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When Extinction is Warranted: Invasive Species, Suppression-Drives, and the Worst-Case Scenario

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When Extinction is Warranted: Invasive Species, Suppression-Drives, and the Worst-Case Scenario

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Most current techniques to deal with invasive species are ineffective or have highly damaging side effects. To this end suppression-drives based on clustered regularly inter-spaced short palindromic repeats (CRISPR/Cas9) have been touted as a potential silver bullet for the problem, allowing for a highly focused, humane and cost-effective means of removing a target species from an environment. Suppression-drives come with serious risks, however, such that the precautionary principle seems to warrant us not deploying this technology. The focus of this paper is on one such risk – the danger of a suppression-drive escaping containment and wiping out the target species globally. Here, I argue that in most cases this risk is significant enough to warrant not using a gene-drive. In some cases, however, we can bypass the precautionary principle by using an approach that hinges on what I term the 'Worst-Case Clause'. This clause, in turn, provides us with a litmus test that can be fruitfully used to determine what species are viable targets for suppression-drives in the wild. Using this metric in concert with other considerations, I suggest that only three species are currently possible viable targets – the European rabbit, ship rat and Caribbean Tree Frog.

Keywords: bioethics, gene-editing, CRISPR/Cas9, invasive species, conservation, precautionary principle

1. Introduction

Invasive species are now considered the top factor in animal extinction rates world-wide, threatening to destabilise wide swathes of the ecosystem (Clavero & García-Berthou, 2005). Moreover, the crisis is accelerating, largely due to globalisation and increased inter-bio-region trade (Seebens et al., 2017; Hulme, 2009), and now poses significant threats to biodiversity, ecosystem functionality, human health, and the economy (Pysek & Richardson, 2010).

Given this, addressing the invasive species[1] crisis is a high-priority goal for most governments and conservation groups. New Zealand, for example, has recently announced its 'predator free 2050' campaign aimed at eliminating invasive mammals that are decimating the local environment.

Unfortunately, most current techniques are ineffective for wide-spread cases or have highly damaging side-effects (Genovesi, 2011; Bax & Thresher, 2009). New tools, then, are a priority in a battle we are losing on a global scale. To this end genetics, and recombinant technologies in particular, have drawn considerable attention in the last few decades. Amongst these, gene-drives based on clustered regularly inter-spaced short palindromic repeats (CRISPR/Cas9) have been touted as a potential silver bullet for the problem, allowing for a highly-focused, humane, and cost effective means of removing a target species from an environment (Webber, Raghu, & Edwards, 2015; Prowse et al., 2017). Gene-drive technology comes with a number of risks, however; risks that currently make it the subject of intense international debate over whether to implement a global moratorium banning use of the technology for germ-line editing ("A Call to Protect Food Systems from Genetic Extinction Technology: The Global Food and Agriculture Movement Says NO to Re-lease of Gene Drives", 2016). Appeals to something like the precautionary principle are common - arguing that we should not

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[1] While the exact definition of an `invasive' species is difficult to pin down (see, for example, the Australian Dingo (Colman, 2014)) I will set this concern aside here as I take the examples I deal with in this paper to be non-controversial examples of the category. As such, we need not worry about fringe cases or a clearer definition than something like that expressed in USA Order 13112, which takes invasives to be "an alien species whose introduction does or is likely to cause economic or environmental harm or harm to human health." (Bulkley, 1999).

implement a technology which has an unknown potential for catastrophic effects despite the benefits it may promise.

Of these risks, three have come to dominate the dialogue - the possibility of unforeseen genetic changes due to the editing itself, the chance of the driven gene jumping to, spreading in, and adversely affecting another non-target species, and the fact that in the extreme gene-drives that aim to suppress a species in a specific range have the potential to significantly impair or even wipe out the target species globally. This last risk is extremely difficult to minimise - quarantine of bio-control techniques has a notoriously high fail rate. Indeed, as I will argue, given the release of a suppression-drive we should treat it as a certainty that it will escape to native ranges. The goal of this paper is to examine this third risk in depth, arguing that while we might think the precautionary principle prevents us from deploying technologies with the potential to wipe out entire species, there are some invasive species which seem to warrant the use of suppression-drives, even in worst case scenarios where the subsequent global extinction of the species is certain. The force of this rests on an application of what I will call the **Worst Case Clause**, a form of limited dominance argument that allows us to sidestep concerns about unknown probabilities and factors by using a methodology which is robust against such factors. This clause, in turn, can then act as a preliminary litmus test by which we can begin determining which species are viable targets for suppression-drive technologies. In demonstrating this I will be looking in some depth at the case for suppression-drive use on the European rabbit but at the end of the paper I suggest that similar arguments might be possible for the ship rat and Caribbean tree frog.

2. Gene Editing, Suppression-Drives, and CRISPR/Cas9

Gene editing is a broader term for a technique of which gene drives are a subset. The term in general refers to any process by which DNA is inserted, deleted, modified, or replaced in a living organism, and can be performed in a number of ways. CRISPR/Cas9 has fast come to dominate the field, however, partly because it can be precisely targeted, and partly because it so cheap. Previous methods could cost upwards of $5000 per modification, while CRISPR/Cas9 can be as little as $30. The technology is modeled on an ability of bacteria that allows them to quickly modify themselves to resist viruses. Taking advantage of this, researchers introduce a Cas9 nuclease complex with a guiding RNA into a cell, and thereby are able to precisely slice genomes and insert new code (Cong et al., 2013)

While there are many potential applications for this technology, ranging from curing diseases to optimising crop yields, in this paper we'll be focusing on one particular implementation known as a suppression-drive. Gene drives in general mimic a natural process that is referred to as 'selfish' genes - genes that have an inheritance probability greater than the normal 50% that develops as a result of segregation of the chromosome pairs during meiosis (Austin, Trivers, & Burt, 2009). The selfish genes discussed here achieve greater than 50% inheritance by copying themselves from one chromosome onto its partner chromosome, changing an individual heterozygous for a gene to one that is homozygous. Because the selfish gene is now present on both members of a chromosome pair, all offspring, rather than only half, get a copy. The gene, in turn, copies itself onto the offspring's partner chromosome and so forth, resulting in the rapid spread of the selfish gene through a population (Caplan, Parent, Shen, & Plunkett, 2015). This class of gene drives occurs naturally, but CRISPR/Cas9 techniques allow for the production of highly efficient 'synthetic' drives that can in theory prevent, reduce, or alter the reproduction of any individual which has it, thereby suppressing a species' population fecundity and viability. The most common ways in which this is done generally involve either altering the driven individuals to have only male offspring, rendering non-viable any embryo which inherits the gene from both parents, or rendering sterile any female which inherits the gene from both parents.

The efficacy of the technique depends on the target population and the context within which it is deployed (Prowse et al., 2017), but all will, in an ideal case, cause the complete elimination within a chosen region of the species to which it is introduced.

Suppression-drives have been tested on a number of species, including mosquitoes (A. Hammond et al., 2016) and rats (Schönig et al., 2012), and current models indicate them to be highly effective at eliminating a target species. Trials in mosquitoes, for example, showed complete spread and subsequent population crash within 11 generations, although this was in lab conditions rather than wild populations (Kyrou et al., 2018).

3. Suppression-Drives: Benefits, Risks, and Worries

The potential benefits of suppression-drives for controlling invasives are significant. Numerous studies have shown that the options currently on the table are insufficient for the task of dealing with the current crisis (Genovesi, 2011; Thresher, 2007; Bax &Thresher, 2009). Examples include restrictions on the efficacy of hunting and trapping in fully eliminating most species (McCrimmon, 1968; Russell, Towns, Anderson, &Clout, 2005; Simberloff, 2008; Myers, Savoie, & Randen, 1998), extensive environmental damage from poisons like 1080 (Innes & Barker, 1999; Ebbert & Burek-Huntington, 2010), the evolution of resistances towards targeted diseases like myxomatosis (Flux,1993; Bull, Mules, et al., 1944; Ross & Sanders, 1984; Kerr & Best, 1998), inhumane suffering from both poisons and diseases (Cowan & Warburton, 2011; Paparella, 2006), and practical limitations on sterile male release (Schliekelman & Gould, 2000; Dyck, Hendrichs, & Robinson, 2006; Nikolouli et al., 2018) and Mendelian inheritance techniques (Harvey-Samuel, Ant, & Alphey, 2017).

In contrast, suppression-drives are often more effective, cost less, do less environmental damage, and are more humane. These drives have minimal impact on the lives of the individuals in question - animals who inherit a suppression-drive live long, full lives. As such, they cause much less pain and suffering than many of the methods above. Similarly, they are kinder to the surrounding environment - there is less risk that native species will be affected, nor will local waterways, pets, or humans. Suppression-drives are also often far better at reducing the numbers of a target population, especially over broader areas. The release of a drive in one small area can lead to the removal of a species as a whole from a large region. By exploiting natural migration and interaction patterns, the drive can reach areas more traditional techniques cannot, and because it doesn't kill the host like diseases, it has a much more effective transmission rate. Finally, they require much less ongoing maintenance than sterile male release or Mendelian approaches, and are easier to implement in cases where the continual mass-release of individuals is difficult or would prove devastating to the environment (Harvey-Samuel et al., 2017).

Downsides obviously include the fact that the drive is, in some cases, much slower than other methods - poisons and diseases are much faster at reducing a population for example - but this is counterbalanced by its theoretical strengths, ideally acting to eliminate rather than suppress in the long-term.

This technology comes with a number of commonly cited worries and risks, however. We can divide these into two broad categories - in-principle concerns, and risk based concerns. In-principle concerns will include things like arguments from the inherent right or intrinsic value of the species, arguments from playing god, arguments from arrogance, and arguments from mistaken technological reliance. Risk based concerns often brought up include arguments from ignorance, arguments from species jump via horizontal gene transfer or hybridisation, and arguments from escape. All of these play some factor in current considerations over whether we have the right to release suppression-drives into the wild

In this paper I'm going to focus on the last of these - the argument from escape and possible subsequent global extinction for the target species. This is partially because many of the other worries have been either explored elsewhere in some depth[2] or, as with many of the pragmatic risks, because they are an acknowledged problem that will necessarily need to be eliminated before the technology could ever get anywhere close to release. Conversely, the escape of a gene-drive to non-target regions is extremely likely, no matter how much effort is put into quarantine and, given this escape, we are likely to see significant suppression or even extinction of the target species in their home-ranges - a risk that has not yet been discussed in any depth in the ethics literature.

4. Escaping Genes

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[2] For a good discussion of playing god see Evans (2002). Intrinsic value we will return to later, but Rolston III (1999) is the only positive argument I can find in favour of this position. For technological reliance both White (1967), and Scott (2011) provide nice overviews of how technological advances interact with environmental concerns. For risk based concerns, work by Roberts et. al (2017), Moran and Jarvik (2010), and Zhang et. Al (2014, 2015) talk about why problems like off-target effects, and horizontal gene transfer are, even today, relatively minimal concerns for the technology.

In many ways this worry is what distinguishes the invasives case from other gene drive applications. Consider, for example, the implementation of a drive into mosquito populations that prevents them from transmitting malaria. If this genetic modification left the region it was released in, such that all individuals of the target mosquito species world-wide eventually possessed this gene, while we would have effectively removed a particular genetic sequence, the insect itself remains in place. Similarly, if we edit the human gene-line to make people smarter, or healthier, the spread of this gene would (barring those cases where we may worry about homogeneity of genetics, or the role social norms have in determining what is 'good' for a human genetically) likely be worrying for other reasons, but not wipe out humans as a whole. What worries we do think hold in these cases are often simply expanded versions of the arguments from ignorance or species jump - where the larger population might make the possibility of off-target effects or jumping more likely. Similarly, we might have some expanded worry from the argument from natural states where we think there is some loss that comes from modifying an entire species, rather than a subset of it, and thus preserving the original.

The use of population suppression-drives, however, changes the stakes. Here, the biggest problem is not the possibility of altering an entire species, but of destroying it completely - a worry that is embedded in the optimisation of the technology itself rather than unpredictable effects from a faulty or off-target drive. Given these stakes, serious consideration needs to be given to the question of global species wipe, or in the less extreme case, a global crash in the target species that significantly reduces its numbers in its native range.

Let's look at this option in more care, then. What are the actual risks involved, how likely is it that we can mitigate them, and how should we weigh them up against the moral obligations we have to solve the invasive species crisis? The answers to these questions should guide our attitudes towards the release of suppression-drives going forwards.

4.1. The Chance of an Escaped Population Suppression-Drive

Suppression-drives have two fundamentally competing requirements. Firstly, they need to be able to drive effectively and efficiently through the target population. Conversely, we also need them to be containable, such that they don't spread to non-target regions. Isolation is often the easiest way to resolve this problem - one reason that most currently proposed applications of gene-drives are on islands.

There are, however, good reasons to think that population-suppressing gene drives will escape even the best quarantine. Primarily amongst these is simply the fact that the species reached the area in the first place. This, in itself, suggests an at least historic transferal of individuals between native and non-native regions. While there are some cases where species were deliberately moved from one area to another (take the eucalyptus in California, for example, or the cane toad in Australia), many transferals were accidental - lanternflies in plane cargo, zebra mussels on the bottom of ships, cats escaping captivity for a life in the wild etc. These mechanisms are, in the majority of cases, still in place, and are often not one-way. Ships still routinely move rats from port to port, people emigrate with pets, warmer weather extends the continuous range of insects and plants. It is difficult, if not impossible, to prevent this movement overlong time-spans, as people battling the initial invasions of invasive species have found (Marshall & Hay, 2012).

This is particularly true of those species which pose the greatest global threats to biodiversity. Ship rats are so named precisely because of their predilection for stowing away on transports, and are now found on over 80% of the world's islands (Towns, Atkinson, & Daugherty, 2006). Restricting their movement is notoriously difficult (Russell et al., 2005; Marshall & Hay, 2012), and while quarantine can be put in place the chance of escape, even for highly immobile species, is non-zero, escalating quickly when we consider those species for which suppression-drives seem like they can do the most good - namely those which are widespread, where traditional methods are ineffective, and where they have significant reintroduction rates. Sparrows, mice, carp, rabbits, mosquitoes, and other major invasives are the target of reduction efforts often precisely because they are difficult to control and are highly mobile, while threatening a large number of native species. What this means is that, despite our best efforts, it is likely that the release of a drive in one region will mean the spread of it to other adjacent areas. This spread, in turn, increases the further chance of escape, creating a runaway effect where any initial quarantine failure significantly increases the chance the drive will eventually effect the target species in its native range. Consider, for example, the use of a suppression-drive on rats in New Zealand. The chance of the drive jumping across to mainland Australia is not inconsequential, for all the reasons we've just discussed. Once in Australia, however, this significantly increases the chance of it migrating upwards into Asia, or jumping to another continent, given the much more extensive trade ties Australia has with other nations. Once it's on more than one continent, it will then be almost impossible to prevent the spread of the drive towards Europe, where the rat is native.

There are, of course, greater and lesser risk species. Carp in Australia are unlikely to reach Europe accidentally via human trade routes, nor are cane toads or foxes. Conversely, we don't always need human movement for a suppression-drive to escape. Lampreys in the Lauritian Great Lakes are a good example of an invasive species that has the potential to naturally migrate back to a native range - while lampreys from the Atlantic are unable to move upstream to reach the lakes, once the fish are upstream there's a non-zero chance that successive generations might migrate downstream and reach the ocean, spreading a suppression-drive with them (Thresher, Jones, & Drake,2018).

On top of this, we have to take into account a long history of humans deliberately spread species and bio-controls to places they will do damage, either through ignorance or malice. While it's unlikely that a suppression-driven carp in Australia will accidentally hitch a ride on a plane to Europe, this doesn't prevent someone from simply capturing a specimen and deliberately moving it across continents. The history of human expansion is marked by instances just like this (Henderson & Murphy, 2008). Consider, for example, the release of non-native species on colonised landmasses by the British for hunting, agriculture or, in one memorable case, as a tribute to Shakespeare (Zielinski, 2011). In the modern day, the introduction of invasive species is often not malicious or with any goal in mind beyond planting a particularly pretty type of exotic flower in one's garden, or keeping an unusual pet, with the mistaken belief that these actions won't cause harm in this one specific case. On the subject of bio-control efforts, we also have cases like French researcher Paul-Félix Armand-Delille catching rabbits deliberately infected with myxomatosis in order to infect rabbits on his estate in Eure-et-Loir to lessen the damage they were causing to his grounds. Less than a year later the rabbit population in France and Iberia had dropped by 45%, with rabbit hunters reporting a 98% drop in yields in the subsequent season (Doherty, 2013). Similarly, farmers deliberately and illegally released the haemorrhagic disease virus to New Zealand in 1997 (O Hara, 2006). Humans, as history reminds us, are often the biggest danger to containment efforts (Henderson & Murphy, 2008; Esvelt & Gemmell, 2017).

With the right quarantine in place, and by selecting the right species, region, and suppression-drive type however, the chance of escape can be extremely low (Champer, Zhao, Champer, Liu, & Messer, 2018; Karlin & McGregor, 1972; Marshall & Hay, 2012), but critically, is never non-zero. In general, then, unlike with the horizontal gene transfer or mutation cases, we cannot dismiss this as an extremely remote possibility, or one that can be solved before the release of the drive. By one means or another for many of the invasive species it is most important we address, in the absence of a viable limitation on the life-span of the drive itself the release of a drive will likely mean the suppression of the species in its native range, and at the most extreme, complete extinction.

4.2. The Chance of Global Extinction given Escape

Given that we can never guarantee the isolation of a suppression-drive, then, what are the chances that an escaped drive actually wipes out the target species, rather than simply temporarily suppressing it?

The actual numbers on this, as with the actual risk of escape, are hard to calculate, and seem to strongly depend on context. Several models have, however, been put forward (Eckhoff, Wenger, Godfray, & Burt, 2017; Beaghton, & Burt, 2016). North et. al (2013), for example, model the propagation of Homing endonuclease genes (HEG) through mosquito populations that are in stable or semi-stable equilibrium. These models are also applicable to Crispr/Cas9 drives, and show that extinction occurs only when population growth is low with sparse density. When breeding and feeding sites are common, the release of a drive results in suppression instead. They also note that the success of these drives depends strongly on the drive being slow enough acting that it has time to spread to the entire target population before wiping out the initially impacted groups. Too fast, and it eliminates itself before it can propagate fully.

There is also a reasonable amount of evidence to show that even stronger drives might not be as effective as we first thought. There is strong evolutionary pressure acting against members of a species that are less viable. A gene-driven individual might, for example, have half their offspring be unable to reproduce. This makes them less fit than a competing non-suppressed member of the same species. Current models suggest that even a fitness viability loss of 25% could be enough to counteract the 'drive' aspect of the suppression-drive, preventing its spread through the population (Drury, Dapper, Siniard, Zentner, & Wade, 2017). There is also significant evidence that this viability mismatch can cause target species to evolve resistances to the drive (Hammond et al., 2017; Karami Nejad Ranjbar et al., 2018). Indeed, in the models given by Unkless et. al (2017) such resistances are almost inevitable given enough time, although it's possible to reduce the chances of them cropping up given the right techniques.

Note, however, that those factors which make extinction unlikely are also the aspects of suppression-drives we are actively trying to 'solve'. Suppression-drives rely on their ability to quickly and effectively spread through a population - there is little point in releasing one to which a species will develop immunity, or one which cannot effectively move between regions containing the target invasives. The Kyrou et al. experiments (2018) which eliminated a lab mosquito population in eleven generations was celebrated precisely because it managed to take a step towards solving the problem of evolved immunity. As such, any version of a suppression-drive which is eventually released will likely have done almost all it can to maximise its chances of becoming an extinction-drive.

Scientists are, however, not blind to the risks involved in a suppression-drive (Esvelt & Gemmell, 2017; Leitschuh et al., 2018; Rode et al., 2019; Beech et al., 2009). Much effort has been put into mitigating escape worries[3], often through the use of artificially limited lifespans for the genes. Daisy-chain drives are a paradigmatic example of this, building into the drive a time-delay that kills it after a certain number of generations, preventing the kind of global spread that we're worried about here. Such systems are termed 'local' drives, as opposed to the 'global' ones we've been talking about up to now. Recent work has suggested that these types of local drives may be less viable than previously thought, however (Min, Noble, Najjar, & Esvelt, 2017; Noble et al., 2019). Tied into this are also calls for a drive to not be released until a counter-drive is also ready to go (Esvelt & Gemmell, 2017). The idea here being that in the case where the drive turns out to have deleterious effects, or escapes the bounds of the target region, a second drive to remove the gene can be released. Recent results by Xu et al. (2020) has suggested that ERACRs (element reversing the autocatalytic chain reaction) and e-CHACRs (erasing construct hitch-hiking on the autocatalytic chain reaction) are promising implementations of this but both have a long way to go. This drive is obviously subject to all the same worries as the original drive in terms of mutation and transfer, but at least theoretically acts as a safeguard against wiping out a whole species.

So then despite what look like good fears about our ability to contain a drive in the wild, the actual current chance of global extinction seem low. Significant

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[3] It is worth noting here that in some cases the global elimination of the species is actually the goal of the project. One approach that has been floated for dealing with the malaria crisis has been to wipe out malaria-carrying mosquito species using a suppression-drive, in which case scientists are obviously not trying to mitigate the chance of escape (A. Hammond et al., 2016)

suppression, however, is a very likely effect of the release of a drive, particularly for those wide-spread species which do the most damage and are the hardest to contain. Suppression, however, can be almost as bad as extinction - just look at all the species on the endangered list whose reduction in numbers are seriously impacting their native habitats. As such, while we should likely not worry too much about the possibility of a suppression-drive causing global wipe-out, this doesn't mean that the risks involved don't have serious stakes.

5. Weighing up the Risks

Unlike other methods of invasives control, gene drives have potentially global implications for a species. We cannot accidentally poison all rabbits on earth, nor would the release of a virus likely prove fatal in the long-run, even if every country got infected simultaneously. Suppression-drives, however, no matter how careful we are will always have a non-zero chance of escape and total species wipe - so how should we think about such scenarios? This is where the precautionary principle is often evoked - given the uncertainties involved, and the potentially serious repercussions, the consensus seems to be that we should hold off on using suppression-drives in any wild-release context.

Still, we can attempt to make some primitive calculations, treating it as a balancing act: If the benefit of act A is n and the act will do damage worth m, and there is a x% chance of the benefit, and a y% chance of the detriment, then we might simply assert that we should do A iff $xn-ym > 0$. That is, if the benefits outweigh the detriments. Such calculations are difficult in real-life, however. Here's one attempt at one - shiprats in New Zealand are responsible for the extinction of 23 local species, and they threaten about 40 more (Towns et al., 2006). If we were to release a suppression-drive on invasive rats in New Zealand, then we are potentially saving many of these species, and potentially eliminating one (the ship rat). This, in the grand scheme of things, seems like an overall win. Even in the case where there is a 100% chance of the drive escaping and killing all ship rats, we have still made a positive contribution to saving species diversity because we've killed one to save many.

This is, obviously, an incredibly naïve position to take. There are a number of salient factors in any such calculation beyond simply brute species diversity. Rats, for example, might be far more numerous globally than the species they are replacing, even before they were invasive. As such, we might think that the sheer number of shiprats gives some weight to the idea that they are more worthy of saving than the native species, as the collective right to continued existence of the first outweighs the additive collective rights of the others. Alternatively, rats may be a keystone species in their native range, as with bees in North America, such that eliminating them would disrupt the entire ecosystem, leading to further extinctions and environmental degradation. On the other hand, it might be the case that rats are one of a number of species that fill a similar ecological niche in their native environment, and thus their elimination wouldn't seriously disrupt the ecosystem, as with the northern and southern white rhinos which are technically genetically distinct but in every other way are identical from an environmental perspective.

We also know that the chance of wiping out rats globally is far from 100% - partially because there will be at least some attempt at quarantine, and partially because unlike poisoning or viruses, the speed of suppression-drive spread is limited by generational considerations. We will have numerous generations of a species to deal with an escaped drive, either by quarantining affected areas, or by introducing reverse drives into the native range being affected. All these factors weigh in favour of suppression-drive release, even in the face of global species wipe risk.

All this is to state the relatively uninteresting conclusion that the release of suppression-drives is incredibly situation dependant, and that many factors will need to be accounted for in each case where it is considered for use. While there will be times when suppression-drives prove to be morally problematic, as with cases where simple trapping or hunting will solve the problem and thus we need not run the risks that CRISPR/Cas9 technology opens up, in other scenarios we might seem more justified in using the suppression-drive approach. These calculations, and the debate around them, form a large part of why suppression-drives are so controversial - no one is entirely sure what constitutes a right to release such a technology, nor what types of risk analysis we should be doing to answer the question.

5.1. The Worst-Case Scenario

It's very easy to get caught up in the details of this complex issue. When do we have the right to release a technology that could wipe out an entire species? What factors should we consider, and what relative weights should we give them? How do we ever analyse the risk of accidental extinction by our own actions? The uncertainty and unknowns make the problem all the more difficult - and is one reason we often take the path of precaution, determined to not take any actions until we have a clearer picture of what the possible problems could be given the severity of getting it wrong

While all this debate is important, and will indeed be critical in our eventual decisions over whether to release suppression-drives into the wild, I don't think that this uncertainty completely precludes the release of suppression-drives in certain specific cases. In fact, I suspect that even without knowing the full impact of what a suppression-drive might do, we can still motivate a case for release on some species that meet certain criteria.

To justify this I will be appealing to what I will refer to as The Worst-Case Clause (WCC),

> **Worst-Case Clause**: If we are warranted in taking action *x* even after assuming that the worst possible outcome will follow, then we are warranted in taking action *x* in general.

That is, if our reason for precaution is that we don't know how risky our action could be, and lack enough information to make an informed decision, then one way to bypass this is to simply assume the worst from the beginning. If, in this context, we still seem warranted in taking the action, then we no longer seem to need to worry about the precautionary principle

In the context of suppression-drives that could, with some unknown probability, eliminate a species, this means assuming that any suppression-drive released is guaranteed to escape quarantine and wipe out the target species globally. For the sake of clarity, we'll refer to suppression-drives with this added worst-case scenario caveat as 'extinction-drives'.

The Worst-Case Clause is a type of dominance argument, albeit one where we have bracketed a number of other relevant factors. The goal here is to zero-in on a particular aspect of the debate which lends itself to a methodology that is robust to changes in the underlying probabilities or uncertainties. We will return to the broader context in the final section to look at how this piece might be seen as one part of the larger debate. Here, however, instead of entering into these types of calculations we're instead examining the idea that for certain species the worst-case scenario of extinction is still such that it is strictly the best outcome for the system as a whole.

Let's look at one example that I think meets the Worst-Case Clause.

European rabbits are one of the most pervasive invasive species in the world[4]. In New Zealand, they have on occasion reached plague-like numbers since their introduction in the early 19th century, ravaging crops, overgrazing native flora, and out-competing native species for resources thereby reducing native biodiversity (Lees & Bell, 2008). For this reason they are included in the New Zealand 2050 'mammal free' goal. Current control methods include hunting, trapping, poisons (via bait, aeroplane drop, and being pumped directly into burrows), the building of rabbit-proof fences, the introduction of competitive and predatory species (including the now invasive ferrets, stoats, and weasels), and targeted disease (Myxomatosis and Rabbit Haemorrhagic Disease (RHD), the former failing to become established, and the latter being introduced by private individuals against the government's wishes. Recent studies have shown that New Zealand rabbits have begun developing a resistance to RHD (B. D. Cooke & Fenner, 2002)). None of these methods have had any long-term impact on rabbit populations in New Zealand

Similar stories may be told throughout the world. In Australia, rabbits have had massively detrimental impacts on agriculture, native flora and native fauna (Clout, 2002; B. Cooke, Jones, & Gong, 2011). Africa and North America have similar problems (Picker, 2013; Hygnstrom et al., 2014) - indeed, European Rabbits are now

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[4] It's been suggested that European rabbits are the first recorded invasive species, with Pliny the Elder noting in the *Naturalis Historia* (VIII.80) that they were invasive to the Balearic Islands around 75AD where they caused famines, brought down trees, and collapsed houses, leading to Divine Augustus sending a troop of soldiers armed with ferrets to help the region.

invasive on ever continent except Antarctica, including over 800 islands worldwide (Lees& Bell, 2008).

Given the failures of current methodology, very few options are left on the table for rabbit control. One of the most promising of these is, unsurprisingly given the contents of this paper, CRISPR/Cas9 gene-editing technology. This method obviously comes with all the risks we've already discussed. There is, in as much as there ever is, the remote chance of horizontal gene transfer via bacteria, although this has a very remote chance of serious damages via random insertion (X.-H. Zhang et al., 2015; Vereset al., 2014). However, there are no recorded instances where European Rabbits have hybridised successfully with native species outside of their own genus in a way that creates viable offspring (Chang, Pickworth, & McGaughey, 1969; Petrescu-Mag, Botha, & Gavriloaie, 2018) making them a good candidate species for a suppression-drive along this dimension. Spread does also means all the worries about 'loose' genes crop up though, where the perpetual existence of the drive may, in remote cases, lead to unexpected off-target effects. Finally, European rabbits are a keystone species in their native range in the south of France and Iberian Peninsula, and should the drive escape and spread world-wide their destruction has potentially devastating implications for these environments.

Imagine, now, that in attempting to remove European Rabbits from New Zealand using CRISPR/Cas9 the worst happens and it is wiped out globally. What then? This is obviously a difficult question to answer - European rabbits have been invasive around the world for centuries and it's hard to predict what removing them might do even in ranges where they're non-native but might now be providing some stop-gap role. As above, there are primitive calculations we can make. Take, for example, the fact that although rabbits are not native to the UK (having been introduced in the 12th and 13th centuries through trade), many studies have proven that they now provide critical services maintaining the natural landscape. So much so that an outbreak of myxomatosis in Southern England led to a radical restructuring of local heathlands, and the subsequent decline of the native *Maculinea arion* butterfly, *Myrmica sabuletiant*, stone curlew, red-billed chough and woodlark (Lees & Bell, 2008). In cases like the UK it is likely that the European rabbit has taken up the role of a now extinct mega-fauna, maintaining environmental stability in a highly-farmed and artificial part of the world. As such, its removal would have serious consequences for the region, despite the rabbit being a non-native transplant.

The rabbit itself is also endangered in parts of its own native range - the Iberian Peninsula - giving us some further insight into what might happen if they were removed completely. In the Iberian Peninsula the species has seen significant decline, threatening the further survival of other endangered species, including the Iberian Sphinx and the Spanish Imperial Eagle (Lees & Bell, 2008). Should the European Rabbit become globally extinct, then, there would be significant knock-on effects for the ecosystem of its home region, likely leading to extinctions.

The actual impact is difficult to calculate. In accordance with the worst-case clause, however, let's assume the worst. If the rabbit goes extinct let's assume it will take down numerous species with it - contributing to the collapse of diversity on the Iberian Peninsula and places like the heathlands in the United Kingdom. This is, of course, only to speak of biological disaster - European rabbits are also central to a number of economic systems in various regions, where hunting and farming the animal is a key source of income.

This worst-case scenario is pretty bad - we are effectively collapsing multiple ecosystems, robbing large groups of people of critical income, and driving multiple species to extinction. It could be argued, however, that this was a mild version of a worst-case scenario - if we really wanted to push things to the extreme it might be possible to argue that the elimination of the European rabbit could have unforeseen devastating consequences globally, perhaps even preceding the total collapse of the global bio-sphere. Or perhaps the European rabbit turns out to be the key to curing the next deadly virus to sweep mankind, or that it somehow has been preventing the complete economic collapse of multiple countries. How, I am unsure, but technically we cannot rule out the possibility if we really are aiming to consider the most devastating version of an extinction-drive. Should we take one of these, then, to be our worst-case scenario, rather than the less extreme one I've proposed here?

Given that I am attempting to distance myself from probabilistic arguments here, it is frustrating to have to turn to one now, but I think we are warranted here in pointing out that the chances that removing the rabbit will be more devastating than the first worst-case scenario are remote. In the absence of any reason beyond wild imagination to think that the European rabbit has become a keystone species in most of its non-native ranges, or that there is some reason to think it is propping up international economies, or that if we attempt to kill of rabbits they'll retaliate by stealing all the nuclear codes and causing thermonuclear devastation, we should act to construct a worst-case scenario based on what we could feasibly see happening at the extreme.

In contrast, consider the determinate damages currently being caused by the rabbit in other environments. Whatever damages may occur by removing the rabbit in Iberia and the UK is already in effect in New Zealand, Australia, South America, and many other ecosystems where rabbits are causing the extinction of numerous native species. Played as a pure numbers game, global biodiversity and stability improves both if the drive works as it's supposed to and only removes rabbits from New Zealand, and if quarantine fails and we see a worst-case scenario of global wipe-out. Moreover, what if one of *these* species are the one that could save mankind from virus, or stabilise global economies? Indeed, the rabbit is driving to extinction many more species than we could reasonably see being threatened by it if it were to disappear, meaning that if we are aiming for a worst-case based on pure speculation we still need to give more weight to the side of rabbit elimination rather than preservation. Given this, we seem warrated in concluding that the potential damages caused by removing the European rabbit globally are much less than the current damages already being caused where the species is invasive.

In many ways this argument is simply a numbers game - weighing up the benefits of removing an overwhelmingly damaging species against the problems removing it may cause. In the European Rabbit case this seems to come out in favour of removal - the species seriously threatens agriculture, and native flora and fauna in almost all it's extensive invasive ranges, and its loss, however serious, would still in turn damage only a limited ecosystem and set of economies. Thus, we seem justified in thinking that even in a worst case scenario we are warranted in releasing a suppression-drive. The European Rabbit is, however, a very distinct case. It has very little evidence of hybridisation, it has a very limited natural range, and it is on the extreme end of invasive species in terms of spread and damage. If, on the other hand, rabbits were only invasive in New Zealand, and not anywhere else in the world, and the damage they did there was on any scale comparable to the damage that would be done by their extinction in Iberia, then even if it were the case that they were driving species to extinction, and that there was no way to remove them other than a suppression-drive, we seem much less warranted in releasing a drive.

5.2. The Right to Cause Extinctions

Here is one possible objection to the argument I have outlined above - throughout this paper I have assumed that the value of species derives from the value of biodiversity, ecological preservation and stability, human utility or some other similar principle. Thus, I have biased the calculations in my favour since invasive species almost by definition are those which threaten biodiversity such that any non-extreme action to remove them will count as a positive mark on the scales towards action.

Here is a different take on the argument. Instead of valuing biodiversity etc (either inherently or for its utility) we might think that either the species itself is inherently valuable, and thus has some primary right to exist, or that we have some duty of care towards species such that we do not have the right to eliminate them. In this way, we might wonder not whether we can balance the scales in favour of saving more species, but whether we ever have the right in the first place to act in a way that will knowingly eliminate it. Perhaps there is some more fundamental principle in play which forbids such actions on the grounds of our inherent duty of care towards these species, particularly given that it is our own interventions which have spread these species to the point where we are now considering taking an action which could wipe them out.

While I suspect that most arguments about our duty of care in this case don't go through, thus rendering this approach nonviable, I do think that even if we accept this premise we can still make the case for worst-case suppression-drives being deployed.

Let's break this objection down a little. Firstly, we have something that looks like the following principle,

> **Duty of Care Principle (DCP):** We have a duty of care towards any given species such that we should allow the species to survive.

This, obviously, is not enough to get the objection up and running. After all, if it is the preservation of species that is important then any scenario where an invasive species threatens to drive more than one species to extinction would license us to release the extinction-drive

I take it, then, that we must add something like the following,

> **Active Participation Principle (APP):** If a species should be allowed to survive, then you should not act such that you knowingly cause the species to go extinct.

The wording of this is to distinguish a difference between actively killing a species and letting one die by omission. I take this to be a core aspect of the objection – that although we might be doing something wrong by not stepping in to save the birds of New Zealand from introduced predatory mammals, it is worse to actively try to eliminate the weasel in order to do so.

I cannot say I find this argument very convincing, but it will be useful to briefly discuss why.

Firstly, 'letting die' implies that we have not had a causal hand in the death of the species, which is patently untrue in most invasives case. While we may not have intended the effects, we as a species are still responsible for the introduction of the invasive pests, and thus the ones who set the extinction mechanisms in place. As such, the distinction between the 'killing' and 'letting die' sides are less straight-forward than in other paradigmatic cases of the action/omission distinction. To lean on an old trope, it is akin to being faced with a trolley problem where you were the person who accidentally set the trolley loose in the first place. In this case, it is unclear that refusing to pull the lever absolves you of the moral responsibility for the subsequent deaths. As such, the claim that the APP tells against extinction drives seems far weaker than the initial formulation suggests.

Direct action is, of course, not the only way we might bear responsibility. Perhaps it was not you who released the trolley (or transported invasive species), but instead you are receiving some benefit that comes from the existence of runaway trolleys as a whole (as we benefit from globalisation and the continued transport of goods which acts to move these species). Similarly, it seems difficult to claim that we should not pull the lever, as the distinction between action and omission is blurred.

There is, however, still a distinction to be made between accidentally killing someone by setting a process in action, and deliberately pulling the trigger. As such, we might think that even though we are still responsible in some way for the deaths of various endangered species, this is still morally preferable to setting out to deliberately wipe-out a species. Note, however, that even if we make the assumption above that releasing a suppression-drive will necessarily eliminate a species, this is not actually the aim of most invasive species controls. In the context of biodiversity conservation it is never the case that we are aiming at the complete global elimination of a species - only ever the removal of them from non-native ranges. Global wipe is, at worst, a foreseeable but unintended repercussion of the act.

Philosophy tends to draw a distinction between an act which aims at doing some-thing, and an act which has the same unintended, but foreseen, consequences.

Most formulations of the doctrine of the double effect have four conditions which must be met for an act to be a morally acceptable (McIntyre, 2019)

The Doctrine of the Double Effect (DDE):

(1) The action in itself must be good or indifferent.

(2) The good effect must be intended, the bad effect must not be intended.

(3) The good effect must cause the bad effect. The bad effect cannot be used to achieve the good effect.

(4) The good and bad effects must be proportional, such that the good sufficiently outweighs the bad.

The extinction-drive case meets all of these. In itself, the release of a gene-drive is at worst indifferent; we intend the good effect of saving the ecosystem and various species therein and by definition do not intend to eliminate the target species globally; the good of saving the ecosystem is the cause of the bad, rather than the other way around; and as we've just discussed in section 5.1 the good outweighs the bad in such a way that it is certainly a proportional action

In the case of an in-principle reason to avoid releasing an extinction-drive then, we can see that

i. the choice between passively allowing a species to go extinct and actively eliminating it is difficult to maintain in the invasive species case due to our broader obligations towards the environment, as well as our either passive or direct hand in causing and benefiting from the problem,
ii. in the case where we actively release an extinction-drive, the global wipe-out is an unintended but foreseen consequence of our bid to save

the environment, something that meets the requirements for the doctrine of the double effect and,

iii. this argument holds regardless of whether we take the value of the species, ecosystem, or individual animals to be inherent or instrumental.

This does not, of course, preclude us from being morally responsible for the ensuing results - just as we as a species have a moral obligation to deal with invasives, we will also have a moral duty to try and prevent the elimination of a species we have introduced an extinction-drive to, even if we have decided that the cost of the species loss is worth the payoff

6. Conclusion

We often appeal to the precautionary principle when we are faced with a new technology that poses a poorly understood but potentially serious risk. Such is the case for suppression-drives which run the risk of accidentally wiping a species out globally, and is one reason that international moratorium have been extensively discussed by both scientists and policy makers. One way around these uncertainties is appeal to a form of dominance argument, assume the worst, and take it that any suppression-drive will become an extinction one, stepping away from the complex risk-analysis questions that underpin most debates on when to use suppression-drives. If it is the case that we can warrant the global extinction of the target species in the name of environmental stability, then it is the case that we can warrant the use of the (likely) less extreme suppression-drive, even in cases where this suppression-drive does serious damage to the population of the species world-wide.

The worst-case clause is a useful litmus test for what species we are warranted in focusing our attentions on. It is only one of a number of factors that I take to be relevant to such calculations, however, including but not limited to,

(1) Worst-Case Clause: It must be the case that if the invasive species went extinct globally we would not cause disproportional damage to the environment, either in the species' native ranges or in ranges where it is invasive but now plays a key part of the ecosystem.

(2) No-Alternatives: There must be no other viable/cost effective alternatives on the table to deal with the invasive species.

(3) Reasonable Timeline: The time between subsequent generations of the species should be sufficiently short to allow the drive to work within a reasonable time-frame.

(4) Proportionality: The damage caused by removing the species must be significantly lower than the damages prevented - if a keystone species with a large native range is invasive on a single island we aren't warranted in releasing the drive from a consequentialist position, nor do we meet the proportionality requirement for the doctrine of the double effect.

(5) Ark-viable: If we assume, as we have here, that a suppression-drive will necessarily be an extinction-drive then the creation of reserves for the species becomes a necessity before the release of a suppression-drive. As such it must be possible to create and maintain an effective ark for the species by which un-modified genetic diversity can be preserved. While this is possible with most terrestrial species, certain aquatic species will be difficult to maintain in isolation in great enough numbers to rebuild the species should the suppression-drive become an extinction one. I expect the onus for creating such an ark will fall primarily on the releasing party.

(6) **Non-Value-ladened:** The target invasive species should not be one to which we attach other types of value that might outweigh environmental damage. This may include criteria like sentimental or cultural value (eg. cats and dogs), research value or uniqueness (eg. lab rats and coelacanths), or being possessed of higher-intelligence (eg. apes and dolphins).

(7) **Non-hybridising:** It must not be the case that it is able to produce fertile hybrids with non-target species unless that species also meets all the other criteria on this list both alone, and in combination with the target species

This is, obviously, not a complete list, nor should it be consider the case that species which meet all of these are thereby automatically an acceptable target fora suppression-drive. I do think, however, that meeting all these criteria, particularly Worst-Case, does warrant us boosting the species to the top of our potential lists, and sidestepping several of the worries that bring the precautionary principle into play

What species meet these criteria? Of the International Union for the Conservation of Nature (ICUN)'s list of top 100 invasive species (Lowe, Browne, Boudjelas,& De Poorter, 2000), if we set aside diseases, plants, and insects as being not well enough understood yet at an ecosystem-wide level, a cursory survey shows that only a few seem like they might currently be possible candidates for a suppression-drive including the Caribbean tree frog, ship rat, and European rabbit. This is, of course, a superficial glance at best, and many of the criteria above are highly circumstantial and subjective judgements, but it is worth noting how rare it will be for a species to meet the minimal criteria I have listed above.

In all of the above I've framed this argument in terms of extinction. As I pointed out earlier, however, the chances of a suppression-drive actually wiping out a species globally is vanishingly low in reality. Realistically a worst-case scenario looks not like extinction, but significant suppression. This, however, can be almost as bad - the practical difference between a species disappearing and simply being massively reduced are minimal. In both cases the species is failing to perform the role needed in the ecosystem, and while in the latter there is hope for recovery, this doesn't mitigate the biome collapse that will occur beforehand. Either way the arguments I've made above can be applied, and seem give the same answers.

In conclusion, then, while there are cases where we might think that the use of suppression-drives involves unwarranted risk, in a small number of scenarios they look to be either the best or the only viable option available to us to stop the massive loss of biodiversity on a global scale caused by invasive species. I have focused primarily on ship rats and European rabbits here, both of which I take to be species which pass the Worst-Case clause and thus allow us to bypass the precautionary principle for the extinction-risk aspect of suppression-drives. In both of these cases the species involved are too pervasive for conventional eradication techniques to be effective, and the current damage being done to the environment seems to tip the scales in favour of CRISPR/Cas9 suppression-drive use despite the remote possibility of species extinction.

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