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UNIVERSITY OF THE WITWATERSRAND



FACULTY OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

Research Report

FACTORS ASSOCIATED WITH VECTOR CONTROL FOR ONCHOCERCIACIS CONTROL IN SUB-SAHARAN AFRICA (2000 – 2023) : A SYSTEMATIC REVIEW

By

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A Research Report Submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the Degree of MSc in Epidemiology, Field of Implementation Sciences.

Supervisors:

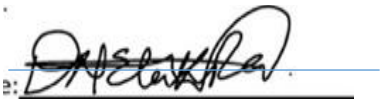
Dr. Juliana Kagura

Prof. Sumaya Mall

May 2024

DECLARATION

I, Elakpa Daniel Ngbede, hereby declare that this MSc Research Report, titled "Factors Associated with Vector Control for Onchocerciases Control In Sub-Saharan Africa (2000 – 2023): A Systematic Review," is the result of my original and unaided research work. It is being submitted for the Degree of Master of Science in Epidemiology in the Field of Implementation Science at the University of the Witwatersrand, Johannesburg. I confirm that this report has not been submitted in any other academic institution for examination or for any other degree.



(Signature of the candidate)

10th day of May 2024 in Abuja, Nigeria

DEDICATION

I would like to dedicate this MSc research report to:

My family: For their unwavering love, support, and encouragement throughout my academic journey. Your belief in me has been a constant source of inspiration and motivation.

My supervisors, Dr Juliana Kagura and Prof. Sumaya Mall: For their guidance, expertise, and valuable insights that have shaped the direction of this research. Your mentorship has been instrumental in my growth as a researcher.

My friends and colleagues: For their camaraderie, discussions, and collaborative spirit that have enriched my academic experience. Your friendship and shared enthusiasm have made this journey memorable.

All the researchers, scholars, and experts in my field: Whose previous work and publications have paved the way for my research. Your dedication and contributions to the field have been a constant source of inspiration.

To myself: For the perseverance, determination, and countless hours invested in this thesis. This accomplishment is a testament to my commitment and passion for knowledge.

Finally, to God: whose grace and mercy was sufficient for me throughout this journey.

May this research report contribute to the advancement of knowledge in the field and serve as a small tribute to all those who have supported and believed in me throughout this academic journey.

ABSTRACT

Background: Onchocerciasis is a neglected tropical disease and the second most common infectious cause of blindness worldwide, after trachoma. The vector which carries this parasite is a blackfly from the *simulium* genus, the parasite is transmitted to humans through the bite of an infected black fly during a blood meal. Alternative control strategies such as local vector control have been employed to complement the mass administration of ivermectin. There remains no synthesis of studies that have examined the use of vector control for onchocerciasis in the Sub-Saharan African (SSA) region.

Objective: To examine the factors associated with vector control in the fight against onchocerciasis in Sub-Saharan Africa as through synthesis of the literature.

Methods: A systematic search was conducted of the Cochrane Library, PubMed, Web of Science, and Scopus databases to identify relevant studies. Studies had to be published in peer-reviewed journals between January 2000 and March 2023. Data were extracted from the studies. Two independent reviewers conducted quality assessments using the Joanna Briggs Institute (JBI) critical appraisal checklist.

Results: Our search identified 343 studies of which 19 were included in this review. Several factors were found to influence blackfly vector control programs. Programmatic factors include intervention duration and effectiveness, implementation challenges, resource availability, and larvicide application practices. Vector-related factors include blackfly susceptibility to larvicides, species variation, and genetic mechanisms of resistance. Environmental factors such as rainfall patterns, river size, and the presence of dams affect blackfly breeding sites. Human-related factors encompassed community knowledge and engagement, commitment to sustainability, and human activities that impacted breeding habitats. Overall, the quality of the included studies was found to be high as per the quality appraisal tool.

Conclusion: This systematic review emphasizes the importance of considering multiple factors in the design and implementation of effective blackfly vector control programs for onchocerciasis in sub-Saharan Africa. Programmatic challenges, vector biology, environmental factors, and human

factors should be considered. Policymakers and public health practitioners should optimize interventions based on these findings.

Keywords: Onchocerciasis, vector control, Sub-saharan África.

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ABBREVIATIONS

APOC – African Programme for Onchocerciasis Control

CDTi – Community Directed Treatment with ivermectin

DALY – Disability Adjusted Life years

MESH – Medical Subject Headings

MDA – Mass Drug Administration

NTD – Neglected Tropical Disease

OCP – Onchocerciasis Control Programme

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO - Prospective Register of Systematic Reviews.

RCT – Randomized Controlled Trials

WHO – World Health Organization

1.0 INTRODUCTION

1.1 Background

The World Health Organization (WHO) uses the term "Neglected tropical diseases (NTDs)" as an umbrella term for 20 different conditions that are mainly prevalent in tropical areas. There is high risk of NTD in tropical regions which are close to the center of the globe i.e., the equator. These areas experience hot weather throughout the year, conditions where vectors can thrive and transmit diseases optimally (1). Examples of NTD include soil-transmitted helminthiases, Buruli ulcer, dengue, dracunculiasis (Guinea-worm disease), leishmaniasis, leprosy (Hansen's disease), lymphatic filariasis, onchocerciasis (river blindness), human African trypanosomiasis (sleeping sickness), schistosomiasis, and trachoma (2).

NTDs have great public health significance both in relation to burden and to their link to poverty related conditions. In a 2009 review of the burden of NTD in the Sub-Saharan Africa (SSA) Hotez and Kamath suggest salient issues that persist until today. They not only suggest that the SSA region accounted for most cases of NTDs, onchocerciasis and schistosomiasis globally, one-third of soil-transmitted helminthes cases and all cases of human African trypanosomiasis and dracunculiasis. Further they suggest that NTDs are related to conditions of poverty, a concept that is further elaborated below (2).

The connection between neglected tropical diseases and poverty was further examined by Magalhães and colleagues in a Brazilian dataset in 2023. They gave thought to proxies to measure poverty which might include sanitation, demography, and income. They conceptualized these proxies to be related to the onset of NTDs in their region and to represent a poverty related experience. Variables such as lack of piped water, high population density or overcrowding and

absence of toilets in a household were found to be related to the onset of NTDs as were eroding vegetation cover (3). In addition, the public health significance is exemplified by NTDs link to high morbidity but are not usually related to high mortality. Thus, their burden is measured in terms of healthy life lost due to some form of disability or even premature death (i.e., DALY). DALY is estimated to be approximately 20 million to 57 million DALYs lost annually (4).

NTDs are referred to as 'neglected' because they are overlooked by research and are not prioritized in the global health agenda. Over the years very little resources have been allocated towards tackling these diseases since they affect a population with little political voice and representation (5,6). However, NTDs did receive significant recognition in 2015 when they were incorporated into the third sustainable development goal. Prioritizing the fight against NTDs will then generally contribute to achieving the SDG goal 3, which is good health and wellbeing (7). In recognition of the experience of poverty described above and how this influences NTD, the WHO recently created a new and updated road map for 2021-2030 to control and eradicate NTDs. With "a target of 90% reduction in people requiring a preventive chemotherapy, and a 75% reduction in DALYs lost due to NTDs and empower at least 100 countries to eliminate at least one NTD" (8). This road map will encourage multi-sectoral collaboration, country ownership and universal health coverage to follow an integrated cross-cutting approach towards controlling NTDs. The aim is to promote a smooth and coordinated scale-up of key interventions through approach like individual case management, preventive chemotherapy (PC), water, sanitation, and hygiene as well as vector control (8).

The NTD of focus in this research report is onchocerciasis, a serious concern for public health practitioners. Following trachoma, it is the second most prevalent infectious factor leading to blindness globally (9,10). It is a multi-system disease mainly affecting the skin and eyes. It is

caused by a parasite called *Onchocerca volvulus (O. volvulus)*. The vector which carries this parasite is a blackfly from the *simulium* genus, the parasite is transmitted to humans through the bite of an infected black fly during a blood meal. The parasite undergoes a two-stage life cycle as illustrated in the figure below.

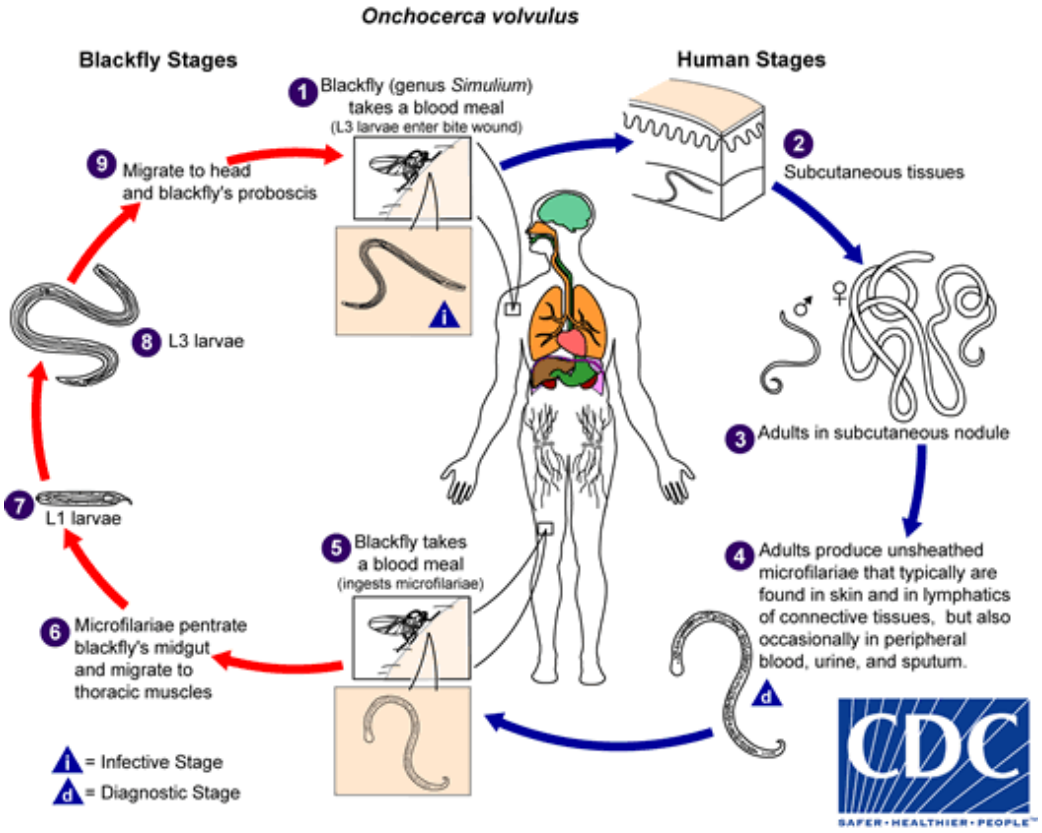


Figure 1 The Life Cycle of *Onchocerca volvulus*

(Illustration by: Center for Diseases Control and Prevention, CDC (11))

In the human stage, an infected blackfly, belonging to the *Simulium* genus, introduces third stage microfilaria larvae onto the skin of a human host during a blood meal. Within subcutaneous tissues, these larvae mature into adult filariae, which can reside in nodules for up to 15 years. Some nodules may contain a mixture of male and female worms, and while they are occasionally found in peripheral blood, urine, and sputum, their typical locations are in the skin and lymphatics of

connective tissues. The blackfly stage commences when a blackfly ingests the microfilariae during a blood meal. Following ingestion, the microfilariae move from the blackfly's midgut, through the hemocoel, to the thoracic muscles, where they transform into first-stage larvae and eventually into third-stage infective larvae. These third-stage infective larvae then migrate to the blackfly's proboscis, where they can infect another human during the fly's subsequent blood meal. The black fly is elaborated below as control strategies described in the literature review target different stages of the black fly cycle (11).

1.2.1 Description of the Blackfly Vectors and Life cycle

Blackflies is an insect, belonging to the Simuliidae family, are widely distributed across the globe, comprising more than 2,000 species in 25 genera (12,13). However, out of these 25 genera, only three, namely *Simulium, ProSimulium*, and *AustroSimulium, are* known to bite humans. Among these, *Simulium* is the most medically significant genus due to its association with several disease vectors like avian malaria, loiasis and masonelliasis (12,14). In Africa, the transmission of onchocerciasis is likely to be facilitated by the *Simulium neavei* group and the *Simulium damnosum* complex. On the other hand, in Central and South America, the *Simulium exiguum*, *Simulium metallicum*, and *Simulium ochraceum* complexes play a role in transmitting the parasitic nematode *Onchocerca volvulus* (12–14).

The lifecycle of *Simulium damnosum* blackflies starts when they deposit their eggs on vegetation that hangs over fast-flowing, well-oxygenated water (13). In contrast, *Simulium. neavei* blackflies lay their eggs on amphibious Potamonautes crabs (12,15). The eggs are laid in batches, typically containing around 100 to 900 eggs, and are attached to the substrate by mucus secretions, which quickly moisten and cement the eggs (12,16). After approximately 1 to 2 days, the blackfly eggs hatch, giving rise to larvae that remain attached to the substrate (12,13,15). The larvae obtain their

nutrition through filter-feeding. The breeding of these blackflies is limited to habitats with fast-flowing, well-oxygenated watercourses, as the larvae require oxygen and rely on filter-feeding for sustenance (16).

A pictorial diagram presenting the lifecycle of blackfly described above is show in Figure 2 below. During the spring or summer, the pupal stage of insects occurs, usually in the same location where the last larval stage took place. However, in some cases, pupae may drift downstream with the current. After spending time as pupae, adults emerge within a period of 4 to 7 days and have a lifespan of a few weeks. Most species of insects are active from mid-May to July (17).

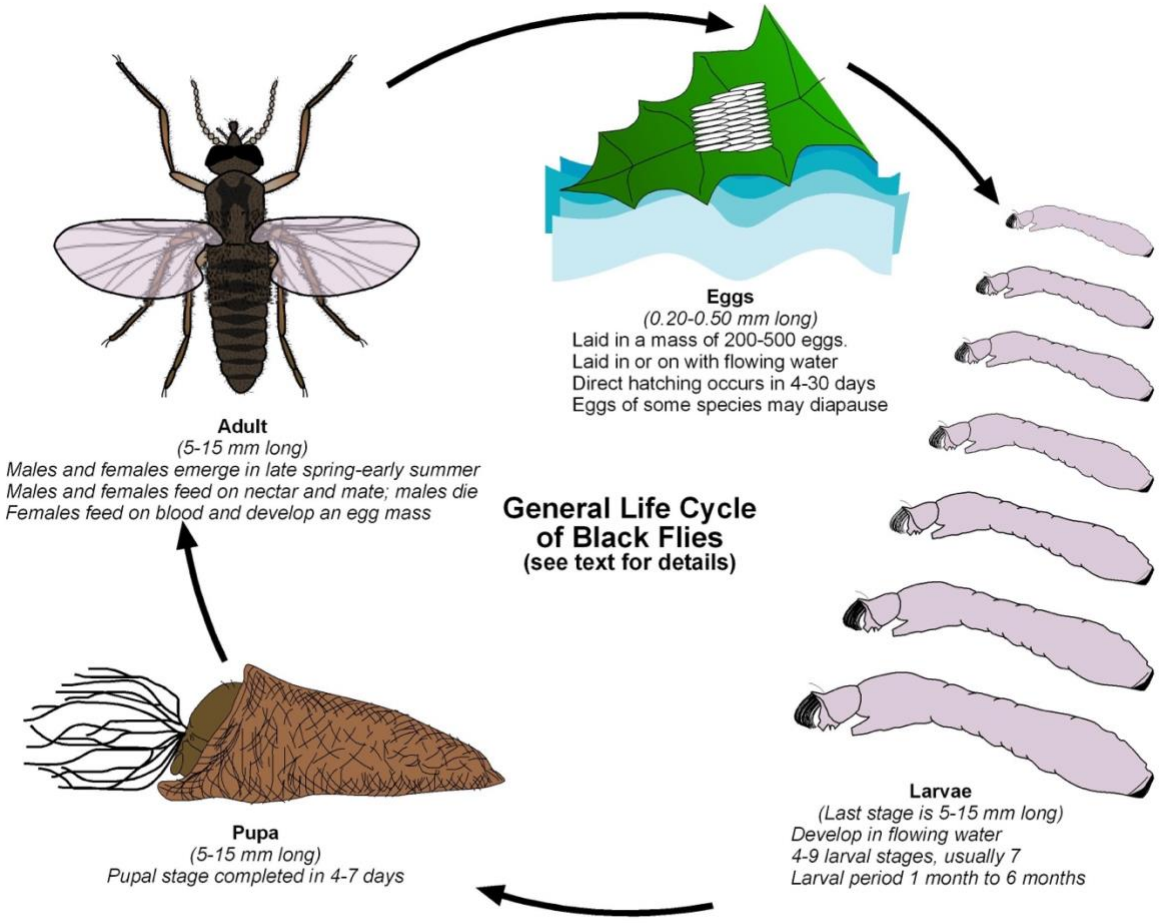


Figure 2 General life cycle of black flies.

(Illustration by: Scott Charlesworth, Purdue University, based in part on Peterson, B.V., IN: Manual of Nearctic Diptera, Vol.1)

Onchocerciasis is referred to as river blindness as the black fly vector thrives and breeds in fast flowing or turbulent rivers. Therefore, those who work near rivers are at high risk of the disease as suggested by previous studies in Guatemala (18,19).

Symptoms of the disease range from severe itching, disfiguration of the skin to some form of eye impairments and finally to permanent or irreversible blindness (20). While onchocerciasis is endemic in South America and the Yemen, in Africa more than 120 million are said to be at risk of onchocerciasis, and around 26 million are infected so far (21). Among these infected persons about 4 million of them have skin related onchodermatitis and more than 265,000 of these infected people are blind (5,22). Another comorbidity associated with onchocerciasis is epilepsy. Fodjo and colleagues explored the relationship between epilepsy and onchocerciasis in a meta-analysis. They pooled data from West African based cross-sectional studies suggesting that high burden of onchocerciasis and short control procedures were associated with epilepsy (23).

Furthermore, onchocerciasis has psychological consequences and has been found to cause serious disabilities, stigmatization, social exclusion, and discrimination (8,24). Qualitative focus group discussions by Okoye and Onwuliri in the Northeastern parts of Nigeria found that participants with onchocerciasis feared social isolation linked to their illness (25).

The literature review below elaborates on various focal points for onchocerciasis and its control and why there is a need for a systematic review focusing on this disease.

1.2 Literature Review

1.2.1 Epidemiology of Onchocerciasis in Sub-Saharan Africa.

As far back as 1987, a prevalence study was conducted in Kwara State, Nigeria to estimate the prevalence of onchocerciasis. This household survey suggested that Kwara was experiencing a moderate burden of onchocerciasis. Prevalence (estimated at 54.6%) was found to be higher in adults than in children and in males compared to females. Farmers were considered a high-risk occupational group given proximity to black fly breeding sites. Symptoms in this sample included blindness and elephantiasis which suggested that the condition had been endemic for some time. Some recent epidemiological studies were published between 2020 and 2022 (26).

According to the WHO in 2022, a disproportionate amount (i.e., 99%) of people infected with onchocerciasis live in 31 African countries mainly in the SSA region. These include Nigeria, Ethiopia, Cameroon, Malawi Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Malawi, Mali, Tanzania (27). This disproportionate burden was confirmed by a geospatial analysis by Schmidt and colleagues (28). Figure 2 below presents the global burden of onchocerciasis.

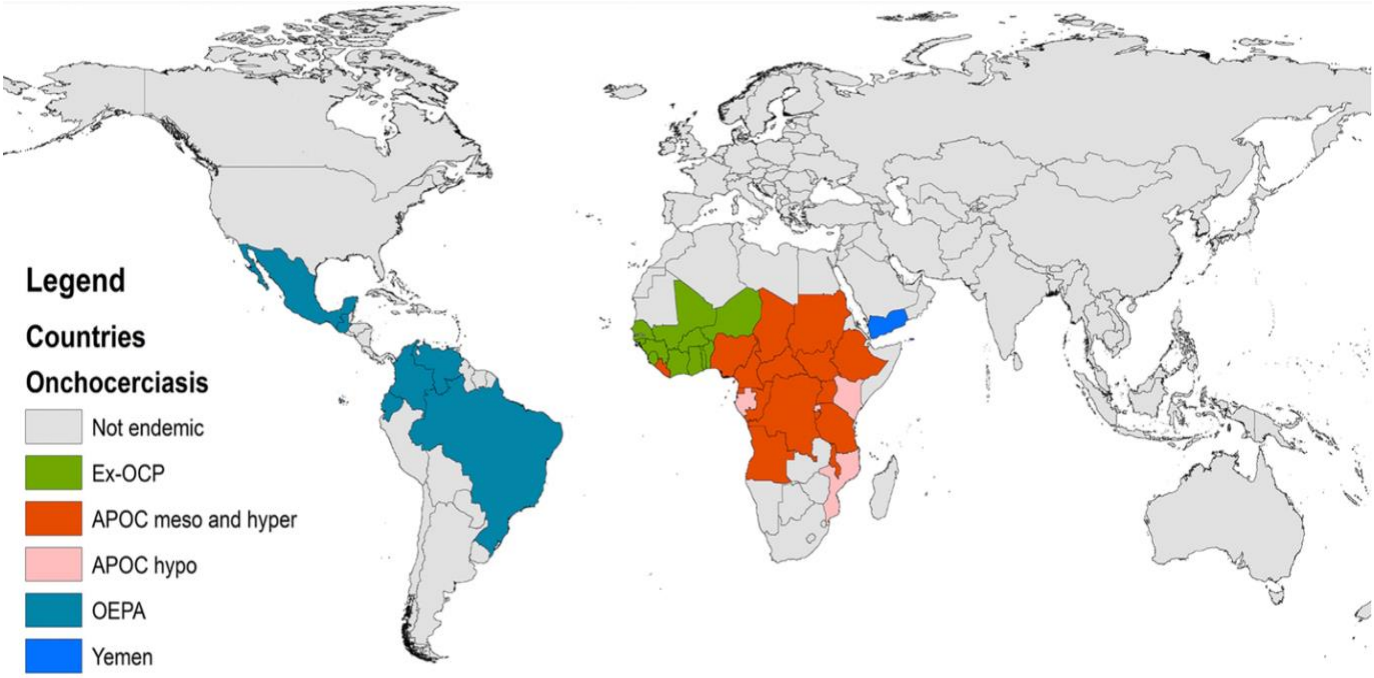


Figure 3 Map of the burden of onchocerciasis.

(Source : Elhassan E, Zhang Y, Richards F et al.) (29)

1.2.2 Onchocerciasis Control and Elimination

The World Health Organization (WHO) defines the elimination of a specific pathogen or disease as the complete reduction of new infections caused by that particular pathogen in a clearly defined geographic region, accompanied by a minimal risk of reinfection. Onchocerciasis control is defined in line with a public health control paradigm for all NTDs i.e., the reduction in the burden, incidence, severity of disease, morbidity and/or mortality of disease (17).

Several studies have reported on vector control, nodule removal and mass drug administration with ivermectin as intervention strategies for onchocerciasis since the start of the onchocerciasis

Control Program (OCP) in 1974. The Onchocerciasis Control Program was a large-scale public health initiative established to combat onchocerciasis, which was implemented in 11 countries in west Africa within the Sahel region (31). These strategies are currently employed by WHO AFRO states and many studies examining their efficacy have been conducted in the SSA region (32–34). Uganda was one of the pioneering nations to act against onchocerciasis transmission by using chemicals to control the *Simulium* species, which is the vector for the disease. Effective control campaigns were carried out to target both *Simulium neavei s.s.* and *Simulium damnosum sensu lato* in the Victoria Nile and Budongo areas. These efforts proved to be remarkably successful, leading to a reduction in the problem of insect bites and allowing for increased utilization of land in these regions of the country (35).

Vector control is an umbrella term for several interventions including aerial larviciding where helicopters are used to spray breeding sites with a chemical substance called temephos or ground larviciding that involves the application of larvicides/chemical substance directly to non-extensive larval habitats on the ground. There were no effective and safe anti-parasitic agents for human use at the time (36). Larvicides were used on the breeding sites (i.e., fast flowing rivers) for a period of 14 years. Furthermore, Benjamin Jacob and colleagues employed a community-based vector control method known as "Slash and Clear" to reduce *Simulium sirbanum* transmission in Maridi, South Sudan, where community members were mobilised to cut down trailing vegetations along fast flowing rivers which usually serves as ideal habitats/attachment sites for black flies (34). Boatin and colleagues reported that people who were already infected with the disease could not benefit from this intervention because the intervention could only prevent the spread of the disease but not useful to treat infected persons (37).

However, when the African Programme for Onchocerciasis Control (APOC) began its operation in 1995, ivermectin was introduced in 16 countries. Infact the aim of the APOC was to provide a sustainable ivermectin programme for onchocerciasis (38). When ivermectin was combined with larviciding, there was direct positive impact on already infected persons as well as reduced transmission rate of the disease (39)(40)(41–44)(45).

In areas of high vector densities, mathematical models predicted by Wilma and colleagues suggests that ivermectin being used alone is insufficient to completely interrupt transmission and control the spread of the disease (46). In addition, recent data from field studies conducted by Moses et al in Cameroon and Uganda showed that ivermectin MDA has been ineffective in eliminating or halting the transmission of onchocerciasis after 15 (in Cameroon) and 18 years (in Uganda) (47,48).

The co-endemicity of *Loa loa* with *onchocerca volvulus* in most part of Africa also poses a significant challenge to mass drug administration of ivermectin. Loiasis is another disease caused by the *Simulium* by transmitting the *Loa loa* parasite. According to a study conducted by Twum-Danso et al, there are incidence of severe adverse effects resulting from use of ivermectin in people with high parasitemia levels of *Loa loa* (49). Another study reported that effective control of onchocerciasis has been achieved using larvicides on the breeding sites and supplemented by mass drug administration of ivermectin. This has brought about notable socioeconomic improvement including agricultural productivity and practices due to back-migration/relocation of people back to fertile and fallow areas free of the vectors and the disease (36).

1.2.4 Approaches in Controlling Vectors of Onchocerciasis

According to a study, when the Onchocerciasis Control Program (OCP) started in 1974 the use of insecticides on breeding sites was the choice of action in the control of the disease. This was either through aerial or ground larviciding using insecticides (36). Wu and colleagues stated in a study analyzing the predicted prevalence of onchocerciasis infections (i.e., a prediction using a host-parasite model) versus the observed prevalence of the disease after 14 years of vector control. The results suggested that the prevalence of onchocerciasis infections declined to almost zero in all villages where the Onchocerciasis Control Program vector control programs were being implemented, such that they even considered stopping the use of larvicides (50).

Over the years, vector control has proved to be an effective approach to tackling the spread of the onchocerciasis due to the lifespan and characteristics of the parasite. Furthermore, another study also reported that vector control was significant in controlling transmission of the disease in many regions, indicating why vector control should still be considered as an effective strategy for the control of the disease in endemic regions (36).

1.2.5 Factors Associated with Vector Control of Onchocerciasis

Vector control has been successfully used in combating the spread of onchocerciasis in many areas in Africa and in the Americas. A range of potential limiting factors have been identified, challenging the upscale of this type of intervention globally. Cost of implementing the vector control programs and diversity of the vectors in different areas are some of the biggest challenges to the use of vector control globally (51). Other vector specific properties such as resistance to larvicides and the temporary recolonization by migrating vectors have also been identified as potential barriers (52–54). In addition, the adverse effects of larvicides on other organisms in the

environment and the in-migration of infected persons from other areas were discussed by Hougard et al as important factors to be considered when deciding to use vector control (55). The impact of the chemicals used as larvicide were found to be deleterious to fishes, other insects, and beneficial organisms as well as the source of water and vegetation (56–59).

1.3 Problem Statement

The Sub-Saharan African region has an excessive burden of onchocerciasis, with more than 99% of infected persons living in this region. This in turn has resulted in significant financial losses and costs in direct health costs, as well as loss in productivity, reduced educational attainment and resultantly makes families and communities remain in the vicious cycle of poverty (60). Despite their adverse health and economic impact, NTDs are mostly ignored and not adequately prioritized in the global health policy agenda like other diseases because they afflict the world's poorest and most vulnerable populations (61). The current major strategy to control onchocerciasis is the community-directed treatment with ivermectin through mass drug administration (MDA). This requires minimum coverage of 80% as recommended by WHO (20), ivermectin use is supplemented by vector control in some settings. However, it is estimated that 2.5 million DALYs were lost annually on account of onchocerciasis before the onset of mass drug administration (1990), this figure declined to 1.4 million in 2020, and it is projected that further decline will need to be achieved to 691 thousand by 2030 (62). Factors that are linked to the sub-optimal control of onchocerciasis are not fully understood. To my knowledge and from the extensive literature review conducted above there is no synthesis of studies examining vector control for onchocerciasis.

1.4 Justification

Models indicate that in circumstances with high annual biting rates, vector abundance must be considered because ivermectin use might not be effective and sufficient in the long run to achieve the goal of elimination alone (63,64). Other challenges facing the elimination efforts of onchocerciasis in Africa include high blackfly vector densities in rural areas, the co-endemicity with the eyeworm *loa loa*, the relatively long-life span of the adult worms of *onchocerca volvulus*

(approximately 14 years). Because of this and the severe anaphylactic reactions (mazotti) linked to the abrupt death of mature worms in the human host, it is difficult to eliminate the disease in one go. This makes it even more challenging to deal with (49,65,66). Therefore, there is a need for an alternative treatment strategies like local vector control that is economical, environmentally safe, and suitable for much of rural Africa as a complement to mass drug administration. However, there are still many uncertainties regarding "where, when, how frequently, for how long and how vector control should be implemented". Thus, the findings from this study will provide synthesis of evidence on the use of vector control as a strategy and factors (barriers and facilitators) associated with the use of vector control in the fight against onchocerciasis in Sub-Saharan Africa. The results will be disseminated and used to support policy and advocacy, resource mobilization and enhance human resource capacity building to deliver integrated strategies within health systems in the fight against onchocerciasis and other NTDs in Africa.

1.5 Research Question

What are the factors that are associated with vector control for onchocerciasis in Sub-Saharan Africa as evidenced from a synthesis of the literature?

1.6 Aim

To synthesize and review studies that examine factors that are associated with vector control for onchocerciasis in Sub-Saharan Africa.

1.7 Objective

To examine the factors associated with vector control in the fight against onchocerciasis in Sub-Saharan Africa as evidenced by synthesis of the literature.

2.0 METHODOLOGY

2.1 Study design

This systematic review follows the reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (67). The systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 28 November 2022 (with the registration number CRD42022376792).

2.2 Study Area

Africa is the second largest continent in the world and is located within the boundaries of the red sea on the north-east end, the Indian ocean on the east side, the Mediterranean Sea on the north and the Atlantic Ocean on the western front (68). The Sub-Saharan African region typically consists of all income level countries (i.e., from low, lower-middle, upper-middle- and high-income countries (69,70). Sub-Saharan Africa is a diverse region characterized by distinct climate patterns, varied vegetation types, and a range of economic activities. In terms of economic activity, countries in the region have economies that rely on sectors such as agriculture, mining, manufacturing, and services. Agriculture is particularly important and takes the center stage as the largest economic activity, with subsistence farming and cash crop production playing a significant role (70). The climate in Sub-Saharan Africa varies widely, encompassing arid and semi-arid regions, savannas, tropical rainforests, and highland areas. The vegetation in the region includes the Sahara Desert, the Sahel region, vast savannas, equatorial rainforests, coastal mangroves, mountainous forests, and wetlands. These different vegetation zones contribute to the region's rich biodiversity. Additionally, the region is rich in mineral resources, and there is growing focus on developing sectors like renewable energy, tourism, and information technology.

2.3 Inclusion and Exclusion Criteria

This review included a synthesis of studies reporting onchocerciasis control using vector control in Sub-Saharan Africa, and the factors associated with vector control. Vector control was defined as any intervention describing methods focused on eradicating the insect '*Simulium specie*' (i.e., black fly) responsible for transmitting onchocerciasis, through habitat or environmental, chemical, or biological methods.

Selected studies were observational and experimental designs of vector control which were peer reviewed and published in peer reviewed journals from the year 2000 till 2023. The rationale behind including both types of study designs was based on the context of vector control programs. The preliminary searches found that some studies evaluated vector control programs through a observational studies, while the majority were quasi-experimental study designs. The observational studies identified important factors which affect various vector control methods. This chosen date range aligns with the need to provide a comprehensive and current overview of factors associated with vector control for onchocerciasis. It ensures the inclusion of the latest research, addresses emerging challenges, and contributes to the ongoing efforts to reduce the burden of this neglected tropical disease.

On the other hand, studies reporting other NTD treatments without onchocerciasis control and other communicable and non-communicable diseases were excluded from this review. I also excluded case reports, conference/poster presentations, commentaries, review articles, case studies and systematic reviews. Studies reported in other languages aside English were excluded from this review. This decision to exclude studies reported in languages other than English is justified by the need for rigorous quality control, the constraints of language proficiency, and the efficient allocation of resources. While it does limit the scope of the review to some extent, it is a practical

approach to ensure the review's accuracy and overall effectiveness. (See table 1 below presenting the full PICOT table whereas table 2 shows the inclusion and exclusion criteria).

Table 1: PICOST Table

P	**Population**	Blackflies in Sub-Saharan African countries
I	**Intervention**	Vector control methods
C	**Comparator**	N/A
O	**Outcome**	Vector control (observed in the control of onchocerciasis/number of disease cases as well as number of bites)
S	**Studies**	Observational and experimental studies.
T	**Timeline**	2000-2022

Table 2 Table presenting inclusion and exclusion criteria.

Criteria	**Inclusion**	**Exclusion**
Time period	1st January 2000 – 31st March 2023	Before 1st January, 2000
Language	English	Non- English
Type of studies	Peer reviewed, experimental and cross-sectional.	Case reports, conference/poster presentations, reviews (scoping/systematic/narrative), case studies
Study area/setting	Africa, sub–Saharan Africa	Outside Africa

2.4 Search Strategy

Multiple systematic searches of the following databases were conducted by the researcher: Cochrane, PubMed, Web of Science, and Scopus. We employed a broad systematic approach through the inclusion of all possible synonyms and abbreviations for the terms of interest, including 'MeSH' and 'EmTree' terms. These keywords combination we used were "onchocerciasis" OR "control", "onchocerciasis" AND "elimination", "onchocerciasis" AND "vector control", "river blindness", "*onchocerca volvulus*", "*simulium sirbanum",* "*simulium damnosun*", "factors" OR "determinants". The search strategy was refined continuously by rearranging the search terms and employing different permutations. (The search strategies for some the databases are in Appendix - 2)

2.5 Data Management

Rayyan, (rayyan.ai) a web-based software was used for study selection and organizing the yield from the search above, as well as to remove duplicates. Articles selection was carried out following the PRISMA guidelines (67). Title and Abstract screening were completed initially using the inclusion and exclusion criteria, and ineligible studies were taken out. This was followed by screening full text of relevant literatures to assess their eligibility. The screening process was conducted by two independent reviewers (both candidates for the Master of Science in Epidemiology) for consistency, and a third reviewer was involved to settle any disagreements between them (71).

2.6 Data Extraction and Analysis

After screening and reading of full text articles, the data were extracted from the result section of the selected papers into a worksheet on Microsoft Excel, and this was conducted in duplicate. Neither “vector control methods” or “factors” were prespecified. The relevant headings were title and year of publications, authors’ names, study design, information on the intervention such as the geographic coverage, the vector control method used, and the factors associated with those methods (71).

We conducted a narrative synthesis of the evidence extracted following guidelines outlined in the "Guidance on the Conduct of Narrative Synthesis in Systematic Reviews" by Popay, J. et al (72), and those used in other similar studies (73). This approach allowed us to organize and interpret the diverse findings from the selected studies, providing a nuanced understanding of the collective evidence and contributing to the robustness and coherence of our systematic review. The narrative synthesis included an iterative process of reading through the selected papers and intermittently discussing the data with my supervisors.

2.7 Quality Appraisal and Assessing the of ‘risk of bias.

The Joanna Briggs Institute (JBI) critical appraisal tool for systematic review of quasi-experimental and analytical cross-sectional studies (74) were used to assess methodological quality and the quality of evidence from various studies included in the review. The quality appraisal was conducted by two independent reviewers (both candidates for the Master of Science in epidemiology and vaccinology respectively). In the event of disagreement, a third reviewer was called in to resolve (75).

3.0 Results

3.1 Literature Search and Screening

The search for relevant literature was conducted on four online databases, which yielded 343 records. After removing 122 duplicates, 221 papers were screened based on their titles and abstracts, resulting in 35 reports after the exclusion of 186 records. The search was further extended by identifying 9 additional papers through reference mining. This reference mining involves systematically analyzing the references cited in a particular publication or across a body of literature to identify other related studies of interest. From a total of 44 full-text articles screened for eligibility, 26 were excluded because they focused on different hosts, were of the wrong study designs, or had inappropriate designs. (See table of excluded and the justification for their exclusion in appendix 6). Ultimately, 18 studies met the inclusion criteria and are listed in Table 2. The results of the search strategy are presented in the PRISMA diagram in Figure 3 below to provide a clear overview.

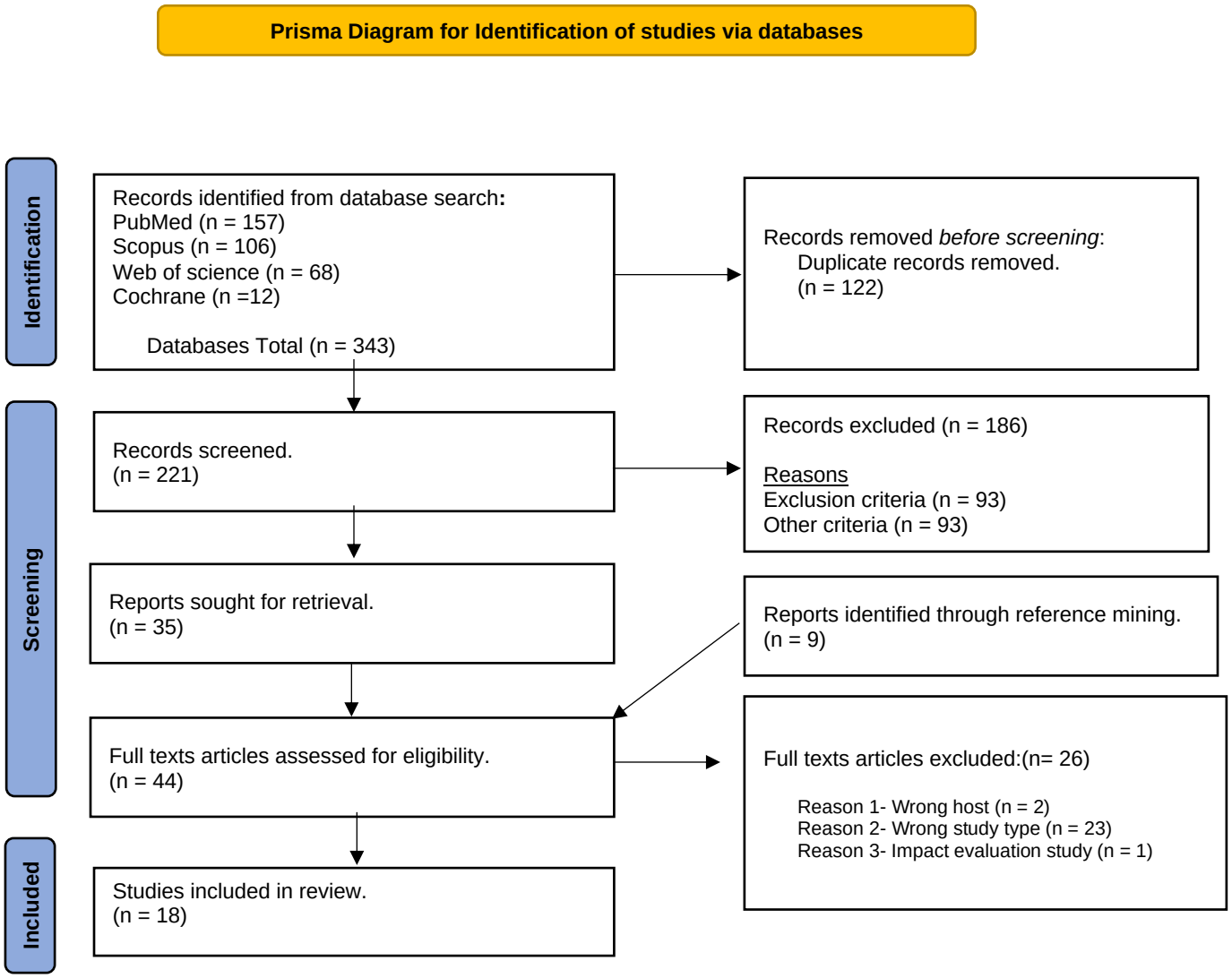


Figure 4 PRISMA flow diagram for the search strategy.

Table 3: Data extraction table presenting included studies' characteristics.

Author/Country/ Year of Publication/Reference	**Study Design**	**Summary of Findings**	**Factors Identified**
B. G. Jacob Et Al, Uganda 2018 (34)	Quasi-experimental	Slash and Clear resulted in 89–99% declines in vector biting rates. The effect lasted up to 120 days post intervention.	Re-colonization of blackflies after treatment of breeding sites.
A.K. Kalinga Et Al, Tanzania 2007 (53)	Quasi-experimental	standard diagnostic dose of 1.25mg/l attained a mortality rate of 100%. The LC50 was from 0.129 – 0.34mg/l (95% CI, P<0.05) After two years of intermittent treatment with temephos, larval mortality rate of 100% was 1.25mg/l	Blackfly Vector susceptibility to larvicides (innate or acquired resistance due to exposure to agricultural insecticides). Incomplete vector elimination Cross migration/re-colonization of treated breeding sites by new or residual. Populations migrating from nearby breeding areas.

Author/Country/ Year of Publication/Reference	Study Design	Summary of Findings	Factors Identified
D. Loum Et. Al, Uganda 2019 (76)	Quasi-experimental	The mean fly collections per trap is 4-fold to 26-fold greater than HLC Deployment of the traps reduced the biting rate in classes by 91%. At the farm fields, each optimized trap collected on average 17 times more than the HLC. The optimization process resulted in a dramatic improvement in the performance of the EWT."	Trap locations- inconsistent with effectiveness. Use of baits and types of baits. Political instability. Difference in species No availability of trap design materials.
R. Ekanya Et Al, Cameroun 2022 (54)	Quasi-experimental	A mortality of 100% was recorded at concentrations between 0.5 and 0.1 mg/l. As the concentration of temephos decreased, mortality of larvae also decreased.	Ground larviciding with temephos was facilitated with the fact that the larvae is susceptible to temephos and this temephos was found not to be harmful to other aquatic fauna. The availability of fast-flowing rivers in this basin contributes to the large numbers of black files necessary for high transmission which may further require more larvicide that may end up harming the non-target aquatic fauna.
R. M. Young Et Al, Burkina Faso 2015 (77)	Quasi-experimental	29 compounds were common to all three individuals. Several short chain carboxylic acids and aliphatic alcohols were stimulatory to *S. damnosum s.l.* and *S. ochraceum s.l.* respectively.	Technical and entomological capacity, variation among species of vector black flies.

Author/Country/ Year of Publication/Reference	Study Design	Summary of Findings	Factors Identified
I. M. A. Zarroug Et Al., Sudan 2019 (78).	Quasi-experimental	The dam complex has produced a positive effect by reducing the breeding sites of black flies in the area. Breeding sites of black flies were reduced due to construction of dams.	Dams alter the pattern of disease transmission, causing issues with public health.
B. K. Olkeba Et Al, Ethiopia 2022 (79)	Cross-sectional	Important drivers of the blackfly population include Altitude, Electrical conductivity, Hardness and Depth of water, Turbidity, Alkalinity	Knowledge of blackfly's ecological preference (e.g., Simulium damnosum larvae more likely present in habitats near shrub). Biotic factors (like predation and competition).
I. Routledge Et Al, Ghana 2018 (80)	Quasi-experimental	The estimated efficacy of large-scale aerial larviciding in the savannah was greater than that of ground-based larviciding in the forest. Larviciding is more likely to succeed in areas with lower water temperatures and where blackfly species have longer gonotrophic cycles. At 93% larvicidal efficacy x 10 consecutive weekly larvicidal treatments would reduce DBRs by 96%. At 70% efficacy x 10 weekly applications, the DBR would decrease by 67%	Duration, frequency/interval of larviciding. River volume and flow; Temperatures; cytospecies identities, population dynamics and vector ecology. Larvicide efficacy or concentration. programmatic difficulties. Poor implementation process and inaccessible breeding sites. Seasonal feasibility of implementation, vector ecology, and the susceptibility of the aquatic stages of the local vector species

Author/Country/ Year of Publication/Reference	**Study Design**	**Summary of Findings**	**Factors Identified**
I. M. A. Zarroug, Sudan 2016 (81)	Cross-sectional	In Abu-Hamed, blackflies appeared in November- April, then declined in wet and flooding months June-July and disappeared from August to October. In the Galabat focus, blackflies appeared in July - December, then decreased in the dry months (February-June).	Black fly vector ecology, distribution and biting activity has obvious implications. Microclimate, seasonality, and proximity of breeding sites to collection sites.
S. Traoré Et Al, Equatorial Guinea 2009 (21)	Quasi-experimental	The biting catches also showed a dramatic fall. At the eight regular capture sites no biting flies were collected or seen for the following 3 years.	Accessibility to the breeding sites. Re-colonization/re-invasion of vectors. inadequately treated breeding sites due to vegetation and insufficient insecticide.
T. L. Lakwo Et Al, Uganda 2006 (38)	Quasi-experimental	After river treatment, a drastic fall mean number of flies/hours from 3 flies/h in 2001 to 0 flies/h in 2003. The annual biting rates were reduced from 14 235 flies in 2001 to only 730 flies in 2003. There was also a reduction in the number of anthropophilic *Simulium* infection and infective rates.	Lack of useful data on transmission rates and elimination efforts may have prevented a comparison on the transmission rates prior to the river treatments. Prospects of success are higher in isolated regions (since there is no repopulation of vectors after treatment).

Author/Country/ Year of Publication/Reference	Study Design	Summary of Findings	Factors Identified
S. Raimon Et Al, Sudan 2021(82)	Quasi-experimental	These monthly biting rates decreased drastically by 99% immediately after the "slash and clear" intervention. However, 2- months post-intervention, MBR spiked in all three sites. Although a rise in MBR was observed from the seventh month, it was not comparable to baseline figures.	The need to repeat the "slash and clear" intervention in the future every 7 months. Inadequate resources for costly larviciding. Lack of adequate entomological workforces. Local commitment and involvement.
R. Garms Et Al, Uganda 2009 (83)	Quasi-experimental	No immature stages were found on 494 crabs examined in January to March 1997. Vector assessment in February/March 2003 confirmed its interruption. No infested crabs have been found since then anywhere in the focus.	The concentration of the larvicide. Efficiency of the larviciding process.
G. Crosa Et Al(A), Guinea 2001 (84)	Quasi-experimental	No evidence of long-term trend in invertebrate community structures were present. There was evidence of medium-term variation for all 3 rivers and reflects seasonal changes in invertebrate densities. Low densities in results of invertebrate communities were identified after a short period.	Effect of larvicide on other biological organisms

Author/Country/ Year of Publication/Reference	Study Design	Summary of Findings	Factors Identified
G. Crosa Et Al (B), Guinea 2001 (85)	Quasi-experimental	A long-term trend is seen, but the fluctuation mainly reflects the seasonal variation of invertebrate densities. There were also seasonal, flow-related variations, showing low values during the high flow periods and high values during the dry seasons.	hydrological and seasonal conditions. The two Guinean rivers were full and fast flowing rivers that contained a lot of fish, this facilitated the evaluation of fish densities before and after the intervention to see if the larviciding was harmful.
M. D. Wilson Et Al, Ghana 2012 (86)	Quasi-experimental	The catchers who used NO MAS caught (224 flies over 11 days - mean DBP of 20.4 flies per person. The duration of complete protection (time to first bite) achieved with NO MAS was 5 h (range = 5–7 h). The estimated overall protection achieved with NO MAS was 80.8%.	Actual protection will vary based on conditions such as temperature, perspiration and water exposure, and repellency may be compromised. Occupation of users influence the duration of repellency.
T. Lakwo Et Al, Uganda 2017 (87)	Quasi-experimental	Vector control trials using temephos revealed a reduction in crab infestation from 51% in July 2003 to 1.6% in February 2004.	Environmental factors (like deforestation and agriculture have led to the temporary disappearance of freshwater crabs. Type of vector species and intensity of transmission.

Author/Country/ Year of Publication/Reference	Study Design	Summary of Findings	Factors Identified
B. G. Jacob, Uganda 2021(33)	Quasi-experimental	The biting rate was reduced by an average of 82% following the first treatment (slashing 0–1 km from a community) 21–42 days later. The bite rate was reduced by 99% overall after the second treatment (slashing 1-2 km away from the communities). Slashing the breeding sites within 0–2 km of the communities in all intervention communities decreased the mean daily biting rate to less than 1 bite/day. However, none of the intervention villages' vector populations had fully recovered by the start of the subsequent rainy season.	vector control using insecticides is expensive and ecologically detrimental. Time of the season in which the (slash and clear) intervention is being conducted. i.e., seasonal variation of rainfall Entomological capacity is an important factor Willingness of community members and community ownership of programs Timing and frequency of slash and clear treatments Very large and dangerous rivers or in areas where the breeding sites are too small to be easily targeted by slash and clear

LC50 – Lethal Concentration 50; CI – Confidence interval; HLC -Human Landing Catch; EWT – Esperanza Window Trap; DBR – Daily Biting Rates; MBR – Mean Biting Rates; NO MAS (NM) – A brand of insect repellent

3.2 Evidence Synthesis

Among the studies included in the review, there were a range of study designs. These included 16 quasi-experimental studies and 2 cross-sectional studies. Out of the studies included, the highest number were conducted in Uganda (n = 6), followed by Sudan (n = 3), Guinea (n = 3), and Ghana (n = 2). Tanzania, Cameroon, Ethiopia, and Burkina Faso each had one study included in the analysis. The number of study sites varied between three and ten for both study designs in terms of sample sizes.

The studies included in the synthesis cover various aspects of onchocerciasis control, including vector control strategies, larviciding interventions, and the evaluation of different approaches. Some of the studies included a preparatory phase before the actual study or data collection began. For example, in 2007, Kalinga and colleagues who work in 3 districts in Southwest Tanzania selected larval sampling sites from rivers known to have considerable levels of *S. damnosum* s. They were guided by a previous study by Pedersen & Maegga who in 1985 identified sites where adult flies were caught to monitor and reduce transmission of onchocerciasis in the area (53). Similarly, Lakwo and colleagues searched rivers in the Western Ugandan region of Mpamba–Nkusi for crabs carrying early stages of infection with *S. neavei s.s* (38). This assisted them with examining the extent of infection and how to proceed with larviciding. Ecological characteristics of the rivers were taken. Thereafter, the process was assisted by local fieldworkers who were able to collect information on the vectors.

In terms of vector control methods, some studies explored the effectiveness of larviciding in reducing transmission. For instance, Garms and colleagues focused on the elimination of the vector *Simulium neavei* from the Itwara onchocerciasis focus in Uganda through ground larviciding (83).

These studies demonstrated the potential of larviciding as an effective approach for controlling onchocerciasis transmission.

Other studies examined specific aspects related to vector ecology and behaviour. Loum et al. evaluated the effectiveness of the Esperanza Window Trap in reducing biting rates of *Simulium damnosum sensu lato* in Northern Uganda. This study highlighted the importance of understanding the ecological preferences and biting behaviours of vector black flies to develop targeted control methods (76) Similarly, Kebede Olkeba and colleagues investigated the habitat preference of blackflies in the Omo Gibe River basin in Ethiopia, which provided insights for onchocerciasis elimination and control efforts (79). Furthermore, a study by Zarroug in 2016 investigated seasonal variations in biting rates and the population dynamics of Simulium damnosum sensu lato, the vector of *Onchocerca volvulus*, in Sudanese foci. These studies emphasized the need to consider seasonal factors and vector ecology when implementing control strategies (81).

The synthesis also includes studies that focused on the assessment of larvicide susceptibility and the impact of larviciding on aquatic fauna. Kalinga and colleagues in 2019 examined the susceptibility of *Simulium damnosum* complex larvae to temephos in southwest Tanzania (53). In 2012, the effects of larvicide treatment on invertebrate communities in Guinean rivers was evaluated by Crosa et al, providing important insights into the potential ecological consequences of larviciding interventions (85).

Overall, the synthesis of these studies shows the significance of a comprehensive and multidimensional approach to onchocerciasis control. The studies highlight the importance of preparatory phases, the efficacy of larviciding interventions, the consideration of vector ecology and behaviour, and the potential ecological impacts of control measures. This synthesis provides

valuable insights for developing effective strategies for the elimination of onchocerciasis in different regions. The figure 5 below shows a conceptual diagram developed from this evidence synthesis.

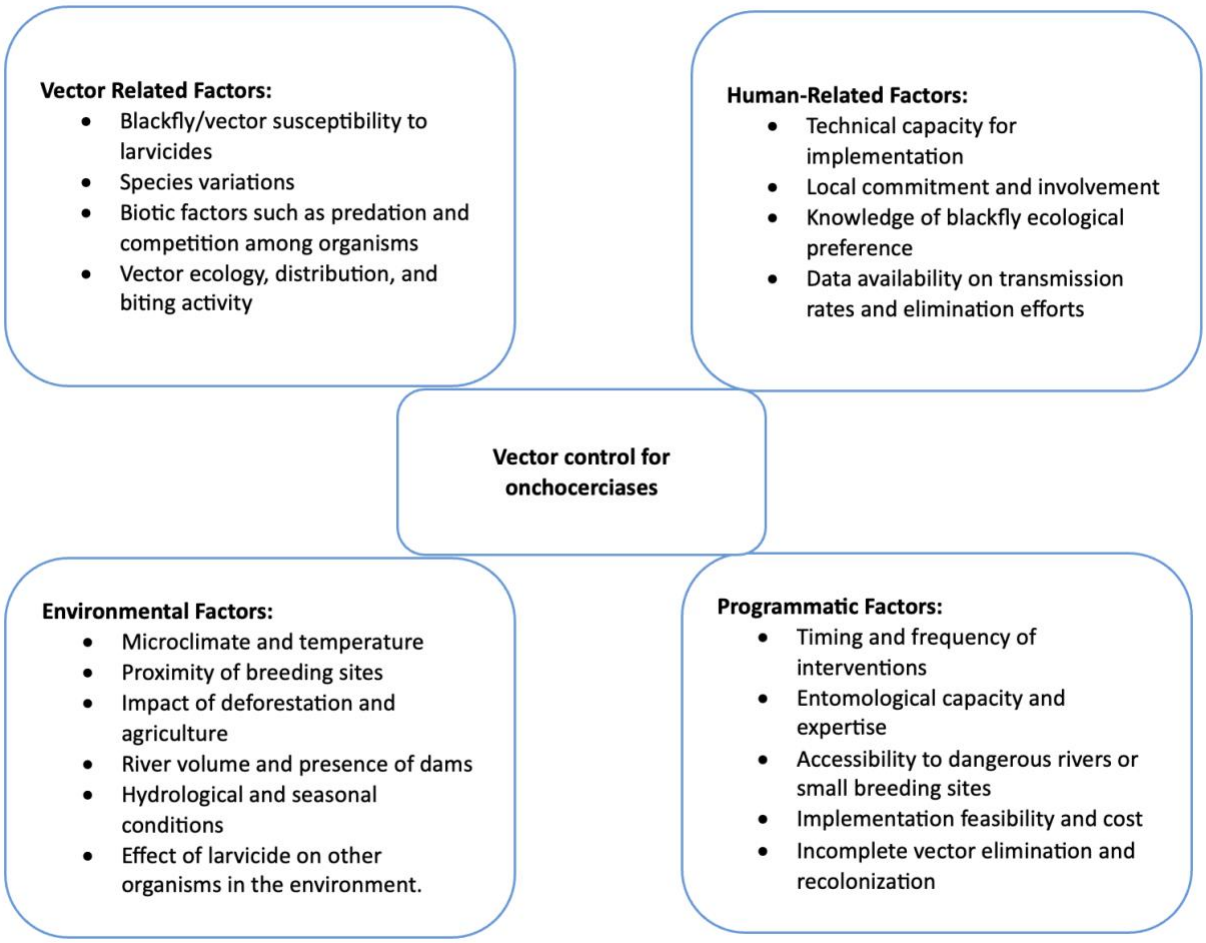


Figure 5 Conceptual Diagram

The findings from this review identified various factors which contribute to the success or failure of blackfly vector control programs. They include programmatic factors, vector ecology and biology, environmental factors, and human related factors which could either be technical

(entomology) capacity or deal with community involvement and commitment as presented in the conceptual framework above.

Programmatic factors refer to different elements essential for the successful and effective implementation of vector control programs. One of these concerns is the duration of effect after a specific type of intervention such as 'slash and clear' (33,34). If this is too short it can lead to a re-colonization of blackflies after treatment of breeding sites (21,53,88). Other program implementation factors such as difficulties faced during implementing specific vector control activities like implementation cost, could impact the availability of resources for costly larviciding programs are important determinants of the success of blackfly control programs. Additionally, the timing and frequency of interventions (80,89), larvicide concentration used during the vector control activities (21,80,83), poor implementation, and re-invasion of vectors into inadequately treated sites can limit the success of vector control programs (21,53,80,83). Wrong implementation of larviciding process can lead to incomplete vector elimination from breeding sites (53,83,84). Also, very high concentrations of larvicide could have deleterious effects on other biological organisms and thus must be taken into significant considerations (53,83,84).

The biological and ecological characteristics of blackflies vectors and their interactions with the environment have been identified by several studies as important determinants of successfully implementing vector control programs (53,54). Blackfly vector susceptibility to larvicides was mentioned in two studies as chief determinants to the success of vector control programs (53,54). The development of resistance which generally occurs innately or acquired through exposure to agricultural insecticides is a significant challenge to the use of larvicides in vector control programs (53,54). Variation among species of black flies is also considered important in vector control programs, this is because the type of species and cytospecies identities differs widely

among the *Simulium* genera (76,77,80,87). The species determines the intensity of transmission, their ecological preference, population dynamics, distribution, and biting activity (76,77,79–81,87).

Understanding these variations, knowing their habitat preference, the biting activity, and genetic mechanisms underlying insecticide resistance in blackflies is essential for developing effective strategies to combat resistance and tackle onchocerciasis. Other biological factors like natural predation and competition may have some consequences in the relative abundance of blackfly vectors (78). Another category relates to the effect of larvicide on other biological organisms and risks of ecological pollution(54,84,89). Particularly in areas with fast-flowing rivers that require higher doses of larvicide, which may end up harming non-target aquatic fauna (54).

Factors related to the environment can also have significant impact on the success or failure of vector control programs in Africa. Seasonal variation of rainfall is one important determinant of seasonal feasibility of vector control interventions(80,81,84,85,89). When the rainfall is high, it leads to large rivers bodies and fast flowing rivers which makes it difficult to reach breeding sites(54,80,89). For instance, during the wet and rainy seasons, river volume increases which makes it dangerous or difficult to target some sites. The rivers could be very large and dangerous in areas where the breeding sites are too small to be easily targeted by slash and clear or larviciding(81,88). Also, the presence of dams can change the pattern of disease transmission by altering the speed and distribution of river flow, as well as creating varying pockets of breeding sites thereby creating more public health problems (78). Isolation of regions or breeding sites such as islands can be considered an important criterion for achieving higher success. After a successful vector control program and a complete elimination is achieved, isolated areas (i.e., Bioko Island)

are protected from re-invasion of blackflies from other regions thus facilitating vector elimination (21,38).

Human related factors such as technical and entomological capacity of those involved in rolling out various vector control programs in Africa are part of the most important determinants of the success of vector control programs for blackfly (33,77,82). Entomological knowledge involves understanding blackfly's ecological preference, their distribution and biting activity, knowing this will aid in the technical planning and preparatory phase for vector control programs as these could have significant implications (33,77,79,82). For example, *Simulium damnosum* larvae more likely present in habitats near shrub (79).

On the other hand, local commitment, willingness of community members and community ownership of programs have been identified by several studies to be factors associated with vector control (33,82). Other factors like presence of vegetation and shrubs are also mentioned, for instance, deforestation and agricultural activities have led to the temporary disappearance of freshwater crabs which are intermediates hosts to the blackfly larvae (21,53,87). Political instabilities and insecurity have also hampered the sustainability and success of vector control activities in some regions (76). These challenges disrupt operations, limit funding and resources, weaken health systems, hinder surveillance, and reporting, impede community engagement, and create coordination issues.

Overall, this study reviews the complex interplay of various factors that affect the success or failure of blackfly control programs. A comprehensive understanding of these factors is essential for designing effective control strategies and achieving long-term elimination of onchocerciasis.

3.3 Quality Appraisal

Table 4 Quality Appraisal.

Study ID	Methodology/Study Design	Overall score
Benjamin G. Jacob et al, Uganda 2018 (34)	Quasi- experimental	9
A.K. Kalinga et al, Tanzania 2007 (53)	Quasi- experimental	8
Dennis Loum et. al, Uganda 2019 (76)	Quasi- experimental	7
Relindis Ekanya et al, Cameroun 2022 (54)	Quasi- experimental	4
Ryan M. Young et al, Burkina Faso 2015 (77)	Quasi- experimental	8
Isam M. A. Zarroug et al., Sudan 2019 (78).	Quasi- experimental	4
Beekam Kebede Olkeba et al, Ethiopia 2022 (79)	Cross-sectional	2
Isobel Routledge et al, Ghana 2018 (80)	Quasi- experimental	8
Isam M. A. Zarroug, Sudan 2016 (81)	Cross-sectional	5
S. Traoré et al, Equatorial Guinea 2009 (21)	Quasi- experimental	5
T. L. Lakwo et al, Uganda 2006 (38)	Quasi- experimental	7
Stephen Raimon et al, South Sudan 2021(82)	Quasi- experimental	7
R Garms et al, Uganda 2009 (83)	Quasi- experimental	5
Giuseppe Crosa et al(A), Guinea 2001 (84)	Quasi- experimental	7

Study ID	Methodology/Study Design	Overall score
Giuseppe Crosa et al (B), Guinea 2001 (85)	Quasi- experimental	6
M D Wilson et al, Ghana 2012 (86)	Quasi- experimental	9
T Lakwo et al, Uganda 2017 (87)	Quasi- experimental	6
Benjamin G. Jacob, Uganda 2021(33)	Quasi- experimental	7

The JBI quality appraisal tools for quasi-experimental and cross-sectional studies were employed for evaluating the quality of the included studies and gaining insights into the limitations of the evidence (74). This transparency in assessing study quality enhances the credibility and reliability of our research findings. In the process of quality assessment, studies scoring between 1 and 3 were categorized as having low quality, those falling within the range of 4 to 6 were classified as medium quality, and studies receiving a score of 7 or higher were deemed high-quality research. Majority of the studies received scores indicating medium to high quality. These studies demonstrated a clear definition of cause and effect, with no confusion regarding the temporal relationships. They also involved pre- and post-measurements of the outcome in a reliable way and employed appropriate statistical analysis methods. Some of these studies further strengthened their design by including control groups for comparison.

However, only one of the studies that scored low, indicating poorer quality. The absence of control groups or group comparisons in these studies made it difficult to assess the true impact of the therapies. Some studies also had issues with the definition and measurement of exposure and outcome variables, raising concerns about the validity and reliability of their findings.

Additionally, a study conducted without statistical analysis and another study lacking a valid comparison were identified as lower-quality studies.

In general, since the majority of the included studies indicated a moderate to high level of quality, the implication is that the findings from this review are somewhat reliable.

4.0 Discussion

This review sought to investigate what factors are associated with vector control for onchocerciasis in Sub-Saharan Africa. The result from the review suggested that several factors contribute to the success or failure of blackfly vector control programs in Africa, and they include programmatic factors, vector ecology and biology, environmental, and human-related factors.

The results suggested that several factors related to the implementation or roll-out of vector control programs clearly affect the success of these programs. For instance, the cost of rolling out new interventions or sustaining an existing vector control program is a big challenge in many sub-Saharan African countries (33,34). This is largely due to scarce resources for aerial or ground larviciding programs, which implies that, rural communities cannot start and sustain larviciding activities without external financial support. This finding was supported by a study conducted in Tanzania, which stated that the start-up costs for implementing a larviciding program can be high and requires international technical and financial support (90). 'Slash and clear' of trailing vegetations along fast flowing rivers are considered the cheap alternative intervention to costly larviciding programs (82). Unfortunately, 'slash and clear' are only effective for few months before the re-growth of the vegetations and thus requires regular repetition of this activity to keep the blackfly vectors away (33,34,82). There is a big risk of re-invasion of the treated sites after a short period of time when the vegetations re-grow (21). This means that sustainability of such program is demanding and depends hugely on the commitment of community members who carry out the slashing activity (33,82). Many studies have found that community commitment, motivation and ownership are major factors related to the success of health programs (33,91). This refers to the level of dedication, involvement, and active participation of community members in

health programs. It involves their willingness to invest time, resources, and efforts to support and sustain the program's objectives and activities.

Our results also reveal that poor implementation of vector control activities/programs like improper application of larvicides or use of sub-optimal concentration could lead to an incomplete elimination of vectors as well as result in the development of insecticide resistance (53). This finding also emerged with a study conducted in South Africa, at the Orange River downstream of Vanderkloof Dam where poor control of blackfly led to an enquiry which confirmed the development of resistance to temephos, one of the most popularly used larvicides in blackfly vector control programs (58). On the other hand, using excessive amount of larvicides can adversely affect other beneficial organisms within the ecosystem. This is supported by the findings from previous studies which demonstrated that, overuse of chemical larvicides leads to disruptions in eco-diversity, pollution, and extinction of aquatic organisms (56,58,59,84,85). For example, if a larvicide is used in a water body where other aquatic organisms like fish, frogs, or aquatic insects are present, it can kill them. Moreover, some larvicides can persist in the environment for a long time and accumulate in the food chain, leading to bioaccumulation and biomagnification (92). This means that higher organisms in the food chain, such as fish or birds, can accumulate the toxic substances over time, leading to toxic effects and potential harm to the health of these animals.

From the results, there was evidence that vector characteristics and their interactions with the environment also determines the success or failure of vector control programs. This is because the various species and cytospecies among the *Simulium* genera have individual genetic make-up, and behave differently in terms of their biting activities, the kind of habitat they prefer and their mechanism of resistance (76,77,79–81,87). Our findings agree with existing literatures which described various species of blackfly and the evolution of their resistance mechanisms, the

interplay of their distribution, competence, and ability to transmit the disease (93–95). Understanding the biology and ecology of blackflies is essential for developing effective vector control strategies. Blackflies have specific habitat requirements, including clean flowing water for their larvae to develop. This can have a significant implication in informing the design of interventions such as environmental management strategies that disrupt or eliminate breeding sites. This highlights the need for entomological surveillance and technical expertise.

Entomological research capacity is the expertise required for studying the role of insects in ecosystems, as well as for developing methods of pest control, disease prevention, and conservation of insect species. Insecticide resistance is a significant challenge for vector control programs, thus, technical knowledge of the vector's competence and biology such as the genetic mechanisms underlying resistance is essential for selecting appropriate interventions (96). Overall, an understanding of vector biology and ecology is crucial for the development and implementation of effective vector control programs for onchocerciasis. By considering the factors related to vector biology and ecology, interventions can be tailored to the specific characteristics of blackflies in different regions, leading to more successful outcomes. Thus, it is imperative to equip community members with entomological and technical capacity to improve their commitment and support for programs (33,82). Communities could utilize control and monitoring tools that make use of the natural attraction of hosts to enhance their ownership of vector control within their territories.

The environment also plays a big role in the success of vector control programs, it involves factors within and around the environment such as climate, rainfall, temperature, vegetation, location of breeding sites, geography, and size of rivers. High rainfall causes vast river bodies and swift river currents, making it challenging for interventions to reach breeding sites (54,80,89). For instance, as river volume rises during the wet and rainy seasons, certain small breeding sites become

inundated, stagnant pools or temporary water bodies become submerged. This aligns with other studies which discussed how high-water volumes causes inaccessibility of breeding sites and makes them difficult to target by slash and clear, which involve physically removing vegetation or debris from the breeding sites (21,34,57). Our result show that high rainfall can result in swift currents in rivers, which can disperse larvae from their original breeding sites (54,57). This is supported by several studies conducted in Nigeria which demonstrated that fast flowing rivers provide conducive environment for blackfly breeding and dispersion of larvae makes it challenging to effectively target and treat specific breeding sites using larviciding techniques (97–100). The fast-moving water can carry the larvae away before the larvicides take effect. In addition, Fast river currents can also pose safety risks for intervention teams as it may be hazardous for personnel to access breeding sites located in areas with strong currents, further complicating intervention efforts. In contrast, two studies conducted in Guatemala and Nigeria have posited that fast flowing river currents can wash away larvae, thereby reducing the fly population (101,102).

Our results also concur with studies that highlighted how the activities of humans can promote breeding of black flies. For instance, larvae and pupae of blackfly vector can use structures like concrete dams and stream channels as good growth environments (17,103). Furthermore, the presence of dams influences the pattern of disease transmission by altering the pace and distribution of river flow, as well as producing different pockets of breeding grounds (103). Some studies have examined how dams affect the dynamics of onchocerciasis transmission in African. According to certain reports (104,105), onchocerciasis is the main issue with environmental health near dams in Africa. There have been linkages made between the building of hydroelectric dams and the proliferation of black flies (106,107) and many new vector breeding sites have been discovered close to dams (108).

Other factors such as isolation of regions (i.e., islands), political instabilities and insecurity were identified in as potential determinants. From our results, after successful roll-out of a vector control program and complete elimination was achieved, an isolated island was protected from re-invasion of blackflies from other regions thus facilitating vector elimination (21,38). Political instabilities and insecurity have also hampered the sustainability and success of vector control activities in some regions (76), describing onchocerciasis control in a post-war environment, where they highlighted political unrest and instability supports the findings from this study.

Overall, this study examined the intricate interactions between many elements that determine whether blackfly management efforts are successful or unsuccessful. Understanding and addressing these factors are essential for developing effective strategies to combat blackfly vector-borne diseases and for the successful implementation of vector control programs in Africa. The presence of well-trained, motivated, and properly financed local entomologists is crucial in leading entomological operations and vector research to ensure vector control capacity.

4.1 Limitations

There are a few potential limitations to consider in this review. Firstly, the availability and quality of studies included in the analysis may have influenced the comprehensiveness and reliability of the findings. The limited number of studies addressing specific factors or interventions in certain regions may have affected the generalizability of the results. Additionally, the review focused specifically on factors associated with vector control for onchocerciasis in Sub-Saharan Africa, which may limit the applicability of the findings to other regions or vector-borne diseases. Further research is needed to explore the factors influencing vector control efforts in different geographical contexts.

Furthermore, several African countries use French as their official language, thus there is a possibility of missing data from studies conducted in those countries and reported in languages other than English. Also, limited access to unpublished data, and the disparities in data collection and reporting methods could be potential bias in this study.

5.0 CONCLUSIONS

In conclusion, this systematic review has identified several key factors associated with vector control for onchocerciasis in Sub-Saharan Africa. The success or failure of blackfly vector control programs in the region is influenced by various programmatic, environmental, vector-related, and human-related factors.

Programmatic factors such as the cost of implementing and sustaining vector control interventions pose significant challenges in many sub-Saharan African countries. Scarce resources for larviciding programs and the high start-up costs for implementing such programs highlight the need for external financial support and international technical assistance. Alternative interventions like "slash and clear" of trailing vegetations along rivers are considered cost-effective but require regular repetition and community commitment. Implementation of vector control activities, including incorrect application of larvicides or sub-optimal concentration, can lead to incomplete elimination of vectors and the development of insecticide resistance. Also, overuse of chemical larvicides can disrupt eco-diversity, cause pollution, and harm beneficial organisms within the ecosystem.

The biology and ecology of blackflies also play a crucial role in the success of vector control programs. Understanding the genetic makeup, biting activities, habitat preferences, and resistance mechanisms of different species of blackflies is essential for developing effective control

strategies. Entomological research capacity and technical expertise are equally necessary for selecting appropriate interventions and addressing insecticide resistance. The environment, including climate, rainfall, temperature, vegetation, and river characteristics, also influences the success of vector control programs. High rainfall and swift river currents during wet seasons make breeding sites inaccessible and larvae dispersion challenging. Dams and human activities, such as the construction of concrete dams, can promote blackfly breeding and alter the distribution of breeding grounds.

5.1 Recommendations

Based on the findings of this review, several recommendations can be made to enhance vector control for onchocerciasis in Sub-Saharan Africa:

1. Increased investment: Adequate financial resources should be allocated to support the program implementation and long-term viability for vector control, including larviciding interventions. International support and technical assistance should be provided to assist countries and communities with limited resources.
2. Community engagement and ownership: Community commitment, motivation, and ownership are crucial for the success of vector control programs. Community members should be equipped with entomological and technical capacity to improve their understanding and support for interventions.
3. Proper implementation: Proper application of larvicides at optimal concentrations should be ensured to avoid incomplete elimination of vectors and the development of insecticide resistance. Careful consideration should be given to the potential ecological impacts of larvicides to prevent disruptions in eco-diversity and harm to beneficial organisms.

4. Understanding vector biology: Comprehensive knowledge of blackfly species, their genetic makeup, biting activities, and habitat preferences is essential for the development and implementation of effective control strategies. Entomological research capacity and technical expertise should be strengthened to support vector control efforts.
5. Environmental management: Considering the environmental factors, such as climate, rainfall, and river characteristics, strategies that disrupt or eliminate breeding sites, taking into account the specific characteristics of blackflies in different regions, should be developed.
6. Addressing political instabilities and insecurity: Political instabilities and insecurity can hinder the sustainability and success of vector control activities. It is important to address these challenges and create a stable and secure environment for effective implementation of vector control programs. Collaboration between government agencies, international organizations, and local communities is crucial in navigating and overcoming these obstacles.
7. Strengthening surveillance and monitoring: Regular entomological surveillance should be conducted to monitor blackfly populations, their distribution, and resistance mechanisms. This will enable early detection of changes in vector behaviour and inform timely interventions. Continuous monitoring of environmental factors, such as rainfall patterns and river conditions, can also guide adaptive vector control strategies.
8. Capacity building: Building and strengthening local capacity in entomology and vector control is essential for long-term success. This includes training and equipping local entomologists with the necessary skills and resources to lead entomological operations, conduct research, and provide technical support for vector control programs. Collaboration

with academic institutions and research organizations can facilitate knowledge exchange and capacity building initiatives.

9. Integrated approach: Adopting an integrated approach that combines multiple interventions can enhance the effectiveness of vector control programs. This may include a combination of larviciding, environmental management, community engagement, and surveillance. Tailoring interventions to the specific characteristics of blackflies in different regions and considering local contexts and resources can maximize the impact of vector control efforts.

10. Research and innovation: Continued research and innovation in vector control technologies and strategies are vital for addressing emerging challenges and improving the effectiveness of interventions. This includes exploring alternative and sustainable methods, such as biological control, as well as evaluating the impact of new interventions on the environment and non-target organisms.

In summary, addressing the complex factors associated with vector control for onchocerciasis in Sub-Saharan Africa requires a multifaceted approach that considers programmatic, environmental, vector-related, and human-related aspects. By strengthening financial support, community engagement, technical expertise, and environmental management, the success of vector control programs can be improved, leading to a significant reduction in the burden of onchocerciasis in the region. However, it is important to acknowledge the potential limitations of the available evidence and further research is needed to expand our understanding and optimize vector control strategies in Africa and globally.

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APPENDIX 1: Plagiarism declaration report



PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Elakpa, Daniel Ngbede (Student number: 2606026) am a student registered for the degree of MSc Epidemiology(Implementation Sc.) in the academic year 2022.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: 12 / July, 2023

APPENDIX 2: Search Strategy

Table 5 Search Strategy for PubMed.

Search number	Query
1	(onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)
2	(onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)
3	((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa South of the Sahara"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh]
4	((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa South of the Sahara"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh]
5	((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh]
6	((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh]
7	((onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)) AND ((onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum))

8	((onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)) AND ((onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)) AND (((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa South of the Sahara"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh]) AND (((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa South of the Sahara"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh]) AND (((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh]) AND (((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh])
9	(onchocercal skin disease OR onchoderm*) AND (Vector manag* OR vector control)
10	#8 AND #9
11	#1 AND #9
12	#2 AND #9
13	#3 AND #9

Table 6 Search strategy for Web of Science

ID	Search	Hits
#1	MeSH descriptor: [undefined] explode all trees	0
#2	[**Error**]==> ((((("Onchocerciasis"[Mesh] OR "Onchocerciasis, Ocular"[Mesh]) AND "Insect Control"[Mesh]) AND "Africa South of the Sahara"[Mesh]) AND "Onchocerca volvulus"[Mesh]) AND "Simuliidae"[Mesh]	
#3	MeSH descriptor: [Onchocerciasis, Ocular] explode all trees	21
#4	MeSH descriptor: [Onchocerciasis] explode all trees	156
#5	MeSH descriptor: [Insect Control] explode all trees	268
#6	MeSH descriptor: [Africa South of the Sahara] explode all trees	7571
#7	MeSH descriptor: [Onchocerca] explode all trees	75
#8	MeSH descriptor: [Simuliidae] explode all trees	6
#9	#3 OR #4 AND #5 AND #6 AND #7 AND #8	22
#10	#3 OR #4	156
#11	#5 AND #10	1
#12	#6 AND #11	1
#13	#7 AND #12	1
#14	#8 AND #13	1
#15	((onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)):ti,ab,kw (Word variations have been searched)	1
#16	((onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)(onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)):ti,ab,kw (Word variations have been searched)	0
#17	(onchocercias* OR river blindness OR onchocercal disease) AND (Vector manag* OR vector control) AND (Sub-saharan africa OR Africa) AND onchocerca volvulus AND (simulium sirbanum OR simulium damnosum)	0
#18	onchocercal skin disease OR onchoderm	12
#19	onchocercal skin disease OR onchoderm AND #15	12

APPENDIX 3: Ethics Waiver Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Innovation)

TO: Mr DN Elakpa
School: Public Health
Department:
Division: Medical School
University

E-mail: 2606026@students.wits.ac.za

CC: Supervisor: Dr J Kagura <Juliana.Kagura@wits.ac.za>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Mr Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 24/03/2023

REF: *R14/49*

PROTOCOL NO: W-CBP-230324-01 (This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)

PROJECT TITLE: *To determine the factors associated with vector control in the fight against Onchocercal disease in Sub-Saharan Africa*

Please find attached the Ethics Waiver Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/ClearScanWaiver.wps

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Innovation)

24/03/2023

Ref: W-CBP-230324-01

TO WHOM IT MAY CONCERN

Waiver: This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical)

Investigator: Mr DN Elakpa
Student No. (if appropriate): 2606026
Staff No. (if appropriate):

Supervisor: Dr J Kagura

School: Public Health
Department: Division of Epidemiology and Biostatistics
Medical School
University

Project title: *Factors associated with vector control for Onchocerciasis in Sub-Saharan Africa (2000-2023): a systemic review*

Reason: Review of information in the public domain
No human participants will be involved in the study

CB Penny

Dr CB Penny
Chairperson: Human Research Ethics Committee (Medical)

Research Office Secretariat:
Third Floor, Phillip Tobias Building, corner of St Andrews and York Roads, Parktown, Johannesburg 2193
Postal address: Private Bag 3, Wits 2050
Tel Nos: +27 (0)11 717 1234/1252/2656/2700
Office E-mail: HREC-Medical.ResearchOffice@wits.ac.za
Website:
https://www.wits.ac.za/research/researcher-support/research-ethics/ethics-committees/

APPENDIX 4: Turnitin Originality Report

Turnitin Originality Report

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T. L. Lakwo, R. Ndyomugyenyi, A. W. Onapa, C. Twebaze. "Transmission of Onchocerca volvulus and prospects for the elimination of its vector, the blackfly Simulium neavei in the Mpamba-Nkusi focus in Western Uganda", Medical and Veterinary Entomology, 2006

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Isam M. A. Zarroug, Kamal Hashim, Arwa H. Elaagip, Abdallah M. Samy et al. "Seasonal Variation in Biting Rates of , Vector of , in Two Sudanese Foci", PLoS ONE

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9965407/

< 1% match ()
Relindis Ekanya, Elisabeth Dibando Obie, Louise Hamill, Sophie Thorogood et al. "The preparatory phase for ground larviciding implementation for chocerciasis control in the Meme River Basin in South West Cameroon: the COUNTDOWN Consortium alternative strategy implementation trial", Parasites & Vectors

< 1% match (T. Lakwo, R. Garms, J. Wamani, E.M. Tukahebwa et al. "Interruption of the transmission of Onchocerca volvulus in the Kashoya-Kitomi focus, western Uganda by long-term ivermectin treatment and elimination of the vector Simulium neavei by larviciding", Acta Tropica, 2017)
T. Lakwo, R. Garms, J. Wamani, E.M. Tukahebwa et al. "Interruption of the transmission of Onchocerca volvulus in the Kashoya-Kitomi focus, western Uganda by long-term ivermectin treatment and elimination of the vector Simulium neavei by larviciding", Acta Tropica, 2017

< 1% match (Arnauld Efon Ekangouo, Hugues Nana Djeunga, Guilhem Sempere, Joseph Kamgno, Flobert Njiokou, Paul Moundipa Fewou, Anne Geiger. "Bacteriome diversity of blackflies gut and association with Onchocerca volvulus, the causative agent of onchocerciasis in Mbam valley (Center Region, Cameroon)", Cold Spring Harbor Laboratory, 2020)
Arnauld Efon Ekangouo, Hugues Nana Djeunga, Guilhem Sempere, Joseph Kamgno, Flobert Njiokou, Paul Moundipa Fewou, Anne Geiger. "Bacteriome diversity of blackflies gut and association with Onchocerca volvulus, the causative agent of onchocerciasis in Mbam valley (Center Region, Cameroon)", Cold Spring Harbor Laboratory, 2020

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APPENDIX 5: PICOS Table

PICOST Table

P	**Population**	Blackflies in Sub-Saharan African countries
I	**Intervention**	Vector control methods
C	**Comparator**	N/A
O	**Outcome**	Vector control (observed in the control of onchocerciasis/number of disease cases as well as number of bites)
S	**Studies**	Observational and experimental studies.
T	**Timeline**	2000-2022

APPENDIX 6: Table of Excluded Studies

STUDY	REASON FOR EXCLUSION
Long-term, large-scale biomonitoring Of the unknown: Assessing the Effects of Insecticides to Control River Blindness (Onchocerciasis) in West Africa. (By Resh et al,)	No study design. No results/outcomes were reported.
Accelerating river blindness elimination by supplementing MDA with a vegetation "slash and clear" vector control strategy: a data driven modeling analysis. (By: Smith et al)	This article was a data driven modelling analysis, had no study design.
Vector control and entomological capacity for onchocerciasis elimination (by: I. Tirados et al)	A review assessing achievements and pitfalls of vector control interventions and has no study design
Longitudinal evaluation of repellent activity of Ocimum gratissimum (Labiatae) volatile oil against Simulium damnosum (By: Usip et al)	An evaluation study and did not focus on the scope of our research question.
Historical Elimination of Onchocerciasis from Victoria Nile Focus in Central Uganda Verified Using WHO Criteria (by: Katabarwa et al)	A routine program-monitoring activity (evaluating the historical effectiveness of vector control from 1974)
Factors affecting onchocerciasis transmission: lessons for infection control. (By Cheke)	This article is a discussion piece/expert commentary
Bacteriome Diversity of Blackflies' Gut and Association with Onchocerca volvulus, the Causative Agent of Onchocerciasis in Mbam Valley (Center Region, Cameroon) (by Ekangouo et al)	Focused on bacteriomes of blackflies and does not answer our research question.

Refocusing vector assessment towards the elimination of onchocerciasis from Africa: a review of the current status in selected countries. (Boakye et al)	A review, and has no primary data nor study design.
Implementation of test-and-treat with doxycycline and temephos ground larviciding as alternative strategies for accelerating onchocerciasis elimination in an area of loiasis co-endemicity: the COUNTDOWN consortium multi-disciplinary study protocol. (By Wanji et al)	A protocol for an ongoing research, thus has no primary data to answer our research question
'Slash and clear' vector control for onchocerciasis elimination and epilepsy prevention: a protocol of a cluster randomised trial in Cameroonian villages (Fodjo et al)	A protocol for an ongoing research, thus has no primary data to answer our research question
The impact of ivermectin treatment alone and when in parallel with Simulium neavei elimination on onchocerciasis in Uganda (by Ndyomugyenyi et al)	This study was comparing effectiveness and did not answer our research question
An 18S ribosomal DNA barcode for the study of Isomermis lairdi, a parasite of the blackfly Simulium damnosum s.l. (Crainey et al)	Focused on exploring a parasite's potential role in reducing blackfly vector population densities, thus not relevant to our study.
Onchocerca volvulus infection and serological prevalence, ocular onchocerciasis and parasite transmission in northern and central Togo after decades of Simulium damnosum s.l. vector control and mass drug administration of ivermectin (Kolman et al)	This was an assessment study and not relevant to our review
Onchocerciasis in West Africa after 2002: a challenge to take up. (Hougard et al)	This article was a discussion piece. Not relevant to our study/wrong type of study
Control of onchocerciasis (By Boatin et al)	This article was a discussion piece. Not relevant to our study/wrong type of study

Review of the National Program for Onchocerciasis Control in the Democratic Republic of the Congo. (By Bof et al)	This study was a review. Not relevant to our study/wrong type of study
The geographic distribution of onchocerciasis in the 20 participating countries of the African Programme for Onchocerciasis Control: (1) priority areas for ivermectin treatment. (By Noma et al)	This was a mapping study. Not relevant to our study/wrong type of study
Deforestation and the spatio-temporal distribution of savannah and forest members of the Simulium damnosum complex in southern Ghana and south-western Togo (By Wilson et al)	This was a mapping study. Not relevant to our study/wrong type of study
Potential effects of warmer worms and vectors on onchocerciasis transmission in West Africa (By Chek at al)	This was a mapping and modelling study. Not relevant to our study/wrong type of study
Population Fluctuations and Effect of Climatic Factors on the Relative Abundance of Simulium damnosum Complex (Diptera: Simuliidae) (By Oforka et al)	This study was an assessment study and not focused on vector control. Not relevant to our study/wrong type of study
Onchocerciasis Elimination: Progress and Challenges (By Lakwo et al)	This study was a review of the current status the disease. Not relevant to our study/wrong type of study
Identification of Human-Derived Attractants to Simulium damnosum Sensu Stricto in the Madi-Mid North Onchocerciasis Focus of Uganda. (By Cozart et al)	Outcomes not relevant to our study
Indices of onchocerciasis transmission by different members of the Simulium damnosum complex conflict with the paradigm of forest and savanna parasite strains. (By Chek at al)	Outcomes not relevant to our study/wrong type of study
Integrated rapid mapping of onchocerciasis and loiasis in the Democratic Republic of Congo: impact on control strategies. (By Tekle et al)	This is a mapping study and impact evaluation
Identification of the onchocerciasis vector in the Kakoi-Koda focus of the Democratic Republic of Congo. (By Post et. al)	Outcomes not relevant to our study

Onchocerciasis control in the Democratic Republic of Congo (DRC): challenges in a post-war environment. (By Bof et al)	Outcomes not relevant to our study