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Letter

Response to the Comments of J.S. Lord

Thierry De Meeûs,[1,*] Sophie Ravel,[1] Philippe Solano,[1] and Jérémy Bouyer[1,2,3]

We thank Dr Lord for her letter [1] that presents criticism on some of the ideas we proposed in [2]. In the following, we answer the different points raised by Dr Lord.

Saying that dispersal of tsetse flies increases ~100-fold with population reduction represents a distortion of what we demonstrated. We showed that populations of tsetse flies with high densities disperse at much smaller distances than populations with low densities. In our graph, the 100-fold dispersal increase raised by Dr Lord would mean a 10^5-fold density decrease, which would be hardly observable.

We agree with Dr Lord that dispersal is species-specific. In our figure, the same species is present more than once. Some species disperse more than others at the same density, or display different densities, but the correlation remains strong. From there, we predict that any other data set of tsetse flies should fit into our graphic. This is the case for a recent paper [3] (density = 169 flies/km^2 and dispersal = 1.12 km/generation, fitting in the middle of our graphic). The population genetics parameters we used were measured in populations in relative migration–mutation–drift equilibrium. Any evaluation undertaken just after treatment would either have provided the same parameters, if no immigration occurred (survivors represent a subsample of the same population), or a change in these parameters in case of recolonization from neighboring sites. The second case seems to describe best what occurred in [3]. Measuring an effect of treatment on tsetse dispersal (as we defined it) would require a follow up of the same sites during several years of continuous control to let the population adjust, or come back several years after a one-time treatment, to check if the population displays again the same parameters as before treatment. Such data seem unavailable to date.

Dr Lord asked us to provide 'a plausible hypothesis for the mechanism behind an increase in dispersal with increased mortality rates'. We did not deal with mortality rate but with increased mortality rate of tsetse flies immigrating in sites with high tsetse densities. We provided arguments for this in our Box 3 and proposed a coevolution model in our main text.

Dr Lord insists on the idea that higher host densities may explain smaller dispersal and higher tsetse fly densities. According to [4], Serengeti National Park probably harbors one of the highest densities of big mammals. However, it displayed the smallest *Glossina* effective population density, and the largest dispersal of our study. At least for this site, host density does not allow a good prediction of tsetse density and dispersal. Besides hosts densities, tsetse presence and densities strongly rely on macroclimatic parameters such as temperature [5–7].

Applying the daily dispersal distance of [8] to our graph, as Dr Lord suggests, is inappropriate since our dispersal distances correspond to the average distance between reproducing adults and their parents of wild and unmanipulated flies, which was not the case in [7]. Tsetse flies both die and disperse faster when released in an unsuitable than in a suitable habitat (J. Bouyer, PhD thesis, Université Montpellier II, 2006, https://www.researchgate.net/publication/334684650_Ecologie_des_glossines_du_Mouhoun_au_Burkina_Faso_interet_pour_l'epidemiologie_et_le_controle_des_trypanosomoses_africaines).

The comment of Dr Lord on our Box 3, and lack of references, is inaccurate. Three references were provided where negative density dependence is discussed. The sentence 'incongruously,…immigrants become 'safely settled' in sparse populations sustained by invasion' is particularly unfair since we never stated such a thing. What we discussed was the possibility that, in sites with low tsetse densities, with untrained hosts, immigrants, even those coming from the most remote sites, can still have a good chance of a successful blood meal.

The last paragraph of Dr Lord's letter confirms a misunderstanding of our paper. Our paper dealt with evolutionary ecology parameters that evolved in

particular ecosystems. The reinvasion risk we discussed is not the instant one but the one that may happen months or years after control campaigns. What we argued was about the sustainable success of control across decades, because this is the right time-window for sustained development of affected countries. However, we acknowledge that our data cope with uncontrolled populations and may not predict accurately what will happen after control. Additionally, what needs to be clarified is that what we measured was not dispersal between favorable and unfavorable (e.g., treated) sites, but colonization and sustained establishment of alleles from one favorable site to another, in each particular situation defined by the tsetse species and the zone of study.

To conclude, the aim of our opinion article was to point out a drastic negative relationship between effective population density and average parent–offspring distance in tsetse fly populations across countries and species. Because this may predict unsustainability of controlled campaigns, especially so in high-density areas, we stressed the need to develop appropriate studies to clarify this issue and then find applicable tools to fix it in case of confirmation. We indeed believe that our ability to implement strategies with long-term sustainability will rely on such approaches.

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Forum

Causal Inference in Spatial Mapping

Moritz U.G. Kraemer,[1,2,3,*] Robert C. Reiner Jr.,[4] and Samir Bhatt[5,6,*]

Disease mapping has evolved to a powerful field in epidemiology and public health to focus interventions. Increased precision has come at the expense of interpretability. We propose that future efforts should focus on causal inference to evaluate and predict the effectiveness of intervention strategies to guide decisions more effectively.

With increasing availability of data, and efficient computational methods, tremendous progress has been made to map human health and related health indicators around the world [1–3]. Maps provide visually interpretable and comparable estimates across geographic areas and time. They have been used to expose large variations in disease risk or incidence rates, thereby providing tools for policy makers to target their efforts, resources, or interventions to particular areas. The temporal and spatial resolution of these precision maps is often chosen opportunistically, depending on computational feasibility and the resolution of the underlying observational data. Research and applications in mapping geographic distributions of disease risk have primarily focused on making the most accurate predictions; this has come at the expense of interpretability, making it difficult to base decisions on how to best curb disease burden directly on these high dimensional maps. In most instances spatial mapping approaches use a suite of covariates that are available to match the observed data but apply machine-learning approaches where the contribution of each covariate cannot be interpreted in isolation. In tandem, novel research in causal inference has shown that there is great potential to extract causal structures (variable A has a causal effect on the outcome of interest) from observational data [4]. In this forum article we argue that causal inference should become a priority area of research in disease mapping, an area of research which we show has all the ingredients for successful implementations of causal inference.

Spatial Mapping and Machine Learning

The central question in disease mapping concerns predicting the