Point prevalence mapping reveals hotspot for onchocerciasis transmission in the Ndikinimeki Health District (Centre Region, Cameroon)

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Research

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Abstract

Background

Ivermectin-based preventive chemotherapy is distributed annually to all at risk eligible individuals to fight onchocerciasis. Data reporting the impact of mass ivermectin administration on onchocerciasis transmission are scanty, and it is tricky to appreciate the progress towards elimination and engage adapted corrective measures. To fill that gap in the Centre Region in Cameroon, this study aimed at assessing onchocerciasis endemicity level in the Ndikinimeki Health District after almost three decades of mass treatments.

Methods

As part of a cluster-based cross-sectional survey, all volunteers aged ≥ 5 years were (i) interviewed on their compliance to ivermectin over the past five years and (ii) underwent clinical (nodule palpation and visual search for onchocercal lesions) and parasitological examinations (skin snip) for onchocerciasis.

Results

The overall *O. volvulus* prevalence was 7.0% (95% CI: 5.2–9.3), significantly higher in the communities Kiboum 1 and Kiboum 2 compared to the other communities (highest prevalence in Makénéné Town Water: 8.5%; 95% CI: 2.3–20.4) (Chi-square = 51.314; df = 11; $p = 0.0001$). The proportion of systematic non compliers was relatively high (23.3%; 95% CI: 19.9–27.1) among individuals interviewed. In the sentinel sites (Kiboum communities), river blindness prevalence decreased from 95.2% (95% CI: 88.3–98.1) to 23.7% (95% CI: 14.7–36.0) thanks to 28 years of annual ivermectin but was still meso-endemic to onchocerciasis.

Conclusions

After almost three decades of preventive chemotherapy, onchocerciasis is now hypo-endemic in the Ndikinimeki Health District. However, transmission is ongoing, with a potential hotspot near Kiboum 1 and Kiboum 2 known as first line communities (closest to breeding sites of the vector). Alternative or complementary strategies to annual ivermectin appear compulsory to accelerate the momentum towards onchocerciasis elimination.

Background

Onchocerciasis is a neglected tropical disease (NTD) affecting over 20.9 million people worldwide, of which 99% reside in Africa. Commonly known as river blindness, this disease is caused by the parasitic nematode *Onchocerca volvulus* and transmitted via the bites of female blackflies of the genus *Simulium*

during blood feeding. People most at risk of acquiring onchocerciasis are those living or working near fast flowing and well oxygenated streams or rivers conducive to blackfly breeding. River blindness is the second leading cause of blindness worldwide after trachoma [1]. This infection rarely causes death but imposes suffering, stigmatization and hardship among affected individuals and communities. The pathogenesis of the diseases is essentially due to microfilariae, adult worms usually causing no pathology or simply stimulating the development of characteristic subcutaneous nodules.

The only known effective and safe drug used for mass treatments against onchocerciasis is Ivermectin (Mectizan®). Since this drug has a limited macrofilaricidal activity [2] and adult *O. volvulus* is lifelong (lifespan > 14 years [3]), treatments must be repeated yearly for more than 15 years to break the transmission cycle. Community-directed treatment with ivermectin (CDTI) has so far remained the main control strategy to eliminate this disease. This strategy has significantly improved Ivermectin treatment coverage [4–5] and succeeded in eliminating the infection in four of the six endemic countries in Latin America (Columbia in 2013, Ecuador in 2014, Mexico in 2015 and Guatemala in 2016) [6]. Unlike Latin America, transmission of the disease has been interrupted only in limited foci in some endemic countries in Africa (Mali, Senegal and Nigeria) [7–9]. In most foci in Africa, including in Cameroon, the burden of onchocerciasis is still heavy, and the disease is persisting despite almost three decades of CDTI [10]. In order to improve current control approaches and define more pinpointed strategy, it is worth to carry out regular surveys to assess the impact of control approaches on the epidemiology of the disease. This study then aimed at investigating onchocerciasis endemicity in the Ndikinimeki Health District (HD) after almost three decades of CDTI.

Methods

Study area

The study was carried out in the Ndikinimeki Health District, consisting of six Health Areas namely Makenene, Nitoukou, Nyokon, Ndokowanen, Ndikinimeki and Boutourou. The Ndikinimeki Health District (4.76° N, 10.83° E) belongs to the Mbam and Inoubou Division of the Centre Region of Cameroon. The climate of this area is of equatorial type divided into four seasons including a long dry season (November-February), a short rainy season (March-June), a short dry season (June-August) and a long rainy season (August-November) [11]. The mean annual temperature is 22.4 °C and the average annual rainfall is 1,440 mm. The region is highly irrigated by the Inoubou, Makombé and Makénéné rivers and their various tributaries. The main activities of the inhabitants are agriculture (cocoa farming, fishing) and sand mining. The Health District has a population size of about 44,519 inhabitants based on the 2017 health population denominators [12].

Study design and participants

A cluster-based cross-sectional survey was carried out in the Ndikinimeki Health District. Clusters were selected using the Probability Proportionate to Estimate Size (PPES) strategy. Eligible individuals were both males and females, aged five years and above, who had already lived in the selected clusters for at

least five years. In each cluster, a structured questionnaire was administered to eligible participants to assess their socio-demographic information and collect their history of, and adherence to, ivermectin treatments during the five years preceding the survey. All volunteers underwent skin snipping and a clinical examination to search for *O. volvulus* microfilariae and clinical signs of onchocerciasis, respectively.

Skin biopsy examination

Two skin snips were taken with a sterile 2 mm Holth-type corneoscleral punch from the two posterior iliac crests of each participant. The skin snips were placed in two separate wells of a microtitration plate containing ~ 200 µL of normal saline (0.9%) and incubated for 24 hours at room temperature. The fluid of each well of the microtitration plate was examined for *Onchocerca* microfilariae using bright field microscopy under low magnification (40×) [13].

Clinical examination

The clinical examination consisted in nodule palpation then visual search for skin disease and anamnesis for pruritus. Nodule palpation was performed on partially disrobed participants in a closed but well-illuminated room. Attention was paid to bony prominences of the torso, iliac crests and upper trochanter of the femurs as was already described as election sites of onchocercal nodules in Africa. Participants were also questioned about pruritus and their skin visually inspected for cutaneous signs of onchocerciasis, especially depigmentation (leopard skin) and skin rashes.

Statistical analyses

All relevant data for onchocerciasis were recorded into a purpose-built Microsoft Access database and subsequently exported into PASW Statistics version 18 (SPSS Inc., Chicago, IL, USA) for statistical analyses. Microfilaridermia and clinical sign prevalence were expressed as the percentage of infected or affected individuals among the total number of individuals examined. Compliance to ivermectin was evaluated as the proportion of individuals eligible to ivermectin who actually ingested the drug. The 95% confidence interval (CI) for proportion/prevalence was calculated using the Wilson method not corrected for continuity [14]. The intensity of infection was evaluated using two metrics, the microfilarial density and the community microfilarial load (CMFL). The Microfilarial density was defined as the arithmetic mean number of microfilariae in the two skin snips (mf/ss), the sampling fluctuations being estimated using standard deviation (SD). The CMFL was computed as the geometric mean number of microfilariae per skin snip (mf/ss) among adults aged 20 years or more, using the log (x + 1) transformation to take into account zero counts [15], especially after multiple rounds of ivermectin treatments. Chi-square, Mann-Whitney and Kruskal-Wallis tests were used to compare onchocerciasis prevalence and mean microfilarial density between clusters, genders and age groups, respectively.

Results

A total of 603 individuals aged 5 to 88 years old (Median: 32; Interquartile range (IQR): 42) were examined in the six health areas of the Ndikinimeki Health District, organized into 12 clusters (communities). The sex ratio was slightly male-biased (50.9%).

Prevalence and intensity of O. volvulus infection

Of the 603 participants examined in the framework of this study, 42 (7.0%; 95% CI: 5.2–9.3) were found to be infected with *O. volvulus*. The prevalence of onchocerciasis was significantly higher in the Boutourou Health Area (21.6% (95% CI: 14.5–30.1) (Chi-square = 48.708; df = 5; $p = 0.0001$), among males (11.1%; 95% CI: 7.7–15.1) (Chi-square = 16.301; df = 1; $p = 0.0001$) and among younger adults (20–34 years old) (18.3%; 95% CI: 11.0-27.6) (Chi-square = 25.727; df = 3; $p = 0.0001$) (Table 1). At the community or cluster level, river blindness prevalence ranged between 23.7% (95% CI: 13.6–36.6), and was significantly higher in the communities Kiboum 1 (19.3%; 95% CI: 10.0-31.9) and Kiboum 2 (23.7%; 95% CI: 13.6–36.6) compared to the other communities (highest prevalence in Makénéné Town Water: 8.5%; 95% CI: 2.3–20.4) (Chi-square = 51.314; df = 11; $p = 0.0001$) (Fig. 1) (Additional file 1: Table S1).

Table 1
Prevalence of onchocerciasis in the Ndikinimeki Health District according to Health Areas, genders and age groups

Variables	No. individuals examined	No. individuals infected	% prevalence (95% CI)
Health Area			
Boutourou	116	25	21.6 (14.5–30.1)
Makénéné	160	8	5.0 (2.1–9.6)
Ndikinimeki	198	7	3.5 (1.4–7.1)
Ndokowonen	37	1	2.7 (0.0–14.2)
Nitoukou	40	0	0.0 (0.0–8.8)
Nyokon	52	1	1.9 (0.0–10.3)
Gender			
Males	307	34	11.1 (7.7–15.1)
Females	296	8	2.7 (1.2–5.3)
Age group			
5–19	217	5	2.3 (0.7–5.3)
20–34	93	17	18.3 (11.0–27.6)
35–49	109	8	7.3 (3.2–14.0)
50-over	184	12	6.5 (3.4–11.1)
Overall	**603**	**42**	**7.0 (5.2–9.3)**

No.: number of; CI: confidence interval

Likewise onchocerciasis prevalence, the overall microfilarial density was 0.557 mf/ss (SD: 3.7843 mf/ss), significantly higher in the Boutourou Health Area compared to the other Health Areas (Chi-square = 47.576; df = 5; $p = 0.0001$), among males compared to females (Mann Whitney test: U = 41645.5; $p = 0.0001$), among young adults aged 20–34 years old compared to the other age classes (Chi-square = 25.703; df = 3; $p = 0.0001$) (Table 2). The intensity of infection was also significantly higher in Kiboum 1 (1.395; SD: 8.4143) and Kiboum 2 (1.814; SD: 5.1986) communities compared to other communities (highest microfilarial density in Makénéné Town Water: 0.979; SD: 4.2643) (Chi-square = 50.490; df = 11; $p = 0.0001$). The overall CMFL in the study area was 0.168 mf/ss, significantly higher in the Kiboum 1 (0.383 mf/ss) and Kiboum 2 (0.538mf/ss) communities (Additional file 1: Table S1).

Table 2
Intensity of *Onchocerca volvulus* infection in the Ndikinimeki Health District according to Health Areas, genders and age groups

Variables	No. individuals examined	Mean microfilarial Density (mf/ss)	Standard Deviation	Min – Max	CMFL (mf/ss)
Health Area					
Boutourou	116	1.608	6.9391	0.0–63.5	0.465
Makénéné	160	0.641	4.0020	0.0–37.5	0.165
Ndikinimeki	198	0.189	1.1893	0.0–12.0	0.103
Ndokowonen	37	0.230	1.3974	0.0–8.5	0.084
Nitoukou	40	0.000	0.0000	0.0–0.0	0.000
Nyokon	52	0.019	0.1387	0.0–1.0	0.021
Gender					
Males	307	0.746	3.5845	0.0–37.5	0.266
Females	296	0.361	3.9776	0.0–63.5	0.079
Age group					
5–19	217	0.168	1.8036	0.0–25.5	-
20–34	93	1.785	7.9075	0.0–63.5	0.357
35–49	109	0.321	1.9239	0.0–18.0	0.096
50-over	184	0.535	2.9449	0.0–27.5	0.125
Overall	**603**	**0.557**	**3.7843**	**0.0–63.5**	**0.168**

No.: number of; mf/ss: microfilariae/skin snip; Min: minimum; Max: maximum; CMFL: community microfilarial load

Morbidity associated with onchocerciasis

The prevalence of onchocercal clinical signs was in general quite low and variable among Health Areas, communities (clusters), gender and age groups. Indeed, the overall prevalence of palpable nodules was 0.3% (95% CI: 0.1–1.2), ranging between 0.0% and 0.6% and the difference was not significant between Health Areas (Chi-square = 1.416; df = 5, $p = 0.923$), communities (Chi-square = 8.768; df = 11, $p = 0.643$), age classes (Chi-square = 2.892; df = 3, $p = 0.409$) and genders (Chi-square = 0.001; df = 1, $p = 1$).

The Skin depigmentation and skin rashes overall prevalence were 3.0% and 0.3%, respectively, and no significant difference ($p > 0.330$) was found across Health Areas (Chi-square = 5.762; df = 5, $p = 0.330$),

genders (Chi-square = 0.154; df = 1, $p = 0.694$), age classes (Chi-square = 1.037; df = 3, $p = 0.792$) and clusters (Chi-square = 9.015; df = 11, $p = 0.620$).

Regarding pruritus, the proportion of individuals affected was significantly higher in the Nyokon Health Area (26.9%; 95% CI: 16.8–40.3) compared to the other health areas (Chi-square = 21.925; df = 5, $p = 0.001$), the difference was also significant when considering clusters (Chi-square = 92.731; df = 11, $p < 0.0001$) and age classes (Chi-square = 18.498; df = 3, $p < 0.0001$), but the difference was not significant when considering genders (Chi-square = 1.436; df = 1, $p = 0.231$).

History and adherence to ivermectin treatment

Overall, 74.8% (95% CI: 71.2–78.1) of enrolees declared that they have swallowed ivermectin at least once during the past five years. The proportion of individuals who declared that they have ingested ivermectin every year for the past five years was 34.5% (95% CI: 30.8–38.4), similar between males (36.2%; 95% CI: 31.0-41.7) and females (32.8%; 95% CI: 27.7–38.3) (Chi-square = 0.76; df = 1, $p = 0.3833$). A significant increase in the trend of Ivermectin compliance was observed across the age groups (Chi-square = 64.08; df = 3, $p < 0.0001$), 22.6% (95% CI: 16.3–30.4) of participants aged 10–19 years old (individuals < 10 excluded), 20.4% (95% CI: 13.5–29.7) of enrolees aged 20–34 years old, 44.0% (95% CI: 35.1–53.4) of interviewees aged 35–49 years old, and 60.3% (95% CI: 53.1–67.1) of participants aged ≥ 50 years old declaring having taken Ivermectin tablets for the past five years. The proportion of systematic non compliers, that is those individuals who never ingested ivermectin tablets during the past five years, was 23.3% (95% CI: 19.9–27.1), similar between males (20.4%; 95% CI: 15.9–25.7) and females (26.3%; 95% CI: 21.3–31.9) (Chi-square = 2.5; df = 1, $p = 0.1138$). Age classes (Chi-square = 24.59; df = 3, $p < 0.0001$). Regarding age classes, a significantly higher proportion of systematic non compliers was found among individuals aged < 34 years old compared to their older counterparts (Chi-square = 64.08; df = 3, $p < 0.0001$). Indeed, 31.6% (95% CI: 24.3–39.9) of participants aged 10–19 years old (individuals < 10 excluded), 36.6% (95% CI: 27.5–46.7) of enrolees aged 20–34 years old, 15.6% (95% CI: 10.0-23.6) of interviewees aged 35–49 years old, and 15.2% (95% CI: 10.7–21.1) of participants aged ≥ 50 years old declaring having never swallowed Ivermectin tablets during the past five years.

20 years trends of onchocerciasis in the Boutourou health area

The follow up of the trends in river blindness prevalence over three decades was carried out only in the Boutourou Health Area where a sentinel site (Kiboum communities) was identified during mapping exercise and baseline data collected. A significant decrease in the prevalence of onchocerciasis was recorded, either between current findings (2019) and baseline data (1991) (Chi-square = 41.59; df = 1; $p < 0.0001$), or the first decade trend (2011) (Chi-square = 15.25; df = 1; $p < 0.0001$) (Fig. 2).

Discussion

The objective of this study was to investigate onchocerciasis endemicity in the Ndikinimeki Health District after almost three decades of CDTI and possibly assess the progress made towards the elimination of the disease. After 28 years of CDTI, the Ndikinimeki Health District changed status, moving from hyper-endemic (prevalence = 95.2%) to hypo-endemic for Onchocerciasis (prevalence = 7.0%). The intensity of infection expressed either by the microfilarial densities (at individual level) or by the CMFL (at the community level), as well as the proportion of individuals presenting clinical signs attributable to onchocerciasis were also quite low. These observations suggest that mass treatment with Ivermectin (CDTI) that have been going in this area for almost three decades have drastically reduced the burden of the disease as previously observed in Cameroon [16].

The high infection observed in males compared to females could be explained by the occupational exposure and susceptibility of individuals. Indeed, males are more involved in outdoor activities thereby exposing themselves to bites from blackflies and therefore infection. This agrees with the findings of Kamga *et al.* [17] who reported a higher prevalence of onchocerciasis in males than in females in the Yabassi Health District (Littoral Region, Cameroon). Furthermore, the high infection observed in the 20–34 years old may be due to the fact that individuals within this age group are usually the most active members in the communities and may have had higher risk of getting infected because of their involvement in outdoor activities such as farming, sand mining and fishing. In addition, because of their very active status, these individuals are usually absent during household-based direct observance mass administration of ivermectin and could therefore exhibit a low adherence to Ivermectin treatment as observed in this study. Our observations disagree with the findings by Ikpo and colleagues [18] who reported a peak prevalence of river blindness among individuals aged 41–50 years old in the Oji River Local Government Area (Enugu State, Nigeria). In fact, onchocerciasis is known to be naturally cumulative, but treatments administered during 28 years might have disrupted this relationship, thus favoring the shift in prevalence peak among individuals highly exposed and poorly compliant vis-à-vis of ivermectin MDA.

Despite the fact that preventive chemotherapies contributed to highly reduce river blindness to hypo-endemic levels (microfilaridermia prevalence 35%) in all the surveyed Health Areas and communities, the trend was still above the expected level (≤ 20% for a pretreatment endemicity ≥ 80% assuming a therapeutic coverage of 65% [19–20] in the Kiboum 1 and Kiboum 2 communities (Boutourou Health Area). This hotspot for transmission of onchocerciasis might be explained by the proximity of these clusters to fast flowing rivers where blackflies breed. This is supportive of a change in the current strategies if one expects transmission interruption of river blindness. Indeed, alternative treatment strategies have been developed by the African Programme for Onchocerciasis Control (APOC), and recently reshaped for adapted implementation purpose [21]. In the current situation with the persistence of onchocerciasis in a restricted hotspot area, implementation of multiple annual rounds of CDTI complemented with localized vector control by using for example ground larviciding might help boosting the momentum towards the elimination of onchocerciasis in the Ndikinimeki Health District, and serve as a proof of concept for strategy improvement for countrywide elimination of onchocerciasis.

Conclusions

This study has revealed that the Ndikinimeki Health District is hypo-endemic for Onchocerciasis after almost three decades of CDTI. Despite the low prevalence and intensity of the disease in the study area, a hotspot for onchocerciasis transmission was found around the communities Kiboum 1 and Kiboum 2 (Boutourou Health Area) where alternative treatment strategies might be useful to prompt the elimination of river blindness.

Abbreviations

CDTI
community-directed treatment with ivermectin
CI
confidence interval
CMFL
community microfilarial load
mf/ss
microfilariae per skin snip
OR
odds ratio
PC
preventive chemotherapy
SD
standard deviation

Declarations

Ethics approval and consent to participate

Ethical clearance was granted by the Centre Regional Ethics Committee for Human Health Research (N°667/CRERSH/2019) and Administrative authorization was granted by the Regional Delegation of Public Health and the Ndikinimeki Health District. After approval of the local administrative and traditional authorities, the objectives and schedules of the study were first explained to community leaders and to all eligible individuals. Before any procedure, informed consents were obtained from participants or their parents or guardians (for minors) who agreed to participate, under the discretion of community leaders. An individual barcode was attributed to each participant for anonymous data analysis.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Competing interest

The authors declare that they have no competing interests.

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Authors' contributions

RAA conceived the study and designed the experiments, collected field data, analyzed the data and drafted the manuscript. LS conceived the study and designed the experiments, supervised and coordinated the study and helped to draft the manuscript. NHN conceived the study and designed the experiments and helped to draft the manuscript. JB collected field data and contributed to the preparation of the manuscript. RHB collected field data and contributed to the preparation of the manuscript. HCND conceived the study and designed the experiments, supervised and coordinated the study, analyzed the data and drafted the manuscript. All authors read and approved the final manuscript. HCND and LS are guarantors of the paper.

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Figures

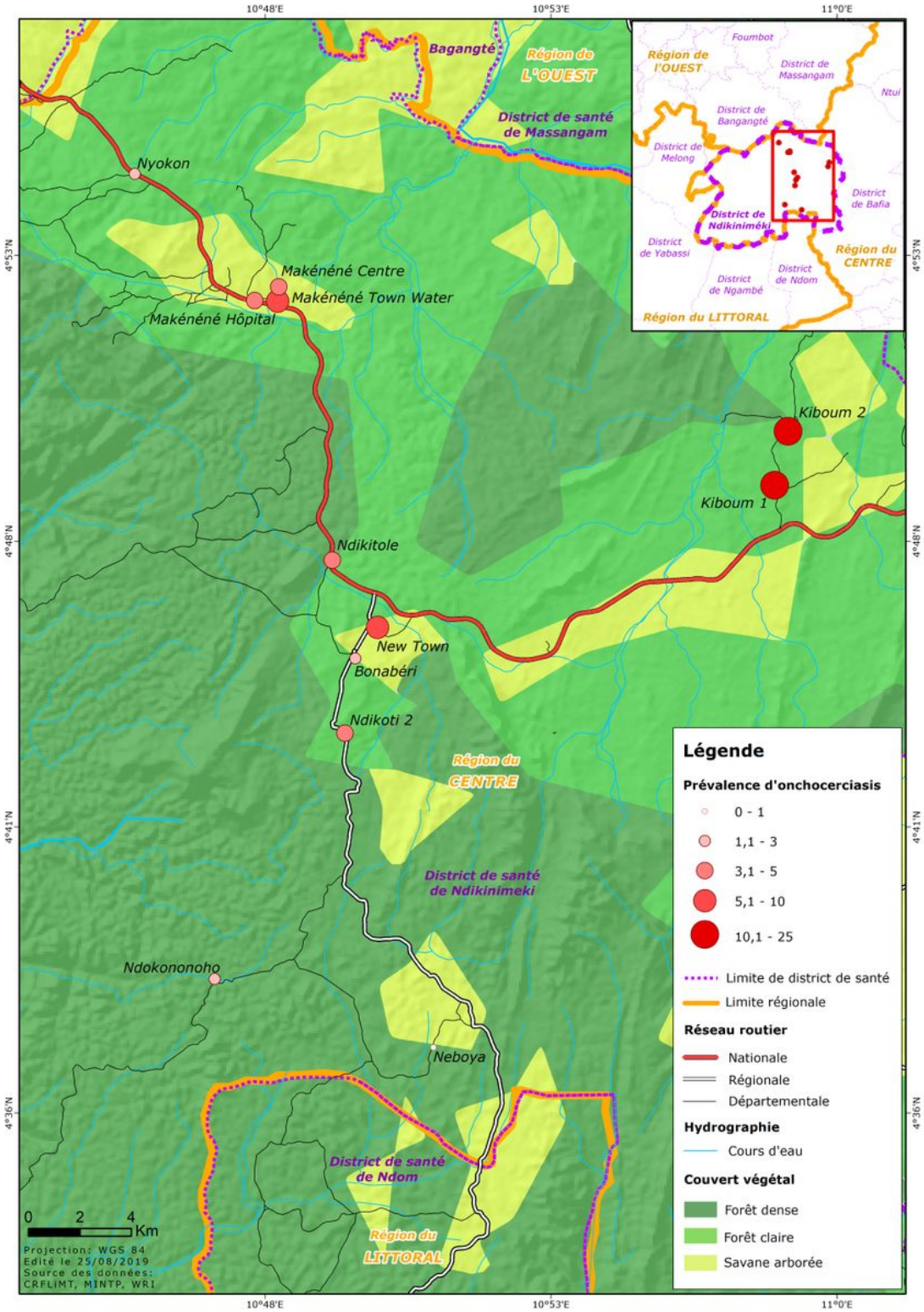

Figure 1

Onchocerca volvulus infection rate in the different communities surveyed in the Ndikinimeki Health District

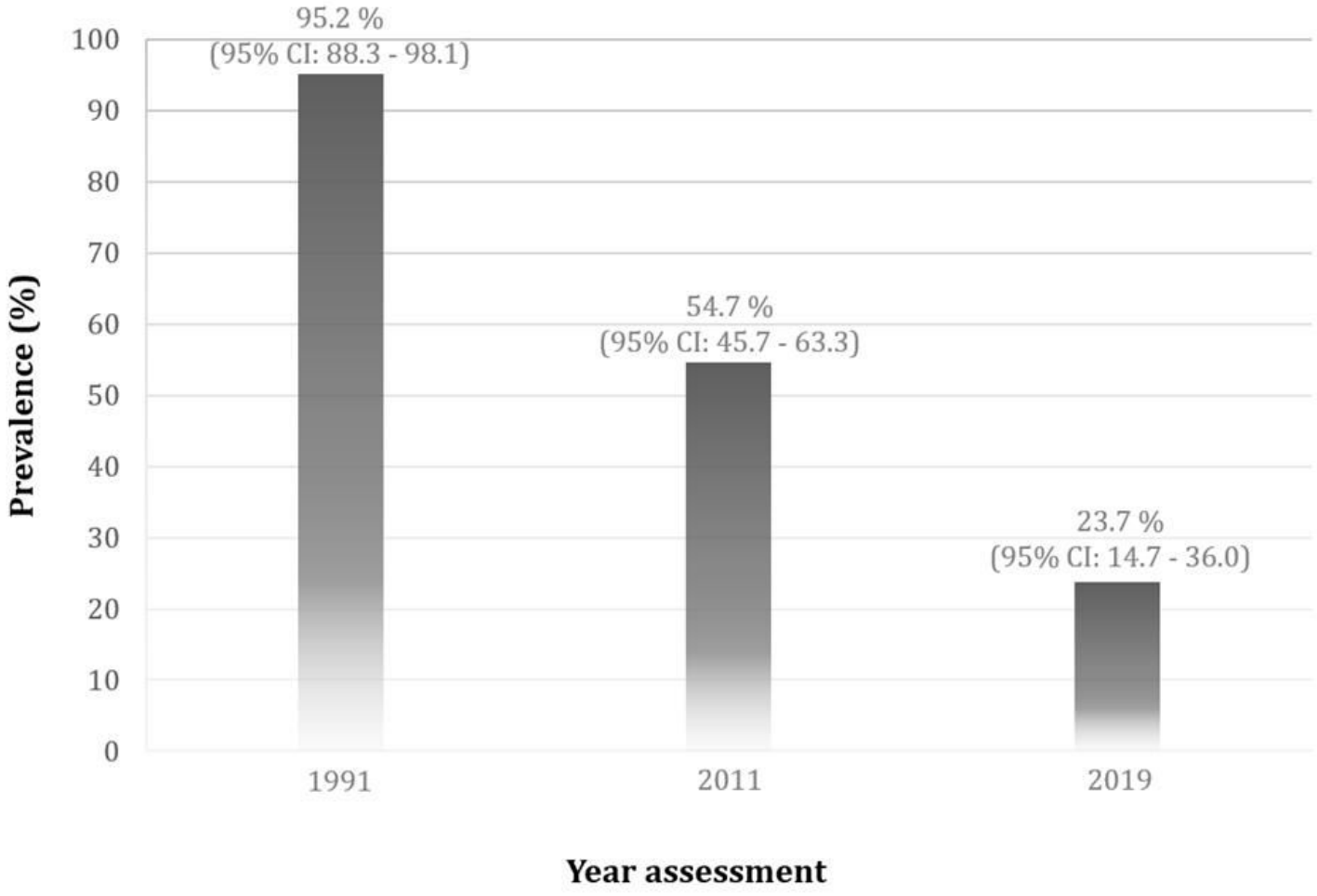

Figure 2

Trends in Onchocerca volvulus infection rates between 1991 (baseline) and 2019 (follow up) in the Ndikinimeki Health District

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- GraphicalAbstract.jpg
- TableS1.docx