BMJ Open

Community delivery of malaria intermittent preventive treatment in pregnancy: protocol of a quasi-experimental evaluation through multistage cluster sampling household surveys in four sub-Saharan African countries

Clara Pons-Duran [1,2] Mireia Llach,[1] Sergi Sanz,[1] Máximo Ramírez,[1] Susana Méndez,[1] Elaine Roman,[3] Maya Tholandi,[3] Franco Pagnoni,[1] Clara Menendez,[1,2] Raquel González[1,2]

For numbered affiliations see end of article.

Correspondence to
Dr Raquel González;
raquel.gonzalez@isglobal.org

ABSTRACT

Background In sub-Saharan Africa (SSA), millions of pregnant women are exposed to malaria infection. The cornerstone of the WHO strategy to prevent malaria in pregnancy in moderate to high-transmission areas is the administration of intermittent preventive treatment (IPTp) with sulfadoxine-pyrimethamine at each scheduled antenatal care (ANC) visit. However, overall coverage remains low. 'Transforming IPT for Optimal Pregnancy' (TIPTOP) project aims at delivering IPTp at the community level (C-IPTp) to complement ANC provision with the goal of increasing IPTp coverage and improving maternal and infant's health. This protocol describes the approach to measure the effect of this strategy through household surveys (HHS) in four SSA countries: Democratic Republic of Congo (DRC), Madagascar, Mozambique and Nigeria.

Methods and analysis A quasi-experimental evaluation has been designed. Delivery of C-IPTp will start first in one area per country, and later it will be extended to two more areas per country. HHS will be carried out before C-IPTp implementation in all study sites, at midterm in initial implementation areas, and after the implementation in all project areas. A multistage cluster sampling method will be followed for the selection of participants. Women of reproductive age who had a pregnancy that ended in the 6 or 12 months prior to the interview, depending on the survey, will be invited to participate by responding to a questionnaire. The main indicators will be coverage of three or more doses of IPTp and attendance to at least four ANC visits. A difference-in-difference analysis will be performed to evaluate the effectiveness of C-IPTp.

Ethics and dissemination The project has been reviewed by the ethics committees of WHO, Hospital Clinic of Barcelona and all project country boards. Project results will be disseminated to in-country stakeholders and at regional and international meetings. TIPTOP project aims to develop and disseminate global recommendations for C-IPTp delivery.

Strengths and limitations of this study

► This is a large-scale multicountry evaluation with a huge potential to generate relevant and useful evidence to inform policies on malaria prevention for the sub-Saharan African region.

► The household surveys (HHS) standardised methodology will make project estimates comparable across areas and countries.

► HHS intrinsic limitations such as recall bias, information and non-response biases will be mitigated by accounting for potential confounding factors in the overall analysis.

► The quasi-experimental evaluation design will not allow determining causal relationships between the intervention and the outcomes, but rather associations between them.

BACKGROUND

Malaria is the most important parasitic disease worldwide. In sub-Saharan Africa (SSA), 215 million people were infected by malaria and about 12 million pregnancies were exposed to the infection in 2019.[1 2] Approximately, 10 000 pregnant women and 200 000 of their newborns die every year due to the infection worldwide, primarily caused by *Plasmodium falciparum*.[2] In endemic areas, the risk of low birth weight doubles when the placenta is infected with malaria, and up to 33% of neonates can be born with congenital infection if the mother is infected during

pregnancy.[3] In addition, pregnant women with malaria more frequently show higher parasitaemia, severe anaemia, hypoglycaemia and acute pulmonary oedema than their non-pregnant counterparts.[4] Recent data also indicate that up to 20% of stillbirths in SSA may be attributable to malaria in pregnancy (MiP).[5]

In 1998, the World Health Organization (WHO) recommended the administration of two doses of intermittent preventive treatment for malaria prevention in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP)—in addition to the use of insecticide-treated bed nets (ITNs) and effective case management—after quickening.[6] In 2012, the WHO updated these guidelines by recommending the administration of IPTp at each scheduled antenatal care (ANC) visit, and at least one month apart, for all women living in moderate to high transmission areas in Africa starting in the second trimester of gestation.[7 8] This recommendation has the objective of ensuring the uptake of at least three doses of IPTp during pregnancy.[9]

Despite the existence of parasite resistance to SP in some areas in Africa, IPTp remains a highly cost-effective, lifesaving strategy to prevent the adverse effects of MiP in the majority of African pregnant women.[10] IPTp decreases the incidence of low birthweight babies, severe maternal anaemia and neonatal mortality.[11] However, despite this evidence, it is estimated that 60% of pregnant women received at least one dose of IPTp in 2018, 49% received two or more doses and only 31% received three or more doses in SSA.[1] These figures reflect the failure of the health system to provide IPTp at ANC facilities. While, on average, around 86% of women in SSA attend the ANC clinic at least once during pregnancy, only two-thirds of women in the region attend the ANC clinic four times as previously recommended.[12] In late 2016, ANC guidelines were updated by the WHO to eight antenatal contacts, which may include community outreach programmes and lay health worker involvement.[13]

TIPTOP (Transforming Intermittent Preventive Treatment for Optimal Pregnancy) is a 5-year project that started in 2017 and will last until 2022. It aims at exploring an alternative, though complementary, approach to the ANC clinic for the delivery of IPTp.[14] It sustains and scales up an innovative, community-based approach to expand coverage of IPTp in four SSA countries: Nigeria, Democratic Republic of Congo (DRC), Madagascar and Mozambique. As part of the project, IPTp is made available to eligible pregnant women close to their homes through a network of purposely trained and supervised, easily accessible community health workers (CHWs). This approach, called community-IPTp (C-IPTp), complements the traditional SP delivery strategy in which eligible pregnant women receive SP when attending ANC clinics. In addition to distributing SP, CHWs also promote ANC attendance by pregnant women to ensure a comprehensive pregnancy follow-up.

The use of CHWs has been shown to improve the provision of some health interventions in children,[15] and there is evidence that they can undertake actions that lead to improved health outcomes.[16] Studies in The Gambia, Ghana, Senegal and Nigeria show that CHWs can successfully deliver malaria preventive interventions.[17–20] Accelerating demand for IPTp primarily through CHWs will be crucial in contributing to increasing coverage of essential indicators, reducing maternal and neonatal mortality and reducing costs.[21]

In a pilot study that evaluated C-IPTp in Burkina Faso, attendance to ANC and coverage of three or more doses and of four or more doses of IPTp significantly increased in the intervention compared with the control areas.[22]

The main goal of TIPTOP project is to contribute to reducing maternal and neonatal mortality in SSA by expanding IPTp and increasing its overall coverage. This protocol describes the methodology that will be used to estimate IPTp and ANC coverage in the project areas. The analysis of these indicators before, during and after project implementation will be used to estimate the effectiveness of C-IPTp.

METHODS
Study design
A quasi-experimental evaluation has been designed to evaluate the effectiveness of C-IPTp. Community-based household surveys (HHS) will be conducted before, during and after C-IPTp delivery in selected project areas. More details on the project's intervention can be found elsewhere.[14] Information about IPTp coverage will be collected from women who have ended a pregnancy in the past 12 months at baseline (before C-IPTp implementation), and in the past 6 months at midline (after one year of intervention in initial intervention areas) and endline (after approximately two years and a half of intervention in initial areas and one year and a half in expansion areas). The C-IPTp implementation strategy will start in the area of initial implementation immediately after the baseline HHS, and after the repeat baseline and baseline HHS in the first and second expansion areas of implementation, respectively. The rationale for including one expansion area in the surveys since the beginning is to strengthen the attribution of a possible increase in the main outcome (IPTp3 coverage) to the intervention. The effectiveness of the C-IPTp strategy will be evaluated by measuring the change across time of the IPTp coverage determined through HHS at baseline, midline and endline timepoints. A diagram of the project design is shown in figure 1.

Objectives
The TIPTOP project aims to increase coverage of IPTp. The HHS have been designed to determine the coverage of three or more doses of IPTp (IPTp3+) in the project areas of Nigeria, DRC, Mozambique and Madagascar before, at midline and at the end of C-IPTp implementation. The secondary objectives of the HHS are to determine the coverages of two or more doses of IPTp (IPTp2+), one or more doses of IPTp (IPTp1+), four
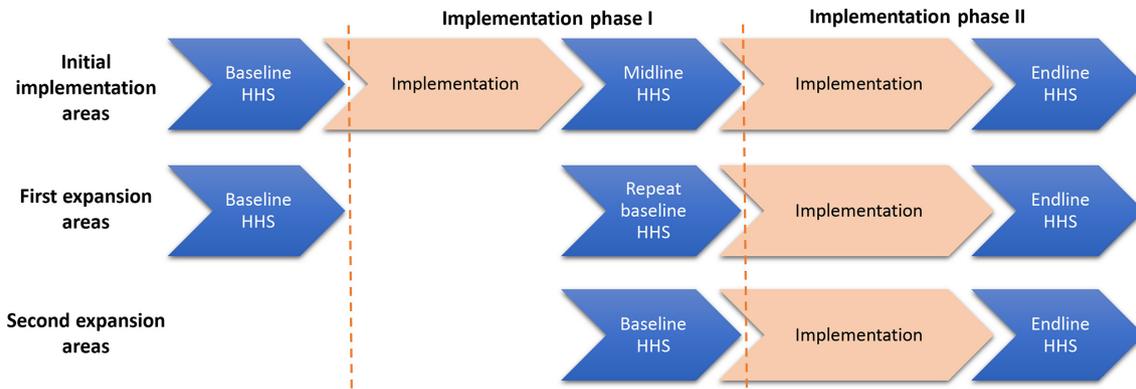
Figure 1 Project phases and evaluation activities of TIPTOP proiect. HHS, household surveys; TIPTOP, Transforming IPT for Optimal Pregnancy.

or more ANC visits (ANC4+), one or more ANC visits (ANC1+), eight or more health contacts during pregnancy, first visit before gestational week 14 and knowledge of IPTp service provided by CHWs, in the same three time points. The ultimate goal of these HHS is to assess the effectiveness of C-IPTp.

Study population
Eligible participants of the HHS will be women of reproductive age (13–50 years old, depending on the country) that had a pregnancy that ended in the 6 months prior to the interview. Exclusively for the first baseline surveys, the target population was composed of women that had a pregnancy that ended in the 12 months prior to the interview. Initially, during the design phase, 12 months was deemed appropriate, but due to a delay in the start of project activities, the criteria had to be changed to 6 months to avoid overlaps in the recall periods of the surveys. The inclusion of legal minors will follow local regulations in each study country.

Project sites
Four countries participate in the TIPTOP project: Madagascar, Mozambique, Nigeria and DRC. The selection of these countries was based on a series of selection criteria including having CHWs and IPTp policies in place, commitment from the Ministry of Health (MoH) and efficient working relationships between the consortium and MoH. Importantly, DRC, Madagascar and Nigeria had the highest estimated increases in cases of malaria in

2017 compared with 2016. Mozambique is among the 10 highest malaria burden countries in SSA.[1]

The complexity and potential demonstration effects of these countries were considered, including geographic and language diversity, size, population and opportunity to meaningfully reach the 'hard-to-reach'. The combination of these factors positions each country for success, ensures the ability to scale up and sustain project gains, and yields critical learning/evidence to inform replication and scale-up throughout SSA.

In each country, an initial implementation area and two expansion areas were selected by the national MoH in collaboration with the project consortium. Baseline surveys will be conducted in the initial implementation area and in one expansion area only at the beginning of the project. A baseline survey in the second expansion area, a second baseline in the first expansion area and a midline survey in the initial implementation area will be conducted at midterm. Endline surveys will be conducted in the three project areas in each country. Project sites are presented in table 1.

Sampling methodology
A multistage cluster sampling method will be followed. This sampling method is adapted from the Malaria Indicator Surveys and the Expanded Programme on Immunisation sampling methods.[23 24] The term 'cluster' is defined as any sampling unit with which one or more listing units can be associated. This unit can be geographical or

Table 1	Project areas by country							
	Madagascar		**Mozambique**		**Nigeria**		**DRC**	
	Provinces	**Districts**	**Provinces**	**Districts**	**States**	**Local Government Areas**	**Provinces**	**Health zones**
Initial implementation areas	Fianarantsoa	Mananjary	Sofala	Nhamatanda	Ebonyi	Ohaukwu	Kwango	Kenge
Expansion areas	Toliara	Toliary 2	Nampula	Meconta	Ondo	Akure South	Kwilu	Bulungu
	Fianarantsoa	Vohipeno	Nampula	Murrupula	Niger	Bosso	Maniema	Kunda

DRC, Democratic Republic of Congo.

temporal in nature. Clusters will be as similar as possible, but highly variable within each one. Since only a subset of the clusters will be included in the HHS, each sampled cluster will be representative of other non-sampled clusters, and the total variation with the population still will be reflected in the overall estimate.

The sampling is done in three stages: (1) the selection of clusters, (2) the selection of households and (3) the selection of women to be interviewed.

First stage

The first step is to obtain, with the collaboration of community leaders, the list of all cities, towns and villages in the study area with as up-to-date population data as possible. This list constitutes the sampling frame from which the sample of clusters will be selected. Generally, the unit of sampling is the smallest with data available, and it may be different across study countries due to variability in the administrative organisation.

Clusters are sometimes too large to be economically feasible for a single survey. In those cases, the area will need to be segmented into smaller subareas for a further subarea selection before doing the household listing.

The number of clusters that will need to be selected is calculated based on the final sample size for each study area. The number of women to be interviewed per cluster was set between 12 and 15 depending on the area, since this is the number expected to be found and interviewed per day per cluster in order to facilitate fieldwork.

Then, the sampling interval will need to be determined. The sampling interval is the number used to select clusters systematically from the sampling frame and it is calculated by dividing the total population to be surveyed by the number of clusters (rounding off the result to the nearest whole number).

The probability proportional to size sampling method will then be applied in order to ensure that the most populated clusters have an increased probability of being selected. First, a random number lower than or equal to the sampling interval (that must have the same number of digits as the sampling interval) will be generated with Excel. The first community listed in which the cumulative population equals or exceeds the random number will be the first cluster selected. Then, the following clusters will be identified by adding the sampling interval to the random number as many times as necessary until the necessary number of clusters has been obtained.

Second stage

This stage consists in selecting the households to be surveyed in each cluster. A census of the households in each selected cluster will be generated to be able to select a random sample of households within each one. If an updated list of households is not available, a map of the cluster including all the households, not only the eligible ones, will be generated prior to the data collection. Based on the number of people living in the study areas and the estimated proportion of women who are pregnant,

Table 2 Estimated sample size for baseline household surveys

Country	Previous estimate of IPTp3-SP uptake (%)*	Estimated sample size
Mozambique		
Nhamatanda	36.1	709
Meconta	19.2	477
Madagascar		
Mananjary	10.3	284
Toliary II	10.3	284
Nigeria		
Ohaukwu LGA	41	744
Akure South LGA	9	277
DRC		
Kenge	17	434
Bulungu	12	325

*Regional estimates from the Malaria Indicator Survey or the national health information systems (latest data available): Mozambique—Sofala and Nampula provinces; Nigeria—Ebony and Ondo States; Madagascar—national; DRC—Kenge and Bulungu Health Zones.
DRC, Democratic Republic of Congo; IPTp3-SP, Three or more doses of intermittent preventive treatment; LGA, Local Government Area.

it is estimated that an average of 60–80 households per cluster will be visited to finally find and interview 12–15 eligible women. For those cases where 60–80 households are not enough to find the required number of eligible women, a systematic procedure to enumerate and select more households will be followed (online supplemental material 1). The households will be randomly selected by equal probability using a table of random numbers or any other method that allows selecting at random a subset of the households (online supplemental material 1).

Third stage

The last stage consists of selecting randomly only one woman meeting the inclusion criteria in each household.

A detailed sampling strategy manual is available (online supplemental material 1).

Sample size calculations

Baseline

Table 2 shows the sample sizes calculated for the baseline HHS.

The sample size calculation is based on the following equation for coverage:

$$n = \frac{DE.1.96^2.p.(1-p)}{precision^2}$$

where design effect (DE)=2, p=expected IPTp3+ coverage and precision=±0.05 with a 95% CI. The final sample size has been increased by 10% in all study areas.

Midline and endline

The sample sizes for midline HHS will be calculated assuming a 10% increase in IPTp3+ coverage in initial implementation areas, whereas for expansion areas, the coverage obtained in the baseline HHS will be used. For the endline HHS, an additional 10% increase with respect to midline results will be applied to the estimations to calculate the sample sizes.

Participant recruitment and inclusion criteria

The interviewers will approach all selected households in each cluster. The household head will also be interviewed in order to obtain household information. If household head's consent for a woman to participate in the survey is needed, field workers will seek their oral consent to proceed.

The inclusion criteria to participate in the HHS are (1) women who had a pregnancy that ended in the 6 or 12 months preceding the interview (depending on the survey), (2) being resident in the study area during for at least 4 months before the end of the pregnancy and (3) willing to participate in the HHS (signing informed consent/assent, in line with country guidelines). By end of pregnancy, it is understood either a delivery of a live birth, a stillbirth or a spontaneous abortion. The exclusion criteria are the lack of willingness to provide informed consent and the impossibility of responding to the interview due to any physical or medical condition.

Survey development and implementation
Logistics, field team and equipment

The field teams will be comprised of a group of interviewers, one local guide, one supervisor and one driver. Field supervisors oversee the teams and report to the HHS country coordinator. Local guides will be people living in each specific cluster that will be selected by local authorities to accompany the interviewers in order to facilitate their work and mobility in the communities. Each team will be responsible for a number of clusters and will move from one cluster to the next. The number of days the team will spend in each cluster will vary between 1 and 3 days, depending on cluster size. The average duration of each interview will be about 40 min.

Each interviewer will carry an electronic device (tablet) to collect HHS data with an integrated high precision Global Positioning System (GPS) to record the latitude and longitude of each household. Regularly, the devices will be connected to the internet, and the data will be uploaded to the centralised server.

Training of field teams

All field team members will undergo 5 days of intensive training. This training will cover aspects such as basic principles of research including ethics, study rationale, aim and design, procedures to ensure high-quality data collection, detailed question by question description of the questionnaire—including the intention behind each question, the data it is supposed to capture, any specific instructions, skip patterns and response categories—and the use of tablets for data collection.

The training will be conducted using various methods including role-plays, skits, question and answer sessions, hypothetical scenarios and lectures. In addition, field teams will conduct a 1-day or 2-day pretest exercise to familiarise themselves with the tools and electronic technology, and identify any errors that may have been missed before. The pretest will be conducted in areas not targeted for the intervention and each fieldworker will be expected to conduct at least four interviews, one of them in the presence of a trainer.

Trainings will be co-facilitated by the national teams, the electronic device experts (data managers) and the country coordinators.

Field manuals and survey instruments

Field manuals and standard operating procedures for the HHS will be developed and will include the objectives of the survey, methods (including the number of clusters to be selected in each project area), logistics, key indicators (outcomes and impact), sample size including its justification and a timetable. The methodology and survey instruments will be standardised for all countries.

Two questionnaires will be used for the survey, one collecting general information about the household and the household head, and another to be responded by the selected woman.

Written informed consent/assent will be sought from all selected women. Informed consent forms will be translated into English, French, Portuguese and local languages. Oral informed consent will be sought from the household head, when necessary.

All questionnaires will also be translated into English, French, Portuguese and Malagasy. The decision on the local language to be used orally if necessary is country specific and this will be discussed and agreed on with the local field teams responsible for the survey.

All questionnaires will be programmed into the electronic devices following the same structure.

Pilot testing of the survey tools

Before the training, the questionnaire will be pilot tested in one subarea per country (not a project area). The aim of the pilot test is to identify questions that may be unclear, difficult to understand or not relevant to the local context, and also to confirm the correctness of the translation. The questionnaires, the instruction manuals and survey methods will be revised after the pilot test is completed.

Data management

The data management systems and procedures used in the HHS will be based on local infrastructures and field sites capabilities, always relying on robust systems based on standards and secure applications. Electronic devices will be used to collect the HHS data. Data will be entered

using specific software for clinical data management, REDCap (Research Electronic Data Capture).[25]

Quality control procedures will be put in place at various stages, during data collection and later with data checking. Rigorous consistency checks will be created in order to reduce errors during data entry. Data checking procedures are conducted at two different levels. The data managers in the field will receive the data collected from the supervisors periodically and will run further checks before transferring the data to a central database. There, an experienced data manager will run analyses to perform the data cleaning before sending the database to the rest of the team to analyse the results.

The database will be stored in a server hosted at a secure data centre with appropriate series of protocols to test and maintain network security, and to provide access management policies for network drives, databases and remote access. The system will be protected from power interruptions.

For data safety purposes, the field teams will be required to define clear data access and backup procedures. The database will only be accessible by the study coordinators. The backup of the data will be done on a timely basis. The final stored data will be anonymous; individual data will be associated with a numerical identification number. This information will uniquely identify project participants and will be associated with the rest of the captured sensitive information. If personal information has to be stored, used or shared, it will be always anonymised and codified.

Data analysis

The following indicators will be analysed: coverage rates of three, two and one or more doses of IPTp (IPTp3+, IPTp2+ and IPTp1+, respectively), the coverage of attendance to at least four and one ANC visits (ANC4 and ANC1), the coverage of attending the ANC clinic before gestational week 14, the coverage of eight or more contacts with health providers during pregnancy and the proportion of women interviewed knowing about the IPTp service provided by CHWs. All the indicators will be disaggregated by IPTp provider type (CHW, health facility), age, gravidity and distance from household to the health facility.

Additional analysis will be performed to determine the presence of potential associations between HHS indicators and confounding factors. An extensive list of potential confounding factors will be collected during the HHS to be used in univariate and multivariate logistic regression analyses to adjust associations. As confounding factors may also have a potential modifier effect, their effect modification will be tested. Clustering will be taken into account in the analyses.

The potential confounding factors and effect modifiers will be socioeconomic factors from the household head and woman's questionnaire —the educational level of the participant, husband and household head, socioeconomic index based on household assets and living conditions, access to health facilities, and so on—and factors related to the health services as per available district statistics—number of hospital beds, health staff in the area or presence of other interventions other than TIPTOP in the study area.

Stata (Stata, College Station, Texas, USA) will be the statistical software used to perform the analyses.

Evaluation of the intervention (C-IPTp)

In order to estimate the effectiveness of the C-IPTp strategy in increasing IPTp3+ coverage in project areas, a difference-in-difference (DiD) analysis will be performed. DiD is a commonly used technique that mimics the experimental research design and calculates the effectiveness of an outcome—IPTp3+ coverage in this case—by comparing the average change over time in the outcome variable in the intervention population versus the average change over time in the non-intervention population.[26] The first expansion area will be used as a false control to carry out the analysis. We will evaluate the effectiveness of the intervention in the short term (first project phase), and the added effect of an additional year and a half of intervention in the long term (phases 1 and 2). The analysis will be controlled for potential explanatory/confounding variables collected through the questionnaires. Standard errors will be clustered to account for potential unobserved correlation among women belonging to the same cluster. A comprehensive analytical plan will be prepared to guide the final evaluation of C-IPTp.

ETHICS AND DISSEMINATION

This multicountry protocol was approved by the WHO Ethics Review Committee (Geneva, Switzerland) and the Hospital Clinic Research Ethics Committee (Barcelona, Spain). Country-specific protocols adapted to each context, though strictly following the methods described here, were approved by the Ethics Committee of the Public Health School of the University of Kinshasa (DRC), the Ethical Review Committee of the Ebonyi, Ondo and Niger States (Nigeria), the National Health Research and Ethics Committee (Nigeria), the Biomedical Research Ethics Committee of the Ministry of Public Health (Madagascar), the Institutional Bioethics Committee of the Centro en Investiçao em Saúde de Manhiça (Mozambique) and the National Health Research Ethics Committee (Mozambique).

The ethical issues described here are those related to the evaluation of the C-IPTp strategy and do not refer to the implementation of the C-IPTp strategy itself.

Written informed consent

It will be sought from all eligible participants. The interviewer will read the informed consent form to the participant and will ask her if she agrees to participate. Where local culture dictates, consent will be sought from household heads in addition. Inclusion of minors will

follow national guidelines at each project country and will require consent from parents/guardians and written assent from the participating minor. Participants will also be informed that a repeat interview may be conducted by a different person to ensure data quality (spot-checks). Women that decide not to participate after consenting will be immediately withdrawn from the study, and their data will be deleted from the project database and the interviewers' tablets.

Privacy

To ensure the privacy of the participant during the interview, the interviewer will ensure that no third party, including the head of the household, is nearby during the interview.

Data confidentiality

Individual participant data will be kept confidential and will not be shared with non-project staff. This will be emphasised to participants during the informed consent-seeking process.

Data management and storage

Personal identifying information will be confidential for both data collected electronically and on paper. In the first case, these variables— including GPS coordinates— will be marked as sensitive variables and protected in the data management application. Therefore, only those users with access to this application and with concrete permissions will have access to sensitive data. For the other users, this information will not be accessible. Moreover, data transferred through the internet will be codified. On the other hand, signed informed consent forms will be stored in a secure warehouse. Access to this warehouse will be restricted and controlled.

Dissemination

Regarding the dissemination of the results, the project partners will keep the WHO informed about project progress. The main findings will be also shared with other relevant stakeholders such as the Malaria in Pregnancy Working Group of the Roll Back Malaria. Results will also be shared in dissemination events, after each round of surveys, where MoH and district representatives will be invited. Findings will be prepared for publication following a publication plan which will be agreed with the partners. Peer-reviewed publications and conference presentations will be prepared. Media press releases aimed at the general public internationally and locally will be also prepared.

Patient and public involvement

Patients or the public will not be involved in the design, conduct, reporting or dissemination plans of this research.

DISCUSSION

This protocol describes in detail the methodology of a large-scale multicountry evaluation that has a huge potential to generate robust evidence to guide the development of malaria in pregnancy prevention policies. Of note, by working in four SSA countries, the conclusions of the final evaluation of the C-IPTp TIPTOP strategy might be easily applicable to other SSA areas.

In TIPTOP, community-based HHS will be used to evaluate C-IPTp in the SSA context. HHS are recommended by the WHO to assess coverage rates of malaria in pregnancy indicators at the community level.[27] The results of HHS will be comparable across areas and countries, since a standardised methodology will be followed. Additionally, the analysis will account for potential confounding factors since this information will be collected in the HHS questionnaires. Unlike indicators calculated through health routine monitoring systems, the HHS allow computing health indicators that are not partial or biased, since the denominators obtained through this community-level methodology are representative samples of the whole study population.

It is estimated that only 34% of pregnant women received three or more doses of IPTp in 2019 in Africa.[1] This figure is far from the optimal universal health coverage of the intervention. Data collected through the HHS will allow comparing study areas' estimates with up to date global, regional and country figures in order to interpret and contextualise the project results.

However, HHS have intrinsic limitations and possible bias to be considered prior to implementation. First, selection bias can occur if field teams are not able to obtain the best sampling frames possible. Non-response bias might also appear if a considerable number of eligible participants decline participation. Finally, information biases such as recall bias or interviewer bias might be of concern when questions asked to eligible participants are related to events far in the past, or if field interviewers are not well trained or do not interpret correctly the questions. To overcome these potential biases in TIPTOP, efforts have been put in obtaining the most precise sampling frames in the study areas, and comprehensive training programmes have been prepared for the interviewers. In addition, ANC cards will be asked to interviewed women, when available, to check self-reported collected information.

The HHS indicators will be used for the quasi-experimental evaluation of C-IPTp. This evaluation method is not as robust as a randomised controlled trial. However, this design was considered the most appropriate considering the overall project's aim, the characteristics of the intervention and the available resources. A cluster randomised controlled design would have implied to find uniform comparison groups (areas) in four African countries with high subnational heterogeneity. Instead, it was considered more efficient to purposely select the study areas mainly due to logistical and budgetary reasons. Besides, the involvement of the country's MoH in the project coordination was considered key and essential for its optimal success. Therefore, priority areas for each country government were selected. On the other hand, the quasi-experimental design will not allow evaluating a direct cause–effect of the intervention as it would have

been the case of an experimental trial. Regardless of this limitation, the present project has the prospect of providing evidence in relation to malaria in pregnancy prevention strategies and ANC attendance indicators at the community level, and C-IPTp performance, thus becoming the basis for future policy updates.

It is envisaged to submit the results of the project to the WHO Global Malaria Program Malaria Policy Advisory Committee (MPAC) within 6 months of its end. The ultimate objective of the project is to generate sufficient evidence for WHO to issue updated policy recommendations and inform MoH policies, in an effort to introduce the intervention strategy over the long-term across SSA countries.

Author affiliations
¹ISGlobal, Hospital Clínic - Universitat de Barcelona, Barcelona, Spain
²CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
³Jhpiego, Baltimore, Maryland, USA

Contributors Conceived and designed the study: CP-D, ML, FP, CM and RG. Gave inputs to protocol methodology: CP-D, ML, SS, MR, SM, ER, MT, FP, CM and RG. Wrote the first draft of the manuscript: CP-D and RG. Wrote and approved the paper: CP-D, ML, SS, MR, SM, ER, MT, FP, CM and RG.

Competing interests None declared.

Patient and public involvement statement Patients or the public will not be involved in the design, conduct, reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iD
Clara Pons-Duran http://orcid.org/0000-0002-9840-7559

REFERENCES
1 WHO. World malaria report. Geneva; 2020. https://www.who.int/publications/i/item/9789240015791
2 Dellicour S, Tatem AJ, Guerra CA, *et al*. Quantifying the number of pregnancies at risk of malaria in 2007: a demographic study. *PLoS Med* 2010;7:e1000221–10.
3 Menendez C, Mayor A. Congenital malaria: the least known consequence of malaria in pregnancy. *Semin Fetal Neonatal Med* 2007;12:207–13.
4 White NJ, Pukrittayakamee S, Hien TT. Malaria. *Lancet* 2014;38322:723–35.
5 Lawn JE, Blencowe H, Waiswa P, *et al*. Stillbirths: rates, risk factors, and acceleration towards 2030. *Lancet* 2016;387:587–603.
6 WHO. A strategic framework for malaria prevention and control during pregnancy in the African region. Brazzaville; 2004. http://www.gfmer.ch/SRH-Course-2010/assignments/pdf/Malaria-pregnancy-Ntirushwa-2010.pdf
7 WHO. Who policy brief for the implementation of intermittent preventive treatment of malaria in pregnancy. Geneva; 2014. http://www.who.int/malaria/publications/atoz/policy_brief_iptp_sp_policy_recommendation/en/
8 WHO. Updated WHO policy recommendation. Intermittent preventive treatment of malaria in pregnancy using Sulfadoxine- pyrimethamine (IPTp-SP) Global Malaria Programme; 2012.
9 WHO. Guidelines for the treatment of malaria. Geneva; 2015.
10 Sicuri E, Bardají A, Nhampossa T, *et al*. Cost-Effectiveness of intermittent preventive treatment of malaria in pregnancy in southern Mozambique. *PLoS One* 2010;5:e13407.
11 WHO. PROGRESS & IMPACT SERIES - The contribution of malaria control to maternal and newborn health. Geneva; 2014.
12 UNICEF. Antenatal care, 2019. Available: https://data.unicef.org/topic/maternal-health/antenatal-care/
13 WHO. WHO recommendations on antenatal care for a positive pregnancy experience. Geneva; 2016. http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/
14 TIPTOP. Advancing prevention of malaria in pregnancy. Available: https://www.tiptopmalaria.org/
15 Lehmann U, Sanders D. *Community health workers: what do we know about them?* Geneva, 2007.
16 Haines A, Sanders D, Lehmann U, *et al*. Achieving child survival goals: potential contribution of community health workers. *Lancet* 2007;369:2121–31.
17 Bojang KA, Akor F, Conteh L, *et al*. Two strategies for the delivery of IPTc in an area of seasonal malaria transmission in the Gambia: a randomised controlled trial. *PLoS Med* 2011;8:e1000409.
18 Greenwood B, Bojang K, Tagbor H, *et al*. Combining community case management and intermittent preventive treatment for malaria. *Trends Parasitol* 2011;27:477–80.
19 Tine RCK, Ndiaye P, Ndour CT, *et al*. Acceptability by community health workers in Senegal of combining community case management of malaria and seasonal malaria chemoprevention. *Malar J* 2013;12:467.
20 Okeibunor JC, Orji BC, Brieger W, *et al*. Preventing malaria in pregnancy through community-directed interventions: evidence from Akwa Ibom state, Nigeria. *Malar J* 2011;10:227.
21 Rogerson SJ, Desai M, Mayor A, *et al*. Burden, pathology, and costs of malaria in pregnancy: new developments for an old problem. *Lancet Infect Dis* 2018;18:e107–18.
22 Brieger WR, Tiendrebeogo J, Badolo O. *Community health workers can enhance coverage of intermittent preventive treatment of malaria in pregnancy and promote antenatal attendance (conference Abstract)*. ASTMH Annual Meeting, 2018.
23 WHO. *Immunization coverage cluster survey – reference manual*. Geneva, 2005.
24 The DHS program. Guidelines for sampling for the malaria indicator survey; 2016. http://malariasurveys.org/toolkitfiles/10 MIS Sampling Guidelines.pdf
25 Harris PA, Taylor R, Thielke R, *et al*. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.
26 Khandker S, Koolwal G, Samad H. *Handbook on impact evaluation: quantitative methods and practices*. Washington, D.C: Group TWB, 2009.
27 WHO. Malaria in pregnancy. Guidelines for measuring key monitoring and evaluation indicators. Geneva; 2007.