



Evaluation of the « Time/Risk » Probability of being Infected and its Evolution Before/After a Long Term Village Scale Malaria Vector Control Programme in Angola

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Three main entomological indicators are classically used in the epidemiology of malaria: the inoculation rate ("h") of Ross, the vectorial capacity ("C") of Garrett-Jones and the reproduction rate ("z") of Macdonald. In spite of their undoubtedly usefulness it appeared that their formulae did not integrate the key parameter of "t" i.e. the time of exposure and therefore the probabilities of being infected according to the entomological condition (density, infectivity, longevity of the vectors) but also the time/risk and the reduction of this risk when some village-scale vector control measures are implemented.

To deal with this approach we used the Briley's formula, elaborated some years ago, to analyze the time/risk of being infected in the framework of a long term village scale vector control programme implemented around Balombo (Benguela Province, Angola) with classical method (inside residual spraying) and newly developed tools (insecticide treated plastic sheeting) used alone or in association with the classical long lasting insecticide treated nets.

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Before vector control the risk was almost 20% in one week, 60% in one month and 100% in 3 months and this explain why plasmodic index are so high in this area without any organized vector control programme.

The 3 methods actually reduced the risks which become of the order of 2% in one week, 10% in one month, 26% in one trimester but 70% in one year; the three methods had the same efficacy in reducing these risks. The fact that the risk reach 70% in one year even with right vector control shows the needs of renewing regularly the operations, the needs of other than entomological methods of prevention but also that immunity could be maintained and feared "rebound" was not observed even during the long term of the programme.

Keywords: Entomological inoculation risk and duration of exposure; new formula for evaluation of time/risk assessment; application in a village scale control programme in Angola.

1. INTRODUCTION

Since the pioneer work of Ross [1], Ross and Hudson [2, 3], several mathematical models were developed to evaluate the intensity of malaria transmission and the efficacy of its control [4-18] with pros and cons mathematical models [19] while noticing the discrepancies between "expected" situation from models and "actual" field situations after vector control [18].

The basic approaches for the evaluation of malaria transmission are based upon 3 main entomological indicators [20]:

- the "inoculation rate" ("h") (also call "Entomological Inoculation Rate" or "EIR") depends on the man biting rate ("ma") multiplied by the infective sporozoite rate ("s") with the classical Ross formula: $h = ma \cdot s$
- the "vectorial capacity" ("C") of vector population; expressed mathematically as $C = ma^2 p^n / -\log_e p$ where ma = man biting rate; a = feeding frequency, p = daily probability of survival; n = duration of the sporogonic development. Vectorial capacity is the "expected inoculations of man per infective case per day"; it is also considered as the "receptivity" to malaria of a defined area. It is a quite common indicator largely used for the estimation of a vector control programme [21,22, 23]
- the "basic reproduction rate" of Macdonald [8] ("z₀") which is "the total expected new infections per case in the absence of immunity" with the mathematical expression

$$z_0 = ma^2 b p^n / -r \log_e p$$

where the entomological parameter are defined as [8]:

"m" = the anopheline density in relation to man;

"a" = the average number of men bitten by one mosquito in one day;

"b" = the proportion of those anophelines with sporozoites in their glands which are actually infective;

"p" = the probability of a mosquito surviving through one whole day;

"r" = the time taken for completion of the extrinsic cycle;

"s" = the proportion of mosquitoes with sporozoites in their salivary glands;

"r" = the proportion of affected people, who have received one infective inoculum only, who revert to the unaffected state in one day.-

In fact "z" represents the "total" new infections expected from one infective case and C the expected inoculations per infective case per day and is easier than the basic reproduction rate where "r" and "b" are of great concern for their evaluation.

It could be used 3 "reproduction rate": the "reproduction rate" = "number of secondary infections distributed by a single primary case"; the "basic reproduction rate" = "the number of secondary occurring in a population-of men and mosquitoes- untouched by malaria until the sources of infection arrives in their midat", also defined as "the potential reproduction capacity of a totally non-immune and untreated case surrounded by a non-immune population" [24]; and the "actual reproduction rate" occurring in endemicity situation and is calculated by the formula $p^n / p^n - s$ (with the example given in Pampana's book : "if $n = 14$ days, and the sporozoite rate 4 per cent (i.e. 0.04) and $p = 0.9$ (i.e. 90 per cent of the vectors survive every day) the expression would be:

$$0.9^{14} / 0.9^{14} - 0.04 = 1.21$$

Meaning that from 1 infected infective human being it could be expected 1.21 new infections and the goal of malaria control will be to get this parameter < 1.

As well underlined by Macdonald “the inoculation rate” which is “the mean daily number inflicted on one individual by mosquitoes infected with sporozoites which are actually infective is sufficient for most purposes” and is commonly used in entomological evaluation of the intensity of transmission.

But one parameter seems to be missing in this classical formula: “t” = the time “exposed” to the risk of inoculation and this is why Birley developed a new formula for the thesis of one of us (PC) [25] with the new expression of $h_B = 1 - (1-s)^{ma.t}$ and s are the same as in classical formula and “t” is expressed in days.

The “ h_B ” therefore means the probability of receiving one infected bite according to the time of exposure and this is very interesting for exemple for travelers exposed, or protected, temporary workers, the evolution of the risk according to the place, or seasons (rainy/dry) or period etc and also the risks while still living in endemic areas with the fear sometimes raised of the loss of immunity if no more infection occurred inducing a rebound of malaria after a malaria vector control programme.

We decided to use this new Birley’s formula of the inoculation rate according to time for an analysis of the risk/time before and after a long term village scale vector control programme implemented in Angola [26].

2. MATERIALS AND METHODS

Since 2007 a long term village scale vector control (VC) programme was implemented in 8 villages around the town of Balombo (Benguela Province, Angola) comparing 4 methods of VC: each one in 2 paired villages, full description of operations done and first results were already described and presented [26, 27].

Entomological evaluation was based on the classical CDC Miniature Light Trap as already used in Tanzania [28] and which were regularly used in 10 randomly selected houses (the same during the whole trial), *Anopheles* caught were determined and biologically analyzed (ELISA test to identify infected specimens).

Inside Residual Spraying was the method of choice for the former Malaria Eradication Programme [24] but in Angola a vector control programme based on this method did not get the expected results [29] while recently developed

Insecticide treated plastic sheetings seems to be an interesting method to replace IRS with a longer durability and better acceptability as it was noticed in Angola and elsewhere [30].

We considered here the situation before and after vector control in 6 paired villages: 2 villages which were sprayed (“Inside Residual Spraying” or “IRS”) with lambda-cyhalothrin, 2 rounds, followed by the installation of δ ITPS; 2 villages which received δ ITPS (model “Wall lining”) only and 2 villages which received both Long lasting insecticide (deltamethrin “ δ ”) treated net and Insecticide treated (deltamethrin) plastic sheeting (“ δ ITPS”) model “Zero Fly©” to see if “2 methods are better than one”.

We compare 2 situations: “before” = years 2007 and 2008; and “after”= years 2009, 2010 and 2011 because vector control operations were done in December 2008 aiming at a full coverage of each house of each village.

Data were gathered in Excel software for their analysis, a programme was especially developed by us to make an immediate calculation of the Birley “ h_B ” when entering data of “ma” and “s” and “t” (in days).

3. RESULTS

3.1 Overall Results

10 *Anopheles* species were collected by the Light Trap (LT) but we analyzed here only the main vectors (MV) which are *Anopheles funestus* and *An.gambiae* gathered in “Main Vectors” (MV). Following Sriwichai et al [31] we divided the number of MV caught by the number of traps used to get the “number of MV/trap” by session to have some proxy of the man biting rate of these MV which are compared according to situation (before/after) and VC method implemented (Table 1).

The infectivity (“s”) correspond to the number of specimens ELISA +/ number of specimens tested.

3.2 Evolution of the Daily Inoculation Rate with the Classical Formula $h = ma.s$

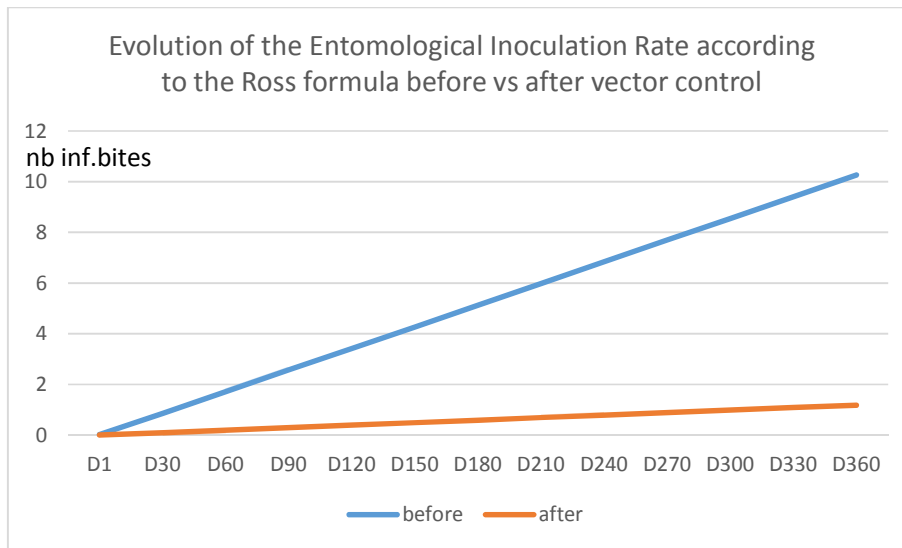
Each method induced a strong reduction of the daily inoculation rate, with an average of 88.5% (Table 2). This daily entomological inoculation rate can easily be calculated for one week, one month and more but appeared linear according to the formula (Graph. 1).

Table 1. Evolution of the “number of MV/traps” and their infectivity according to the method of vector control implemented and the situation before/after VC (LLIN = long lasting insecticide treated nets; ZF = insecticide treated plastic sheeting model Zero Fly; ITPS WL = insecticide treated plastic sheeting model Wall Lining; IRS = inside residual spraying; MV= *An.gambiae*+ *An.funestus*)

Method of VC	Before		After	
	ma	s	ma	s
LLIN + ZF	0.745	0.0420	0.23	0.0145
ITPS WL	0.396	0.0454	0.064	0.0476
IRS	0.5	0.0714	0.127	0.0263
Average	0.547	0.0520	0.140	0.0234

Table 2. Evolution of the daily inoculation rate according to the method of VC implemented and estimated by the classical formula

Methods of VC	Before	After	Difference
LLIN + ZF	0.0313	0.00333	- 89.4%
ITPS WL	0.01797	0.00305	- 83.3%
IRS	0.0357	0.00334	- 90.6%
average	0.0285	0.00328	- 88.5%



Graph 1. Evolution of the number of infected bites by main vectors calculated with the Ross formula (h= ma.s.) (nb.inf.bites= number of infected bites; D1 to D360 = number of days)

3.3 Evolution of the Inoculation Rate with Time, According to the Birley’s Formula

in one month; these percentages are respectively #7% and # 9% after vector control.

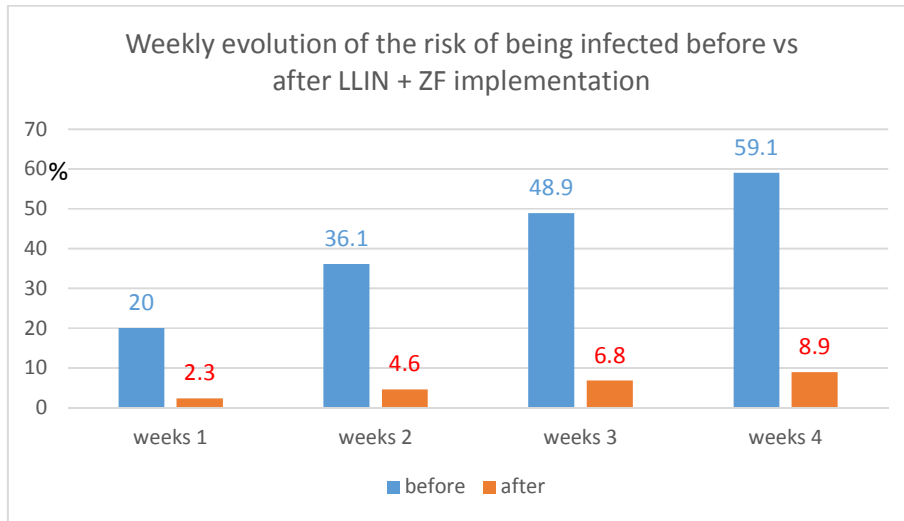
3.3.1 With LLIN + ZF Vector Control

3.3.1.2 Evolution of the monthly risk

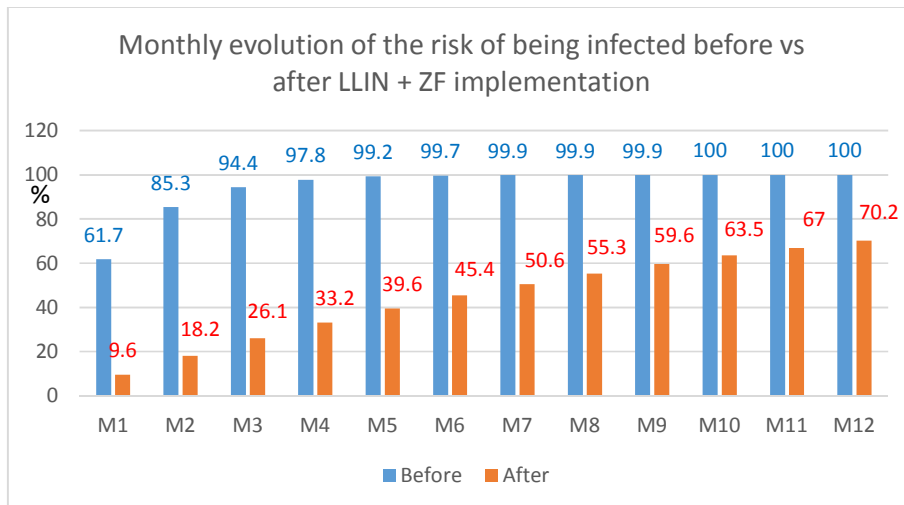
3.3.1.1 Evolution of the weekly risk

Before LLIN + ZF implementation the risks are #62% of getting infected in one month; 85% in 2 months, 94% in 3 months, 98% in 4 months and >99% after (Graph 2b). These percentages are respectively # 10%; 18%, 26%; 33% and reached 50% the 7th months and 70% in one year.

Before full coverage in LLIN and ZF the risk was about 20% in one week and 10 times less after protection of houses (Graph 2a); the risk was # 50% in 3 weeks (50.5% the 22nd day) and # 60%



Graph 2a. Weekly evolution of the risk of being infected in villages before and after implementation of vector control based on LLIN on beds and ZF on walls



Graph 2b. Evolution of the monthly risk of being infected before vs after LLIN + ZF implementation

3.3.1.3 Evolution of the yearly risk

Before vector control in these villages the risk was 100% since the first year and remained as such while after LLIN + ZF the risks could be estimated at 70% the first year then 91% and 97% the two following years.

3.3.2 With WL alone for vector control

3.3.2.1 Evolution of the weekly risk

Before installation of wall lining in every houses the risks were 12%, 23%, 32% and 40% from the first to the fourth week and these percentages dropped respectively to 2%, 4%, 6% and 8%

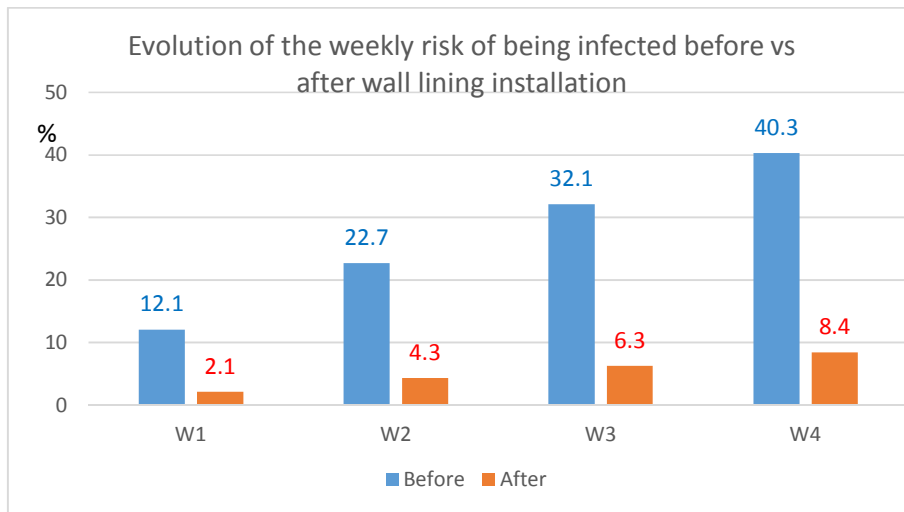
after full coverage in insecticide treated WL (Graph 3a).

3.3.2.2 Evolution of the monthly risk

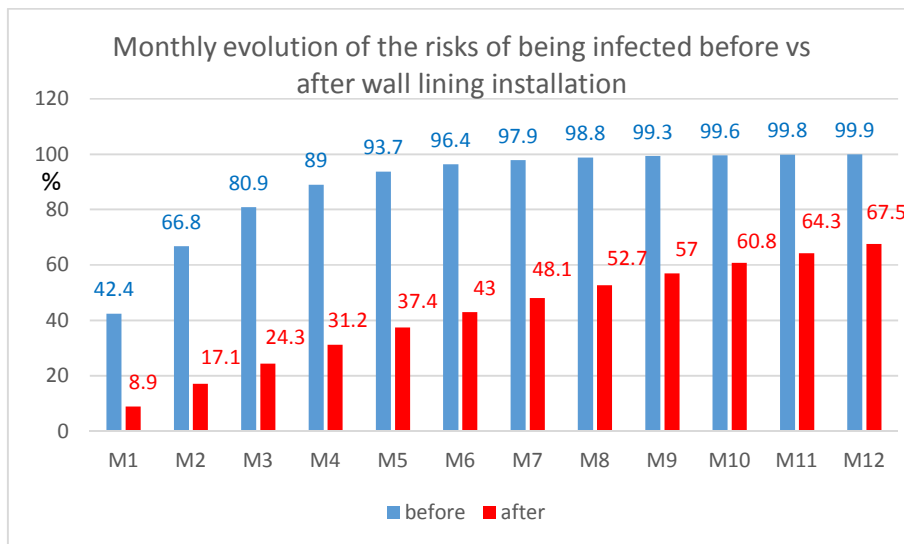
It appeared that a 50% risk occurred in less than 2 months and reached > 90% as soon as the 5th month before vector control while 50% is reached the 8th month after vector control with a 67% risk in one year (Graph 3b).

3.3.2.3 Evolution of the yearly risk

The yearly risks are 99.9% the first year then 100% the following years but 67.5% then 89.4% and 96.6% the following two years with WL.



Graph 3a. Evolution of the weekly risk of being infected before vs after full coverage in wall lining



Graph 3b. Evolution of the monthly risk of being infected before vs after WL installation in every houses

3.3.3 With IRS for vector control

3.3.3.1 Evolution of the weekly risk

In the villages where IRS was carried out the risks were 23% the first week, 40% the 2nd, 54% the 3rd and # 65% in one month while they were as low as 2%, 5%, 7% and 10% in one month after vector control operations (Graph 4a).

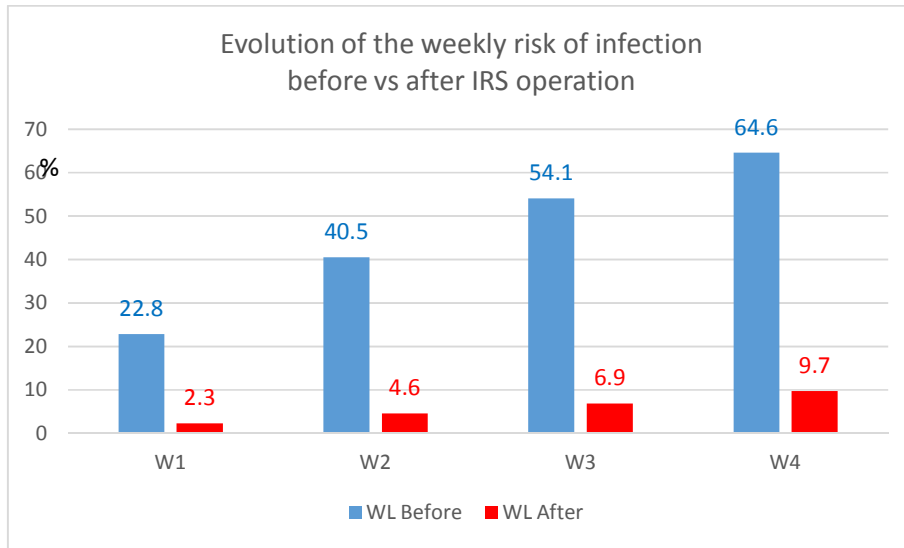
3.3.3.2 Evolution of the monthly risk

In the villages before IRS the risks were near 70% in one month, then # 90% the second

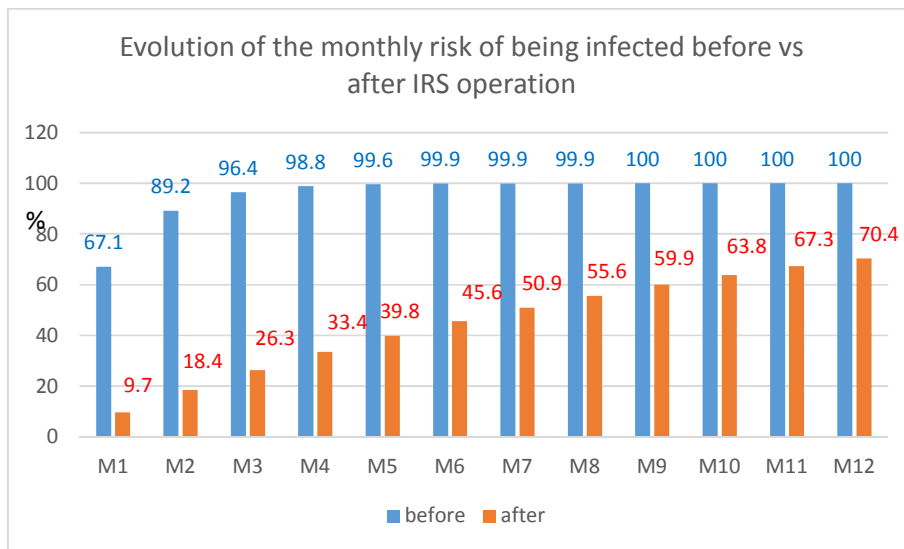
month and > 96% the third one then > 99% ;while remaining around 10% the first month then 20% the second month reaching 50% the 7th month and 70% in one year after VC (Graph 4b).

3.3.3.3 Evolution of the yearly risk

The yearly risks were always 100% since the first year before IRS while reaching 70% the first year then 91% and 97.4% the following years after IRS operation.



Graph 4a. Evolution of the weekly risks of being infected before vs after IRS operations



Graph 4b. Evolution of the monthly risks of being infected before versus after IRS operations

3.3.4 Average with vector control

3.3.4.1 Evolution of the daily risk

The analysis of the daily risk of being infected before and after a vector control programme (Graph 5a) shows that the risk reached 50% in 24 days and almost 60% in one month before VC implementation while the risk is lower than 10% in one month after VC.

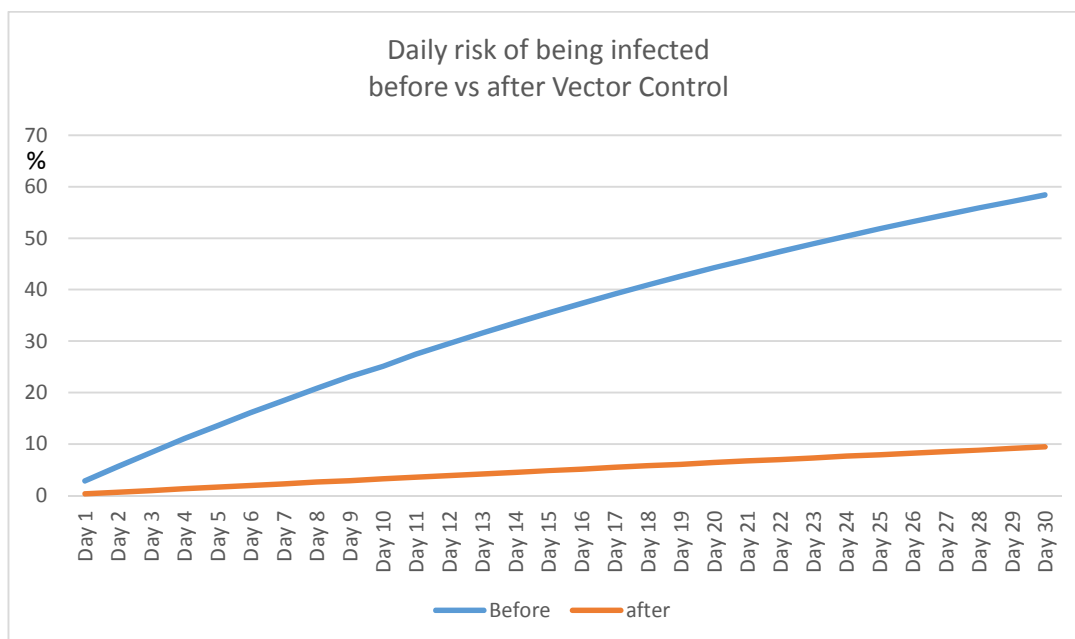
3.3.4.2 Evolution of the weekly risk

It is worth underlying the sharp evolution of the weekly risk with a 18% risk in one week and 33%

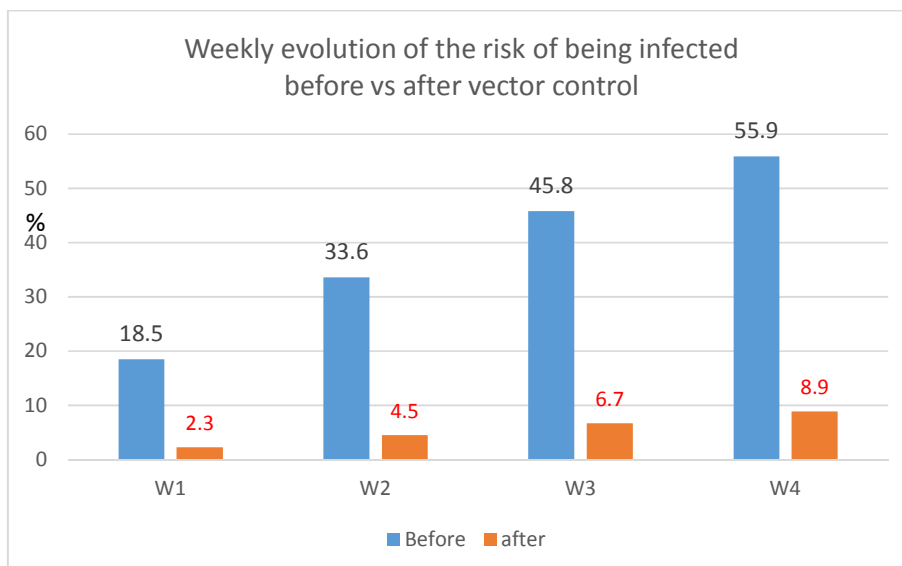
risk in 2 weeks before vector control compared to respectively 2% and less than 5% after VC (Graph 5b) with # 56% and # 9% in one month before versus after vector control.

3.3.4.3 Evolution of the monthly

Comparing the monthly risk shows that it reach > 90% in 3 months before VC and > 99% in 6 months, meaning a “total infection”, while it is # 26% in 3 months and # 45% in 6 months; 50% the 7th month and 70% in one year after VC (Graph 5c).



Graph 5a. Daily evolution of the risk of being infected in one month before vs after vector control

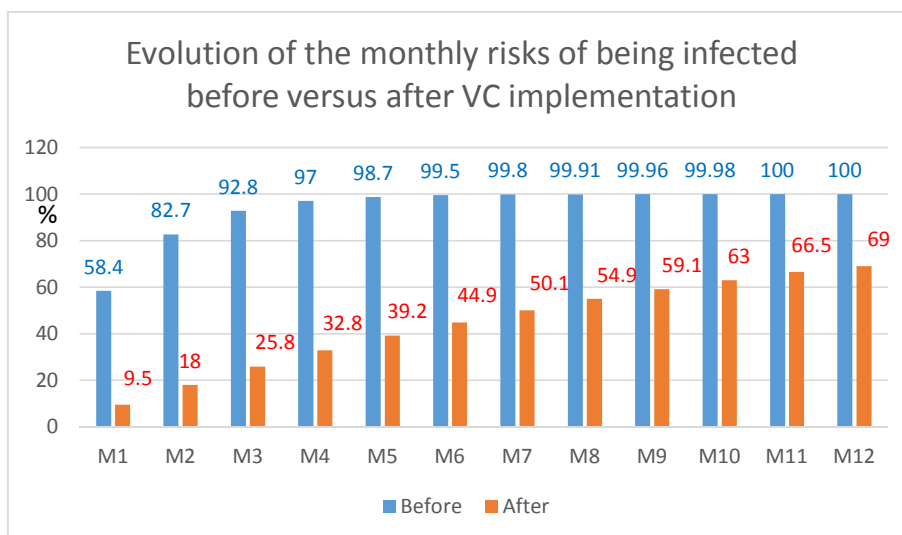


Graph 5b. Average evolution of the weekly risks of being infected before and after implementation of vector control

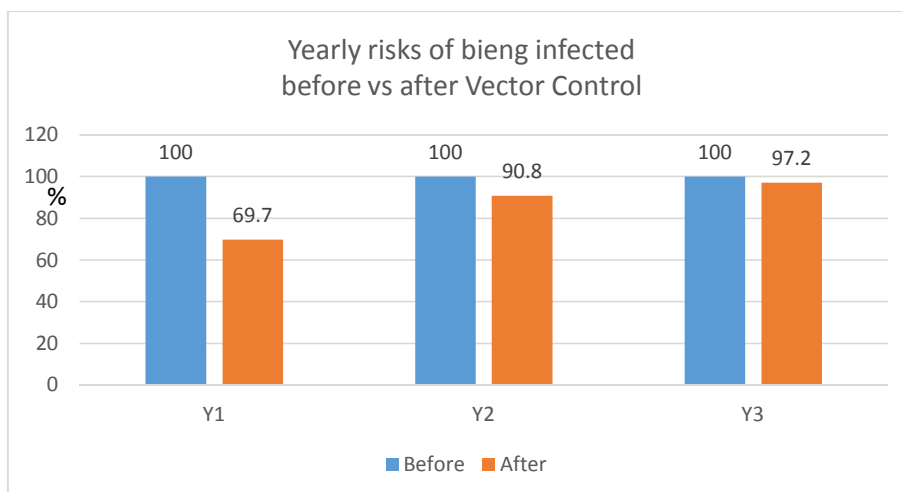
3.3.4.4 Evolution of the yearly risk

Before vector control it clearly appeared that the risks were 100% (Graph 5d) and this “explain” the high level of Plasmodic Index noticed in these area before the Balombo vector control programme [32].

After vector control the risks sharply decreased at the beginning but with time they reach 70% in one year and more than 90% as soon as the 2nd year, meaning that the immunity was still stimulated and this “explain” why plasmodic index remained at low level during several years after vector control operation [26].



Graph 5c. Evolution of the monthly risks of being infected before vs after implementation of vector control



Graph 5d. Evolution of the yearly risks of being infected before vs after vector control operations

3.4 Synthesis

In analyzing the evolution of risk every trimester it is noteworthy the remarkable homogeneity of the situation before (Graph 6a) and after (Graph 6b) of the evolution of risks whatever the method of vector control was.

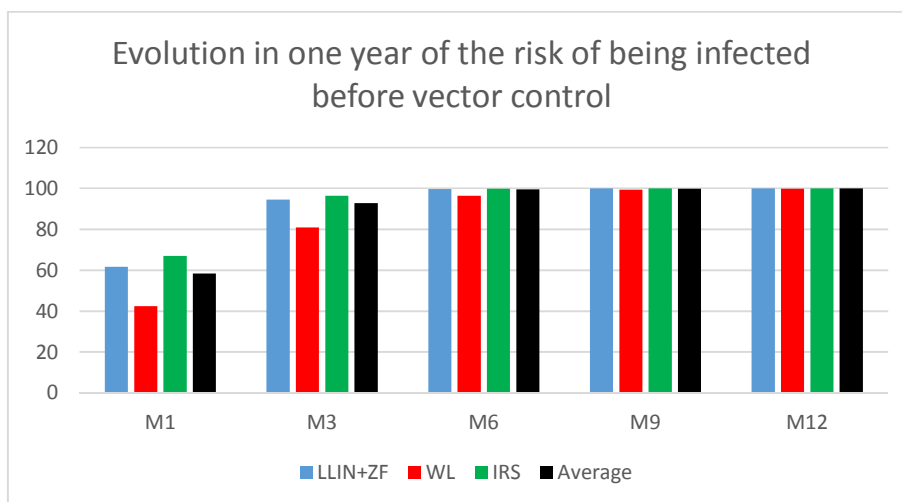
It is clear that the probabilities of being infected reached almost 60% in one month and #100% in 3 months before VC.

After vector control the risks are sharply reduced, about 10% the first month but reaching

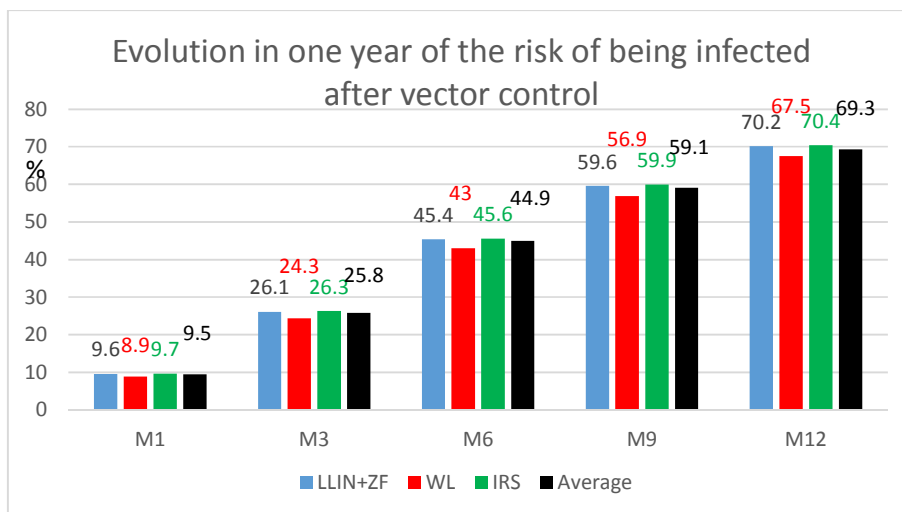
nevertheless 70% in one year underlying the need of regular campaign to “boost” the impact of vector control to reduce the risk of receiving a malaria infected bite.

The similar efficacy of the 3 methods shows that:

- adding 2 tools (mosquito nets + insecticide treated sheeting) and therefore increasing the amount of insecticide (and selective pressure) did not reduced the risks of being infected in studied conditions;



Graph 6a. Evolution every 3 months of the probabilities of being infected before implementation of one of the three methods of vector control (LLIN + ZF= Long lasting insecticide treated nets+ insecticide treated plastic sheeting model Zero Fly; WL= insecticide treated plastic sheeting model Wall Lining; IRS= inside residual spraying)



Graph 6b. Trimestral evolution of the risks of being infected after implementation of 3 measures of vector control

- Insecticide treated plastic sheeting can replace the classical inside residual spraying considering its same efficacy (and even longer) without the well-known operational and ethical issues which quite often prevent the regularity of the scheduled rounds of spraying.

exposure to malaria infection will vary according to the area visited, type of accommodation, time and duration of stay and effectiveness of prevention measures used”. Intuitively it is clear that the longest the time of exposure the highest the risks of being infected but it is interesting to be able to measure this risk and its evolution with implementation of preventive measures such as vector control.

4. DISCUSSION AND CONCLUSION

In their “assessment of risk” Zucker and Carnevale [33] considered that the “risks of

2 main situations could be envisaged: people living in endemic areas and being immune (or

semi immune) and a balance must be found between reducing the risks and maintaining immunity; and non-immune people coming in “at risk” area for more or less time and must be aware of these risks to adopt correct adapted behaviour.

The “time/risk” assessment is also important when developing new settlement for refugees or displaced population knowing, for example, that in such place at such time of the year it could be expected 50% of the population being infected by *Plasmodium* and health structure must be prepared to care about these malaria cases.

As well underlined by Orlandi-Pradines et al [34] “malaria remains a major threat, to both travelers and military personnel deployed to endemic areas. The recommendations for travelers given by the World Health Organization is based on the incidence of malaria in an area and do not take the degree of exposure into account” and they developed some studies “to evaluate the exposure of travelers by entomologic methods, which are the commonly used measures of the intensity of malaria transmission”.

For Kelly-Hope and McKenzie [35] “the “entomological inoculation rate” is the commonly-used measure of the intensity of malaria transmission, yet the methods used are currently not standardized. For them “Understanding the dynamics of malaria transmission in a population is critical; it provides insight into the magnitude of the problem, helps to define when and where the greatest risk occurs and facilitates the development of appropriate control strategies [36-38]. “Furthermore, it is important to determine how the level of risk within a population may compare with other (or surrounding) populations – this will help identify key differences and similarities and highlight corresponding risk factors” [35].

Birley and Charlowwod [39] considered that studies on infectivity of vectors (by ELISA test and parasite prevalence in children in Papua-New Guinea “provide a unique opportunity to compare sporozoite rate, biting density and prevalence. These seminal data will fuel debates about the epidemiology of malaria which may provide insights into potential control strategies”.

What is actually of paramount importance is that with 3 parameters only: “human biting rate (“ma”) infectivity (“s”) and now the time (“t”) of exposure it is possible to quickly evaluate the risk

of being infected when spending one night, one week, one month, one year in some more or less “malarious” areas and how these risks could be sharply reduced in protected “vector control” area still keeping in mind that “risk zero” doesn’t exist but almost 0 when staying one night in protected area is actually achievable. The issue remains in term of sustainability as even in protected area the risk reach 10% in one month, 26% in 3 months, 50% in 7 months and could be of 70% in one year.

This dynamic approach of malaria risks of transmission with duration of exposure open a new way of planning and evaluating strategies of control.

Knowing these risks, adapted measures could be undertaken in due time, adding community protection by large scale vector control, personal protection with insecticide treated net and drug prophylaxis as needed with accurate case management to reduce the malaria burden for its foreseen global elimination.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This mathematical analysis is a part of a comprehensive evaluation of a vector control programme done with the Angola National Malaria Control Programme and Provincial Public Health Authorities.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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