

The epidemiology and genomics of a virulent emerging fungal pathogen in an Australian reptile

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Abstract

Emerging infectious fungal diseases (EIFDs) represent a major conservation concern worldwide. Here, we provide early insights into the potential threat that *Nannizziopsis barbatae* (*Nb*), a novel EIFD, poses to Australian herpetological biodiversity. First known to the reptile pet trade as a primary pathogen causing untreatable severe dermatomycosis, since 2013, *Nb* has emerged in a growing number of phylogenetically and ecologically distant free-living reptiles across Australia. Observing its emergence in a long-term study population of wild eastern water dragons (*Intellagama lesueurii*), we demonstrate the pathogen's virulence-related genomic features, within-population spatiotemporal spread, and survival costs, all of which imply that *Nb* could pose a threat to Australian reptiles in the future. Our findings highlight the need to closely monitor this pathogen in Australian ecosystems.

1 **Introduction**

2 Emerging infectious fungal diseases (EIFDs) pose a serious threat to the conservation of global
3 biodiversity (1–3) and are responsible for some of the most severe mass mortality events in wild
4 populations (1–4). Notable examples include chytridiomycosis, which has now impacted over 500
5 species of amphibians in 54 countries, driving the extinction of 90 species worldwide (5); white-
6 nose syndrome, which has resulted in a devastating 75% population decline across bats in Canada
7 and the USA (6, 7); and the more recent snake fungal disease (8), which poses a significant threat
8 to snake populations in eastern North America (9). Whilst EIFDs make up less than three percent
9 of infectious agents reported amongst animal hosts, they are nonetheless responsible for over 70
10 % of disease-driven population declines and extinctions (1).

11 Members of the fungal genus *Nannizziopsis* are well known to the pet trade as primary pathogens
12 that cause serious cutaneous and systemic fatal disease in a diverse range of reptiles across the
13 world (10–13). *Nannizziopsis barbatae* was first identified in captivity in 2009 (14), and remained
14 confined to captivity until, in 2013, two-free living eastern water dragons (*Intellagama lesueurii*)
15 from locations separated by 30 km across Brisbane (Queensland, Australia) were identified with
16 proliferative dermatitis, necrosis, ulceration and emaciation (15). *Nb* has since emerged in a
17 growing number of phylogenetically and ecologically distant free-living lizards (2 x agamid
18 species and 2 x skink species) across Australia (6 sites in Qld, 1 site in NSW and 1 site in WA)
19 (15) and is known to cause disease in 9 species (data combined from captive and wild cases, see
20 Table S1). This recent emergence in the wild, followed by a rapid expansion of its geographical
21 distribution and host range, indicate that this fungal pathogen may present a pressing new threat
22 to Australia's herpetological biodiversity. While we know that *Nb* causes untreatable severe
23 dermatomycosis (15), mitigating its impact will require a thorough understanding of its ecology.

24 Taking advantage of its recent emergence in a long-term study population of eastern water dragons
25 (15) and using an innovative combination of comparative genomics and spatiotemporal
26 autocorrelation models, we assess the potential threat that *Nb* may pose to Australia's
27 herpetological biodiversity.

28 **Results**

29 *Nb* emerged in 2013 in two geographically isolated populations of eastern water dragons in the
30 city of Brisbane (QLD, Australia). One of these populations (Roma Street Parkland, 27°27'46'S,
31 153°1'11'E) has been monitored with frequent behavioral surveys and yearly catching since 2010.
32 This population comprises 336 individuals on average and behavioral surveys were performed 2-
33 3 times per week along a transect which covered 85% of this population (16). During behavioral
34 surveys, individuals' GPS position were systematically recorded and profile photographs taken to
35 allow later identification based on unique scale patterns (17). Disease diagnosis was based on the
36 presence or absence of characteristic skin lesions (15), which observers were trained to recognize
37 from season 9 (2018-2019) onwards. Individuals' disease status for earlier years was hence
38 determined retrospectively using photos from catching and, when not available, behavioral
39 surveys. Once diagnosed, individuals were assumed to remain diseased even when not caught
40 again. Amongst the diseased individuals repeatedly captured between February 2020 and August
41 2021, some individuals (20/61) showed a reduction in the severity of their lesions, although this
42 reduction was mainly observed in individuals exhibiting mild lesions (15/20, Data S1). Using this
43 decade-long individual-based data, we found that the disease prevalence has continuously
44 increased throughout the population since *Nb*'s emergence. Starting with one individual in 2013,
45 a total of 158 individuals have now presented with clinical signs of the disease (n =1221 for field
46 seasons 3-11) and in the last field season (2020-2021), the prevalence was 26.4% (95% CI: 24.2-
47 28.4, Fig. S1, Table S2). The majority (96.7%) of these individuals were adults, and males

48 (58.3%). Only five juveniles were found with clinical signs of the disease (0.07 to 5.5% of
49 juveniles) between late 2018 to early 2021, despite juveniles representing on average 17.8% of
50 observed individuals during these years.

51 *N. barbatae* shares genomic characteristics with other fungal pathogens

52 *Nb* is a member of the Onygenales, an order of fungi that are able to degrade keratin, the main
53 component of the vertebrate outer skin layer. Some members of this order are important primary
54 pathogens of animals and humans and recent comparative genomic studies have helped resolve
55 differences in gene content between pathogenic and non-pathogenic species (18). With this in
56 mind, we performed a comparative whole-genome analysis incorporating the full set of genes of
57 *Nb* (8,012 predicted protein-coding sequences) together with 16 other species of fungi (Table 1)
58 to uncover genomic features likely to contribute to *Nb*'s pathogenicity.

59 First, we identified that the *Nb* genome contains a gene repertoire rich in proteases, known to
60 increase fungal virulence (19), and shares similarities with other pathogenic Onygenaceae (Fig.
61 1A). Most notable is an expansion of trypsin domain-containing genes (PF00089) (Fig. 1B) found
62 only in *Nb* (7 genes) and the fungus causing snake fungal disease, *O. ophidiicola* (29 genes). Both
63 of these species are capable of primary infection in reptiles (9, 20) suggesting a role for this gene
64 family in influencing host range. *Nb* has a degradome that bears resemblance to important
65 dermatophytes and the enrichment of proteases including, subtilase (PF00082) and deuterolysin
66 (PF02102), suggest extensive proteolytic capacity. Second, *Nb* has a large number of protein
67 kinase domain-containing genes (PF00069) which may contribute to its capacity to infect a broad
68 range of reptile taxa (15). Last, we identified a higher number of LysM domain-containing genes
69 (PF01476) in the *Nb* genome than most of the other fungi in this analysis. Together, these

70 characteristics of the *Nb* genome highlight factors which may be key to determining its propensity
71 to infect herpetofauna.

72 *N. barbatae* infection is spatially structured within the population

73 To investigate the phenotypic and spatiotemporal predictors of fungal infection, we constructed
74 spatiotemporal autocorrelation models using the Integrated Nested Laplace Algorithm.
75 Comparison of disease prevalence models (Fig. S2) provided strong support for spatial structuring
76 ($\Delta\text{DIC}=-117.24$ relative to the base model), but relatively little evidence for spatiotemporal
77 structuring ($\Delta\text{DIC}=-4.11$ relative to the spatial model) (Fig. S2). That is, disease prevalence varied
78 more spatially (assuming no time effect) than spatiotemporally. Indeed, spatial effects were
79 strongly correlated across field seasons ($\rho>0.9$) and disease prevalence has remained
80 consistently higher in the East (up to 33%) compared to the West (<10%, Fig. 2). Models also
81 showed lower prevalence in juveniles than adults, and in females compared to males (Fig. S2).

82 *N. barbatae* infection is associated with survival costs

83 To investigate the survival costs of infection, we fitted a binomial survival model, where survival
84 of an individual was coded based on whether they were observed in any subsequent year. The full
85 population model showed effects of cohort, field season and sex on the yearly probability of
86 survival but failed to detect any effect of the disease (Fig. 3A). In contrast, randomly subsampling
87 diseased and non-diseased individuals from matching cohorts and accounting for age (number of
88 days in the population), sex, and field season in subsequent models revealed a small but significant
89 individual survival costs of the disease (Fig. 3B-D). All subsampled models found a significant
90 effect of the disease (Fig. 3B); the overall mean survival cost was 12% (Fig. 3C), so that the mean
91 predicted annual survival of diseased individuals was 74% compared to 86% for non-diseased

92 individuals (Fig. 3D). Controlling for spatial autocorrelation did not improve model fit ($\Delta\text{DIC} > -2$
93 relative to the base model), demonstrating that this survival cost did not vary spatially.

94 **Discussion**

95 Gaining early insights into disease virulence, spatiotemporal spread, and survival costs is
96 particularly urgent in the case of novel emerging infections that have the potential to severely
97 threaten biodiversity. Yet such data are challenging to obtain in the wild, greatly impeding our
98 abilities to predict and mitigate the impact of infections on wildlife. Our study investigates within-
99 population spread and impacts of *Nannizziopsis barbatae*, a novel emerging infectious fungal
100 disease which should give us cause for vigilance.

101 ***Genomic signatures of pathogenicity***

102 We show that the free-living *Nb* genome sampled from our long-term study population of eastern
103 water dragon contains many gene families implicated in fungal pathogenicity, including several
104 proteases, protein kinases, and LysM effector proteins. Virulence in wildlife fungal pathogens has
105 often been associated with expansions of protease gene repertoires and their expression (e.g.
106 chytrid (21); WNS (22–24)). *Nb* has a gene repertoire rich in proteases with features similar to
107 those identified in other wildlife fungal pathogens such as snake fungal disease (e.g. trypsin
108 domain-containing genes) and chytrid fungus (e.g. M36 metalloproteases). Additionally, a
109 comprehensive and novel repertoire of protein kinases can provide fungal species with plasticity
110 in occupying different ecological niches and responding to environmental change (25, 26). LysM
111 effector proteins may contribute to fungal virulence by suppressing the host immune system
112 response via interactions with chitin (27). Comparative studies strongly suggest an association
113 with the enrichment of LysM domain-containing genes and virulence in the keratin-degrading
114 dermatophytes (26). Furthermore, chitin-binding CBM18 gene family proteins (PF00187) are also

115 found expanded in *B. dendrobatidis*, and are thought to play a role in evasion of the amphibian
116 host immune response (26). While understanding the molecular mechanisms of this pathogen is
117 central to mitigating its impact on wildlife, the exact source of *Nb*, its current free-living genetic
118 diversity, and its mode of introduction into our dragon population remain unknown. Genomic
119 resources for *Nannizziopsis* spp. will enable the development of tools to answer these questions.
120 The emergence of this disease urgently necessitates the identification of its origin to better
121 understand and thus predict the impact it will likely have on the Australian herpetofauna. For
122 instance, it is critical that we determine whether or not we are dealing with a novel pathogen and
123 thus naïve hosts, or whether the population has had historical exposure to the pathogen.

124 ***Within-population spread***

125 Even though central to the forecasting and control of wildlife disease management, quantifying
126 the contribution of different transmission pathways of a pathogen is notoriously challenging to
127 achieve in nature (28). Using an intensively-studied lizard population, we provide a much-needed
128 early assessment of *Nb*'s spatiotemporal spread since its emergence in 2013. We show that the
129 disease has spread relatively rapidly across an increasing portion of the population, providing the
130 first likely evidence for within-population *Nb* transmission in the wild. From a single individual
131 dragon identified with *Nb*-like clinical signs in 2013, more than 150 individuals have displayed
132 apparent clinical signs of *Nb* and the disease prevalence has reached 26.4% of the population.
133 Worryingly, prevalence of the disease has been continuously increasing since 2016 and shows no
134 signs of slowing down. Although it is unclear what the transmission route of this pathogen is in
135 this population (e.g. physical contact or environmental latency), our results show that over the
136 years, the disease prevalence has remained higher in the eastern part of the park than in the western
137 area, which could be due to spatial variation in environmental factors influencing the pathogen's

138 survival, transmission, or virulence (29). Analyses of the dragons' spatial and social behaviors
139 coupled with molecular diagnostics capabilities will help identify transmission routes, predict
140 geographic spread of the pathogen, and inform potential future interventions (30).

141 ***Low but detectable survival costs***

142 Survival costs of *Nb* infection were detectable at an individual level. Although individuals showing
143 clinical signs of the disease varied in their survival costs, they were still relatively likely to survive
144 from one year to the next (>70% chance), demonstrating that adults are relatively tolerant to the
145 pathogen and can carry it for multiple years once skin lesions become apparent. Although the
146 disease has been shown to be incurable in captive reptiles (15), some rare individuals in this
147 population showed reductions in the severity of their lesions (Data S1) and we are yet to determine
148 whether individual diseased dragons can entirely clear the infection (as shown in chytridiomycosis
149 (31) and white-nose syndrome (32)). Additionally, we were only able to detect survival costs when
150 we subsampled our dataset to cohort-matched (age and sex) diseased and non-diseased individuals,
151 thereby reducing extraneous variation in survival probability. Evidence for individual survival
152 costs remains similarly equivocal for other EIFDs, some of which have been studied for much
153 longer than *Nb* (31–33). We also acknowledge some uncertainty in our estimates of survival costs
154 due to potential errors in diagnosis, our visual assessment being particularly prone to miss
155 asymptomatic or cryptic infections in the population. Additionally, because lesions are easier to
156 observe in caught individuals, this underestimation may be particularly severe for individuals or
157 classes of individuals that were less likely to be caught (e.g. juveniles). Taken together, these facts
158 imply a general difficulty detecting survival costs of fungal pathogens in long-lived reptiles.

159 Despite identifying individual-level costs of infection, predicting *Nb*'s impacts on population
160 dynamics remains difficult. Such uncertainty is likewise common to other EIFDs, as some

161 populations affected by chytridiomycosis and white nose syndrome have not declined
162 systematically (44, 45). Predicting *Nb*'s impacts on the viability of our studied population of
163 eastern water dragons will require key information about: i) *Nb*'s prevalence and survival costs at
164 different life stages (36, 37), which should be achieved with higher certainty through the use of
165 molecular diagnosis; ii) *Nb*'s potential reproduction costs, as was documented for snake fungal
166 disease (38) and chytridiomycosis (39); iii) the mechanisms underlying *Nb*'s spatiotemporal
167 spread. In addition, assessing whether the pathogen's transmission dynamics are density-
168 dependent might be crucial to understanding whether the epidemic will become self-limiting (40).

169 ***A novel threat for the Australian biodiversity?***

170 EIFDs constitute an increasing cause for concern regarding global health, food security and
171 biodiversity conservation (1). With *Nb*, we may be witnessing the early days of a novel fungal
172 threat to Australian herpetological biodiversity. While other infamous EIFDs with global impacts
173 on wild animal populations were only reported after mass mortality events had already occurred
174 (41, 42), we have the unique opportunity to monitor the emergence of this pathogen and take action
175 early enough to limit its spread. Although the origin and long-term population impacts of *Nb*
176 remain unknown, its genomic similarity with other pathogenic EIFDs, capacity to spread in the
177 wild, and detectable survival costs, combined with its repeated emergence across the country and
178 broad host range, highlight the critical need to closely monitor this pathogen in Australian
179 ecosystems.

180

181 **Materials and Methods**

182 *Study system*

183 The population of Eastern water dragons has been monitored since 2010, with frequent
184 behavioral surveys and regular catching during the active season, (i.e. early September to late
185 April). During behavioral surveys (2-3 times per week), individuals' behavior and GPS position
186 were recorded and photographs taken to allow later identification based on unique scale patterns
187 (see (17)). Individuals were also caught during 1-2 weeks catching events in the years 2013, 2014,
188 and yearly since 2016. Morphometric measurements, head and body photographs and DNA
189 samples (blood or tip of the tail) were taken, and unique PIT-tags were inserted in their right upper
190 hind leg. EWD are sexually dimorphic, males being overall larger than females, with more
191 developed jaw and dorsal crest and a red ventral coloration (43). Age class (adult vs. juvenile) was
192 determined for each breeding season using a combination of approaches (snout-vent length when
193 individuals were caught; general appearance when individuals were not caught) and taking into
194 account individuals' observation history (individuals being considered adults after 3 years (43)).
195 Disease diagnosis was based on the presence or absence of characteristic skin lesions (15), which
196 observers were trained to recognize from season 9 (2018-2019) onwards. Individuals' disease
197 status before season 9 was hence determined retrospectively using pictures from behavioral
198 surveys and catching (75-100% for the latter). From season 9 onwards, disease status was assessed
199 directly in the field during behavioral surveys and catching (65-92% for the latter). From February
200 2020 onwards, disease severity was rated for captured individuals using scores ranging from 0 (no
201 lesions, not diseased) to 5 (severely diseased, Table S3).

202

203 *Genome annotation and comparative analysis*

204 The genomes of *N. barbatae*, *O. ophidiicola* and *C. queenslandicum* were annotated using
205 the Funannotate (v1.7.4) gene prediction pipeline (<https://funannotate.readthedocs.io/>). Genomes
206 were firstly screened for repeats using custom generated databases for each species using
207 RepeatModeler (v2.0.1) and masked using RepeatMasker (v4.1.0; <http://www.repeatmasker.org>).
208 Repeat masked assemblies were then cleaned and sorted before initial gene prediction using
209 GeneMark-ES (v4.65) (44). Protein sequences from high-quality fungal genomes used in this study
210 were used for protein-to-genome alignments as evidence for gene predictors AUGUSTUS (45),
211 SNAP(46), and Glimmer (47) before being passed to EVM (48) to build consensus gene structures.
212 All other predicted protein sequences were downloaded directly from GenBank (Table 1). The
213 newly annotated gene models were evaluated for completeness using BUSCO (v5) (49) in protein
214 mode against the ascomycota_odb10 database (Table S4).

215 Gene families within each fungal genome were identified from searches of the protein-coding
216 sequences for Pfam (50) domains to assign gene function. We used HMMER (v3.1) (51)
217 (hmmScan) to search the Pfam A database (release 32.0) for 4312 different domains of 16 different
218 species of fungi. To test for significantly expanded gene families, a Fisher's exact test was then
219 conducted iteratively using R (52), comparing the number of counts in Pfam families found in an
220 individual genome, normalised by the total gene count for that species, against the background,
221 which we defined as the average of the counts in the remaining species. Multiple testing corrections
222 were done using the FDR method in R for all calculated *p*-values. A Pfam domain was considered
223 expanded if it showed a corrected *p*-value < 0.05. Counts of each domain were collated for each
224 species with domains that occurred multiple times in a protein sequence being counted only once.
225 Heatmap was generated using the package pheatmap with data normalised using the scale function
226 in R. Protein sequences were aligned using Muscle (v3.8.425) (53) and phylogenetic inference

227 made using FastTree (v2.1.12) (54) built in to the commercially available Geneious Prime
228 (v2021.1.1) software.

229 *Drivers and spatiotemporal dynamics of infection*

230 To investigate the phenotypic and spatiotemporal predictors of fungal infection, we
231 constructed spatiotemporal autocorrelation models using the Integrated Nested Laplace Algorithm,
232 implemented in the `inla` package in R (55). These models fitted binary fungal infection as a
233 response variable, where an individual was coded as a 1 if it had previously been diagnosed with
234 fungal infection, and a 0 otherwise. All covariates were categorical, and included Age class (3
235 levels: Adult, Juvenile, and Unknown); Sex (2 levels: Female and Male); Field season (9 levels:
236 one for each sampling year 2012-2021). The model used a binomial logit error distribution:

237 Fungus (0/1) ~ Season + Sex + Age

238 We first fitted these fixed effects as a “Base” model. To investigate spatiotemporal patterns
239 of infection, we then added Stochastic Partial Differentiation Equation (SPDE) random effects
240 using individuals’ mean map locations in a given season (“annual centroids”). This random effect
241 models two-dimensional patterns of the response variable based on distances between individuals
242 using Matérn correlation (56, 57) The “Spatial” model used a static field, where the spatial
243 distribution of infection was modelled to be unchanging across the study period; the
244 “Spatiotemporal” model allowed this field to change from year to year, using an autoregression
245 (AR1) correlation across years, to examine how the infection’s distribution changed over the
246 course of the study period. We compared these three models using deviance information criterion
247 (DIC) as a measure of model fit to investigate whether spatiotemporal correlation significantly
248 improved the model.

249

250 *Survival costs*

251 To investigate the survival costs of infection, we fitted a binomial survival model, where
252 survival was coded based on whether the individual was seen in a subsequent year (we hence
253 excluded the most recent year, 2019). The model was specified as follows:

254 $\text{Survived (0/1)} \sim \text{Season} + \text{Sex} + \text{Cohort} + \text{ActiveFungus}$

255 Following this model, we used a subsampling routine that allowed us to reduce extraneous
256 variation in survival by compensating for the low proportion of infected individuals in the study
257 period (120/1151=10.4%) and for the unknown age of infected individuals. We 1) assigned each
258 individual a cohort based on the first season that they were observed in the population; 2) selected
259 the 101 individuals that were ever observed with an infection between 2012 and 2018; and 3) age
260 matched each diseased individual with a random non-diseased individual from their cohort.
261 Between 2018 and 2020, six diseased individuals that were caught in a very poor condition were
262 euthanized. These individuals were hence excluded from these analyses. Having subsampled the
263 population, we then ran the same model as before. This protocol was repeated 1000 times to ensure
264 an even and different selection of non-diseased individuals and survival effect estimates.

265 We summarized the findings from these models by predicting survival probability for each
266 individual and comparing these values between uninfected and infected individuals. To produce
267 conservative estimates, we randomly drew one effect estimate from each model's fungal effect
268 estimate posterior distribution and used these estimates to predict the survival probability for all
269 infected and uninfected individuals. We then took the mean survival probability for these groups
270 of individuals and subtracted the infected individuals' survival probability from those of the
271 uninfected individuals to estimate a survival cost of infection.

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280 Conceptualization: BC, JT, CF, DP, GA, SB

281 Data curation: BC, CD, CF

282 Methodology: GA, DP, BC

283 Investigation: BC, DP, JT, CF, CD

284 Visualization: DP, GA

285 Funding acquisition: CF

286 Project administration: CF

287 Supervision: CF, SB

288 Writing – original draft: BC, JT, CF

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290 **Competing interests:** Authors declare that they have no competing interests.

291 **Data and materials availability:** Genome annotation data, individual data and R code used for
292 statistical analyses are available from Figshare using the following link
293 <https://doi.org/10.6084/m9.figshare.16599245> .

294 **Supplementary Materials**

295 Figs. S1 to S2

296 Table S1 to S4

297 Data S1

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Table 1. Details of the fungal species used in the comparative analysis.

Species	Division	Order	Family	Host	Disease	GenBank Accession	Genome Size (MB)	Genome N50 (Kb)	Number predicted proteins
<i>Nannizzia barbatae</i>	Ascomycota	Onygenales	Onygenaceae	Reptiles	Dermatomycoses	GCA_014964245.1	31.543	6,192	8,012*
<i>Ophidiomyces ophiodiicola</i>	Ascomycota	Onygenales	Onygenaceae	Snakes	Ophidiomycosis (snake fungal disease)	GCA_002167195.1	21.865	1,499	6,983*
<i>Uncinocarpus reesii</i>	Ascomycota	Onygenales	Onygenaceae	-	Non-pathogenic	GCF_000003515.1	22.349	5,232	7,760
<i>Coccidioides immitis</i>	Ascomycota	Onygenales	Onygenaceae	Humans	Coccidioidomycosis (valley fever)	GCA_004115165.2	27.474	3,797	7,815
<i>Chrysosporium queenslandicum</i>	Ascomycota	Onygenales	Onygenaceae	-	Non-pathogenic	GCA_001430955.1	32.335	173	11564*
<i>Microsporium canis</i>	Ascomycota	Onygenales	Arthrodermataceae	Humans, animals	Dermatophytosis	GCF_000151145.1	23.263	2,919	8,765
<i>Trichophyton rubrum</i>	Ascomycota	Onygenales	Arthrodermataceae	Humans	Dermatophytosis	GCF_000151425.1	22.530	2,156	8,706
<i>Trichophyton equinum</i>	Ascomycota	Onygenales	Arthrodermataceae	Humans, horses	Dermatophytosis	GCA_000151175.1	24.158	397	8,676
<i>Nannizzia gypsea</i>	Ascomycota	Onygenales	Arthrodermataceae	Humans, animals	Dermatophytosis, onychomycosis	GCF_000150975.2	23.272	3,227	8,921
<i>Paracoccidioides brasiliensis</i>	Ascomycota	Onygenales	Ajellomycetaceae	Humans	Paracoccidioidomycosis	GCF_000150735.1	29.952	2,149	8,390
<i>Blastomyces dermatitidis</i>	Ascomycota	Onygenales	Ajellomycetaceae	Humans, animals	Blastomycosis	GCA_000151595.1	73.633	400	11,443
<i>Pseudogymnoascus destructans</i>	Ascomycota	Incertae sedis	Pseudeurotiaceae	Bats	White-nose syndrome	GCF_001641265.1	35.818	1,168	9,405
<i>Saccharomyces cerevisiae</i>	Ascomycota	Saccharomycetales	Saccharomycetaceae	-	Non-pathogenic	GCF_000146045.2	12.157	924	6,002
<i>Candida albicans</i>	Ascomycota	Saccharomycetales	Saccharomycetaceae	Humans	Candidiasis	GCF_000182965.3	14.282	2,231	6,030
<i>Aspergillus fumigatus</i>	Ascomycota	Eurotiales	Trichocomaceae	Humans	Aspergillosis	GCA_000002655.1	29.384	3,948	9,630
<i>Cryptococcus neoformans</i>	Basidiomycota	Tremellales	Tremellaceae	Humans	Cryptococcosis	GCF_000091045.1	19.051	4,438	6,863
<i>Batrachochytrium dendrobatidis</i>	Chytridiomycota	Rhizophydiales	Batrachochytriaceae	Amphibians	Chytridiomycosis	GCF_000203795.1	24.315	1,484	8,677

* Gene annotations produced in this study.

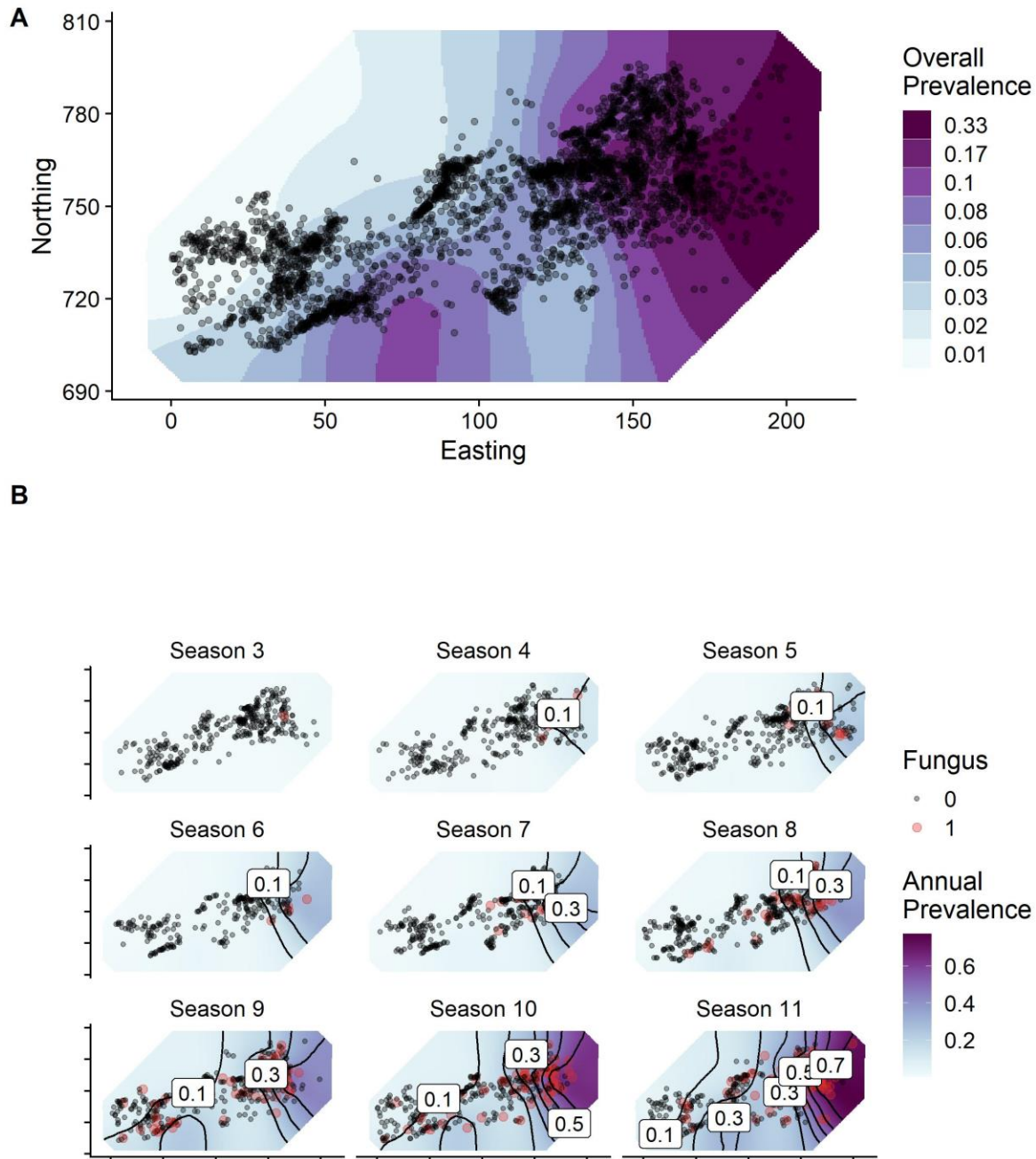


Fig. 2. Spatial distribution and temporal spread of *N. barbatae* infection within the population. These are represented as the spatial distribution of the spatial random effect from the Spatial model (A) and the annually stratified Spatiotemporal model (B), respectively. The spatial effects were estimated using a stochastic partial differentiation equation (SPDE) in an integrated nested Laplace approximation (INLA) model. Adding these SPDE components substantially

improved model fit. In (A), points represent individuals' average annual locations. The axes in (B) are identical to those in (A), with the labels removed for plotting clarity. In (A), the spatial effect is categorized into eight quantiles to facilitate visualization over a range of prevalence values.

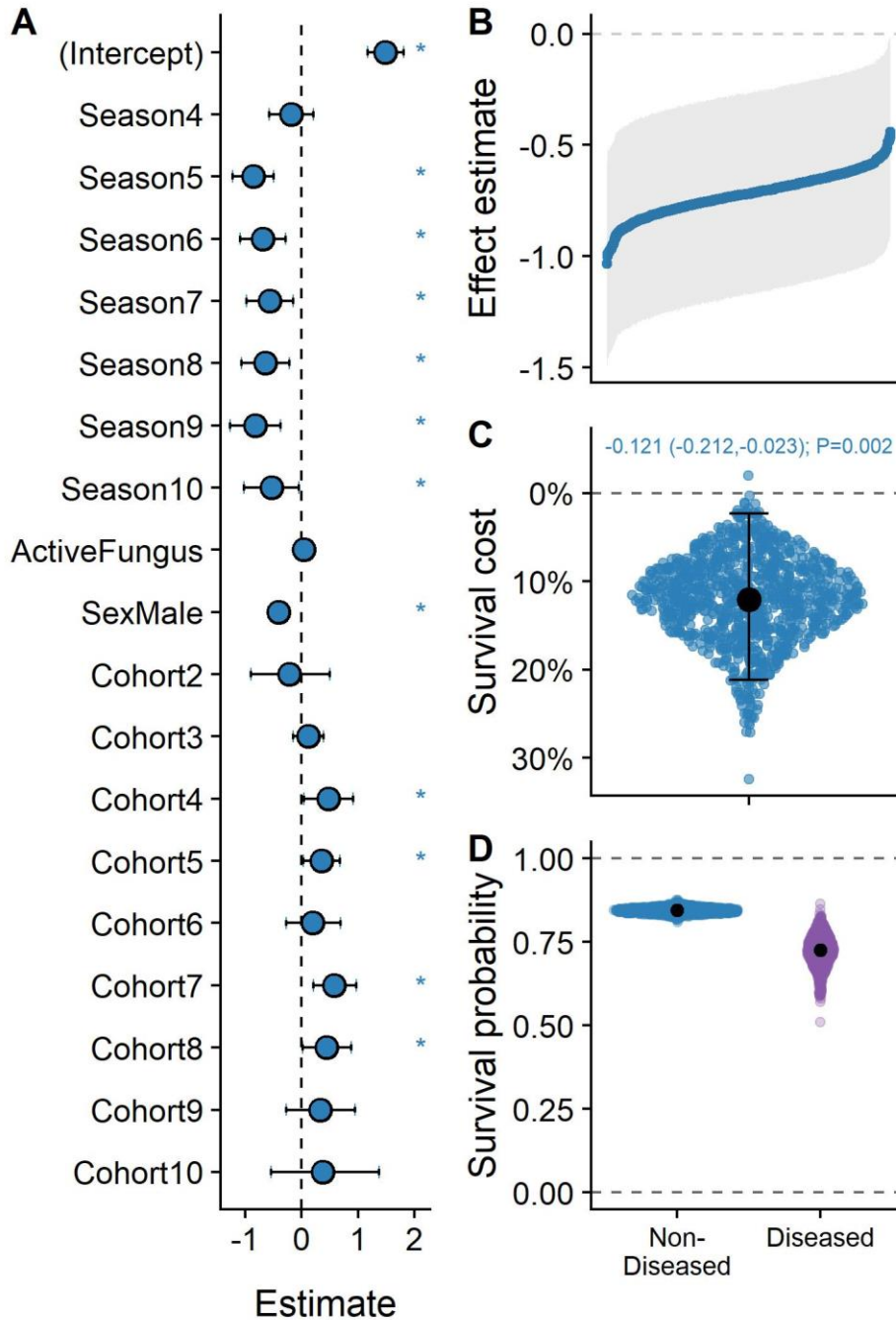


Fig.3. Survival effects of *N. barbatae* infection in the population. Survival effects of the disease are estimated using a full-population model (A), and an approach combining model uncertainty and subsampling regime uncertainty (B, C, D). The second approach provided estimates of survival effects across all subsamples (B) and survival costs (C) and probabilities (D) of diseased

vs. non-diseased individuals. The large black points represent means across all 1000 replicates. The text at the top of panel C displays the effect estimate for the survival cost across all models, with 95% credibility intervals in brackets and the P value. The error bars represent the 95% credibility intervals.