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A 5-year *Chlamydia* vaccination programme could reverse disease-related koala population decline: Predictions from a mathematical model using field data

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ABSTRACT

Background: Many koala populations around Australia are in serious decline, with a substantial component of this decline in some Southeast Queensland populations attributed to the impact of *Chlamydia*. A *Chlamydia* vaccine for koalas is in development and has shown promise in early trials. This study contributes to implementation preparedness by simulating vaccination strategies designed to reverse population decline and by identifying which age and sex category it would be most effective to target.
Methods: We used field data to inform the development and parameterisation of an individual-based stochastic simulation model of a koala population endemic with *Chlamydia*. The model took into account transmission, morbidity and mortality caused by *Chlamydia* infections. We calibrated the model to characteristics of typical Southeast Queensland koala populations. As there is uncertainty about the effectiveness of the vaccine in real-world settings, a variety of potential vaccine efficacies, half-lives and dosing schedules were simulated.
Results: Assuming other threats remain constant, it is expected that current population declines could be reversed in around 5–6 years if female koalas aged 1–2 years are targeted, average vaccine protective efficacy is 75%, and vaccine coverage is around 10% per year. At lower vaccine efficacies the immunological effects of boosting become important: at 45% vaccine efficacy population decline is predicted to reverse in 6 years under optimistic boosting assumptions but in 9 years under pessimistic boosting assumptions. Terminating a successful vaccination programme at 5 years would lead to a rise in *Chlamydia* prevalence towards pre-vaccination levels.
Conclusion: For a range of vaccine efficacy levels it is projected that population decline due to endemic *Chlamydia* can be reversed under realistic dosing schedules, potentially in just 5 years. However, a vaccination programme might need to continue indefinitely in order to maintain *Chlamydia* prevalence at a sufficiently low level for population growth to continue.

1. Introduction

The numbers of koalas (*Phascolarctos cinereus*) around Australia are decreasing, with populations in the states of Queensland, New South Wales and the Australian Capital Territory recently listed as vulnerable by the Australian government. A panel of experts estimated that the number of koalas in Southeast Queensland has declined by 51% over the past three generations (15–21 years) [1], and by 51% in the three years up to 2008 in the Koala Coast [2].

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The main reasons for population declines are habitat loss and fragmentation, vehicle collision mortality, dog attack and disease [2]. Of these, the largest contributor in situations where ongoing habitat loss is not a major factor is likely to be disease, mostly attributable to severe sequelae from chlamydial infections. It has been estimated that a 59% reduction in the disease mortality rate of a presently declining koala population in Southeast Queensland would stabilise the population [3].

Chlamydia is highly prevalent in many koala populations in eastern Australia. The largest survey yet conducted found prevalence rates of *C. pecorum* ranging from 20% to 61% in eight wild populations [4]. The amount of associated disease varies, being commonly observed in Queensland and New South Wales but less frequently in Victoria and South Australia [5–8]. Sequelae arising from chlamydial infection include blindness and sterility [9], and koalas may die as a result of infection [10]. Research into koala *Chlamydia* vaccines is yielding positive results, with the development of an effective prototype vaccine demonstrated to be safe in early trials [11,12]. The expected efficacy and rate of waning of this vaccine when implemented in koala populations is not yet known, but a field trial is underway in Queensland. Although high protective efficacy is often assumed to be required of an effective vaccine, this is not necessarily the case: modelling of a human immunodeficiency virus vaccine has suggested that a vaccine with just 30% efficacy might avert 33–36% of infections in South Africa [13].

In this study, we aim to assist in planning for vaccine programme implementation by simulating the impact of various vaccine deployment strategies on Southeast Queensland koala populations in decline due to the effects of chlamydial disease. This is done to estimate the minimum vaccine characteristics (efficacy and waning levels) in combination with population coverage levels and dosing intensities that would be necessary in order to reverse population declines. We also aim to identify the most efficient programmatic strategies in terms of targeting koalas of specific age, sex and mass categories to attain maximal population impact. These simulations are based on a novel individual-based model of *Chlamydia*–koala population dynamics.

Based on the Koala Coast's estimated population size of 2279 koalas in 2008 and an approximate population halving time of three years [2], we simulate a koala population of around 500 koalas. We assume that it is decreasing in size due to *Chlamydia*-related disease, as seen in Southeast Queensland. We calibrate the prevalence of infection, the prevalence of disease and the rate of decline of the population to be the same as those estimated for a field trial group in Southeast Queensland, and assume that habitat area and other potential sources of impact remain constant over the vaccine deployment period. Not all koala populations fit this profile of disease-driven decline, but it is precisely these declining populations in which a *Chlamydia* vaccine would be deployed and thus it makes sense to model these populations.

2. Materials and methods

2.1. Data sources

We informed the structure and parameterisation of the model by reference to the published literature and to field data. Male body mass has been found to be correlated with annual reproductive output [14], so we hypothesised that targeting large males for capture and vaccination may be an effective vaccination strategy. In order to incorporate mass into the model, we generated age/mass growth curves using data from a sample of 38 male koalas, captured in the wild around Brisbane, Queensland [15].

2.1.1. Model

We developed a stochastic individual-based model, run with monthly time steps. Koalas in the model were categorised as susceptible, infected or recovered. Recovered koalas have some temporary natural immunity to reinfection [10]. Disease in the model is temporary (with associated temporary infertility in females), permanent (with associated permanent sterility in females) or fatal [10,16,17]. See Supplementary material for further details, and Table 1 for input parameters.

2.1.2. Modelled vaccine scenarios

We assumed that vaccination would confer some immunity of partial efficacy, which would then wane exponentially over time. We simulated vaccines with average protective efficacy over five years of 35–75%. We assumed that a vaccine would have a probability of resolving an existing infection equal to its initial efficacy. We considered vaccines that protected against infection and development of disease. We also considered the potential effect of boosting (i.e., vaccinating a previously vaccinated koala) to increase the initial protective efficacy up to 100% or back to the initial efficacy level; and whether mating with an infected koala acted as a boost for a previously vaccinated koala.

Simulated koala capture and vaccine coverage levels and frequencies were based on experience in the field to inform what is likely to be feasible. We assumed three capturing rates, being around 10, 15 and 20% captures/vaccinations annually as a percentage of the original 500-koala population. We assumed that on capture, diseased koalas would be taken to hospital and given antibiotics (assumed to always resolve infection) if *Chlamydia*-positive. Those with terminal illness would be euthanised; all captured koalas not euthanised would be vaccinated. Another programmatic variation included in secondary analyses was the provision of antibiotics to *Chlamydia*-positive captured koalas in addition to the vaccine.

We investigated scenarios in which koalas of specific age, sex and mass categories were targeted for vaccination. The individuals captured and vaccinated were chosen at random from the targeted koalas. We assumed that 16% of the koala population could not be located at any given time [18].

2.1.3. Model implementation and calibration

The model was implemented in Matlab, using some third-party functions [19,20]. Calibration involved choosing 100,000 parameter sets from a Latin hypercube sample of the parameter space, and then using a two-stage Monte Carlo filtering process. The first stage consisted of simulating *Chlamydia*-free populations, and retained only those parameter sets that resulted in the population remaining stable or growing with a doubling time greater than or equal to 2.7 years [21] (the fastest doubling time we found in the literature). The second stage considered the infection parameters, and involved simulating an infected population; parameters retained were those that produced a population halving time of between 5 and 10 years, with chlamydial infection and disease prevalence between 35 and 70%, as is estimated for the field trial population.

Of the parameter sets that passed both stages of calibration, 100 were randomly selected and each vaccine scenario was simulated over all of these retained parameter sets. Further details are provided in the Supplementary material.

3. Results

In Fig. 1 we show the time course predicted in the absence of an intervention, and by comparison, the administration of a *Chlamydia* vaccine with a 75% average efficacy over 5 years administered to around 10% of koalas every year (as a percentage of the initial population). Optimistic boosting assumptions are made: that is, that

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