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SUPPLEMENT ARTICLE

Predictive Value of Microfilariae-Based Stop-MDA Thresholds After Triple Drug Therapy With IDA Against Lymphatic Filariasis in Treatment-Naive Indian Settings

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Mass drug administration (MDA) of antifilarial drugs is the main strategy for the elimination of lymphatic filariasis (LF). Recent clinical trials indicated that the triple-drug therapy with ivermectin, diethylcarbamazine, and albendazole (IDA) is much more effective against LF than the widely used two-drug combinations (albendazole plus either ivermectin or diethylcarbamazine). For IDA-based MDA, the stop-MDA decision is made based on microfilariae (mf) prevalence in adults. In this study, we assess how the probability of eventually reaching elimination of transmission depends on the critical threshold used in transmission assessment surveys (TAS-es) to define whether transmission was successfully suppressed and triple-drug MDA can be stopped. This analysis focuses on treatment-naive Indian settings. We do this for a range of epidemiological and programmatic contexts, using the established LYMFASIM model for transmission and control of LF. Based on our simulations, a single TAS, one year after the last MDA round, provides limited predictive value of having achieved suppressed transmission, while a higher MDA coverage increases elimination probability, thus leading to a higher predictive value. Every additional TAS, conditional on previous TAS-es being passed with the same threshold, further improves the predictive value for low values of stop-MDA thresholds. An mf prevalence threshold of 0.5% corresponding to TAS-3 results in ≥95% predictive value even when the MDA coverage is relatively low.

Lymphatic filariasis (LF), a neglected tropical disease (NTD), is a leading cause of preventable morbidity and disability due to lymphedema, hydrocele, and acute inflammatory episodes with resultant fevers (acute dermatolymphangioadenitis) and still affects more than 50 million people worldwide [1]. The most common causative agent is the parasitic filarial nematode worm *Wuchereria bancrofti*. Adult worms are found in lymph vessels, whereas the worm's offspring microfilariae (mf), which are released by fertilized female worms, are picked up from blood and transmitted to humans by mosquitoes. The Global Programme to Eliminate Lymphatic Filariasis was initiated in 2000 with the aim of interrupting the transmission of LF by implementing mass drug administration (MDA) with the 2-drug combinations of diethylcarbamazine and albendazole (DA) in onchocerciasis-free areas or ivermectin and albendazole (IA) in areas where onchocerciasis prevails [2, 3]; where loiasis is present, twice yearly albendazole is the recommended treatment regimen [3]. This is to be combined with improved morbidity management to alleviate the suffering of people with clinical manifestations.

Recent clinical evidence indicated that MDA with a triple-drug regimen of ivermectin, diethylcarbamazine, and albendazole (IDA) is even more effective than the 2-drug regimens [4–7], leading to the World Health Organization (WHO) recommendation in 2017 of using IDA for LF control in LF-endemic areas not co-endemic with either onchocerciasis or loiasis [8]. This includes India, where approximately 55% of the current global burden of LF is located, with approximately 487 million people at risk of infection [3]. MDA was initiated in 2004 in 202 Indian districts with diethylcarbamazine and in 2007 in all 256 endemic districts at that time with DA [9]. In 2018, IDA was introduced in 5 districts that either failed a transmission assessment survey (TAS) or never undertook MDA despite the identification of LF transmission. This was followed by the selection of 21 additional districts for IDA implementation in the next year. In 2020, 16 districts were newly classified as endemic for LF, increasing the total number to 272.

MDA programs that use the various drug regimens have successfully reduced LF prevalence in many affected areas so that the infection is either eliminated as a public health problem (mf prevalence <1% or antigen prevalence <2%) or elimination is close to being achieved. To save resources and time, it is important to establish threshold prevalences below which MDA can be

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stopped as soon as possible but with minimal risk of disease resurgence. For areas treated with a 2-drug regimen, the stop-MDA decision is made based on TAS-1 that assesses the prevalence of circulating filarial antigenemia (CFA) in children aged 6–7 years [10]. Elimination is considered validated if antigenemia prevalence in this age group is sustained below the predefined threshold in two subsequent TAS-es (TAS-2 and TAS-3), with intervals of two years minimum between surveys. However, compared with 2-drug regimens, IDA leads to a faster mf clearance and potential sterilization of adult worms, resulting in fewer required treatment rounds. This means that after the last MDA round, antigens are likely to persist [11]. WHO recognizes that new diagnostics are needed, and target product profiles have been developed [12, 13]. Until such new tests are available, testing for mf is the best way to identify persons with reproducing adult worms. Because adults, in contrast to children, are the most likely to be mf-positive and have the lowest MDA coverage, it might be useful to target TAS in IDA-treated areas at adults [14].

Mathematical models have been helpful in assessing the validity of stop-MDA thresholds [15, 16]. Here, we use the already established LYMFASIM model [16] to simulate IDA-MDA in treatment-naive Indian settings and to assess the probability of achieving elimination of LF transmission in relation to the chosen mf-based stop-MDA threshold used in TAS-1, TAS-2, and TAS-3. To understand the impact of the treatment regimens used, including the uncertainty regarding the effect of IDA on adult worms [17], we compare the results for MDA with IDA and DA. We identify situations for which predictive values as high as 95% are possible.

METHODS

We adopted the same methods that were used in a previous publication on assessing stop-MDA thresholds for the African context [16]. To simulate population-level LF transmission dynamics, we used the individual-based LYMFASIM model, which accounts for interhost variation in exposure to transmission and uptake of MDA. The model was quantified for Indian settings using data from approximately 25 000 individuals from Pondicherry in 1981 and longitudinal measurements of human infection status in 1981, 1986, 1989, and 1991 [18]. This Indian model variant includes a host immunity mechanism that regulates parasite establishment [18, 19], which is absent for the African version of LYMFASIM [16]. As a result, transmission can better maintain itself at low levels without incoming infections from neighboring areas. For the analysis presented here, we simulated a single community with a population of approximately 1000 people.

We performed simulations for a range of baseline mf prevalences between 5% and 20%, assuming that simulated communities underwent no previous treatment. Baseline mf prevalences were determined using two transmission parameters: the monthly biting rate and the shape of the gamma distribution that describes exposure variation between individuals. We repeatedly sampled values for these two parameters from a predefined parameter space (Supplementary Figure 1); individual sets of parameter values were adopted until we had 250 parameter combinations for each 1%-wide bin between 5% and 20% (ie, 15 bins). Next, we simulated the impact of 3–6 rounds of annual MDA using either IDA or DA, implemented at either 65% or 80% of the total population and comprising all age groups (ie, 16 MDA scenarios). We assumed the macrofilaricidal effect of IDA to be the same as that of DA (55%) but with 100% mf killing and permanent sterilization of female adult worms (denoted as "IDA1" by Irvine et al. [17]). As such, we ran 3750 simulations per MDA scenario (15×250) and 60 000 simulations in total (16×3750). Each simulation was marked as having achieved elimination (or not) if the mf prevalence in the entire population was zero (above zero) 20 years after the last MDA round. To evaluate the predictive value of TAS-es for achievement of elimination, we saved the annual post-MDA mf prevalence, starting one year after the last MDA round, for each simulation. We also repeated TAS-1 defining elimination within a 50-year period post-MDA instead of 20.

We evaluated the predictive value of a series of three TAS-es that take place one, three, and five years after the last MDA round, which was first quantified in terms of receiver operating characteristic (ROC) curves. For each LYMFASIM simulation ($N = 60\,000$), we simulated 100 repeated series of TAS-es, assuming a binomial sample of 200 or 400 individuals of ages ≥5 or ≥15 years (ie, four TAS scenarios). For each simulated TAS scenario, varying the stop-MDA threshold, we evaluated the positive predictive values (PPVs; ie, the probability of achieving elimination if the measured prevalence is below the threshold), where a particular threshold value was always used for all TAS-es in the same series. (We did not evaluate negative predictive values since overtreatment was outside the scope of this study.) For TAS-2 and TAS-3, we evaluated the PPV on the condition that previous TAS-es in the same series had been passed. We quantified the impact of TAS(-es) in terms of the maximum increment in PPV as the decision threshold is lowered. Finally, we determined the maximum stop-MDA threshold that achieves a PPV of ≥95%. We repeated this analysis with one of the TAS-es being delayed by two years.

In Supplementary Table 1, we describe our adherence to the five principles of the Neglected Tropical Diseases Modelling Consortium on good practice for policy-relevant modeling [20].

RESULTS

First, we evaluated the amount of information available from TAS-1 targeting age group 5+ with IDA using the ROC curve (Figure 1). The curve was fairly close to the diagonal, suggesting TAS-1 provides only limited information relative to the *a priori*

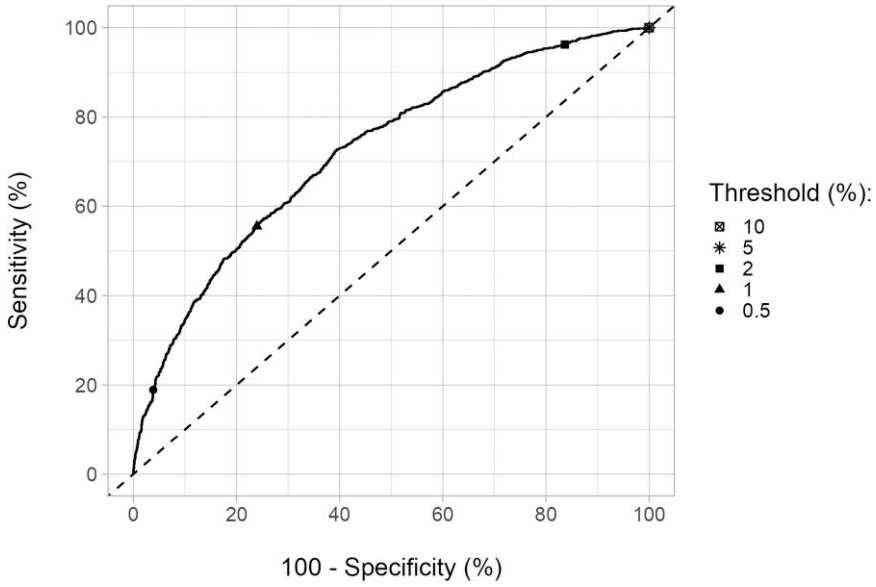

Figure 1. Receiver operating characteristic (ROC) curve at 1-year post–MDA (TAS-1) for age group 5+ under MDA with ivermectin, diethylcarbamazine, and albendazole (IDA). The MDA duration was three years, and coverage was 65%. The ROC curves for a wide range of parameters can be found in Supplementary Figure 2. Note that sampling is not included for the ROC curve(s). Sensitivity (*y*-axis) is the percentage of runs ending in elimination within 20 years post-MDA that are correctly identified based on microfilariae prevalence below a range of thresholds. The *x*-axis, 100%-specificity, represents the percentage of runs falsely classified as having elimination among all the runs that did not result in elimination in the same period.

probability of achieving elimination. Even for a wide range of MDA scenarios, the ROC curves showed similar trends (Supplementary Figure 2). However, the ROC curve for age group 5+ was always further away from the diagonal than age group 15+, indicating that the former is a better option for measuring mf prevalence.

Next, we evaluated how the PPV of TAS-1 changes as a function of the stop-MDA threshold for mf prevalence in age group 5+ for IDA-treated areas (Figure 2). One common feature of the PPV curves was that as the stop-MDA threshold increased, the PPV decreased to a plateau, equaling the *a priori* probability of achieving elimination across all simulation runs. For IDA-based MDA scenarios, adopting a lower stop-MDA threshold increased the PPV (relative to the plateau) up to approximately 30 percentage-points (Supplementary Figure 3). The corresponding increment associated with DA was approximately 48 percentage-points. Also, sampling 400 instead of 200 individuals increased the maximum PPV by, at most, approximately 10 percentage-points for IDA (Figure 2). As the probability of elimination increased with MDA coverage and duration, so did the PPV; to a degree, this was comparable to the magnitude of increase in PPV when lower stop-MDA thresholds were adopted. Those aged ≥5 years had a higher PPV by, at most, 5 percentage-points compared with those aged ≥15 years for IDA (Supplementary Figure 3). With 80% coverage, PPVs of 85%–95% were possible when the stop-MDA threshold was ≤0.5% mf prevalence, although surveys to assess mf prevalence led to only a small increment in PPV compared with the *a priori* probability of elimination.

For TAS-1, we considered some alternate situations as well. First, given that the exact values of coverage are often unknown in actual settings, we repeated the above analysis by lumping together simulations with 65% and 80% coverage levels (Supplementary Figure 4). The resulting PPV increments were intermediate (with the maximum increments being approximately 25 percentage-points for IDA and approximately 42 percentage-points for DA) between those when the two coverage levels were considered separately. Next, to determine if the predictive power of TAS-1 would improve, we considered elimination within 50 years instead of 20 years (Supplementary Figure 5). The *a priori* probability of elimination was higher if measured 50 years after stopping than if measured 20 years after stopping, resulting in higher absolute PPVs. However, the maximum PPV increments were lower for the former for both drug regimens, indicating its weaker predictive power. The maximum PPV increments were approximately 20 percentage-points and approximately 30 percentage-points for the two periods for IDA-based MDA, whereas they were approximately 35 percentage-points and approximately 48 percentage-points for the DA-based one.

Finally, keeping the time to achieve elimination as 20 years, we explored the predictive value of TAS-2 and TAS-3, conditional on previous TAS-es being passed (with the same stop-MDA threshold as used in later TAS-es), when based on

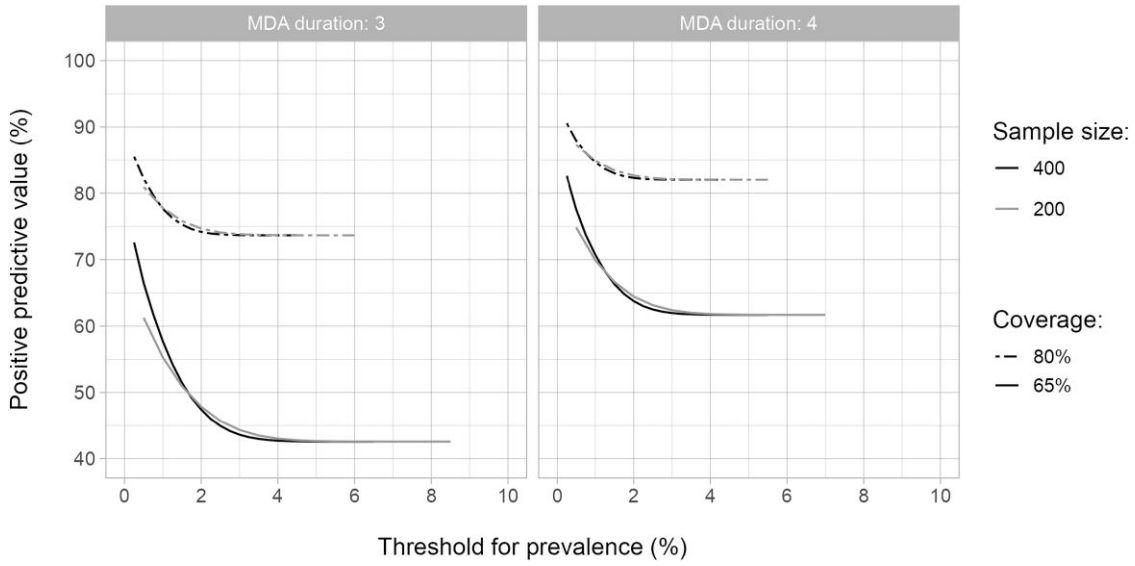

Figure 2. Positive predictive values (PPVs) as a function of stop-MDA threshold for MDA durations three (left panel) and four (right panel) years. PPV was defined as the probability of achieving elimination within 20 years after the last round of IDA-MDA if the microfilariae prevalence 1-year post-MDA (transmission assessment survey-1) was below a given threshold. The results shown are for those aged 5+ years and for two different values of sample sizes (400 and 200) and MDA coverages (65% and 80%). The PPV curves with sample size being 400 for a wide range of other parameters can be found in Supplementary Figure 3.

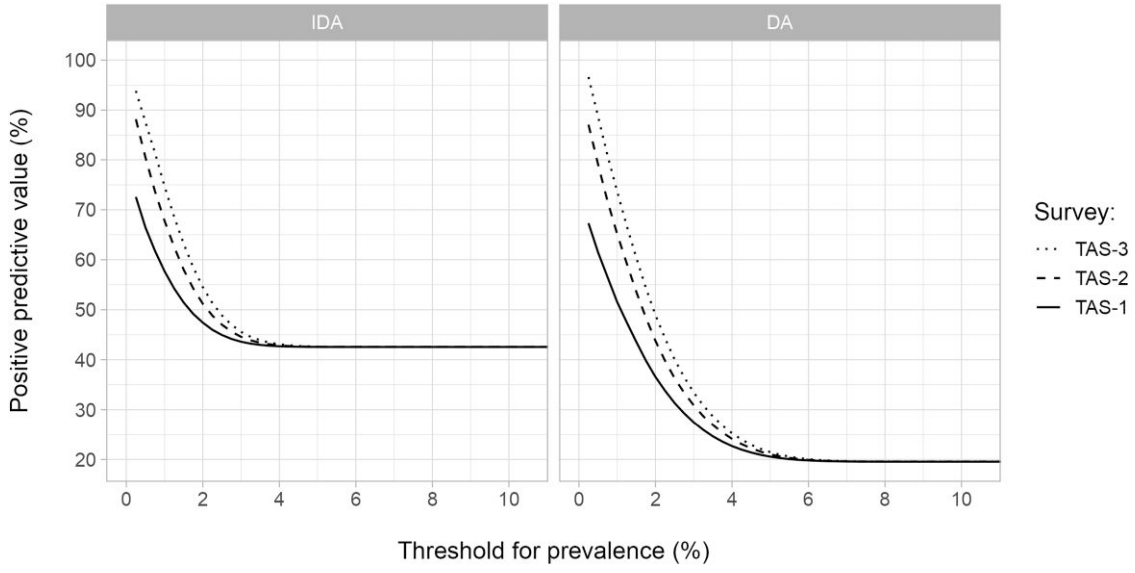

Figure 3. Positive predictive value (PPV) of TAS-1, TAS-2, and TAS-3 for elimination of lymphatic filariasis after three years of mass drug administration (MDA) at 65% coverage using IDA (left panel) or DA (right panel) treatment. Elimination was defined as zero microfilariae prevalence 20 years after the last MDA round. PPVs were calculated as a function of the stop-MDA threshold for prevalence of infection in the age group 5+ (horizontal axis). For TAS-2 and TAS-3, PPVs are conditional on all previous TAS-es being passed with the same prevalence threshold. TAS-1, TAS-2, and TAS-3 were scheduled one, three, and five years post-MDA, so that the gap between consecutive TAS-es was two years. For each TAS, we assumed a sample size of 400.

a sample of ages 5+ (Figure 3). PPV increased with each additional TAS for lower thresholds. This trend remained consistent across all the MDA scenarios that we considered (Supplementary Figure 6). Following TAS-2 and TAS-3, the maximum PPV increments associated with IDA became approximately 45 percentage-points and approximately

52 percentage-points, respectively, compared with the maximum increase of approximately 30 percentage-points for TAS-1 only. The corresponding values for DA were approximately 68 percentage-points and approximately 76 percentage-points, respectively, compared with the approximately 48 percentage-points for TAS-1 only. Thus, PPVs following TAS-3 can be as high as approximately 95 percentage-points for decision thresholds ≤0.5% mf prevalence, even for low values of MDA coverage (65%) and duration (three years).

We also found that delaying TAS-1 by two years so that TAS-es occurred at three, five, and seven years post-MDA had only a limited impact on PPVs (Supplementary Figure 7). The PPV increment was the highest for TAS-1 by approximately 5 percentage-points for both drug regimens. The PPV increments associated with increasing the gap between one of the TAS-es, keeping TAS-1 at one year post-MDA, were even more negligible (not shown).

DISCUSSION

Our results show that, by itself, TAS-1 conducted to measure mf prevalence one year after the last MDA round with IDA provides relatively little information on the prospect of elimination, which is dictated largely by MDA duration and coverage. However, TAS-2 and TAS-3, conducted three and five years post-MDA (but only if TAS-1 is passed), are more informative in this regard. For TAS-3, PPVs ≥95% are possible with a stop-MDA threshold of ≤0.5% mf prevalence for ages 5 years and above. Further, using a larger sample size for TAS (ie, greater number of individuals) as well as testing the age group of 5+ instead of 15+ increase the PPV of mf surveys. The latter is due to the fact that if MDA successfully suppresses transmission, young individuals are less likely to contract their first worm infection; therefore, in age groups for which prevalence would normally strongly increase with age pre-MDA (ages 5–15 years), a low infection prevalence is indicative of a significant impact on transmission. Including this age group in surveys therefore adds useful information for decision-making [15].

The surveys provide more information in settings with DA than in settings with IDA, which is due to IDA being more effective than DA in clearing LF infection. Results pertaining to DA are helpful in hypothesizing the consequence of an alternate assumption of IDA having no sterilizing effect (denoted as "IDA2" by Irvine et al. [17]), which is contrary to the 100% (permanent) sterilization of female adult worms we considered here. In case of no sterilizing effect, the only difference between IDA2 and DA is IDA2's ability to kill 100% mf instead of the widely accepted value of 95% mf killing of DA [21]. Therefore, we expect that the results for an analysis of IDA2 would be similar to what we present here for DA.

Previous modeling studies on elimination or stop-MDA thresholds for LF considered 40–50 years after the last MDA round as the time horizon to define elimination (0% mf prevalence) [16, 19, 22], whereas we adopted a time horizon of 20 years. Following the assumption that the parasite numbers are so low by the time MDA is stopped, as per the breakpoint theory [23], the number of new infections post-MDA is not enough to sustain transmission. Hence, when past this breakpoint, a 50-year period would allow for the complete natural attrition of the remaining parasite population in our simulations, resulting in a higher (*a priori*) elimination probability than for a 20-year period. This is why TAS-es added less information in the former case than the latter. More importantly, a 50-year time horizon is far beyond the political scope of most governments and probably not realistic since a lot can happen in 50 years (eg, secular developments or disasters). Although still long, a 20-year time horizon is much closer to the reality in which we develop and use NTD control strategies. For this time horizon, it is more feasible to also compare our model predictions with results from actual settings than from the 50-year period. In real-life settings, before TAS-1, a pre-TAS is often conducted in up to eight communities to determine whether mf prevalence is <1% (CFA prevalence <2%). The purpose of the pre-TAS is to decide whether TAS-1 should be conducted across the evaluation unit (typically a district), which would encompass a large number of communities. As our simulations focus on single communities and not larger areas that consist of multiple communities, we did not account for pre-TAS.

Although testing for mf may be the best way to identify persons with reproducing adult worms, implementing this strategy at scale can be challenging due to the nocturnal periodicity of mf in India and most other countries, with serious cost and resource implications for all programs. Therefore, mf tests will likely not be performed population-wide but will only be done in people who tested antigen-positive in an antigen survey carried out during the day, as in recent studies such as the one by Eneanya et al. [24]. In our study, we did not explicitly consider a pre-screening for CFA and assumed that the probability of an mf-positive individual testing negative on CFA is negligible. Taken together, our results may represent a strategy with decision-making based solely on the estimated mf prevalence. Another concern relates to the limited sensitivity/reliability of mf detection using finger-prick blood in post-treatment settings when parasitemia levels are expected to be low. Our model accounts for this by simulating variation in mf counts, assuming that mf counts follow a negative binomial distribution with aggregation parameter $k = 0.35$. Better sensitivity can be achieved by filtration of larger blood samples, but this is not feasible at a large scale. If the CFA prevalence itself would also be considered in the decision-making (eg, via a second threshold for CFA prevalence), the predictive value of TAS-es might be somewhat higher than we predict here. Further, the timing of TAS-es may not be as we assumed here (every

two years, starting one year after the last MDA round). For instance, it is also possible that TAS-es could be delayed in some settings due to external reasons such as coronavirus disease 2019. However, we found such delays to only slightly increase the predictive value of TAS-es, which is reflective of the slow dynamics of LF recrudescence [25].

To assess the status of LF elimination, only mf and CFA prevalences are used as indicators, with the latter not being recommended for IDA-based MDA. For other NTDs, the vector infectivity rate is also often used as an indicator. For example, stop-MDA decisions for onchocerciasis are based on black fly infectivity in addition to antibody seroprevalence [26]. However, in the case of LF, there is no established practice for collecting mosquito infectivity data. This is also because the mosquitoes would need to be captured in many different locations (eg, households) to obtain a representative picture of a community [27], unlike the onchocerciasis-transmitting black flies that circulate throughout a village, making it easy for data to be collected.

In this work, we only considered regions in India that were previously untreated and ignored the impact of other interventions potentially affecting LF infection and transmission, such as the National Deworming Day (NDD) program, initiated in 2015, in which albendazole is administered biannually in those aged up to 19 years [28]. Based on evidence from the Republic of Congo, twice yearly albendazole can strongly reduce antigenemia rates [29, 30], but no information is available yet on the effectiveness of the strategy in the Indian context. Given that a big fraction of the population remained untreated, NDD alone is unlikely to lead to elimination. Still, accounting for this effect could lead to more accurate predictions for areas that are treatment-naive for LF where the NDD strategy is applied. There might also be settings that failed TAS even after multiple rounds of DA and where IDA could be administered for 1–3 rounds, for which a similar analysis would be interesting. IDA can also be administered in LF-endemic African regions that are not endemic to both onchocerciasis and loiasis, such as Madagascar. Our analysis could be extended to such settings as well.

We conclude that when only TAS-1 is included, PPVs are always <95% for threshold values ≥0.5% mf prevalence. However, with two additional TAS-es, spaced two years apart and conditional on all three TAS-es being passed with the same threshold, PPVs of ≥95% are possible for a stop-MDA threshold of 0.5%, even when the coverage is as low as 65%. This study supports the WHO strategy of repeating the TAS twice during post-MDA surveillance, although the PPV could be improved by lowering the decision threshold from approximately 4% to 0.5%.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Dovato
dolutegravir/lamivudine

EVIDENCE SUPPORTS THE HIGH BARRIER TO RESISTANCE OF DOVATO UP TO 5 YEARS[1-3]

CONFIDENCE IN DOVATO ACROSS TREATMENT SETTINGS[4–9]

Treatment-naïve resistance rates, with up to **3 years of evidence**[5–7]

0% (n=0/1,885)*,[4]
REAL-WORLD EVIDENCE

0.1% (n=1/953)**,†,‡,§,5–7
RANDOMISED CONTROLLED TRIALS

Treatment-experienced resistance rates, with up to **5 years of evidence**[1–3]

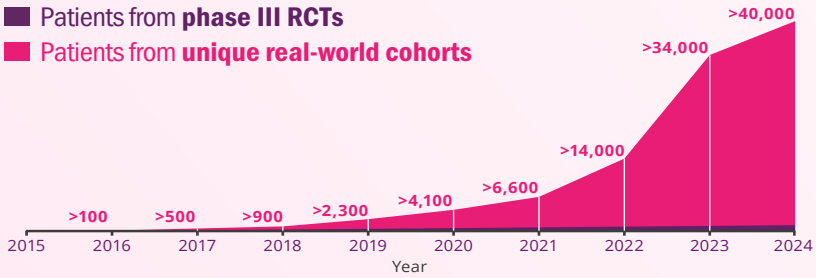
0.03% (n=10/35,888)*,[4]
REAL-WORLD EVIDENCE

0% (n=0/615)||,¶,#,8,9
RANDOMISED CONTROLLED TRIALS

>300,000 PEOPLE LIVING WITH HIV HAVE BEEN TREATED WITH DOVATO GLOBALLY[10]

DOVATO is supported by a wealth of evidence, with the outcomes of **>40,000** people living with HIV captured within clinical trials and real-world evidence, including those with:[4–9,11,12]

- **NO PRIOR TREATMENT EXPERIENCE**[13]
- **NO BASELINE RESISTANCE TESTING**[13]
- **HIGH BASELINE VIRAL LOAD** (>100,000 copies/mL and even >1M copies/mL)[6,13]
- **LOW CD4 + COUNT** (≤200 cells/mm³)[13]



IS IT TIME TO RECONSIDER THE VALUE OF THE 2ND NRTI?

LEARN MORE

DOVATO is indicated for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adults and adolescents above 12 years of age weighing at least 40 kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine.[13]

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk/** or search for MHRA Yellowcard in the Google Play or Apple App store. Adverse events should also be reported to GSK on 0800 221441

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ABBREVIATIONS

3TC, lamivudine; **CD4,** cluster of differentiation 4; **DTG,** dolutegravir; **FDA,** United States Food and Drug Administration; **FTC,** emtricitabine; **HIV,** human immunodeficiency virus; **ITT-E,** intention-to-treat exposed; **NRTI,** nucleoside/nucleotide reverse transcriptase inhibitor; **RCT,** randomised controlled trial; **RNA,** ribonucleic acid; **TAF,** tenofovir alafenamide fumarate; **TDF,** tenofovir disoproxil fumarate; **XTC,** emtricitabine.

FOOTNOTES

*Data extracted from a systematic literature review of DTG+3TC real-world evidence. Overlap between cohorts cannot be fully excluded.

**The reported rate reflects the sum-total of resistance cases calculated from GEMINI I and II (n=1/716, through 144 weeks), STAT (n=0/131, through 52 weeks), and D2ARLING (n=0/106, through 24 weeks).[5–7]

†GEMINI I and II are two identical 148-week, phase III, randomised, double-blind, multicentre, parallel-group, non-inferiority, controlled clinical trials testing the efficacy of DTG/3TC in treatment-naïve patients. Participants with screening HIV-1 RNA ≤500,000 copies/mL were randomised 1:1 to once-daily DTG/3TC (n=716, pooled) or DTG + TDF/FTC (n=717, pooled). The primary endpoint of each GEMINI study was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 48 (ITT-E population, snapshot algorithm).[13]

‡STAT is a phase IIIb, open-label, 48-week, single-arm pilot study evaluating the feasibility, efficacy, and safety of DTG/3TC in 131 newly diagnosed HIV-1 infected adults as a first line regimen. The primary endpoint was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 24.[6]

§D2ARLING is a randomised, open-label, phase IV study designed to assess the efficacy and safety of DTG/3TC in treatment-naïve people with HIV with no available baseline HIV-1 resistance testing. Participants were randomised in a 1:1 ratio to receive DTG/3TC (n=106) or DTG + TDF/XTC (n=108). The primary endpoint was the proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 48.[7] Results at week 24 of the study.

||The reported rate reflects the sum-total of resistance cases calculated from TANGO (n=0/369, through 196 weeks) and SALSA (n=0/246, through 48 weeks).[8,9]

¶TANGO is a randomised, open-label, trial testing the efficacy of DOVATO in virologically suppressed patients. Participants were randomised in a 1:1 ratio to receive DOVATO (n=369) or continue with TAF-containing regimens (n=372) for up to 200 weeks. At Week 148, 298 of those on TAF-based regimens switched to DOVATO. The primary efficacy endpoint was the proportion of subjects with plasma HIV-1 RNA ≥50 copies/mL (virologic non-response) as per the FDA Snapshot category at Week 48 (adjusted for randomisation stratification factor).[8,13]

#SALSA is a phase III, randomised, open-label, non-inferiority clinical trial evaluating the efficacy and safety of switching to DTG/3TC compared with continuing current antiretroviral regimens in virologically suppressed adults with HIV. Eligible participants were randomised 1:1 to switch to once-daily DTG/3TC (n=246) or continue current antiretroviral regimens (n=247). The primary endpoint was the proportion of subjects with plasma HIV-1 RNA ≥50 copies/mL at Week 48 (ITT-E population, snapshot algorithm).[9]

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