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PERSPECTIVES AND PARADIGMS

Scenario analysis on the use of rodenticides and sex-biasing gene drives for the removal of invasive house mice on islands

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Abstract Since the 1960s conservation efforts have focused on recovering island biodiversity by eradicating invasive rodents. These eradication campaigns have led to considerable conservation gains, particularly for nesting seabirds. However, eradications are complex and lengthy endeavors and are even more challenging when humans are co-inhabitants of the targeted island. Furthermore, the method of eradication matters and recent proposals to consider genetic technologies for rodent eradication require specific scrutiny. One such technology is the potential use of a gene drive for biasing offspring sex ratios in invasive house mice, *Mus musculus*, that would spread and prevent the production of one sex, allowing die-off from lack of reproduction and natural attrition. Practitioners can gain insight into the potential for adoption of this technology from examining stakeholder engagement. This paper uses scenario analysis to address the eradication of rodents on inhabited and uninhabited islands, by specifically comparing the traditional approach of using rodenticides with sex-biasing gene drives. Concurrently the International Union for Conservation of Nature is assessing the risks and value of gene drives in general for conservation. Hence, we make the case that the ethical challenges with the use of gene drive sex-biasing techniques and the effectiveness of this tool will rely as much on its public acceptance and its democratic use as the actual science used to construct the technology.

Keywords Preserving island biodiversity · Rodent eradications · Synthetic biology · Stakeholder engagement · Public perceptions

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Introduction

Island biodiversity threatened by invasive rodents

Islands represent only a small portion of total terrestrial habitat at 5% of global land mass, but host a disproportionate share of biodiversity. Importantly, island endemics also account for a disproportionate

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share of critically endangered species (37%; Tershy et al. 2015). Invasive species negatively impact island ecosystems (Bellard et al. 2016). In particular, 80% of the world's islands harbor invasive rodents; the most common are house mice (*Mus musculus*) and three species of rats (*Rattus rattus, R. norvegicus, R. exulans*) (Caut et al. 2008). Because invasive rats and mice are so widespread and interact with native species in a range of ways including predation and competition, their impacts are pervasive and significant (Mulder et al. 2008; Drake and Hunt 2009). Impacts are particularly dramatic for seabirds because these taxa use islands as breeding habitat and rodents predate eggs, chicks and even attack adults (Fukami et al. 2006; Caut et al. 2008). The eradication of invasive rodents leads to significant and diverse conservation benefits (Capizzi et al. 2014; Jones et al. 2016). In addition to seabirds, conservation benefit examples include sea turtles through reduced predation on eggs and hatchlings (Caut et al. 2008; Gronwald et al. 2019) and even indirect effects such as enhancement of coral reef productivity due to increased effects on nutrient cycling through seabird populations (Graham et al. 2018). Eradication of invasive rats on Palmyra Atoll led to another, surprising indirect effect as another invasive species, the disease vectoring Asian tiger mosquito (*Aedes albopictus*), also disappeared following rat removal (Lafferty et al. 2018). Economic impacts can also be very significant as invasive rodents can destroy crops both in the field and storage (Brown and Singleton 2000). Lastly, invasive rodents are also important vectors of Leptospirosis and other human diseases and their removal can benefit human health (Vanasco et al. 2003).

Rodenticide eradications

Eradications of invasive rodents from islands rely almost exclusively on rodenticides that are anticoagulant toxicants (Campbell et al. 2015). These rodenticides are distributed in bait form either aerially or using bait stations (Capizzi et al. 2014). The first successful rodent eradication campaign occurred in New Zealand on Maria Island in 1964 (Russell and Broome 2016). The use of aerial baiting has increased the size and scope of these efforts to South Georgia island (30,000 ha), in the southern Atlantic ocean. This represents the largest campaign to date and the island is now rodent free (Simberloff et al. 2018). Modern rodenticides are second-generation anticoagulants that are slower acting, which helps prevent bait shyness, and allows the rodents to consume multiple baits (Howald et al. 2007; Capizzi et al. 2014).

While this rodenticide-based approach has been quite successful overall (> 80% of 650+ operations worldwide, Holmes et al. 2015a, b), there are also very significant drawbacks (Parkes et al. 2011; Campbell et al. 2015; Rueda et al. 2016). The rodenticides available are not species-specific and therefore can kill non-target species that consume bait. This concern can necessitate the capture and holding of these non-target species for months and sometimes years (Howald et al. 2010). Additionally, resistance to rodenticides can develop in the invasive target species (Campbell et al. 2015). Another enormous challenge is that most islands with species threatened by invasive rodents are also inhabited, which complicates implementation because of potential accidental exposure to humans and domestic animals (Oppel et al. 2011; Glen et al. 2013; Campbell et al. 2015). Finally, success rates are high, but not 100% and repeated efforts are costly and difficult (see below and Howald et al. 2007; Angel et al. 2009).

From inception to implementation, a rodenticide-based eradication campaign can take 5–10 years (Howald et al. 2010). Island eradication campaigns have been carried out through the coordination with land managers and non-governmental organizations such as Island Conservation (Island Conservation 2018). These campaigns are labor and cost intensive and implementation is highly dependent on several factors: island size, remoteness, native species present, whether it is inhabited by people, and their support or lack thereof for the campaign (Holmes et al. 2015a). Because of these concerns and limitations, many conservation practitioners have stated they are quickly running out of islands that can be restored using current methods (Goldson et al. 2015). This situation, along with ethical concerns about using rodenticides, has led to a push for the investigation of newer technologies, such as sex-biasing gene drives (Campbell et al. 2015, 2019; Goldson et al. 2015; Sutherland et al. 2018).

Sex-biasing gene drive strategies

Gene drives are a potential rodent eradication methodology that would avoid use of rodenticides. Gene drive methods draw on sterile insect technique approaches developed in the 1950s (Knipling 1955) and refined by Oxitec to develop genetically-engineered mosquitoes (Capurro et al. 2016). Gene drives are genetic constructs that exhibit super-Mendelian inheritance and thus can potentially be used to spread a particular trait into a population. Because gene drives bias their probability of transmission above the Mendelian expectation of 50%, they can be inherited at near 100% frequency in offspring. This can allow for transmission of phenotypic effects such as an offspring sex bias or infertility, which is why gene drives have stimulated great interest as a potentially effective form of pest control (Burt 2003; Sinkins and Gould 2006; Esvelt et al. 2014). Natural gene drives do exist in a variety of systems and have been well studied (Burt 2003; Burt and Trivers 2009; Silver 1993). Likewise, synthetic gene drives have been developed in a number of invertebrates but have not been released into the wild (DiCarlo et al. 2015; Esvelt et al. 2014; Gantz and Bier 2015; Harris et al. 2012). Active and mathematical modeling suggests that low threshold engineered drives could spread through a target population even if introduced at low frequencies (Harvey-Samuel et al. 2017; Prowse et al. 2017) Gene drives are being researched and considered for rodent eradication that would bias the sex ratio of target populations, leading to local extirpation through lack of reproduction (Backus and Gross 2016; Campbell et al. 2019; Leitschuh et al. 2018; Piaggio et al. 2017) (Fig. 1).

While gene drives are considered species-specific and non-lethal (Harvey-Samuel et al. 2017), they present other environmental concerns. Gene drives in at least their basic form are designed to be self-sustaining and could spread beyond the targeted geographic region if containment measures are not in place (Moro et al. 2018). In 2016 the National Academy of Sciences, Engineering, and Medicine called for caution in studying gene drives in the laboratory and urged phased testing throughout the entire project (National Academies of Sciences, Engineering and Medicine 2016). Similar reports have been developed in Australia and New Zealand (Australian Academy of Science 2017; Royal Society Te Apārangi Gene Editing Panel 2017). Scientists in the USA, Australia, and New Zealand are examining the potential use of sex-biasing gene drives in house mice working within biosecure facilities (National Academies of Sciences, Engineering and Medicine 2016; Australian Academy of Science 2017; Royal Society Te Apārangi Gene Editing Panel 2017). A future goal is to release altered mice on an uninhabited island as part of carefully monitored field trials, in a country with a robust regulatory environment, perhaps in one of the three above mentioned countries (Genetic Biocontrol of Invasive Rodents 2017).

Public perceptions of rodents

People who live with rodents often express concerns about rodents' effects on food-stocks, clothes, and overall human health, and want the rodents removed (Reiter et al. 1999; Morzillo and Mertig 2011; Panti-May et al. 2017). However, there is sometimes opposition to removal, motivated by concerns towards the target animal, the humaneness and effectiveness of control methods, unknown environmental impacts, ability to target specific animals, and cost (Dubois et al. 2017; Fitzgerald 2009; Reiter et al. 1999). Animal welfare and the number of organisms to be killed are points of contention (Dubois et al. 2017). Opponents report strong ethical concerns about killing for conservation and generally prefer no-kill methods (Courchamp et al. 2017). The results of a survey that measured New Zealander's perceptions of lethal methods for wildlife control indicated that 'poisoned baits for rodents' is an acceptable form of lethal control (Reiter et al. 1999). A US-based study that measured perceptions of lethal methods found respondents to be most concerned about species specificity, pain level, and efficiency of method (Sanborn and Schmidt 1995; Fitzgerald 2009). A study of news media coverage of rodent eradications indicated that media coverage of eradications was supportive of eradications, although a majority of the islands addressed were uninhabited (Valdez et al. 2019).

Important here are the bases for opposition to eradication. Managers often attribute opposition to ignorance, but studies show that public education designed specifically to garner support does not necessarily increase acceptance and can heighten conflict (Owens 2000; Crowley et al. 2017). Therefore, public engagement campaigns should be at least

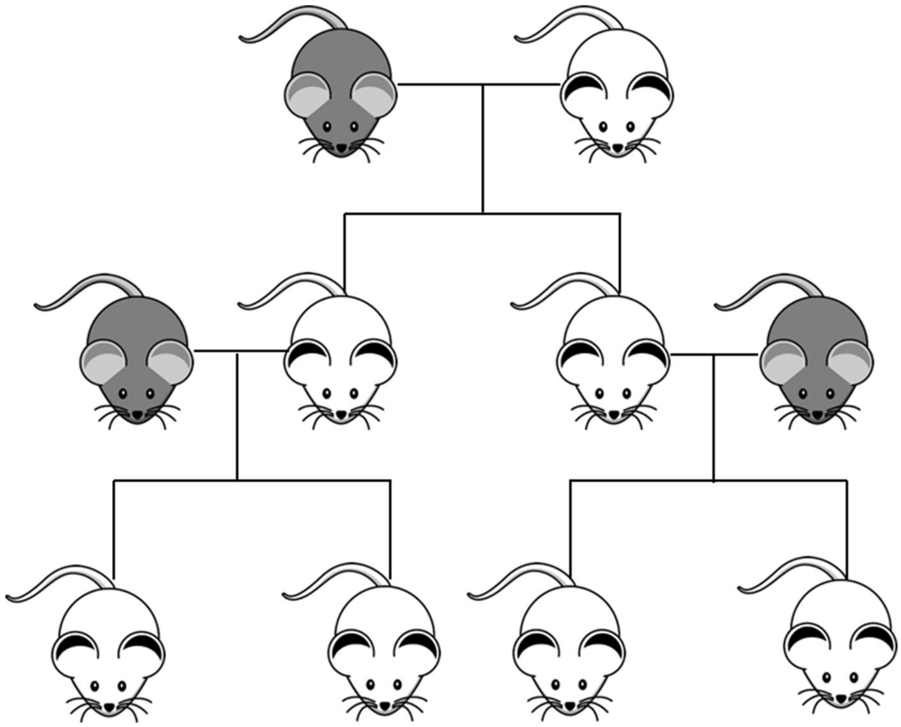

Fig. 1 Depiction of how a sex biased gene could spread through a population. The grey color depicts the wild-type and the white is the gene drive

as much about public deliberation as they are public education. Public perception of rodenticides may also differ depending on the country and the community in which they are deployed and on the scale of use. The use of rodenticides on large scale agriculture in Australia has occurred for decades to control invasive rodent outbreaks (Moro et al. 2018). This technology has been welcomed by the farming community as a means to save crop production and storage (Singleton et al. 2001).

The range of cultural perspectives about rodents as invasive species is also often overlooked. Some Indigenous Australians do not view invasives as incompatible with native species, or the invasive species may be viewed as a resource (Fitzgerald 2009). The Maori of New Zealand view the Pacific Rat (*R. exulans* or Kiore) as sacred (Haami 1994). Some people will never support an eradication campaign. Others argue it is the only way to save endangered species. Thus, stakeholder groups on different islands have shifting social dynamics that eradication managers need to address, acknowledge, and adapt to (Morrison et al. 2011; Crowley et al. 2017; Dubois et al. 2017; Novoa et al. 2018).

Governance of gene drive rodents for conservation

A number of institutions could regulate gene drive rodents. In the United States, for example, invasive species eradications are regulated by the National Environmental Policy Act (NEPA), which requires an Environmental Impact Statement (EIS) as a decision-making tool (Meghani and Kuzma 2018). Within this framework, NEPA uses quantitative risk assessments to evaluate courses of action (including no action). Similarly, the Coordinated Framework for the Regulation of Biotechnology also relies on "verifiable scientific risk" as the basis for decisions about the release of genetically engineered organisms (Office of Science and Technology Policy 1986; Kuzma 2016). Both NEPA and the Coordinated Framework require mechanisms for public input as explicit dimensions of the decision-making process. For example, NEPA review requires an EIS and public comment period (Hayes et al. 2018), and the release of genetically engineered organisms also requires public comment periods (Kuzma 2016). Similarly, Australia's Environmental Protection and Biodiversity Act (EPBC Act) also requires risk assessments when examining wildlife management strategies and encourages public input (EPBC 1999; Hayes et al. 2014). New Zealand's Royal Society Te Aparangi and Landcare Research have been investigating the potential of gene drives with a panel that solicits public input (Royal Society Te Apārangi Gene Editing Panel 2017; Dearden et al. 2017). From a global perspective, the UN's Convention on Biological Diversity is currently deliberating on how to address the governance of gene drives (Convention on Biological Diversity 2019; Callaway 2018a). However, the United States has not ratified the Convention, and while the US continues to send delegations to the relevant negotiations, the absence of a binding commitment will likely add to the complexity of regulating gene drives (Oye et al. 2014). Adding to decision-making complexity are the tensions between different scales of governments, governance, and interests. There are calls for nested governance considerations that explore the interplay between local and global interests (Kofler et al. 2018). They also highlight the need to consider that gene drives may well be global decisions but will have localized material impacts and vice versa. Again, governance and regulatory contexts point to a need for complementary systems of decision-making that attend to broader complexity.

Because emerging gene editing technologies outpace the regulatory structures that govern them, scholars and stakeholders have drawn attention to the *governance* of these technologies (Kuzma 2016; Kofler et al. 2018). Governance goes beyond governmental regulations to include more responsible parties, and can include ethical considerations and community impacts (National Academies of Sciences, Engineering and Medicine 2016). Public comment periods that are built into regulatory systems (described above) are important starting points for soliciting public input but may not account for the complex views associated with gene drive rodents. As such, more deliberative processes are warranted. A distinguishing component of governance is its potential for broader inclusivity and deliberation beyond the public comment approach to public input.

A particular form of governance which lends itself to nuanced viewpoints is deliberative stakeholder, community and public engagement (National Academies of Sciences, Engineering and Medicine 2016). A stakeholder is defined as having some personal or professional interest, while a community is often defined by having geographic proximity to a project and or its impacts. Meanwhile, public engagements are comprised of audiences (individuals and or groups) who have an interest or concern in the matter. A defining character of deliberative engagement is it allows for the discussion of technological innovation, its benefits and potential risks, while allowing for the explicit incorporation of values (Kuzma et al. 2018).

In complex cases such as the potential use of gene drive house mice, more deliberative public engagement efforts, such as stakeholder workshops may be of benefit. These should occur early in the process, and stakeholder groups should consider establishing appropriate timelines for goals and final decision-making. This should help maintain consistent engagement and prevent stagnation. In fact, building on a landscape analysis (Delborne et al. 2019) some of the authors of this paper organized and facilitated a stakeholder workshop about the potential use of gene drive mice that generated important deliberation about trade-offs (see Farooque et al. 2019). Citizen/stakeholder advisory committees may be well-suited for making decisions regarding invasive rodent management (Chess and Purcell 1999). These deliberative engagement efforts will likely require more time and resources, but there are a number of reasons to invest in these types of engagement efforts. Citizens should have a right to know, and a right to participate in decisions that impact their lives (Cox 2012). Additionally, deliberative public engagement offers a potentially better process for incorporating input because participants have a space to communicate their preferences and better understand the preferences of other participants (Parkins and Mitchell 2005). Scenario analysis is a potentially useful tool for deliberative engagement because the process allows for the integration of complexity, uncertainty, and values all within the framework of imagined futures (Joshi et al. 2015; Quay 2010) Finally, deliberative public participation can lead to better outcomes, or better eradication plans in this case, because multiple stakeholder perspectives are discussed, knowledge can be shared between parties and consensus or near-consensus decisions can be developed (Parkins and Mitchell 2005; Walker 2007). A recent paper has argued for and described an articulation of free, prior and informed consent (FPIC) that attends to issues of transparency, iterative community-scale consent, and shared power through co-development among Indigenous peoples, local communities, researchers and technology developers. In realizing a comprehensive FPIC process, researchers and developers have an opportunity to incorporate enhanced participation and social guidance mechanisms into the design, development and implementation of engineered gene drive applications (Dalton et al. 2019). How to incorporate public participation into a final decision will be challenging. One option is to incorporate the outcomes of public participation into an analytical process, such as structured decision making (Martin et al. 2009). Whichever process is used, stakeholders should know, going into the process, how their involvement will impact the final decision.

Scenario analysis

In this section we analyze four scenarios that illustrate the complexity of eradications. A scenario analysis can help organize insights into a framework that integrates qualitative and quantitative information, and gauges risks (Swart et al. 2004). Stakeholders can also participate in scenario analyses, which is particularly useful when considering scenarios that include gene drive rodents. Results of scenario analyses can then be communicated to broad audiences and can provide guidance for planning (Swart et al. 2004). With this in mind, we present the following scenarios to demonstrate the differences between applying rodenticides and gene drives on uninhabited and inhabited islands. We draw attention to the ecological, financial and social contexts that are important to consider when developing rodent eradication proposals on similar islands.

Eradication with rodenticides on an uninhabited island

The uninhabited Subantarctic Antipodes are a known nesting site for 21 species of seabirds where house mice were the only invasive mammal (Elliott et al. 2015). Nicknamed the "Million Dollar Mouse Project", the 2016 invasive house mouse (*M. musculus*) eradication in the New Zealand's Subantarctic Islands region (2045 ha) marks a milestone for mouse eradication in terms of island size (Russell and Broome 2016: Wickes 2016: Horn et al. 2019). The campaign used 65,500 kg of rodenticide-laced bait to remove an estimated 200,000 mice from the island (Wickes 2016). The project's planning phase began in 2012 and was deemed a success in 2018 when mice were no longer found, after the typical 2 year monitoring period (Horn et al. 2019).

Public engagement was quantified by recording the number of media articles discussing the project as well as activity on websites designed for the project (Horn et al. 2019), which contrasts with the deliberative engagement processes proposed in subsequent scenarios. The cost of the aerial eradication was around 2.6 million USD, with New Zealand Government, Morgan Foundation, World Wildlife Foundation, Island Conservation and New Zealanders contributing funds (Wickes 2016). Now that the mice have been eradicated, biosecurity measures need to be in place to prevent reinvasion, requiring more time and expenditure (Russell and Broome 2016).

Eradication with rodenticides on an inhabited island

Australia's Lord Howe Island (1455 ha) will likely soon become the largest human-inhabited island to eradicate rodents (Walsh et al. 2019). Popular among tourists, the island supports an abundance of unique fauna including an endemic giant stick insect, *Dryococelus australis* (Priddel et al. 2003). Lord Howe's year-round population is approximately 350, but doubles with tourists (capped by the island governing board at 400) (Oppel et al. 2011; Reis and Hayward 2013; Cavanagh 2018). Greater than 75% of Lord Howe is a permanent park preserve aimed at protecting and preserving land and is a UNESCO world heritage site (Reis and Hayward 2013). Unfortunately, rodents were negatively impacting over 70 plant and animal species on the island and have already caused the extinction of several species of birds, insects, and plants (Wilkinson and Priddel 2011). Ongoing rodent control efforts have been in place since the 1920s while eradication efforts began being tested for feasibility in 2001 (Walsh et al. 2019). In accordance with existing Australian laws and governance, eradications need to account for the safety of the 350 year-round residents (along with their pets and livestock) and considered a a limited ban on tourism (Oppel et al. 2011; Wilkinson and Priddel 2011). Similar to previous eradications using rodenticide, the Lord Howe Island eradication required the temporary housing of two bird species of special concern, the Lord Howe Woodhen (*Gallirallus sylvestris*) and Lord Howe Currawong (*Strepera graculina crissalis)* (Lord Howe Island Rodent Eradication Project 2019). Currently, the project is estimated at 7 million USD (Gillespie and Bennett 2017) but failure the first time rodenticides are deployed can drive up costs (Russell et al. 2018). Cost–benefit analyses that compare current methods of rodent management to the eradication campaign have been made public to show that the eradication could financially benefit the island (Gillespie and Bennett 2017). The Lord Howe Island Board (LHIB), which oversees the eradication, also incorporated an open public comment period in accordance with Australia's EPBC Act (Lord Howe Island Rodent Eradication Project 2019). However, the eradication of mice and rats was delayed several times due to the community's opposition to the campaign (Wilkinson and Priddel 2011; Tolj 2016: Cavanagh 2018). Opposing voices expressed concern over potential risks to endemic species, human health, livestock, and potential impacts to tourism (Wilkinson and Priddel 2011; Gillespie and Bennett 2017). After strong vocal opposition in 2014 delayed implementation the LHIB decided to divide the project into sequential stages and go back to the community with a renewed effort on community engagement (Walsh et al. 2019). The LHIB have also conducted social impact assessments to address key issues and the eradication took place in 2019. Lord Howe is now waiting the standard 2 years to see if the eradication was a success. Lord Howe would demonstrate that eradications could be performed on inhabited islands, but also shows that eradications are more complicated when people also reside on the island.

Eradication with a gene drive on an uninhabited island

Sex-biasing gene drives in mice are currently in the research and design phase (Callaway 2018b; Cohen 2018; Grunwald et al. 2019) but will likely require unique planning and assessment efforts before being used in the field. First, the viability of gene drive mice needs to be addressed. Gene drive mice that succeed in laboratory environments may not survive and reproduce in the wild if the fitness cost of a drive mechanism is too high or the drive may not persist if wild populations develop resistance to it (Manser et al. 2015; Champer et al. 2017; Prowse et al. 2017; Sudweeks et al. 2019). Another major concern for rodent gene drives is their potential ability to penetrate and spread to non-target populations (Esvelt et al. 2014; Leitschuh et al. 2018). Scientists need to better understand and limit off-target effects, to ensure that the drive will not spread to other species, or spread outside the intended uninhabited island location (Esvelt et al. 2014; National Academies of Sciences, Engineering and Medicine 2016). Methods to contain gene drives both temporally, spatially, and molecularly are being designed and considered (Leitschuh et al. 2018; Sudweeks et al. 2019).

To prevent the unwanted escape of gene drive organisms, or even the intentional spread, control measures will need to be established and enforced. Methods and lessons on control can be gained by studying islands post rodenticide eradication and the majority of this work has been conducted in Australia and New Zealand (Greenslade et al. 2013; Russell and Broome 2016). Researchers have suggested that a remote offshore island might be the best location to trial a gene drive sex-biasing mouse as the uninhabited island provides physical containment as recommended by Champer et al. (2016). Additionally, if the gene drive were to fail, existing regulations should permit following up with rodenticides as a failsafe.

There are ecological concerns related to rodent gene drives as well. If not timed properly a release could temporarily add more invasive mice to the population, which might have cascading ecological consequences, including increased competition for food resources, and increases in predation pressures (Esvelt et al. 2014; Backus and Gross 2016; Esvelt and Gemmell 2017).

The cost of a gene drive mouse is as yet unknown, but development and upfront costs would be in the millions (Backus and Gross 2016; Leitschuh et al. 2018). It is also important to note that while the same monitoring and biosecurity costs to prevent reinvasion would still be present, there would not be the additional cost of housing threatened species off the island since a gene drive mechanism would be species-specific (unlike a rodenticide).

Deliberative public engagement will be important for an uninhabited island because the application of gene drive mice will be novel, complex, and it is difficult to predict how people will react to this method. In a nationwide survey of New Zealanders, 32% were comfortable with gene drives being deployed to control invasive species but 18% believed that gene drives should not be used, leaving 50% undecided (MacDonald 2017). In a survey of US residents, 37.6% of respondents stated it is not morally acceptable to edit genes to control invasive species, 30.1% neither agreed or disagreed, and 32.3% agreed it is morally acceptable, though not all participants said they understood how a gene drive functions (Brossard et al. 2018). Another recent US survey found that around 85% of Americans thought gene editing wildlife is somewhat risky but half were unsure on whether it would be beneficial even if posing a risk (Kohl et al. 2019). In short, public opinion about gene drive technologies is complex and divided. Opposition to sex-biasing gene drives may be based on perceptions of what is natural, and how much humans should interfere with nature (Redford et al. 2014; Piaggio et al. 2017; Brossard et al. 2018). Another avenue for public engagement is to have community discussions about gene drives and animal welfare concerns in parallel to let the community discuss the pros and cons of rodenticides versus gene drives.

In terms of gene drives, the development of methods to contain them temporally, spatially, and molecularly may actually erode public trust because people may become concerned that if gene drives potentially need fail-safes then the gene drive organisms should not be released. There has also been some discussion with stakeholders amid concern that uninhabited islands might be viewed as more 'pristine' and that we should not interfere with areas 'untouched' by humans (Gomez-Pompa and Kaus 1992; Farooque et al. 2019).

Eradication with a gene drive on an inhabited island

Currently, there are no known plans to release a gene drive mouse on any island and a logical first step would be a remote uninhabited island (as discussed above). However, we discuss the inhabited island scenario because the planning for this type of eradication will require considerable foresight; an inhabited island will likely be more ecologically and socially complex. The ecology of urban rodents differs from rodents on uninhabited islands. Non-commensal rodents on islands have been documented eating a higher number of invertebrates as opposed to grasses and on islands with strong seasonality they can dramatically increase in number during periods of food abundance (Angel et al. 2009; Backus and Gross 2016). Commensal rodents may also behave and move differently than those living on islands non-commensally (Gray and Hurst 1998). The regulatory structure for gene drive mice on an inhabited island is not likely to fundamentally differ from regulations on an uninhabited island but assessments for impacts to domestic animals and livestock will likely be necessary to build relationships with residents, even if risks seem minimal (Ogden and Gilbert 2011).

The justifications for eradicating invasive rodents from an island will affect public perceptions, and this is likely to be particularly true for a genetic approach and a no-kill method of rodent eradication (such as gene drives) may be preferred over rodenticides (Campbell et al. 2015; Leitschuh et al. 2018). In addition to biodiversity losses, rodent populations can boom in agricultural areas. In Australian agricultural environments, invasive mice regularly reach "plague" densities, at over 2000 per hectare, causing severe financial and emotional hardships for farmers (Singleton et al. 2001). Concerns for rodents are often even higher in cities either because the desire to remove rodents is stronger or there is more educational information on costs of rodents to human health and food security (Morzillo and Mertig 2011; Garba et al. 2014; Panti-May et al. 2017). People may not be as willing to deploy sex-biasing gene drives for conservation purposes as they are for rodents impacting human health because support for genetically modified organisms is generally higher in the context of human health (Widmar et al. 2017; Funk and Hefferon 2018).

Developing trust with island residents becomes a critical management goal in this scenario, especially if a gene-drive system would need to be deployed over several years (e.g., Backus and Gross 2016). This is because residents will become active eradication partners and their cooperation will be necessary for success. At a minimum, they can help eradication efforts by excluding rodents from food sources and minimizing available nesting sites in personal homes and other buildings. Residents will be more likely to cooperate if they trust the management agency and believe the eradication can be successful (Stern and Coleman 2015). Deliberative public participation methods can help foster relationships and lead to eradication plans that are acceptable to stakeholders and communities (Parkins and Mitchell 2005).

Conclusion

Rodent eradications are complex and no technique, including sex-biasing gene drives, offers a "silver bullet". Any method may fail to eradicate pest species and people will still bear the conservation and economic burden of invasive species. Yet, inaction also maintains these same burdens. The above case studies introduce the complexity of eradicating invasive rodents on islands. They also highlight the social and political complexity of conservation. We feel strongly that for any rodent eradication project, eradication campaigners must carry out a genuine, thorough public engagement process by balancing the advantages of gene drives with the risks and benefits for conservation, health, and agriculture.

Despite much discussion and calls for public engagement on gene-drive sex-biasing technology for rodents on islands, presently only one group is exploring the technique in house mice. The Genetic Biocontrol of Invasive Rodents Program (GBIRd, http://www.geneticbiocontrol.org/) involves seven institutions exploring all aspects of the technique: science, safety, stakeholder engagement, ethics, and regulation (Genetic Biocontrol of Invasive Rodents 2017). Drawing on principles of responsible research and innovation (Stilgoe et al. 2013), this group is working together to build a transparent innovative process that engages stakeholders early and often. While explorations of rodent sex-biasing gene drives are starting with house mice, it is also foreseeable that in the future this organization or others expand into sex-biasing gene drives targeting rats, which are more damaging to island flora and fauna (Towns et al. 2006).

If sex-biasing gene drive mice are determined to be a viable approach, eradication planners will need to navigate uncertain and potentially evolving biotechnology regulations. In the United States, the Coordinated Framework for the Regulation of Biotechnology does not provide clear insight into how a gene drive mouse would be regulated (Kuzma 2016), but regulation may fall to one of the following three regulatory agencies: Food and Drug Administration, Environmental Protection Agency, or the USDA's Animal and Plant Health Inspection Service (USDA-APHIS) (Office of Science and Technology Policy 1986). The Australian Academy of Sciences has been exploring gene drives for conservation (Australian Academy of Science 2017), while the Commonwealth Scientific and Industrial Research Organisation has been examining the regulatory aspects of sex-biasing gene drive mice (Commonwealth Scientific and Industrial Research Organisation 2018). For New Zealand, sex-biasing gene drive mice would fall under the Hazardous Substances and New Organisms Act and would be evaluated on a case-by-case basis by the Environmental Protection Authority (Royal Society Te Apārangi Gene Editing Panel 2017). Given that sex-biasing gene drives could spread beyond national borders, these technologies may warrant further international regulations. On an international level, the Convention on Biological Diversity has continued to discuss and evaluate the safety and potential use of gene drives for conservation (Secretariat of the Convention on Biological Diversity 2015). In conjunction, the International Union for Conservation of Nature (IUCN) has decided to formulate an IUCN Synthetic Biology and Biodiversity Conservation assessment with recommendations for the 2020 World Conservation Congress (IUCN: Development of an IUCN policy on Synthetic Biology 2018). Moreover, the majority of rodent eradications have occurred on islands that are territories of wealthy countries and there is concern that eradication managers may dismiss or overlook groups of people with less privilege (Brown et al. 2017).

Given the urgent conservation needs and the limits of existing technologies, now is the time to discuss the potential of sex-biasing gene drive mice as an alternative to rodenticides for island mouse eradication. As an emerging technology, it remains to be seen exactly how or if sex-biasing gene drive mice will be effective as compared to traditional rodenticide-based approaches. Regardless of technology deployed, one of the greatest steps forward in terms of eradication has been the call for not only increased engagement, but in studying the social aspects of eradication for conservation. With over 460,000 islands globally, and invasive rodents present on the majority of these, society will need to decide whether to eradicate, and if eradicating, which method to use (United Nations Environment World Conservation Monitoring Centre 2015; UNEP-WCMC 2018).

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