	Megwara	7	0.01	Ol Pusimoru	24	0.00	Dagoretti	32	0.00
Ololaimutia	40	0.11	Irbaan	12	0.02	Olesere [Ψ]	7	0.00	Olesere [Ψ]	24	0.00	Empopongi [Ψ]	31	0.00
Empopongi [Ψ]	36	0.09	Megwara	10	0.01	Tipilikwani	7	0.00	Lolgorien	22	0.00	Olesere [Ψ]	26	0.00
Ololorok	34	0.07	Losho	10	0.00	Ingoso	7	0.00	Naikara	22	0.00	Ilpoori	19	0.00
Tanzania[*]	26	0.05	Ololaimutia	9	0.01	Irbaan	6	0.00	Trans Mara	18	0.00	Naikara	17	0.00

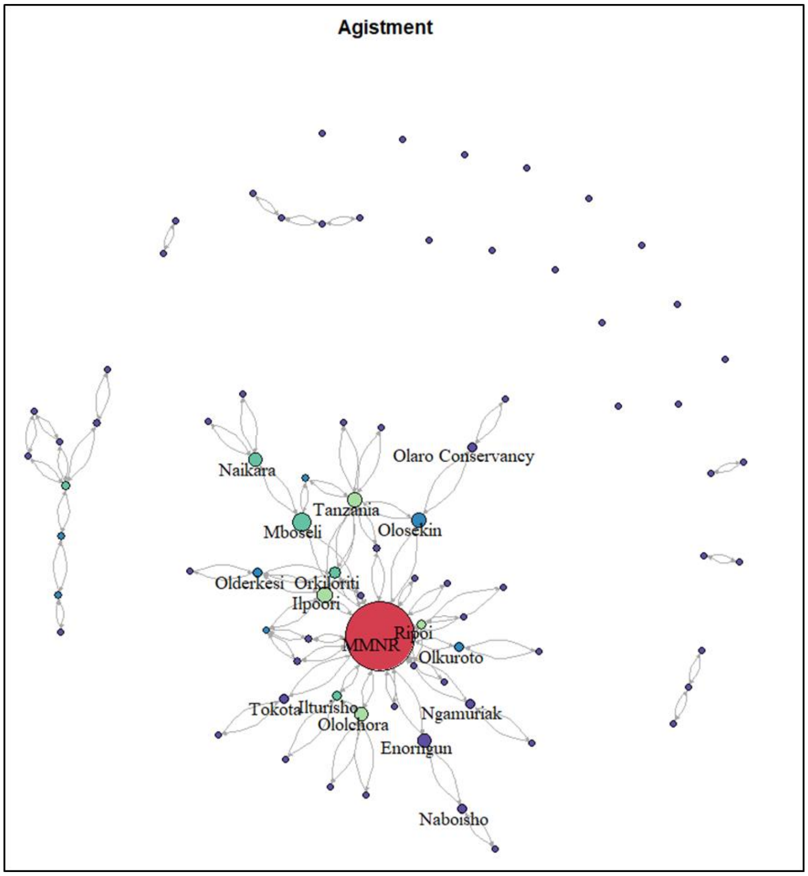
Effectiveness of targeted interventions

Consistent with our hypothesis, targeted removal based on degree or betweenness outperformed random removal of nodes in terms of increasing the extent to which villages are disconnected (Table 4.4). Across all network types, targeted removal of nodes based on their degree or betweenness resulted in substantially higher fragmentation than random removal of nodes; the fragmentation indices for the targeted removals always exceeded the upper bounds of the 95% interval of that achieved through random removals. This result was consistent regardless of whether the top 2, 5, or 10 nodes with highest degree or betweenness were removed. Although the fragmentation indices based on either degree or betweenness were comparable, removal based on degree performed considerably better than betweenness, especially in the buying and selling networks (Table 4.4, and Figure 4.4).

Table 4.4. Fragmentation index of the five networks evaluated in this study following the removal of 2, 5 and 10 nodes, with nodes removed either selected randomly or targeted based on degree (A) or betweenness (B). For random removals, the median (95% confidence interval) fragmentation is reported, summarized across 1,000 iterations.

A. Fragmentation of the network following targeted versus random node removal by degree							
Reason	Full Network	Removal of 2 villages		Removal of 5 villages		Removal of 10 villages	
		Random	Targeted	Random	Targeted	Random	Targeted
Agistment	0.38	0.41 (0.41 0.45)	0.45	0.46 (0.45 – 0.51)	0.60	0.55 (0.51 – 0.61)	0.85
Gifting	0.77	0.79 (0.77 – 0.83)	0.86	0.82 (0.80 – 0.87)	0.92	0.86 (0.83 – 0.92)	0.99
Bride Price	0.84	0.86 (0.85 – 0.88)	0.86	0.88 (0.86 – 0.92)	0.93	0.92 (0.89 – 0.96)	0.99
Buying	0.45	0.48 (0.48 – 0.56)	0.51	0.51 (0.51 – 0.61)	0.75	0.59 (0.57 – 0.68)	0.96
Selling	0.46	0.49 (0.49 – 0.51)	0.66	053 (0.53 – 0.66)	0.86	0.59 (0.59 – 0.73)	0.99
B. Fragmentation of the network following targeted versus random node removal by betweenness							
	Full Network	Removal of 2 villages		Removal of 5 villages		Removal of 10 villages	
		Random	Targeted	Random	Targeted	Random	Targeted
Agistment	0.38	0.41 (0.41 - 0.45)	0.48	0.46 (0.45 – 0.51)	0.60	0.55 (0.51 – 0.61)	0.85
Gifting	0.77	0.79 (0.77 – 0.83)	0.83	0.82 (0.80 – 0.87)	0.89	0.86 (0.83 – 0.92)	0.98
Bride Price	0.84	0.86 (0.85 – 0.88)	0.86	0.88 (0.86 – 0.92)	0.88	0.92 (0.89 – 0.96)	0.97
Buying	0.45	0.48 (0.48 – 0.56)	0.61	0.51 (0.51 – 0.61)	0.68	0.59 (0.57 – 0.68)	0.75
Selling	0.46	0.49 (0.49 – 0.51)	0.64	0.53 (0.53 – 0.66)	0.69	0.59 (0.59 – 0.73)	0.73

Figure 4.4. Plot of the agistment animal movement network following removal of top 10 villages based on their degree. Node sizes are scaled by their betweenness. Larger circles also had a higher total degree. The large node is the Maasai Mara National Reserve



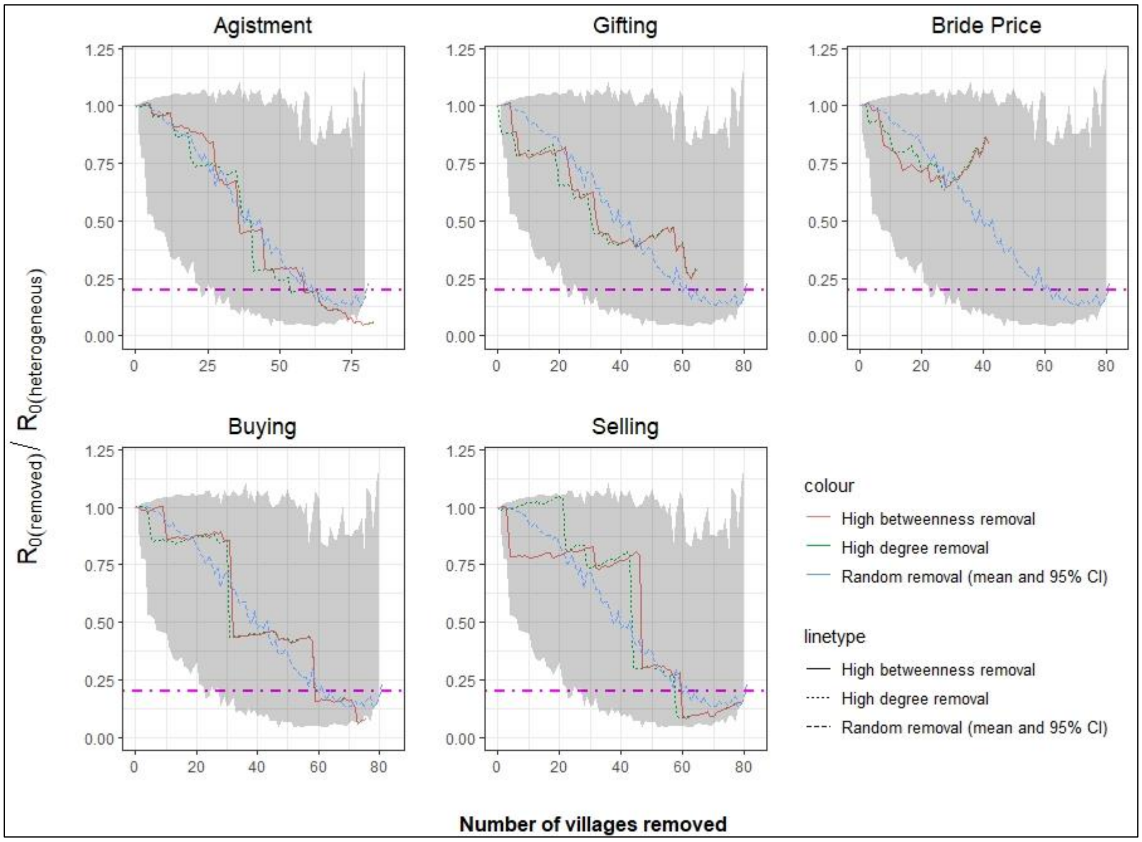
The relative effect of variability in contact rates on R_0 in the five networks are presented in Table 4.2. The agistment network had the largest relative effect with the R_0 estimated to be 177% followed by the gifting network at 135% larger than if the network had a homogeneous contact rate equivalent to mean degree (Table 4.2). The Pearson's correlation coefficient for agistment and gifting movement networks were positive and statistically significant, and with the high variances in contact, explain the higher relative magnitude of R_0. Those of the buying and bride price movement networks were weakly positive but not statistically significant, while that of the selling network was -0.06.

Despite weak or negative correlations, the high variances of between village contacts resulted in a net high relative R_0 in these networks.

For all the networks apart from selling, the total degree and betweenness were positively correlated (p-value <0.001), with their respective Spearman's rank correlation coefficients being 0.9, 0.66, 0.53, 0.34, and 0.26 for agistment, gifting, bride price, buying and selling networks. The inference here is that villages with a higher than average number of contacts were also potential conduits for pathogen flow in the respective networks (Figure 4.2). Overall, village removal, equivalent to vaccination, ban on movement or surveillance measures, was effective in reducing the basic reproductive number across all networks (Figure 4.5).

Across all networks apart from gifting, although there was some reduction in R_0 when a village was removed based on its degree or betweenness, targeted removal did reduce R_0 more rapidly than random removal of villages (Figure 4.5). In the agistment network, targeted removal of >65% and 73% of the villages based on degree and betweenness, respectively, was required to reach an 80% reduction in the R_0 (Figure 4.5). This 80% threshold was also achieved when 75% of the villages were removed randomly. In the buying and selling networks, random removal of villages achieved the threshold reduction in the magnitude of R_0 when 69% and 47% of the villages were removed, respectively, compared to 74% and 70% of villages when removed based on their degree. In the gifting and bride price networks, an 80% reduction in the magnitude of the R_0 was not achievable using any of the three strategies.

Figure 4.5. Plot of the agistment, gifting, bride price, buying and selling movement networks showing change in the proportion of $R_{0\ (removed)}/R_{0\ (heterogeneous)}$ when village are removed based on their degree (dashed line), betweenness (solid line) or random removal (long dashed line). Horizontal dot dash line represents 80% reduction in R_0.



Discussion

In this study, our goal was to characterize the network patterns associated with five classes of animal movements in rangeland pastoralist communities in the Maasai Mara Ecosystem in Kenya, and evaluate their potential role in disease control and management. The agistment network showed the highest level of connectivity, and coupled with long distances (median of ~40 km) and seasonal regularity of movements, agistment is potentially an important avenue for disease dissemination in the ecosystem. Paths existed between 79% of villages in the giant strongly connected component of the agistment network, pointing to an interconnected ecosystem for dry season grazing. Recently, the

MMNR has become especially attractive following increased fencing within the ecosystem that has disrupted traditional animal foraging routes and grazing lands (Løvschal et al., 2017; Weldemichel and Lein, 2019). Although grazing in MMNR is banned, illegal grazing has been previously reported in the literature (Ogutu et al., 2009; Green et al., 2019). We demonstrate that villages adjacent to MMNR are common destinations for agistment, which may point to their use as entry points to MMNR. The proximity of these villages to a major wildlife area coupled with mixing of livestock herds from different villages makes these villages priority areas for disease control interventions and surveillance. Although some villages that ranked highly based on their agistment degree and betweenness were not adjacent to the MMNR, these villages appear to function as bridges between areas that would otherwise be poorly connected. Indeed, Ololaimutia, Aitong, Olesere, Megwara, Ingoso, Gishoromuruak, Olesheke, Oldapash, Enkoika, Molibany, Esukuta, Nkoiroro, Irbaan and Oltorotwa may be potential cut-points in the network, and such villages may function as a firebreak or gate-keeper during a disease epidemic (VanderWaal et al., 2014; Motta et al., 2017). In addition, 15% of the respondents identified Tanzania as an agistment location. Despite the distance, the motivating reasons included cross-border kinships and having hired herders (personal communication).

Gifting of animals was associated with the shortest median distances, a degree of 2 villages and the lowest network density, indicating that this type of movement involved a smaller range of more localized villages compared with other movement classes. Bride price was associated with a median degree of 2.5 villages and a low network density, but had a longer median distance that was similar to buying and selling. These results indicate that moving animals for gifting and bride price contributes less to the risk of disease propagation within the study area compared with buying, selling and agistment. Interestingly, the highest-ranking villages in the bride price and gifting networks included villages around the MMNR. Livestock grazing patterns in the Maasai community have been shown to follow familial social networks, including patrilineal and matrilineal kin (Grandin, 1991). Taken together, these findings show that bride price and gifting might be strategically used to enhance relationships beneficial to the household livelihood (Aktipis et al., 2011; Aktipis et al., 2016) by increasing accessibility to agistment destinations close to MMNR.

Although buying and selling median distances were identical, a closer look at the network reveals more context. First, buying commonly included transactions with villages outside Narok County (the study area). For instance, the respondents indicated that in addition to the villages listed in Table 4.3, they bought their cattle from Tanzania, Kajiado, Kiserian, Emali, and Laikipia, all of which fall outside the county boundaries. This could be a strategy to acquire different or "better" livestock genetics (Ilatsia et al., 2012). On the contrary, selling of livestock mostly occurred in local markets. These included major markets such as Aitong, Nkoilale, Ololaimutia, Ewaso Ngiro, and Ol Pusimoru. In addition, a few farmers sold livestock in larger, peri-urban markets (e.g. Dagoretti, Ngong and Ongata Rongai) serving the capital city of Nairobi, possibly as a means of getting higher returns (Alarcon et al., 2017). A few local non-formal markets were identified, pointing to opportunistic trading of animals independent of formal markets. The presence of a large giant weakly connected component in both the buying and selling networks, is an important consideration for disease control. While the risks of introducing disease to a herd through buying animals are apparent, selling of livestock also poses a particular danger because of the occasional bi-directionality of movement when all animals are not sold. This could serve to introduce acute diseases such as foot-and-mouth disease to the village of origin (Motta et al., 2019).

Effectiveness of network-based interventions: Network-based disease control relies on identifying a population's contact structure and evaluating the role of different nodes (e.g. villages, households, or farms) that could influence connectivity and whose removal may fragment the transmission network (Kiss et al., 2005; Volkova et al., 2010; Tanaka et al., 2014; Marquetoux et al., 2016). We compared the effect of random versus targeted removal of nodes on the networks' topological structure using the fragmentation index. Random removal of nodes requires no prior information on the network structure, but has been shown to be an inefficient approach (Motta et al., 2017; Kinsley et al., 2019). In our study, targeted removal of village nodes based on degree or betweenness outperformed random removal in terms of fragmenting the network, demonstrating the utility of network analysis for more strategic disease control or surveillance in this pastoralist system. Here, node removal mimics the effect of vaccination or depopulation on interrupting the disease transmission pathways, depending on the disease and context of infectious disease control (Keeling and Eames, 2005; Bansal et al., 2010). However, node removal based on degree performed marginally better than betweenness. Unlike betweenness, estimations of degree are not as dependent on comprehensive network analysis, allowing for a simpler mode of data collection, such as ego-based approaches (Bronsvoort et al., 2004), to understand movement risk factors relevant for control. This makes a degree-based approach attractive in a system where comprehensive network data are not routinely collected.

Ideally, an efficient fragmentation strategy should be one that removes a minimal number of nodes as it represents, for instance, the minimum number of villages to be vaccinated to prevent further spread of an infection (Chen et al., 2007). We demonstrated that the removal of the top five nodes with the highest degree was effective at fragmenting all the networks. The agistment network, however, was more robust to node removal in that the removal of the top 5 or 10 villages resulted in fragmentation indices of 60% and 85%, whereas this value was close to 100% for the other networks in this study. This might be due to the fact that we cannot remove MMNR from the network (no feasible way to vaccinate when the presence of livestock is technically illegal).

While fragmentation captures the extent to which villages are directly or indirectly connected in the network (allowing flow of a pathogen through the network), R_0 calculations capture variation amongst villages in their potential contribution to disease spread. Highly right-skewed scale-free degree distributions are generally indicative of the presence of super-spreaders (Dorjee et al., 2013), which may contribute disproportionately to disease spread within the system (Figure 3). We show that all the evaluated networks displayed scale-free properties, highlighting the important role of hubs in these networks. The presence of a few nodes having more connections while the majority having few is an important aspect of networks for risk-based disease control interventions (Woolhouse et al., 1997; Motta et al., 2017). Evaluation of R_0 provides a method to assess the impact of such heterogeneities on the potential for pathogen invasion (May and Lloyd, 2001; Volkova et al., 2010; Marquetoux et al., 2016). In populations where the probability of contact is equal, the magnitude of R_0 is proportional to the mean number of contacts made by a village (May and Lloyd, 2001). However, in networks where the contact patterns are heterogeneous, the magnitude of R_0 is also influenced by the variance and covariance in contact rates between villages (May and Lloyd, 2001; Volkova et al., 2010; Marquetoux et al., 2016). When in- and out-degree are correlated, nodes with high degree are not only more likely to become infected, but also have a higher potential to transmit a pathogen onwards, thus amplifying the realized R_0 of the network.

In our study, we observed a strong correlation between the in and out-degree for the agistment network, due to the bidirectional nature of this movement, and documented the presence of super-spreader villages (Figure 4.3). This suggests a high risk of disease occurrence in the villages engaged in agistments, which is further supported by a higher prevalence of various livestock diseases, including zoonotic pathogens, in villages closer to MMNR (Lekolool, 2011; Nthiwa et al., 2019b; Nthiwa et al., 2020). The relative magnitude of R_0 (Table 4.2) favors invasion of highly transmissible diseases such as foot-and-mouth disease, especially in the agistment network. However, if large number of animals moved especially in the agistment network were high, the relative magnitude of R_0 would also favor chronic diseases such as *Mycobacterium bovis* (Kiss et al., 2006; Kovanen et al., 2011; Marquetoux et al., 2016). In addition, movements associated with agistment, buying, and selling occur much more frequently than gifting and bride price, thus have potentially greater implications for pathogen dissemination (Macpherson, 1995; Bett et al., 2009).

Degree and betweenness were highly correlated, thus rankings of villages based on these metrics were largely similar. Overall, apart from in the gifting network, village removal based on degree or betweenness was not effective at reducing the R_0 when compared to random removal (Figure 4.4). This may not be surprising as the sampling was focused on a small geographical area; contact rates may not have been substantially different between respondents.

Our study has several limitations. First, data were collected cros-sectionally, and temporal changes in a network's topology is a common phenomenon, especially in pastoralist production systems (Volkova et al., 2010; VanderWaal et al., 2017; Pomeroy et al., 2019b). Secondly, respondents were asked about movements made during the last five years, which limits the temporal resolution of when movements occurred and introduces potential recall bias. For example, the respondents are less likely to remember villages where they sold or bought animals hence underestimating the representativeness of the buying and selling networks as compared to agistment networks, which are used regularly. Third, because data were collected in a defined geographical area, the results may not be generalizable to other areas. However, the principles of using network analysis to identify highly connected nodes and targeting those nodes for disease control measures are transferable to other pastoralist systems. Finally, our network structure did not account for common areas of daily contact, such as congregation during daily herding and at water resources, which may be important for localized disease transmission. Thus, our networks may under-represent connectivity amongst villages, particularly at local scales.

Conclusions

We show that using network analysis to identify highly connected villages could be beneficial in designing disease control programs so that measures can be implemented to fragment potential transmission pathways in the livestock population. Our findings demonstrate that even at a restricted spatial scale, network centrality measures may provide sufficient information to fragment networks, thus showing their utility not only for disease control but also in developing targeted risk-based surveillance approaches. Our approach of identifying villages rather than households has multiple advantages. First, targeting disease control measures at a population level rather than at individual level is cost effective, especially in the study population where livestock mobility is common. The fact that degree outperformed betweenness in increasing the number of components means application of low-cost data collection techniques such as ego-based approaches may yield sufficient information to identify disease control targets.

Chapter 5 | Conclusions

The importance of sociocultural factors in disease control has been demonstrated through challenges in the management of various diseases including Ebola (Whembolua et al., 2015; Carrión Martín et al., 2016), HIV/AIDS (Chitnis et al., 2000; Leclerc-Madlala et al., 2009) and parasitic diseases (Mata, 1982). At a minimum these factors help enhance the understanding of mechanisms of exposure, infection, and pathogenesis at the population level (CDSH, 2008), which are critical for effective control.

Tuberculosis is a community disease whose dynamics are driven by social and cultural determinants that modulate exposure, infection, progression to active disease, access to therapy and outcome (Hargreaves et al., 2011). Its control depends on both hospital-based approaches and integration of both social and cultural factors (Lonnroth et al., 2009; Hargreaves et al., 2011; Rasanathan et al., 2011; Bonadonna et al., 2017; Baah et al., 2019). The goal of this dissertation was to evaluate the role of sociocultural factors in shaping tuberculosis patterns in a pastoralist population in Maasai Mara, Kenya and assess their potential role in disease control. In Chapter 1, I reviewed the complexity of TB and the need for new approaches to surveillance and control. This was in light of inequities such as those experienced in traditional pastoralist cultures where their social and cultural practices may expose them to multiple MTBC species, and due to their marginalization have limited access to health systems, and where available the diagnostic techniques employed cannot tease apart these species. In chapter 2, I further characterized *Mycobacterium tuberculosis* complex species (MTBC) in suspected tuberculosis cases identified in local clinics in the Maasai Mara ecosystem, and evaluated their spatial distribution. *Mycobacterium tuberculosis* complex species in this system include both human, animal and environmental pathogens (De Jong et al., 2010; Brites and Gagneux, 2017; Gagneux, 2018). Here molecular analysis showed the possibility of four MTBC, *Mycobacterium bovis, Mycobacterium bovis* BCG, *Mycobacterium canettii*, and *Mycobacterium caprae* co-circulating in the ecosystem, with villages adjacent to Maasai Mara National Reserve being at a high risk of zoonotic tuberculosis caused by *Mycobacterium bovis*, while those along the Tanzania border being at a higher risk of *Mycobacterium caprae*. These findings may reflect increased contacts and spread during the dry season when the community (livestock and humans) utilizes the villages around the Maasai Mara National Reserve for strategic access to forage-rich lands for their animals (Omondi et al., 2021). Using a multinomial spatial scan statistic, I show that there are four clusters where different MTBC species are more important. The primary cluster comprised of twelve villages located in a belt within 3 kilometers of the Maasai Mara National Reserve with the risk for *M. bovis* being highest, while in the three villages in cluster 2 that were located along the Tanzanian border, the risk for *M. caprae* was highest. I further demonstrate that even at geographical locations near each other (clusters 1 and 4), the relative risks of zoonotic tuberculosis due to *Mycobacterium bovis* and *Mycobacterium caprae* differed, potentially reflecting the influence of community structure and social determinants (CDSH, 2008; Hargreaves et al., 2011). An important next step is to contextualize the transmission through evaluation of livestock sources of *Mycobacterium bovis* and *Mycobacterium caprae*, especially through milk, and generate genetic sequence profiles to allow for the exploration of potential community spread.

Chapter 3 took a broad view of the community and the ecosystem, exploring the role of social and cultural practices on patterns of human tuberculosis. This stemmed from a need to investigate potential competing factors for MTBC in general (Koech, 2001; Meisner et al., 2019). Pastoralist, including Maasai observe their cultural traditions as a way fostering community values, leadership, cultural identity and resilience (Smith, 1992; Anderson, 1993; Straight, 1998; Leslie et al., 2013; Carabine, 2014; Jandreau and Berkes, 2016). Here, this study found that livestock-associated social and cultural factors are important for predicting tuberculosis occurrence in this ecosystem. Specifically, there was an increased risk of tuberculosis with frequency of consumption of raw milk, sheep kidney and consumption of raw milk from cattle. In addition, households' selling degree and bride price degree also ranked high in predicting household tuberculosis. Overall, these factors point more towards the possibility of zoonotic tuberculosis in the ecosystem, which was demonstrated in Chapter 2. These findings are an important contribution to tuberculosis research, especially in pastoralist communities with multiple interacting and sometimes contradictory predictors (Koech, 2001; Meisner et al., 2019) as they raise awareness on the need to characterize sociocultural variables not just as attributes of the community but as a continuum with multiple layers necessary for the localization of One Health approaches.

In Chapter 4, I explored further, the role of livestock movements, highlighting locations in which zoonotic tuberculosis could be explored further. It has been shown that under the right conditions, although rare, human-to-human transmission of *Mycobacterium bovis* is possible (Evans et al., 2007). In this dissertation, I show that dry season grazing plays an important role in the connectivity of villages within the ecosystem, with villages around the Maasai Mara National Reserve being the most common destinations for grazing. These are the same villages (not all) in cluster 1 in

Chapter 2, showing that potentially, movement patterns may influence spatial patterns of MTBC. Through analysis of livestock movement, this study reveals the existence of bridge villages (Clusters 1, 2, 3 and 4 in Chapter 2) that serve to link seemingly poorly connected villages in the ecosystem. These villages were also important spatial clusters for zoonotic tuberculosis. Interestingly, the highest ranking villages in the bride price and gifting networks included villages adjacent to the MMNR, a potential further piece of evidence for maintaining strategic familial ties as a gateway to survival and livelihoods (Aktipis et al., 2011; Aktipis et al., 2016). In exploring potential network-based disease control options, first, this study shows that targeted removal of >65% and 73% of nodes (villages) that lie on the paths that control information flow within the ecosystem, resulted in 80% decrease in the agistment network, with a higher percentage of villages needing to be removed using the random approach. In addition, we show that the Maasai Mara National Reserve drives the livestock, and by extension human movement, within the Maasai Mara Ecosystem, with the caveat that although it is technically not a village, focusing disease control measures or surveillance in areas around it would be most effective. Although we show that targeted removal always outperformed random removal of nodes in fragmenting the networks, the agistment network was more robust to node removal due to the influence of the MMNR. Thus, this study shows the utility of strategically incorporating villages as potential surveillance points or areas of joint surveillance of humans and animals.

Taken together, this thesis identifies sociocultural factors contributing to the spread and potential management of tuberculosis in the Maasai Mara Ecosystem. Specifically, this thesis shows that the community within this ecosystem is potentially at a high risk of zoonotic tuberculosis with sociocultural practices including consumption of raw milk, livestock movement and congregation around the MMNR increasing exposures. This thesis also shows that One Health approaches can yield benefits if combined with an understanding of the social and cultural practices. In conclusion, this thesis provides a framework for developing a community profile taking into account social and cultural practices to enrich and localize One Health approaches for the surveillance and control of tuberculosis in a high exposure community.

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Appendix

Table 5. Definition of predictors, their code and associated Pearson’s Chi-squared test p-value. All predictors with p-value<0.15 were included in the machine learning models.

	Predictor (code)	Levels	No. TB positive	No. TB negative	Justification	X^2 p-value
1	Sex of the respondent (sex)	Male	20	94	The number of persons in a household has been positively correlated with the occurrence of tuberculosis, with females more likely to be infected (Teklu et al., 2018; Meisner et al., 2019). In addition, it has been suggested that households may present complex interacting system leading to increased risk for tuberculosis positive contacts (Guwatudde et al., 2003).	1
		Female	9	41		
2	Number of males in the family (males)	Low	14	61		0.795
		Medium	5	31		
		High	10	43		
3	Number of females in the family (females)	Low	11	48		0.642
		Medium	8	49		
		High	10	38		
4	Level of education of the respondent (education)	None	22	85	Tuberculosis occurrence in pastoralist populations have been shown to be associated with lower levels of education (Berg et al., 2015a). However, in some studies, persons with higher levels of education were shown to be more at risk , with those educated more likely to seek healthcare in formal health facilities (Ringo et al., 2018).	0.217
		Primary	1	22		
		Secondary	3	20		
		College	3	8		
5	Years respondent has lived in the village (residence)	Low	11	49	Due to the nature of contact among pastoralists due to their sociocultural practices (Omondi et al., 2021), length of time in a village or an area may be correlated with increased contact within	0.486
		Medium	6	42		
		High	12	44		

					the community and potentially exposure to pathogens including tuberculosis.	
6	Formal employment (formal)	Yes	3	18	Being a pastoralist has associated with increased risk of tuberculosis, however, some studies have shown that in comparison to being a pastoralist, other occupational undertakings have higher odds of TB infection (Teklu et al., 2018).	0.896
		No	26	117		
7	Business person (merchant)	Yes	4	5		0.09
		No	25	130		
8	Hunting of wild animals for food (hunting)	Yes	27	123	Consumption of raw animal products has been linked with a higher risk of testing positive for tuberculosis, especially in pastoralists (Gumi et al., 2012; Kirui, 2014; Berg et al., 2015a), with showing a strong positive association between exposure to bovine tuberculosis, caused by Mycobacterium bovis, and tuberculosis positivity in humans (Mengistu A et al., 2015). However, a few studies have also shown contradictory results with consumption of raw animal products being assumed to be protective against tuberculosis (Koech, 2001; Meisner et al., 2019). Understanding the frequency of consumption of raw animal products is important as this can be manipulated, together with other public health measures, to develop preventive measures aimed at reducing human exposure to tuberculosis of animal origin (Roug et al., 2014).	1
		No	2	12		
9	Consumption of raw cattle milk (rawmilkcattle)	Yes	19	40		0.0006
		No	10	95		
10	Consumption of raw goat milk (rawmilkgoat)	Yes	1	24		0.096
		No	28	111		
11	Consumption of raw sheep milk (rawmilksheep)	Yes	2	23		0.274
		No	27	112		
12	Consumption of raw cattle liver (cattleliver)	Yes	8	35		1
		No	21	100		
13	Consumption of raw cattle kidney (cattlekidney)	Yes	16	57		0.286
		No	13	78		
14	Consumption of raw sheep liver (sheepliver)	Yes	9	39		0.996
		No	20	96		
15	Consumption of raw sheep kidney (sheepkidney)	Yes	20	70		0.140
		No	9	65		
16	Consumption of raw goat liver (goatliver)	Yes	9	40		1
		No	20	95		
17	Consumption of raw goat kidney (goatkidney)	Yes	20	72		0.183
		No	9	63		
18	Consumption of raw blood from cattle (rawbloodcattle)	Yes	11	41		0.566
		No	18	94		
19		Yes	8	36		1

	Consumption of raw blood from sheep (rawbloodsheep)	No	21	99		
20	Consumption of raw blood from goat (rawbloodgoat)	Yes	8	34		0.870
		No	21	100		
21	Frequency of consumption of raw milk (rawmilkfreq)	Never	10	95		0.0001
		Sometimes	1	10		
		Always	18	35		
22	Frequency of consumption of raw meat (rawmeatfreq)	Never	9	58		0.229
		Sometimes	0	5		
		Always	20	72		
23	Frequency of consumption of raw blood (rawbloodfreq)	Never	17	86		0.809
		Sometimes	1	6		
		Always	11	43		
24	A household resident coughing for a more than a month prior to the interview (cough1month)	Yes	10	17		0.009
		No	19	118	Sharing of poorly ventilated spaces and household utensils with TB patients has been associated with tuberculosis infections among TB patients contacts (Aman and Zeidan, 2017).	
25	Sharing housing with livestock (sharehouse)	Never	10	55	Sharing of household space with livestock has been associated with higher risk of tuberculosis (Berg et al., 2015a). In addition, increased contact with livestock has been shown to be associated with human tuberculosis, especially those with tuberculosis reactors, however, there are contradictory findings where wealthier households and those with larger cattle herds have more tuberculosis reactors and less human tuberculosis (Meisner et al., 2019).	0.635
		Sometimes	0	2		
		Always	19	78		
26	Number of cattle in the household (hscattle)	Low	13	47		0.523
		Medium	7	45		
		High	9	43		
27	Number of goat in the household (hsgoat)	Low	8	46		0.601
		Medium	9	46		
		High	12	43		
28	Number of sheep in the household (hssheep)	Low	9	46		0.809
		Medium	11	55		
		High	9	34		

29	Distance cattle are herded to forage (grazingcattle)	Less than 5km	13	56	Pastoralists graze for shorter daily distances (Turner and Schlecht, 2019), but also engage in long distance grazing and movement of livestock to areas with good forage and water. These areas include protected areas, thus contact with wildlife, and transboundary movements which have implications for disease in livestock herds (Cleaveland et al., 2007; Caron et al., 2013; Omondi et al., 2021) and by extension human health (Cosivi et al., 1998; Mfinanga et al., 2004b; Olea-Popelka et al., 2017).	0.946
		5km to 10km	8	39		
		More than 10km	8	40		
30	Distance goat are herded to forage (grazinggoat)	Less than 5km	24	106		0.593
		5km to 10km	4	27		
		More than 10km	1	2		
31	Distance sheep are herded to forage (grazingsheep)	Less than 5km	24	106		0.593
		5km to 10km	4	27		
		More than 10km	1	2		
32	Observed interaction between wildlife and livestock during forage or watering (livestock.wildlife)	Yes	28	127		0.935
		No	1	8		
33	Frequency of interaction between wildlife and livestock during forage or watering (livestock.wildlifefreq)	Never	2	10		0.398
		Sometimes	0	8		
		Always	27	117		
34	Grazing cattle in the protected Maasai Mara National Reserve (maracattle)	Never	5	27		0.544
		Sometimes	18	69		
		Always	6	39		
35		Never	27	124		0.918
		Sometimes	1	4		

	Grazing goat in the protected Maasai Mara National Reserve (maragoat)	Always	1	7		
36	Grazing sheep in the protected Maasai Mara National Reserve (marasheep)	Never	27	124		0.918
		Sometimes	1	4		
		Always	1	7		
37	Transboundary movement of cattle to Tanzania during the dry season (tanzania)	Never	23	116		0.221
		Sometimes	4	17		
		Always	2	2		
38	Long wet season grazing in the Maasai Mara National Reserve (wet.long)	Yes	4	19		1
		No	25	116		
39	Dry season grazing in the Maasai Mara National Reserve (dry)	Yes	24	108		0.935
		No	5	27		
40	Short wet season grazing in the Maasai Mara National Reserve (wet.short)	Yes	4	23		0.879
		No	25	112		
41	Use of surface water in the household (surface.water)	Yes	18	81	Surface water is usually shared between humans, domestic animals and wildlife with the potential for sharing pathogens among the triad. In addition, the use of untreated water carries the risk of nontuberculous mycobacteria which complicates diagnosis of tuberculosis in humans (Mnyambwa et al., 2018a).	1
		No	11	54		
42	Use of underground/borehole water in the household (underground.water)	Yes	8	38		1
		No	21	97		
43	Use of piped water in the household (piped)	Yes	4	32		0.356
		No	25	103		
44	Drinking water from streams/rivers/ open pans during grazing of livestock (opendrinking)	Never	1	16		0.276
		Sometimes	0	3		
		Always	28	116		
45	Agistment degree (agist_deg)	Low	10	45	A household’s role in disease transmission is determined by its degree and/or betweenness where those with	0.427
		Medium	12	42		
		High	7	48		

46	Agistment network betweenness (agist_bet)	Low	11	46	high degree engage more with other households thus may play an important role in disease introduction or dissemination in the ecosystem. Those with a high betweenness lie in the middle of the path between other households thus, indirectly connecting other households, with their ‘removal’ fragmenting the network (Wasserman and Faust, 1994). Different animal movement reasons exist in this ecosystem with implications for disease transmission and control (Omondi et al., 2021).	0.713
		Medium	10	41		
		High	8	48		
47	Gift degree (gift_deg)	Low	16	63		0.521
		Medium	4	31		
		High	9	41		
48	Gift betweenness (gift_bet)	Low	21	86		0.583
		Medium	0	2		
		High	8	47		
49	Bride price network degree (bride_deg)	Low	16	102		0.047
		High	13	33		
50	Bride price network betweenness (bride_bet)	Low	24	126		0.138
		High	5	9		
51	Buying network degree (buy_deg)	Low	11	44		0.454
		Medium	11	42		
		High	7	49		
52	Buying network betweenness (buy_bet)	Low	14	41		0.071
		Medium	10	43		
		High	5	51		
53	Selling degree (sell_deg)	Low	14	40		0.007
		Medium	3	55		
		High	12	40		
54	Selling betweenness (sell_bet)	Low	14	40		0.140
		Medium	9	51		
		High	6	44		

Table 6. Metrics of the top 25 villages in the combined movement network in the Maasai Mara Ecosystem. $^{\gamma}$ Not a village in the ecosystem.

Village	Degree	In-degree	Out-degree	Betweenness
Nkoilale	220	101	119	0.16
Ololaimutia	180	72	108	0.15
Ngoswani	156	92	64	0.14
Aitong	142	76	66	0.11
Olesere	130	60	70	0.08
Empopongi	127	67	60	0.06
Talek	108	44	64	0.05
MMNR$^{\gamma}$	108	54	54	0.04
Sekenani	90	41	49	0.04
Nkineji	75	36	39	0.03
Trans Mara	68	25	43	0.03
Ilpoori	65	35	30	0.03
Losho	60	34	26	0.02
Naikara	58	22	36	0.02
Ol Tepesi	57	31	26	0.02
Ewaso Ngiro	56	47	9	0.02
Ololchora	53	25	28	0.02
Irbaan	49	28	21	0.02
Megwara	47	23	24	0.02
Ripoi	47	26	21	0.02
Ololorok	45	21	24	0.01
Ilturisho	39	21	18	0.01
Mboseli	37	19	18	0.01
Tipilikwani	36	17	19	0.01
Tanzania$^{\gamma}$	35	13	22	0.01