analysis, Hsiang *et al*. found that their results were unaffected by modelling choices, including those involving the way in which civil conflict and ENSO conditions are measured. Although this work[1], like other studies in the field, was motivated in part by interest in the effects of global climate change, the authors take pains to note that ENSO-related variability is no proxy for long-term climate change.

Careful statistical analyses such as this one[1], which relate complex human behaviour to environmental factors, can be invaluable, but they need to be complemented by more detailed studies focusing on the underlying human dynamics. Hsiang *et al*. clearly understand that any effect of climate on conflict is likely to be indirect — people do not start wars simply because they are hot. One plausible hypothesis to explain the authors' findings is that the warm, dry conditions during El Niño years reduce agricultural yields, leading to conflict related to food availability.

However, as Hsiang and colleagues note[1], their analysis hints at an alternative hypothesis: civil conflicts do not originate with climate variations, but they do wax and wane, possibly as part-time fighters move in and out of agriculture. Interestingly, the same possibility was proposed[5] to explain the earlier work of Burke *et al*.[2]. Whether global climate variations give rise to new civil conflicts or modulate existing ones would seem to have somewhat different implications for improving the situation. For example, if the first theory is correct, then efforts could be made to address simmering problems that might erupt into conflict. But if the second suggestion is true, then peace-keeping efforts should focus mainly on situations that have already boiled over. Hsiang and colleagues' results should encourage a deeper look into this issue. ■

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DENGUE FEVER

Mosquitoes attacked from within

Infection with a harmless bacterium makes the mosquitoes that transmit dengue virus resistant to viral infection. The resistant population can rapidly replace the natural, susceptible population. SEE LETTERS P.450 & P.454

JASON L. RASGON

Dengue fever is the most prevalent mosquito-borne viral disease in humans. The virus is transmitted mainly by the mosquito *Aedes aegypti*, and so targeting this insect has been considered a viable option for controlling the incidence of the disease. In two papers in this issue (Walker *et al.*[1] and Hoffmann *et al.*[2]), a team of researchers reports an unusual approach for making *A. aegypti* almost completely resistant to infection, and thereby blocking transmission of dengue virus. Moreover, when the authors released their dengue-resistant mosquitoes into the wild, the insects replaced nearly 100% of the natural, susceptible mosquito population within a matter of months.

Around 40% of the world's population is at risk of infection with dengue virus. Every year, the virus infects 50 million to 100 million people, causing classical dengue fever as well as more severe symptoms such as dengue haemorrhagic fever and dengue shock syndrome. In the absence of an effective vaccine, controlling dengue is limited to targeting the mosquitoes that transmit the virus[3]. Many mosquito-control strategies are based on suppressing or eliminating the insect population. By contrast, population-replacement strategies aim to replace the pathogen-susceptible mosquito population with a resistant one[4].

The bacterium *Wolbachia* is a common endosymbiotic associate of many insects, including mosquitoes, and lives inside their cells. It is maternally inherited, and manipulates the reproduction of its invertebrate hosts in various ways to maximize the number of infected females in the next generation; this allows *Wolbachia* to spread rapidly

NATURE

50 Years Ago

Repeated investigations by the Medical Research Council have shown no evidence of a higher incidence of lung cancer or respiratory disease among persons exposed to increased amounts of Diesel exhaust fumes … Mr. Freeth [the Parliamentary Secretary for Science] also said that the Warren Spring Laboratory of the Department of Scientific and Industrial Research has examined methods for removing smoke from the exhausts of Diesel-propelled road-vehicles, but no device yet tested has proved satisfactory. The British Internal Combustion Engine Research Association is undertaking fundamental work on the combustion process in Diesel cylinders which it is hoped may lead to remedial measures. Mr. Freeth said it is a fact that correct setting of the injectors and their proper maintenance and operation provide a simple and effective remedy.
From *Nature* 26 August 1961

100 Years Ago

As a supplement to the literary and historical Biblical exhibition which has been arranged at Bloomsbury for the tercentenary of the Authorised Version, an exhibition of the animals, plants, and minerals mentioned in the Bible has been arranged in one of the bays of the Central Hall of the Natural History Museum, South Kensington … The collection, and the guide to it, will be of special interest to those to whom the Bible plants and animals are rich in picturesque associations; but it is, of course, part of a liberal education to know that the "unicorn" was probably the extinct wild ox or aurochs, "behemoth" the hippopotamus, the "coney" the hyrax, and the "leviathan" of Job the crocodile.
From Nature 24 August 1911

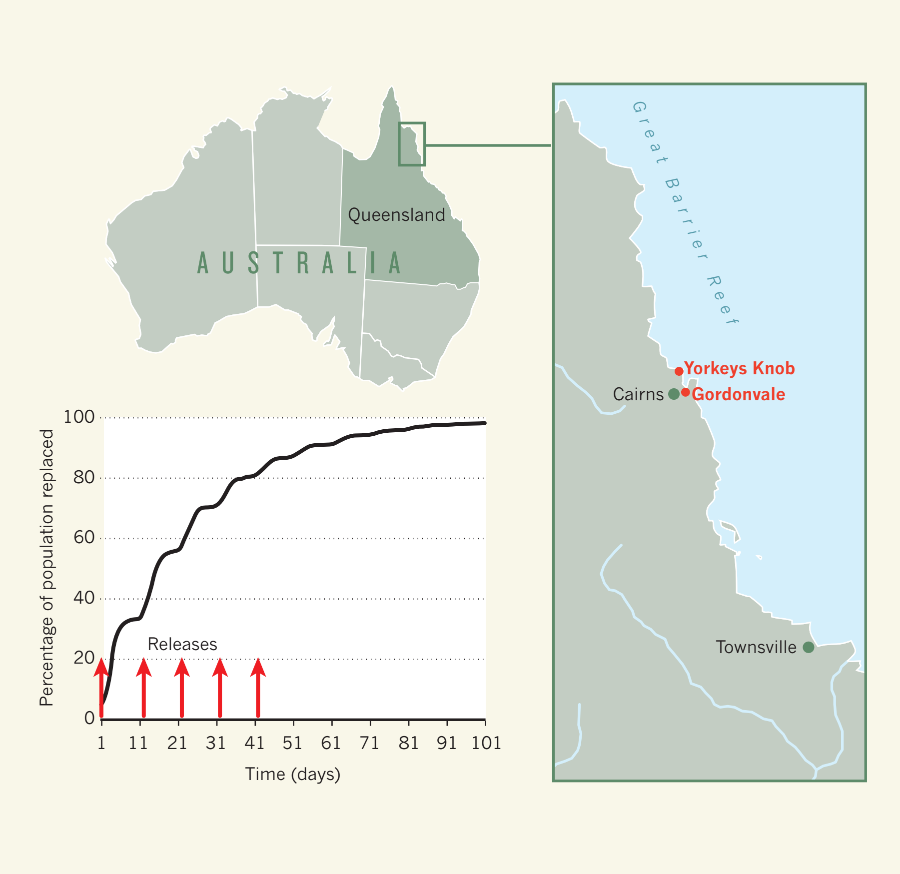

Figure 1 | Dengue-virus control. Hoffmann *et al.*[2] released *Aedes aegypti* mosquitoes infected[1] with the wMel strain of *Wolbachia* in two locations — Yorkeys Knob and Gordonvale — near Cairns in Queensland, Australia. After several releases, these dengue-virus-resistant mosquitoes replaced almost the entire natural, virus-sensitive *A. aegypti* population.

through populations[5]. Infection with the bacterium can make insects such as mosquitoes resistant to infection by many pathogens, including viruses, malaria parasites and filarial nematodes[6]. If *Wolbachia* is artificially introduced into an uninfected vector population, it can spread and replace the wild-type population with one in which pathogen transmission is blocked[5].

Researchers showed[7] a few years ago that wMelPop — a virulent *Wolbachia* strain from a laboratory colony of the fruitfly *Drosophila melanogaster* — almost completely blocked dengue infection in *A. aegypti*. This *Wolbachia* strain, however, severely affected the mosquitoes' fitness, making its spread into natural *A. aegypti* populations difficult or even impossible[8].

Going back to the source, Walker *et al.*[1] (page 450) noted that wMel, the natural, avirulent *Wolbachia* strain in *Drosophila*, can inhibit fly infection with RNA viruses. As dengue is an RNA virus, the authors reasoned that wMel might also block infection with this virus in mosquitoes, without having the virulent effects of wMelPop. Lo and behold, when they infected *A. aegypti* with wMel, the mosquitoes became highly resistant to infection by dengue virus. In experiments on caged mosquitoes, Walker and colleagues further showed that the wMel infection could spread through laboratory mosquito populations at a rate consistent with predictions based on theoretical modelling.

Many studies would stop there. But the investigators took the astonishing next step of attempting a release of *Wolbachia*-infected mosquitoes into the wild, and, even more astonishingly, they did it in their own backyard. Queensland, Australia, has a recurring dengue problem[9], and so seemed an ideal location for an initial test release.

After extensive public engagement, and development of a regulatory framework governing the release of the *Wolbachia*-infected insects, in January this year Hoffmann *et al.*[2] (page 454) began releasing wMel-infected mosquitoes at two locations — Yorkeys Knob and Gordonvale, both near Cairns in Queensland (Fig. 1). The authors continued to release the insects at regular intervals over the next two and a half months, with a total of roughly 150,000 mosquitoes released at each location. The frequency of *Wolbachia* infection increased extensively during the releases, but more crucially, continued to climb in both areas after releases were stopped, approaching 100% in Yorkeys Knob and more than 80% in Gordonvale[2].

Hoffmann and colleagues estimated that wMel exerts only a moderate (10–20%) fitness cost on the mosquitoes it infects. This suggested that a 'wave' of infection with this bacterial strain should eventually spread from local areas in which the infection was introduced. And spread it did — infected mosquitoes were detected several kilometres away from both release areas, probably owing to occasional long-distance movement of infected insects. Although in these experiments the infection is unlikely to increase in frequency outside the release area, but rather will be swamped by the local wild-type mosquitoes, the data suggest that long-range spread is possible[2].

These studies mark the first time that a deliberate *Wolbachia*-mediated population-replacement strategy has been attempted in nature, and herald the beginning of a new era in the control of mosquito-borne diseases. The advantage of population-replacement approaches is that, once established, they are self-propagating. And because the mosquito population is simply changed rather than eliminated, effects on the ecosystem should be minimal[4].

Theoretically, these strategies can also be applied to other vector-borne diseases, including malaria[10]. The next step will be to attempt release of *Wolbachia*-infected mosquitoes in an area with endemic, rather than sporadic, dengue transmission, such as southeast Asia or South America. It remains to be seen whether the introduction and spread of *Wolbachia* can be achieved across the highly variable worldwide range of dengue virus, and whether *Wolbachia* can provide consistent protection against viral strains of different genetic make-up. Nevertheless, these experiments[1,2] are a groundbreaking first step towards *Wolbachia*-mediated replacement of *A. aegypti* and so elimination of the scourge of dengue fever. ■

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