found that, for 15 VL and 47 PKDL patients (comprised of 21 patients with nodular and 26 patients with macular PKDL), nodular PKDL was more likely (86%) and macular PKDL less likely (35%) to result in infected sand flies compared with VL (67%) [7]. When taking into account the distribution of the different forms of PKDL in this region, with 48% being macular and 52% nodular [8], the relative infectiousness of PKDL is 0.9 compared with VL (1.0), making PKDL cases nearly equally infectious.

Figure 1 shows the implications of these new findings in a typical high-endemic setting (precontrol incidence of 10 VL cases/10 000/year), using both model variants now incorporating the empirically based PKDL infectiousness of 0.9 relative to that of VL. Clearly, 5 years of intensive WHO strategy (solid curves) led to a rapid incidence reduction to about the target of 1/10 000/year, but when the WHO strategy changed to less-intense interventions after year 5, incidence reductions slowed down. The relative contribution to transmission of the different infection stages during the WHO strategy (two panels above) indicate that the contribution of PKDL cases to transmission more than triples for both models after 5 years of intensive WHO interventions, clearly highlighting the need for a PKDL control strategy. When adding a hypothetical PKDL control strategy (here: preventing 95% of PKDL) to the existing WHO strategy, the elimination target is achieved as much as 8 years earlier for model E0 (dashed line). Elimination of transmission (0/10 000/year) will also be achieved several years sooner. The relative contribution of PKDL to transmission, as well as the impact of a PKDL control strategy, will be larger in settings where 20% instead of 2.5% of VL cases develop PKDL.

PKDL control is currently not included in the main intervention programs, and the options are limited. Straightforward but operationally difficult strategies could entail active PKDL case-finding and treatment, long-term follow-up of VL patients, patient education on the need to report to the clinic in case of a rash, and educating community workers on recognizing PKDL, all requiring the availability of safe and effective treatment. For the future, we hope for better VL treatment, including a vaccine or immunomodulator to avert any PKDL development.

Obviously, we also eagerly await the outcomes of ongoing xenodiagnosis studies on the infectiousness of asymptomatic individuals to further complete the VL puzzle (helping us to choose between both model variants). If the model-estimated infectiousness of asymptomatic cases in Model E1 is true (i.e., 1–2% relative to VL), then several hundreds of asymptomatic patients need to be tested in order to identify the few that lead to infection of sand flies.

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Forum

Can We Recommend Practical Interventions to Prevent Neurocysticercosis?

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The cystiSim model was used to compare strategies for the control of *Taenia solium*. A three-monthly intervention in pigs for 3 years was substantially more effective than biannual treatment for taeniasis in the human population for 5 years. The intervention period could be shortened further by combining pig and human interventions.

The World Health Organization (WHO) identifies neurocysticercosis as a neglected tropical disease and has prioritized *Taenia solium* as the focus for new control initiatives [1]. At this time, there is no consensus as to

the relative effectiveness and practicality of different approaches to control of *T. solium* transmission [1]. Treatment of taeniasis is an attractive option because of the direct causal link between taeniasis and human cysticercosis. However, the duration requirement for a programme to achieve a substantial level of control would be at least several years if based only on treatment of taeniasis [2,3].

A recently published study described a successful intervention in pigs for control of *T. solium* [4]. The study combined vaccination of pigs with Cysvax, a commercial vaccine based on the TSOL18 antigen, together with medication with oxfendazole, undertaken at 3-monthly intervals. The medication cleared any existing infection in the pigs while the vaccine prevented any subsequent infections. These and other authors [5–7] suggest that strategic treatment of taeniasis in the human population, after an intervention in the pig population had already removed the source of new cases of taeniasis, may provide a rapid and effective method for *T. solium* control.

Several mathematical/computational models have been developed which aim to simulate the impacts of various *T. solium* control measures [8–11], as well as a logical model based on basic aspects of the parasite biology and a dynamic pig population [7]. Here we use the cystiSim model [8] to compare the relative effectiveness of repeated mass drug administration (MDA) for taeniasis with a three-monthly intervention in pigs involving vaccination and medication as described by Poudel *et al*. [4], as well as a combination of pig interventions with strategic MDA in the human population. The model settings and assumptions used were similar to those described by Braae *et al*. [8] which were developed based on *T. solium* transmission data adapted to an observed setting using field data from Tanzania.

The outcomes of the simulations are summarized in Figure 1, which displays the predicted impacts of various intervention strategies on porcine cysticercosis (PC), immunity to *T. solium* infection in the pig population (PR), and human taeniasis (HT).

Four scenarios were simulated involving only MDA in humans using 80% coverage (Figure 1A–D): annual treatments for 5 or 10 consecutive years (Figure 1A and B, respectively) and biannual MDA for 5 or 10 consecutive years (Figure 1C and D, respectively). Annual MDA in humans for even as long as 10 years was predicted to be relatively slow in reducing the prevalence of taeniasis in the community and poorly effective in reducing taeniasis and porcine cysticercosis after the cessation of the MDA. Six-monthly MDA was more effective. In some countries, six-monthly MDA is conducted for the control of soil-transmitted helminths; therefore, although more cumbersome, it was considered feasible. Biannual MDA for 10 years was predicted to achieve the elimination of transmission with a probability of >80%.

Two scenarios were simulated which involved interventions in the pig population. These are different to the control simulations that have been published by others because they are based on specific aspects of the biology of the parasite [7,12] or on a control scenario which has already been demonstrated to be effective in a short-term intervention [4]. Both simulated scenarios included three-monthly vaccination and oxfendazole medication of the pig population. The first involved only vaccination and medication in pigs (Figure 1E) for a period of 3 years and with a coverage of 75%. The duration of the intervention was selected based on the lifespan of the adult tapeworm parasite, which is believed to be, on average, up to 3 years [12]. For this reason, interventions only in pigs lasting for less than this time, such as that considered by Gabriel *et al*. [13], would be expected to be relatively ineffective. The 3-year duration intervention simulated here (Figure 1E) was predicted to achieve the elimination of transmission with a probability >90%. The simulation illustrates that a porcine intervention approach without human interventions has the potential for success if the programme is implemented and run for at least 3 years. The second simulation involved pig interventions for only 2 years, but also included three MDA treatments in the human population, at 6, 12, and 18 months after the initiation of the interventions in pigs (Figure 1F). MDA was started 6 months after the pig intervention, when pigs present a reduced risk for transmission because of the interventions already undertaken in the pig population. With a coverage of 75%, this intervention in pigs, together with strategic MDA, was predicted to achieve the elimination of transmission with a probability of >85% and had a relatively immediate impact on the prevalence of taeniasis.

A three-monthly intervention only in pigs for 3 years was substantially more effective in reducing both human taeniasis and porcine cysticercosis than was biannual MDA in the human population for 5 years, but the intervention period could be shortened by the inclusion of MDA in the human population.

The predictions made in these simulations should be considered in the light of several limitations in the modelling. For example, the scenarios considered a population coverage of 80% (MDA only models) or 75% (pigs only and combined models), which may be difficult to achieve. The WHO coverage target for preventive chemotherapy for soil-transmitted helminths is 75%. The model does not consider reintroduction of infected humans or pigs from outside the intervention area. The effectiveness of the human treatment, and both oxfendazole and the vaccine, was set at 90% and might differ under programmatic conditions.

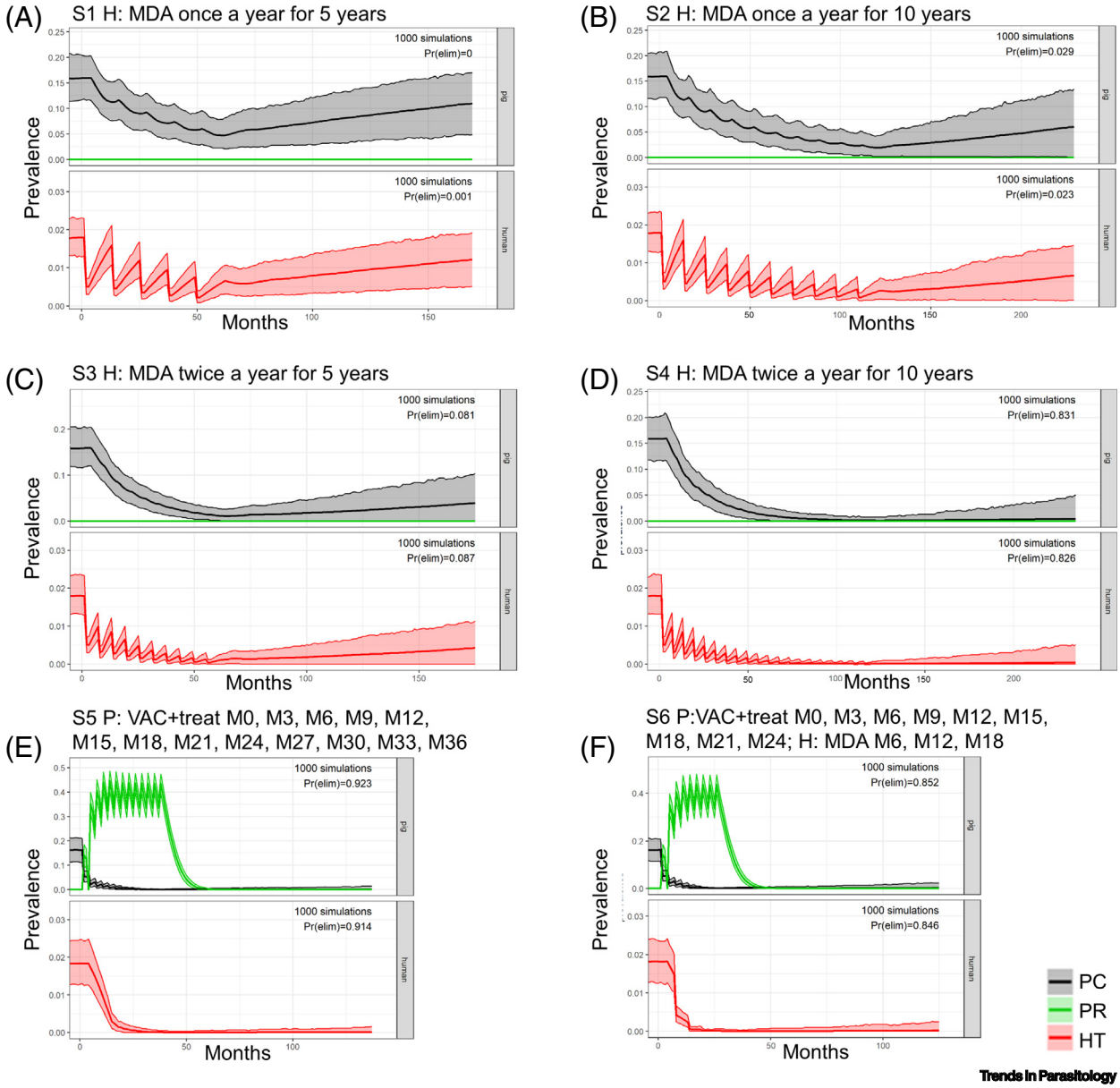

Figure 1. Simulation of Various Control Scenarios for *Taenia solium* Using cystiSim. The effectiveness of repeated mass drug administration (MDA) in humans (H) for taeniasis is compared with three-monthly interventions in pigs (P) involving vaccination and medication, or a combination of pig interventions with strategic MDA in the human population after 1000 simulations (S). The impacts are shown on porcine cysticercosis (PC), immunity to *T. solium* infection in the pig population (PR), and human taeniasis (HT). The coloured areas demarcate the 95% uncertainty intervals for prevalence. Pr(elim) indicates the predicted probability of elimination occurring in the given scenario. Four scenarios are simulated which involve only MDA in humans (A–D): annual treatments for 5 or 10 consecutive years (A and B, respectively), and biannual MDA for 5 or 10 consecutive years (C and D, respectively). Two scenarios are simulated which involve interventions in the pig population. Each included three-monthly vaccination and oxfendazole medication of the pig population. The first involves only vaccination and medication in pigs (E) for a period of 3 years. The second (F) also involves pig interventions, but includes three MDA treatments in the human population, at 6, 12, and 18 months after the initiation of the interventions in pigs, over a total period of 2 years.

Long-term interventions against *T. solium* that involve only MDA in humans ([8,13]; Figure 1D), or medication of pigs with oxfendazole alone [13], may eventually lead to elimination of the parasite's transmission; however, the impact of these programmes on the incidence of cysticercosis in humans could be expected to be delayed substantially in comparison to the 3-year vaccination+oxfendazole intervention in pigs or the shorter intervention involving both pigs and humans, that were

simulated here. Although these control scenarios have been compared on the basis of their probability to achieve elimination of parasite transmission, in most continental situations they could be expected to achieve control rather than actual elimination of transmission due to the potential for reintroduction of the parasite through immigration of either humans with *T. solium* taeniasis or pigs with cysticercosis.

Simulation of different *T. solium* control scenarios with cystiSim indicate that a 10-year biannual MDA for treatment of taeniasis in the human population would lead to a substantial reduction in the parasite's transmission; alternatively, a strategy of vaccinating and medicating the pig population could also achieve the same objective in 3 years, or the same pig strategy combined with three MDA treatments of the human population could achieve a high level of control within an intervention period of 2 years.

The relative costs of a long-term human MDA programme, versus intervention in pigs for 3 years, or a combination of intervention in pigs and human MDA over a period of 2 years, are unknown; however, it may be more satisfactory and realistic to implement an intensive control programme over a period of 2 or even 3 years, than securing support of an ongoing intervention for a decade in order to achieve a similar impact on *T. solium* transmission.

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