

# SYSTEMATIC REVIEW ON IMPACT OF MASS DRUG ADMINISTRATION ON LYMPHATIC FILARIASIS PREVENTION

Mohd Fathulzhafran Mohamed Hanan<sup>1</sup>, Hanani Nabilah Mohd Sobri<sup>1</sup>, Noor Dalila Inche Zainal Abidin<sup>1</sup>, Mohd Rohaizat Hassan<sup>1</sup>, Azmawati Mohammed Naw<sup>1</sup>, Norfazilah Ahmad<sup>1</sup>, Syed Sharizman Syed Abdul Rahim<sup>2</sup> and Mohammad Saffree Jeffree<sup>2</sup>

<sup>1</sup>Department of Community Health, National University of Malaysia Medical Centre 56000, Kuala Lumpur Malaysia

<sup>2</sup>Department of Public Health Medicine, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, 88400 Kota Kinabalu Sabah Malaysia

\*Corresponding author: [syedsharizman@ums.edu.my](mailto:syedsharizman@ums.edu.my)

## ABSTRACT

**Introduction:** Lymphatic filariasis (LF) is a disease caused by filarial parasites transmitted to human by mosquitoes and infecting 120 million people worldwide. Mass drug administration (MDA) involves delivering treatment to every person living in a defined geographical area, is the current practice in place and has shown to be very useful in reducing the global transmission of LF. This review aims to explore into the effectiveness of MDA in interrupting the transmission of LF in terms of the types of MDA, number of cycles, coverage, and percentage of transmission reduction. **Methods:** A systematic search via Scopus, PubMed, and Cochrane was done for articles published from 2015 to 2019 by using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. The articles identified from the databases searched and any that appeared to relate to the research questions were included. A total number of 14 articles fulfilled the criteria for review. **Results:** Overall, the review showed a reduction in LF indices of more than 50% and up to 100% post-MDA in endemic communities with high prevalence. The entomological assessment revealed a reduction in LF transmission post-MDA, which strongly supported the reduction of LF indices. Biannual MDA conducted further showed a marked reduction in LF indices compared to annual MDA. Double therapy of MDA significantly reduced the transmission indices to almost nil compared to single therapy. **Conclusion:** Review of MDA showed promising effects in which it reduced the prevalence microfilaraemia (mf) and Circulating Filarial Antigen (CFA) from baseline, as well as the clinical prevalence and entomological indices. Combination therapy showed better outcome compared to single therapy. Therefore, complementary vector control is suggested in addition to MDA, as well as education delivery to the endemic communities.

**Keywords:** Lymphatic filariasis, mass drug administration, systematic review, transmission assessment survey

## Introduction

Lymphatic filariasis (LF) is a disease caused by filarial parasites that are transmitted to human by mosquitoes. This infection is usually obtained during childhood and can damage the lymphatic system in the body. As the disease progresses over the years, the patients will present with swelling over bilateral limbs, as well as scrotum. The appearance of lower limb swelling looks similar to elephant leg; thus, this disease is also known as elephantiasis. Despite being considered as a neglected tropical disease, LF has infected 120 million people worldwide, with 886 million people in 72 countries living in prone areas (World Health Organization, 2021).

There are three species of filarial parasites responsible for causing this disease. In most areas in the world, it is caused by *Wuchereria bancrofti*. Two other parasites, namely *Brugia malayi* and *Brugia timori* affect those in the Asia region (CDC, 2021). These parasites are transmitted by a wide range of mosquitoes, such as *Anopheles*, *Culex*, *Mansonia*, and *Aedes*. The types of mosquito species involved are highly dependent on their geographic distribution. For example, *Anopheles* is commonly found in rural areas, *Culex* is found in urban and semi-urban areas, and *Mansonia* and *Aedes* are the common vectors in the Pacific Islands and Asia (World Health Organization, 2021).

An adult filarial parasite lives in the human lymphatic system and reproduces microfilariae. Due to its small size, the mf can enter blood vessels and then circulates. When a mosquito bites a human, the mf will enter into mosquito's gut and grows in it. The mf will then be passed to another human when the mosquito bites them before entering the lymphatic system and growing into an adult worm. It will stay in the lymph vessels for five to six years, before mating and releasing more mf (CDC, 2021). The presence of adult worms can block the lymph vessels and cause limb and genitalia swelling. The mf will present at the blood capillaries at night-time so that it can be taken by the mosquito during the bite.

Majority of the patients are asymptomatic, whereby the clinical manifestation usually appears in chronic infection due to lymphatic damage. The patients will have lymphoedema of the limbs, hydrocele, and chylocele. Recurrent acute attacks are also common, such as acute adenolymphangitis, which is characterised by fever associated with swelling and pain of the lymph nodes and vessels (CDC, 2021; World Health Organization, 2021).

In 2000, World Health Organisation (WHO) launched the Global Programme to Eliminate Lymphatic Filariasis (GPELF) in response to the quest to eliminate LF worldwide. Elimination of LF is achieved when mf rate is less than 1% and less than 1/1000 children infected over five cumulative years (Noordin, 2007). Two objectives were highlighted in this programme: (i) to interrupt the transmission of LF, and (1) to control the morbidity caused by LF. Endemic areas were mapped, and community-wide treatment programmes were administered. Patients with morbidity were included in morbidity management and

disability prevention (MMDP) programme and they were taught on the care of lymphoedema and hydrocele (World Health Organization, 2021).

Mass drug administration (MDA) is a programme designed to treat the entire population at risk by delivering treatment to every person living in a defined geographical area. This programme is implemented using the smallest administrative unit, which is called the Implementation Unit (IU) (2). Every person in the IU, excluding children under two years old and pregnant ladies, is given either 6 mg/kg of body weight diethylcarbamazine citrate (DEC) + 400 mg albendazole, or 150 µg/kg of body weight ivermectin + 400 mg albendazole annually for at least five years. The coverage of annual MDA must be at least 65% of total population (World Health Organization, 2018). After completing the MDA rounds, transmission assessment survey (TAS) is done to quantify the impact of MDA on the prevalence of mf in the IU. Once the prevalence is very low and there is no risk of new transmission, the programme can be stopped.

Since the GPELF has been set up to eliminate LF by 2020, many countries have scaled up MDA in their endemic districts, such as in the African region. A WHO progress report in 2017 stated that 87% of IUs conducting MDA globally had achieved effective coverage of more than 65% (World Health Organization, 2018). Despite having a good coverage for MDA, the number of people who suffers from the complications of LF are still increasing in trend (Molyneux, 2018).

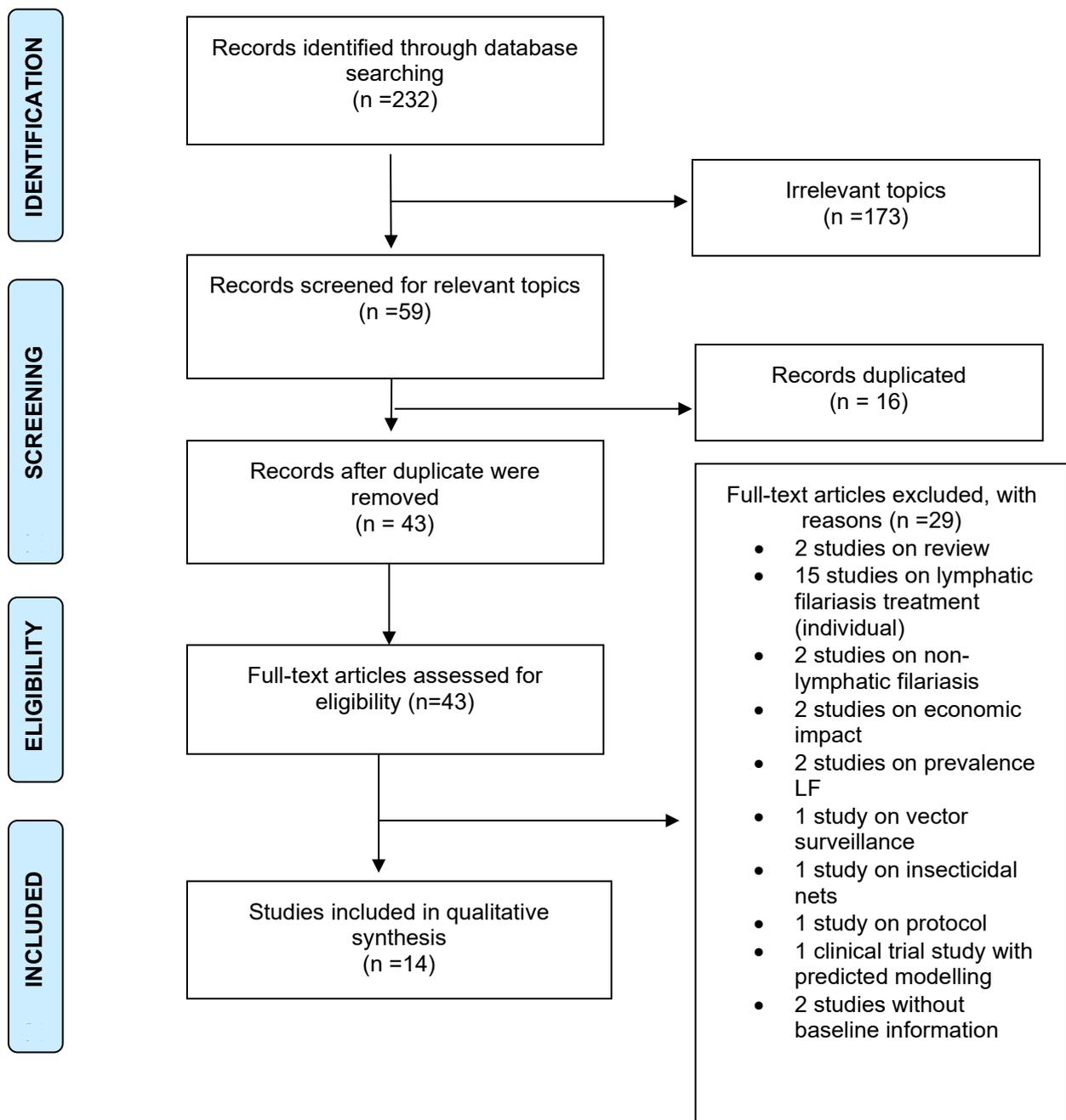
It is agreed that MDA is very useful in reducing the transmission of LF. However, some countries have reported an increasing resistance towards the antihelminthic drugs used in MDA. The prolonged exposure to these drugs can cause drug pressure on the parasites and trigger the production of drug-resistant strains (Cobo, 2016). Therefore, it is important to evaluate the impact of MDA conducted globally. This review will look into the effectiveness of MDA in interrupting the transmission of LF globally in terms of the types of MDA, number of cycles, coverage, and percentage of transmission reduction.

## **Methods**

### *Literature Search*

A systematic search for relevant published articles with three major search engines, namely Scopus, PubMed, and Cochrane were conducted. To yield the most current studies, retrieval was restricted to articles published from the year 2015 to 2019. The systematic review is performed using the PRISMA checklist (Moher et al., 2015) in which the workflow of publication search is presented in Figure 1. The three major selected databases were accessed using the following keywords: “filariasis\*” OR “elephantiasis\*” AND “mass drug administration” OR “chemoprevention” OR “antibiotic prophylaxis” AND “effectiveness” OR “impact” OR “outcome”. For the articles identified from the database search, the titles were screened according to those which were relevant to the research questions. Any articles that appeared to provide an answer to the research questions were also included. Then, articles that were duplicated in the pool of screened articles were discarded and the total number of articles left after

duplication were assessed for eligibility. The eligible articles were retrieved and evaluated based on the inclusion and exclusion criteria. Inclusion criteria were: (a) community-based study, (b) epidemiological or entomological assessment as the outcome, (c) included studies that were done all over the world, and (d) availability of baseline information. The studies were excluded based on: (a) non-lymphatic filariasis, (b) review or clinical trial, and (c) vector surveillance. Articles were also excluded if the English version of the full text was not available. The three electronic database searches revealed a total number of 14 articles that fulfilled the aforementioned criteria for review (Table 1). The selected articles were assessed for quality using the Newcastle-Ottawa Quality Assessment Scale in which the reviewers consisted of three medical doctors with public health background.



**Figure 1: Workflow showing process of articles selection for the review**

## Results

### *Characteristics of Studies*

As mentioned in the methodology section, the systematic review included studies from the year 2015 to 2019 from various countries in the world, which were prominently from the endemic region of African countries and other regions including South Asia, Southeast Asia, and Oceania. All of the studies used the observational type of quantitative study, whereby 13 studies were cross-sectional, and one was cohort/longitudinal in design. Sample population involved in the studies were from various range of ages, including both children and adults. Most of the studies used thousands of sample size and the quality of the selected articles was fair to good quality based on the Newcastle-Ottawa Quality Assessment Scale. Epidemiological assessments such as CFA and mf were carried out as an outcome impact in most studies, while only two studies assessed entomological indices as an outcome impact. Results are further specified according to the type of MDA conducted and outcome reduction (Table 2).

### *Impact of MDA*

All of the studies showed a reduction in LF indices, namely CFA and mf of more than 50% and up to 100% post-MDA in the community over endemic regions with a high prevalence of LF infection. Few studies also demonstrated the reduction of both CFA and mf prevalence to 0% after five to six rounds of MDA (Allen et al., 2017). The entomological assessment also revealed a reduction in LF transmission post-MDA, which strongly supported the reduction of LF indices. Biannual MDA that was previously conducted also showed a marked reduction in LF indices compared to annual MDA (Supali et al., 2019). On top of this, single therapy of MDA (diethylcarbamazine alone) showed higher transmission rates compared to the double therapy of MDA (diethylcarbamazine plus albendazole), whereby the double therapy of MDA significantly reduced the transmission indices to almost nil compared to single therapy (Sunish et al., 2015). However, in both comparisons of MDA frequency (annual versus biannual) and type of MDA prescribed to the community (double versus single therapy), more studies needed to be included for comparative review. For this study, the objective and keywords in the search engines should be expanded accordingly. In the systematic review, one study was included for an assessment of MDA effectiveness in the vulnerable group, which was individual with HIV (Human Immunodeficiency Virus) co-infection (Pitter, Mgeni, Mabuye, Kowuor, & Mwingira, 2016). In the study, they found that the effectiveness of MDA was not reduced by concomitant HIV infection. Again, the effectiveness of MDA towards the vulnerable population needs to be systematically reviewed using different operational keywords in order to capture more related studies and make more comparisons.

**Table 1: Characteristics of studies reviewed**

Article & Author/year	Study Population/country	Study design	Mass Drug Administration (MDA)	Other intervention	Outcome impact	Barriers (if applicable)
Lymphatic filariasis transmission in Rufiji District, south-eastern Tanzania: infection status of the human population and mosquito vectors after twelve rounds of mass drug administration Jones et al. 2018	Population in Rufiji District, south-eastern Tanzania N=854	Community-based cross-sectional study (7 months post 12 <sup>th</sup> annual MDA round-April 2015)	12 annual rounds of MDA (ivermectin and albendazole) between 2002-2014 with 54-94% of coverage Drug uptake among respondents ranging from 70% to 83%	None	Reduction of CFA prevalence from baseline 49% to 1.1% and mf prevalence from baseline 18% to 0.1% Reduction of hydrocele prevalence from baseline 12% to 4.8% and elephantiasis prevalence from baseline 4% to 2.9% None of the indoor filarial vectors was found to be infected with <i>W. bancrofti</i> An estimated <i>W. bancrofti</i> infection rate of 0.1% among outdoor filarial vectors Individuals who did not participate in any of the previous rounds of MDA were significantly more infected (CFA) compared with those with a recent history of participating in MDA	Not stated
Progress on the elimination of lymphatic filariasis in Sierra Leone Koroma et al. 2018	Population in all 12 districts of Sierra Leone N=4230	Community survey using selected sentinel and spot-check sites (2013)	5 annual rounds of MDA (ivermectin and albendazole) in 2008-2012 with coverage >65%	None	Reduction of mf prevalence from baseline 2.6% to 0.3% at midterm 2011 and slightly increase to	Not stated

					0.54% in the current study	
Mapping and modelling the impact of mass drug administration on filariasis prevalence in Myanmar Aye et al. 2018	12 provinces (45 districts) in Myanmar with high endemicity status of LF transmission N=4660	Community-based survey; TAS via sentinel and spot-check sites in districts with at least 5 rounds of MDA	Annual MDA conducted in a stepwise manner over 13 years period from 2001-2013 with coverage 60-98%	None	Only 5 provinces (22 districts) completed TAS post 5 rounds MDA Reduction of mf prevalence from 1.5-5.2% to 0.2-2.8%.	Challenges: drug supply, local conflict interrupted MDA in some districts
The interruption of <i>Onchocerca volvulus</i> and <i>Wuchereria bancrofti</i> transmission by integrated chemotherapy in the Obongi focus, North-Western Uganda Luroni et al. 2017*	Population in Obongi focus in Moyo District, northwestern Uganda N=1532	Community-based survey (2014) using selected sentinel sites and TAS	5 annual rounds of MDA (ivermectin and albendazole) in 2006-2011 with 70% coverage	Malaria prevention (long-lasting insecticide-treated nets)	Reduction of mf prevalence from pre-MDA 2.5% to 0.8% in 2011 and 0% in 2014 TAS among children aged 6-7 years old in 2014 revealed negative (0.0%) for antibodies of <i>W. bancrofti</i>	Not stated
Persistent 'hotspots' of lymphatic filariasis microfilaraemia (MF) despite 14 years of mass drug administration in Ghana.  Biritwum et al. 2016	98 endemic districts in Ghana 29 hotspots 69 stopped MDA districts N=not stated	Community based survey	14 annual rounds of MDA 2001-2014 with coverage 75% (hotspots) 10 annual rounds of MDA 2001-2012 with coverage 77.5% (stopped MDA) *type not specified	1. Average LLIN coverage (SD) hotspots: 19.7 (1.5) stopped MDA: 20.1 (12.2)	Hotspots: Reduction of mf prevalence from baseline (2000-2004) 41.6% to 11.5% at midterm (2003-2009) to 0.7% during recent study (2009-2014) Stopped MDA: Reduction of mf prevalence from baseline (2000-2004) 4.7% to 2.0% at midterm (2003-2009) to 0.1% during recent study (2009-2014)	Not stated
Impact of mass drug administration for elimination of lymphatic filariasis in Nepal.	10 selected districts in Nepal N=9495	Community-based survey (pre-TAS; post 5 annual MDA)	5 annual rounds of MDA (DEC and albendazole) in 2010-2014 6 districts achieved MDA	None	Reduction of mf prevalence from baseline 1.06-20% to <2% at pre-TAS	Not stated

Ojha et al. 2017*		rounds 2014) (TAS in 2015)	coverage of 65%		TAS mf prevalence: All 6 districts achieved the prevalence threshold (<1%)	
Effect of 3 years of biannual mass drug administration with albendazole on lymphatic filariasis and soil-transmitted helminthic infections: a community-based study in Republic of the Congo Pion et al. 2017	Seke Pembe, a village located in Mabombo Health District (Bouenza division) in Republic of the Congo N=1574	Community-based survey (2015)	Biannually (6 rounds) MDA with albendazole in 2012-2015 MDA coverage: 77-83%	Coverage bednet usage: 76%	Reduction of CFA prevalence from 17.3% (2012) to 4.7% (2015) Reduction of mf prevalence from 5.3% (2012) to 0.3% (2015)  72.8% reduction in CFA prevalence and 94.3% reduction in mf prevalence	Not stated
Reaching endpoints for lymphatic filariasis elimination- results from mass drug administration and nocturnal blood surveys, South Gujarat, India. Modi et al. 2017*	5 districts in South Gujarat Region N=17551	Community-based survey (2010-2015)	10 annual rounds of MDA from 2005-2015 with coverage of 89.2-96.7% for the last 5 years (2010-2015) *type of MDA not specified	None	Reduction of mf prevalence from 1.4% (2005) to 0.44% (2015)	Not stated
Comparison of the Impact of Annual and Semi-annual Mass Drug Administration on Lymphatic Filariasis Prevalence in Flores Island, Indonesia. Supali et al. 2019	3 villages in Sikka district, Flores Island, Indonesia N=2804 (2104)	Community-based survey (2014)	MDA with DEC combined with ALB in 2011-2013  No. of MDA rounds: Paga and Lewomada: 3 (annual) Pruda: 5 (semi-annual)	None	1. Baseline mf prevalence: Paga: 3.9% Lewomada: 5.0% Pruda: 14.2% 2. Current mf prevalence: Paga: 0.0% Lewomada: 0.3% Pruda: 1.2%	Not stated
The first evidence of lymphatic filariasis transmission interruption in Cameroon: Progress towards elimination.	North and Far North Regions of Cameroon; 5 health districts divided into 3 Evaluation unit (EU) Mokolo Ngong/Poli Tchollire/Rey-Bouba N=5292	Community-based TAS in 2014	6 Annual MDA rounds in 2008 – 2013	None	Baseline CFA prevalence in 2007 was 2.7% Current CFA prevalence: EU #1: 0.13% EU #2: 0.57% EU #3: 0.45%	Not stated

Nana-djeunga et al. 2017*					overall: 0.40%	
Impact of the Lymphatic Filariasis Control Program towards the elimination of filariasis in Vanuatu, 1997–2006 Allen et al. 2017*	51 villages throughout the 6 provinces of Vanuatu N=4363	Community-based survey (2005/2006)	5 annual rounds of MDA from 2000 to 2004 with coverage of 75.5-81.5%	None	Reduction of mf prevalence from baseline (1997/1998) 2.48% to 0% (current study) Reduction of CFA prevalence from baseline (1997/1998) 4.79% to 0.16% (current study)	Not stated
Prevalence of Lymphatic Filariasis and Treatment Effectiveness of Albendazole/ Ivermectin in Individuals with HIV Co-infection in Southwest-Tanzania Kroidl et al. 2016	Population in the Kyela district/ Mbeya region Southwest Tanzania (aged 0–94 years) N=2104	Community-based cross-sectional study (part of cohort-study; Surveillance of Lymphatic Filariasis)  *6 months post 2 <sup>nd</sup> round of MDA	2 annual rounds of MDA (ivermectin and albendazole) from 2007-2009 *coverage not specified in article	None	Prevalence CFA reduced from 21.6% to 19.7% after 2 rounds of annual MDA (relative drop of 8.8%, McNemar's exact p = 0.036) * The effectiveness of MDA was not reduced by concomitant HIV-infection	Not stated
The Impact of Six Annual Rounds of Mass Drug Administration on Wuchereria bancrofti Infections in Humans and Mosquitoes in Mali Coulibaly et al. 2015	6 endemic villages in Sikasso, Mali N=1334	Community-based cross-sectional study between 2002-2008	Six consecutive annual MDA albendazole and ivermectin from 2002 to 2007 with coverage of 69% to 89%	None	Adults: reduction of mf prevalence from 21.4% (pre-MDA) to 0% (12 months post 6 <sup>th</sup> round of MDA)  Children: reduction of CFA from 53% (pre-MDA) to 0% (12 months post 6 <sup>th</sup> round of MDA)  Number of infective bites/ human/ year decreased from 4.8 in 2002 (pre-MDA) to 0.04	Not stated

					in 2007(post-MDA).  Only one mosquito containing a single infective larva was observed 12 months post a final round of MDA	
Decline in lymphatic filariasis transmission with annual MDA using DEC with and without albendazole over a 10-year period in India  Sunish et al. 2015	Endemic districts (revenue blocks) in Tamil Nadu State, South India.  N=not stated	Longitudinal study from 2001-2009	6 rounds of annual MDA carried out over a period of 10 years (2001, 2002, 2003, 2004, 2007 and 2009)  Tirukoilur block (DEC + albendazole)  Mugaiyur block (DEC alone).	None	Entomological indices derived from the collection of indoor resting adult female mosquitoes; -99% reduction in TTI for DCE + albendazole -72% reduction in TTI for DEC alone -86% reduction in infectivity rate for DCE + albendazole -54% reduction in infectivity rate for DEC alone  DEC alone arm showed higher transmission rates, compared to the DEC + ALB arm. Albendazole along with DEC has significantly reduced the transmission indices to almost nil level, compared to DEC alone	MDA not conducted in 2005. 2006, 2008 due to administrative reason

\*good quality study using Newcastle Ottawa Scale Assessment, TTI= transmission intensity index

**Table 2: Outcome reduction in relation to the type of MDA therapy**

Type of MDA therapy		Outcome	Articles	
Combination DEC/ ivermectin with albendazole	Annual MDA	≥ 5 rounds of MDA	Reduction of 98% CFA prevalence Reduction of 88-100% mf prevalence <b>Reduction of 99% TTI and 86% infectivity rate</b>	Jones et al. 2018 Dolo et al. 2015; Jones et al. 2018; Koroma et al. 2018; Luroni et al. 2017; Ojha et al. 2017 Sunish et al. 2015
		< 5 rounds of MDA	Reduction of 8.8% CFA prevalence Reduction of 94% mf prevalence	Kroidl et al. 2016 Supali et al. 2019
	Biannual MDA	≥ 5 rounds of MDA	Reduction of 91.5% mf prevalence	Supali et al. 2019
		< 5 rounds of MDA	-	-
Albendazole alone/ DEC alone	Annual MDA	≥ 5 rounds of MDA	<b>Reduction of 72% TTI and 54% infectivity rate</b>	Sunish et al. 2015
		< 5 rounds of MDA	-	-
	Biannual MDA	≥ 5 rounds of MDA	Reduction of 72.8% CFA prevalence and 94% mf prevalence	Pion et al. 2017
		< 5 rounds of MDA	-	-
Not specified		≥ 5 rounds of MDA	Reduction of more than 80% CFA prevalence and more than 50% mf prevalence	Allen et al. 2017; Aye et al. 2018; Biritwum et al. 2016; Modi et al. 2017; Nana-djeunga et al. 2017

TTI= transmission intensity index

## Discussion

### Single MDA VS Double MDA

Most of the studies revealed a reduction in either microfilariae count, CFA by using double therapy and employing a combination of either Albendazole or DEC (Sunish et al., 2015; Supali et al., 2019) or Albendazole and Ivermectin (Coulibaly et al., 2015; Jones et al., 2018; Koroma et al., 2018; Kroidl et al., 2016; Luroni et al., 2017). Using a single therapy of Albendazole alone as per is due to its delayed use in central Africa as a result of the risk of serious adverse events in subjects with Loiasis. Using single-dose therapy shows a reduction in the mf count and CFA, however, they are not significant (Bastien et al., 2015). Nevertheless, the use of a single dose is still promising as it reduces the geometric mean mf count and the hookworm infection rate in the community. A double-blind study in South India by has shown no difference between single dose in terms of its efficacy in the clearance of microfilaria and the overall incidence of adverse reactions (Pani et al., 2002). By contrast, another community-based study in India showed higher and sustained benefits with regard to filarial and soil-transmitted helminthic infections for the combination therapy (Rajendran et al., 2006). This review showed that

combination therapy was better in the reduction of transmission intensity index and infectivity rate compared to single therapy, which could be due to the positive effect of the drug combination.

#### *Additional control*

The articles included using MDA mainly of three drugs, which were Albendazole, DEC, and Ivermectin, whether as a single therapy or in combination. Besides, the insecticide net was mentioned in addition to pharmacotherapy (Bastien et al., 2015; N.-K. Biritwum et al., 2016; Luroni et al., 2017) as a part of vector control. To achieve LF elimination, a suggestion that supplementary vector control needs to be added alongside mass therapy due to persistent transmission in villages in the study (Sunish et al., 2015).

#### *Annual VS Semi-annual*

A randomised clinical trial in Egypt showed that multi-dose DEC/Alb was significantly more effective than single-dose therapy for reducing and clearing microfilaraemia. It can be used to quickly reduce the community mf loads and transmission rates, especially in endemic places (El Setouhy et al., 2004). A study conducted in Indonesia has also stated that the annual MDA rounds are sufficient in areas with low to moderate baseline prevalence compared to more frequent biannual rounds (Supali et al., 2019). However, the study showed that in areas of higher endemicity, semi-annual MDA was useful for rapidly reducing of the microfilariae prevalence. A study in Congo as mentioned earlier showed semi-annual use of Albendazole could reduce both the CFA and mf. In this review, both annual and semi-annual MDA outcomes were almost the same.

#### *Round of Treatment*

In this review, the rounds of treatment were from two rounds up to 12 rounds in annual MDA, while five to six rounds were done in semi-annual MDA. Meanwhile, an ecology study in Ghana stated the average number of MDA rounds in hotspots was 11.5 (N.-K. Biritwum et al., 2016). One round of MDA has been reported to have a reduction of microfilariae prevalence by 26% to 41%, five to six rounds led to 88%–90% reduction (Ramaiah & Ottesen, 2014). Generally, in the included articles, more or equal to five rounds of treatment look promising in reducing the circulating filarial antigen for annual combination MDA, however, this is not conclusive and needs further comparison. The required rounds of annual MDA increase with higher baseline endemicity and lower MDA coverage (Jambulingam, Subramanian, De Vlas, Vinubala, & Stolk, 2016). If the MDA coverage rate is high, a higher treatment index can be achieved in the early rounds of the programme, and fewer rounds of MDA may be required to maximise both impact and cost-effectiveness.

#### *Coverage of MDA*

The coverage in the articles is only from 54% up to 98%, showing that the coverage of MDA is not 100%. It can be due to geographical reasons, logistics such as drug supply and local conflict (Aye et al., 2018), and country capacities. A review (Ramaiah & Ottesen, 2014) has also stated that all at-risk countries and all regions within these countries have not yet reached 100% geographic MDA coverage.

This review cannot compare between coverage in terms of the outcome as the studies included have used a range of coverage that is not a discrete value, while some did not mention the coverage level. It is crucial to achieve a 100% MDA coverage in order to eliminate filariasis in endemic countries. Programmes in India implementing the Global Programme for Elimination of Lymphatic Filariasis (GPELF) are an example to increase the coverage.

#### *Method of Detection*

The included studies showed many methods of assessment and evaluation of microfilaria. The most common method is CFA (Allen et al., 2017; Coulibaly et al., 2015; Jones et al., 2018; Kroidl et al., 2016; Nana-Djeunga et al., 2017; Ojha et al., 2017; Pion et al., 2017) and microfilaria prevalence (Aye et al., 2018; N.-K. Biritwum et al., 2016; Coulibaly et al., 2015; Koroma et al., 2018; Luroni et al., 2017; Modi et al., 2017; Ojha et al., 2017). Meanwhile, other methods are vector or entomological indices like mosquito transmission indices (Sunish et al., 2015), mosquito infectivity rate, mosquito containing a single infective larva (Coulibaly et al., 2015; Jones et al., 2018), number of infective bites/ human/year, clinical signs such as hydrocele and lymphoedema (Jones et al., 2018), and transmission assessment survey (TAS) (Aye et al., 2018; Luroni et al., 2017; Ojha et al., 2017). The GPELF diagnostic principles are simple and efficient: diagnostic techniques for field diagnosis of infection by simple, finger-prick, anytime-of-day antigen-detection tests and for clinical diagnosis by ultrasound identification of living adult parasites (Ottesen, Hooper, Bradley, & Biswas, 2008).

#### **Conclusion**

From all of the studies included, MDA showed promising effect in which it reduced the prevalence of MF and CFA from baseline, the clinical prevalence, and entomological indices. Combination therapy showed better outcome compared to single therapy. However, most of the studies did not eliminate the prevalence by a total of 100%. This can be due to the incomplete coverage of the MDA programme. Besides, vector control is required, in addition to mass therapy and education to the endemic communities.

#### **Limitation**

This review is only a scoping review and does not compare the information statistically. We recommend using a metanalysis of the outcomes of the included studies. The review also mixed the parameters of treatment regimes, assessment method, and study population.

#### **Abbreviations**

CFA: Circulating Filarial Antigen; LF: Lymphatic filariasis; MDA: Mass drug administration; mf: microfilaraemia; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; WHO: World Health Organization.

#### **Conflicts of Interest:**

The author declares no conflicts of interest.

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