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Corresponding author mail-id:elkelly@student.unimelb.edu.au

How many, and when? Optimising targeted gene flow for a step change in the environment

Optimising targeted gene flow for conservation

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Targeted gene flow is an emerging conservation strategy that involves introducing individuals with particular traits to places where these traits are of benefit. One obvious application is to adapt a recipient population to a known threat, but questions remain as to how best to achieve this. Here, we vary timing and size of the introduction to maximise our objective – survival of the recipient population’s genome. We explore a generic population model as well as a specific example – the northern quoll, an Australian marsupial predator threatened by the toxic cane toad. We reveal a trade-off between preserving the recipient genome and reducing population extinction risk, but key management levers can often optimise this so that nearly 100% of the recipient population’s genome is preserved. Any action was better than none but the size of the benefit was sensitive to outbreeding depression, recombination rate, and the timing and size of the introduction.

Keywords: conservation genetics; evolutionary rescue; assisted gene flow; population modelling; population viability analysis

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Corresponding author: Ella Kelly: Biosciences 4, The University of Melbourne, Parkville, Australia 3010

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Abstract

Targeted gene flow is an emerging conservation strategy that involves introducing individuals with particular traits to places where these traits are of benefit. One obvious application is to adapt a recipient population to a known threat, but questions remain as to how best to achieve this. Here, we vary timing and size of the introduction to maximise our objective – survival of the recipient population’s genome. We explore a generic population model as well as a specific example – the northern quoll, an Australian marsupial predator threatened by the toxic cane toad. We reveal a trade-off between preserving the recipient genome and reducing population extinction risk, but key management levers can often optimise this so that nearly 100% of the recipient population’s genome is preserved. Any action was better than none but the size of the benefit was sensitive to outbreeding depression, recombination rate, and the timing and size of the introduction.

Main Text

Introduction

Rapid environmental change is causing declines in biodiversity across the globe (Barnosky *et al.* 2011), and as threats become harder to mitigate, threatened species must adapt to survive (Hoffmann & Sgrò 2011). Existing genetic variation in relevant traits coupled with strong selection imposed by a threatening process may allow some populations to rapidly adapt; staving off extinction through evolutionary rescue (Bolnick *et al.* 2011; Sih *et al.* 2011). Unfortunately, for many threatening processes, beneficial traits are either locally absent or at low frequencies, and this makes extinction more likely than evolutionary rescue (Gomulkiewicz & Holt 1995; Frankham 2015). Targeted gene flow has emerged as a conservation strategy for helping promote these favourable traits in threatened populations (Kelly & Phillips 2016). This strategy involves translocating individuals with key traits to areas where the traits would have a conservation benefit.

Although targeted gene flow is being explored with regard to climate change (“assisted gene flow”, e.g., Aitken & Bemmels 2016), it has yet to be robustly assessed: climate change is a relatively slow change, making assessment difficult. Targeted gene flow, however, could provide benefits for populations facing more rapidly-acting threats, such as disease and invasive species. Here it can enhance the capacity of these populations to adapt to predictable, imminent changes in their environment, and so skew outcomes towards evolutionary rescue rather than extinction (Kelly & Phillips 2016). Targeted gene flow is similar to the idea of genetic rescue, where populations of low genetic diversity are bolstered by the introduction of individuals from elsewhere, however targeted gene flow aims to increase the proportion of specific traits instead of just increasing genetic variance in a non-directed way (Tallmon *et al.* 2004; Whiteley *et al.* 2015; Frankham *et al.* 2017). By increasing the chance of evolutionary rescue, we also promote the persistence of the local genome: the aim being to manipulate populations so that they are not only locally adapted, but also carry genes that allow them to survive the current threat (Kelly & Phillips 2016; Ralls *et al.* 2017).

Here, we address questions on the implementation and risks of targeted gene flow using a population viability analysis that incorporates micro-evolutionary process. Conservation managers considering any adaptive relocation must decide on the optimal timing for their translocation, as well as the composition of the introduced cohort (McDonald-Madden *et al.* 2011). Targeted gene flow is no different, with timing and number of introductees likely to have large effects on the benefits for conservation. This presents managers with a “management space” within which we seek the optimum solution. Evolutionary processes clearly have strong influences on population persistence, but are rarely included in models of population viability (Pierson *et al.* 2015). For those models that do incorporate rapid evolution, few look at the potential impact of outbreeding depression (Frankham *et al.* 2011), and none have yet assessed the potential use of targeted gene flow (Frankham *et al.* 2017). For any conservation action, it is wise to assess the action prior to implementation – particularly to determine the best way to implement the strategy, and to assess possible negative effects (Coulson *et al.* 2001). We addressed these key aspects of conservation decision making (timing and number of introductees) in our model. We also examined how key uncertainties (i.e. population dynamics, outbreeding depression, recombination rate) changes outcomes.

We seek a strategy that, within our management space (timing and size of introduction), maximises expected return for conservation. To identify this strategy requires a clear statement of our management objective (Regan *et al.* 2005). In our case we would like to keep our recipient population extant, but we would like to do so without replacing the local genome. Replacing the local genome with a genome from elsewhere is equivalent to a reintroduction, but one of the main potential benefits of targeted gene flow is the possibility that we preserve local genetic diversity. A sensible objective, then, is analogous to a gambler’s expected return: the probability of winning, multiplied by the payout. In our case the payout is the proportion of the recipient population’s genome still extant, (calculated as mean proportion of recipient genome within each individual; $\bar{r}_i$), and our probability of winning it, $1 - x$, where x is the extinction probability. Thus, our objective is to maximise the expected return:

$$E(Y) = \bar{r}_i(1 - x)$$

The problem here is a general one: how does varying key management levers (timing and number of introductees) influence the expected return of targeted gene flow following a stepwise change in the environment? A step change, where the environment goes from one state to another, is the simplest possible example to begin to explore these ideas. This could be applicable to any population dealing with a rapid change in their environment (i.e. arrival of a disease or invasive predator), where the population has some proportion of individuals who are resistant to the threat. While modelling evolutionary response to a step change is possible (e.g. Gomulkiewicz & Holt (1995)), modelling population response following targeted gene flow is complicated by the non-normal trait distribution, and linkage disequilibrium that results from the introduction. These issues render an analytical model intractable, so we require an individual-based population model to examine this idea. We execute this here, exploring the idea of targeted gene flow with a generic population model and a generic adaptive trait, and then grounding the ideas in reality with a particular case study – the endangered carnivorous marsupial, the northern quoll (*Dasyurus hallucatus*) and the arrival of toxic cane toads.

Northern quolls are a potential candidate for targeted gene flow: they are threatened by the invasion of the toxic cane toad (*Rhinella marina*) because quolls unknowingly eat the toxic toads and are fatally poisoned (Tingley *et al.* 2017). The great majority of quoll populations (more than 95%) go extinct after the large step-change in their environment caused by the arrival of cane toads (EPBC 1999). Cane toads continue to spread westward, and will eventually inhabit the quolls' entire range (Tingley *et al.* 2017). Evidence suggests a small number of scattered populations have adapted to the threat (Kelly & Phillips 2017, 2018) by evolving to avoid toads as prey. Recent work shows the behaviour has a heritable basis (Kelly & Phillips 2018). It is this "toad-smart" behavioural trait that we can make use of with targeted gene flow.

Here, we optimise targeted gene flow following a step change in the environment for both a generic individual-based population model and one whose demographic sub-model has been rendered specific to northern quolls. We use a population viability analysis, to explore our management space (timing of the introduction and size of the introduced cohort) to maximise the expected return for conservation.

Methods

We developed two discrete-time individual-based population models. The first was a generic model, with generalised population dynamics. We then used northern quolls as an example to apply the model to a specific scenario. The models differ only in their population dynamics: the mechanics of sexual reproduction and trait inheritance remained consistent across both. In both models we introduced a stepwise change in the environment, an arrival of a threat that imposed hard selection – in the quoll model this represented the arrival of toads. The step change led to selection-driven mortality imposed only in the first year juvenile stage. Animals surviving this event were considered to have survived the threat thereafter. For both models we explored assumptions using a sensitivity analysis of key parameters.

Population dynamics

The two models – the generic population model and the northern quoll specific model – differed only in their population dynamics. The general population model was developed using the Beverton–Holt model of density dependence (Beverton & Holt 2012). For the quoll model, we gave individuals age- and sex-specific annual survival and fecundity rates, and imposed density dependence on juvenile survival.

Generic population model

Individuals in the generic population have a maximum rate of reproduction, R_{max} , modified by density dependence, described using the Beverton–Holt model (Beverton & Holt 2012), which yields their expected reproductive output, $E(W)$:

$$E(W) = \frac{R_{max}}{1 + \left(\frac{R_{max} - 1}{N^*} N\right)}$$

In this formulation, N is the number of individuals in the population. N^* represents the carrying capacity that would be achieved if all individuals achieved a fecundity of R_{max} . We set $R_{max} = 3$ and $N^* = 500$, but also ran a sensitivity analysis on R_{max} and N^* to determine the

impact of population dynamics on our results (see Scenarios). All individuals are treated as sexual hermaphrodites and all have the chance to breed with a randomly selected mate. The population is considered an annual species, with individuals only living for one breeding season (survival = 0 for all individuals over one year of age).

Northern quoll population model

The northern quoll population model is more complex, grounded in demographic data collected by previous studies. It incorporates survival rates that differ by sex and age. Within time intervals, reproduction (including pre-weaning survival of babies) is followed by survival of juveniles and adults. Baseline survival probabilities and fecundity were inferred for this model using the average of values drawn from the literature, and density dependence (driven by density of adult females) acted on the probability that offspring survived to weaning (full details in supplementary material; Table S1).

Sexual reproduction

In both the generic and northern quoll-specific population models the animal's genotype consists of a number of diploid, biallelic loci. A number of loci, n_p , contribute to the organism's phenotype; n_c are involved in incompatibility; and another subset n_n were neutral and used to track the recipient genome (see below). Each offspring from each pair inherits a genotype determined by the fusion of gametes from the sire and dam. In all cases, a gamete is the result of random recombination of the parent's genotype into haploid form. All loci are randomly placed on a chromosome (represented as a line from 0 to 1) at the beginning of a simulation (so that, across simulations we integrate over all possible linkage arrangements). For each gamete, random cuts are made to produce a recombined haploid genome. Genome-wide pairwise recombination rate was calculated as the average proportion of pairwise crossover events between loci. We manipulated recombination rate by adjusting the expected number of cuts made (actual number drawn from a poisson distribution). In the primary models, we set the expected number of cuts on the chromosome to 50 to simulate an approximately 0.5

recombination rate (based on 30 loci). We also explored a lower recombination rates (0.25, set by 1.33 cuts) in the sensitivity analysis (see supplementary material).

Evolutionary dynamics

Each individual expresses a continuous trait, A , determining whether or not the individual survive the threat (generic, or toads for the northern quoll model), or not. Thus, A experiences threshold selection. The trait is determined by the animal's genotype, and also by environmental variation according to the underlying mechanisms of a simple quantitative genetic model in which the total phenotypic variance is the sum of genetic and environmental contributions: $V_T = V_G + V_E$. Within all our simulations, the environmental variation imposed on the trait remains constant ($V_E=1$).

The genotype and expected trait value

A specified number of loci, n_p , contribute to the organism's phenotype. Each phenotype-influencing locus has an equal additive effect on the individual's expected trait value, $E(A)$. Two alleles are possible at each locus, with alleles having an additive effect size of either 0, or e , where e represents an increment towards being fitter after the environmental step-change (more toad-smart in the quoll model). The effect size, e is calculated as a function of the environmental variance (V_E), and the heritability (h^2), and is chosen such that the stated heritability is achieved at initialisation given the stated environmental variance and number of loci. Under a simple quantitative genetic model (with no dominance or epistasis),

$$h^2 = \frac{V_G}{V_G + V_E}$$

or equivalently,

$$V_G = \frac{h^2 V_E}{1 - h^2}$$

Under a binomial distribution, the expected genetic variance is,

$$V_G = 2e^2 n_p f_0(1 - f_0),$$

where f_0 is the initial frequency of favourable alleles (i.e., those with effect sizes of e). Thus, at initialisation, our effect size can be calculated as:

$$e = \sqrt{\frac{h^2 V_E}{2n_p f_0 (1 - h^2) (1 - f_0)}}$$

An individual's genotypic value (its expected phenotype) is then:

$$E(A_i) = e \sum_{j=1}^{n_p} \sum_{k=1}^2 a_{ijk}$$

where a_{jk} references the allelic value (either 0 or 1) at allele k of locus j . i indexes the individual.

In the results presented here, the heritability of the trait in the recipient population (h^2) was set to 0.2, based on the estimate of behavioural trait heritability given by Roff (2012). We explored the impact of h^2 in the sensitivity analysis (Fig. 3 & S3). We assume that the population initially has low mean fitness with regard to the threat, and that alleles conferring threat-adapted behaviour are rare in the population. We set the initial frequency of threat-adapted alleles in our recipient population, $f_0 = 0.05$.

The phenotype

An individual's realised phenotypic value, A_i incorporates environmental variation on the expected trait value, and is determined stochastically, as a draw from the normal distribution.

$$A_i \sim N(E(A_i), V_E)$$

Selection

The model implements threshold selection in which all individuals with trait values for $A_i \leq A^*$, will be killed prior to breeding, while all individuals with $A_i > A^*$ will survive. The selection threshold, A^* , is defined as the $(1 - \bar{w}_0)$ th quantile of the initial expected phenotype distribution, where $\bar{w}_0$ is the initial post step-change fitness at a population level. $\bar{w}_0$ was

determined by running the simulations with different values of $\bar{w}_0$ to get the model to generate an observed population extinction rate (with no management intervention) of 0.95 after the stepwise change. Selection threshold is determined as a function of the environmental variance and the heritability at initialisation. Therefore values of $\bar{w}_0$ varied based on these parameters and are presented in Table S2 & S3. The expected phenotype distribution is,

$$N(2en_p f_0, V_T)$$

Where V_T is the total phenotypic variation, $V_G + V_E$.

As is likely the case in reality (small population sizes and short time spans), selection acts on this standing variation in the population; we do not consider mutation important (Elena *et al.* 2007).

Loci involved with incompatibility

To allow us to incorporate outbreeding depression, each individual also carries n_c loci involved with incompatibility. These loci carry fixed differences between recipient (=0) and introduced (=1) populations.

These loci were used to implement outbreeding depression using the model of two-locus incompatibilities developed by (Turelli & Orr 2000). This model encapsulates the idea that lowered hybrid fitness can be explained by between-locus Dobzhansky-Muller incompatibilities. The Turelli and Orr model includes three types of incompatibilities: those between heterozygous loci (H_0), those between a heterozygous and a homozygous (or hemizygous) locus (H_1), and those between homozygous loci (H_2). Using this model, we determine the “hybrid breakdown score” $E(S)$ of each individual based on the composition of alleles in their set of loci involved with incompatibility (proportion of loci that are homozygous from population 1 (p_1), the proportion that are homozygous from population 2 (p_2), and the proportion that are heterozygous for material from the two populations (p_H)). Following Turelli and Orr, the hybrid breakdown score is given as,

$$E(S) = n_c[p_1p_2h^2 + (p_1 + p_2)p_Hh_1 + p_H^2h_0]$$

where n_c is the number of loci that are contributing to incompatibilities. We then used a simple negative exponential function to link hybrid breakdown score to fitness,

$$s_h = e^{-\alpha E(S)}$$

where α is a constant value, and s_h is the probability of survival from outbreeding depression. When outbreeding depression is activated in the model, all baseline survival probabilities are multiplied by individual s_h values, and survival is then determined by a draw from a Bernoulli distribution with the resultant survival probability.

We used simple dosage ratios for the different classes of incompatibilities: $(H_1) = 0.5$, $(H_2) = 1$ and $(H_0) = 0.25$, to generate the hybrid breakdown score. We then varied the value of α in the fitness function to manipulate the strength of outbreeding depression.

Neutral loci

To track the proportion of the recipient population's genome remaining, we also initialised n_n neutral loci, also carrying fixed differences between recipient (=0) and introduced (=1) populations. We measured changes in the recipient genome in two different ways — the first ($\bar{r}_i$) was calculated as the proportion of recipient population alleles within each individual, averaged over all individuals in the population. This was used, along with probability of extinction (x) to calculate the expected return of our management objective ($E(Y)$: the proportion of the local genome surviving) for each scenario. Therefore, maximum expected return equated to the population with the highest proportion of recipient genome likely to survive the threat (calculated by $E(Y) = \bar{r}_i(1 - x)$).

$\bar{r}_i$, however, underestimates the true proportion of the recipient genome still extant in the population, because the original genome will be scattered across individuals within the population. Therefore, we also calculated r_p , the proportion of loci which retained recipient alleles across the population. This gives us the true estimate of recipient genome retention, because it counts alleles even when they are at low frequency. While r_p is the true proportion of the recipient genome still extant, it will likely decline over time due to loss of rare alleles

through drift. Because of this, we ran our optimisation using the more conservative metric, $\bar{r}_i$, and make a comparison of the two metrics using the generic population model (Fig. S2).

Scenarios

All our scenarios begin with an initially poorly adapted population of N individuals — our “recipient population” (where N = carrying capacity – for generic model $N = N^*$, and for the quoll model $N = K$). The recipient population is initiated with initial fitness of $\bar{w}_0$ where post step-change probability of extinction with no management is 95% (Table S2 & S3). The number of loci was set to 30 ($n_c = 10$ relating to incompatibility, $n_p = 10$ relating to the trait and $n_n = 10$ neutral loci). Carrying capacity of breeding individuals (N^* or K in generic and quoll models respectively) was set to 500. The recipient population was allowed to grow for 30 years before the step change in the environment, which happens at the beginning of a generation. For the quoll model, this sudden change reflects the reality of toad arrival (Phillips 2007).

In each scenario we recorded whether the population went extinct or not over 50 years following the step change. For populations that survived we also calculated the proportion of the recipient population’s genome remaining. Using these measures, we calculated the expected return — the proportion of recipient genome likely to survive the step change.

Targeted gene flow

To simulate targeted gene flow we introduced a number of threat-adapted individuals to our recipient populations prior to reproduction in a specified year. Our “source population” was a threat-adapted population, initialized with $f_0 = 0.9$, age = 1, and (in the quoll model) sex randomly allocated. We explored a management space, varying the timing of introduction and the number of introducees: introduction times ranged from ten years prior to ten years post the step change (in 1 year increments); and the proportion of threat-adapted individuals introduced ranged from 0 - 0.3 in 0.02 increments. This proportion was converted to number of individuals introduced by multiplying by the carrying capacity of the population and rounding down to the nearest whole number. For our standard population size (carrying capacity = 500) this meant we introduced a range of 0-150 threat-adapted individuals. We ran 100 simulations

for each scenario to estimate extinction probability, x , and the proportion of the recipient genome remaining, $\bar{r}_i$ or r_p (averaged over the 100 simulations).

Sensitivity analysis

The above scenario was repeated across a broad sample of parameter space to produce a global sensitivity analysis around key parameters (Table S2 & S3).

For the generic model we systematically sample the 3-dimensional parameter space in a fully factorial design to determine the impact of varying carrying capacity (N^*), growth rate (R_{max}) and heritability (h^2) on model output (Table S2; 27 parameter sets). For each parameter set, we explore the full management space and record the maximum expected return ($E(Y)_{max}$) as well as where in the management space this maximum occurred.

For the northern quoll model we ran the global sensitivity analysis on just carrying capacity (K) and trait heritability (h^2 ; Table S3). We sampled this 2-dimensional parameter space (9 parameter sets), and again for each parameter set record the maximum expected return ($E(Y)_{max}$), and the management strategy that delivered the maximum expected return.

For both models, we also examined the impact of outbreeding depression (leading to lowered fitness of hybrids) and lower recombination rate. For the scenarios with increased outbreeding depression we ran the simulations described above (“Scenarios”) but added in varying recombination rates and strengths of outbreeding depression. We set outbreeding depression to have a low and high impact on hybrid individuals by reducing the fitness of F1 hybrids by 10% and 50% of baseline fitness. This was achieved by changing the value of α that converts hybrid breakdown score into fitness (10% reduction in F1 hybrids $\alpha=0.04$; 50% reduction in F1 hybrids $\alpha=0.28$). For recombination rate, we lowered pairwise recombination rate from 0.5 to 0.25 by reducing the number of cuts on the chromosome. In the generic model, we also explored the combined effect of recombination rate and outbreeding depression (10% and 50% reduction in hybrid fitness combined with 0.25 recombination rate; Table S2 & S3).

Model simulations were implemented in R (Team 2016) and run using *Spartan*, a High Performance Computing system operated by Research Platform Services at The University of

Melbourne (Lafayette *et al.* 2016). All code and model output is available at <https://github.com/elkelly/TGFquolls>.

Results

We found that the success of targeted gene flow was strongly influenced by the timing of the introduction, and the proportion of individuals introduced (Fig. 1 & 2). The results varied between the two population models (generic and quoll), however a general pattern did emerge. Our management objective (Y) was optimised when a larger proportion of individuals ($> 0.1 \times$ carrying capacity) were introduced in the years immediately preceding the step change (Fig. 1 & 2).

Although this pattern remained relatively consistent, adjusting population parameters did alter the effectiveness of targeted gene flow, and the optimal management strategy (Fig. 3 & Fig. S3 - S5). From the global sensitivity analysis conducted on the genetic population model, we were able to capture these trends (Fig. 3). We found that as population size (N^*) increased, the effectiveness of targeted gene flow increased. For scenarios with a higher population size ($N^* = 500$ or 1000) our maximum expected return was higher, and we required a small proportion of threat-adapted introducees to gain this benefit. Changing the growth rate of a population (R_{max}) had little effect on the outcome of targeted gene flow (Fig. 3). Heritability (h^2) also impacted the success of the management action, with higher heritability leading to an increase in population survival – particularly in small populations, driving an increase in expected return (Fig. 3). These broad patterns were also seen in the sensitivity analysis for the northern quoll population model (Fig. S3), suggesting they are consistent trends robust to population dynamics.

Generally, outbreeding depression reduced the success of targeted gene flow in both models. 10% reduction in fitness produced relatively similar results to no outbreeding depression, however a 50% reduction in fitness increased the probability of extinction and decreased the proportion of recipient population genes, reducing the proportion of scenarios with a high value of Y (Fig. 4 & Fig. S1). Outbreeding depression also drove optimal timing towards later

action: with weak outbreeding depression the introduction needs to happen closer to the step change to effect high returns; with extremely high outbreeding depression, the optimal timing occurs after the step change (Fig. S1). Lowering recombination rate led to a lower retention of the recipient genome, and thus lower overall expected returns for both the generic and quoll population model (Fig. S4). The combined affect of high outbreeding depression and low recombination rate caused extremely low expected returns (though still better than no action; Fig S5).

Discussion

Our model demonstrates that our management objective – retention of the recipient population and genome, Y – is sensitive to the timing and size of the introduction. There is also an apparent trade-off between maintaining the local recipient genome, and population survival. Generally, a larger number of introductees in the years immediately preceding and following the stepwise threat produce the lowest probability of extinction, but this also produces lower retention of the recipient genome. The trade-off can be optimised, however, with the highest expected return when we introduce a higher proportion of pre-adapted individuals prior to the arrival of the threat. This strategy produces hybrids in the years prior to the step change so that when selection begins, individuals who carry the recipient genome as well as resistant genes survive. These more optimal strategies retained almost 100% of the recipient population alleles spread across the genome (r_p). Our results fit with previous assessments of assisted colonisation (that do not consider evolution) that show the timing and number of introductees to be primary considerations for conservation managers undertaking such endeavours (McDonald-Madden *et al.* 2011).

Despite difference in population dynamics, the optimal strategy for targeted gene flow was similar for both the generic population model and specific northern quoll model. This indicates that the underlying trade-off between timing and size of the introduction is likely a general one. The specific population dynamics still play an important role in determining the best course of action, however. For instance, implementing targeted gene flow after the step change exhibited

low returns in the generic model. Here, individuals only breed for one year, so the population cannot sustain itself under selection for as long as in the quoll model, which had individuals breeding over multiple years. This suggests that timing of an introduction will perhaps be particularly sensitive in short lived species.

The importance of population dynamics was further demonstrated when we considered broader parameters in our global sensitivity analyses. For instance, carrying capacity had a major bearing on the effectiveness of targeted gene flow, with larger populations generating a substantially higher return than small populations. This result matches theoretical expectations in that larger populations are less affected by stochastic processes. As such, natural selection is more effective in these populations, and they are less prone to stochastic extinction processes (Lande 1993; Charlesworth 2009). By contrast to carrying capacity, growth rate (explored only in the generic model), had only a minor impact on expected return. This result may reflect model assumption in that we chose initial fitness levels guaranteed to generate 95% extinction probability for each growth rate, and relative fitness in our model was predicated on survival rather than reproductive rate. While the effect of growth rate may be larger than we unearth here, in reality managers focussing on a particular species may get to choose among sites varying in carrying capacity, but will have substantially less choice with regard to growth rate. Finally, heritability of the threat-adapted trait also affected returns, with less heritable traits causing an increased chance of extinction (particularly in small populations). This is unsurprising given heritability determines the response to selection, but there are still some management strategies that are effective even under low heritability. Overall, targeted gene flow decreased extinction probability, and this is consistent across all scenarios.

There is, however, an oft-cited risk when hybridising populations: outbreeding depression can reduce population fitness (Edmands 2007; Frankham *et al.* 2011). Reduced fitness in hybrids could arise from breakdown of local adaptation, or from genetic incompatibilities, both of which are difficult to predict (Frankham *et al.* 2011). Our model incorporated the possibility of genetic incompatibilities and showed outbreeding depression generally reduced the success of targeted gene flow. These results are unsurprising: we have introduced both a barrier to introgression and a mechanism for reducing fitness. Importantly, however, even with high

hybrid dysfunction it was typically still beneficial to act. Outbreeding depression did not increase extinction probability above the baseline “do nothing” level of 95% (scenario where 0 individuals are introduced). Although every situation has its own peculiarities, recent reviews suggest that the risk of outbreeding depression is overstated in the literature: in most realistic cases outbreeding should cause only minor and transitory effects (Frankham *et al.* 2011; Aitken & Whitlock 2013), and work on hybrid zones show that beneficial alleles rapidly introgress despite strong selection against hybrids (e.g., Barton & Bengtsson 1986). Of course, crossing small inbred populations sometimes also leads to hybrid vigour, by masking deleterious alleles (Frankham 2015), an effect which should decrease the extinction probability (Weeks *et al.* 2017), though potentially at some cost to the recipient genome. In our particular case study, it is likely that northern quolls will experience only minor, if any, effects of outbreeding depression (due to low genetic divergence across their range; Firestone (2000)). Generally, the likely fitness benefits gained from carrying favourable alleles that help individuals survive a current and overwhelming threat will likely outweigh any small impact of outbreeding depression (How *et al.* 2009; Weeks *et al.* 2011, 2016; Aitken & Whitlock 2013), and recombination ensures that maladaptive genetic combinations are rapidly lost.

Recombination, however, is the key variable affecting linkage disequilibrium, and, by affecting the independence of loci can potentially lower the effectiveness of targeted gene flow. When recombination rate was set to 0.25, there were lower expected returns overall because, although populations survived, a lower proportion of the recipient genome was retained. Lower recombination causes selection to capture larger chunks of the introduced genome: the introduced population’s neutral alleles are carried along with the threat-adapted (strongly favoured) alleles (Aquadro 1997). Therefore in a scenario where recombination is low, the introduction of pre-adapted individuals would need to occur a significant time prior to the step change, to allow time for linkage disequilibrium to decay. When outbreeding depression is also a factor, however, selection against hybrids renders early introductions ineffective. Thus when low recombination rate and strong outbreeding depression occur together, we see low returns. Unfortunately, both of these factors are complex and difficult to predict in advance (Jensen-Seaman *et al.* 2004; Frankham *et al.* 2011). Again, however, even with outbreeding and low

recombination, our returns for a targeted gene flow action are still greater than a do nothing approach.

We have, of course, been unable to capture the full potential complexity in our model. We used timing, population sizes and number of introductees that would be feasible for terrestrial fauna, but using this parameter space we were still able to capture the variation in the global sensitivity analysis. The model lacks complexity around genetic architecture: in reality, genes influence traits to varying degrees (i.e., there is a distribution of effect sizes, e), loci are non-randomly linked, and there are interactions within and between loci (Gomulkiewicz & Holt 1995). Although we have incorporated recombination, the picture is, of course, far more complex in reality. For example, dominance in the target trait (which is hinted at in northern quolls; Kelly & Phillips (2018)) would result in a faster adaptive shift if dominance effects are in the direction of selection, and depending upon the distribution of dominance effects, may also generate heterosis. But in the absence of detail on the distribution of fitness effects and genetic architecture of the key trait, we have chosen the simplest model possible. Our model was simplified also to not include spatial effects, giving all individuals (including introductees) equal chances of survival and finding a mate.

Here we consider a threat that constitutes a step change in the environment. This is broadly relevant to such threatening processes as invasive species and disease that move into a population and alter it from one state to another. There are, however, other threatening processes, such as climate change, that cause gradual change (McDonald-Madden *et al.* 2011; Aitken & Whitlock 2013). Our management objective – maximising the expected proportion of recipient genome, $\bar{r}_i(1 - x)$ – can of course be applied to a gradual change also, and this is a challenging future problem. For now, however, our results with regard to a step change suggest that timing is important. Introducing beneficial traits early and generating hybrids prior to the step change is our optimal action (particularly with low recombination rates), but the timing for this becomes tighter as outbreeding increases, generating selection against hybrids. Ultimately, at high levels of outbreeding depression, the introduction is best made after the step change. Unfortunately, we will rarely know in advance the strength of outbreeding depression, nor the genetic architecture of a polygenic trait. Such uncertainty is common in conservation

management (Kujala *et al.* 2013), and modelling, along with decision-theoretic approaches can provide useful framework for optimising actions in particular cases (Regan *et al.* 2005; Polasky *et al.* 2011).

Overall our model suggests that targeted gene flow could provide substantial benefits to populations at risk from step change to their environment. No scenario we explored caused more damage than not acting at all. Despite the variation of different population dynamics, our model suggests it is generally possible to use targeted gene flow to reduce population extinction risk while still maintaining much, if not all, the local genetic diversity of the population. We have also identified a useful objective to optimise: the surviving proportion of the recipient population's genome. This objective directly addresses the trade-off between reducing extinction probability and retaining the recipient genome, and it proved sensitive to management levers. It would be straightforward, in many circumstances, to anchor this optimisation process with a cost model that adds the economic and logistical constraints particular to a given system (e.g., Southwell *et al.* 2017). While each case will have its own particularities, it appears that targeted gene flow can be a valuable tool in an era of rapid environmental change.

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Figure Legends

Fig 1. Generic population model results across our management space: varying the timing of targeted gene flow (years) and the proportion of pre-adapted individuals introduced. **A:** The probability of extinction of a generic population (x ; red = high chance of extinction) for varying implementations of targeted gene flow. **B:** The proportion of recipient population genome ($\bar{r}_i$; dark blue is recipient genome) in eventual population after varying implementations of targeted gene flow. **C:** Expected return of the recipient genome (i.e. the proportion of the recipient genome surviving, calculated by $E(Y) = \bar{r}_i(1 - x)$). Management scenario that produced the maximum expected return is represented by a black point ($E(Y)_{max} = 0.89$).

Fig 2. Northern quoll population model results across our management space: varying the timing of targeted gene flow (years) and the proportion of toad-smart individuals introduced. **A:** The probability of extinction of a northern quoll population (x ; red = high chance of extinction) for varying implementations of targeted gene flow. **B:** The proportion of recipient population genome ($\bar{r}_i$; dark blue is recipient genome) in eventual population after varying implementations of targeted gene flow. **C:** Expected return of the recipient genome (i.e. the

proportion of the recipient genome surviving, calculated by $E(Y) = \bar{r}_i(1 - x)$ using probability of extinction (x) and proportion of recipient genome ($\bar{r}_i$). Management scenario that produced the maximum expected return is represented by a black point ($E(Y)_{max} = 0.83$).

Fig 3. Generic population model: global sensitivity analysis exploring three dimensional parameter space; population size (N^* : represented by point colours), growth rate (R_{max} : represented in panels) and heritability (h^2 : represented as point shapes). Showing **A**: Maximum expected return ($E(Y)_{max}$) from a scenario, and **B**: the location in the management space (the timing of targeted gene flow and the proportion of pre-adapted individuals introduced) that produced maximum expected return.

Fig 4. Generic population model results across our management space considering **A**: 10% and **B**: 50% reduction of fitness for F1 hybrids. Expected return of the recipient genome (calculated by $E(Y) = \bar{r}_i(1 - x)$ using probability of extinction (x) and proportion of recipient genome ($\bar{r}_i$)).

Fig. 1. Generic population model results

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Fig. 2. Northern quoll population model results

Fig. 3. Generic population model: global sensitivity analysis exploring three dimensional parameter space: population size (N^* : represented by point colours), growth rate ($R_{\max}$: represented in panels) and heritability (h^2 : represented as point shapes). Showing **A**: Maximum

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Kelly, E;Phillips, B

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