Genetic, social and maternal contributions to *Mycobacterium bovis* infection status in European badgers (*Meles meles*)

Running title: Variation in badger infection status

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34 **Genetic, social and maternal contributions to *Mycobacterium bovis* infection status in European**

35 **badgers (*Meles meles*)**

36

37 **Abstract**

38 Within host populations, individuals can vary in their susceptibility to infections and in the severity
39 and progression of disease once infected. Though mediated through differences in behaviour,
40 resistance or tolerance, variation in disease outcomes ultimately stems from genetic and
41 environmental (including social) factors. Despite obvious implications for the evolutionary, ecological
42 and epidemiological dynamics of disease traits, the relative importance of these factors has rarely
43 been quantified in naturally infected wild animal hosts. Here, we use a long-term capture-mark-
44 recapture study of group-living European badgers (*Meles meles*) to characterise genetic and
45 environmental sources of variation in host infection status by *Mycobacterium bovis*, the causative
46 agent of bovine tuberculosis (bTB). We find that genetic factors contribute to *M. bovis* infection
47 status, whether measured over a lifetime or across repeated captures. In the latter case the
48 heritability (h^2) of infection status is close to zero in cubs and yearlings but increases in adulthood.
49 Overall, environmental influences arising from a combination of social group membership (defined
50 in time and space) and maternal effects appear to be more important than genetic factors. Thus,
51 while genes do contribute to among-individual variation, they play a comparatively minor role,
52 meaning that rapid evolution of host defences under parasite-mediated selection is unlikely
53 (especially if selection is on young animals where h^2 is lowest). Conversely, our results lend further
54 support to the view that social and early-life environments are important drivers of the dynamics of
55 bTB infection in badger populations specifically, and of disease traits in wild hosts more generally.

56

Keywords: bovine tuberculosis, infection status, quantitative genetics, *Mycobacterium bovis*, *Meles meles*

Introduction

Pathogens and parasites are key drivers of the ecological and evolutionary dynamics of their wild host populations (Schmid-Hempel 2011). In response, hosts have evolved a myriad of defence strategies that include behavioural avoidance of infection (Behringer et al. 2006), immune responses that limit parasite growth (resistance; Rigby et al. 2002), and repair of parasite-induced damage to minimise costs of infection (tolerance; Medzhitov et al. 2012). However, there can be considerable variation amongst individuals in these traits which gives rise to differences in susceptibility to infection and the subsequent progression of disease. The importance of among-individual variation for population-level processes has become increasingly clear in recent years (e.g. Madritch & Hunter, 2002; Grist et al., 2014; Svanbäck et al. 2015), particularly with respect to our understanding of infection dynamics (Kramer-Schadt et al. 2009; van der Waal & Ezenwa, 2016). However, while among-individual variation can generally be viewed as stemming from both genetic and environmental (including social) effects, we currently have little knowledge of their relative importance in wild and unmanaged host populations where environmental factors can exert considerable influence on infection dynamics.

From an evolutionary point of view, parasites (in which we include pathogenic bacteria, viruses, fungi, protozoa and macroparasites) are expected to select for improved host defences. However, any response to selection is contingent on the presence of genetic variance in the host. A partial genetic basis of variation in host defence strategies against infectious disease is well-established in humans, model organisms, and livestock studies (Morris, 2007; Yan et al. 2006; Breitling et al., 2008). For instance, selective breeding for resistance to specific parasites is important to agriculture and aquaculture (Stear et al. 2001; Yáñez et al. 2014). In addition to enabling host

82 selection responses, genetic variation among individuals may also impact on parasite transmission
83 dynamics, and patterns of disease emergence and prevalence (Yates et al., 2006; Doeschl-Wilson et
84 al., 2011) with consequences for host behaviour, mortality and fecundity. Among-host genetic
85 variation can therefore influence the population-level (demographic) consequences of infection
86 through multiple routes (Nath et al. 2008; Lough et al. 2015).

87 At present, relatively little is known about the extent of genetic variation in disease
88 susceptibility in wild host populations. This is largely due to the difficulties of obtaining appropriate
89 immunological data coupled to genetic information (e.g. pedigree or relatedness measures over
90 multiple generations). Several quantitative genetic studies have investigated variation in avian
91 immune response traits, with findings ranging from an apparent absence of genetic effects (Pitala et
92 al. 2007) to moderate heritability (h^2, the proportion of variance explained by additive genetic
93 effects) of immune function (e.g. phytohaemagglutinin response in house sparrows, *Passer*
94 *domesticus*, h^2 (± SE) = 0.46 ±0.19, Bonneaud et al. 2009; in common kestrels, *Falco tinnunculus*, h^2=
95 0.47 ±0.10, Kim et al. 2013) . Genetic variation in resistance and tolerance to ectoparasites has been
96 reported in a cyprinid fish (*Leuciscus leuciscus*; Blanchet et al. 2010; Mazé-Guilmo et al. , 2014), while
97 analyses of helminth infection in Soay sheep (*Ovis aries*) revealed genetic variation in host
98 resistance but not tolerance (Hayward et al., 2014a; Hayward et al., 2014b). There is also growing
99 evidence that consistent differences in host behaviours, likely to influence infection risk (e.g.
100 dispersal, sociability; Barber & Dingemanse, 2010), are heritable in natural populations (Korsten et
101 al. 2013; Petelle et al. 2015). However, whether this behavioural variation represents an important
102 source of genetic variation in infection status remains to be determined.

103 As studies to date have yielded mixed conclusions about the importance of genetic variation
104 in disease traits in wild animal hosts, we also have limited understanding of how environmental
105 factors contribute to among-host variation. Abiotic factors (e.g. rainfall, seasonality) can play an
106 important role in shaping disease dynamics at the population level (Altizer et al. 2006), as can biotic

107 environmental influences such as the distribution and social structure of host populations (Keiser et
108 al. 2018). However, social effects, broadly defined as influences of phenotype arising from
109 interactions with conspecifics, are also strongly associated with heterogeneity in disease dynamics.
110 On the one hand, transmission of pathogens within groups of closely interacting individuals is
111 thought to represent a major cost of group living (Kappeler et al. 2015). On the other hand, social
112 immunity processes – whereby the immune response of one individual offers protection to group
113 members - can sometimes occur (e.g. in Nicrophorus burying beetles; Palmer et al. 2016). More
114 generally, social systems in which close-knit groups have limited among-group contact can inhibit
115 the spread of disease over larger (among-group) scales (e.g. Delahay et al., 2000b; Rozins et al.
116 2018).

117 The importance of social effects on disease traits can also change with age, precisely
118 because social behaviours and contexts are themselves frequently age- or stage-specific. For
119 example, sexually transmitted infections may be prevalent in a population, but be restricted to
120 adults that engage in sexual activity (Rhule et al. 2010). Earlier in life, parental effects arising from
121 interactions of offspring with parents (and/or helpers in cooperative systems) can influence both
122 exposure and infection risk. In birds and mammals, for instance, immunocompetence in early life can
123 depend entirely on the transfer of maternal antibodies (Grindstaff et al. 2003; Grindstaff et al. 2006).
124 More generally, environmental effects on maternal state (e.g. food availability) will influence
125 investment in care, with downstream consequences for offspring immune development and disease
126 resistance (Karell et al. 2008; Garbutt et al. 2014). A common finding across other trait types (e.g.
127 growth, morphology, life history; Wilson et al. 2005a; Houde et al., 2015; Falica et al. 2017) is that
128 the importance of maternal effects as a source of phenotypic variance declines with (offspring) age
129 (while h^2 often shows the opposite pattern). However, this does not mean that adult phenotypes
130 should be assumed to be free from early life influences (see e.g., Clark et al. 2014) and 'silver spoon'
131 effects on later health are certainly well documented in the context of non-communicable diseases
132 (Gluckman and Hanson 2004).

133 Here, we examine the relative importance of genetic and environmental (including social
134 and maternal) sources of variation in *Mycobacterium bovis* (the causative agent of bovine
135 tuberculosis; bTB) infection status in a wild population of European badgers (*Meles meles*). Badgers
136 are an important wildlife reservoir for bTB in the United Kingdom, where the disease in livestock is a
137 longstanding socioeconomic burden on the industry and taxpayers (Defra, 2014). The primary route
138 of infection in badgers is thought to be inhalation of infectious aerosol, occurring during close
139 contact with infectious individuals (Gallagher and Clifton-Hadley 2000). Some of the drivers of
140 disease in badgers have been described, such as sexual dimorphism, whereby bTB infection
141 probability, disease progression and mortality risk are all greater in males (Graham et al., 2013;
142 McDonald 2014). Age effects have also been observed (Graham et al., 2013; McDonald et al., 2014;
143 Beirne et al. 2016), while at the population-level, bTB incidence and prevalence exhibit seasonal
144 variation (incidence being highest in spring and prevalence peaking in autumn; Delahay et al. 2013).
145 However, the potential contribution of additive genetic variation has not previously been
146 investigated, not least because badgers live in kin-biased social groups making disentangling genetic
147 from environmental (social) effects challenging.

148 Badgers are facultatively social, forming groups in medium to high density populations but
149 adopting a more solitary lifestyle when living at low density (Roper 2010). At the level of the
150 population, natal philopatry and territorial defence limit mixing of animals amongst social groups,
151 which in turn is expected to reduce inter-group disease transmission (Delahay et al. 2000b), while at
152 the same time being associated with relatively high within-group transmission rates. Social group
153 structure should thus drive spatial clustering of bTB, and high among-group variation in disease
154 status, relative to that found within-groups, has been previously reported (Delahay et al. 2000b).
155 However, genetic data suggest alternative explanations for observed spatial clustering may also have
156 merit. Parentage analyses show that among-group breeding dispersal is limited, leading to greater
157 relatedness within than among groups (Dugdale et al., 2008). Crucially for current purposes though
158 some individuals are known to make permanent moves away from their natal group (Rogers et al.

159 1998) while breeding between adults of different groups also occurs (Annavi et al 2014; Marjamäki
160 et al. 2019). For instance, in this population an estimated 37% of cubs born are sired by an extra-
161 group male (Marjamäki et al. 2019). Recent work has also shown that bTB infection risk for cubs is
162 increased by the presence of closely related infected adults (including but not limited to mothers)
163 within the natal group (Benton et al. 2016). Spatial heterogeneity in host disease status is consistent
164 with within-group (and by extension kin-biased) social interactions impacting infection risk, maternal
165 effects, and/or genetic variation in one or more host defence strategies. These alternative
166 explanations are in no sense mutually exclusive and we also acknowledge that inbreeding
167 depression (IBD) could play a role (e.g. if breeding dispersal and therefore inbreeding differ among
168 groups; Benton et al. 2016). Heterozygosity-fitness correlations have provided some evidence of IBD
169 on *M. bovis* disease progression although this is limited to older (senescent) females (Benton et al.
170 2018)

171 It is therefore clear that *M. bovis* infection status in badgers can be influenced by numerous
172 factors at multiple scales. The long-term life-history and genetic pedigree data from the
173 Woodchester Park study initiated in the 1970s (McDonald et al. 2018) affords a rare opportunity to
174 assess the relative importance of genetic and environmental effects. We adopt a quantitative
175 genetic animal model approach to decompose the variance in bTB infection status into its
176 component parts and examine the relative contributions of genetic and environmental factors. We
177 ask: i) whether variation in host infection status has a detectable additive genetic basis; ii) what are
178 the relative contributions of additive genetic and social (including maternal) effects on the observed
179 variation in host bTB status; and, iii) do the relative contributions of additive genetic and social
180 effects on bTB status vary in relation to host age?

181

182 **Methods**

183 *Study site and sampling*

184 A population of approximately 200–300 wild badgers has been the subject of an ongoing capture-
185 mark-recapture study at Woodchester Park (Gloucestershire) since 1976. The study area is
186 approximately 11 km^2 and consists of a steep-sided wooded valley surrounded by farmland, set in an
187 area where *M. bovis* infection is endemic in cattle and wildlife. Badger dens (setts) in the study area
188 have been the focus of trapping operations up to four times a year. During each quarterly 'trap-up',
189 badgers are trapped for two consecutive nights using steel mesh box traps baited with peanuts,
190 (after 4–8 days of pre-baiting). Trapped badgers are anaesthetized (de Leeuw et al. 2004) and their
191 capture location, sex and age class (cub, yearling, adult) recorded. Biological samples are collected to
192 allow determination of *M. bovis* infection status and to provide a DNA source for microsatellite
193 genotyping (full details presented below). After a recovery period, all badgers are released at the
194 point of capture. Social group boundaries are also determined for each year of the study by bait
195 marking (Delahay et al. 2000a). Further details on determination of group membership are discussed
196 in Marjamäki et al. (2019) and references therein.

197 Overall, the mark-recapture dataset used here contained 14846 observations of *M. bovis*
198 infection status on 2945 individual badgers captured between 1976 and 2014. For individuals first
199 caught as cubs or yearlings (readily identifiable from size, pelage and toothwear; Delahay et al. 2013)
200 age at subsequent captures is known. Unsurprisingly the age distribution is highly skewed (Figure 1);
201 cubs, yearling and adults (i.e. age ≥ 2) account for 31.8%, 24.4% and 43.8% of observations,
202 respectively. Among known-age adult captures the modal age is 2 years (which accounts for 32.9%
203 of adult observations) and the mean is 4.06 (SE 0.03) years. At all ages the capture records are
204 numerically dominated by putative uninfected animals (based on a recorded infection status score of
205 zero; explained in full below). The data included 398 individuals first captured as adults for which
206 ages were unknown. However, since capture records for individuals span multiple years, they still
207 contain valuable information about within-individual changes with advancing age. In order to retain
208 these individuals for analysis we elected to assume that age=2 years at their first capture. This is

209 both the most likely true age (based on the distribution of known age individuals) and also
210 represents the minimum possible age (as cubs and yearlings are readily distinguished).
211
212 *Microsatellite genotyping and parentage analysis*
213 Guard hairs taken at capture were used for DNA extraction, allowing microsatellite genotyping and
214 parentage analysis. Full details are described in Marjamäki et al. (2019). Briefly, DNA was extracted
215 from hair samples using either the protocol outlined in Carpenter et al. (2005), or an ammonium
216 acetate extraction method (Richardson et al. 2001). We used a minimum of five hair follicles with
217 visible roots per individual for extraction. Individuals were genotyped using a minimum of 16
218 (Carpenter et al. 2005) and maximum of 22 fluorescently labelled autosomal microsatellite markers.
219 We used a 2 µl Qiagen Multiplex PCR reaction (Qiagen Inc., Valencia, USA), before separation of the
220 amplicons on an ABI 3730 DNA Analyzer and genotype scoring using GENEMAPPER 3.7.
221 Microsatellite genotypes and spatial data were then used for Bayesian parentage analysis performed
222 using the R 3.3.0 (R Core Team 2016) package *MasterBayes* 2.54 (Hadfield et al. 2006). Markov
223 chains were run separately for each year (i.e. cub cohort) for 2 million iterations, with a thinning rate
224 of 100 and burn-in period of 500,000. Tuning parameters were specified for each cohort to ensure
225 that the Metropolis–Hastings acceptance rates were within acceptable limits (0.2–0.5; Hadfield
226 2017). The presence of unsampled males (per population) and females (per social group) was also
227 allowed for each cohort. Assignments were accepted and used in downstream analyses when a
228 confidence threshold of 80% was met, resulting in a total of 1175 parentage assignments (579
229 maternities and 596 paternities). A total of 617 cubs were assigned at least one parent (35% of
230 genotyped cubs included in the analyses), and of these, 556 (89%) were assigned both parents.
231 Marjamäki et al. (2019) provides a thorough description of available pedigree information (see also
232 archived data for this paper). The genetic pedigree is far from complete which may have implications
233 for our analyses (as discussed below). We note that, in contrast to comparable long-term avian and

234 mammalian studies, maternal identities cannot be determined by observation in badgers owing to
235 their nocturnal and fossorial habits. Thus, pedigree analysis is especially challenging because
236 maternities must be estimated simultaneously with paternities based on genetic and spatial data in
237 the presence of multiple related candidate mothers and fathers.

238

239 *Infection status*

240 For each captured badger, *M. bovis* infection status is determined from the bacterial culture
241 of a standardised set of clinical samples (as described in Clifton-Hadley et al. 1993), and a serological
242 test for the presence of antibodies to *M. bovis* (Brock Elisa used 1982 to 2006 (Goodger et al., 1994)
243 and BrockTB Stat-Pak test used 2006 to 2014 (Chambers et al., 2008)). Clinical samples of
244 oesophageal and tracheal aspirates, urine and faeces, are collected from all animals, with additional
245 samples collected by swabbing open bite wounds if present. Results of these diagnostic tests are
246 used to assign badgers to one of four bTB infection status categories on an ordinal scale following
247 Graham et al. (2013). Individuals that returned negative results for both the bacterial culture and
248 serological test were classified as test-negative (N) and treated as free of infection. Badgers that
249 tested antibody-positive but had negative culture results were assigned test-positive (P) status,
250 taken to indicate recent exposure to *M. bovis.* Positive test results could also indicate cross-reaction
251 or presence of maternal antibodies (Maas et al., 2013; but see Tomlinson et al, 2012). To account for
252 this possibility, and reduce the false positive rate, we elected to reclassify single test-positive results
253 as N (i.e. test negative) if individuals (i) had one or more subsequent recapture(s) and (ii) all
254 subsequent tests were negative. Badgers that tested positive for the presence of *M. bovis* by
255 bacterial culture were assigned as either one-site (O) or multi-site (M) excretors, based on the
256 number of sampled body sites (i.e. distinct clinical samples) that tested positive at each capture.
257 Although culture has relatively low sensitivity as a diagnostic test, a positive result is a strong

258 indicator of established bTB infection (Drewe et al. 2010). These latter two categories (O, M) are
259 therefore considered to represent more advanced infection states.
260
261 *Quantitative genetic analyses*
262 To model variation in infection status we defined two different response variables. Firstly, we
263 reduced infection status data for each individual to a single binary "lifetime" score ($bTB_{lifetime}$). Thus,
264 each individual has a single observation of either 0 (if they did not test positive for bTB during their
265 entire recorded lifetime) or 1 (if they did). Secondly, we analysed the repeated measures collected
266 on individuals over multiple trapping events, to investigate the possibility that contributions of
267 genetic and/or environmental effects to variance in infection status are age dependent. Based on
268 models of bTB immunopathogenesis in badgers (Mahmood et al., 1987; Lesellier et al., 2008), we
269 assumed the four infection status categories described above can reasonably be ordered to reflect
270 the progression of bTB within a host. We thus converted them to a numerical score (N=0, P=1, O=2,
271 M=3) which we refer to hereafter as $bTB_{capture}$. Each individual thus has a number of $bTB_{capture}$ records
272 equal to its number of captures during the study. We elected to make $bTB_{capture}$ score progressive,
273 whereby values can increase (or remain constant) for an individual but cannot decrease. Both
274 $bTB_{lifetime}$ and $bTB_{capture}$ were analysed in conjunction with pedigree information using 'animal models'
275 (i.e. linear mixed effect models that include a random effect of an individual's additive genetic merit;
276 Wilson et al., 2010) to estimate additive genetic variance (V_A). Variance components attributable to
277 specified environmental effects were also estimated, and fixed effects were included (as specified
278 below) to control for several known sources of variance not directly relevant to the current
279 hypotheses. Note that fixed effect results are not presented or discussed in detail but are shown in
280 full in the supplemental materials.
281

282 *Modelling lifetime bTB status*

283 $bTB_{lifetime}$ was modelled using a Bayesian animal model implemented using the package *MCMCglmm*
284 2.26 (Hadfield 2010) in R 3.6.1 (R Core Team 2019). Sex was included as a fixed effect together with a
285 cubic function of age at last capture. All else being equal, we would expect the probability of
286 $bTB_{lifetime}$= 1 to increase monotonically with observed lifetime (even if risk of infection is not itself
287 age-dependent) but a cubic function was chosen simply to avoid making strong assumptions about
288 the functional form of the relationship. The additive genetic merit, maternal identity, natal group,
289 and birth year were included as random effects. We also included a (natal) group x birth year
290 interaction. All random effects are assumed to be drawn from distributions with zero means, and
291 variances to be estimated of V_A, V_M, V_{NGr}, V_{BY} and V_{NGrxBY}, respectively. Note that 'group' designations
292 are based on sett locations that are consistent across the timeline of the study. Consequently, any
293 variance explained by (natal) group is likely to reflect spatial heterogeneity within the study area. In
294 this model, V_{NGrxBY} serves (albeit imperfectly) to identify sets of individuals that clustered strongly in
295 both space and time (i.e. same cohort and same spatial location). Note that we assumed the natal
296 group is the group where badgers first sampled as a cub or yearling were found. We elected to
297 exclude badgers with missing predictors from this analysis which, in practice meant exclusion of
298 individuals first caught as adults (as they had missing natal group information, even after
299 assumptions about age at last capture). Additionally, several (3) individuals captured only once as
300 cubs with missing sex data were excluded. However, we did include individuals with unknown
301 mothers subject to all other predictors being available. Since the mother is unknown for the majority
302 of individuals this was a necessary compromise. Consequently we ran this model on a data set
303 comprising 2319 badgers of which 606 (23.7%) have $bTB_{lifetime}$ = 1.

304 The Markov chain was run using the "ordinal" family (which uses a probit link for binary
305 data) with residual variance fixed to 1. We used a parameter-expanded priors for random effects as
306 suggested in Hadfield 2019; more specifically parameter-expanded X^2 priors (by specifying V = 1, nu

307 = 1000, alpha.mu = 0, alpha.V = 1) and normally distributed diffuse priors for fixed effects.
308 Convergence of the MCMC chain was checked using Heidelberger and Welch's convergence
309 diagnostic test for stationarity (implemented in the R package *coda 0.19-3*; Plummer et al 2006), and
310 the level of autocorrelation checked to ensure adequate (>1000) effective sample size for each
311 estimated parameter. To enable more intuitive biological interpretation, estimated variance
312 components (conditional on fixed effects) on the latent scale were transformed to the
313 corresponding intra-class correlations values (i.e. including heritability, h^2) on the observed scale.
314 This was done using the functions 'QGparams' and 'QGicc' from the R package *QGglmm 0.7.4* and
315 the model 'binom1.probit' (de Villemereuil et al. 2016).

316

317 *Modelling bTB status with age*

318 We then modelled $bTB_{capture}$ on the observed (0–3) scale using a series of animal models fitted by
319 REML in *ASReml-R* 4 (VSN International). In all models we assume Gaussian residuals, an assumption
320 that is necessarily violated given that the response variable is bounded. While some caution with
321 respect to our statistical inference is thus appropriate, we nonetheless consider this assumption very
322 reasonable as residuals from all models showed unimodal distributions with strong central
323 tendencies. We also note inferences from linear mixed models are relatively robust to even large
324 departures from distributional assumptions (Schielzeth et al 2020). Significance of fixed effects was
325 determined using conditional Wald F-tests, while statistical inference on random effects was by
326 likelihood ratio test (LRT) comparison of the full model to reduced formulations in which the tested
327 random effect was omitted. Twice the difference in log-likelihood between the full and reduced
328 models was assumed to have a χ^2 distribution. Following Visscher (2006), we assumed the test
329 statistic to be asymptotically distributed as an equal mix of χ^2_0 and χ^2_1 (denoted as $\chi^2_{0,1}$) when testing
330 a single variance component.

331 We sought to estimate age-specific quantitative genetic parameters for $bTB_{capture}$ for two
332 reasons. First, we wanted to determine if the relative contributions of genetic and environmental
333 effects to variance change with age. Second, since $bTB_{capture}$ can increase (but not decrease) across
334 observations within individuals we expect among-individual variance (partitioned as additive genetic
335 and/or permanent environmental variance) to increase with age (at least initially). Variance
336 compounding is thus expected from trait definition as effects on the phenotype of any individual at
337 age *x* will have 'permanent' effects (i.e. impact phenotype at all ages > *x*). We wanted our models to
338 accommodate this feature of the data, and to ensure that compounding of environmental variance
339 could not cause upward bias in the estimate of additive genetic variance at later ages. In principle,
340 an initial increase in among individual variance with age would be followed by a decrease among the
341 oldest badgers if infection and disease progression were inevitable consequences of sufficient
342 longevity. In this scenario badgers living long enough would eventually all converge on a single
343 phenotype ($bTB_{capture}$=3). However, this does not happen here and across all ages observed records
344 are strongly dominated by captures of putatively uninfected badgers (i.e. $bTB_{capture}$= 0; Figure 1). For
345 instance, in cubs, yearlings, all adults (age ≥ 2) and 'older' adults (age ≥ 4) the proportions of capture
346 records with $bTB_{capture}$ = 0 are 88.3%, 79.6%, 76.2 %, and 75.1%, respectively.

347 We adopted two complementary strategies to incorporate this age-specificity of variance
348 components. The first was to analyse stage specific data subsets corresponding to cubs (age=0;
349 $n_{badgers}$= 2407, $n_{observations}$=4723), yearlings (age=1; $n_{badgers}$=1521, $n_{observations}$= 3620), and adults (age≥2;
350 $n_{badgers}$=1483, $n_{observations}$=6503). This allowed us to avoid assuming homogeneity of variance
351 components across age categories (though the assumption of homogeneity with increasing adult age
352 remains). We fitted an animal model to each data subset, including fixed effects of *sex*, *season*
353 (spring = Mar–May, summer= Jun–Aug, autumn= Sep–Nov, winter = Dec–Feb), and for adults only
354 we included a cubic function of *age*. Random effects included the *additive genetic merit*, a
355 *permanent environment* effect (to account for non-genetic sources of repeatable differences),
356 *maternal identity*, *year* (of observation), *group* (defined by spatial location of home sett), and a

357 factor defined by the *group-by-year* interaction. The latter serves here as a proxy for social
358 environment as it defines the set of individuals interacting most closely in time and space (i.e. within
359 a year of observation at a spatial location). Random effects are assumed to be normally distributed
360 with means of zero and variances (V_A, V_{PE}, V_M, V_{Gr}, V_Y and V_{GrxY}, respectively) to be estimated. For
361 each stage-specific model, we calculated phenotypic variance as the sum of the estimated
362 components and used this to calculate intra-class correlations (conditional on fixed effects). We also
363 tested the significance of V_A, V_M, V_{Gr}, V_Y and V_{GrxY} by LRT. Note we do not test V_{PE} separately or
364 provide an overall test for among-individual variance (V_A+V_{PE}) as its presence is inevitable given the
365 progressive definition of $bTB_{capture}$.

366 Our second strategy for dealing with age-specificity was to analyse the full $bTB_{capture}$ data set
367 using a random regression animal model. Specifically, we included random slopes on age (as well as
368 random intercepts) for the additive and permanent environment effects that combine to determine
369 among-individual variance. Other fixed and random effects were specified as described above for
370 the models applied to data subsets. Though this method is widely used to characterise (genetic)
371 variation in reaction norm slopes (interpretable as ageing or plasticity, depending on the x-axis),
372 here the rationale is to fit a model that can accommodate the expected compounding of among-
373 individual variance with age. The random regression model yields estimates of genetic variances in
374 random intercepts and slopes (and the slope-intercept genetic correlation) that can be projected to
375 obtain a 'character state' estimate of the genetic variance-covariance matrix (**G**) among age-specific
376 $bTB_{capture}$ traits (see e.g. Roff and Wilson 2014 for equations and a didactic treatment of this
377 strategy). Permanent environment effects are then treated analogously. In practice, we first fitted
378 the model using slopes on a rescaled version of age; we subtracted 2 so that 'zero' on the new scale
379 corresponds to 2 year old badgers (the modal age class of adults). With this scaling of age, additive
380 genetic and permanent environment intercept variances represent V_A and V_{PE} respectively in 2 year
381 olds (the model class of adults). We then projected the estimated covariance functions to derive
382 corresponding estimates of V_A and V_{PE} at actual ages 0 (cubs), 1 (yearlings), and 4 (the approximate

383 mean age of adult observations in the data) which were used to derive age-specific ICC estimates.

384 Note that while the model assumes that the variance components, except V_A and V_{PE}, are

385 homogeneous, all ICCs are expected to show age-sensitivity (as changes in V_A and/or V_{PE} will alter V_P).

386

387 **Results**

388 *Analysis of $bTB_{lifetime}$*

389 Diagnostics on initial MCMCglmm runs suggested poor chain mixing and high levels of

390 autocorrelation across consecutive saved samples of many model parameters. Although this was not

391 readily resolved by adjusting run parameters, the estimated variance components were highly

392 consistent across three runs, all based on a chain length of 3000000 with a burn in of 10000 and

393 thinning interval of 100 (resulting in 29900 samples in the posterior). We present results based on a

394 single one of these chains. Diagnostic plots and tests for this model fit are presented in

395 Supplemental Appendix 1. Autocorrelation levels between saved samples remained high but the use

396 of such long chain allowed us to obtain reasonably large effective sample sizes (>1500 across all

397 variance components; Supplemental appendix 1) and tests for stationarity were passed for all fixed

398 effects and variance components. Posterior distributions (on the latent probit scale) were clearly

399 distinct from zero for V_{NGr}, V_{BY} and V_{NGrxBY} but not for additive and maternal variance components

400 (Supplemental appendix 1). For V_A the posterior shows a local peak that is distinct from zero but also

401 has high density close to zero. For V_M there is no non-zero peak in the posterior distribution visible.

402 Posterior means of variance components on the probit scale used to generate point

403 estimates ICC on the observed scale (Table 1) indicated that additive genetic effects (h^2 = 0.092) and

404 birth year (ICC=0.110) and natal group x birth year effects (ICC =0.087) explain similar amounts of

405 variance in $bTB_{lifetime}$ while maternal effects were (effectively) absent (posterior mean ICC of <1%).

406 Fixed effect estimates from this model are not directly relevant to hypotheses being tested but for

407 completeness are shown in Supplemental appendix 2 (together with estimated variance components
408 on the probit scale).
409

410 *Repeated measures models of age specific $bTB_{capture}$*

411 Analysis of $bTB_{capture}$ provided evidence for changes in the relative importance of genetic and
412 environmental influences on phenotype with age. Analyses of age specific data subsets provided
413 statistical support for the presence of maternal, year, group and year x group effects in cubs,
414 yearlings and adults (all LRT yielding P<0.05; Table 2). In contrast, statistically significant additive
415 genetic variance was only found in the adult (2+ years) data subset. Estimated heritability (SE) was
416 low in cubs (h^2<0.001 (0.053)) and undetectable in yearlings (with V_A bound to zero in the model fit),
417 but somewhat higher and statistically significant in adults (h^2=0.119 (0.062), $\chi^2_{0,1}$= 3.75, P=0.026).
418 Group effects are low with the highest ICC being just 2.4% (in cubs) suggesting little (fixed) spatial
419 heterogeneity in bTB risk. However, ICC for year and group x year effects were somewhat higher
420 (Table 2). Notably in cubs and yearlings these two components together explain approximately 20%
421 of observed variance in $bTB_{capture.}$ Thus, there is temporal (among year) variation, some of which is
422 general to the study area, and some of which is specific to particular groups. The estimates of the
423 variance components used to calculate ICC are presented in Supplemental appendix 3. As in the
424 analysis of $bTB_{lifetime}$ we note that fixed effects are being used to control for 'nuisance' sources of
425 variance here rather to address any specific hypotheses. Nevertheless, for completeness, fixed
426 effects estimates and the corresponding statistical inference are shown in Supplemental appendix 4
427 for all REML models.

428 As expected, when modelling all ages simultaneously, the inclusion of random slopes on age
429 for additive and permanent environment effect greatly improved the model (LRT comparison to the
430 equivalent random intercept only model; χ^2_4=4491, P<0.001). The random regression model
431 indicated significant contributions of V_M, V_{Gr}, V_Y and V_{GrxY} to variance in $bTB_{capture}$ (Table 2), while

432 support for genetic variance was slightly equivocal. This is because while the presence of genetic
433 variance (modelled as a first order covariance function of age) was marginally non-significant (LRT
434 χ^2_3=7.59, P=0.055), we also expect that use of 3 DF in the likelihood ratio test will be rather
435 conservative here (since boundary constraints strictly apply to both slope and intercept variances for
436 which negative values are precluded). Furthermore, the REML estimate of the slope-intercept
437 genetic correlation was fixed to +1 to keep the genetic covariance structure within allowable
438 parameter space (i.e. variances ≥ 0, -1≤ correlation ≤ +1). The perfect slope-intercept correlation
439 means that projected to a character state view, estimated genetic correlations between age-specific
440 $bTB_{capture}$ traits are strongly positive (and effectively +1 among all ages >1) while there is a strong
441 pattern of increasing V_A with age (Supplemental appendix 3). For permanent environment effects,
442 the equivalent projection reveals a pattern of increase from cubs onwards (as expected given
443 inevitable accumulation of among-individual variance). Estimates of r_{PE} are strongly positive
444 (effectively +1) between observation ages 1, 2 and 4, but are less between these ages and $bTB_{capture}$
445 at age 0 (with a minimum of r_{PE} = 0.38 between 0 and 4; Supplemental appendix 3).

446 Scaling the variance components estimated with the random regression models to ICC
447 reveals broadly similar patterns to those obtained by age specific analysis (Figure 2). Specifically,
448 both approaches to modelling $bTB_{capture}$ indicate that heritability is very low in early life while social
449 environment effects (maternal and group x year) are important in the youngest badgers. Conversely,
450 heritable variation is present in adults. Under the random regression model, estimated heritability
451 (SE) goes from zero in cubs, to 0.134 (0.580) at the modal adult age of 2 years and increases to 0.206
452 (0.078) at 4 years. Some differences between the results of the two modelling strategies are also
453 apparent. Most notably the age-specific subset analysis actually indicates increasing relative
454 importance of maternal effects with age, while m^2 (the ICC corresponding to maternal variance)
455 declines under the random regression model (from m^2=0.21 at age 0 (cubs) to 0.04 at age 4).
456 However, interpretation is slightly nuanced here, as maternal influences at early ages will tend to
457 contribute to fixed-among individual differences (and so be partitioned as V_{PE}) at later ages under

458 the random regression formulation. This will not happen to the same extent in models of yearling
459 and adult data subsets. The same effect may also explain the slightly lower estimates of the group x
460 year ICC under the random regression model.

461

462 **Discussion**

463 Here we examined *M. bovis* infection status in a naturally infected population of European badgers,
464 to ask whether, and to what extent, genetic and environmental (including social and maternal)
465 effects contribute to variation among individuals in disease risk and progression. Using two
466 measures of infection status ($bTB_{capture}$, a progressive measure of disease at each capture event and
467 $bTB_{lifetime}$, a binary lifetime infection score), animal model analyses support the presence of a
468 relatively small, but non-zero, heritable component of infection status. Analyses of $bTB_{capture}$ shows
469 that heritability is very low in cubs and yearlings but higher in adults. Temporal (among-year)
470 variation is present in the population as a whole, as expected, while group identity effects
471 (interpretable as temporally fixed spatial heterogeneity) are detectable, but do not explain much
472 variance in either $bTB_{lifetime}$ or $bTB_{capture}$. In contrast, group x year effects are important in all analyses
473 and are most parsimoniously interpreted as social effects, reflecting shared infection risk of animals
474 closely associating in space and time. The importance of maternal identity effects – both in relative
475 and absolute terms is less clearly resolved by our analyses (discussed further below).

476

477 *Genetic variation in bTB status and progression*

478 Variation in the lifetime risk of infection and in progression of bTB (as measured by $bTB_{capture}$ across
479 repeated measures) both have a partial genetic basis. The heritability of the former is estimated at
480 0.092, while our models suggest h^2 for $bTB_{capture}$ is very low among young animals but increases with
481 observation age (e.g. to 0.134 in two year old adults, based on the random regression model). Most

482 variation in bTB infection status therefore arises from environmental effects (broadly defined) rather
483 than genetic factors. This is not surprising and mirrors findings in cattle where estimates of h^2 for
484 bTB resistance range from 0.06 to 0.18 (Allen et al. 2010). Interestingly, using an experimental
485 infection approach, h^2 of bTB resistance to *M. bovis* was estimated at 0.48 in a population of farmed
486 red deer (*Cervus elaphus*; Mackintosh et al., 2000), a species that, in some ecological contexts, is also
487 thought to act as an important wildlife reservoir for this disease (Vicente et al. 2006; Delahay et al.,
488 2007). This much higher estimate was obtained from parent-offspring regression (a method which
489 can be more prone to upward bias from common environment effects), but could also reflect the
490 experimental infection design used. Specifically, we stress that neither $bTB_{lifetime}$ nor $bTB_{capture}$ provide
491 a measure of resistance alone. Rather these phenotypes will be outcomes of multiple contributing
492 traits and processes (e.g., behavioural exposure risk, resistance, tolerance) that may themselves
493 differ in their extent of genetic control.

494 Since there are few heritability estimates for disease traits in wild vertebrate populations a
495 consensus on the importance of standing genetic variation is yet to emerge. A number of studies
496 have found additive genetic variation for host defence traits, including resistance to strongyle
497 nematodes in feral sheep (h^2= 0.13 SE 0.04) inferred from nematode-specific antibody titers;
498 Hayward et al., 2014a) and both resistance (inclusive heritability 0.176 CI 0.072-0.322) and tolerance
499 to copepod parasites in a freshwater cyprinid fish (Mazé-Guilmo al. 2014). Conversely, experimental
500 studies failed to detect any influence of host genotype on cell-mediated immune responses in house
501 martins *Delichon urbica* (Christe et al. 2000) and house wrens *Troglodytes aedon* (Sakaluk et al.
502 2014). Interestingly, across three populations of tree swallow *Tachycineta bicolor*, Ardia and Rice
503 (2006) found no heritable variation for immune function in two populations, while an estimate of h^2
504 =0.42 was reported for the third.

505 While it seems quite possible that generalisations about the contribution of genetic factors
506 to variation in disease outcomes will be difficult (even among populations of the same species), our

507 analyses of $bTB_{capture}$ do highlight the importance of considering age-specificity. At least initially, an
508 increase in phenotypic variance with age is an inevitable consequence of trait definition and
509 measurement here; the pattern of increasing h^2 with age thus arises because V_A goes up
510 proportionately faster than the total phenotypic variance V_P. Importantly, age-specificity of
511 heritability does not however imply that underlying risk factors themselves (whether genetic or
512 otherwise) must have age specific action. This is because small (but age-invariant) differences in
513 infection risk will generate more and more variance in infection status as time available to acquire
514 infection increases. So, while age- (or stage-) specific gene action could contribute to the pattern of
515 increasing h^2, it is not required to explain the pattern. Regardless, the main implication of low trait
516 heritability in cubs and yearlings is that any early life natural selection acting through juvenile
517 viability has very limited scope to affect an evolutionary response. Conversely, a response is
518 predicted if selection against bTB infection acts through adult fitness components. Though we do not
519 have formal estimates of selection, two recent studies have both failed to detect costs of infection
520 on reproductive success in this badger population (Tomlinson et al. 2013; McDonald et al. 2016).
521 However, adult badgers (particularly males) with advanced infection states do show increased
522 mortality rates (Graham et al. 2013; McDonald et al. 2016).

523 An important caveat in interpreting our heritability estimates is that the serological tests and
524 bacterial culture used to define phenotypes have relatively low levels of sensitivity. This means that
525 an unknown, but certainly non-zero, proportion of truly infected animals will not have been correctly
526 phenotyped. For example, intermittent excretion and latent infection characteristic of *M. bovis*
527 infection (Clifton-Hadley et al. 1993; Gallagher et al. 1998) limit the sensitivity of bacterial culture
528 whilst antibody tests may fail to detect infection either due to the absence or low concentrations of
529 antibody produced or inclusion of an inappropriate antigenic target. Assuming that propensity to
530 test negative when truly infected is not itself a heritable trait, this form of measurement error
531 should be partitioned into generic residual and (for $bTB_{capture}$) permanent environment variances and
532 so may contribute to relatively low heritabilities (as well reducing ICC for all non-generic

533 environmental effects). If so, improved confidence in assigning individual infection status (e.g. use of
534 probabilistic approaches to incorporate full test histories, Buzdugan et al., 2016) may be needed to
535 gain greater resolution on genetic factors predisposing to disease.

536

537 *Social effects tend explain more variation than genetic factors*

538 In total, social environment effects, estimated as the sum of group x year and maternal variances
539 appeared to explain more variation in $bTB_{capture}$ than genetic factors. This is certainly the case for
540 cubs and yearlings and was also true for the estimates derived from analysis of the adult data only.
541 Under the random regression model, genetic and social effects account for similar proportions of
542 variance at age 2 years, while genetic effects are predicted to dominate at 4 years. However, as
543 noted earlier, under this modelling approach where only V_A and V_{PE} were allowed to vary with age
544 we expect 'permanent' non-genetic effects from early life (that may include, for instance maternal
545 influences) to accumulate in V_{PE} with age, somewhat complicating interpretation. In principle it is
546 possible to allow age-dependence of all random effects within the random regression model, but
547 initial exploration of models with additional random slopes led to instability, convergence problems
548 and implausible levels of predicted phenotypic variance in adults.

549 Spatial clustering of infection at the social group level has been reported previously in
550 badger populations, with some groups in the Woodchester Park population remaining test-negative
551 for long periods (Delahay et al., 2000b; Vicente et al. 2007). As (natal) group identity coincides with
552 main sett location in the study area, whether this observation can be explained by spatial
553 heterogeneity in the habitat rather than social effects *per se* has remained unclear. However, our
554 finding that most group effects were year-specific (i.e. partitioned as group by year variance)
555 strongly suggests a social origin (since group composition varies on a year-to-year basis whereas
556 location is fixed in time). It also corroborates previous studies that suggest the importance of social
557 processes (but which did not control for potentially confounding genetic or maternal effects). For

558 instance, social network analyses have revealed evidence suggesting a positive association between
559 bTB infection and levels of extra-group contact (Weber et al. 2013; Silk et al. 2018). Extra-group
560 contacts may include temporary excursions for breeding purposes, the rates of which have recently
561 been found to vary among social groups (Marjamäki et al. 2019). Seasonal variation in bTB incidence
562 (accounted for in our models by the fixed effect structure) has also been shown to correlate with
563 peaks of within-group social contact (Silk et al., 2017), although indirect transmission (e.g. via
564 environmental contamination of communal latrines and setts) may also occur (Courtenay et al.
565 2006; Drewe et al. 2010).

566 The contribution of maternal (identity) effects to bTB risk and progression in Woodchester
567 Park badgers is not fully resolved by our study. In particular, the Bayesian analysis of $bTB_{lifetime}$
568 provided no evidence of among-mother variance in offspring lifetime risk, while maternal identity
569 was a statistically significant predictor of $bTB_{capture}$ in all REML models fitted. Based on the results in
570 their entirety, we cautiously conclude that maternal effects exert at least some influence on bTB
571 status among badgers in the present study. Assuming so, this adds further support to the view that
572 early-life environments impact bTB infection risk (Tomlinson et al. 2013). It also suggests the
573 reported positive association between cub infection and presence of infected relatives (Delahay et
574 al., 2000; Benton et al. 2016) could be driven by a combination of both maternal and additive
575 genetic effects. Though widely observed for life-history, reproductive and growth traits, maternal
576 effects on disease risk have been less well documented in other wild vertebrates (but see e.g., Hall &
577 Ebert, 2012; Seppälä & Langeloh, 2016). However, in Soay sheep maternal effects on offspring
578 parasite load appear, at least in part, to occur through maternal age and parasite load (Hayward et
579 al., 2010). However, in that population and in some domestic sheep quantitative genetic analyses
580 also support a contribution of maternal effects to nematode resistance (Coltman et al., 2001; Stear
581 et al., 2001) and to helminth-specific immune responses in lambs (Sparks et al. 2019). Our data are
582 not informative for specific mechanisms, although similarity among maternal siblings (over and
583 above that attributable to additive genetic and social group effects) could arise from maternal

584 provisioning of antibodies, variation in maternal infection status, or differential contact time with
585 cubs. Second order mechanisms are also possible, for instance if maternally influenced nutritional
586 status has consequences for cub immune responses.

587 Whether or not the magnitude of maternal effect contributions to variation in bTB status
588 declines with age in Woodchester Park badgers is unclear. On the one hand, maternal effects on
589 $bTB_{lifetime}$ were absent and random regression model for $bTB_{capture}$ yielded only a small maternal ICC
590 estimate (5%) in adults by age 4. On the other, this second result may be a consequence of model
591 specification (with early acting maternal effects having permanent effects that are partitioned to V_{PE}
592 rather than V_M in late life) while the highest maternal ICC estimated was for $bTB_{capture}$ in the adults-
593 only data subset (18%). We suspect this lack of consistency arises from a data structure that is far
594 from ideal for partitioning additive genetic from maternal (and common environment) effects. In
595 particular the pedigree is very incomplete and while some females contribute multiple offspring (to
596 a maximum of 11), the mean number of offspring among the 537 known mothers is just 1.07. For
597 this reason, we also elected not to attempt further decomposition of the estimated maternal
598 variances into maternal genetic and environmental components (e.g. following Wilson et al. 2005b,
599 McAdam et al. 2014).

600

601 *Caveats arising from the consideration of genotype-(social) environment correlation*

602 As noted earlier, the preponderance of within-group paternities in the Woodchester Park population
603 (63% within-group vs 37% extra-group paternity, Marjamäki et al. 2019) means that genetic
604 relatedness is, on average, greater for pairs of individuals that share a (natal) social group
605 environment than for pairs that do not. Similarly, siblings necessarily share a maternal environment.
606 The population is thus characterised by a 'genotype-environment correlation' that cannot easily be
607 disentangled. Since experimental approaches (e.g. cross-fostering; Kruuk & Hadfield, 2007) are not
608 appropriate in this or similar systems, we have taken the conservative approach (with respect to

609 estimation of h^2) of simultaneously modelling additive genetic, maternal and social group (including
610 group x year) effects. Failure to model common environment effects, including mothers and shared
611 habitat use by relatives is a well-known potential source of upward bias in h^2 estimates (e.g. Wilson
612 et al. 2005b; Stopher et al., 2012; Regan et al. 2015). However, accurate separation of correlated
613 genetic and environmental effects necessarily depends on data structure and quality. Here
614 incomplete parentage data is likely to have produced errors in the pedigree (e.g. unrecognised
615 relatedness among true siblings) even in the unlikely event that all parentage assignments made are
616 correct. Although pedigree error will usually downwardly bias the estimation of h^2 (Morrissey et al.
617 2007) the consequences are not so readily predicted here, given the kin-biased social group
618 structure, and the fact that maternal and paternal identities are both similarly uncertain.

619

620 **Conclusions**

621 The long-term study of the Woodchester Park badger population provides a unique and valuable
622 opportunity to investigate the factors driving among-individual variation in *M. bovis* infection status.
623 We have found that genetic factors play a small but significant role in structuring variation in
624 infection status, particularly in older (adult) badgers. However, it is clear that social influences arising
625 from interactions among animals clustered in space (group) and time (year) and from maternal
626 effects are also important. Genetic and social effects may influence observed bTB infection status
627 through multiple pathways, including via infection risk (e.g. through behavioural traits), resistance,
628 and/or ability to limit damage caused (tolerance). Though not mutually exclusive, resistance and
629 tolerance in particular are predicted to have very different consequences for parasite fitness; by
630 limiting parasite growth, resistance will negatively impact parasite fitness, while tolerance can, in
631 fact, promote parasite fitness by increasing the period over which transmission might occur. Given
632 the implications of individual variation in infectiousness for the long-term persistence of parasites
633 (Kramer-Schadt et al. 2009) and microevolutionary dynamics of both host and parasite (Best et al.

634 2008), determining whether genetic and environmental determinants of *M. bovis* infection status
635 and the severity and progression of bTB operate through resistance, tolerance, or both should be a
636 useful – if empirically challenging – priority.

637

638 **Data accessibility** Data used in this study are publicly archived in Open Research Exeter (ORE) at
639 https://doi.org/10.24378/exe.3104

640

641 **References**

642 Akaike, H. (1974). A new look at the statistical model identification. *IEEE Transactions on Automatic*
643 *Control*, 19, 716–723.
644 Allen, A. R., Minozzi, G., Glass, E. J., Skuce, R. a, McDowell, S. W. J., Woolliams, J. A, & Bishop, S. C.
645 (2010). Bovine tuberculosis: the genetic basis of host susceptibility. *Proceedings of the Royal*
646 *Society*, 277(1695), 2737–45.
647 Altizer, S., Dobson, A., Hosseini, P., Hudson, P., Pascual, M., & Rohani, P. (2006). Seasonality and the
648 dynamics of infectious diseases. *Ecology Letters*, 9(4), 467–484.
649 Annavi, G., Newman, C., Buesching, C.D., Macdonald, D.W., Burke, T., & Dugdale, H.L. (2014)
650 Heterozygosity–fitness correlations in a wild mammal population: accounting for parental
651 and environmental effects. *Ecology and Evolution*, 4, 2594– 2609
652 Ardia, D. R., & Rice, E. B. (2006). Variation in heritability of immune function in the tree swallow.
653 *Evolutionary Ecology*, 20(5), 491–500.
654 Barber, I., & Dingemanse, N. J. (2010). Parasitism and the evolutionary ecology of animal personality.
655 *Philosophical Transactions of the Royal Society B: Biological Sciences*, 365(1560), 4077–4088.
656 Behringer, D. C, Butler, M. J., Shields, J. D. (2006). Avoidance of disease by social lobsters. *Nature*,
657 441, 421.

658 Beirne, C., Waring, L., McDonald, R. A., Delahay, R., & Young, A. (2016). Age-related declines in
659 immune response in a wild mammal are unrelated to immune cell telomere length.
660 *Proceedings of the Royal Society B: Biological Sciences*, 283(1825), 20152949.
661 Benton, C. H., Delahay, R. J., Robertson, A., McDonald, R.A., Wilson, A. J., Burke, T. A., & Hodgson, D.
662 (2016). Blood thicker than water: kinship, disease prevalence and group size drive divergent
663 patterns of infection risk in a social mammal. *Proceedings of the Royal Society B*, 283,
664 20160798.
665 Benton, C. H., Delahay, R. J., Smith, F. A. P., Robertson, A., McDonald, R. A., Young A. J., Burke, T. A.,
666 & Hodgson, D. (2018). Inbreeding intensifies sex- and age-dependent disease in a wild
667 mammal. *Journal of Animal Ecol*ogy, 87, 1500– 1511.
668 Best, A., White, A., & Boots, M. (2008). Maintenance of host variation in tolerance to pathogens and
669 parasites. *Proceedings of the National Academy of Sciences of the United States of America*,
670 105(52), 20786–20791.
671 Blanchet, S., Rey, O., & Loot, G. (2010). Evidence for host variation in parasite tolerance in a wild fish
672 population. *Evolutionary Ecology*, 24, 1129–1139.
673 Bonneaud, C., Sinsheimer, J. S., Richard, M., Chastel, O., & Sorci, G. (2009). Mhc polymorphisms fail
674 to explain the heritability of phytohaemagglutinin-induced skin swelling in a wild passerine.
675 *Biology Letters*, 5(6), 784–787.
676 Breitling, L. P., Wilson, A. J., Raiko, A., Lagog, M., Siba, P., Shaw, M., & Quinnell, R. J. (2008).
677 Heritability of human hookworm infection in Papua New Guinea. *Parasitology*, 135, 1407–
678 1415.
679 Carpenter, P. J., Pope, L. C., Greig, C., Dawson, D. A, Rogers, L. M., Erven, K., Wilson, G. J., Delahay, R.
680 J., Cheeseman, C.L & Burke, T. (2005). Mating system of the Eurasian badger*, Meles meles*, in
681 a high density population. *Molecular Ecology*, 14(1), 273–84.
682 Carter, S. P., Delahay, R. J., Smith, G. C., Macdonald, D. W., Riordan, P., Etherington, T. R., Pimley, E.
683 R., Walker, N. J., & Cheeseman, C. L. (2007). Culling-induced social perturbation in Eurasian

684 badgers *Meles meles* and the management of TB in cattle: an analysis of a critical problem in
685 applied ecology. *Proceedings of the Royal Society B*, 274, 2769–2777.
686 Chambers, M. A., Crawshaw, T., Waterhouse, S., Delahay, R., Hewinson, R. G., & Lyashchenko, K. P.
687 (2008). Validation of the BrockTB Stat-Pak Assay for Detection of Tuberculosis in Eurasian
688 Badgers (*Meles meles*) and Influence of Disease Severity on Diagnostic Accuracy. *Journal of*
689 *Clinical Microbiology*, 46(4), 1498–1500.
690 Christe, P., Møller, A. P., Saino, N., & De Lope, F. (2000). Genetic and environmental components of
691 phenotypic variation in immune response and body size of a colonial bird, *Delichon urbica*
692 (the house martin). *Heredity*, 85(1), 75–83.
693 Clark, E. S., Pompini, M., Marques da Cunha, L., & Wedekind, C. (2014). Maternal and paternal
694 contributions to pathogen resistance dependent on development stage in a whitefish
695 (*Salmonidae*). *Functional Ecology*, 28(3), 714–723.
696 Clifton-Hadley, R. S., Wilesmith, J. W., Stuart, F. A. (1993). *Mycobacterium bovis* in the European
697 Badger (*Meles meles*): Epidemiological Findings in Tuberculous Badgers from a Naturally
698 Infected Population. *Epidemiology and Infection*, 111(1), 9–19.
699 Coltman DW, Pilkington J, Kruuk LEB, Wilson K, Pemberton JM (2001). Positive genetic correlation
700 between parasite resistance and body size in a free-living ungulate population. *Evolution*, 55,
701 2116–2125.
702 DEFRA 2014, Department for Food and Rural Affairs - The Strategy for achieving Officially Bovine
703 Tuberculosis Free status for England, April 2014. Available 21/09/2015:
704 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/300447/p
705 b14088-bovine-tb-strategy-140328.pdf
706 Delahay, R. J., Langton, S., Smith, G. C., Clifton-Hadley, R. S., & Cheeseman, C. L. (2000). The spatio-
707 temporal distribution of *Mycobacterium bovis* (bovine tuberculosis) infection in a high-
708 density badger population. *Journal of Animal Ecology*, 69(3), 428–441.

709 Delahay, R. J., Smith, G. C., Barlow, A. M., Walker, N., Harris, A., Clifton-Hadley, R. S., & Cheeseman,
710 C. L. (2007). Bovine tuberculosis infection in wild mammals in the South-West region of
711 England: A survey of prevalence and a semi-quantitative assessment of the relative risks to
712 cattle. *Veterinary Journal*, 173(2), 287–301.
713 Delahay, R. J., Walker, N., Smith, G. S., Wilkinson, D., Clifton-Hadley, R. S., Cheeseman, C. L.,
714 Tomlinson, A. J., & Chambers, M. A. (2013). Long-term temporal trends and estimated
715 transmission rates for *Mycobacterium bovis* infection in an undisturbed high-density badger
716 (*Meles meles*) population. *Epidemiology and Infection*, 141(07), 1445–1456.
717 de Villemereuil P., Schielzeth H., Nakagawa S., & Morrissey M. (2016). General methods for
718 evolutionary quantitative genetic inference from generalised mixed models. *Genetics*,
719 204(3), 1281-1294.
720 Doeschl-Wilson, A. B., Davidson, R., Conington, J., Roughsedge, T., Hutchings, M. V. (2011).
721 Implications of Host Genetic Variation on the Risk and prevalence of infectious diseases
722 transmitted through the environment. *Genetics*, 188(3), 683–693.
723 Drewe, J. A., Tomlinson, A. J., Walker, N. J., & Delahay, R. J. (2010). Diagnostic accuracy and optimal
724 use of three tests for tuberculosis in live badgers. *PLoS ONE*, 5(6).
725 Dugdale, H. L., Macdonald, D. W., Pope, L. C., Johnson, P. J., & Burke, T. (2008). Reproductive skew
726 and relatedness in social groups of European badgers, *Meles meles*. *Molecular Ecology*,
727 17(7), 1815–1827. Falica, B. K., Lehnert, S. J., Pitcher, T. E., Heath, D. D., & Higgs, D. M.
728 (2017). Ontogenetic shifts in genetic and maternal effects on length and survival in Chinook
729 salmon (*Oncorhynchus tshawytscha*). *Aquaculture*, 468, 218–225.
730 Gallagher, J., Monies, R., Gavier-Widen, M., & Rule, B. (1998). Role of infected, non-diseased badgers
731 in the pathogenesis of tuberculosis in the badger. *The Veterinary Record*, 142(26), 710–4.
732 Gallagher J., Clifton-Hadley, R. S. (2020) Tuberculosis in badgers; a review of the disease and its
733 significance for other animals. *Research in Veterinary Science*, 69: 203–217.

734 Garbutt, J. S., Scholefield, J. A., Vale, P. F., & Little, T. J. (2014). Elevated maternal temperature
735 enhances offspring disease resistance in *Daphnia magna*. *Functional Ecology*, 28(2), 424–
736 431.
737 Gluckman, P. D. & Hanson, M. A. (2004). Living with the past: Evolution, development, and patterns
738 of disease. *Science*, 305, 1733-1736.
739 Goodger, J., Nolan, A., Russell, W.P., Dalley, D.J., Thorns, C.J., Stuart, F.A., Croston, P., Newell, D.G.,
740 1994. Serodiagnosis of *Mycobacterium bovis* infection in badgers: development of an
741 indirect ELISA using a 25 kDa antigen. *Veterinary Record* 135, 82–85.
742 Graham, J., Smith, G. C., Delahay, R. J., Bailey, T., McDonald, R. A., & Hodgson, D. (2013). Multi-state
743 modelling reveals sex-dependent transmission, progression and severity of tuberculosis in
744 wild badgers. *Epidemiology and Infection*, 141(7), 1429–36.
745 Grindstaff, J. L., Brodie, E. D., & Ketterson, E. D. (2003). Immune function across generations:
746 integrating mechanism and evolutionary process in maternal antibody transmission.
747 *Proceedings of the Royal Society B: Biological Sciences*, 270(1531), 2309–2319.
748 Grindstaff, J. L., Hasselquist, D., Nilsson, J.-A., Sandell, M., Smith, H. G., & Stjernman, M. (2006).
749 Transgenerational priming of immunity: maternal exposure to a bacterial antigen enhances
750 offspring humoral immunity. *Proceedings of the Royal Society B: Biological Sciences*,
751 273(1600), 2551–2557.
752 Grist, H., Daunt, F., Wanless, S., Nelson, E. J., Harris, M. P., Newell, M., Burthe, S., Reid, J. M. (2014).
753 Site fidelity and individual variation in winter location in partially migratory European shags.
754 *PLoS ONE*, 9(6).
755 Hadfield, J. D. (2010). MCMC Methods for Multi-Response Generalized Linear Mixed Models: The
756 MCMCglmm R Package. *Journal of Statistical Software*, 33(2) 2-22.
757 Hadfield, J. D. (2019). MCMCglmm Course Notes, https://cran.r-
758 project.org/web/packages/MCMCglmm/vignettes/CourseNotes.pdf

759 Hadfield, J. D., Richardson, D. S., & Burke, T. (2006). Towards unbiased parentage assignment:
760 combining genetic, behavioural and spatial data in a Bayesian framework. *Molecular*
761 *Ecology*, 15, 3715–3730.
762 Hadfield, J. D. 2017. MasterBayes: Maximum Likelihood and Markov chain Monte Carlo methods for
763 pedigree reconstruction, analysis and simulation. Available 11/6/2018: https://cran.r-
764 project.org/web/packages/MasterBayes/vignettes/Tutorial.pdf
765 Hall, M. D., & Ebert, D. (2012). Disentangling the influence of parasite genotype, host genotype and
766 maternal environment on different stages of bacterial infection in *Daphnia magna*.
767 *Proceedings of the Royal Society B: Biological Sciences*, 279(May), 3176–3183.
768 Hayward A. D., Pilkington J. G., Pemberton J. M., Kruuk L. E.B. (2010). Maternal effects and early-life
769 performance are associated with parasite resistance across life in free-living Soay sheep.
770 *Parasitology* 137, 1261–1273.
771 Hayward, A. D., Garnier, R., Watt, K. A., Pilkington, J. G., Grenfell, B. T., Matthews, J. B., Pemberton,
772 J. M., Nussey, D. H., & Graham, A. L. (2014a). Heritable, heterogeneous, and costly resistance
773 of sheep against nematodes and potential feedbacks to epidemiological dynamics. *The*
774 *American Naturalist*, S58-S76.
775 Hayward, A. D., Nussey, D. H., Wilson, A. J., Berenos, C., Pilkington, J. G., Watt, K. A., Pemberton, J. A.
776 & Graham, A. L. (2014b). Natural Selection on Individual Variation in Tolerance of
777 Gastrointestinal Nematode Infection. *PLoS Biology*, 12(7), e1001917.
778 Houde, A. L. S., Black, C. A., Wilson, C. C., Pitcher, T. E., Neff, B. D., & Morán, P. (2015). Genetic and
779 maternal effects on juvenile survival and fitness-related traits in three populations of
780 Atlantic salmon. *Canadian Journal of Fisheries and Aquatic Sciences*, 72(5), 751–758.
781 Kappeler, P. M., Cremer, S., Nunn, C. L., & Kappeler, P. M. (2015). Sociality and health: impacts of
782 sociality on disease susceptibility and transmission in animal and human societies.
783 *Philosophical Transactions of the Royal Society B* 370: 20140116.

784 Karell, P., Kontiainen, P., Pietiäinen, H., Siitari, H., & Brommer, J. E. (2008). Maternal effects on
785 offspring Igs and egg size in relation to natural and experimentally improved food supply.
786 *Functional Ecology*, 22(4), 682–690.
787 Keiser, C. N., Rudolf, V. H. W., Sartain, E., Every, E. R., & Saltz, J. B. (2018) Social context alters host
788 behavior and infection risk, *Behavioral Ecology*, 29(4), 869–875.
789 Kim, S. Y., Fargallo, J. A., Vergara, P., & Martínez-Padilla, J. (2013). Multivariate heredity of melanin-
790 based coloration, body mass and immunity. *Heredity*, 111(2), 139–146.
791 Korsten, P., van Overveld, T., Adriaensen, F. & Matthysen, E. (2013). Genetic integration of local
792 dispersal and exploratory behaviour in a wild bird. *Nature Communications*, 4, 1–7.
793 Kramer-Schadt, S., Fernández, N., Eisinger, D., Grimm, V., & Thulke, H.-H. (2009). Individual
794 variations in infectiousness explain long-term disease persistence in wildlife populations.
795 *Oikos*, 118(2), 199–208.
796 Kruuk, L. E. B., & Hadfield, J. D. (2007). How to separate genetic and environmental causes of
797 similarity between relatives. *Journal of Evolutionary Biology*, 20(5), 1890–903.
798 de Leeuw, A. N. S., Forrester, G. J., Spyvee, P. D., Brash, M. G. I., Delahay, R. J. (2004). Experimental
799 comparison of ketamine with a combination of ketamine, butorphanol and medetomidine
800 for general anaesthesia of the Eurasian badger (*Meles meles L.*). *The Veterinary Journal*, 167,
801 186–193.
802 Lesellier, S., Corner, L., Costello, E., Sleeman, P., Lyashchenko, K., Greenwald, R., Esfandiari, J., Singh,
803 M., Hewinson, R. G., Chambers, M., & Gormley, E. (2008). Antigen specific immunological
804 responses of badgers (*Meles meles*) experimentally infected with *Mycobacterium bovis*.
805 *Veterinary Immunology and Immunopathology*, 122(1–2), 35–45.
806 Lough, G., Kyriazakis, I., Bergmann, S., Lengeling, A., & Doeschl-Wilson, A. B. (2015). Health
807 trajectories reveal the dynamic contributions of host genetic resistance and tolerance to
808 infection outcome. *Proceedings of the Royal Society B: Biological Sciences*, 282(1819),
809 20152151–20152151.

810 Maas, M., Michel, A. L., & Rutten, V. P. M. G. (2013). Facts and dilemmas in diagnosis of tuberculosis
811 in wildlife. Comparative Immunology, *Microbiology and Infectious Diseases*, 36(3), 269–85.
812 Mackintosh, C. G., Qureshi, T., Waldrup, K., Labes, R. E., Dodds, K. G., Griffen, J. F. T. (2000). Genetic
813 Resistance to Experimental Infection with *Mycobacterium bovis* in Red Deer (*Cervus*
814 *elaphus*). *Infection and Immunity*, 20(1), 1620–1625
815 Madritch, M. D., & Hunter, M. D. (2002). Phenotypic Diversity Influences Ecosystem Functioning.
816 *Ecology*, 83(8), 2084–2090.
817 Mahmood, K. H., Stanford, J. L., Rook, G. A. W., Stuart, F. A., Pritchard, D. G., & Brewer, J. I. (1987).
818 The immune response in two populations of wild badgers naturally infected with bovine
819 tubercle bacilli. *Tubercle*, 68(2), 119–125.
820 Marjamäki, P.H., Dugdale, H., Dawson, D., McDonald, R.A., Delahay, R.J., Burke, T.A., Wilson,
821 A.J. (2019). Individual variation and the source-sink group dynamics of extra-group paternity
822 in a social mammal. *Behavioura*l Ecology, 30(2), 301-312.
823 Mazé-Guilmo E, Loot G, Páez DJ, Lefévre T, Blanchet S. 2014 Heritable variation in host tolerance and
824 resistance inferred from a wild host–parasite system. *Proceedings of the Royal Society B,*
825 281, 20132567.
826 McAdam, A., Garant, D., Wilson, A. J. (2014). Chapter 6 – *The effect of others' genes: maternal and*
827 *other indirect genetic effects* in *Quantitative Genetics in the Wild*. Oxford University Press
828 McDonald, J. L., Smith, G. C., McDonald, R. A, Delahay, R. J., & Hodgson, D. (2014). Mortality
829 trajectory analysis reveals the drivers of sex-specific epidemiology in natural wildlife-disease
830 interactions. *Proceedings of the Royal Society B: Biological Sciences*, 281, 20140526.
831 McDonald, J. L., Bailey, T., Delahay, R. J., McDonald, R. A., Smith, G. C. & Hodgson D.J. (2016).
832 Demographic buffering and compensatory recruitment promotes the persistence of disease
833 in a wildlife population. *Ecology Letters*, 19(4), 443-449.

834 McDonald, J. L., Robertson, A. & Silk, M. J. (2018) Wildlife disease ecology from the individual to the
835 population: Insights from a long-term study of a naturally infected European badger
836 population. *Journal of Animal Ecology*, 87, 101– 112.
837 Medzhitov, R., Schneider, D. S., & Soares, M. P. (2012). Disease Tolerance as a Defense Strategy.
838 *Science*, 335(6071), 936–941.
839 Morris, C. A. (2007). A review of genetic resistance to disease in *Bos taurus* cattle. *Veterinary Journal*,
840 174(3), 481–491.
841 Morrissey, M. B., Wilson, A. J., Pemberton, J. M., & Ferguson, M. M. (2007). A framework for power
842 and sensitivity analyses for quantitative genetic studies of natural populations, and case
843 studies in Soay sheep (*Ovis aries*). *Journal of Evolutionary Biology*, 20(6), 2309–2321.
844 Nath, M., Woolliams, J. A., & Bishop, S. C. (2008). Assessment of the dynamics of microparasite
845 infections in genetically homogeneous and heterogeneous populations using a stochastic
846 epidemic model. *Journal of Animal Science*, 86(8), 1747–1757.
847 Palmer W. J., Duarte A., Schrader M., Day J. P., Kilner R., Jiggins F. M. (2016) A gene associated with
848 social immunity in the burying beetle Nicrophorus vespilloides. *Proceedings of the Royal*
849 *Society B*, 283, 20152733.
850 Petelle, M. B., Martin, J. G. A., & Blumstein, D. T. (2015). Heritability and genetic correlations of
851 personality traits in a wild population of yellow-bellied marmots (*Marmota flaviventris*).
852 *Journal of Evolutionary Biology*, 28(10), 1840–1848. http://doi.org/10.1111/jeb.12700
853 Pitala, N., Gustafsson, L., Sendecka, J., & Brommer, J. E. (2007). Nestling immune response to
854 phytohaemagglutinin is not heritable in collared flycatchers. *Biology Letters*, 3(4), 418–421.
855 R Core Team (2019). R: A language and environment for statistical computing. R Foundation for
856 Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.
857 Regan, C.E., Pilkington, J.G., Pemberton, J.M. & Crawley, M.J. (2015). Sex differences in relationships
858 between habitat use and reproductive performance in Soay sheep (*Ovis aries*). *Ecology*
859 *Letters*, 19, 171–179.

860 Rhule, E. L., Majerus, M. E. N., Jiggins, F. M., & Ware, R. L. (2010). Potential role of the sexually
861 transmitted mite *Coccipolipus hippodamiae* in controlling populations of the invasive
862 ladybird *Harmonia axyridis*. *Biological Control*, 53(2), 243–247.
863 http://doi.org/10.1016/j.biocontrol.2009.12.006
864 Richardson, D. S., Jury, F. L., Blaakmeer, K., Komdeur, J., & Burke, T. (2001). Parentage assignment
865 and extra-group paternity in a cooperative breeder: The Seychelles warbler (*Acrocephalus*
866 *sechellensis*). *Molecular Ecology*, 10(9), 2263–2273.
867 Rigby, M. C., Hechinger, R. F., & Stevens, L. (2002). Why should parasite resistance be costly? *Trends*
868 *in Parasitology*, 18(3), 116–120.
869 Roff, D. A., & Wilson. A. J. (2014). Quantifying genetic by environmental interactions in laboratory
870 systems. In: *Genotype-by-environment interactions and sexual selection. Hunt, J. & Hosken,*
871 *D. eds.* John Wiley & Sons, Ltd.
872 Rogers, L. M., Delahay, R., Cheeseman, C. L., Langton, S., Smith, G. C., & Clifton-Hadley, R. S. (1998).
873 Movement of badgers (*Meles meles*) in a high-density population: individual, population and
874 disease effects. *Proceedings of the Royal Society B*, 265(1403), 1269–1276.
875 Roper T. J. (2010) *Badger*. London, UK: Collins.
876 Rozins, C., Silk, M., Croft, D. P., Delahay, R. J., Hodgson, D., McDonald, R. A., Weber, N. & Boots, M.
877 (2018). Social structure contains epidemics and regulates individual roles in disease
878 transmission in a group-living mammal. *Ecology and Evolution* 2018; 00:1–12.
879 https://doi.org/10.1002/ece3.4664
880 Sakaluk, S. K., Wilson, A. J. Bowers, E. K., Johnson, S. L., Masters, B. R., Johnson, B. G. P., Vogel, L. A.,
881 Forsman, A. M., & Thompson, C. F. (2014). Genetic and environmental variation in condition,
882 cutaneous immunity, and haematocrit in house wrens. *Evolutionary Biology*, 14(242), 1471–
883 2148.
884 Schielzeth, H., Dingemanse, N. J., Nakagawa, S., Westneat, D. F., Allegue, H., Teplitsky, C., Réale,
885 D., Dochtermann, N. A., Garamszegi, L. Z., & Araya-Ajoy, Y. G. (2020). Robustness of linear

886 mixed-effects models to violations of distributional assumptions. *Methods in Ecology and*
887 *Evolution*, https://doi.org/10.1111/2041-210X.13434
888 Schmid-Hempel, P. 2011. *Evolutionary Parasitology: The Integrated Study of Infections, Immunology,*
889 *Ecology, and Genetics*. Oxford University Press, New York.
890 Seppälä, O., & Langeloh, L. (2016). Estimating Genetic and Maternal Effects Determining Variation in
891 Immune Function of a Mixed-Mating Snail, *PLoS ONE* 11(8): e0161584.
892 Silk, M., Weber, N., Steward, L., Hodgson, D., Boots, M., Croft, D. Delahay, R., McDonald, R.A.
893 (2017a). Contact networks structured by sex underpin sex-specific epidemiology of infection,
894 *Ecology Letters*. 21:2, 309-318.
895 Silk, M. J., Weber, N., Steward, L. C., Delahay, R. J., Croft, D. P., Hodgson, D. J., Boots, M. &
896 McDonald, R. A. (2017b). Seasonal variation in daily patterns of social contacts in the
897 European badger *Meles meles*. *Ecology and Evolution*, 7(21), 9006–9015.
898 Sparks, A. M., Watt, K., Sinclair, R., Pilkington, J.G., Pemberton, J.M., McNeily, T. N., Nussey, D. H.,
899 Johnston, S. E. (2019) The genetic architecture of helminth-specific immune responses in a
900 wild population of Soay sheep (*Ovis aries*). *PLOS Genetics*, 15(11), e1008461.
901 Stear, M. J., Bishop, S. C., Mallard, B. A., & Raadsma, H. (2001). The sustainability, feasibility and
902 desirability of breeding livestock for disease resistance. *Research in Veterinary Science*,
903 71(1), 1–7.
904 Stear, M. J., Boag, B., Cattadori, I. and Murphy, L. (2009). Genetic variation in resistance to mixed,
905 predominantly *Teladorsagia circumcincta* nematode infections of sheep: from heritabilities
906 to gene identification. *Parasite Immunology* 31, 274–282.
907 Stopher, K. V, Walling, C. A., Morris, A., Guinness, F. E., Clutton-Brock, T. H., Pemberton, J. M., &
908 Nussey, D. H. (2012). Shared spatial effects on quantitative genetic parameters: accounting
909 for spatial autocorrelation and home range overlap reduces estimates of heritability in wild
910 red deer. *Evolution*, 66(8), 2411-26.

911 Svanbäck, R., Quevedo, M., Olsson, J., & Eklöv, P. (2015). Individuals in food webs: the relationships
912 between trophic position, omnivory and among-individual diet variation. *Oecologia*, 178(1),
913 103–114.
914 Tomlinson, A. J., Chambers, M. A., Carter, S. P., Wilson, G. J., Smith, G. C., McDonald, R. A., &
915 Delahay, R. J. (2013). Heterogeneity in the risk of *Mycobacterium bovis* infection in European
916 badger (*Meles meles*) cubs. *Epidemiology and Infection*, 141(7), 1458–66.
917 Tomlinson, A. J., Chambers, M. A., Wilson, G. J., McDonald, R. A., & Delahay, R. J. (2013). Sex-related
918 heterogeneity in the life-history correlates of *Mycobacterium bovis* infection in European
919 badgers (*Meles meles*). *Transboundary and Emerging Diseases*, 60(1), 37–45.
920 van der Waal, K. L., & Ezenwa, V. O. (2016). Heterogeneity in pathogen transmission: mechanisms
921 and methodology. *Functional Ecology*, 30(10), 1606–1622.
922 Vicente, J, Höfle, U, Garrido, J M, Fernández-de-Mera, I G, Juste, R, Barral, M, Gortazar, C. (2006).
923 Wild boar and red deer display high prevalences of tuberculosis-like lesions in Spain.
924 *Veterinary Research*, 37, 107–119.
925 Vicente, J., Delahay, R. J., Walker, N. J., & Cheeseman, C. L. (2007). Social organization and
926 movement influence the incidence of bovine tuberculosis in an undisturbed high-density
927 badger *Meles meles* population. *Journal of Animal Ecology*, 76(2), 348–60.
928 Visscher, P. M. (2006). A note on the asymptotic distribution of likelihood ratio tests to test variance
929 components. *Twin Research and Human Genetics*, 9(4), 490–495.
930 Weber, N., Carter, S. P., Dall, S. R. X., Delahay, R. J., McDonald, J. L., Bearhop, S., & McDonald, R. A.
931 (2013). Badger social networks correlate with tuberculosis infection. *Current Biology*, 23(20),
932 R915-6.
933 Wilson, A. J. (2018). How should we interpret estimates of individual repeatability*? Evolution Letters*,
934 4–8.

935 Wilson, A. J., Kruuk, L. E., & Coltman, D. W. (2005a). Ontogenetic patterns in heritable variation for
936 body size: using random regression models in a wild ungulate population. *American*
937 *Naturalist*, 166(6), E177-92.
938 Wilson, A. J., Coltman, D. W., Pemberton, J. M., Overall, A. D. J., Byrne, K. A., & Kruuk, L. E. B.
939 (2005b). Maternal genetic effects set the potential for evolution in a free-living vertebrate
940 population. Journal of *Evolutionary Biology*, 18(2), 405–414.
941 Yan, B.-S., Kirby, A., Shebzukhov, Y. V, Daly, M. J., & Kramnik, I. (2006). Genetic architecture of
942 tuberculosis resistance in a mouse model of infection. *Genes and Immunity*, 7, 201–210.
943 Yáñez, J. M., Houston, R. D., & Newman, S. (2014). Genetics and genomics of disease resistance in
944 salmonid species. *Frontiers in Genetics*, 5, 1–13.
945 Yates, A., Antia, R., & Regoes, R. R. (2006). How do pathogen evolution and host heterogeneity
946 interact in disease emergence? *Proceedings of the Royal Society B: Biological Sciences*,
947 273(1605), 3075–3083. http://doi.org/10.1098/rspb.2006.3681
948 Young, J. S., Gormley, E., & Wellington, E. M. H. (2005). Molecular detection of *Mycobacterium bovis*
949 and *Mycobacterium bovis* BCG (Pasteur) in soil. *Applied and Environmental Microbiology*,
950 71(4), 1946–1952. http://doi.org/10.1128/AEM.71.4.1946
951

952 **Table 1.** Intra-class correlations (ICC) for the binary measure of lifetime risk of *Mycobacterium bovis*
953 infection ($bTB_{lifetime}$). Estimates presented relate to the observed data scale but are obtained from a
954 generalised model using a probit link. Posterior means are used as point estimates of ICC and 95%
955 credible intervals are also shown.

Variance component	ICC	95% CI
additive genetic	0.092	<0.001-0.195
maternal	0.009	<0.001-0.033
birth year	0.110	0.060-0.169
natal group	0.040	0.013-0.073
natal group x birth year	0.087	0.051-0.125

956

957

958 **Table 2**: Likelihood ratio tests of random effect in animal models of $bTB_{capture}$ fitted to age specific
959 data subsets, and random regression animal model fitted to all data.

Age class	Component	χ^2	DF	P
O (cubs)	additive genetic	0.10	0,1	0.377
	maternal	5.05	0,1	0.012
	year	50.4	0,1	<0.001
	group	19.7	0,1	<0.001
	group x year	86.6	0,1	<0.001
1 (yearling)	additive genetic[1]	0.00	0,1	0.500
	maternal	6.46	0,1	0.006
	year	79.6	0,1	<0.001
	group	10.1	0,1	0.001
	group x year	75.7	0,1	<0.001
2+ (adult)	additive genetic	3.75	0,1	0.026
	maternal	8.31	0,1	0.002
	year	36.1	0,1	<0.001
	group	9.36	0,1	0.001
	group x year	234	0,1	<0.001
All (random regression)	additive genetic[2]	7.59	3	0.055
	maternal	53.4	0,1	<0.001
	year	143	0,1	<0.001
	group	21.7	0,1	<0.001
	group x year	288	0,1	<0.001

960 [1]Additive variance was bound to zero leading to identical log-likelihoods of full and reduced models

961 [2]Reduced model contains three fewer parameters, although since negative genetic variances in
962 intercept and slope are precluded use of 3 DF is conservative for statistical inference.

963

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967 Figure 1: Histogram of *Mycobacterium bovis* infection status records by age and infection status
968 score $bTB_{capture}$. Note that individuals may contribute multiple records (within and across ages), and
969 only records of known age badgers are included. Badgers have known age at capture if fist sampled
970 as a cub (age 0) or yearling (age 1) .

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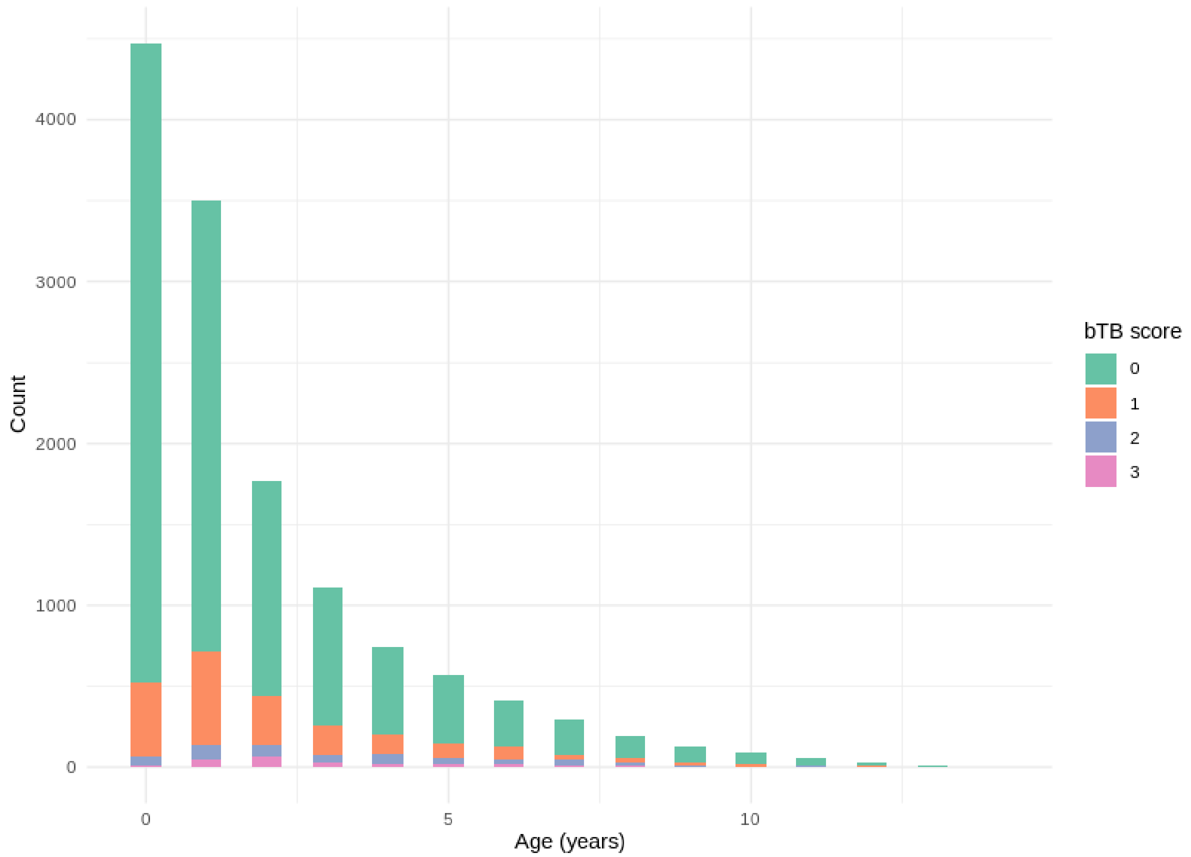

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974

975 Figure 2: Estimated heritabilities and intra-class correlations for $bTB_{capture}$. Estimates from analyses of age class specific data subsets (cubs, yearlings, adults)
976 are shown, together with estimates from the random regression (RR) model evaluated at ages 0, 1, 2 and 4 years. Error bars indicate ± 1 standard error but
977 could not be obtained for ICC at age 0 under the random regression model (see supplemental appendix 3 for explanation of this).

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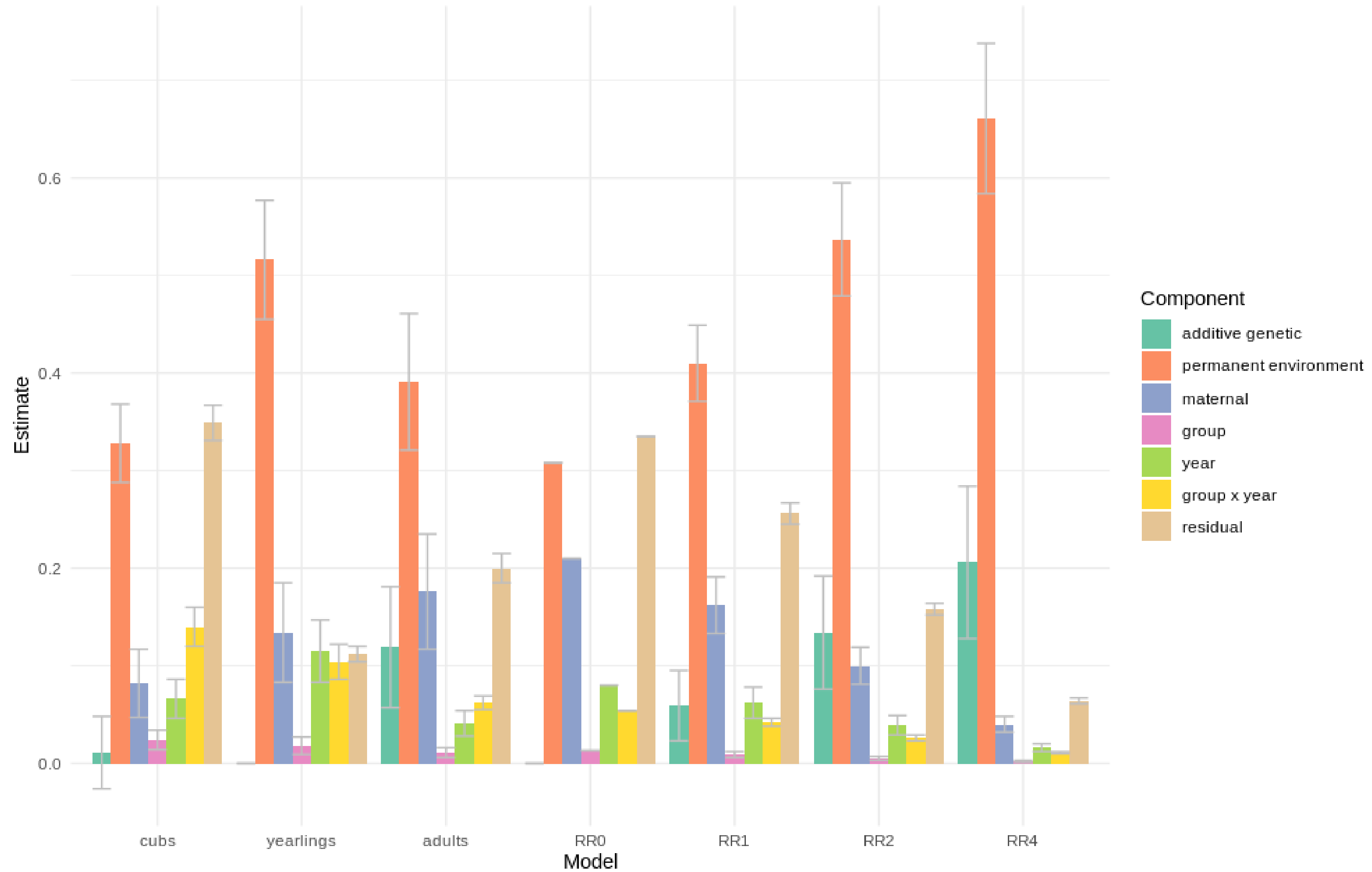

981 **Supplemental appendix 1: Diagnostic information from mcmcglmm model of $bTB_{lifetime}$**

982 Here we present diagnostic plots and test results produced using *MCMCglmm* to assess convergence
983 of our model of lifetime bTB status as a binary trait (see method for description). For information on
984 how to use these diagnostics and why they are useful checks on the validity of *MCMCglmm* model
985 outputs, the interested reader should refer to Hadfield 2019, Plummer et al 2006 and de
986 Villemereuil et al. 2016).
987
988 **a) Posterior plots for fixed effects**
989 Note `sex2` denotes the effect of being male (relative to female) while `lastage`, `latage_sq`,
990 and `lastage_cub` are regression coefficients associated with linear (first order), quadratic, and
991 cubic effects of age at last capture
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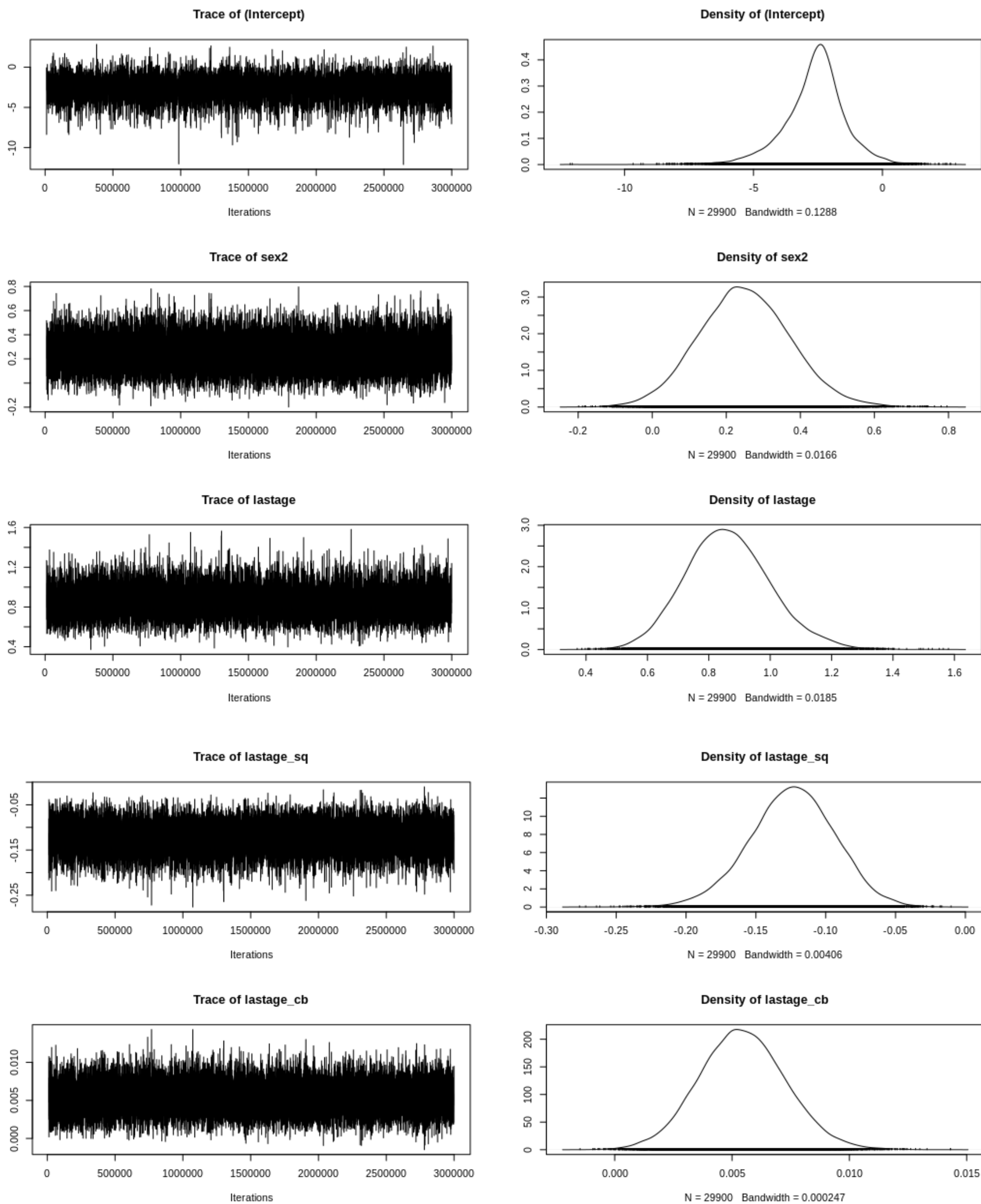
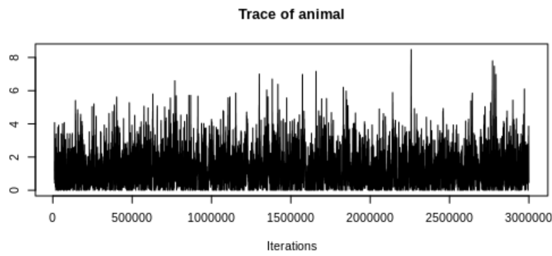
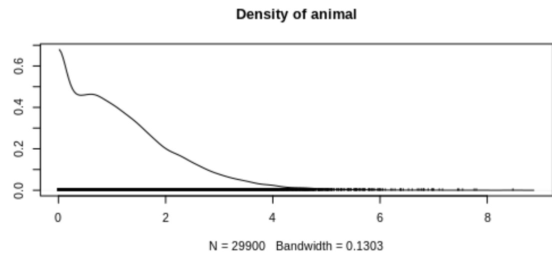
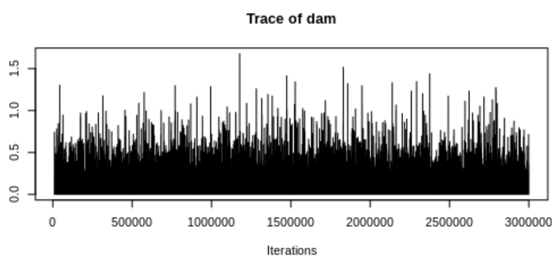


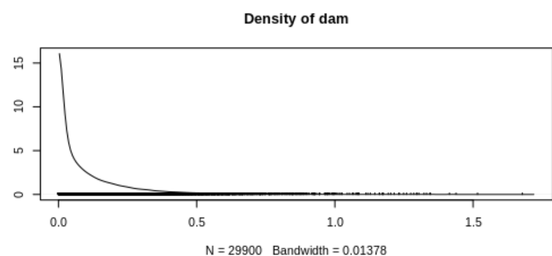
b) Posterior plots for random effect variances

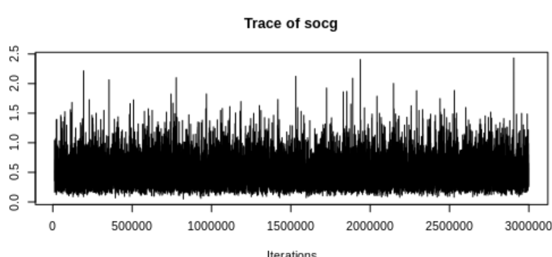
Note `animal`, `dam`, `socg`, `byearF` and `socg:byearF` denote the variance estimates (on the probit link scale) labelled as additive (V_A), maternal (V_M), natal group (V_{NGr}), birth year (V_{BY}) and natal group by birth year (V_{NGrxBY}) in main text

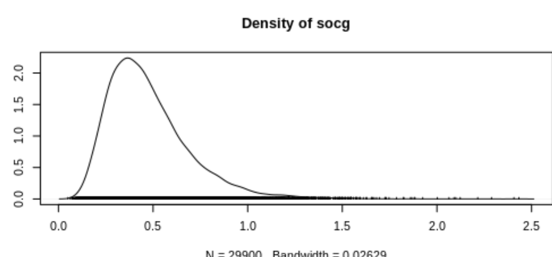


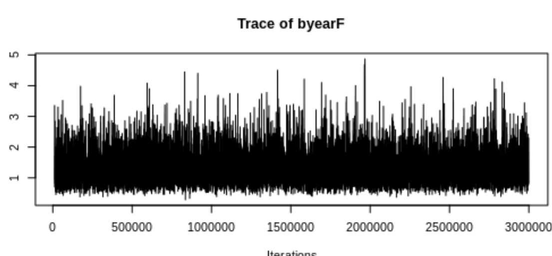


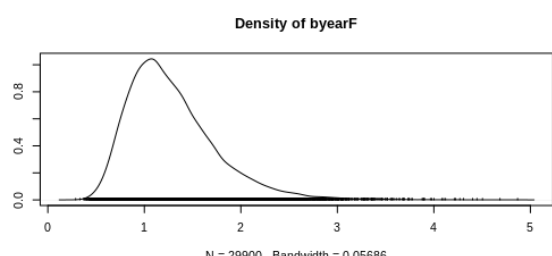


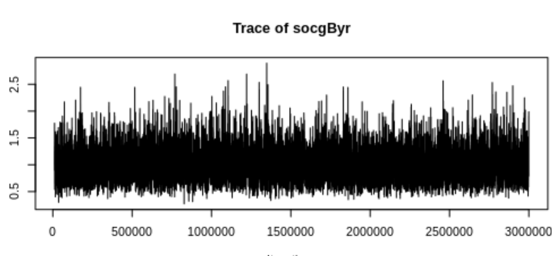


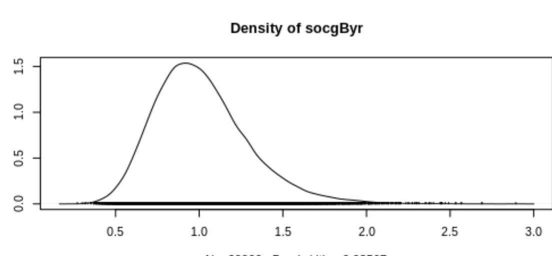












1052
1053 **c) Effective parameter sample sizes (given autocorrelation)**
1054

Fixed effect parameters	Intercept	17994.381
	sex (male)	20611.472
	lastage	5751.063
	lastage_sq	10113.619
	lastage_cub	14029.229
Random effect variances	animal	1582.926
	dam	1582.926
	socg	8024.905
	byearF	5097.583
	socg:byearF	3962.126
	units	0

1055
1056
1057
1058 **d) Heidelberger and Welch's convergence diagnostic test for stationarity**

	Stationarity test	**start iteration**	**P**	**Halfwidth test**	**Mean**	**Halfwidth**
Fixed effects						
Intercept	passed	1	0.383	passed	-2.6128	1.72E-02
Sex (male)	passed	1	0.225	passed	0.25004	1.68E-03
Lastage	passed	1	0.245	passed	0.86265	3.60E-03
Lastage_sq	passed	1	0.224	passed	-0.12406	5.97E-04
Lastage_cub	passed	1	0.183	passed	0.00546	3.05E-05
Random effects						
animal	passed	1	0.577	passed	1.234	0.04942
dam	passed	1	0.211	passed	0.109	0.00194
socg	passed	1	0.65	passed	0.476	0.00479
byearF	passed	1	0.766	passed	1.288	0.01267
socg:byearF	passed	1	0.307	passed	1.013	0.00873
units	failed	NA	NA			

1059

1060 **Supplemental appendix 2: Estimated fixed effects and random effect variances on link (probit)**
1061 **scale from mcmcglmm model of $bTB_{lifetime}$**

1062

1063 Here we present the primary output results of the mcmcmglmm model of $bTB_{lifetime,}$ showing point es
1064 timates of fixed effects and random effect variances (as posterior means) with 95% credible interval.
1065 All estimates relate to the link (probit) scale while ICC on the observed (0,1) data scale are presented
1066 in the main text.

1067

1068 **Fixed effect estimates**

1069

1070 Note sex2 denotes the effect of being male (relative to female) while lastage, latage_sq,
1071 and lastage_cub are regression coefficients associated with linear (first order), quadratic, and
1072 cubic effects of age at last capture

1073

1074

	Posterior mean	Lower 95% CI	Upper 95% CI	eff.samp	pMCMC
(Intercept)	-2.6128	-5.17603	-0.27206	17994	0.02876
sex2	0.250042	0.011991	0.497298	20611	0.03853
lastage	0.862648	0.597814	1.148476	5751	<3.00E-05
lastage_sq	-0.12406	-0.18532	-0.06485	10114	<3.00E-05
lastage_cub	0.005455	0.001775	0.009028	14029	0.00187

1075

1076

1077 **Estimated random effect variances**

1078

1079 Note animal, dam, socg, byearF and socg:byearF denote the variance estimates (on the
1080 probit link scale) labelled as additive (V_A), maternal (V_M), natal group (V_{NGr}), birth year (V_{BY}) and natal
1081 group by birth year (V_{NGrxBY}) in main text

1082

	Posterior mean	Lower 95% CI	Upper 95% CI	eff.samp
animal	1.234	4.209e-10	3.166	1583
dam	0.1091	1.16e-11	0.4052	21908
socg	0.4765	0.1379	0.913	8025
byearF	1.288	0.547	2.214	5098
socg:byearF	1.013	0.5099	1.575	3962
units	1	1	1	0

1083
1084
1085

1086 **Supplemental appendix 3: Estimated variance components and intraclass correlations $bTB_{capture}$.**
1087
1088 Here we present the REML-based estimates of variance components for $bTB_{capture}$ as well as the
1089 corresponding intra-class correlations (ICC; i.e. variance components as a ration of phenotypic
1090 variance conditional on fixed effects). Estimates are presented from analyses of stage specific data
1091 subsets (cubs, yearlings, and adults) and from the random regression animal model (RR). Note under
1092 RR model V_A and V_{PE} change with age while other components are estimated under assumed
1093 homogeneity and are therefore constant). Approximated standard errors are presented in
1094 parentheses where available.
1095
1096 **a) Estimated variances and ICC from REML animal models fitted to age specific data subsets and to**
1097 **all data using random regression (RR).**

Model (age)	Component	V (SE)	ICC (SE)
Cub (0)	additive genetic	0.002 (0.005)	0.011 (0.037)
	permanent environment	0.048 (0.006)	0.328 (0.040)
	maternal	0.012 (0.006)	0.082 (0.035)
	group	0.003 (0.001)	0.024 (0.010)
	year	0.010 (0.003)	0.066 (0.020)
	group x year	0.021 (0.003)	0.140 (0.020)
	residual	0.051 (0.001)	0.349 (0.018)
Yearling (1)	additive genetic[1]	0.000 (-)	0.000 (-)
	permanent environment	0.181 (0.020)	0.516 (0.061)
	maternal	0.047 (0.020)	0.134 (0.051)
	group	0.006 (0.003)	0.018 (0.009)
	year	0.040 (0.013)	0.115 (0.032)
	group x year	0.036 (0.006)	0.104 (0.018)
	residual	0.039 (0.001)	0.112 (0.008)
Adult (2+)	additive genetic	0.073 (0.038)	0.119 (0.062)
	permanent environment	0.240 (0.038)	0.391 (0.070)
	maternal	0.108 (0.043)	0.176 (0.059)
	group	0.007 (0.003)	0.011 (0.005)
	year	0.025 (0.008)	0.041 (0.013)
	group x year	0.038 (0.004)	0.062 (0.007)
	residual	0.122 (0.003)	0.200 (0.015)
RR (0)[2]	additive genetic	0.000 (-)	0.000 (-)
	permanent environment	0.069 (-)	0.308 (-)
	maternal	0.047 (-)	0.210 (-)
	group	0.003 (-)	0.013 (-)
	year	0.018 (-)	0.080 (-)
	group x year	0.012 (-)	0.054 (-)
	residual	0.075 (-)	0.335 (-)
RR (1)	additive genetic	0.017 (0.011)	0.059 (0.036)
	permanent environment	0.120 (0.011)	0.410 (0.039)
	maternal	0.047 (0.010)	0.162 (0.029)
	group	0.003 (0.001)	0.009 (0.003)
	year	0.018 (0.005)	0.062 (0.016)
	group x year	0.012 (0.001)	0.042 (0.004)
	residual	0.075 (0.001)	0.256 (0.011)

RR (2)	additive genetic	0.063 (0.028)	0.134 (0.058)
	permanent environment	0.254 (0.028)	0.537 (0.058)
	maternal	0.047 (0.010)	0.100 (0.019)
	group	0.003 (0.001)	0.005 (0.002)
	year	0.018 (0.005)	0.039 (0.010)
	group x year	0.012 (0.001)	0.026 (0.003)
	residual	0.075 (0.001)	0.158 (0.006)
RR (4)	additive genetic	0.242 (0.092)	0.206 (0.078)
	permanent environment	0.774 (0.093)	0.661 (0.077)
	maternal	0.047 (0.010)	0.040 (0.008)
	group	0.003 (0.001)	0.002 (0.001)
	year	0.018 (0.005)	0.016 (0.004)
	group x year	0.012 (0.001)	0.011 (0.001)
	residual	0.075 (0.001)	0.064 (0.003)

1098 [1]Additive variance bound to zero in this model so no SE obtained

1099 [2] We were unable to obtain standard errors on variance components and ICC as estimated from the
1100 random regression model at age 0 (cubs). As described in the main text, the RR model fitted genetic
1101 and permanent effects as first order (linear) functions of age. We initially used a rescaled age
1102 (subtracting 2 from actual age) such that the random intercept variances (and their estimated SEs)
1103 directly estimated by the model describe V_A and V_{PE} at age 2. We then used the estimated random
1104 intercept-slope covariance structures to project estimates of V_A and V_{PE} at different ages (0, 1 and 4).
1105 However, it is not mathematically trivial to obtain SEs for these projected estimates at different
1106 ages. To obtain those as a measure of uncertainty we therefore refitted the RR model with adjusted
1107 scalings of age, such that zero on the adjusted scale corresponded to 0, 1 or 4 instead of 2). In
1108 principle this should allow refitting of an identical model with slightly different parameterisations,
1109 such that intercept variance (and their SEs) would now correspond to for V_A and V_{PE} at the other
1110 (true) ages. In practice, this was achieved as expected to generate SEs on variances (and ICC) at ages
1111 1,2 and 4. However, we could not achieve the same model fit with age standardised to a zero point
1112 corresponding to a real age of zero (cubs). This is because, with this scaling the random genetic
1113 intercept variance was fixed to the boundary of allowable parameter space. This prevented us
1114 generating directly comparable SEs on the variance components and ICC for the RR model at age 0.

1115 **b) Estimated 'character-state' additive genetic (G) and permanent environment (PE) variance-**
1116 **covariance-correlation matrices across ages for bTB$_{capture}$ projected from the random regression**
1117 **model.** Point estimates of variance (shaded diagonal), covariance (below diagonal) and correlation
1118 (above diagonal) for ages 0, 1, 2 and 4 years are derived from a model in which additive genetic and
1119 permanent environment effects are treated as first order functions of age.

1120

G	*Age 0*	*Age 1*	*Age 2*	*Age 4*
Age 0	0.000	0.708	0.675	0.657
Age 1	0.002	0.017	0.999	0.998
Age 2	0.003	0.033	0.063	1.000
Age 4	0.005	0.065	0.124	0.243

1121

PE	*Age 0*	*Age 1*	*Age 2*	*Age 4*
Age 0	0.069	0.809	0.590	0.377
Age 1	0.074	0.120	0.952	0.850
Age 2	0.078	0.166	0.254	0.970
Age 4	0.087	0.259	0.430	0.773

1123 **Supplemental appendix 4:** Estimated fixed effect coefficients (with SE) and associated conditional F
1124 tests from all animal models of $bTB_{capture}$ fitted by REML.

Model	Effect	Estimate (SE)	F	DF	P
cub	Intercept	0.202 (0.195)	0.202	1,2624.8	0.653
	sex (F)	-0.003 (0.194)	0.167	2,2347.4	0.846
	sex (M)	-0.011 (0.194)			
	season (Winter)	0.164 (0.025)	89.71	3,3098.2	<0.001
	season (Spring)	-0.154 (0.015)			
	season (Summer)	-0.097 (0.008)			
yearling	Intercept	0.300 (0.044)	39.42	1,38.5	<0.001
	sex (M)	0.024 (0.026)	0.858	1,1373.1	0.355
	season (Winter)	-0.096 (0.011)	23.72	3,2166.6	<0.001
	season (Spring)	-0.058 (0.013)			
	season (Summer)	-0.043 (0.011)			
adult	Intercept	0.132 (0.062)	5.63	1,50.7	0.021
	sex (M)	0.079 (0.035)	5.257	1,1286.1	0.022
	season (Winter)	-0.065 (0.017)	5.197	3,4939.9	0.001
	season (Spring)	-0.041 (0.018)			
	season (Summer)	-0.026 (0.013)			
	age	0.085 (0.03)	8.114	1,5277.5	0.004
	age^2	-0.005 (0.005)	1.017	1,5179.4	0.313
	age^3	9.21×10^{-5} (2.74×10^{-4})	0.113	1,5123	0.736
random regression	Intercept	0.237 (0.224)	0.615	1,3756.8	0.433
	sex (F)[1]	-0.059 (0.223)	1.593	2,2948.1	0.204
	sex (M)	-0.083 (0.223)			
	season (Winter)	-0.071 (0.009)	37.71	3,11093.1	<0.001
	season (Spring)	-0.068 (0.009)			
	season (Summer)	-0.054 (0.006)			
	age	0.099 (0.009)	122.9	1,2205.3	<0.001
	age^2	0.001 (0.002)	0.266	1,12380.1	0.606
	age^3	3.77×10^{-5} (1.23×10^{-4})	0.094	1,12313.3	0.760

1125 Note cub data included some individuals with missing sex. For **cub** and **RR** models we included these
1126 records and sex=missing was treated as the reference factor level. For yearling and adult models sex
1127 effects indicate males relative to females. Autumn provides the reference level of season in all
1128 models.

1129