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Letter to the Editor

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Letter to the Editor

Gene drive: communication, hype, and the publics

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Engineered gene drive (EGD) systems are probably the most high-tech approach considered for their potential role in the control of vector-borne diseases. Interestingly, the rhetoric around it often goes along with a negative presentation of the current "conventional" tools and exaggerated promises about EGD themselves, leading to a situation of hype.

Keywords: hype, engineered gene drive, malaria, communication, trust

The discovery of CRISPR has accelerated the development of engineered gene drive (EGD) systems that could be used to spread desired traits in a target species (population replacement) or to exterminate a population within a few generations. This controversial and disruptive technology has raised hopes and fears regarding its application for public health (malaria control), conservation (protection of endangered species, elimination of invasive ones), or agriculture (pest control). Among the different domains where an approach relying on EGD is considered, the fight against malaria is at the forefront. While aiming ultimately at the same goal of reducing malaria burden, the 2 different approaches result in different entomological outcomes. In the case of population removal, the vector is expected to be suppressed leaving its ecological niche vacant and, theoretically without the persistence of modified mosquitoes in the environment. In a strategy based on population replacement, the release of modified mosquitoes designed to be nonvectors should lead to them remaining in the environment without contributing to disease transmission. While most of the work on EGD has been conducted on some malaria vectors, *Aedes aegypti* (L.)*(L.)(L.)*, a major dengue vector, is now also the target of such approaches (Anderson et al. 2023, 2024). Promoters of EGD in vector control often showcase a number of potential advantages usually falling into the semantic category associated with hypes as defined in Millar et al. (2022) for this technology: its novelty, its cost-effectiveness, its scalability, and the ability to reach last-mile. Note that clearly modeling is seen as a key field of research to determine the potential entomological and epidemiological outcomes for population replacement (Boëte and Koella 2002) or population suppression (Hancock et al. 2024), but it also highlights several critical aspects and limitations of gene drive (crucial efficacy of the refractoriness, persistence of nonmodified vector species, dispersal to name a few). In this context, this is then essential to consider the discourse about the malaria situation and the control of its vectors.

What Do We Hear and Read About Malaria Vector Control?

Resistance to insecticides and antimalarial drugs is a recurring theme in malaria literature, frequently serving as a prelude to discussions on optimizing current methods for controlling vectors and parasites. Unsurprisingly, this topic also features prominently in publications advocating for the development of engineered genetic drives (EGD), often cited as a key justification for their future implementation. The limitations and obsolescence of existing tools are commonly highlighted in a pessimistic narrative that emphasizes their shortcomings, reinforcing the notion that new tools are needed rather than improving the use of those currently available. This perspective, however, tends to narrow the focus on biological explanations for the persistence and spread of vector-borne diseases, overlooking the broader, more complex factors at play. While biological resistance is important, it is insufficient to explain the full picture, which includes demographic, environmental, cultural, political, and socioeconomic influences. As Packard emphasizes in the Making of a Tropical Disease (Packard 2021) rise in vector-borne diseases cannot be attributed solely to biological factors; rather, it results from the intricate interplay of various systemic forces. Despite this, the discourse often falls short of critically examining health policies or calling for socioeconomic changes. Given the complex drivers of disease spread, it is essential to consider both the current global malaria situation and future projections in a more nuanced light. It is then essential to examine the recent evolution of the worldwide malaria situation and the associated forecasts.

Malaria, Where Are We Now?

The recent World Malaria Report 2024 (WHO 2024) provides valuable insights into both the progress made over the past 2 decades and the future outlook for malaria control. Nearly half of the global population remains at risk of malaria, and in 2022, the disease caused 597,000 deaths, with a case incidence of 60.4 per 1,000 people at risk and a mortality rate of 13.7 per 100,000. While there was a slight increase in malaria cases in 2021 due to disruptions caused by the COVID-19 pandemic and humanitarian crises, overall, malaria situation has improved since 2000. Several countries reported zero malaria deaths or indigenous cases since 2022, including Cabo Verde, São Tomé and Príncipe, Comoros, Egypt, Bhutan, Timor-Leste, and Thailand, while others, such as Argentina, Belize, China, El Salvador, and Paraguay, have been certified malaria-free for several years. Despite a plateau in recent years, there has been a significant global decline in malaria incidence, dropping from 81 cases per 1,000 population at risk in 2000 to 57 in 2019 (WHO 2020). During this period, an estimated 1.5 billion cases and 7.6 million deaths were averted. In the African region, while progress has fallen short of targets, there has still been a noticeable decline, with a malaria mortality rate of 52.4 per 100,000 people at risk in 2023. In contrast, the WHO South-East Asia region has surpassed expectations, with projections indicating that the malaria case incidence could drop to 0.8 per 1,000 people at risk by 2030 if current trends continue. These achievements, conducted with the use of LLINs and IRS but also via cases surveillance, the establishment of a network of diagnostic laboratories as well as socioeconomic improvement and the implementation of poverty alleviation projects demonstrate that effective tools for malaria control exist. To explain failure or delay in reducing malaria incidence, one might blame the highly anthropophilic behavior of major African malaria vectors compared to vector species elsewhere but, again, this strictly biological explanation does not hold when one recalls the successful elimination of the African malaria vector *An. gambiae* in northeast Brazil. Taking advantage of the anthropophilic behavior of this vector, the heavily financed campaign was conducted in a rigorous and integrated manner largely based on larval control and was repeated with similar success in Egypt and Zambia (Killeen et al. 2002, Killeen 2003). However, chronic shortages of skilled health professionals and limited resources in endemic countries continue to hinder progress. Meanwhile, new strategies, such as chemoprevention, intermittent preventive treatment (IPTp and IPTi), and seasonal malaria chemoprevention, are being developed, and innovation is evident in other vector control efforts, such as the successful *Wolbachia* trial against *Aedes* mosquitoes and dengue in Indonesia (Utarini et al. 2021).

The Rhetoric About EGDs

Despite the demonstrated success of existing tools and methods—evidenced by several countries, including African ones achieving malaria-free certification and progress in many regions—a pessimistic narrative still pervades discussions around vector-borne disease control. This often accompanies the promotion of gene drive technology, highlighting its purported advantages: innovation, precision (Schairer et al. 2021), and, in some cases, the term "precision drive" is used to emphasize its accuracy (Esvelt et al. 2014). Additionally, proponents sometimes frame gene drive as a biocontrol method rather than a genetic intervention, as reflected in publications (James et al. 2018). One of the key arguments for gene drive is its potential to revolutionize vector control by employing a modified mosquito as the active tool, a real shift in vector control transforming a disease-bringing agent to a benevolent public health tool (Beisel and Boëte 2013). Advocates suggest this could offer significant benefits, such as self-sustainability, resilience against financial limitations, and reduced reliance on community participation in control efforts. While lab research has indeed shown promising results—such as the elimination of *Anopheles gambiae* populations in cage trials (Hammond et al., 2021) and high transmission rates of modification drives to nearly all offspring in *Anopheles gambiae* (Carballar-Lejarazú et al. 2020) and *Anopheles stephensi* (Adolfi et al. 2020)—these successes are limited to a few (even major) malaria vectors and restricted to laboratory settings. Moreover, once released in the wild, gene drives may not function as expected especially in the long term. In the case of population suppression, secondary vectors might become substantially more important, eroding the expected initial benefits of a gene drive release for a given vector. Importantly, the contribution of vector species to malaria transmission has changed over the last 20 years, and *Anopheles funestus* has now become a major vector in East and Southern Africa (Msugupakulya et al. 2023). Given that its genetic modification is still in its early stages (Quinn et al. 2021), the optimism around gene drive's potential should again be viewed with caution.

Furthermore, when considered within the broader research and development landscape for malaria eradication (Feachem et al. 2019), gene drive systems are projected to have only an average probability of successful development, with a timeline extending to 2030. In contrast, several other strategies—including new insecticides, medicines, data hubs, and improved program management—are expected to deliver similar impacts but with higher success rates of development and shorter development times. Thus, the prospects for gene drive, while promising, do not stand out. The positive rhetoric about gene drive is often found in mainstream (Crisanti and Kyrou 2018; Wade 2018) and scientific publications that make bold promises and overpromote certain technologies. The gene drive approach is frequently portrayed as a groundbreaking and exciting tool in the fight against malaria, likely to encourage public acceptance. This reflects the phenomenon of "hype," which has been well-documented in biotechnology (Caulfield 2004) and that corresponds here to what Fleising described as a "possessing nature" form of hype (Fleising 2001). Years ago, a similar situation arose during the Human Genome Project, where exaggerated claims about DNA's potential to cure diseases led to the term "Genohype" being coined (Holtzman 1999). Such hype often stems from the interactions between geneticists, funding bodies, and the public (Caulfield and Condit 2012) and, at that time, the sequencing of the human genome was accompanied by unrealistic expectations and hyperbole. Once again, there is a risk of a gap between the promises made and the actual outcomes delivered.

When discussing the causes of this hype, it is tempting to pinpoint a single source, but the reality is more complex. As shown in previous studies on genetic research the situation of hype is not only the result of an inaccurate convey of research results by the media but an overemphasis on benefits and under-representation of risks in both scientific and newspaper articles (Bubela and Caufield 2004). While the mass media amplifies the hype, it is shaped by input from various stakeholders: scientists, funding agencies, businesses, and the public itself (Caulfield 2004, Caulfield and Condit 2012). In the case of gene drive technology, press releases play a significant role, but there is also a broader distortion in how science is portrayed. Rather than focusing on the collective efforts of research teams, there is an emphasis on individual scientists or inventors, simplifying the narrative and making it more relatable. This, in turn, contributes to a skewed presentation of the science, often highlighting uncertain benefits for

public applications while downplaying the limitations (Woloshin et al. 2009). Another issue tied to the hype is the risk of a creation of a "scientific bandwagon," when a large number of people, organizations commit their resources to one approach to a problem as described by Fujimura about cancer research (Fujimura 1988). This occurs when research projects become driven by exaggerated claims, partly to secure ongoing funding. In this context, negative results are often minimized, while any positive outcomes are disproportionately emphasized, further fueling the cycle of hype.

Any Risk to Research?

While EGD (Engineered Genetic Drives) is often positioned as a promising long-term investment in malaria control or eradication, focusing research efforts on its development may unintentionally bias policy discussions and divert resources away from simpler, proven approaches as already discussed years ago with the investment in genomics in the fight against malaria (Curtis 2000), a situation that could undermine more immediate solutions.

Moreover, the hype surrounding EGD could foster unrealistic public expectations, given the high level of trust placed in researchers. If the results fail to meet these expectations, there is a genuine risk of eroding public trust—an essential factor in the success of vector control initiatives.

Beyond the sociological impact of overhyping EGD, there is also the risk of distorting perceptions of the actual risks involved. This could lead to a poorly informed policy debate about EGD's benefits and risks, potentially resulting in its premature implementation before all implications are fully understood.

Conclusion

The current communication around EGD often borders on propaganda rather than fostering a balanced, 2-way dialogue. While this manuscript does not advocate for a status quo over innovation in the fight against malaria, it is clear that researchers should avoid sensationalism with providing achievements in the field first. Research institutions must also exercise caution when promoting scientific advancements in press releases and media, ensuring that accurate, reliable information reaches the public. There is little doubt that misinformation about science can fuel or exacerbate public distrust, a dangerous path that scientists cannot afford to take, especially when public health is at stake.

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