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Stakeholder engagement to inform the risk assessment and governance of gene drive technology to manage spotted-wing drosophila

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ABSTRACT

Emerging biotechnologies, such as gene drive technology, are increasingly being proposed to manage a variety of pests and invasive species. As one method of genetic biocontrol, gene drive technology is currently being developed to manage the invasive agricultural pest spotted-wing drosophila (Drosophila suzukii, SWD). While there have been calls for stakeholder engagement on gene drive technology, there has been a lack of empirical work, especially concerning stakeholder engagement to inform risk assessment. To help address this gap and inform future risk assessments and governance decisions for SWD gene drive technology, we conducted a survey of 184 SWD stakeholders to explore how they define and prioritize potential benefits and potential adverse effects from proposed SWD gene drive technology. We found that stakeholders considered the most important potential benefits of SWD gene drive technology to be: 1) Decrease in the quantity or toxicity of pesticides used, and 2) Decrease in SWD populations. Stakeholders were most concerned about the potential adverse effects of: 1) Decrease in beneficial insects, 2) Increase in non-SWD secondary pest infestations, and 3) Decrease in grower profits. Notably, we found that even stakeholders who expressed support for the use of SWD gene drive technology expressed concerns about potential adverse effects from the technology, emphasizing the need to move past simplistic, dichotomous views of what it means to support or oppose a technology. These findings suggest that instead of focusing on the binary question of whether stakeholders support or oppose SWD gene drive technology, it is more important to identify and assess the factors that are consequential to stakeholder decision making - including, for example, exploring whether and under what conditions key potential adverse effects and potential benefits would result from the use of SWD gene drive technology.

1. Introduction

Enabled by gene editing techniques such as CRISPR, a broad range of novel emerging biotechnologies are being proposed to manage a variety of invasive species and pests (Adelman et al., 2017; Hartley et al., 2019; IUCN, 2019; Neuhaus and Caplan, 2017). Gene drive technology, RNAi, and genetically engineered insects and microorganisms are all under different stages of development to address invasive species and endemic agricultural and human health pests such as soybean aphids (*Aphis glycines*) (Yan et al., 2020), diamondback moths (*Plutella xylostella*) (Shelton et al., 2020), mosquitoes (e.g., *Aedes aegypti*) (Li et al., 2020), and invasive rodents (Barnhill-Dilling et al., 2019). One example of an emerging biotechnology proposed to address an invasive species is the

use of gene drive technology to manage the invasive agricultural pest spotted-wing drosophila (*Drosophila suzukii*, SWD). Since 2009, SWD has rapidly expanded its known range and is now found on all continents except Australia and Antarctica (de la Vega et al., 2020). Economic damage from SWD results when females lay their eggs into ripening soft-skinned berries, grapes, and other fruit crops and the resulting larvae consume the inner flesh of the fruit. Current pest control methods rely on prophylactic insecticide sprays when ripe fruit are present and labor-intensive manual removal and disposal of infested and overripe fruit (Diepenbrock et al., 2016, 2017; Haviland and Beers, 2012). These methods are not sustainable in the long term. For example, secondary pest problems have already arisen in some regions due to depletion of natural enemies from insecticide overuse (Lopez and Liburd, 2020).

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Given the problematic nature of SWD and the limitations of current management techniques, a variety of emerging biotechnologies have been proposed to aid in its management (Schetelig et al., 2018). One such biotechnology being researched for SWD control, which we examined in this study, is gene drive technology for population suppression (Buchman et al., 2018). The SWD gene drive technology aims to reduce or eliminate SWD populations at local or larger scales using a gene that interrupts female reproduction (Buchman et al., 2018). This gene drive technology works by causing mutations to a sex determination gene that leads female flies to have non-functioning genitalia while males develop functional genitalia (Li and Scott, 2016). Modified males that reproduce with wild, non-gene drive females produce female offspring with no reproductive potential and a new generation of gene drive-carrying males. Over time, the number of fertile, wild female SWD, and thus the population as a whole, is reduced. This specific gene drive technology is currently in a proof-of-concept research stage of development. It is as yet not determined whether this technology would include a self-limiting attribute or would be designed to spread unencumbered (Backus and Delborne, 2019). Similar to other applications of gene drive technology, there are a variety of concerns surrounding the potential use of this technology, from potential ecological risks to the potential for the technology to further corporate control over agriculture (Devos et al., 2020b; ETC Group, 2018; Montenegro de Wit, 2019).

The novelty, power, and controversy of gene editing-enabled technologies such as SWD gene drive technology has led to calls for both risk assessment and robust stakeholder engagement. Risk assessment – a formal process used to identify and characterize potential adverse effects from a technology – is used to study potential harms from gene drive technology and inform governance decisions about whether and under what conditions gene drive technology should be used (Devos et al., 2020a). While there are active discussions concerning what form risk assessment should take to adequately assess the risks from gene drive technology, the importance of risk assessment for gene drive governance is widely recognized (Devos et al., 2020a; Kuzma, 2019; National Academies of Sciences, Engineering, and Medicine, 2016; Simon et al., 2018).

Engagement – simply defined as including a diverse set of disciplines and worldviews in decision making - has also been widely called for in the context of gene drive technology (Brossard et al., 2019; National Academies of Sciences, Engineering, and Medicine, 2016). There is a widespread recognition that the decisions concerning whether and how to use these novel and powerful technologies should be informed by broad societal discussion and not just the views of a small group of technology developers (George et al., 2019; Jasanoff and Hurlbut, 2018; Kofler et al., 2018; Long et al., 2020; Thizy et al., 2019). Ensuring the inclusion of a diversity of disciplines and worldviews can help avoid problematic blind spots in decision making for gene drive technology. Engagement can help inform a variety of key decisions related to gene drive technology such as: What product attributes are desirable and undesirable? What level of reduction in a pest population is required to deem a technology successful? How (in)adequate are existing management options? What are the most important potential harms from a technology that should be avoided? Many existing areas of scholarship are well suited to inform engagement efforts for gene drive technology including: responsible innovation (e.g., Stilgoe et al., 2013), ecological risk assessment (e.g., Nelson et al., 2007), and invasive species management (e.g., Shackleton et al., 2019). In a previous article we reviewed these relevant literatures and explored the diversity of forms engagement could take in the context of emerging biotechnologies to address invasive species (Kokotovich et al., 2020).

In the context of gene drive technology, calls for engagement are often separated from calls for risk assessment, yet engagement is also needed in risk assessment itself (Hartley and Kokotovich, 2018; Hayes et al., 2018; Kuzma, 2020; Stirling et al., 2018; Thompson, 2018). Although there are different views concerning who should be involved in engagement for risk assessment, where in the risk assessment process they should be involved, and how they should be involved, engagement

is seen as particularly useful during the problem formulation stage of risk assessment (Nelson et al., 2004). Many key judgments concerning the scope and scale of the risk assessment are made during problem formulation, including selecting protection goals and identifying and prioritizing potential adverse effects. Incorporating community and stakeholder engagement within risk assessment can help ensure that the results are relevant, rigorous, and trusted for a particular context (Kokotovich et al., 2020; Kuzma, 2019). For example, engagement can help ensure that risk assessment addresses the most important topics and concerns of key stakeholders.

1.1. Engagement for gene drive risk assessment and governance

To contextualize our study, we briefly review existing examples of engagement relating to SWD and gene drive technology, more broadly. This review will help make clear where our study fits into the existing literature and the different types of engagement activities that can be useful for gene drive-related decision making. While widely called for, existing engagement related to the potential use of gene drive technology to manage SWD has been limited in nature. In one engagement study involving SWD gene drive technology, Jones et al. (2019) conducted a statistically representative survey of 1018 adults in the United States to examine whether and under what conditions they would support the use of gene drive technology in agriculture. In the survey they used two case studies (SWD and Asian citrus psyllid) to describe how gene drive technology could be used in agriculture, choosing them because they were examples where conventional control options were failing and costly. They found that support for the use of the gene drive technology in agriculture depends most on whether it is used on native or non-native species and whether the gene drive is designed to spread or is self-limiting. Support was highest for a self-limiting gene drive for a non-native species (61% Support; 25% Neither; 14% Oppose) and support was lowest for a non-self-limiting gene drive for a native species (22% Support; 32% Neither; 46% Oppose). In response to a question on the most important uncertainty to resolve before deciding whether gene drive insects should be used to control pest damage to crops, respondents most highly ranked human health effects and the environmental consequences of pest removal. Notably for our study, this was a randomized sample of adults in the United States - not individuals who necessarily had experience with SWD or emerging biotechnologies.

The European Food Safety Authority conducted a stakeholder workshop with 38 representatives from industry, academia, non-governmental organizations and government to explore issues concerning the risk assessment of gene drive technology in insects (Devos et al., 2020b). As part of the workshop, a risk assessment problem formulation exercise for gene drive technology was conducted for the case studies of SWD and the Asian tiger mosquito. Through this workshop, participants created a broad set of, sometimes conflicting, general insights and recommendations for gene drive risk assessment (Devos et al., 2020b). Findings specific to the SWD case study, however, were not reported (Devos et al., 2020b).

While very little engagement has been conducted specifically on SWD gene drive technology, there has been more engagement conducted for other potential uses of gene drive technology. For example, Teem et al. (2019) reported on stakeholder engagement conducted for gene drive mosquitos that sought to, in part, have participants discuss some of the potential harms that could result from the use of gene drive mosquitoes for malaria control in Africa. This stakeholder engagement took the form of four workshops, each in a different country (Ghana, Kenya, Botswana, and Gabon), and each lasting four days with a mixture of presentations and breakout sessions. Participants included African human health and environmental agencies, local and international scientists, and other government officials who the organizers deemed to have no known bias for or against gene drive technology. The potential harms from the use of gene drive mosquitoes most frequently mentioned by participants during these workshops included: 1) Increase in other

mosquito-borne diseases; 2) Increase in malaria incidence; 3) Decrease in mosquito predators; 4) Decrease in water quality; 5) Impacts on other mosquito species; 6) Livestock animals sickened; 7) Decrease in soil quality; and 8) Increase in mosquito invasiveness. In addition to identifying these potential harms, participants identified pathways to each of these harms, how plausible each step along the pathway was, and additional information needed to further analyze the potential harms (Teem et al., 2019).

Hartley et al. (2021) conducted in-depth interviews with 19 stakeholders in Uganda to explore their hopes and concerns surrounding the potential use of gene drive mosquitoes for malaria reduction. Participants included biosafety experts, entomologists, medical doctors, a veterinary doctor, representatives of the community living near an important research center, biotechnology experts, a legal expert, an environmentalist, and a social scientist. Key hopes for the gene drive technology included reducing malaria, causing less environmental harm than existing chemical pesticides, increasing socio-economic productivity, and decreasing malaria-related costs. Key concerns included: 1) the inability of gene drive mosquitoes to address malaria (e.g., gene drives are ineffective; lack of public or political support hinders gene drive deployment), 2) detrimental impacts of gene drive technology (e. g., decrease in non-target organisms and/or species diversity; emergence of new diseases and/or increase in prevalence of existing diseases; negative impacts on the economy and society; costs and benefits unfairly distributed), and 3) other gene drive governance issues (e.g., alternative approaches to malaria are neglected; political conflict with neighboring nations; lack of regulatory capacity; lack of transparency and independence; lack of clarity on liability and responsibility).

MacDonald et al. (2020) conducted a representative national survey of 8199 individuals who live in New Zealand to ask about their support for gene drive technology for pest control for conservation purposes and how it compared to two other pest management techniques. Using case studies of rats, stoats, and wasps, they found the overall percentage of participants supportive of gene drive technology to be 32%, compared to 42% for the Trojan Female Technique and 52% for pest-specific toxin baiting. In addition, support for gene drive technology varied across 4 worldviews held by participants (Humanitarian, Individualist, Pragmatic, Scientific), with the highest support for gene drive technology expressed by those who held a scientific perspective (i.e., emphasizes trust in science and scientists - 53% supportive) and the lowest support expressed by those holding a pragmatic perspective (i.e., emphasizes the economic impact of pest control - 22% supportive).

Finally, Farooque et al. (2019) conducted a stakeholder engagement workshop to explore issues concerning the use of gene drive technology to manage invasive mice on islands to benefit biodiversity. The two-day workshop at North Carolina State University consisted of a mixture of presentations and small group breakout sessions and included 21 individuals from academic institutions, US federal agencies, Australian and New Zealand agencies, and non-governmental organizations. Through workshop activities, participants provided insights and recommendations on a variety of different governance decisions concerning mouse gene drive technology including research design decisions (e. g., how self-limiting gene drives may address issues of containment), testing in simulated natural environments (e.g., the importance of staff training protocols), selection criteria for islands for first field trials (e.g., the importance of an established regulatory system), and future community and stakeholder engagement (e.g., the importance of upstream engagement).

These six examples of engagement for gene drive technology reveal that a breadth of different methods (e.g., workshops, surveys, interviews) with a range of possible participants (e.g., stakeholders, academics, government agency personnel; members of the broader public) can be useful for informing a variety of risk assessment and governance questions related to gene drive technology (e.g., What level of support exists for gene drive technology? What are key potential harms to study in risk assessments? What are desirable attributes of a technology? What

are key governance issues that need to be addressed?). The diversity found within these examples reinforces the idea that engagement for emerging biotechnologies should be broad in nature: conducted at many points in the research to deployment pipeline, asking a breadth of questions, using many methods, and involving a diversity of participants. In other words, a particular use of one technology would benefit from many different forms of engagement. At the same time, whatever combination of methods, participants, and questions are followed for engagement for gene drive technology, it is important to follow good design practices (Kokotovich et al., 2020; Rowe and Frewer, 2000, 2005).

To help address the dearth of engagement work conducted specifically on SWD gene drive technology and given that SWD gene drive technology is still in the research and development phase, the main goal of our study was to better understand some foundational views of SWD stakeholders concerning the potential benefits and potential adverse effects of SWD gene drive technology. To do this we conducted a survey of 184 SWD stakeholders to explore whether they support SWD gene drive technology and how they prioritize potential adverse effects and potential benefits from SWD gene drive technology. The fact that the SWD gene drive technology is still in the research phase means that the insights garnered in this study can help inform future product development as well as risk assessment and other governance decisions.

2. Methods

To inform the risk assessment and governance of proposed SWD gene drive technology, we designed and conducted an Institutional Review Board-approved survey (North Carolina State University #18012) of SWD stakeholders from October to December in 2019. In this survey we asked SWD stakeholders a variety of questions concerning the potential benefits and potential adverse effects of gene drive technology used to manage SWD. In addition to the questions on gene drive technology reported here, participants were also asked these same questions for one other emerging biotechnology for SWD management, either genetically engineered sterile SWD or RNA interference expressed in genetically engineered yeast. In this publication we focus solely on the gene drive technology results, and future work will examine differences between technologies. To form our sample of participants, we defined SWD stakeholders to include the following individuals:

- Scientists in academia, government, or industry studying SWD and related topics
- Scientists in academia, government, or industry studying genetic pest management
- State and federal government employees working on invasive species or biotechnology regulation
- Growers of crops impacted by SWD
- Extension or agribusiness professionals who advise growers on SWD pest management
- Fruit wholesalers or marketers impacted by SWD
- Representatives of conservation or environmental advocacy nongovernmental organizations that work on issues relating to biotechnology

We identified potential participants in a variety of ways. First, we identified academics by reviewing grants related to SWD in the United States Department of Agriculture (USDA) Specialty Crop Research Initiative and Organic Research and Education Initiative. These large, multidisciplinary, nationally representative grants include entomologists, ecologists, geneticists, social scientists, and extension professionals. Second, we identified farmers growing SWD-affected fruit crops from grower organization email lists and from stakeholder advisory boards for USDA grants. We identified regulatory officials using publicly available lists of state level USDA Animal and Plant Health Inspection Service (APHIS) Coordinated Agricultural Pest Survey

personnel. We found additional participants from the attendee lists of an extension webinar series on SWD management. Finally, using a literature review and a search of organization websites, we identified individuals from conservation or environmental advocacy nongovernmental organizations that work on issues relating to biotechnology.

We sent study invitations to 681 potential participants. The invitation contained an introduction to our project and the link to our online survey. We sent follow-up email reminders one week after the initial invitation. A total of 184 stakeholders completed the survey, including 42 academics, 89 growers, 8 individuals from non-governmental organizations, 7 individuals from industry, 27 regulators and other government officials, and 11 people who categorized themselves as "other" without further specifying their affiliation. With 270 respondents initiating the survey and 184 respondents completing the gene drive section of the survey relevant to this paper, we had a 27.0% response rate and a 68.1% completion rate.

This survey was designed and administered using the survey software program Qualtrics. The survey consisted of 9 substantive questions on gene drive technology divided into three sections: introduction, potential adverse effects, and potential benefits (Tables 1-3). In the introduction section, we first asked participants to report their level of familiarity with both SWD and genetic pest management techniques. We then provided a general description of gene drive technology and how it could be used to manage SWD (see Supplementary Information). Due to the fact that this research is ongoing, we kept this a broad description and did not provide specific attributes of the technology (e.g., whether the gene drive would be self-limiting) or where it would be used. Following this description, we asked participants an open-ended question about what factors influence their decision making concerning whether to support gene drive technology. The introductory section concluded with a question asking to what degree they personally support or oppose the use of gene drive technology to control SWD (Table 1).

The survey continued by asking stakeholders to judge the importance of potential benefits and their degree of concern about potential adverse effects (Tables 2–3). In other words, which potential benefits are most important to assess and realize and which potential adverse effects are most important to assess and prevent. The list of potential adverse effects and potential benefits that stakeholders assessed was compiled from three previous focus groups with SWD stakeholders (See description in Kokotovich et al., 2020) and verified for completeness by a review of the literature. In addition to Likert scale questions, we also asked stakeholders to do a forced ranking of the potential benefits and potential adverse effects. For the potential benefits, we also asked stakeholders to identify what decrease in SWD populations would need to result from the use of this gene drive technology for them to support using it.

Concerning our analysis of the data, first, for the Likert scale questions of the Introduction (#1, 2, and 4), we simply identified the percentage of stakeholders who selected each choice. For the open-ended question (#3) on the factors influencing their decision making, we reviewed these factors and paid attention to how they highlight the reasoning used by participants in their answers to the questions on

Table 1 Introductory survey questions.

Question

- 1 How familiar are you with spotted-wing drosophila? [5 point Likert scale]
- 2 How familiar are you with genetic pest management techniques (e.g., gene drive technology or genetically engineered insects)? [5 point Likert scale]
- 3 When considering whether to support gene drive technology for managing SWD, what are the 3 most important factors that influence your decision making? These may be economic, ecological, social, or political factors. [Open-ended]
- 4 Overall, to what extent do you personally support or oppose the use of gene drive technology to control SWD? [5 point Likert scale]

Table 2

Survey questions on potential adverse effects from the use of gene drive technology to control SWD.

Ouestion

5 How concerned would you be if the following potential adverse effects occurred as a result of the use of gene drive technology to control SWD? [5 point Likert scale]

Agricultural and environmental potential adverse effects:

- Increase in non-SWD secondary pest infestations but below the current level of SWD infestation
- Increase in non-SWD secondary pest infestations above the current level of SWD infestation
- c. Decrease in beneficial insects (e.g., natural enemies and pollinators) that leads to a measurable reduction in their pollination or predation rates
- d. Decrease in beneficial insects (e.g., natural enemies and pollinators) that leads to an over 50% reduction in pollination rates
- e. Decrease in other non-target animals (e.g., birds and bats)
- f. Extinction of the SWD species in its native range (East Asia) resulting from the spread of the gene drive SWD to the native range of the SWD

Socio-economic potential adverse effects:

- g. Decrease in profits from decreased sales e.g., from negative consumer or regulatory reaction to gene drive technology (domestic or international)
- h. Decrease in profits from increased costs e.g., cost of management or postharvest screening
- Loss of organic certification to growers using, or exposed to, gene drive technology – e.g., from the detection of residue of gene drive organisms on the target crop
- j. Decrease in grower autonomy e.g., from not being able to avoid a gene drive that is designed to spread without limit
- becrease in public reputation of those involved in the development and use
 of this technology e.g., from public disapproval of the technology
- l. Decrease in research and management funding for other, non-gene drive, methods to control SWD $\,$
- 6 Please rank the following potential adverse effects from most to least important for informing your decision making on whether to support gene drive technology for managing SWD. [Forced ranking]
 - a. Increase in non-SWD secondary pest infestations
 - b. Decrease in beneficial insects
 - c. Decrease in other non-target animals
 - d. Extinction of the SWD species in its native range
 - e. Decrease in profits
 - f. Loss of organic certification to growers using, or exposed to, gene drive technology
 - g. Decrease in grower autonomy
 - Decrease in public reputation of those involved in the development and use of gene drive technology
 - Decrease in research and management funding for other, non-gene drive, methods to control SWD

potential adverse effects and potential benefits (Questions #5–9). We intersperse these qualitative answers within our findings to shed light on the participant reasoning.

For the Likert scale questions on potential adverse effects and potential benefits (#5 and 8), we looked at how participant support or opposition to the SWD gene drive technology related to the degree of importance they assigned for each potential benefit and the degree of concern they assigned for each potential adverse effect. For each potential adverse effect and potential benefit, we performed a hypothesis test using a two proportion Z-test to see whether there was a statistically significant difference in the proportion of stakeholders who expressed Moderate, High, or Extreme levels of concern (or importance) vs. Slight or None at all. The null hypothesis in these tests is that the proportions are the same and actual proportions are presented in Figs. 3–5. We conducted these tests at the 95% and 99% confidence levels.

The potential adverse effects and potential benefits forced ordinal ranking total scores were calculated using a point-based system. For example, Question #9 on potential benefits contained six choices being ranked, so all first place votes received 6 points, all second place votes 5, and so on with all sixth place votes receiving one point. For Question #7 on the decrease in SWD populations needed for support of the

Table 3

Survey questions on potential benefits from the use of gene drive technology to control SWD.

Ouestion

- 7 What decrease in SWD populations would need to result from the use of this gene drive technology for you to support using it? That is, you would not support the use of this technology unless it reaches or exceeds this level of reduction in SWD populations. [Multiple choice a through f]
 - a. Extirpation of SWD This gene drive technology would need to completely eliminate SWD in the entire United States for me to support this technology.
 - Very high level of decrease in SWD populations This gene drive technology would need to achieve complete local eradication of SWD for me to support it
 - c. High level of decrease in SWD populations This gene drive technology would need to reduce SWD populations to prevent any measurable crop damage for me to support it.
 - d. Moderate level of decrease in SWD populations For me to support his technology, it would need to keep the SWD population below the Economic Injury Level (EIL) for pesticide use. That is, this gene drive technology would have to prevent pesticides from needing to be used. (EIL = The smallest number of SWD that will cause losses equal to the insect management costs.)
 - Low level of decrease in SWD populations Any decrease in SWD populations would be enough for me to support this technology.
 - f. My support (or lack of support) of this technology does not depend on its ability to suppress the SWD population
- 8 How important to you are each of the following potential benefits that could result from the use of gene drive technology to control SWD? [5 point Likert scale]
 - a. Decrease in the quantity or toxicity of pesticides used
 - b. Increase in beneficial insect (e.g., natural enemy and pollinator) population size, pollination rates, predation or parasitism
 - c. Increase in grower profit
 - d. Increase in knowledge about gene drives & emerging biotechnologies for pest management
- e. Increase in consumer acceptance of emerging biotechnologies in agriculture
 Please rank the following potential benefits from most to least important for informing your decision making on whether to support gene drive technology for managing SWD. [Forced ranking]
 - a. Decrease in SWD populations
 - b. Decrease in the quantity or toxicity of pesticides used
 - c. Increase in beneficial insects
 - d. Increase in grower profit
 - e. Increase in knowledge about gene drives & emerging biotechnologies for pest management
 - f. Increase in consumer acceptance of emerging biotechnologies in agriculture

technology, we show how stakeholder answers varied with regards to whether they supported or opposed the use of the gene drive technology.

3. Results

Overall, our sample of SWD stakeholders was made up of individuals who were well aware of SWD, with 71% reporting being *Highly* or *Extremely* familiar with SWD, and only 9% being *Slightly* or *Not at all* familiar (Fig. 1). Familiarity with genetic pest management techniques was markedly lower with only 14% being *Highly* or *Extremely* familiar and 51% being *Slightly* or *Not at all* familiar. SWD stakeholders largely indicated that they were personally supportive of the gene drive technology for managing SWD with 74% of respondents indicating that they *Support* or *Strongly Support* the use of gene drive technology to control SWD, and only 7% indicating that they *Oppose* or *Strongly oppose* its use (Fig. 1).

3.1. Potential benefits

There are three key components of our findings on the potential benefits from using gene drive technology to manage SWD: 1) Reduction of SWD required for support of the gene drive technology, 2) Importance of potential benefits, and 3) Ranked importance of potential benefits. Understanding how stakeholders prioritize potential benefits and what

levels of SWD reduction are required for stakeholder support of the technology can help inform technology development and broader governance decisions.

First, we analyzed what level of reduction in SWD populations needed to result from gene drive technology for stakeholders to support the technology (Fig. 2). High levels of required reduction indicate a high threshold for support. Our results show that over 80% of respondents indicated that SWD gene drive technology would have to result in at least a moderate level of reduction (i.e., "Keep the SWD population below the Economic Injury Level (EIL) for pesticide use. That is, this gene drive technology would have to prevent pesticides from needing to be used."). Only 8% of respondents said they would support the SWD gene drive technology if it provided any decrease in SWD populations. This finding indicates that stakeholders hold a high SWD suppression threshold for their support of gene drive technology. The high threshold of support was shared across stakeholders regardless of support or opposition to the technology. There are, however, proportionally far more stakeholders who oppose or neither support nor oppose the technology who selected "My support (or lack of support) does not depend on its ability to suppress SWD," implying that some of those who do not currently support gene drive technology SWD have concerns that are not addressed by whether and to what degree it can suppress SWD. At the same time, the only stakeholders who indicated that their support was dependent upon extirpation of SWD from the United States were those who oppose or neither support nor oppose the technology, perhaps implying that the lack of support may also be related to stakeholders judging it to be unlikely that the technology will realize the high amount of benefit needed justify the associated costs and risks.

Second, to understand stakeholder views on other potential benefits from using gene drive technology to address SWD, we asked stakeholders to judge the importance of 5 potential benefits (see Table 3). To examine whether support or opposition to the technology influenced stakeholder views about the importance of potential benefits, we present the findings on potential benefits according to degree of stakeholder support or opposition to the technology (Fig. 3). We found that stakeholders, regardless of support for the technology, largely judged all of the potential benefits to be important, with the proportion of respondents that chose *Moderately*, *Highly*, or *Extremely* important statistically larger than those chose *Slightly* or *Not at all* important for all potential benefits (significant at the 99% confidence level).

Finally, we also wanted to know which potential benefit was most important for stakeholder decision making concerning whether to support the technology, which we learned through the forced ranking of potential benefits. The forced ranking revealed three tiers of potential benefits (Table 4). The two most important potential benefits, by total rank score, were *Decrease in the quantity or toxicity of pesticides used* and *Decrease in SWD populations*. The importance of these potential benefits was reflected in the open-ended answers, as one respondent noted:

"If we can reduce the numbers of this pest, we as farmers can reduce the amount of pesticides we use, the money we spend on them, and the quality and overall safety of our products we sell to the consumers. No one likes to spray. We do this because this pest has left us no other options."

Another respondent noted that "eliminating SWD without pesticides is safer for human consumers, growers, ... the environment and fellow insects." The next two most important potential benefits were *Increase in grower profit* and *Increase in beneficial insects*. Finally, the least important potential benefits according to stakeholders were *Increase in knowledge about gene drives & emerging biotechnologies for pest management* and *Increase in consumer acceptance of emerging biotechnologies in agriculture*.

3.2. Potential adverse effects

There are three parts of our findings concerning potential adverse

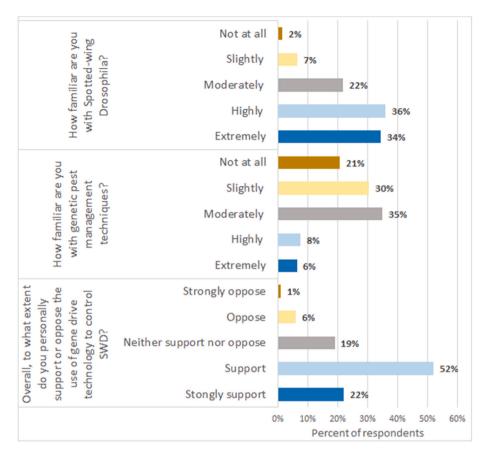


Fig. 1. Stakeholder familiarity with SWD and genetic pest management, as well as level of support or opposition to the use of gene drive technology to control SWD. Percentages rounded to the nearest percent.

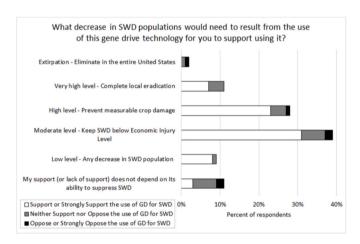


Fig. 2. Respondent answers to the question: "What decrease in SWD populations would need to result from the use of this gene drive technology for you to support using it? That is, you would not support the use of this technology unless it reaches or exceeds this level of reduction in SWD populations." Full wording of the multiple choice answers provided in Table 3.

effects from the use of gene drive technology to manage SWD: 1) Level of concern about agricultural and environmental potential adverse effects, 2) Level of concern about socio-economic potential adverse effects and 3) Ranked importance of all potential adverse effects. Knowing how SWD stakeholders prioritize different potential adverse effects can help inform what to include in future risk assessments on SWD gene drive technology and can help gene drive technology developers understand undesirable technology-related impacts.

First, we asked SWD stakeholders to indicate how concerned they would be if each of 6 agricultural and ecological potential adverse effects occurred as a result of the use of SWD gene drive technology. To examine whether support or opposition to SWD gene drive technology impacted this level of concern, we present these findings according to the degree of stakeholder support or opposition to the technology (Fig. 4). To assess how stakeholder views varied based on the degree of severity of the potential adverse effect, we included two degrees of secondary pest infestations (i.e., i. Below the current level of SWD infestation, and ii. Above the current level of SWD infestation) as well as two levels of decrease in beneficial insects (i.e., i. Measurable reduction in pollination or predation rates, and ii. 50% reduction in pollination rates). We found that stakeholders were most concerned about the following four agricultural and ecological potential adverse effects, shown by significantly more stakeholders indicating that they were Moderately, Highly, or Extremely concerned compared to Not at all or Slightly concerned (all statistically significant at the 99% confidence level):

- Increase in non-SWD secondary pest infestations above the current level of SWD infestation
- Decrease in beneficial insects (e.g., natural enemies and pollinators) that leads to a measurable reduction in their pollination or predation rates
- Decrease in beneficial insects (e.g., natural enemies and pollinators) that leads an over 50% reduction in pollination rates
- Decrease in other non-target animals (e.g., birds and bats)

Interestingly, the high level of concern about these 4 potential adverse effects was present regardless of the degree of support or opposition one held for the technology. As discussed further in Section 4, this shows that support for the technology does *not* equate to a lack of

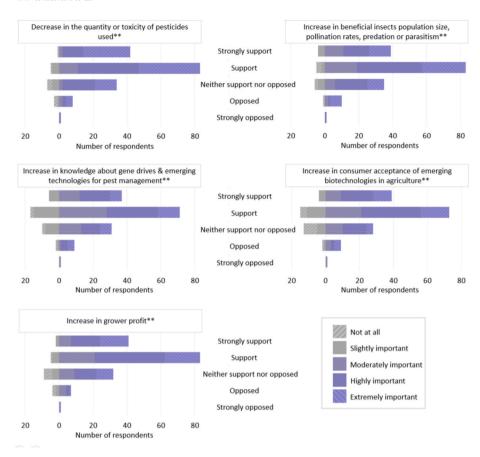


Fig. 3. Importance of potential benefits of SWD gene drive technology presented according to degree of support for or opposition to the use of SWD gene drive technology. The "**" indicates that across all stakeholders for a specific potential benefit, the difference between those indicating (1) Moderately, Highly, and Extremely important and (2) Not at all and Slightly important is significant at the 99% confidence level. These graphs show that the belief that the potential benefits are important is shared across SWD stakeholders and is not just held by those who support the technology. For example, for the Decrease in the quantity or toxicity of pesticides used potential benefit. of the 11 SWD stakeholders who indicated that they "Oppose" the use of the technology, 2 expressed that the potential benefit was Moderately important, 2 Highly important, and 4 Extremely important, while 1 SWD stakeholders expressed that the potential benefit was Slightly important and 2 expressed it was Not at all important.

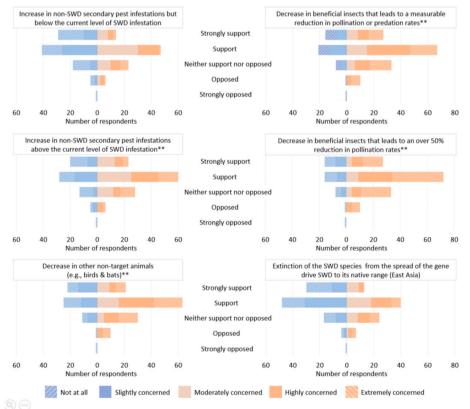


Fig. 4. Level of concern about agricultural and ecological potential adverse effects of SWD gene drive technology presented according to degree of support for or opposition to the use of SWD gene drive technology. The "**" indicates that across all stakeholders for a specific potential adverse effect, the difference between those indicating (1) Moderately, Highly, and Extremely concerned and (2) Not at all and Slightly concerned is significant at the 99% confidence level. These graphs show that the concern about potential adverse effects is shared across SWD stakeholders and is not held solely by those who oppose the technology. For example, for the Decrease in beneficial insects that leads to a measurable reduction in pollination or predation rates potential adverse effect, of the 88 SWD stakeholders who indicated that they "Support" the use of the technology, 15 expressed that they were Moderately concerned about the potential adverse effect, 32 were Highly concerned, and 20 were Extremely concerned, while 14 SWD stakeholders were Slightly concerned and 7 were Not at all concerned.

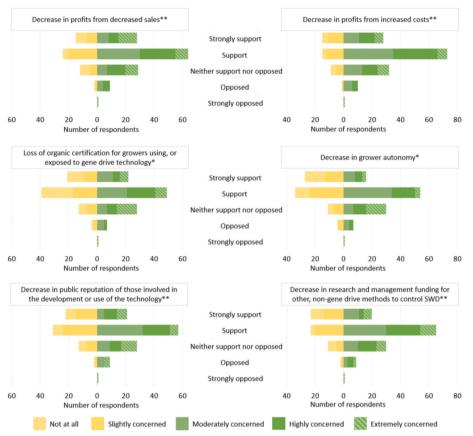


Fig. 5. Level of concern about socio-economic potential adverse effects of SWD gene drive technology presented according to degree of support or opposition for the use of SWD gene drive technology. The "**" indicates that across all stakeholders for a specific potential adverse effect, the difference between those indicating (1) Moderately, Highly, and Extremely concerned and (2) Not at all and Slightly concerned is significant at the 99% confidence level, and the "*" indicates the difference is significant at the 95% confidence level. These graphs show that the concern about potential adverse effects is shared across SWD stakeholders and is not held solely by those who oppose the technology. For example, for the Decrease in profits from increased costs potential adverse effect, of the 88 SWD stakeholders who indicated that they "Support" the use of the technology, 35 expressed that they were Moderately concerned about the potential adverse effect, 31 were Highly concerned, and 7 were Extremely concerned, while 12 SWD stakeholders were Slightly concerned and 3 were Not at all concerned.

Table 4

Rank order of potential benefits by total rank score resulting from the question: "Please rank the potential benefits that you have selected from most to least important for informing your decision making on whether to support gene drive technology for managing SWD." Percentage of respondents who ranked each potential potential benefit 1st, 2nd, and 3rd is also shown. The total rank score was calculated using a simple, point-based ranking. All first place votes received 6 points, all second place votes 5, and so on with all sixth place votes receiving one point.

Rank order of potential benefits	1st choice	2nd	3rd	Total rank score
Decrease in the quantity or toxicity of pesticides used	32%	38%	21%	721
2. Decrease in SWD populations	41%	31%	10%	692
3. Increase in grower profit	19%	12%	14%	520
4. Increase in beneficial insects	3%	13%	41%	519
 Increase in knowledge about gene drives & emerging biotechnologies for pest management 	1%	2%	10%	316
6. Increase in consumer acceptance of emerging biotechnologies in agriculture	3%	5%	4%	295

concern about potential adverse effects. This level of concern was not held for the potential adverse effects Increase in non-SWD secondary pest infestations but below the current level of SWD infestation and Extinction of the SWD species in its native range (East Asia) – resulting from the spread of the gene drive SWD to the native range of the SWD for which there is no significant difference between Moderately, Highly, or Extremely concerned compared to Not at all or Slightly concerned. The low level of concern about the extinction of SWD in its native range may have to do with the fact that these stakeholders are based in the United States and many may not be aware of the role SWD plays in its native range while they are currently and intimately experiencing negative impacts from

SWD.

Second, we asked SWD stakeholders to indicate how concerned they would be if each of 6 socio-economic potential adverse effects occurred as a result of the use of SWD gene drive technology. Once again, to examine whether support or opposition to SWD gene drive technology impacted this level of concern, we present these findings according to the degree of stakeholder support or opposition to the technology (Fig. 5). We found that stakeholders were most concerned about the following four socio-economic potential adverse effects, shown by significantly more stakeholders indicating that they were Moderately, Highly, or Extremely concerned compared to Not at all or Slightly concerned (statistically significant at the 99% confidence level):

- Decrease in profits from decreased sales e.g., from negative consumer or regulatory reaction to gene drive technology (domestic or international)
- Decrease in profits from increased costs e.g., cost of management or post-harvest screening
- Decrease in public reputation of those involved in the development and use of this technology – e.g., from public disapproval of the technology
- Decrease in research and management funding for other, non-gene drive, methods to control SWD

Similar to the agricultural and ecological potential adverse effects, the high level of concern was present for both those who supported and opposed the use of the technology. The level of concern was lower for the potential adverse effects Loss of organic certification to growers using, or exposed to, gene drive technology – e.g., from the detection of residue of gene drive organisms on the target crop and Decrease in grower autonomy – e.g., from not being able to avoid a gene drive that is designed to spread without limit as the differences between Moderately, Highly, or Extremely concerned compared to Not at all or Slightly concerned were significant at the 95% confidence level.

Finally, to understand stakeholder prioritization across all potential

Table 5

Rank order of potential adverse effects by total rank score resulting from the question, "Please rank the following potential adverse effects from most to least important for informing your decision making on whether to support gene drive technology for managing SWD." Percentage of respondents who ranked each potential adverse effect 1st, 2nd, and 3rd is also shown. The total rank score was calculated using a simple, point-based ranking. All first place votes received 9 points, all second place votes 8, and so on with all ninth place votes receiving one point.

Rank order of potential adverse effects	1st choice	2nd	3rd	Total rank score
1. Decrease in beneficial insects	30%	26%	16%	1141
Increase in non-SWD secondary pest infestations	19%	21%	19%	988
3. Decrease in grower profits	19%	7%	11%	984
4. Decrease in other non-target animals	4%	19%	20%	890
 Loss of organic certification to growers using, or exposed to, gene drive technology 	7%	8%	8%	669
6. Decrease in grower autonomy	4%	2%	6%	643
 Decrease in public reputation of those involved in the development and use of gene drive technology 	8%	6%	6%	633
Decrease in research and management funding for other, non-gene drive, methods to control SWD	2%	7%	9%	608
Extinction of the SWD species in its native range	7%	4%	5%	598

adverse effects we had them complete a forced ranking (Table 5). By far, the most important potential adverse effect was *Decrease in beneficial insects*. In other words, *Decrease in beneficial insects* is the potential adverse effect that stakeholders are most keen on avoiding - the adverse effect that if it were to occur would impact their support for the technology most. For SWD gene drive technology to be successful, therefore, it is important to both rigorously study the potential for, and seek to avoid, adverse effects on beneficial insects. The importance of beneficial insects was reflected in the qualitative data as numerous respondents wrote about the importance of avoiding non-target effects across the landscape and across different species. For example, one respondent argued that the gene drive technology needed to be a:

"targeted action [that] ONLY affects SWD and NO other flies" as "the environment ... does not need yet another pressure, it's so messed up [that] I worry [about] when we are going to pull the wrong brick out of the ecosystem and the whole thing will collapse. I am especially concerned about insects."

Another stakeholder expressed this concern in a more specific way, expressing concern about the "Effect on non-target organisms, specifically *Drosophila melanogaster*. These two species are closely related. Is there a potential for this gene to cross over to melanogaster from SWD? What are the potential implications of that?" The next most important potential adverse effects were *Increase in non-SWD secondary pest infestations* and *Decrease in grower profits*. Concerning grower profits, one stakeholder emphasized, "You can't stay in business if you can't afford the control measures." Across these potential adverse effects, then, one can see a pragmatic trio of most important concerns: not wanting SWD gene drive technology to reduce beneficial insects, lead to secondary pest infestations, or lead to a reduction in grower profits.

4. Discussion

4.1. Support for the SWD gene drive technology does not equate to a lack of concern about potential adverse effects

One of the most noteworthy findings from this study is that SWD stakeholders who indicated support for the use of gene drive technology

still expressed concern about potential adverse effects from the technology (Figs. 4 and 5). In other words, support for the gene drive technology does not equate to a lack of concern about the potential adverse effects from the technology. Furthermore, many of the respondents who indicated support for the use of the technology still expressed the need for high SWD suppression thresholds for their support - that is, the vast majority of stakeholders who supported or strongly supported the use of gene drive technology stated that their support is conditional on the technology keeping SWD populations at least below the Economic Injury Level (Fig. 2). These findings challenge a simple, dichotomous view of stakeholders as either completely supporting and accepting or completely opposing and questioning all aspects of SWD gene drive technology. It shows that stakeholders may express overall support for the use of a technology while still expressing concern about potential adverse effects and desiring a certain threshold of effectiveness. In this case, the fact that 51% of our respondents were Slightly or Not at all familiar with genetic pest management techniques may also contribute to the broad support for the technology while at the same time being concerned about potential adverse effects and requiring a high SWD suppression threshold for support. Since SWD stakeholders are aware of or experiencing the consequences of SWD, it is perhaps not surprising that they would be supportive of a potential solution (even one they know little about) if it performs well and does not cause adverse effects.

One of the implications of these findings concerns the importance of risk assessment and benefits assessment for SWD gene drive technology. Given the widespread concern about certain potential adverse effects, across degree of support for the technology, it will be important to conduct rigorous risk assessments to understand whether and under what conditions the use of SWD gene drive technology would lead to those potential adverse effects. These findings mirror the broader prescriptive literature that has called for thorough and trusted risk assessments on gene drive technology (Kuzma, 2020). In addition, the high threshold of support (i.e., Keep SWD populations below the Economic Injury Level) and the highest ranked potential benefit (i.e., Decrease in the quantity or toxicity of pesticides used) indicate the importance of benefits assessment. Given the value SWD stakeholders place on these potential benefits, it will be essential to consider whether and under what conditions proposed SWD gene drive technologies can actually realize such a SWD population reduction and decrease in pesticide usage. This finding is supported by Hartley et al. (2021) who argue that it is important not to assume that the benefits from gene drive technology will necessarily materialize. Instead, they suggest that the same level of scrutiny provided to risks needs to be paid to the technical, ecological, and social conditions that must be realized for the benefits to

Our results also point to the need for nuance in discussions concerning whether and how to use SWD gene drive technology and emerging biotechnologies, more broadly. Public or stakeholder perception research often focuses on simple notions of support or opposition, but by focusing only on this binary, other important issues are ignored. Focusing only on determining stakeholder support or opposition to the SWD gene drive technology would have overlooked stakeholder views on potential adverse effects and potential benefits that inform those decisions. In addition, the support/opposition binary neglects the views that are shared across respondents who indicated different levels of support or opposition. For example in this survey, SWD stakeholders largely shared concerns about key potential adverse effects (e.g. decrease in beneficial insects and decrease in profits) and deemed important certain potential benefits (e.g., decrease in SWD populations and decrease in pesticide usage).

Furthermore, these findings show the need to interrogate what it means to support or oppose the use of a technology. While some may assume that support for a technology means, "I want this technology used now or as soon as possible", these findings suggest it may actually mean, "I support the use of this technology if it achieves certain benefits

and avoids certain adverse effects." In reality, then, someone who supports a technology may not differ that much from someone who opposes the use of a technology while thinking, "I oppose the use of this technology because I don't think it will be effective and I don't think that certain adverse effects have been adequately assessed." Gene drive technology for SWD is still in development such that we do not yet know what level of effectiveness will be realized in any particular context, nor do we know how likely or severe certain adverse effects are going to be in any particular context. As a result, at this point, it seems to matter less whether one supports or opposes a technology and more what key factors influence one's decision making. In this regard, our findings highlight both potential adverse effects and potential benefits that are important to consider in the context of gene drive technology to manage SWD.

4.2. Engagement for gene drive risk assessment and benefit assessment

In addition to highlighting the importance of risk assessment and benefit assessment to the governance of gene drive technology for SWD, our findings also provide an example of how to use stakeholder engagement to inform these assessments. The problem formulation stage of risk assessment contains a host of important judgments that influence what form the resulting risk assessment will take. One of the most consequential judgments is which potential adverse effects to prioritize if a potential harm is not assessed, then it cannot inform decision making. And while there have been continued calls for stakeholder engagement to inform risk assessment for emerging biotechnologies, there is a lack of empirical work doing so. In this study, we used an online survey to have SWD stakeholders prioritize potential adverse effects from the use of SWD gene drive technology. Of the potential adverse effects that we asked about, the three most important for SWD stakeholders were: Decrease in beneficial insects, Increase in non-SWD secondary pest infestations, and Decrease in grower profits. In any future risk assessments of SWD gene drive technology, it will be important to assess whether and under what conditions these potential adverse effects would occur from using the technology.

While benefits assessment is much less theoretically developed than risk assessment, a similar initial problem formulation process is also required. Such a process can, for example, identify the most important potential benefits and can be informed by the views of stakeholders and other relevant parties. In the context of SWD gene drive technology, we have identified some of the most important potential benefits, according to stakeholders. All potential benefits that we asked about were deemed important, however when we asked stakeholders to do a forced ranking, clear preferences emerged with a first tier of *Decrease in the quantity or toxicity of pesticides used* and *Decrease in SWD populations* followed by *Increase in grower profit* and *Increase in beneficial insects* (Table 4). In any future benefits assessment for SWD gene drive technology, it will be important to assess the technical, ecological, and social conditions needed to recognize these potential benefits.

Concerning next steps, it is important to note that once a specific gene drive technology has been developed to manage SWD in a particular location, it will be necessary to conduct further engagement to inform risk assessment for that technology. Because this technology is still in development and not proposed for use in a particular area, we asked about general types of potential adverse effects (e.g., beneficial insects) and not about specific species in a particular area. The potential adverse effects and potential benefits that we asked about emerged from previously conducted focus groups on broadly defined gene drive technology for SWD (see Kokotovich et al., 2020) and were verified for completeness by a review of the literature. If, however, a specific gene drive technology for a specific location were to be developed, it would be important to conduct additional engagement to further specify and prioritize the potential adverse effects and potential benefits. For example, what specific species should be assessed (e.g., a particular pollinator species) and what amount of change to a particular attribute

is considered harm and/or unacceptable harm (e.g., a 25% decrease in a population size). Furthermore, in addition to further specifying and prioritizing potential adverse effects, it will also be important to incorporate engagement into other aspects of problem formulation and other components of risk assessment (Hartley and Kokotovich, 2018; Kokotovich et al., 2020; Stirling et al., 2018).

5. Conclusion

Emerging biotechnologies, such as gene drive technology, are increasingly being proposed to address a variety of pest, invasive species, and human health issues. There have been wide calls for societal engagement to inform the research and development, risk assessment, and governance decisions surrounding these technologies. One component of rigorous, relevant, and inclusive risk assessment involves understanding how stakeholders define and prioritize potential adverse effects from these technologies. Understanding how stakeholders define and prioritize potential benefits from these technologies is important for governance. In the context of proposed gene drive technology to manage SWD, we conducted a survey of 184 SWD stakeholders to explore how they define and prioritize potential benefits and potential adverse effects of SWD gene drive technology.

Key findings from this study include that SWD stakeholder identified the most important potential benefit as Decrease in the quantity or toxicity of pesticides used. In addition, over 80% of SWD stakeholders expressed that their support for SWD gene drive technology was dependent upon the technology reaching at least a moderate level of SWD suppression (i. e., "Keep the SWD population below the Economic Injury Level (EIL) for pesticide use"). Stakeholders were most concerned about the potential adverse effects Decrease in beneficial insects, Increase in non-SWD secondary pest infestations, and Decrease in grower profits. Furthermore, we found that even stakeholders who supported and strongly supported the use SWD gene drive technology still expressed moderate, high and extreme levels of concern about many of the potential adverse effects. In other words, support for the technology did not equate to a lack of $concern\ about\ potential\ adverse\ effects-emphasizing\ the\ importance\ of$ risk assessment and moving away from simplistic, dichotomous notions of what it means to support or oppose a technology. The outcomes of our research can help inform SWD gene drive technology development and risk assessment going forward. Our findings can also help inform future engagement around SWD gene drive technology, such as in the design of broader public surveys, stakeholder workshops and community meetings.

Author contributions

AK designed the survey, contributed to the survey analysis, and drafted and revised the manuscript; KB administered the survey, contributed to the survey analysis, and reviewed and provided feedback on the manuscript; JE designed and conducted the focus groups that informed the survey, provided feedback on survey design and analysis, created Figs. 3–5 for manuscript, helped draft the manuscript sections on SWD biology and management, and reviewed and provided feedback on the manuscript; RL conducted the statistical analysis of the survey and reviewed and provided feedback on the manuscript; JD provided feedback on the study design and analysis and reviewed and provided feedback on the manuscript; HB obtained funding for and oversaw the project, provided feedback on the study design and analysis, helped draft the manuscript sections on SWD biology and management, and reviewed and provided feedback on the manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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