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# Community Directed Ivermectin Treatment Coverage in Burundi: A Spatio-Temporal Analysis for 2030 World Health Organization Road Map

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## ABSTRACT

**Background:** Integrated national programme for the control of neglected tropical diseases and blindness aims to achieve a paradigm shift from control of morbidity to interruption of transmission and ultimately elimination.

**Objective:** The aim of this study was to understand onchocerciasis epidemiology and control strategies in the context of Burundi. Specifically, the study sought to understand the coverage of Ivermectin treatment in onchocerciasis endemic zones, to assess the impact of African Programme for Onchocerciasis Control (APOC) approach on treatment coverage and forecast the therapeutic coverage to 2030 horizon in Burundi.

**Methods:** We used retrospective data collected from 2005 to 2019 in four onchocerciasis endemic provinces in Burundi. For mapping and ivermectin coverage rates comparison, we respectively used a spatial analysis and welch testing methods. After, we forecasted the therapeutic coverage using the Autoregressive Integrated Moving Average (ARIMA) model, a statistical analysis model which uses time series data to predict future trends. All analysis were done using Quantum Geographic Information System (QGIS) and the R 3.5.3 software.

**Results:** During study period, a mean population of 1,536, 392 (95% CI: 1,114 ,870-1,932 ,403) has been targeted by ivermectin treatment in all the four provinces. The ivermectin coverage rate was 77.8% (95% CI: 67.8% to 81.6%). Specifically, ivermectin coverage rates were 76.4%, 76.6% and 78.7% in Rutana, Bururi and Cibitoke - Bubanza respectively. After six years of massive drug administration under World Health Organization community guidelines launched in 2011, the coverage rates were, except the 2016 year, above 80%. Forecasts for 2030 showed that the coverage rate for treatment could increase.

**Conclusion:** This study showed that the ivermectin coverage rate significantly increased during the community-directed treatment approach period. The coverage rate should remain over 80% until 2030 in endemic regions, a strategy which should contribute to decrease the onchocerciasis prevalence and lead to onchocerciasis elimination.

## BACKGROUND

Onchocerciasis is of public health concern in 31 sub-Saharan African countries where 99% of the infected population live.[1, 2] Nigeria is one of the countries with the heaviest burdens of onchocerciasis in the world, accounting for almost one-third of the global prevalence.[3] As study on the geographic distribution of onchocerciasis in the 20 participating countries of the African Programme for Onchocerciasis Control (APOC) identified high risk areas in 18 APOC countries with 86 million of people living in high risk areas.[4] Five countries among them have a high risk area covering 48% of the total surface area, and 31% to 48% of the population.

In Burundi, many control programmes have been implemented to tackle onchorcerciasis, a parasitic disease caused by the filarial worm onchocerca volvulus.[5] In that way, large-scale and regional interventions have also been implemented in the last decades.[6] The public health problem due to onchocerciasis has been reduced through these programs.[7,8] However, onchocerciasis remains concern to the public health in sub-Saharan.

Despite control and elimination efforts through Mass

Drug Administration (MDA), vector control and recent intervention trials, the onchocerciasis still present in some areas with high prevalence.[9, 10] Therefore, the World Health Organization (WHO), International foundations, Governmental and Non-Governmental Organisations worked together to reduce the burden of onchocerciasis in endemic zones.[11, 12] They used insecticide sprays as well as bi-annual mass administration of ivermectin and a positive impact has been achieved.[13]

Before 2007, Burundi hosted two ministerial programmes related to treatment of parasitic diseases.[14] The National Programme for the Control of Transmissible Diseases and Deficiencies for malaria, worm infections, and nutrition (Lutte contre le Maladies Transmissibles et Carentielles [LMTC]) for management and the onchocerciasis control programme.[15] Supported by APOC[16] and Christian Blind Mission (CBM), the onchocerciasis control programme conducted the annual administration of ivermectin in ten endemic health districts (namely Cibitoke, Bubanza, Bururi, Rutana, Mpanda, Rumonge, Matana, Gihofi, Mabayi, and Makamba [in Kayogoro commune ]) through the Community Directed Ivermectin Treatment with Ivermectin (CDTI) strategy.[14, 17] That new treatment policy based on both ivermectin mass distribution and community health workers involvement in control and elimination of onchocerciasis have been implemented. Moreover, the most endemic health districts of Cankuzo, Mutaho and Nyanza-Lake have been targeted by serologic testing towards achieving onchocerciasis elimination.

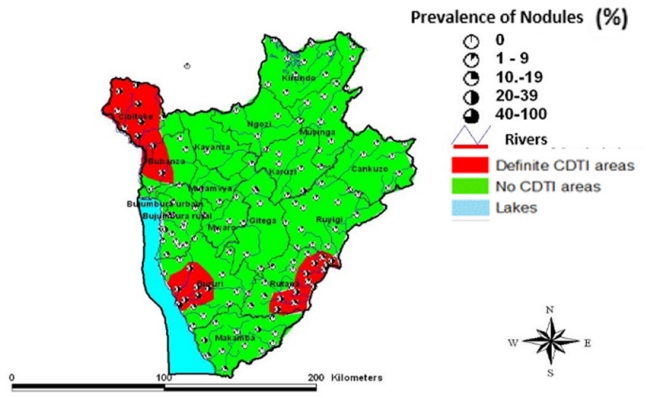
Despite the WHO efforts to end NTDs by 2030,[18-20] onchocerciasis as well as other NTDs still cause significant health and socio-economic issues.[21-23] Since 2012, the onchocerciasis control goal changed into onchocerciasis elimination goal since 2012.[24] In that context of onchocerciasis elimination, studies aiming to understand onchocerciasis' epidemiology and control strategies in Burundi are lacking, which prompts the need to conduct this study. Therefore, the main objective of this study is to assess spatio-temporal distribution of ivermectin coverage in Burundi. Specifically, this study wants to show the onchocerciasis distribution, to highlight the ivermectin coverage rate in all the four provinces, to assess the impact of APOC approach and forecast the therapeutic coverage to 2030 horizon in Burundi. Knowing these onchocerciasis aspects could support effective public health planning and facilitate policy makers to formulate plausible policies towards onchocerciasis elimination.

## MATERIALS AND METHODS

This study was conducted in three regions of Burundi which are the North-West, South-West and South-East. These regions include Cibitoke-Bubanza, Bururi and Rutana provinces. Cibitoke is located at 2° 53′ 19″ S, 29° 07′ 12″ E, Bubanza is located at 3° 05′ 00″ S, 29° 24′ 00″E. Bururi is located at 3° 57′ 00″ S, 29° 37′ 00″ E. Rutana is located at 3° 55′ 40.4″ S, 29° 59′ 31.2″E (Figure 1). They were selected because they have been targeted by Mass Drug Administration trough community health workers involvement.

These regions were classified as hypo, meso and hyper-endemic for onchocerciasis. Some of them are remotely located and are not easily accessed by road. No basic health services are provided in these regions. So, the residents walk several hours to reach the nearest health facility which provides basic health services. Those conditions explain why the treatment under community guidelines approach was adopted.

**FIGURE 1: Onchocerciasis Endemic Regions and Nodule Prevalence**




### Data Source, Inclusion and Exclusion Criteria

Data used in this study was collected by the integrated national NTDs program in collaboration with the Ministry of Health (MoH).This study was conducted in accordance with required ethical considerations.[25, 26] The MoH works closely with the national institute of public health in charge with ethical approval at the national level. The sampling of suspected individuals with onchocerciasis was based on individuals' risk, i.e. these residents of areas previously reported as meso or hyper-endemic. Every child who reached 5 years old was added in the targeted population. The untreated provinces included areas defined as hypo endemic (<40% microfilaremia or <20% microfilaremia with nodules). These areas with less than 40% of microfilaremia were therefore not targeted to receive ivermectin treatment under community guidelines and consequently not included in this study.

### Statistical Analysis

Using Quantum Geographic Information System (QGIS),[27, 28] the spatial analysis was done to map the study area and the distribution of nodule's prevalence. To compare proportions and means before and after 2012, we used the welch test in R software.[29-31] The Auto-Regressive Integrated Moving Average (ARIMA) model,[32] which is also known as the Box–Jenkins methodology was used to model the time series.[33] This methodology was based on the presence of autocorrelation within the time series.[34] The time interval was equally spaced, while the model's construction was done on stationary data (constant mean and variance over time).[34] The descriptive method was performed for plotting the onchocerciasis data through autocorrelation function (ACF) and partial autocorrelation function (PCF) to identify the order of differentiation function for both seasonal and non-seasonal effects.

The residuals of the models fitted were inspected with the ACF and PCF plots, and further verified with the Ljung-Box test. The best ARIMA model was selected for analysis according to the lowest Akaike Information Criterion (AIC). The ARIMA models were represented by the form as (p, d, q), where p is the order of auto-regression, d is the order of differencing (or integration), and q is the order of moving average for non-seasonal series. P, D, Q are their seasonal counterparts, and S is the seasonal period. If the parameters p and q or P and Q are together present in the non-seasonal or seasonal series, the model was termed as mixed ARIMA model. We estimated the parameters of ARIMA models with the "arima" function implemented in R software.[35] The model's fitted values were also graphically compared with the observed data. Both data processing and statistical analysis were done in R 3.5.3.

### Ethics Approval

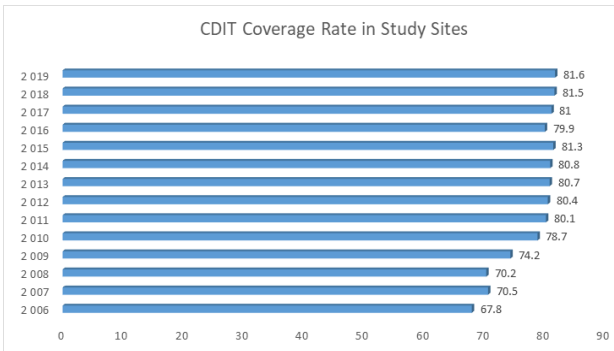
No ethics approval was required as the study used secondary data from the Integrated national NTDs control program of Burundi.All methods were carried out in accordance with the declaration of Helsinki.

## RESULTS

From 2006 to 2019, CDTI was performed in the three meso and hyper endemic regions of Burundi. Each year, a mean population of 1,536 392 (95% CI:1,114,870 to 1,932,403) have been targeted by ivermectin treatment in all the four provinces (Figure 2). In the first three years, the coverage was relatively low (<71%). The overall mean coverage rate was 77.8% (67.8 to 81.6). The lowest and the highest coverage rate were respectively observed in 2006 and 2019. During this period, the treated population doubled from 755, 870 to 1,576,933 (Figure 2). The annual treatment coverage recommended by WHO (80%) was not achieved in 2010 and in 2016.

During the two periods, i.e (2006 to 2011) and (2012 to 2019), the range ivermectin coverage rate was 76.4%, 76.6% and 78.7% in Rutana, Bururi and Cibitoke-Bubanza respectively (Table 1). The highest coverage rate (81.6%) was observed in 2019. Bururi province comes on the last position after Rutana, Cibitoke and Bubanza provinces.

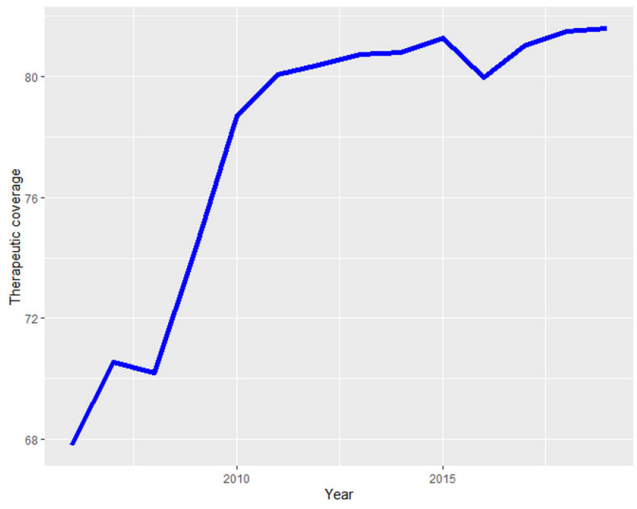
**FIGURE 2: Coverage of Community Directed Ivermectin Treatment in Study Sites**




The targeted population significantly increased during the onchocerciasis elimination project than before the project in Cibitoke and Bubanza ($p$<.001), Bururi ($p$=.001). Even if the targeted population globally increased, the variation in Rutana province was not significant ($p$=.170).

The treated population increased significantly in Rutana ($p$=.038), Bururi ($p$<.001) and Cibitoke-Bubanza ($p$<.001) during the onchocerciasis elimination project. Consequently, the coverage rate of ivermectin in Rutana ($p$=.010), in Bururi ($p$=.023) and Cibitoke-Bubanza ($p$=.019) significantly increased.

**FIGURE 3: Evolution of Ivermectin Treatment Coverage in Burundi**




More than 80% of coverage was observed after six years of massive drug administration under community guidelines (Figure 3). From 2011, except the 2016 year where this coverage rate was 79.9%, the coverage rate was increasing. The figure 3 shows the evolution of Treatment Coverage From 2006 to 2019 in Burundi.

According to the current data on onchocerciasis therapeutic coverage in Burundi, the Box-Pierce test suggested that data were not independent ($p$=.006). There was a simple autocorrelation on the first peak of the autoregressive graph and partial autocorrelation on the first peak of the moving average graph (Figure 4). So, the figures of simple and partial autocorrelation showed that the data were not independent because they tend to zero when h (the horizon) tends to infinity. It was positively correlated.

As a stationary time-series supposed to have a constant mean, variance and covariance properties, the Augmented Dickey-Fuller (ADF) showed that our data were not stationary ($p$ =.8745). It means that our data were trendy. The differentiation method which shows that the series was or not stationary was needed. The second differentiation showed that the data was stationary

(Figure 5). These results are boosted by the Phillips-Perron test with $p$=.010. The figure 5 shows the simple and partial correlation of the second Differentiation.

As we obtained stationary series without differentiation, we decided to model by the arima function. In the arima function (p, d, q), where p equals 1, d=2 and q=1, only one model can be estimated, namely arima1 (1, 2, 1).

**TABLE 4: Simple and Partial Autocorrelation of the First Differentiation**

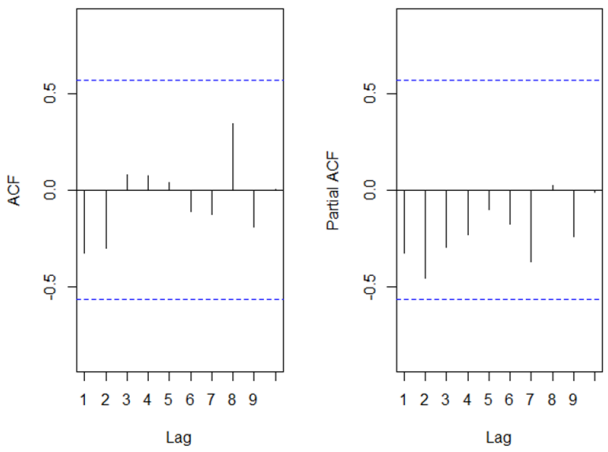
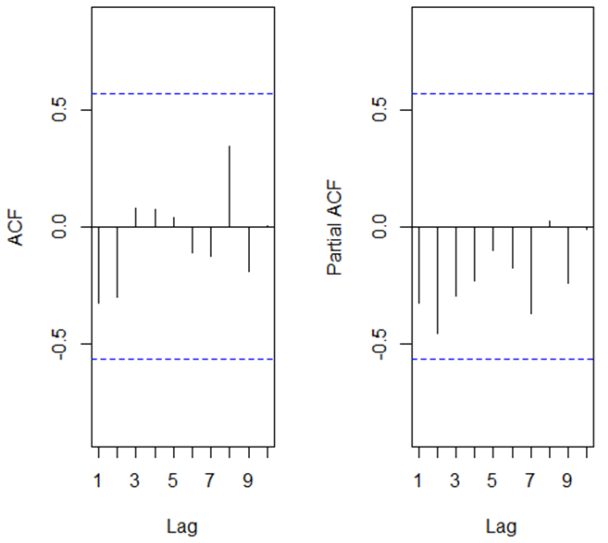



**FIGURE 5: Simple and Partial of the Second Differentiation**




The ACF plot of the residual from ARIMA (1,21) model showed that all autocorrelation are within the threshold limits, indicating that the residuals are behaving like white noise (Figure 6).

The portmanteau test returned a large $p$ value ($p$=.237), also suggesting that the residuals are white. The Box-Pierce test ($p$=.499) and Jarque Bera test ($p$=.5089) suggested respectively that residuals were not auto correlated and normally distributed. The figure 6 shows the residuals assessment and iteration of the arima model.

The figure 7 shows the trend of Ivermectin coverage from 2006 to 2021. It illustrates also the trend of Ivermectin coverage to 2030. The statistics projections on 2030 horizon shows that the coverage rate could remain high and increasing (Figure 7). From 2022 to 2030, the coverage will remain over 80%. The figure 7 shows the trend of Ivermectin coverage rate up to 2030.

The Ivermectin coverage rate is expected to remain over 80%. It will vary from 82.58 % in 2022 to 85.28% in 2030. Even if a high coverage rate is expected, more variations should also be expected near the 2030 horizon (Figure 8).

**FIGURE 6: Model's Residuals Assessment and Iteration**

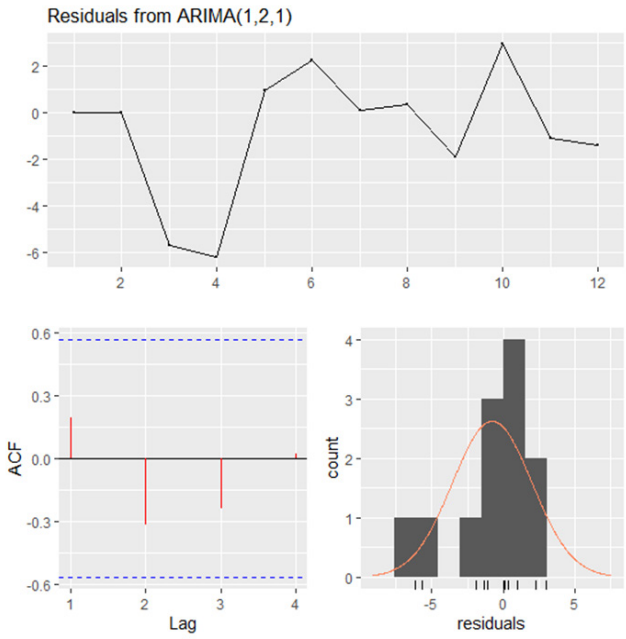


**TABLE 1: Comparison of Ivermectin Treatment Coverage Rate Distribution Before and After Implementation of APOC Programme**

| Region | CDTI indicators | Before APOC 2006-2011 | After APOC 2012-2019 | *p* |
|---|---|---|---|---|
| Cibitoke-Bubanza | Targeted population | 765 006.2 | 962005.2 | <.001 |
| | Treated population | 579246.2 | 781661.1 | <.001 |
| | Coverage rate (%) | 75.4 | 81.2 | .019 |
| Bururi | Targeted population | 244 192.2 | 385371.8 | .001 |
| | Treated population | 3094 40.1 | 176380.3 | <.001 |
| | Coverage rate (%) | 71.5 | 80.3 | .023 |
| Rutana | Targeted population | 347 580.4 | 315774.0 | .170 |
| | Treated population | 224998.7 | 280895.4 | .038 |
| | Coverage rate (%) | 70.6 | 80.8 | .010 |
| Overall | Targeted population | 1 324 972 | 1694957 | <.001 |
| | Treated population | 980625.2 | 1371996.6 | .001 |
| | Coverage rate (%) | 74.0 | 80.9 | .015 |

**FIGURE 7: Ivermectin Coverage Trend up to 2030 Horizon**

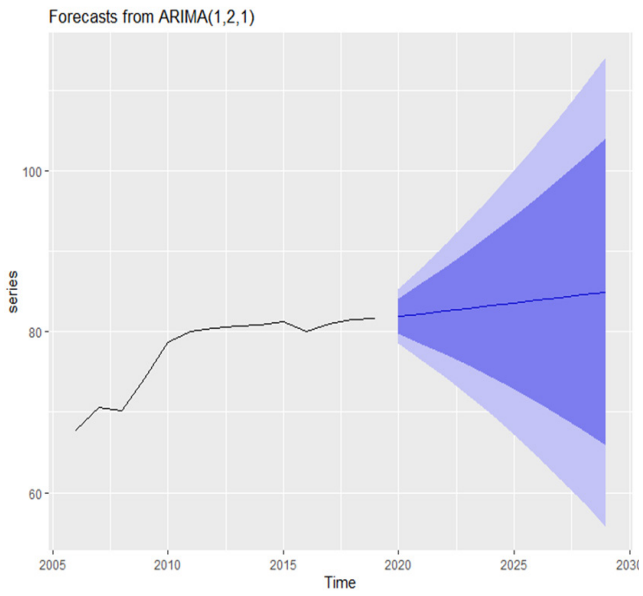
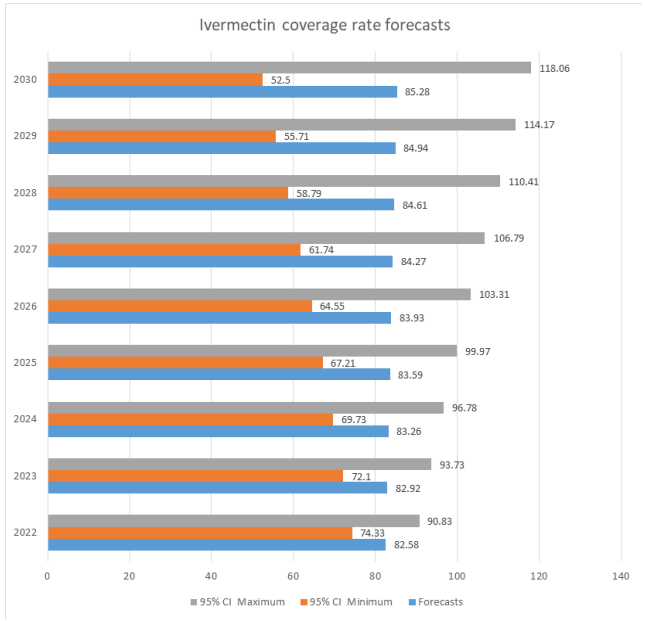



**FIGURE 8: Projection of Ivermectin Coverage Rate to 2030 Horizon**




## DISCUSSION

The current study sought to understand the spatio-temporal distribution of ivermectin coverage before and during APOC program in Burundi. Therefore, this study assessed the onchocerciasis distribution, targeted and treated population, and the coverage rates of treatment in the provinces where CDTI programme was rolled out. This study assessed also the trend of ivermectin coverage by 2030 horizon according to WHO road map to end NTDs.

According to the areas of study, the ivermectin treatment covered the meso and hyperendemic provinces. The treatment with ivermectin in people at risk of onchocerciasis infections has been the key component in the control of onchocerciasis disease in Burundi. During APOC program period, the lowest average treatment coverage under than the annual treatment coverage recommended by WHO (80%) was observed only in

in 2016.[36] This could be due to the political situation that country went through during the 2015 year. Moreover, the ivermectin coverage rates were relatively high (≥70%) in Rutana, in Bururi, and in Cibitoke-Bubanza but under the WHO's recommendation. Similar findings were reported in a recent population based cross sectional study conducted in Cameroon which showed a treatment coverage rate at an average of 74.1%.[37]

The ivermectin coverage significantly increased in the time and particularly during APOC program. Overall, it increased from 74.0% before APOC to 80.9% during APOC program. This should be due to role of health workers in onchocerciasis control through CDTI approach. Time series analysis and projections showed that the ivermectin coverage was 80% and above till 2030 year, a potential way to end onchocerciasis. Those finding are consistent with evidence from Uganda,[38] Sudan,[39] and Americas,[40] and from modelling studies[41, 42] which suggests that annual or more frequent MDA reaching at least 80% of the eligible population may halt onchocerciasis transmission. Indeed, the success observed in these settings has led stakeholders to consider the elimination of onchocerciasis across Africa.[43, 44] This is one of strategies which would probably decrease the onchocerciasis prevalence and lead to onchocerciasis elimination in Burundi.[45] Even if this coverage rate will remain high, a small increase of less than 3% will occurs the whole period while 100% would be the most perfect coverage rate. The low increase could be due to the impact of Covid-19 and /or others outbreaks on Burundian health system especially on NTD programme.[46, 47] In fact, unpredictable changes in all sectors of economies and societies are expected manifest themselves over the coming months and years.[48] Based on the projections trend, a small decrease of coverage rate is expected. These findings are in accordance with previous studies which argued that Covid-19 will also have un intended positive impact on NTDs control.[49]

The current study has strengths and weaknesses. The first strength of this study is the ability to assess trend of the onchocerciasis treatment coverage on a long period. The second strength of this study is that the study assessed the CDTI strategies (community health workers involvement) in the control and elimination of onchocerciasis. Despite these strengths, some limitations should be taken into consideration when interpreting the results and formulating policy as our study used secondary data. Caution should be taken when generalizing findings on onchocerciasis as data used were reported from all the three hyper endemic provinces without any information's in neighbour transmission provinces. Also, the lack of annual prevalence data in these areas and in close transmission zones remain the problem to know impact of CDTI program in control and elimination of onchocerciasis. The next evaluative study should be focused on prevalence of onchocerciasis in these areas and in close transmission zones.

### Policy Implications

Findings from this study feed into the Burundian context. They highlight the significant increase in ivermectin coverage for onchocerciasis control, especially during the APOC program period, demonstrating the effectiveness of community-directed treatment strategies. Despite achieving coverage rates above 80%, challenges such as political instability and potential impacts of external factors like COVID-19 on healthcare systems could hinder further progress. Projections indicate sustained high coverage rates through 2030, contributing to onchocerciasis elimination efforts. Findings from this study on Burundi highlight the importance of continued support for community-directed treatment approaches, investment in healthcare infrastructure resilience against external shocks, and ongoing surveillance to assess progress and adapt strategies accordingly.

## CONCLUSION

This study indicates a notable enhancement in the treatment coverage rate for onchocerciasis infection within the country. Projections for 2030 suggest a sustained coverage rate of approximately 80%, which holds potential for mitigating onchocerciasis prevalence and ultimately achieving its elimination. Despite resource constraints in Burundi, addressing the substantial burden of neglected tropical diseases necessitates the establishment of systems for early detection and timely treatment, particularly for high-risk populations.

At the community level, there should be intensified efforts aimed at enhancing innovative and inclusive health promotion initiatives. Simultaneously, government policies at the health system level should incorporate provisions for targeting high-risk populations to ensure early detection and tailored treatment approaches.
Such measures are crucial for ensuring the sustainability and efficacy of public health interventions directed towards combating onchocerciasis, as well as other prevalent infectious diseases.

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