

Exposure and susceptibility drive reinfection with gastrointestinal parasites in a social primate

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Abstract

1. Increased risk of infectious disease transmission has been proposed as one major cost of group living. While factors corresponding to transmission via exposure to infectious stages and susceptibility to contracting infections upon contact are relatively well understood, both aspects are rarely investigated simultaneously.
2. Here, we assessed the influence of exposure and susceptibility measures on strongyle nematode reinfection after experimental deworming of Barbary macaques (*Macaca sylvanus*) ($n = 57$). We investigated impacts of behaviour (social bonds, grooming and ground use) and physiology (faecal glucocorticoids, urinary C-Peptides, urinary neopterin, gastrointestinal [GI] helminth coinfection) on the likelihood of reinfection, using patch occupancy modelling and information theoretic model selection to determine the best models predicting reinfection patterns.
3. Coinfection was the most consistent risk factor, spending time on presumably contaminated soil, interacting with many partners and forming strong same-sex bonds also tended to increase infection risk. In contrast, strong social bonds with opposite-sex partners had a consistently protective effect.
4. Our results indicate that coinfections could serve as an integrative measure of individual disease susceptibility. Furthermore, we show that social contact contributes to both exposure and susceptibility to environmentally transmitted parasites, with the outcome depending on specific interaction patterns.

KEYWORDS

anthelmintic treatment, exposure, gastrointestinal parasites, non-human primate, reinfection, social relationships, susceptibility

1 | INTRODUCTION

Parasitic infections are ubiquitous in wildlife, and increased parasite transmission has been suggested as a major cost of group living in social animals (Altizer et al., 2003; Freeland, 1976). Disease transmission depends on two distinct processes: exposure to infectious agents and host susceptibility, that is the host's likelihood to become

infected upon exposure (Hawley, Etienne, Ezenwa, & Jolles, 2011). Both aspects of transmission vary within and between individuals and with individual characteristics such as sex, age and dominance rank (Habig & Archie, 2015; Hawley et al., 2011). Individual differences in behaviour, susceptibility and capacity to transmit infectious diseases shape infection dynamics within populations (Drewe, 2009; Ezenwa, Etienne, Luikart, Beja-Pereira, & Jolles, 2010), with

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certain individuals contributing disproportionately to disease transmission (Hawley & Altizer, 2011; Lloyd-Smith, Schreiber, Kopp, & Getz, 2005). Comprehensive studies incorporating both susceptibility and exposure and their potential interactions are rare (Hawley et al., 2011), yet crucial for understanding the proximate mechanisms underlying disease transmission and the subsequent impact on individual health and fitness.

Sociality is linked to both, exposure and susceptibility to infectious diseases. While for directly transmitted diseases, direct physical contact carries infection risks (Drewe, 2009; Hamede, McCallum, & Jones, 2008), spatial association patterns predict transmission of environmentally transmitted parasites (Altizer et al., 2003; Nunn, Jordan, McCabe, Verdolin, & Fewell, 2015). In primates, for example, being socially central and directly interacting with many partners increases the risk of gastrointestinal (GI) parasite infections (MacIntosh et al., 2012; Wren, Remis, Camp, & Gillespie, 2016), suggesting a social component of transmission. While direct and indirect transmission via contact or shared space are often studied in combination (Friant, Ziegler, & Goldberg, 2016; Rimbach et al., 2015), the role of environmental contamination is more difficult to measure and consequently assessed less frequently.

Social behaviour not only affects parasite transmission via modulating exposure to infections, but also by affecting susceptibility. Social interactions influence individual physiology and immune function (Hawley et al., 2013; Snyder-Mackler et al., 2016), and by extension alter the propensity to acquire and survive infections (Capitanio, Mendoza, Lerche, & Mason, 1998; Cohen, Tyrrell, & Smith, 1991). One mechanism is social modulation of the hypothalamic–pituitary–adrenal axis: Socio-positive interactions like grooming and agonistic support are frequently linked to decreased stress hormone, that is glucocorticoid (GC) levels (Shutt, MacLarnon, Heistermann, & Semple, 2007; Young, Majolo, Heistermann, Schülke, & Ostner, 2014), while socio-negative interactions and group-level social instability can increase GC levels (Abbott et al., 2003; Sapolsky, 2005). GCs are essential for energy metabolism and immune regulation (Hart, 1988; Konsman, Parnet, & Dantzer, 2002), with immunostimulatory effects of short-term and immunosuppressive effects of long-term and high GC level elevations (Cain & Cidlowski, 2017). Higher GC levels have thus frequently been linked to increased infection risk (reviewed in Glaser & Kiecolt-Glaser, 2005), also with GI nematodes (Friant et al., ; Pedersen & Greives, 2008). GC levels and GI nematode prevalence are often, but not always, correlated (Fleming, 1997; MacIntosh et al., 2012), but since experimental studies are rare, both the directionality of the link and whether sociality impacts infection risk via GC levels remains largely unclear.

While susceptibility assessment using GC levels is common, more comprehensive approaches, incorporating health correlates like immune function, are still rare outside laboratory settings. Recent advances in the field of wildlife endocrinology now allow quantification of non-invasively assessed immune markers (Behringer & Deschner, 2017). GI nematodes usually evoke Th2 responses of the immune system (Carvalho et al., 2009), with failure to mount efficient Th2

response leading to chronic rather than transient infections with GI nematodes in laboratory studies (Finkelman et al., 1997). Stronger Th1 immune function, indicative of suppressed Th2 response (Long & Nanthakumar, 2004), has been linked with higher GI nematode infection risk in experimental studies on wild buffaloes (Ezenwa et al., 2010). Thus, urinary neopterin (uNEO), a marker of Th1 immune activation (Murr, Widner, Wirleitner, & Fuchs, 2002), can serve not only as a non-invasive marker of acute microparasite infection (Behringer, Stevens, Leendertz, Hohmann, & Deschner, 2017), but potentially of individual immune status and, indirectly, susceptibility to GI nematodes.

As immune responses are energetically costly (Colditz, 2008; Derting & Compton, 2003), individuals in worse physical condition or nutritional status are considered at higher risk of contracting infections (Coop & Kyriazakis, 1999). This pattern holds true for infection with GI parasites in various taxa (Díaz & Alonso, 2003; Ezenwa, 2004), including humans (Stephenson, Latham, & Ottesen, 2000). As a valid marker of energy balance and nutritional status in non-human primates, urinary C-Peptide (uCP) (Emery Thompson & Knott, 2008; Girard-Buttoz et al., 2011) can be employed as a marker to investigate links between individual physiology and susceptibility.

Coinfections with multiple parasites, commonly observed across the animal kingdom (Rynkiewicz, Pedersen, & Fenton, 2015) but less frequently incorporated in wildlife health studies, may also predict susceptibility to infections (Ezenwa, 2016; Graham, 2008). While infections can be the result of individual immune physiology (Ezenwa et al., 2010; Vaumourin, Vourc'h, Gasqui, & Vayssier-Taussat, 2015), GI nematode infections can increase susceptibility to micro- and macroparasites via immunosuppressive effects or be protective against infections with other GI nematode taxa due to cross-immunity or competition among the pathogens (Cox, 2001; Vaumourin et al., 2015).

Faeco-orally transmitted GI nematodes are an excellent system to study transmission and address several of the above issues in wildlife. Utilizing experimental deworming and tracking reinfection by dense repeated sampling from known individuals, we aimed to comprehensively assess predictors of reinfection with strongyle nematodes in semi-free ranging Barbary macaques (*Macaca sylvanus*). More specifically, we considered possible effects of environmental (ground use and time spent in areas presumably contaminated with infective strongyle stages) and social exposure (number of grooming partners and overall grooming duration). Given the beneficial health effects of social bonds (Cohen et al., 1991; Holt-Lunstad, Smith, & Layton, 2010), we included measures of social bond strength to test for beneficial effects of social interactions on health via reduced GI parasite infection risk. We included three physiological markers, faecal glucocorticoid metabolites (fGCM), uNEO and uCP levels, and coinfection with other GI nematodes as possible predictors of individual susceptibility. To account for uncertainty in parasite detection, we used patch occupancy modelling (MacKenzie et al., 2002) in combination with information theoretic model selection

(Garamszegi, 2011) to assess the effects of the measured predictors on reinfection.

2 | MATERIALS AND METHODS

2.1 | Study site and anthelmintic treatment

The study was conducted at Affenberg Salem, a 20 ha forested outdoor enclosure in Germany (de Turckheim & Merz, 1984), on all adult individuals of two groups of semi-free ranging Barbary macaques during two field seasons (June to December 2014, group C, $n = 36$; June to November 2015, group H, $n = 41$, see Supporting Information Table S1 for detailed information on group composition). Anthelmintic treatment was administered orally by distributing food items containing ivermectin (approximately 0.4 mg/kg body weight). All individuals of group C received treatment on 5 August 2014; 21 individuals of group H were treated on 17 August 2015, 20 individuals served as an untreated control group for other studies (Müller, Heistermann, Strube, Schülke, & Ostner, 2017; Müller-Klein et al., 2018). Control individuals were included for construction of social variables, but excluded from reinfection analysis.

2.2 | Behavioural data collection and construction of social variables

Behavioural data were collected using continuous focal animal sampling (Martin & Bateson, 2007), recording affiliative and aggressive behaviours (3,245.6 focal hours; 2014: 48.1 ± 4.6 hr/individual; 2015: 36.9 ± 1.4 hr/individual), with instantaneous recording of focal animal substrate use (ground vs. non ground) every minute. Individual dominance rank was constructed from all decided dyadic aggressive interactions recorded during focal protocols and ad libitum. Dyadic sociality indices (CSI) (Silk, Altmann, & Alberts, 2006) were calculated and sum of top three partners used as a measure of social bonding as described in Müller-Klein et al. (2018). As interaction patterns differed markedly between the sexes, CSIs were calculated separately for same- and opposite-sex relationships (see Supporting Information Appendix S2 for detailed information).

2.3 | Assessing environmental exposure (2014 only)

All spatial data were recorded as cardinal direction in 22.5° increments and distance in metres from 166 individually marked positions with known GPS location (GPS device: eTrex 10, Garmin, Garching, Germany) spread approximately every 10 m within the homerange of study group C. A "risk area" was delineated from the location of 257 defecations prior to anthelmintic treatment as the 33% Kernel polygon in ArcGIS (version ARCMAP 10.5.1). We used a search radius of 15 to obtain the best compromise between smooth edges of the area and not overestimating the risk area. To estimate individual exposure to contaminated soil, we calculated the proportion of time each individual was observed on the ground in the risk area from 283 spatially explicit 10-min group scans (Altmann, 1974) prior to

deworming (6,163 data points, mean \pm SD = 167.25 ± 18.41 data points/individual; Figure 1).

2.4 | Sample collection

Faecal samples were collected immediately after defecation 0–4 times per individual per week for parasite analysis, with separate aliquots stored for fGCM analyses if possible as described previously (Müller et al., 2017; Müller-Klein et al., 2018). Over the six weeks prior to anthelmintic treatment, 2.0 ± 0.8 urine samples were collected opportunistically from 40 of the subjects as described previously (Müller et al., 2017, see Supporting Information Appendix S2).

2.5 | Parasite analysis

We analysed one sample per individual per week if available and every available sample for the first two weeks after treatment ($n = 953$, 16.7 ± 2.8 samples/individual; $n = 338$ before treatment, $n = 615$ after treatment) using the McMaster method as described in Müller et al. (2017). We focussed our statistical analyses on strongyle nematodes successfully cleared by treatment, but include co-infection with two other parasites not fully cleared by treatment, *Capillaria* spp. and *Trichuris* spp., as predictor of reinfections (Müller et al., 2017, see Supporting Information Appendix S2).

2.6 | Analyses of physiological markers

For fGCM analysis, faecal samples ($n = 267$ samples, 4.7 ± 1.1 samples/individual) were analysed as described in Paschek, Müller, Heistermann, Ostner, and Schülke (2018). fGCM levels are expressed in ng/g faecal dry weight. We measured uNEO levels ($n = 82$ samples, 2.1 ± 0.8 samples/individual) and uCP levels ($n = 78$ samples, 2.0 ± 0.8 samples/individual) in duplicates as described previously (Müller et al., 2017, see Supporting Information Appendix S2). uNEO and uCP concentrations are expressed as ng/ml corrected for the sample's specific gravity.

2.7 | Patch occupancy modelling and model selection

The Cox proportional hazards models often used to assess reinfection (Friant et al., 2016) assume precise information on the time of reinfection. Microscopic parasite analyses from faeces are inherently prone to imprecisions (Gillespie, 2006), especially false-negative scores, creating considerable uncertainty in the exact time of reinfection. To account for this uncertainty, we used a patch occupancy modelling approach (MacKenzie et al., 2002) utilizing the *unmarked* package (Fiske & Chandler, 2011) to assess the influence of various predictors of individual exposure and susceptibility on reinfection risk with strongyle nematodes in R, version 3.4.3 (R Core Team, 2014). Each individual was considered as one patch, and each week post treatment was considered as one time step. The availability of several samples per time period (at least for some time periods) is essential for applying patch occupancy modelling, as the

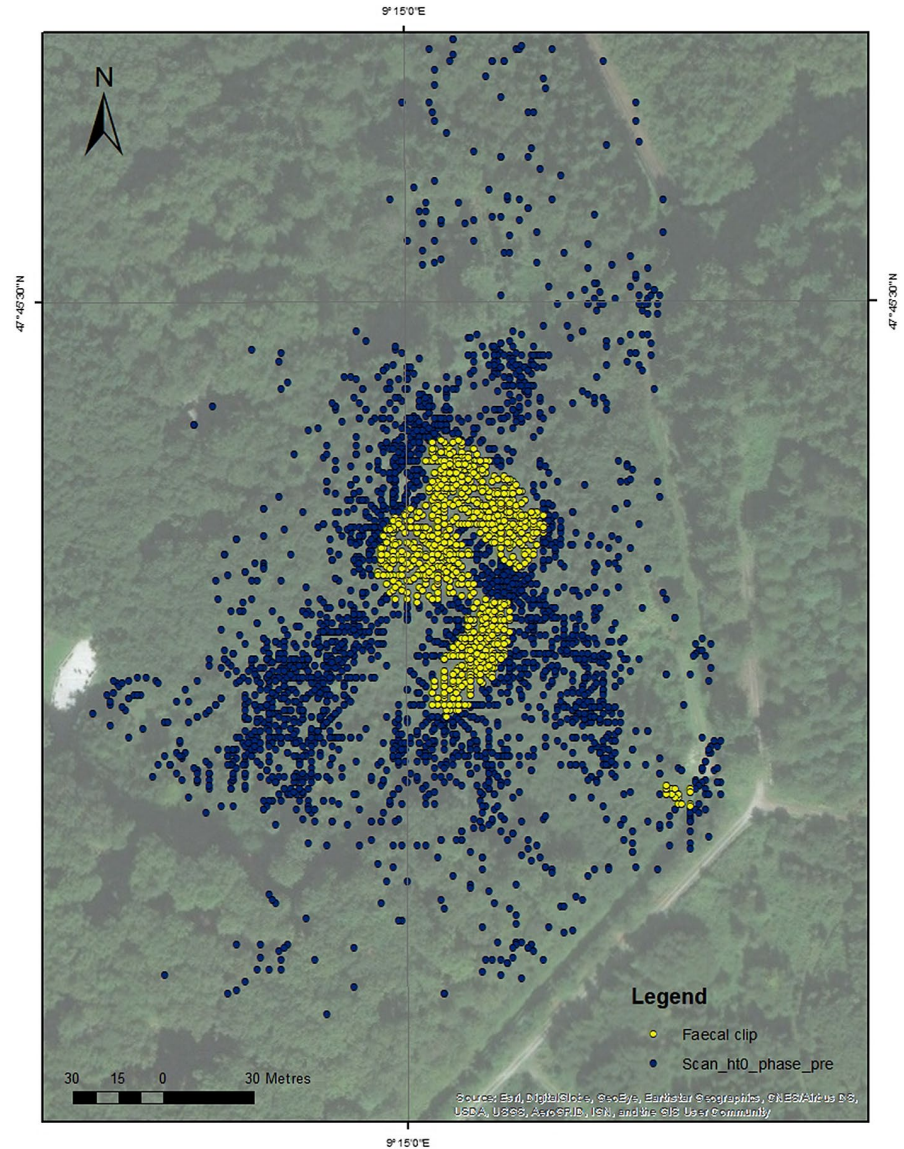


FIGURE 1 Area of high faecal contamination mapped onto ranging data from study year 2014. The risk area of presumably high faecal contamination was defined as the density kernel including 33% of all faecal samples. Each dot represents one recorded individual location, with records on the ground in the risk area shown in yellow. Individuals were observed on the ground in the risk area between 17.7% and 34.8% of all observations (mean \pm SD = 27.3 \pm 4.1%)

probability of false negatives is estimated from multiple samples, also enabling the estimation of reinfection probabilities. In contrast to a Cox model, patch occupancy models do not assume that a negative sample is a true negative. Instead, the model simultaneously estimates whether reinfection occurred and whether an infection was also detected. Based on available samples, we included a maximum of four samples (i.e. observation events) available per time step, coding the presence/absence of strongyle eggs and assigned NAs to missing observations. Six positive samples collected within 2 days of treatment were excluded from analyses, as individuals remained coproscopically negative for at least 3 weeks after treatment afterwards, indicating ongoing gut passage of eggs after successful treatment (Müller-Klein et al., 2018).

For all analyses, we estimated the following set of parameters: (a) a constant probability of detecting true positives, (b) a constant probability of initial infection (which corresponds to the probability that deworming was not successful) and (c) a constant probability of “extinction” (i.e. natural parasite clearance by the host). For

modelling “colonization”—that is parasite reinfection—we used a set of predictors, employing information theoretic model selection based on Akaike's information criterion (AIC) (Garamszegi, 2011) to assess which factors are included in the model best predicting reinfection. The predictors included were environmental (proportion of time spent on ground and proportion of time spent in the risk area) and social (number of grooming partners and grooming duration) exposure factors and physiological (fGCM, uCP and uNeo, coinfection with *Capillaria* and *Trichuris*) and social (same- and opposite-sex CSI) predictors of susceptibility (Table 1).

As social contact patterns and space use cannot be assessed on a day-to-day basis, but require large amounts of data, and imprecise information on the exact time of reinfection prohibited time-matching for other predictors, we used the pre-treatment phase to quantify individual differences in all predictors of reinfection. Grooming data were included as summarized data over the entire pre-treatment phase, physiological marker levels as average values over all samples from the pre-treatment phase.

TABLE 1 Overview of the predictors considered for model selection assessing the best predictors of reinfection. For all predictors except CSI, we considered data before anthelmintic treatment

Exposure				
Measure	Ground use	Contaminated soil use	Grooming partner number	Grooming duration
Abbreviation	Proportion on ground	(proportion in) risk area	NA	NA
Expected effect on reinfection	Positive	Positive	Positive	Positive
Mechanism	Environmental transmission	Environmental transmission	Social transmission	Social transmission
Physiology				
Measure	Faecal glucocorticoid metabolites	Urinary neopterin	Urinary C-Peptide	Coinfection
Abbreviation	fGCM	uNEO	uCP	NA
Expected effect on reinfection	Positive	Positive	Negative	positive or negative
Mechanism	Immunomodulation	Immune function	Physical condition/energy availability	Parasite community effects
Social bonds				
Measure	Sum top 3 CSI, same-sex partners		Sum top 3 CSI, opposite-sex partners	
Abbreviation	Same sex CSI		Opposite-sex CSI	
Expected effect on reinfection	Negative		Negative	
Mechanism	Social buffering		Social buffering	

All variables were rather stable over the entire study period as indicated by high correlations between values before treatment and for the entire study period (Pearson correlation, $p < 0.001$, $R > 0.58$, see Table 1).

We further included sex, age and rank of each animal as control variables. We considered the potential for group differences in temporal effects on reinfection and accordingly included week after treatment, study year and their interaction in all models (week treated as a continuous predictor). A nonlinear (quadratic) fit of study week improved AICs for the full dataset only and could not be included in the exposure dataset due to indications of problems with model fitting. The overall results were highly similar between linear and nonlinear fit of week, so we report the linear model fit here for consistency, providing the results for nonlinear fit of week as Supporting Information (<https://doi.org/10.5061/dryad.rr379bp>). Linear predictors except week were z-transformed prior to analyses. Sex and rank as well as grooming partner number and grooming duration showed signs of collinearity (variance inflation factors > 6). Therefore, all models were restricted to include either sex or rank and either grooming partner number or duration. Including an interaction between sex and CSI measures to account for sex-specific effects of social bond strength did not improve AIC values of the models and was thus not retained for the final analyses.

As data for all predictors were available for only 19 individuals and patch occupancy models did not allow for NAs in predictors, we

used three different datasets to the best compromise between sample size and predictor inclusion: (a) the “full dataset,” which included all treated individuals ($n = 57$), but lacked measurements of time in risk area, uNEO and uCP; (b) the “susceptibility dataset”, which included all individuals for which urine samples were available ($n = 40$), with all predictors except time in risk area; and (c) the “exposure dataset,” which included only data from 2014 ($n = 36$) and proportion of time spent in risk area in addition to all predictors except uNEO and uCP. Consequently, only 19 individuals are included in all three datasets, whereas 21 individuals included in the susceptibility dataset and 17 individuals in the exposure dataset are included only in the full and the respective dataset.

Given the high number of models to compare, we chose a cut-off of $\Delta AIC \leq 2$ for models to be considered plausible. To not select overly complex models, we followed the approach suggested by Richards, Wittingham, and Stephens (2011) to exclude models which were a more complex version of a better fitting model and which had a higher AIC than the less complex better fitting model.

2.8 | Ethical statement

This study was approved by the Animal Welfare Body of the German Primate Centre (No. E9-16) and adhered to the standards on the protection of animals used for scientific purposes as defined by the European Union Council Directive 2010/63/

EU and the Animal Behaviour Society's guidelines for the treatment of animals in behavioural research and teaching (Animal Behavior Society, 2012). The Veterinary Office of the district office of county Lake Constance authorized anthelmintic treatment as defined by the European Union Council Directive 1999/22/EC. Treatment was performed as part of the routine veterinary care on Affenberg Salem.

3 | RESULTS

AIC-based model selection resulted in eleven models (with $\Delta AIC \leq 2$) across the three datasets, three models in the full and susceptibility dataset, respectively, and five models in the exposure dataset, all with a better fit than the respective null model (Table 2, detailed information available at <https://doi.org/10.5061/dryad.rr379bp>).

Across the three datasets, reinfection risk increased with progression of the study (Figure 2). The most consistent predictor of reinfection probability was coinfection, which was included in all selected models with an estimated threefold to fourfold increase in odds of reinfection (Figure 3a). A higher CSI with opposite-sex partners was another highly consistent effect, included in all but three selected models. In all cases, opposite-sex CSI was estimated to reduce the odds of reinfection by a factor of 0.6 to 0.7 per standard deviation (Figure 3b).

In the exposure dataset, the proportion of individuals spent in the likely contaminated areas was included in three of five models, increasing the odds for reinfection by a factor of ~ 2.2 per 10% increase in time spent in the risk area (Figure 3d). Apart from environmental exposure, exposure via social contact also affected reinfection risk. High same-sex CSI was included in one model of the full and in all models of the exposure dataset, leading to a 1.3- to

1.8-fold increase in the odds of reinfection per standard deviation (Figure 3c). Similarly, the number of grooming partners was included in two of the models of the full dataset, with the odds for reinfection increasing by a factor of ~ 1.1 per additional grooming partner (Figure 3e). The same models also included sex, with males having ~ 3 fold higher odds of reinfection than females.

Age and uCP appeared in single models of the susceptibility dataset and will thus be considered as potentially influential predictors, with the odds for reinfection decreasing by a factor of 0.1 per year of age, and increasing by a factor of 1.6 per standard deviation increase in uCP levels. Considering the low number of samples available for uCP analysis, this result needs to be considered with caution.

4 | DISCUSSION

Aiming at a comprehensive study of GI nematode transmission in a non-human primate, the Barbary macaque, we combined experimental parasite clearance, patch occupancy modelling and model selection to simultaneously measure the effects of exposure and susceptibility on reinfection risk after parasite clearance. Taking into account physiological parameters (i.e. stress, energy and immune markers) and measures of both environmental and social exposure, we found indications for simultaneous effects of susceptibility and exposure, mediated both environmentally and behaviourally.

Coinfection with other GI parasites emerged as the most consistent predictor of reinfection risk in our analysis. Rather than providing a protective effect based on cross-immunity or competition between GI nematode taxa within hosts (Vaumourin et al., 2015), coinfections with *Trichuris* or *Capillaria* increased strongyle nematode reinfection risk. This could be the result of negative health

TABLE 2 Overview of the selected models predicting reinfection probability with strongyle nematodes after treatment in Barbary macaques using three different datasets: full, $n = 57$ individuals, including predictors available for all individuals; susceptibility, $n = 40$ individuals, including individuals with urine samples available to assess the effect of urinary physiological markers of susceptibility; and risk, $n = 36$ individuals, including only data from 2014 to assess effect of direct exposure to highly contaminated ("risk") areas. Models were excluded if they represented more complex versions of nested, better fitting models. Interpretation of effects of predictors on reinfection is based on the final retained models. For detailed overview over the predictor estimates from models used in model selection, see the full summary provided in the Dryad Data Repository at <https://doi.org/10.5061/dryad.rr379bp>

Dataset	Predictors of reinfection	AIC	ΔAIC
Full	week \times year + Coinfection + CSI (opposite sex) + CSI (same sex) + grooming partner number + sex	584.88	0.00
Full	week \times year + Coinfection + CSI (opposite sex) + grooming partner number + sex	585.12	0.24
Full	week \times year + Coinfection + CSI (opposite sex)	586.15	1.27
Susceptibility	week \times year + uCP + Coinfection + CSI (opposite sex)	385.58	0.00
Susceptibility	week \times year + age + Coinfection + CSI (opposite sex)	386.22	0.64
Susceptibility	week \times year + Coinfection + CSI (opposite sex)	386.47	0.89
Exposure	week + Coinfection + CSI (opposite sex) + CSI (same sex) + proportion in risk area	386.41	0
Exposure	week + Coinfection + CSI (same sex) + proportion on ground + proportion in risk area	386.51	0.10
Exposure	week + Coinfection + CSI (opposite sex) + CSI (same sex)	386.55	0.14
Exposure	week + Coinfection + CSI (same sex) + proportion in risk area	387.13	0.72
Exposure	week + Coinfection + CSI (same sex)	387.20	0.79

Bold font indicates predictors, in contrast to week \times year as control variable.

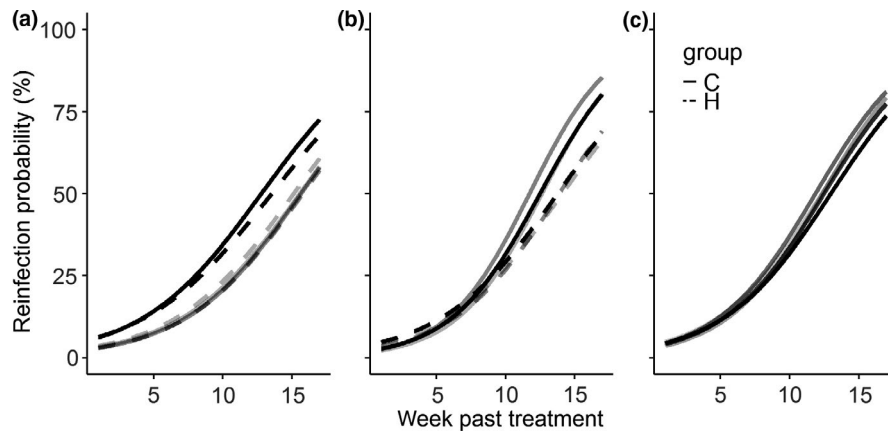


FIGURE 2 Temporal effects on re-infection risk for (a) the full dataset, (b) the susceptibility dataset and (c) the exposure dataset. The three datasets were used for the best compromise between sample size and including all possible predictors (full dataset: $N = 57$ Barbary macaques; susceptibility dataset: $N = 40$ Barbary macaques; exposure dataset: $N = 36$ Barbary macaques). For the full and susceptibility dataset, effects are plotted separately for the two study groups (solid line group C, dashed line group H). Effects for all best models ($\Delta AIC < 2$; full dataset: $N = 3$; susceptibility dataset: $n = 3$; exposure dataset: $N = 5$) are plotted for mean value of all other predictors. The temporal effects depicted here are included as control variables in all further analyses

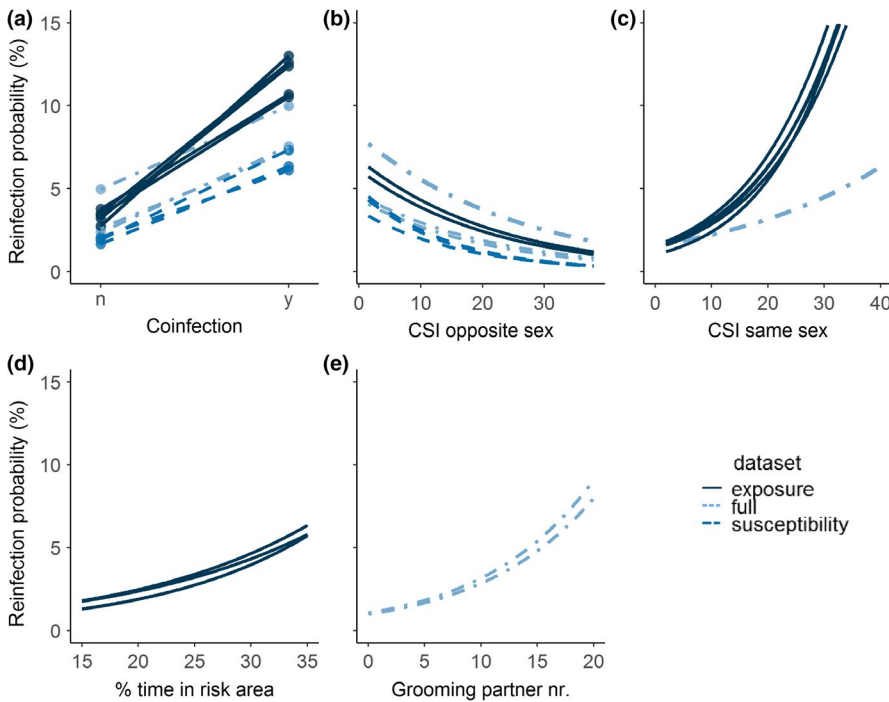


FIGURE 3 Effects of (a) coinfection, (b) social bonds with opposite-sex partners, (c) social bonds with same-sex partners, (d) time spent in risk area and (e) number of grooming partners on re-infection probability, assessed by patch occupancy modelling of egg presence data for the full (dashed lines), susceptibility (broken lines) and exposure (solid lines) datasets. All predictors were included in all or the majority of the best models ($\Delta AIC < 2$). Effects are plotted for week post treatment = 1 and mean values of all other predictors

impact of pre-existing infections or parasite-mediated immunosuppression (Andreasen et al., 2015; Lello, Boag, Fenton, Stevenson, & Hudson, 2004) or reflect an overall propensity of the individual immune system to inefficiently defend against nematodes. Studies on rodents and ungulates showed that individuals tending towards a Th1 type immune response and failing to mount efficient Th2-type responses are more likely to suffer from GI nematode infections, developing chronic rather than transient infections (Ezenwa et al., 2010; Loukas, Constant, & Bethony, 2005). However, uNEO, our indicator for Th1-type immune system activation, was not included as a predictor of re-infection in any of the best models, nor strongly related with coinfection. As mixed Th1-Th2 type responses

against *Trichuris* and *Oesophagostomum* spp. have been described (Andreasen et al., 2015), Th1 type immune responses suppressing Th2 responses may not be the mechanism linking coinfection to higher susceptibility in our study species. Future studies might provide some clarity with regard to parasite community effects by measuring the cost of infections (e.g. energetic costs or reduced activity) (Friant et al., ; Hayward et al., 2014) or taking actual parasite burden into account (Jackson et al., 2014; Lello et al., 2004).

Coinfections with enoplid parasites (*Capillaria* and *Trichuris* spp.) were not cleared by anthelmintic treatment in all individuals (Müller et al., 2017), limiting the interpretation of our results with regard to the underlying mechanism linking coinfection to increased re-infection risk.

Whether increased reinfection reflects overall susceptibility of individuals to GI nematode infections (Vaumourin et al., 2015), or parasite community effects at time of reinfection (Cox, 2001; Lello et al., 2004) is unclear. Possibly, coinfection may be best viewed as an integrative measure, because it is driven by both susceptibility and exposure, in ways that might not have been captured by the physiological markers of our study.

Strong opposite-sex social bonds consistently decreased the risk of reinfection. The beneficial effect of social bonds on health and survival has been well documented in primates (Archie, Tung, Clark, Altmann, & Alberts, 2014; Holt-Lunstad et al., 2010), although bonding has, to our knowledge, not been linked with GI parasite transmission to date. Social bonds and affiliative behaviours decrease physiological stress correlates in primates (Shutt et al., 2007; Young et al., 2014), an effect that is considered a major mechanism linking sociality to positive health outcomes (Cohen & Wills, 1985; Hawkley et al., 2013). In our study, the positive effect of opposite-sex social bonding did not seem to be mediated by fGCM levels, as a mediating effect should become apparent by selected models including fGCM levels in absence of opposite-sex bonds as predictor of reinfection. Social bond strength may instead be an integrative measure of social contact modulating physiology, for example of inflammatory pathways (Uchino, 2006), endogenous endorphins or oxytocin (Crockford et al., 2013; Curley & Keverne, 2005; Uchino, 2006), possibly promoting immune function and health.

While we found quite clear evidence for opposite-sex social bonds reducing reinfection risk, our results also indicate that bonds with same-sex partners increase infection risk. Given the reported salubrious effects of bonding for survival regardless of partner sex (Archie et al., 2014; McFarland & Majolo, 2013), the negative effect of same-sex bonds is unexpected, but could be linked to different nature of same- and opposite-sex bonds. Same-sex bonds are more heterogeneous than opposite bonds, and female–female interactions are ~ 10 times more frequent than male–male interaction, possibly leading to same-sex interactions contributing more to exposure risk. A moderate correlation between same-sex bond strength and number of grooming partner numbers (Pearson correlation, $R = 0.32$, $p = 0.01$)—another measure implied to increase reinfection risk—supports this suggestion. In contrast, opposite-sex bond strength was not closely related to number of grooming partners (Pearson correlation: $R = 0.10$, $p = 0.93$). Similarly, high network integration has been shown to be either protective or a risk factor to GI parasite infections in captive macaques (Balasubramaniam, Beisner, Vandeleest, Atwill, & McCowan, 2016), highlighting the dual function of sociality. Another possibility is that the female propensity to form strong bonds with close kin (Silk, Alberts, & Altmann, 2003) leads to frequent contacts between genetically similar individuals potentially more similar in susceptibility or exposure than unrelated individuals. Which specific correlates of physiology, immunology and exposure connected to same- versus opposite-sex social interactions contribute to parasite transmission, and whether those components are traded off against each other (Hawley et al., 2011) poses interesting questions for future studies.

Assessing both social and environmental components of exposure to infective parasite stages, we found no indication that the overall time spent on the ground explained reinfection. However, we found some indication that more time spent on soil presumably contaminated with faeces increased the risk of parasite infection, indicative of environmental transmission. By linking defecation and individual space use, we extend approaches using social network parameters to estimate such exposure (Friant et al., 2016; Rimbach et al., 2015). As behavioural avoidance strategies are well documented (Poirotte et al., 2017; Weinstein, Moura, Mendez, & Lafferty, 2018), it will be interesting for future studies to assess whether interindividual differences in environmental exposure are linked with behavioural adjustments to mitigate risk of parasite transmission, for example hygienic tendencies (Sarabian & MacIntosh, 2015).

Parasite transmission often has a social component (Balasubramaniam et al., 2016; Drewe, 2009; MacIntosh et al., 2012), but is not always linked to direct contact (Friant et al., 2016; Gear, Luong, & Hudson, 2013), suggesting parasite-specific patterns, for example different transmission pathways in parasites with mobile (free-living larvae) versus immobile (embryonated eggs) infective stages (MacIntosh et al., 2012). In vervet monkeys and our study, grooming many different partners increased infection risk with GI nematodes (Wren et al., 2016), indicating a social component of transmission. Both transmission pathways contributed to individual reinfection risk, highlighting the importance to consider both components of transmission even in predominantly environmentally transmitted pathogens and possibly explaining the dual effect of sociality as both a protective and risk factor.

Several predictors emerged in a few selected models, indicating a link to parasite transmission. In accordance with numerous previous studies (Habig & Archie, 2015), males had a markedly higher risk of reinfection. Older age predicted lower reinfection risk, possibly a sign of acquired immunity against repeated parasite infections (Wilson et al., 2002). Contrary to our assumption that individuals with poor physical condition are more susceptible to GI nematodes (Beldomenico & Begon, 2010), higher uCP levels were linked with increased reinfection risk, possibly reflecting different defence strategies against GI nematodes. High uCP levels prior to treatment could indicate low energetic costs of infection in some individuals, similar to findings in Soay sheep (Hayward et al., 2014), where some individuals tolerate GI nematode infections with lower weight loss. The differences in the results between the datasets could be attributable to sample size-driven differences in statistical power or the fact that different datasets held different individuals (only 19 of 57 individuals were included in all datasets). To disentangle these explanations, a larger and more complete dataset is needed, which will allow to assess the impact of the less consistent predictors in our analyses, that is age, physical condition and sex in relation to exposure and coinfection in future studies.

In summary, we found exposure and susceptibility to contribute simultaneously to individual risk of acquiring strongyle nematode infections, with sociality feeding into both aspects. Although we cannot exclude the possibility that predictors not emerging in our selected

models have an impact on reinfection, the consistent patterns allow us to draw some conclusions about the host–parasite relationships between Barbary macaques and strongyle nematodes, and synthesize on transmission pathways. We suggest that direct contact to infective parasite stages, which can be mediated by spatial centrality within a social group, is the probable mechanism linking social integration to GI parasite infection risk based on direct measurements of this environmental exposure. While in case of strongyle nematodes with mobile larvae a social component of transmission is evident, this might not be the case for parasites with different transmission pathways, explaining the discrepancy with regard to an impact of direct contact on parasite transmission. Incorporating several physiological markers, we show that they are not necessarily the best predictor of susceptibility, but that individual infection status or previously existing infections might serve as an integrative measure of individual physiology and immune status. While social bonds have emerged as the major protective factor against strongyle infection, they are also implied as a risk factor, indicating covariation between sociality, exposure and susceptibility. Disentangling this covariation is beyond the scope of this study, but we encourage future studies to simultaneously incorporate distinct susceptibility and exposure predictors in experimental approaches to understand their respective roles for host–parasite relationships in wildlife (Hawley et al., 2011).

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AUTHORS' CONTRIBUTIONS

N.M.K., J.O. and O.S. conceived the study design; N.M.K. collected the data presented; C.S. and N.M.K. performed parasite analyses; M.H. performed enzyme immunoassays; M.F. contributed patch occupancy modelling and model selection. All authors participated in writing the manuscript and approved the final version.

DATA ACCESSIBILITY

Data used for the analyses in this article are deposited in the Dryad Digital Repository <https://doi.org/10.5061/dryad.rr379bp> (Müller-Klein et al., 2019).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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