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than in a meta-analysis⁶ that included 423 patients who received pegylated interferon plus ribavirin. Despite the small number of patients included in Abergel and colleagues' study (mainly because of the low frequency of HCV genotype 5 in Europe), their study represents the first strong evidence that sofosbuvir plus ledipasvir is effective for the treatment of HCV genotype 5 infection and should therefore be considered as a first-line option for treating HCV in this setting.

Abergel and colleagues detected no differences in SVR with respect to the presence of liver cirrhosis or previous treatment experience. Nonetheless, reduced SVR was reported for patients with the *IL28B* TT genotype (a genetic marker that was associated with a low probability of treatment response during the era of interferon treatment for HCV).⁷ The two patients who did not achieve SVR both had the *IL28B* TT genotype. SVR for patients with *IL28B* TT genotype was 50% (achieved by two of four patients). This result agrees with the findings of a clinical trial by Feld and colleagues, who assessed a new combination consisting of sofosbuvir plus velpatasvir once per day for 12 weeks.⁸ Among the 35 patients with HCV genotype 5 infection recruited to the study, just one patient (who had the *IL28B* TT genotype) did not achieve SVR, and SVR in patients with the *IL28B* TT genotype (two [67%] of three patients) was similar to that reported by Abergel and colleagues. Because of the small numbers of patients included in both studies, no association can be established between the *IL28B* TT genotype and reduced SVR in patients with HCV genotype 5 infection who are receiving interferon-free regimens. Nevertheless, these results show that studies to assess this possible association

will be important for the optimisation of treatment for patients with HCV genotype 5 infection and the *IL28B* TT genotype. These findings could also reopen the debate about the need to establish *IL28B* as a predictive factor in the interferon-free era. The fact that HCV genotype 5 does not represent a major health problem in high-income countries should not preclude larger clinical trials being done to assess the efficacy of interferon-free combinations in this subset of patients. Meanwhile, the combination of sofosbuvir and ledipasvir represents a substantial advance for the treatment of patients with HCV genotype 5 infection.

*Antonio Rivero-Juárez, Antonio Rivero

Infectious Diseases Unit, Instituto Maimonides de Investigación Biomédica de Córdoba (IMIBIC), Hospital Universitario Reina Sofía de Córdoba, Universidad de Córdoba, 14004, Córdoba, Spain
arjvet@gmail.com

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How much more malaria could be prevented?

Measurement of the global burden of malaria is difficult, because many deaths from malaria occur outside the health-care system and other infections might be misdiagnosed as malaria unless a diagnostic test is done. However, there is general agreement that a substantial reduction in both deaths from malaria and cases has occurred during the past decade.^{1,2} WHO estimates that between 2000 and 2015, the annual incidence of malaria

cases fell by 37% and that the malaria mortality rate fell by 60%.³ These reductions have been achieved largely through scale-up of insecticide-treated bednets and provision of prompt access to effective treatment. Can even better results be obtained from more of the same? WHO estimated that in 2015, about 68% of individuals at risk from malaria slept under an insecticide-treated bednet; this is probably a generous estimate, which might



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not account for intermittent use of nets, and additionally only few cases received treatment with artemisinin combination therapy. Thus, further scale-up of these interventions is needed.

In the *Lancet Infectious Diseases*, Jamie Griffin and colleagues⁴ used a well established model of malaria transmission^{5,6} that accounts for increasing population size to predict what would happen if coverage of established interventions was increased to 80% or 90% with or without the addition of rectal artesunate. The model accounted for treatment of cases of severe malaria, and expansion of seasonal malaria chemoprevention to additional areas where it has not been recommended because suitable drugs are not available. Finally, they predicted what would happen if the status quo of coverage is maintained or allowed to fall back to the 2006 level. If the current level of coverage with insecticide-treated bednets and artemisinin combination therapy is sustained they predicted that the incidence of malaria would increase by 21% (95% CrI 18–23) and malaria mortality by 11% (7–16) between 2015 and 2030 due to population-level loss of immunity caused by successful reduction in the incidence of malaria during the previous years. With the scaling up of existing interventions to 90%, adoption of immediate treatment of severe malaria with rectal artesunate, and expansion of seasonal malaria chemoprevention they estimate that by 2030, malaria incidence would be reduced by 74% (95% CrI 70–77) and malaria mortality by 81% (76–87) preventing an estimated 3.37 billion cases (95% CrI 2.37 billion–4.33 billion) and 11.5 million deaths (4.6 million–16.0 million) over the 15-year period.

However, an important issue not covered by Griffin and colleagues in this Article⁴ is the cost of scale-up. As coverage improves, extending it will become more difficult and costly because access will be needed to communities living in remote areas or those who are suspicious of the formal health system and prefer to seek treatment elsewhere. Increasing coverage from 60% to 90% cannot be assumed to be half the cost of increasing coverage from 0% to 60%. Additionally, some communities are likely to be more receptive of one intervention than another and obtaining their views will be an important requisite to achieving very high coverage levels.

Novel interventions for the control of malaria are being developed and some difficult decisions will be needed to

determine how to balance investment in the deployment of these new interventions with efforts to further scale-up existing methods to very high levels of coverage. Use of models that include a range of costs for each intervention, old and new, could help guide the best approach in specific epidemiological situations, as has been shown in investigations of how best to deploy the malaria vaccine RTS,S/AS01.⁷

WHO has published a technical report that sets out the strategy for malaria control from 2016 to 2030.⁸ This report lists targets for reducing malaria cases and deaths from 2015 levels, by 40% in 2020, 75% in 2025, and 90% in 2030 with 10, 20, and 35 countries achieving malaria elimination by these dates. The modelling undertaken by Griffin and colleagues⁴ suggests that these goals are not unrealistic, but this is the case only if they are not derailed by the spread of high-level resistance to drugs and insecticides, a supposition that cannot be assumed and that is not included in the model. Therefore, while strenuous efforts to scale-up existing interventions continue, research must continue for the development of new insecticides and antimalarial drugs, and on the development of vaccines and novel vector-control methods, which will almost certainly be needed before malaria is finally vanquished.

Brian Greenwood

Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, WC1E 7HT, UK
 Brian.Greenwood@lshtm.ac.uk

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