Technical consultation to assess evidence on community-based delivery of intermittent preventive treatment in pregnancy for malaria

Report of a virtual meeting
21–23 June 2022

World Health Organization

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This publication contains the report of a technical consultation to assess evidence on community-based delivery of intermittent preventive treatment in pregnancy for malaria and does not necessarily represent the decisions or policies of WHO.

Contents

ABBREVIATIONS

ANC	antenatal care
CHW	community health worker
CI	confidence interval
c-IPTp	community-based intermittent preventive treatment in pregnancy
DALY	disability-adjusted life-year (generic measure of health effect)
DHFR	dihydrofolate reductase (enzyme in malaria parasite)
DHPS	dihydropteroate synthase (enzyme in malaria parasite)
ICER	incremental cost-effectiveness ratio
IPTp	intermittent preventive treatment in pregnancy
FGD	focus group discussion
GMP	Global Malaria Programme
HMIS	health management information system
ISGlobal	Barcelona Institute for Global Health
ITN	insecticide-treated net
MMV	Medicines for Malaria Venture
NMCP	national malaria control programme
PMI	United States President's Malaria Initiative
PNLP	National Program for the Fight Against Malaria
SP	sulfadoxine–pyrimethamine
TBA	traditional birth attendant
TIPTOP	Transforming Intermittent Preventive Treatment for Optimal Pregnancy
WHO	World Health Organization

MEETING OBJECTIVES AND EXPECTED OUTCOMES

Presenter: **Silvia Schwarte**

Participants (Annex 1) in the meeting were:

- technical consultation expert members;
- country participants (from Burkina Faso, Democratic Republic of the Congo, Madagascar, Malawi, Mozambique, Nigeria, Senegal and Sierra Leone); some of these countries are participating in the Transforming Intermittent Preventive Treatment for Optimal Pregnancy (TIPTOP) project, and some are non-TIPTOP countries;
- representatives from Jhpiego, the Barcelona Institute for Global Health (ISGlobal) and Medicines for Malaria Venture (MMV), who were involved in the conduct of the TIPTOP study; and
- representatives from the United States Centers for Disease Control and Prevention; the United States Agency for International Development; the Bill and Melinda Gates Foundation; the Global Fund to Fight AIDS, Tuberculosis and Malaria; Unitaid; the World Health Organization (WHO) (Global Malaria Programme, Maternal and Perinatal Health, Child Health Development); WHO country offices; and the WHO Regional Office for Africa.

Silvia Schwarte provided a brief background on the burden of malaria in general and malaria in pregnancy. With regard to intermittent preventive treatment in pregnancy (IPTp), uptake of IPTp3+ (at least three doses of sulfadoxine–pyrimethamine (SP)) has been slow in the past 10 years, estimated at 32% in 2020 *(1)*. WHO guidelines changed in 2017, from four recommended antenatal care (ANC) visits to eight contacts during pregnancy. The TIPTOP project – the main study on community based IPTp (c-IPTP) – was designed before this change in ANC recommendations. WHO also changed its policy-making process around 2020, with a focus on two components: guidelines on *what* to do, based on a systematic review of the evidence (e.g. the best way to reduce adverse effects of malaria in pregnancy); and guidance on *how* to do it (e.g. to increase IPTp coverage), based on experiences and operational research. "Guidance" is a term reserved for operational manuals and information notes, based on programmatic consideration. In contrast to "guidelines", it is not necessarily based on a systematic review of the evidence.

As of 3 June 2022, the WHO IPTp guidelines state that, in malaria-endemic areas, pregnant women of all gravidities should be given antimalarial medicine at predetermined intervals to reduce disease burden in pregnancy, and adverse pregnancy and birth outcomes *(2)*.

- SP has been widely used for malaria chemoprevention during pregnancy and remains effective in improving key pregnancy outcomes.
- IPTp using SP (IPTp-SP) should start as early as possible in the second trimester and not before week 13 of pregnancy.
- Doses should be given at least 1 month apart, with the objective of ensuring that at least three doses are received.
- ANC contacts are an important platform for delivering IPTp. Where inequities in ANC service and reach exist, other delivery methods (such as the use of community health workers (CHWs)) may be explored, ensuring that ANC attendance is maintained and underlying inequities in ANC delivery are addressed.

- IPTp is generally highly cost-effective, widely accepted, feasible for delivery and justified by a large body of evidence generated over several decades.

The meeting objectives were to:

- assess the effectiveness and impact of c-IPTp on IPTp coverage and ANC attendance
  - review, discuss and assess the evidence generated in the context of the TIPTOP project
  - review, discuss and assess the evidence obtained from additional (non-TIPTOP) countries where c-IPTp was piloted;
- discuss molecular markers of SP resistance monitored in the TIPTOP project; and
- agree on best practice for implementation of c-IPTp, if proven successful.

Outcomes expected from the meeting were:

- determination of the impact of c-IPTp on IPTp coverage and ANC attendance;
- formulation of guidance for the implementation and scale-up of IPTp-SP through community-based delivery approaches, if proven successful; and
- development of a meeting report, with summary findings and results to serve as basis for an implementation guide or operational manual to guide the implementation and scale-up of c-IPTp.

After the meeting, a meeting report and operational guidance will be developed, and c-IPTp guidance will be presented in the Malaria Policy Advisory Group meeting (11–13 October 2022); it is planned to finalize and disseminate guidance end 2022.

All 10 Expert Members attending the meeting submitted their declarations of interest, which were assessed by the WHO Secretariat. One Member reported a conflict of interests, which was deemed to be not relevant to topics for decision on the agenda (Annex 2). A due diligence search was undertaken and found nothing significant that was not already declared the Expert Members.

TIPTOP OVERVIEW AND DATA SOURCES

Presenter: **Elaine Roman**

Elaine Roman presented an overview of TIPTOP, a 5-year multi-country project to support ministries of health in introducing, testing and expanding c-IPTp with quality-assured SP. TIPTOP aims to generate evidence, increase coverage of IPTp and increase demand for quality-assured SP. Community engagement and strong partnerships are important to set the stage for scale-up. The COVID-19 pandemic has had an impact on the project.

Around 2017, when the TIPTOP project started, there were many missed opportunities for IPTp3+ doses in the countries involved, as illustrated by the discrepancy between the number of women making at least four ANC visits and reporting to have received at least three doses of IPTp (e.g. in the Democratic Republic of the Congo, 47% and 11%, respectively). In addition, there was a market access problem, with no quality-assured SP manufactured in Africa, and there was a misconception that SP was a failed

medicine because of drug resistance. The TIPTOP project was designed to generate evidence on c-IPTp as a means to safely increase IPTp3+ coverage, create equitable access to SP, and set the stage for scale-up of community delivery of IPTp, if this approach was proven to be successful.

Partnerships are critical to success in the short and long terms. The consortium was led by Jhpiego, which implemented and managed the project, and included ISGlobal as a research partner. The two organizations collaborated closely with MMV to bring quality-assured SP to the market, and with WHO for technical guidance and for evidence review (MMV and WHO received separate enabling grants from Unitaid for this project). The ministries of health of the respective countries provided support at the community, facility, district and national levels. The project steering committee involved senior members among the consortium partners and representatives of the United States President's Malaria Initiative (PMI), the Global Fund, and the Bill and Melinda Gates Foundation. All these partners have a key role in supporting programming for malaria in pregnancy in Africa and may play a role in further expansion of c-IPTp after the project ends.

The project was implemented in the Democratic Republic of the Congo, Madagascar, Mozambique and Nigeria, which have some of highest burdens of malaria in Africa. The choice of countries was also influenced by governments committed to testing this strategy, with community programmes already in place, and existing low IPTp coverage. In addition, a diversity of settings was important for the final selection of countries.

The goal of the project was to reduce maternal and neonatal mortality by increasing IPTp3+ uptake to a minimum of 50% without decreasing use of ANC. There were four intended project outputs:

- demonstrated and fully implemented c-IPTp with quality-assured SP without reducing ANC attendance;
- improved supply of quality-assured SP and adapted packaging through the supply grant with MMV;
- an established environment that supports adoption of c-IPTp by ministries of health for policy, scale-up and sustainability; and
- development and dissemination of global recommendations and guidance for c-IPTp-SP delivery (following the project).

The TIPTOP approach aimed to increase the number of eligible pregnant women receiving IPTp by reaching them in the community where they live, complementing IPTp distribution through ANC. The project worked closely with nationally recognized CHWs in every country, who had been trained by their governments. CHWs were initially trained in c-IPTp and promotion of ANC. ANC providers were additionally trained in the c-IPTp approach. In Nigeria and the Democratic Republic of the Congo, CHWs could administer the first dose of SP if the pregnant woman felt fetal movements; in Madagascar and Mozambique, the first dose was given during an ANC visit, but subsequent doses could be given by the CHW. In Mozambique, the number of CHWs was low, and they served larger communities than in the other countries. With the help of the National Malaria Control Program and the Division of Reproductive Health in Mozambique, lay community counsellors were added to help identify pregnant women, promote IPTp, and refer women to ANC and CHWs. These lay community counsellors did not distribute IPTp. A key component of the programme was reinforcement of messages, in close collaboration with civil society organizations and community leaders, to mobilize communities and support information dissemination on malaria in pregnancy, c-IPTp and, at a later stage, COVID-19.

Setting the stage for scale-up of c-IPT involved a strong partnership between the consortium and the ministry of health in each country at all levels; health system strengthening, based on rapid facility assessments, and capacity-building and supervision of health-care facility workers and CHWs; community engagement using multiple channels; and continuous programme learning from evidence generated during programme implementation. Two virtual learning meetings were conducted during the project, focused on sharing and disseminating results, and sharing best practices and lessons learned. These meeting were attended by representatives from both TIPTOP and non-TIPTOP countries, relevant donors and other key malaria stakeholders.

The COVID-19 pandemic occurred during this project, and the TIPTOP project focused on supporting countries with continuity of care and the safety of health workers. Appropriate job aids were developed with the help of WHO on how to safely deliver c-IPTp. This guidance was adapted in the four countries, and the project was able to provide personal protective equipment so that staff could continue their work. The COVID-19 pandemic reinforced the importance of community engagement. Unexpectedly, the CHWs remained motivated and in service during the entire pandemic.

ISGlobal conducted the research component, which comprised household surveys, anthropological and cost-effectiveness studies, SP resistance monitoring (in collaboration with the Institut Pasteur for the molecular analysis), and an exploratory study on the acceptability of quality-assured SP and packaging of SP. Jhpiego evaluated the use of routine data for monitoring coverage in all countries and the reviews of maternity record books in Nigeria for this purpose.

Strengthening both CHW and ANC platforms is paramount for success – strengthening of either CHWs or ANC alone would not work. Partnerships are key for both short- and long-term success to drive momentum and ensure sustainability. Finally, a data-driven design set the stage for effective implementation and learning.

Questions and responses

- **The ANC visits in the TIPTOP countries as presented are rather low. Has anything been done to address this situation?**
  Response: These data were from 2017, and reflected at least four visits, but the number was still low.
- **Was a follow-up planned for when the study had stopped, and the support would fall away?**
  Response: A formal assessment after a couple of years was not planned. The hope is that other programmes (e.g. PMI) will support ministries of health to move forward

SESSION 1. TIPTOP PROJECT: HOUSEHOLD SURVEY RESULTS

Presenter: **Franco Pagnoni**

Franco Pagnoni presented the structure of data collection in TIPTOP using baseline, mid-term and final household surveys in test and expansion districts. The baseline survey was undertaken in the test district and the first expansion district, followed immediately by the intervention in the test district. After 1 year, a repeat survey was undertaken in the test district (the "midline survey") and another baseline survey in the first expansion district. A baseline survey was also conducted in the second expansion district. The intervention was continued in the test district after the midline survey, and

started in the first and second expansion districts after the baseline surveys. At endline, surveys were conducted in all districts (test, first expansion and second expansion districts).

The first surveys took place in early 2018, except in Mozambique where cyclone Idai delayed the surveys. The second series of surveys took place in the second half of 2019, and the last series in June–August 2021. Results for each district were shown for the coverage of IPTp3+ by country. In the Democratic Republic of the Congo, IPTp3+ in the test district increased from 21.8% at baseline to 61.9% at midline (slope 2.23 percentage points per month); however, between the midline and endline, the increase was more modest (61.9% at midline; 65.3% at endline; slope 0.16 percentage points per month). The increases in the first and second expansion areas were from 23.9% to 78.0% (slope 2.46 percentage points per month) and from 18.4% to 51.0% (slope 1.36 percentage points per month), respectively. The differences between baseline and endline were significant in each district in the Democratic Republic of the Congo.

IPTp3+ coverage in the Democratic Republic of the Congo, comparing baseline and endline in the three districts

Zone	Baseline	Endline	□	*P* value
Kenge	21.8	64.9	+198%	<0.0001
Bulungu	23.9	77.7	+225%	<0.0001
Kunda	18.4	51.1	+177%	<0.0001
Overall	21.2	65.2	+207%	<0.0001

Kenge: test district; Bulungu: first expansion district; Kunda: second expansion district.

Patterns were similar for Madagascar and Nigeria, with fast and significant increases in IPTp3+ coverage in each district after implementation of c-IPTp (slopes of 1.3–2.9 percentage points per month).

IPTp3+ coverage in Madagascar, comparing baseline and endline in the three districts

Zone	Baseline	Endline	□	*P* value
Mananjary	23.3	70.1	+201%	<0.0001
Toliary II	19.1	68.8	+261%	<0.0001
Vohipeno	36.6	84.1	+130%	<0.0001
Overall	27.9	74.9	+169%	<0.0001

Mananjary: test district; Toliary II: first expansion district; Vohipeno: second expansion district.

IPTp3+ coverage in Nigeria, comparing baseline and endline in the three districts

Zone	Baseline	Endline	□	*P* value
Ohaukwu	11.3	71.2	+533%	<0.0001
Akure South	10.2	56.5	+453%	<0.0001
Bosso	14.2	54.5	+284%	<0.0001
Overall	11.5	62.7	+448%	<0.0001

Ohaukwu: test district; Akure South: first expansion district; Bosso: second expansion district.

However, patterns were slightly different in Mozambique: baseline IPTp3+ coverage was significantly higher (45.0–63.3%), and only two of the three districts experienced a modest increase compared with baseline. Possible reasons for these differences were a different health system in Mozambique (e.g. low ratio of CHWs to people served compared with other countries, with a multitude of tasks) and contextual factors in districts (e.g. cyclone, security issues).

IPTp3+ coverage in Mozambique, comparing baseline and endline in the three districts

Zone	Baseline	Endline	□	*P* value
Nhamatanda	63.3	69.4	+9.6%	<0.01
Meconta	45.0	58.0	+28.8%	<0.001
Murrupula	49.1	48.7	-0.7%	NS
Overall	52.7	58.6	+11%	<0.0001

Nhamatanda: test district; Meconta: first expansion district; Murrupula: second expansion district.

The introduction of c-IPTp was associated with increases in ANC4+ (i.e. four or more ANC visits) coverage in two countries: the Democratic Republic of the Congo (an overall increase from 40.1% to 49.3%, with a non-significant increase in one district) and Madagascar (an overall increase from 44.8% to 66.2%, with a non-significant increase in one district). In Nigeria, the overall ANC4+ attendance showed no significant difference, changing from 69.2% to 68.4%, with mixed results in the three districts: a significant increase in the test district (67.1% to 74.9%), a non-significant decrease in the first expansion area (76.0% to 71.8%) and a significant decrease in the second expansion area (from 63.6% to 55.6%). Similar mixed results were seen in Mozambique, with a non-significant difference in overall ANC4+ attendance from 38.6% before introduction of c-IPTp to 37.1% after; this involved a non-significant decrease in the test district (from 64.6% to 60.2%), a significant increase in the first expansion area (from 23.0% to 34.5%) and a significant decrease in the second expansion area (from 26.1% to 17.6%). The absence of significant increase in Nigeria could be related to a high baseline coverage of ANC4+ (69%), with a potentially limited opportunity for further increases. The mixed results in Mozambique may be due to district-specific contextual factors.

Results were similar for ANC1+, with significant increases in the Democratic Republic of the Congo (from 89.0% to 94.5%) and Madagascar (from 85.8% to 94.2%), and no significant differences in Nigeria (from 91.1% to 92.4%) or Mozambique (from 91.5% to 92.8%).

The introduction of c-IPTp did not lead to an increase in early ANC attendance, defined as start of ANC visits before 14 weeks gestational age (Democratic Republic of the Congo: from 16.4% to 18.4%; Madagascar: no change, at 11.1%; Nigeria: from 25.1% to 25.8%; Mozambique: from 12.1% to 12.5%).

Some limitations were noted in the study design (ecological, non-controlled) and sites (purposely chosen, not being representative for the whole country). The impact of c-IPTp on IPTp coverage seemed to be higher in districts with lower baseline coverage of IPTp3+. In addition, c-IPTp shifted the distribution of the number of IPTp doses, with fewer women receiving zero doses, and a significantly higher mean number of IPTp doses per pregnant woman in each country (Democratic Republic of the Congo: from 1.3 at baseline to 2.7 at endline; Madagascar: from 1.5 to 3.4; Nigeria: from 0.8 to 3.0; Mozambique: from 2.6 to 2.8). Similarly, the number of women not attending ANC decreased in all countries, whereas the number of women who visited more frequently increased.

In conclusion, c-IPTp was associated with a dramatic reduction in the proportion of women not receiving any IPTp, an increase in the proportion of women receiving more doses of IPTp and an increase in the mean number of IPTp doses per pregnant woman. More modest increases were evident for ANC attendance: fewer women did not attend any ANC visits, and more women attended more frequently.

Questions and responses

- **What did the project do in the non-intervention areas when the intervention was started in the test area? Did TIPTOP promote ANC attendance in these areas using CHWs, or engage in a community effort to increase ANC attendance? Were there differences between countries in these non-intervention areas?**
  Responses: During the non-intervention phase in the first expansion district, there was no active promotion of ANC. Training of CHWs for the implementation phase was conducted during the implementation phase and not in advance. However, a general introduction about the programme was provided to community leaders to prepare them before implementation.

- **Were the data on IPTp dose derived from interviews or corroborated with ANC card information?**
  Response: The data on IPTp dose were from both interviews and ANC cards.

- **What proportion of women had eight or more visits/contacts?**
  Response: This information is available in the report. Comparing baseline and endline, this changed from 4.4% to 7.0% in the Democratic Republic of the Congo, from 5.3% to 21.7% in Madagascar, from 23.0% to 34.9% in Nigeria and from 1.7% to 2.1% in Mozambique. Note that, when the project started, eight or more ANC visits had not yet been adopted as a WHO guideline (this occurred in 2017); countries adopted this strategy at different times.

- **Can you disaggregate the data on ANC visits that were made in the third trimester? Third-trimester visits have been associated with reduced perinatal morbidity and mortality.**
  Response: The available data do not allow assessment of the proportion of ANC visits that were made in the third trimester.

- **What went into the implementation of c-IPTp apart from training CHWs, to ensure that pregnant women were sufficiently motivated?**
  Response: Besides reorienting the ANC providers and the CHWs, the project worked with national governments, district teams and community leaders to determine how to roll the intervention out in the context of each country. The CHWs involved were selected by the communities, which provided a sense of ownership of the programme from the beginning. CHWs were trained and supervised by ANC providers; this included monthly meetings at the health-care facilities for resupply of SP and data reporting. Documentation of IPTp was very important; ANC providers and CHWs knew when pregnant women were eligible for IPTp through adapted ANC books that were used to track doses administered by both CHWs and ANC providers. Supplementary data collection and reporting systems were established to routinely track and report c-IPTp use. Existing data systems were used as much as possible, together with supplementary data collection for community-based distribution of SP.

- **Was there an intervention to ensure sufficient SP supplies in the facilities during the study?**
  Response: Yes, the project procured the SP needed for the communities and a 10% buffer stock for each facility, which resulted in a low number of short-lived stockouts.

- **Did the pregnant women visit the CHW or did the CHW visit the pregnant woman?**
  Response: The CHW usually identified the pregnant women and visited them. However, pregnant women could also reach out to the CHW.

- **Would it be possible from your household surveys to identify whether specific groups are benefiting from c-IPTp?**
  Response: Yes, we will present these other data at a later stage (we focused in the first part of the project on IPTp coverage).

- **Was there any monitoring of SP resistance in the sites?**
  Response: Yes, these data will be presented later. This was conducted in one intervention district and one control district in each of the four project countries.

SESSION 2. TIPTOP PROJECT: ROUTINE MONITORING

Presenter: **Christina Maly**

Christina Maly presented on behalf of the four monitoring and evaluation country teams on how routine monitoring data were used to track progress of the project. The project collaborated with ministries of health and leveraged existing data systems. Supplementary data collection was only used when it was critical for monitoring implementation of c-IPTp. There was a focus on data quality and use of data at all levels, from community to national levels (e.g. through technical working groups). Indicators such as ANC1, ANC4 and IPTp coverage were primarily obtained from the country's health management information system (HMIS). In Mozambique, where a cohort system is used to register ANC data, a supplementary summary form for collecting information on key indicators was used to enable comparison with other countries. In Madagascar, a supplementary form was used to track data on early ANC attendance. The national bureau of statistics or the district health authority provided estimates of the number of pregnant women in the study districts. The coverage of c-IPTp was obtained from TIPTOP CHW monthly registers and summary forms.

During the course of the project, WHO changed the recommendations on tracking IPTp coverage from using ANC1 attendance as the denominator to using an estimate of the number of pregnant women in the population as the denominator. The project made that shift as well. However, there were some challenges. The estimated number of pregnant women is not always up to date. In Madagascar, data from 2017–2018 were available, whereas, in the Democratic Republic of the Congo, the most recent census was in 1984. There may be issues with precision, but the more constant denominator improved the accuracy for monitoring trends.

Trends in ANC1, ANC4 and IPTp3 were shown for each country from early 2017 to early 2022. The data before and after implementation were not fully comparable, because the project included several interventions that focused on improving data quality, so the quality of data may have been greater after implementation began.

- In the Democratic Republic of the Congo, the introduction of c-IPTp led to a peak in ANC1, followed by a decrease (but not to the same level as before) and then a more gradual increase over time in the test district. IPTp3 and ANC4 showed more gradual increases. The same pattern was seen in the expansion districts; however, this was interrupted by a health worker strike, resulting in a temporary drop in all indicators.

- In Madagascar, a similar pattern was seen initially in the test district; however, after about a year, the indicators increased in the test district, whereas increases were more gradual in the expansion districts.

- For Mozambique, no data were available pre-implementation because of the cohort system used. IPTp3 and ANC4 increased gradually over time. ANC4 was at a higher level than ANC1, because ANC4 was provided as ANC4+ (including

ANC4, ANC5, ANC6 and so on). However, the gaps are closing between ANC1 and ANC4 – this was also seen in the other countries.

- In Nigeria, IPTp3 was not separately registered but grouped with IPTp3+. This made it difficult to look for trends, so the data collection system was altered to isolate IPTp3. In the test district, indicators decreased as a result of communal clashes after an initial rise after implementation. In the expansion districts, ANC1 and IPTp3 increased, but ANC4 decreased after an initial peak.

Where women received their third dose varied widely by district and country.

- In the test district in the Democratic Republic of the Congo, CHWs initially dispensed most doses, but this changed gradually over time to ANC providers. In the expansion districts, ANC providers dispensed most SP doses.
- In Madagascar, women initially received more doses from CHWs than from ANC providers. This was corrected by emphasizing to CHWs the importance of ANC visits under the TIPTOP project. In the expansion districts, the contribution of CHWs varied.
- In Mozambique, an increasing contribution of CHWs in delivering IPTp could be seen over time across all districts. The test district was affected both by a cyclone and by security issues that resulted in low access to health-care facilities.
- In Nigeria, only data on IPTp3+ were available, with a massive increase in all districts. A large contribution of CHWs was noted in the test district, and a smaller contribution in the expansion districts.

The introduction of c-IPTp affected the cascade of IPTp. The first dose of IPTp increased regardless of who gave the first dose; CHWs were able to give the first dose in the Democratic Republic of the Congo and Nigeria, and ANC providers in Madagascar and Mozambique. Doses 1–4 increased across all districts after implementation of c-IPTp, but gaps persisted in some districts.

- In the Democratic Republic of the Congo, there was an initial sharp increase in all doses – especially dose 1 – which levelled off over the years at a higher level than before introduction of c-IPTp, with smaller gaps between the doses. The changed eligibility for SP (starting from 13 weeks gestational age or fetal movement) was not yet updated in the HMIS to reflect that pregnant women could receive more than four doses.
- In Madagascar, information by dose was only available after implementation of c-IPTp. There was a gradual increase for all doses. All IPTp4+ doses were grouped together as IPTp4.
- In Mozambique, data were only available from the time of project implementation, showing more modest increases in IPTp doses.
- In Nigeria, data were available before and after implementation of c-IPTp, and the increases were more dramatic. As in Madagascar, IPTp4+ doses were grouped with IPTp4. After a sharp initial increase, there was a more gradual increase in the implementation districts, but not in the test district.

The routine data suggested that c-IPTp has not had a negative impact on early ANC initiation.

- In the Democratic Republic of the Congo, early ANC attendance was defined as an ANC visit before 16 weeks gestational age. Early ANC visits increased in all districts after implementation of c-IPTp, especially in the later months of the project.

- In Madagascar, early ANC attendance was defined as a visit before 14 weeks. In all districts, there was a modest increase in early ANC visits; increases were larger in the expansion districts.
- In Mozambique, an early ANC visit was defined as a visit before 12 weeks gestational age. No data on early visits were available before implementation of c-IPTP. A modest increase in early visits over time was seen in the test district, and a larger increase in the expansion district.
- In Nigeria, early ANC was defined as a visit before 20 weeks gestational age. There was no clear change in this indicator during the project.

Overall, the routine data show similar findings to the household surveys: c-IPTP improved overall IPTp coverage without a negative impact on ANC use. Most routine data to monitor c-IPTp were available from the national HMIS; only minor adaptations were needed, and these were acceptable to the ministries of health. Challenges included inaccurate population estimates, and an inconsistency between policy and HMIS indicators. Routine data quality assessments and data review meetings were institutionalized for review and use of IPTp data. Routine data can and should be used to inform approaches to reach pregnant women with IPTp.

Questions and responses

- **Is it correct that there was no difference if the first dose was started by ANC providers or CHWs? How was this decision made; what were the reasons for this?**
  Response: The routine data showed no difference in coverage according to who gives the first IPTp dose. The decision was based on ministry of health preference in each country.
- **What problems did you find with using routine data, and how did you manage to solve them?**
  Response: Before implementation, rapid facility assessments were done for all the facilities involved, which included routine data quality assessment. The routine data quality improved over time. The type of problems encountered were quite typical – for example, overreporting and underreporting of some indicators, because of high workloads and inefficient tracking mechanisms (registers). This was addressed by conducting routine data quality assessments, once every 6 months in conjunction with the ministry of health, which resulted in action plans and supervisory visits. We adapted the measure evaluation tool, which was a standard tool for that purpose. The more people look at data, the more they may develop questions about the data; they may become aware that the data have meaning and purpose, and can also contribute to improvements in the system.
- **There were challenges in estimating the number of pregnant women, and some countries changed the denominator during the study. What are the lessons to be learned from this?**
  Response: In our countries, the assumption about the rate of pregnant women varied between 4% and 5%. However, census dates ranged from 1984 to 2017, and some countries conducted a census during the project. Lessons include: know your data sources, talk with the people who know best, and know your limitations. Routine data will be used after the TIPTOP project ends, so we have to evaluate these data. We can learn from the immunization community about this because they face similar challenges when calculating immunization coverage. WHO has a useful "How to" guideline discussing these limitations and problems with denominators *(3)*.

- **How do you promote quality of data in these countries after the project ends? Were the CHWs chosen by the communities involved in the health worker strikes?**
  Response: Even when the ANC health workers were on strike, the CHWs continued to distribute SP, as long as they had SP available (they were restocked by the ANC providers). We had relatively low attrition of CHWs, although some countries have limits on the duration of service of CHWs. Overall, CHWs remained engaged during strikes and security issues. With regard to data quality, it is not clear what will happen after the project. Usually, there is some loss in data quality and rigour in the move from a small project to scale. Since the system built by the TIPTOP project was part of institutionalized data collection, it will likely be sustained in the project districts. There is a need for investments and resources to assure data quality.

- **Did CHWs provide SP at women's homes or in the ANC setting? How did you measure impact of c-IPTP?**
  Response: The CHWs went to women's homes and provided SP; sometimes pregnant women went to the home of the CHW for SP. Overall trends for IPTp coverage showed a meaningful increase without negative impacts on ANC attendance.

- **Was the dose delivered by the CHW recorded on the ANC card?**
  Response: Yes, doses given by CHWs were reported in the ANC card and in the CHW records.

- **In the cascade graphs of some countries, the IPTp doses and lines were messy, with IPTp2 higher than IPT1 in some countries.**
  Response: Information in the cascade graphs for dose could be noisy, with doses 1–4 not in the expected order. In all countries, IPTp doses 1–3 were categorized, but doses >3 were reported in heterogeneous ways. When IPTp2 was higher than IPTp1, this was clearly a data quality issue. This was particularly challenging in Mozambique, where the project had to move from a cohort approach to a monthly dose system.

- **How do you measure IPTp3 coming from the CHW or ANC provider, if the doses given can be delivered by both CHWs and ANC providers?**
  Response: IPTp doses were reported in monthly summary forms disaggregated by dose and distribution point – ANC or CHW. As the routine monitoring data are collected, reported, analysed and used by month, in any given month reviewing IPTp3 doses distributed will be a very close proxy to analysing the number of pregnant women receiving a third dose (as per WHO policy, a pregnant woman should only receive one dose per month).

- **Were some of the reporting tools digitalized and used at the community level?**
  Response: In Madagascar and Nigeria, CHWs used mobile phones for some data collection. In Nigeria, there was a pilot for a community HMIS module for c-IPTp, as well as other community-based interventions. These approaches were implemented if there was interest and support from the ministry of health.

- **Was cIPTp combined with community malaria treatment for the CHWs involved?**
  Response: No, CHWs involved in this project were not treating clinical malaria episodes, but they were trained to refer.

- **Was cost of ANC visit removed? In many countries, ANC visits are subject to user fees. Did a system like that exist in any of the TIPTOP countries?**
  Response: TIPTOP did not change if there was a fee associated with ANC. In most districts, ANC was free. SP was always provided for free by the TIPTOP project.

SESSION 3. C-IPTP: LITERATURE REVIEW

Presenter: **Anna Maria van Eijk**

Anna Maria van Eijk presented data on c-IPTp based on a review of the literature. Uptake of IPTp2+ was slow during the first 10 years of the IPTp SP policy. This has also been the case for IPTp3+ in the past 10 years. Many articles have been devoted to factors associated with IPTp uptake, including stockouts, user fees, confusing guidelines at the general health-care level, poor organization, overburdened staff, lack of directly observed therapy, prescription of SP at the health-care facility level, confusion on timing of first dose, lack of training/retraining/supervision, perception of low efficacy of SP because of drug resistance at the health-care provider level, poor or late attendance of ANC and distrust of SP by pregnant women.

Higher rates of IPTp uptake are associated with higher maternal education or education of the husband, higher maternal employment, better knowledge about malaria in pregnancy, higher socioeconomic status, higher parity, proximity to a health-care facility, urban residence, being married, having health insurance and being exposed to media messages *(4, 5)*. Some of the issues with IPTp uptake may be mitigated by c-IPTp, which may reduce travel distances, and costs and time spent at ANC for the pregnant woman. As well, pregnant women may receive more personalized attention and receive ANC services earlier, and workload for ANC staff may be reduced. However, c-IPTp also has its own set of requirements: CHWs need training and supervision, and incentives for motivation, and supplies need to be restocked. CHWs need to be accepted by the community as caregivers and medicine suppliers. And c-IPTp may be perceived by pregnant women as a replacement for ANC and lead to reduced ANC attendance.

A literature search on studies that reported on c-IPTp and results for IPTp coverage and ANC attendance identified seven studies, conducted between 2002 and 2020. Five were quasi-experimental (of which two were cluster adjusted), and two were cluster randomized trials. In the cluster randomized trials, the first dose of SP was delivered at the ANC visit. In one study in Uganda, a parallel system was set up with little interaction between CHWs and ANC providers. In studies with information before and after intervention, the risk difference for IPTp2+ ranged from –15 to 57% (five studies); for IPTp3+, from 11% to 21% (two studies); and, for ANC4+, from 10% to 19% (three studies). In studies with information on intervention and control areas, the risk difference for IPTp2+ ranged from –1% to 55% (seven studies); for IPTp3+, from 6% to 45% (three studies), and, for ANC4+, from –19 to 24% (four studies). Two studies out of seven showed a decrease in ANC visits. Two studies reported that they did not see adverse events when using c-IPTp. One study noted that women who lived further away from the ANC were more likely to receive IPTp3+ in the intervention arm than in the control arm. Another study noted that health-care facilities were attended by a higher proportion of primigravidae and adolescents. Finally, a cluster randomized trial in which CHWs promoted ANC visits reported IPTp and ANC coverage that were in line with c-IPTp. In conclusion, IPTp generally increased after c-IPTp but did not do so in all settings, and a decrease in ANC visits was not common when c-IPTp was implemented.

Questions and responses

- **Was ANC promoted in the control area?**
  Response: ANC promotion is well described in the control arm of the studies by Dr Gutman et al. *(6)*, Dr Rubenstein et al. *(7)*, and in the study by Dr Msyamboza et al. *(8)*, but not in the other studies. A decrease in ANC visits was not common and was seen in the two earliest studies.

SESSION 4. EXPERIENCES FROM NON-TIPTOP COUNTRIES WITH C-IPTP: SUCCESSES AND CHALLENGES IN BURKINA FASO, SENEGAL, MALAWI AND SIERRA LEONE

Burkina Faso

Presenter: **Yacouba Nombre**

Yacouba Nombre gave a presentation on behalf of his colleague Gauthier Tougri on the c-IPTp pilot project in Burkina Faso, conducted in 2017–2018, to assess the impact of c-IPTp on IPTp and ANC coverage.

ANC visits in Burkina Faso are free, but women often come late because of security issues or geographical difficulties. In 2019–2020, the national coverage was around 35–40% for ANC4 and around 55–60% for IPTp3. There are about 17 669 CHWs in Burkina Faso, who are paid 20 000 West African CFA francs (corresponding to about US$ 35 per month), and trained in a package of preventive (including IPTp), promotional, curative and supportive activities.

In the pilot project, CHWs were trained in providing IPTp from the second dose onwards, following the first dose given at the ANC visit. The first dose at ANC was given if the woman was >16 weeks pregnant, with a fundal height >9 cm. For the 2-year pilot study, CHWs were recruited with a preference for females; they were trained in provision of IPTp and data recording, and supervision was provided by health-care facility staff and the malaria control programme. SP was available throughout the study. CHWs visited the pregnant woman at home for follow-up doses of SP. The pilot study was conducted in six intervention areas and compared with six control areas where IPTp was only available through routine ANC visits. Forty-eight health-care facility workers and 407 CHWs were involved.

In the Po district, IPTp3 increased from 35% to 44%, whereas in the control area it remained around 24%. ANC4 visits increased from 40% to 47% in the intervention area and from 48% to 60% in the control area. IPTp3 increased from the beginning of the intervention compared with the control area, and the majority of doses were given by CHWs. IPTp4 also increased in the intervention area. The programme had no stockouts of SP, was well received and accepted by the community, and increased the proportion of women with four ANC visits and four IPTp doses.

Limitations were the limited resources for supervision, insecurity in the areas involved, the absence of a cost-effectiveness analysis or a study on the impact of the intervention on clinical episodes for pregnant women, and the absence of an alternative option in case of SP allergy. Challenges included maintenance of effective supervision; follow-up of pregnant women referred to ANC by the CHW, particularly in areas with security issues; irregular payment of CHWs, which negatively impacted motivation and the quality of the intervention; and issues with expansion and sustainability of the approach. Key conditions for success were the availability of SP, the ability to effectively monitor and supervise the strategy on the ground, and the safety and accessibility of the areas involved.

In conclusion, with the contribution of CHWs and communities, the intervention led to an increase in IPTp3 and IPTp4 in the intervention area. In some regions, there was room for improvement to recruit more female CHWs.

The study described here has been published by Gutman et al. *(6)*.

Questions and responses

- **Has the project continued? If not, do you think it should continue?**
  Response: The intervention could not be continued after 2018 because of insufficient financial resources and security issues. Additionally, new CHWs were recruited who were not familiar with this intervention. However, an extension is included in the strategic plan for 2021–2025.

- **Are the evaluation data from surveys or from routine data?**
  Response: Evaluation data are from baseline and endline household surveys.

Malawi

Presenter: **John Munthali**

John Munthali presented the c-IPTp study conducted in Malawi. Factors that have been associated with low ANC attendance include distance to the health-care facility, transport costs, user fees, knowledge and attitudes of the pregnant woman, and facility-level factors (e.g. no SP available, low health worker performance, poor documentation of SP doses). Malawi became the first country to adopt IPTp-SP in 1993. In 2017, there was 40% coverage of IPTp3+ and 50% coverage of ANC4+. In 2019, the ANC guidelines were updated to recommend eight ANC contacts.

To assess how IPTp uptake and ANC attendance can be improved, Malawi conducted a cluster randomized trial between 2017 and 2020 comparing c-IPTp in addition to routine IPTp at ANC versus routine IPTp at ANC only. Primary study outcomes were IPTp3+ and ANC4+. The study was conducted in 20 health-care facility catchment areas of the Ntcheu and Nkhata Bay districts. Cross-sectional household surveys were conducted at baseline (December 2017; n = 370) and endline (August 2020; n = 687); the intervention lasted from early 2019 to August 2020. Women aged 16–49 years who had a pregnancy resulting in a live birth in the previous 12 months were interviewed. Data were analysed using a difference-in-difference model to estimate crude and adjusted intervention effects (adjusted for gravidity, maternal age and maternal education). Overall, all doses of IPTp increased during the study period (across both arms): IPTp3+ increased from 50% to 66% and IPTp4+ from 13.1% to 27.8%. The intervention effect (taking the baseline and control area findings into account) was 6.9% for IPTp3+ (95% confidence interval (CI): –5.9% to 19.6%), with a P value of 0.29 for the crude estimate and 0.19 for the adjusted estimate. IPTp1+ increased from 83.0% to 93.3% in the intervention arm, with an intervention effect of 13.5% (95% CI: 4.7% to 22.3%; $P < 0.01$ for crude estimate; $P = 0.01$ for adjusted estimate). In further analyses, it appeared that few women received IPTp from CHWs; the vast majority received IPTp at ANC visits. Although more than 80% of women make three or more ANC visits, ANC4+ visits were around 50% (ANC5+ around 14%), showing that ANC visits drop off after three visits. ANC4+ visits increased from 46.9% to 56.8% in the intervention arm, with an intervention effect of 25.3% (95% CI: 1.3% to 49.3%; $P = 0.04$ for crude estimate and adjusted estimate). Women in the intervention area did start ANC significantly earlier than those in the control area: the mean gestational age at first ANC visit decreased from 21.2 weeks to 20.4 weeks, with an intervention effect of –2.5 weeks (95% CI: –3.7 to –1.4 weeks; $P < 0.0001$ for crude estimate and adjusted estimate). Analysis of CHW records showed that CHW follow-up visits were infrequent, and CHWs spent most of their time accompanying the pregnant woman to the first ANC visit. From the household surveys, it appeared that CHWs were rated less favourably than ANC health workers, with ANC health workers perceived as being more knowledgeable and showing more respect.

In summary, the IPTp3+ coverage in these districts was quite high to start, and the interventions did not have the intended effect on IPTp3+. However, there was a beneficial effect on ANC outcomes. No stockouts of SP occurred during the study.

Follow-up visits by CHWs were infrequent. Challenges were travel distances for CHWs, high work burdens for CHWs with competing priorities, the high need for supervision of CHWs and problems with data entry in registries. The ratio of CHWs to population was about 1:1945 in Ntcheu and 1:1150 in Nkhata Bay. Some operational issues to be considered for scaling up of c-IPT include the role of Community Health Advisory Groups in supporting the CHWs, the need for CHW follow-up of pregnant women at home if they did not present at scheduled visits, the transition from supportive supervision and mentorship to senior village health workers, and elaboration of strategies to identify women early in pregnancy. Before new strategies are put in place, a more in-depth assessment is needed of the relatively low delivery of IPTp by CHWs, to better understand operational issues and the workload of CHWs.

The study described here has been published by Rubenstein et al. *(7)*.

Questions and responses

- **Did c-IPTp increase IPTp3+?**
  Response: There was an increase, but it was not statistically significant.
- **Was there a difference in proportion of women who did not any receive dose of SP (0 dose)?**
  Response: This is not currently known. In the article by Rubenstein et al. (2022; Table 3), IPTp1+ increased from 83.0% to 93.3% in the intervention arm, with an intervention effect of 13.5% (95% CI: 4.7% to 22.3%; $P < 0.01$ for crude estimate; $P = 0.01$ for adjusted estimate).

Senegal

Presenter: **Seynabou Gaye**

Seynabou Gaye presented data from Senegal, where the national policy of three doses of IPTp was adopted in 2016. The WHO eight-contact guidelines for ANC are currently integrated in the policy, but the primary collection tools have not yet been updated. There are two types of CHW: community care workers, and community prevention and promotion agents. They receive 4 days of training at the district level, and a practical period of 15 days at the health post with which they will collaborate. CHWs are volunteers, but they receive an incentive per visit for certain activities. At a national level, between 2016 and 2021, IPTp3 increased from 45% to 65%.

SP is free of charge for pregnant women. National and regional pharmacies store SP and distribute it to the districts (health centre, health post, health huts and home care providers), and SP is kept at room temperature. The supply of SP is well integrated in the national health system. CHWs are supervised weekly by the community supervisor, monthly by the chief of the health unit and quarterly by the district health management team. Educational supervision of CHWs is provided by nurses, midwives and the district teams. Early identification of pregnant women, including adolescents, in the community is conducted by a village committee, with personalized follow-up throughout pregnancy and after delivery by CHWs. CHWs are informed either by the midwife at the health post or by the community committee about pregnant women.

The study was implemented in 15 districts with low IPTp3 coverage, with the first dose to be given at the ANC visit. Home visits are made as part of the PECADOM+ strategy. As well as being supervised, CHWs are supported by the community supervisors within the framework of PECADOM+ and by members of the village committee. Supervisors were trained at the start of the implementation on the strategic approach of c-IPTp, the roles and responsibilities of the different actors, pharmacovigilance elements,

and monitoring and evaluation tools. The c-ITPp approach was implemented in the southern area of Senegal, starting in 2020. During the 2 years of the programme in the 15 districts involved, the ANC completion rate (at least four visits) remained similar, at an average of 55.6% in 2020 and 58.3% in 2021, whereas IPTp3 increased from an average of 48.7% in 2019 to 55.9% in 2020 and 62.9% in 2021. In all 15 districts, there has been an increase in ANC1+ visits, IPTp1, IPTp2, IPTp3 and IPTp4+ in 2020 and 2021, compared with 2019.

Strengths of the programme included community ownership, improved access to care and adherence to guidelines. The collaboration with village leaders and women leaders was very important in enabling the programme to reach a large number of women for IPTp and promotion of ANC visits. The c-IPTp approach strengthened the credibility of CHWs, and the acceptability of, and adherence to, IPTp-SP for pregnant women. The strategy was well suited for areas with difficult access and high levels of poverty.

Challenges were the need for a consistent supply of commodities, regular supervision and adequate funding. Key requirements for c-IPTp include constant supply of SP, regular supervision by qualified health-care facility staff and stability of funding. A small incentive payment to CHWs for home visits was essential for their motivation. In conclusion, c-IPTp was well received by the communities, health post nurses and the district management teams, and may contribute to a significant decrease in the burden of malaria in pregnancy and an increase in ANC attendance.

Questions and responses

- **Can you explain the name PECADOM+?**
  Response: PECADOM stands for "prise en charge à domicile", which can be translated as "home-based case management". The programme started in 2008 with home-based malaria case management, involving rapid diagnostic tests and artemisinin-based combination therapy. In 2013, a variation named PECADOM+ was piloted by Peace Corps volunteers and the Saraya District (Kédougou region). In this approach, CHWs (called DSDOMs or "dispensateur de soins à domicile") visited each household in their communities weekly during the malaria high-transmission season (July–December) to identify and test any fever cases, and treat or refer any cases of malaria among all age groups, and diarrhoea or acute respiratory illness among children under 5 years of age. The PECADOM+ strategy was adopted by the National Malaria Control Programme (NMCP) in 2014 and scaled up to four regions (Kédougou, Kolda, Sédhiou and Tambacounda), comprising 708 villages in 16 districts, by 2016. It has now expanded to a total of 35 districts with PMI support. The package has been further extended and now includes deworming, vitamin A supplementation and identification of children who are late for immunizations. Currently PECADOM+ is being implemented by 1944 DSDOMs monitored by 560 community supervisors *(9)*.

- **Did you receive reports on any side effects of SP?**
  Response: The first dose of SP is given at the ANC visit, where allergies to sulfonamides can be assessed and SP can be given under direct observation. No severe adverse events have been reported by CHWs; only mild adverse events were noted.

Sierra Leone

Presenter: **Wani Kumba Lahai**

Wani Kumba Lahai presented the experiences in Sierra Leone. Malaria is endemic, with stable and perennial transmission throughout the year. Pregnant women and children under 5 years of age are at higher risk of malaria. In 2017, Sierra Leone adopted the policy of a minimum of three doses of SP for IPTp, as recommended by WHO. IPTp-SP is delivered free both at health-care facilities and in communities by traditional birth attendants (TBAs, until 2020) and CHWs (from 2017). In May–June 2018, a total of 1814 TBAs (all female) were trained nationwide in IPTp3 administration. The training was conducted for 5 days; it included home visits and promotion of insecticide-treated nets (ITNs) among pregnant women. The Ministry of Health and Sanitation (MoHS) developed and implemented two national CHW policies (2012-2016 and revised for 2016- 2020). The updated 2021 national CHW policy incorporates the recommendations from assessments and lessons learned from implementation of the 2016 policy, under which 15 000 CHWs were trained. These recommendations included improved management and support for CHWs to improve the provision of preventive, promotive and basic curative services at people's doorsteps. The Ministry of Health and Sanitation is committed to the effective operationalization of the 2021 national CHW policy to realize the vision for human capital development in Sierra Leone.

National-level data on ANC coverage showed that ANC1+ decreased from 89% in 2016 to 78% in 2020; in the same period, ANC4+ decreased from 66% to 57%. National-level data on IPTp showed that IPTp3+ increased from 31% in 2016 to 52% in 2021. Under the 2021 national CHW policy, some TBAs have been recruited as CHWs to deliver c-IPTp. Currently, 8700 CHWs are undergoing training nationwide. The first phase of training in eight districts has been completed. CHWs receive training in community profiling and surveillance (Module 1, 6 days); malaria, pneumonia, diarrhoea and malnutrition (Module 2, 6 days); reproductive, maternal and newborn child health (Module 3, 6 days) and peer supervision (Module 4, 2 days). Funding has been secured from GAVI, PMI and the Global Fund. CHWs take pregnant women to the health-care facility for the first dose of IPTp. The second and third doses can be administered by CHWs in their communities. CHWs submit monthly reports to the health-care facilities, and summary data are reported using health-care facility community intervention reporting forms. In easy-to-reach areas (3–5 km radius), CHWs take care of about 100–170 households (500–1000 people) and provide all services under their scope of work. In hard-to-reach areas (>5 km away or 3–5 km with difficult terrain), CHWs take care of about 50–60 households (300–350 people) and provide all services under their scope of work, as well as integrated community case management and nutrition services. CHWs (or TBAs) distributed 3.6% of the third doses of IPTp in 2017, 7.2% in 2018, 10.5% in 2019 and 9.1% in 2020. There is a wide range of IPTp3 coverage among the districts, ranging from 31.2% in Western Area Rural to 83.6% in Kambia (data from Sierra Leone Malaria Indicator Survey 2021).

A strength of the system is that experiences to date are guiding the updated CHW policy. TBAs contributed about 10% to IPTp3 in 2019–2020. CHWs were recommended by community stakeholders and stayed in the communities: they showed willingness and commitment to work. The CHW programme is within the directorate of primary health care, and coordinates all support for, and activities of, CHWs. Multiple partners support the programme, and this has led to high coverage of IPTp3 in 2021, despite decreasing ANC attendance.

Challenges include the irregular payment of incentives and the irregular supply of SP. IPTp3 is mostly recorded as aggregated data under IPTp3+, which includes IPTp4, IPTp5 and so on. There is inadequate supportive supervision from districts (district health management team, primary health unit) to the community and limited mobility support. There are more male than female CHWs (because of education requirements), and there is a high attrition rate.

In conclusion, CHWs are contributing positively to IPTp and ITN coverage, and promote early referral of pregnant women for ANC services. The government should increase support to the CHW programme.

Questions and responses

- **Is there an impact on ANC attendance?**
  Response: National-level data on ANC coverage showed that ANC1+ decreased from 89% in 2016 to 78% in 2020; ANC4+ decreased from 66% to 57% in the same period. National-level data on IPTp showed that IPTp3+ increased from 31% in 2016 to 52% in 2021. Note that the COVID-19 pandemic may have affected ANC attendance from 2020 onwards.

- **What other health promotion or preventive activities do TBAs and CHWs undertake in Sierra Leone?**
  Response: Health promotion and preventive functions provided by CHWs in Sierra Leone include home visits to promote ITN use, sensitize people on local food intake, recognize danger signs in pregnancy and refer pregnant women to health-care facilities.

- **Do you have information on the distribution of ITNs at health-care facilities or by the TBAs/CHWs in the community?**
  Response: Routinely, ITN distribution is done at health-care facilities (during ANC contact) and during outreach campaigns by health workers. During mass campaigns, ITNS are distributed to every household every 3 years, giving one ITN for every two people in a household, to a maximum of three ITNs in a household of six people.

SESSION 5. ANTHROPOLOGICAL STUDY FINDINGS FROM THE TIPTOP PROJECT

Presenters: **Yara Alonso, Cristina Enguita**

Yara Alonso described qualitative research on acceptability of c-IPTp in the context of TIPTOP. The study aimed to understand the social and cultural context of the study settings, identify barriers and opportunities for delivery of c-IPTp, and assess the acceptability of c-IPTp in the four countries. Findings included those common to the four countries on the factors influencing acceptability of c-IPTp at the community level, based mainly on perceptions by pregnant women and health-care workers (facility and community based – that is, CHWs). The approach to acceptability of the intervention was based on two conceptual frameworks: a socioecological model, and a barriers and opportunities analysis model.

The socioecological model conceptualizes the different layers that may influence individuals' behaviour. It considers the individual level (knowledge, attitude, practices), the interpersonal level (families, friends, social networks), the community level (relations between groups), the organizational level (organizations, social entities) and the political level (policies, enabling environment). The barriers and opportunities analysis model has allowed anthropologists to study acceptability of c-IPTp from a multidimensional perspective. It considers different axes of analysis that are adapted, reframed and/or removed over time, based on data saturation and research needs. These include the perceived susceptibility to a disease, the perceived severity of the disease and risk of disease in pregnancy, the attributes of ANC, the perceived efficacy and social acceptability of treatment, perceived self-efficacy, cues for action, perception of divine will and attributes of c-IPTp.

The socio-anthropological study was longitudinal and had four fieldwork phases, one per year, and four in total. The start was in 2018 before implementation (exploratory phase), followed by data collection phases in the subsequent years up to 2021 (in both test and expansion districts). The study followed an iterative approach, which meant that data analysis was combined with periods of data collection. Therefore, findings from each data collection phase informed the design and scope of the following data collection period. In addition to pregnant women and health-care providers, the study targeted other groups of participants, such as women of reproductive age, relatives of pregnant women, community leaders, traditional healers, traditional birth attendants and local government health authorities. Data collection tools consisted of focus group discussions (FGDs), in-depth interviews, direct observation of different activities (i.e. ANC visits, CHW activities, dissemination and communication activities for IPTp and maternal health promotion, day-to-day activities of pregnant women) and informal conversations. A total of 265 FGDs and 796 in-depth interviews were conducted, and 388 direct observations were made, involving a total of 3235 participants.

There were differences between countries in how c-IPTp was delivered.

- In Mozambique and Madagascar, pregnant women were identified and mapped in the community by CHWs and referred to ANC for their first dose of IPTp. Subsequent doses could be given by the CHW at their location or at the pregnant women's home; however, pregnant women were always referred to ANC after receiving SP in the community. CHWs were supported in identifying and mapping pregnant women by lay community counsellors in Mozambique (specifically introduced by TIPTOP because of the low numbers of available CHWs) and TBAs in Madagascar.
- In Nigeria and the Democratic Republic of the Congo, CHWs identified and mapped pregnant women, and were allowed to give the first dose of SP in the community after assessing eligibility. They referred the pregnant women to ANC after receiving SP doses at the community. In Nigeria, CHWs were also supported by TBAs.

Cristina Enguita presented the important actors with influence on pregnant women identified using the socioecological model. Similar actors were identified across countries. At the individual level, sources of influence included past experiences with SP and ANC; knowledge and awareness of IPTp; maternal health; and levels of autonomy, self-efficacy and empowerment. At the interpersonal level, sources of influence included husbands, parents, in-laws, uncles, siblings and peers; these may vary depending on the situation of the pregnant women (e.g. single women, adolescent girls). At the community level, sources of influence included community and religious leaders, TBAs (not in the Democratic Republic of the Congo), traditional healers, local associations and local norms. At the organizational level, sources of influence included health-care workers; at the political level, they included state laws, standards and directives. CHWs are at the interface between the community and organizational levels, given their dual attachment to the community and the health system. In Madagascar, the Dinam pokolona is a local community law that also regulates maternal health practices (which can be located at the interface between the community and political spheres). It is a local system of justice, based on agreements and conventions in a community or between several communities. In some districts of Madagascar, the Dinam requires that pregnant women attend ANC and fines those who deliver outside health-care facilities.

Based on the barriers and opportunities analysis model, findings can be classified into two categories: factors related to health-seeking behaviours (with or without c-IPTp), and factors associated with the intervention itself. Barriers to c-IPTp involving health-seeking behaviours include perceived side effects of SP, pregnant women's lack of

autonomy, barriers to health-care facility access (financial or logistical) and pregnancy disclosure norms. Another barrier specific to c-IPTp is CHWs' working conditions, such as work overload and insufficient remuneration. Despite their cross-cutting nature, these findings might be more relevant in some countries than in others. For instance, barriers to health-care facility access were identified in all countries but might be more relevant to the intervention in Mozambique and Madagascar, where IPTp1 should be administered at the health-care facility. Pregnant women's autonomy also involves different aspects – for example, pregnant women's need for their husband's permission or financial support to attend ANC, or even to receive the CHW in their homes, and their reliance on other influential relatives (e.g. mothers-in-law, male relatives from the maternal lineage). Adolescent girls who depend on their parents or caretakers may also have limits placed on their decision-making. Finally, this lack of autonomy can be reflected in some husbands' preferences for female CHWs (specially in Muslim communities).

Opportunities for c-IPTp at the health-seeking behaviour level include trust in efficacy of SP, awareness of malaria symptoms and severity of the disease in pregnant women, and medical pluralism. The researchers found that the use of traditional medicine and c-IPTp or SP from ANC were not mutually exclusive. Opportunities for c-IPTp include the active involvement of influential actors in project activities, reduced geographical distance to access SP, increased awareness among different groups of SP and ANC as necessary measures to improve pregnant women's well-being, and appreciation of CHWs. The project is generally not perceived as reducing ANC attendance.

With regard to involvement of influential actors in c-IPTp, some nuances can also be identified.

- In Madagascar, TBAs play an important role in identifying and referring pregnant women, and have collaborated with CHWs in identifying pregnant women.
- In Mozambique, community leaders play an important role in addressing refusals.
- In Nigeria, TBAs are integrated into the project referral system. Their participation is incentivized.
- In the Democratic Republic of the Congo, TBAs in one district are integrated by the local health system into the maternal health-care circuit as ANC promoters.

In the exploratory phase of the study, before c-IPTp implementation, several factors were identified that were expected to influence acceptability of c-IPTp. These included health-seeking factors, such as use of traditional medicine, lack of women's autonomy, limited awareness of strategies to prevent malaria in pregnancy and taboos around pregnancy disclosure. With regard to access to ANC, factors included perceived quality of care and related costs. Additional factors included the perceived competence of the CHW to deliver SP and handle maternal health issues, community bonds and reduction of ANC visits because of easy access to SP.

Some factors influencing c-IPTp acceptability have fluctuated over time. Pregnant women's lack of autonomy and barriers to facility-based ANC access have persisted throughout the study. ANC access barriers are particularly relevant to Madagascar and Mozambique, which require that pregnant women only receive c-IPTp after having sought the first dose at the health-care facility. Perceived side effects of SP emerged as an unanticipated, yet significant barrier. Barriers that were ruled out included the perception that c-IPTp would reduce ANC attendance, and that traditional medicine would compete with c-IPTP. Barriers that were overcome through

implementation included mistrust in CHWs' competence in delivering IPTp, and lack of awareness by pregnant women of strategies to prevent malaria in pregnancy. Although cases of refusal – both treatment refusal and refusal to participate in the project – have been reported, c-IPTp is widely accepted by its beneficiaries and different sectors in project areas. Nevertheless, the research identified barriers to acceptability and overall uptake that should not be dismissed.

In conclusion, the key factors that have made the strategy more likely to be accepted are alignment with social norms surrounding pregnancy and maternal health practices, involvement of trusted actors outside the biomedical system (e.g. TBAs), use of existing social structures/hierarchies (e.g. traditional authorities, communal laws) that may lead to an enabling social environment, improving pregnant women's self-efficacy (e.g. overcoming financial issues and associated lack of autonomy), and existing (and reinforced) trust in CHWs. Implementers should revisit and expand the information and instructions provided to pregnant women during ANC counselling, to address their concerns and ensure a clear understanding of SP side effects. Counselling should include an explicit recommendation of eating before taking SP (to diminish the risk of experiencing nausea and vomiting) and promote ANC attendance through incentives (e.g. pregnancy kits). Continuous community engagement is important and needs to be strengthened, particularly with regard to the involvement of traditional medicine providers, who play an important role in pregnant women's health care. Implementers also need to ensure sufficient incentives and means for CHWs.

Questions and responses

- **Did the CHWs express any concerns about the workload they would be taking on when delivering c-IPTp among all their other duties?**
  Response: All CHWs expressed concerns about workload, transport allowances and incentives. Workload varied depending on the setting. For example, there were complaints that no difference was made in payment between rural and urban areas, when the cost of living is higher in urban areas.

- **Were the perceived side effects of SP based on previous personal experiences or was it more a general concern (e.g. among primigravidae)?**
  Response: It was both. Sometimes women referred to personal experiences, and sometimes to socially shared knowledge.

- **It is important to involve the partner of the pregnant woman. Were FGDs conducted for partners of pregnant women?**
  Response: Men were included as part of FGDs and interviews under the category of "relatives of pregnant women".

- **Was there mistrust between CHWs and ANC providers? If so, was the mistrust from the perception of pregnant women, from the perception of health workers or both?**
  Response: Mistrust was expressed at the beginning of the study by CHWs, pregnant women, health-care facility workers and members of the community.

- **Did pregnant women complain about distance to ANC as a deterrent to visit?**
  Response: Yes, there were complaints about the distance and transport costs.

- **Did any pregnant woman report benefits of SP leading to improved birth outcome as a motivation for them to take SP?**
  Response: Yes, we have captured experiences from women realizing how they have a healthy pregnancy without malaria episodes since the project has started, and they see this as a positive experience with SP.

SESSION 6. COST AND COST-EFFECTIVENESS ANALYSIS OF THE TIPTOP PROJECT

Presenter: **Laia Cirera**

Laia Cirera gave a presentation on the cost-effectiveness analysis of c-IPTp. The objective was to estimate and compare the incremental costs and health gains associated with c-IPTp delivery in addition to routine IPTp at ANC visits versus routine IPTp delivery exclusively at ANC visits. The analysis calculated the incremental cost-effectiveness ratio (ICER), which refers to the incremental costs of c-IPTp (when compared with routine delivery exclusively at ANC) divided by the incremental effectiveness of c-IPTp (when compared with routine delivery exclusively at ANC) leading to the costs per disability-adjusted life-year (DALY) averted. The incremental effectiveness of c-IPTp is measured as DALYs averted, which is a measure of the burden of disease. The cost-effectiveness of c-IPTp was calculated in TIPTOP test areas by the end of Year 4 (after almost 4 years of implementation), and the analysis was conducted at the country level.

Different kinds of cost data were collected, and two approaches were used. In the first approach, the costs of c-IPTp delivery as part of TIPTOP were calculated using Jhpiego country work plans, activity reports and face-to-face discussions. In the second approach, the cost of c-IPTp delivery was estimated in "programmatic mode", when c-IPTp would be managed and implemented by ministries of health. To collect data for this second approach, meetings were held with key ministry of health stakeholders (malaria programme managers, district health directors, CHW coordinators), and data were gathered using questionnaires with questions on activities and resources (quantities and costing inputs) likely to occur in programmatic mode for c-IPTp. In addition, information was collected on costs of an episode of malaria in pregnancy for the health system (health workers questionnaire; n = 133) and for the household (ANC exit survey; n = 2031), to assess cost savings related to treating fewer episodes of clinical malaria in pregnancy. Through the ANC exit survey, around 2000 pregnant women were interviewed when leaving the ANC visit –an average of 500 pregnant women per country. This survey provided a better understanding and estimate of the household costs associated with malaria in pregnancy (i.e. costs associated with transport, medicines and other expenses, and the opportunity cost of time – the value of time spent being ill). For health provider costs, 133 health workers were interviewed from different health centres – and asked what they do to manage an episode of malaria. To translate coverages into additional women receiving IPTp3+, the number of targeted pregnant women was multiplied by the increase in IPTp3+ coverage. The malaria episodes averted in pregnancy were calculated as the additional number of

Methods: epidemiological parameters for effectivness calculations

INDICATOR	SOURCE	VALUE
SP efficacy in reducing maternal clinical malaria incidence	Menéndez et al, 2008	40%
SP efficacy in reducing maternal anaemia st delivery	Menéndez et al, 2008	8%
SP efficacy in reducing neonatal mortality rate	Eisele et al, 2012	18%
SP efficacy in reducing LBW	Eisele et al, 2012	21%
Incidence of non-complicated malaria in pregnancy*	TIPTOPANC exit survey	Country specific
Incidence of complicated malaria in pregnancy*	TIPTOPANC exit survey	Country specific
Anaemia prevalence among pregnant women	Gonzalez et al. 2015	43.4%
Incidence of LBW in SSA	UNICEF DATA 2015	13.9%
Neonatal mortality rate (deaths per 1 000 live births)	WHO, 2019 SSA Region	28%

*Self-reported information from pregnant women attending ANC clinics and participating in the survey.

pregnant women receiving IPTp3+ multiplied by the incidence of malaria in pregnancy (SP protective efficacy). Estimates from the literature were used to calculate the reduction in outcomes for mothers and newborns related to SP.

A case fatality rate for malaria in pregnancy of 0.33% was used, as calculated by Sicuri et al. *(10)*.

During the study period (2018–2022), the estimated number of maternal malaria cases averted in the TIPTOP study ranged from 958 in Mozambique to 20 148 in Nigeria. The estimated number of maternal malaria deaths averted ranged from 3 in Mozambique to 66 in Nigeria. Corresponding numbers for maternal anaemia at delivery were 283 for Mozambique and 2107 in Nigeria, and for neonatal deaths 40 in Mozambique and 295 in Nigeria. When converted to DALYs averted per 1000 pregnant women, a major part of DALYs were attributed to the health effects on the newborn.

Costs estimates of TIPTOP activities to implement and maintain c-IPTp in the test districts were made for CHW materials used (T-shirt, cap, backpack, waterproof jackets, register books, referral forms, monthly summary forms), CHW incentives (monthly transport allowance to attend review meetings), cascade training (annual training for CHWs, service providers and supervisors), supervision visits (monthly and quarterly provincial visits), monitoring and evaluation (mobile phone and monthly airtime, monitoring and evaluation tools, data review meetings) and sensitization campaigns (monthly community gatherings, campaigns). The total estimated costs per 1000 pregnant women of these activities in "TIPTOP mode" ranged from US$ 32 492 in Madagascar to US$ 53 558 in the Democratic Republic of the Congo. Cost estimates of c-IPTp in "programmatic mode" (when implemented and maintained by the ministry of health) were made for CHW materials used (T-shirt, cap, backpack, waterproof jackets, register books, referral forms, monthly summary forms), CHW training (annual training for new CHWs, with a dropout rate of 5–20%, and refreshments for existing CHWs), training of trainers (annual training for service providers and CHW supervisors) and supervisory visits (monthly visits by CHWs to districts, and quarterly visits for provincial supervision visits). It should be noted that, in programmatic mode, c-IPTp activities would be integrated with other tasks, and costs allocated to c-IPTp were based on assessment of time devoted to c-IPTp-specific tasks. The total estimated costs per 1000 pregnant women of these activities in programmatic mode ranged from US$ 6492 in Madagascar to US$ 12 519 in the Democratic Republic of the Congo. The unit cost per activity in programmatic mode was also calculated: Mozambique had the lowest ratio of CHW to 1000 pregnant women (5) and the Democratic Republic of the Congo the highest (47). In Mozambique, CHWs received a monthly salary equivalent to US$ 18 per month; in all other countries, CHWs were volunteers. CHW training costs per CHW ranged from US$ 20 in Madagascar (3–4 days) to US$ 300 in Mozambique (4–5 months). The cost of training of trainers (overall costs) ranged from US$ 3500 per year and district in Madagascar to US$ 5,000 per year and district in Nigeria. The cost per trainer trained ranged from US$ 48 for 4–5 days in Madagascar to US$ 119 for 12 days in Nigeria. The monthly cost of supervision ranged from US$ 426 per month and district in Madagascar to US$ 696 per month and district in the Democratic Republic of the Congo.

Health system costs to treat uncomplicated malaria ranged from US$ 3.61 in Madagascar to US$ 4.69 in the Democratic Republic of the Congo; for complicated malaria requiring hospitalization, costs ranged from US$ 63.33 in Madagascar to US$ 101.41 in the Democratic Republic of the Congo. For household costs, two components were included: the out-of-pocket expenditure (travel cost and medical costs) and the opportunity cost of time (the income lost when spending time being sick and seeking care). Household costs for uncomplicated malaria ranged from US$ 16.60 in Madagascar to US$ 22.80 in the Democratic Republic of the Congo; for complicated malaria, they ranged from US$ 35.70 in Madagascar to US$ 61.30 in Mozambique.

For the programmatic model, the ICER (cost/DALY averted) ranged from US$ 2 in Nigeria to US$ 104 in Mozambique; in TIPTOP mode, it ranged from US$ 53 in Madagascar to US$ 543 in Mozambique. These outcomes were compared with the WHO thresholds, which are 3 times or 1 times gross domestic product (GDP) per capita. An ICER below these thresholds is considered cost-effective. All ICER estimates (TIPTOP and programmatic mode) were below the WHO threshold for 3 times GDP per capita and, except for Mozambique in TIPTOP mode, also below the WHO threshold of 1 times GDP per capita. The ICER in Nigeria is lower (more cost-effective) than in any other TIPTOP country, due to the sharp increase in IPTp3+ following c-IPTp in all sites, and the high numbers of cases of maternal malaria averted, which translates into a high number of DALYs averted and cost savings. The ICER in Mozambique is higher (less cost-effective) than in any other TIPTOP country because the impact of c-IPTp coverage was not as evident as in other countries, and the IPTp coverage values at baseline were higher than in other countries. The lower ICER in Madagascar is explained by lower local input costs (low overall costs) and the high effectiveness of c-IPTp. The ICER in the Democratic Republic of the Congo is higher than in Nigeria and Madagascar because the overall costs are the highest, as a result of country-specific health system factors (e.g. the ratio of CHWs to pregnant women is much higher than in the other countries).

The main conclusion is that c-IPTp significantly increased IPTp3+ at an additional low cost for the health system. Results from the TIPTOP intervention areas show that c-IPTp may be a cost-effective intervention when incorporated into routine governmental programmes. Compared with other health interventions such as the rotavirus vaccine or prevention of mother to child transmission for HIV, c-IPTp may be more cost-effective. Delivery of c-IPTp may also result in cost savings for the health system and households. Governments should consider c-IPTp for the prevention of malaria in pregnancy and prioritize resources towards c-IPTp.

Questions and responses

- **The number of episodes of malaria averted in Mozambique is the lowest, but the costs of the programme are high. Is this really cost-effective?**
  Response: There is still a lot of discussion among experts on the cost-effectiveness threshold. When using the standard WHO threshold for Mozambique, it is still cost-effective. However, the ministry of health in Mozambique should evaluate the public health priorities and its willingness to pay to avoid malaria cases in pregnancy. When compared with other interventions, the costs are still low; for the health system, c-IPTp needs a relatively small amount of additional resources.

- **Were payments of CHWs included in Nigeria but not in Mozambique?**
  Response: For sustainability of c-IPTp strategies, CHW incentives are important for motivation. Two scenarios were presented: one for what happened during the TIPTOP study and one for programmatic mode. In programmatic mode, a monthly stipend is only provided in Mozambique. It is a big cost component and may affect motivation of CHWs.

- **Costs of CHWs would be shared by other activities and programmes.**
  Response: Indeed, in pilot mode, the CHW activities are exclusive to c-IPTp, but in programmatic mode there may be integration of different programmes. There are important synergies, and an approximation is that CHWs may only contribute 20–30% of their time to c-IPTp.

- **Is the effectiveness of SP evaluation from the literature outdated? There are some old references.**
  Response: Indeed, one of the main limitations of this study is that parameters used are old, and some were not obtained in the context of IPTp. However, in sensitivity analysis, we checked the impact of different inputs, and the results were quite robust.

- **Moving from project to programme, when you modelled the costs, did you look at any changes in effects? You might expect effects to change if you leave something out.**
  Response: In deterministic and probabilistic models for sensitivity analyses, the most important component is the protective efficacy of SP. This has been considered for threshold analysis, to identify the cut-off value beyond which c-IPTp is no longer cost-effective. Due to lack of time, this was not reported here, but it will be in the manuscript.

- **You talked with the ministry of health; what did they sound like about this programme? Did they want to sustain it?**
  Response: Some parts of the ministry of health were a bit more sceptical about continuing this programme. CHWs, especially in the Democratic Republic of the Congo, were more motivated towards the programme, despite a lack of incentives; they showed commitment to key activities, but were not sure what will happen in the future. The reaction from the ministry of health was regularly along the lines of "once we go into programmatic mode, we will not be able to sustain all the activities supported as part of the pilot project, despite having already a CHW programme in place".
  Response: All the data from TIPTOP were shared with the countries in dissemination meetings, where we showed the results, including the cost analysis. In these meetings, there was a lot of discussion on sustainability issues. In each country, TIPTOP has started discussion on ongoing activities, continuation and sustainability with the ministry of health.
  Response: Discussion with ministries and partners on the ground are ongoing about sustainability.

SESSION 7. CONSIDERATIONS ON METHODOLOGICAL ASPECTS AND STUDY DESIGN OF THE TIPTOP PROJECT

Presenters: **Issaka Sagara, Lucy Paintain**

Issaka Sagara and Lucy Paintain presented observations on the design and methods of TIPTOP. Evaluation of TIPTOP has involved a comprehensive mixed methods approach. This includes repeated cross-sectional household surveys at baseline, midline and endline; routine data collection in a longitudinal fashion; a longitudinal anthropological study; a cost-effectiveness analysis; SP resistance monitoring at baseline, midline and endline; additional studies of maternal record review in Nigeria; a quality-assured SP and packaging study in the Democratic Republic of the Congo and Nigeria; an equity analysis; and sustainability and scalability assessments. The household surveys were part of a quasi-experimental study design. The phased implementation allowed a difference-in-difference analysis. In terms of plausibility of findings, for this design, it is important to consider context in detail to assess whether other interventions might have influenced the outcomes of interest. To strengthen the attribution of changes to c-IPTp, the project could assess which doses were given by CHWs versus routine ANC, or the effect of exposure to TIPTOP behaviour change communication activities. There was an appropriate and adequate sample size calculation for the household survey. The recall period for respondents can be an issue, but participants' recall was verified using ANC cards. It would be useful to have maps of the districts involved, to understand whether contamination between intervention and expansion districts was possible. There was some limited variation in timing of the surveys, which probably excludes a major influence of seasonality on the study results.

The routine data analysis was very interesting, given the limitations of data quality. Routine data are important for flagging issues for action – for example, overreporting (Democratic Republic of the Congo) or adherence to approach (Madagascar). There

were challenges with the denominator, derived as recommended by WHO from the estimated number of pregnant women in the study areas. Using triangulation of household survey and routine data strengthened the findings; however, there are challenges in comparing cross-sectional and longitudinal data. The anthropological studies were fascinating, and there are probably many more interesting findings that could have been presented. Data collection for the anthropological studies was thorough; all major stakeholders were included, and a range of methods were used over multiple rounds. Interesting and important themes were identified that would influence success of c-IPTp. Changes in themes over time (e.g. for barriers and opportunities) would influence success of c-IPTp, and it would be interesting to explore this further. The cost-effectiveness study provided an interesting and detailed analysis. With regard to the reporting of the cost-effectiveness analysis, the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 statement could be used *(11)*; this checklist is recommended for use in reporting methods and results of a cost-effectiveness analysis. It was sometimes unclear which perspective of analysis was taken, and whether these were financial and/or economic costs. Some further detail on some of the methods would be helpful for reporting – for example, formulae for modelling effectiveness, DALY calculations, formulae for intervention costs, and whether the same outcomes were used for the effects and the cost savings analyses.

The strengths of the SP resistance monitoring study are the ability to compare an intervention with a control area, having baseline and endline samples, and using well-described laboratory methods for blood sample analysis. As recommended by WHO, blood samples were collected only in children to avoid the systematic bias of selection of SP molecular markers in pregnant women exposed to repeated doses of SP for IPTp.

Overall, evidence from the TIPTOP project suggests that c-IPTp has potential to increase IPTp3 coverage without decreasing ANC attendance; however, there is variability between districts and countries. Results should be interpreted by country, reflecting differences in the intervention (e.g. first dose by ANC provider or not) and influences of possible contextual factors on results. Questions remain on the transferability of findings – for example, which context c-IPTp may be suited to and at what costs (e.g. implemented at the national level or only at subnational level in problem areas with low coverage of IPTp).

Response to issues raised: The TIPTOP investigators advocated for a randomized controlled trial in the project design phase, but this was refused by the donor. Also, a difference-in-difference (DiD) analysis was done using the midline data from the first intervention and first expansion districts. This was presented last year in the Regional Program Learning Meeting, and results are available in that report. In essence, the DiD analysis showed that the intervention effect was significant in all models, ranging from 0.27 in Madagascar to 0.39 in the Democratic Republic of the Congo and 0.61 in Nigeria. The intervention effect in Mozambique was significant but negative, at –0.17. However, the sites were not chosen randomly but purposefully, based on a variety of criteria, so they may not be comparable. For example, some sites have very different malaria transmission profiles, and socioeconomic and cultural profiles. This prevents a rigorous DiD analysis.

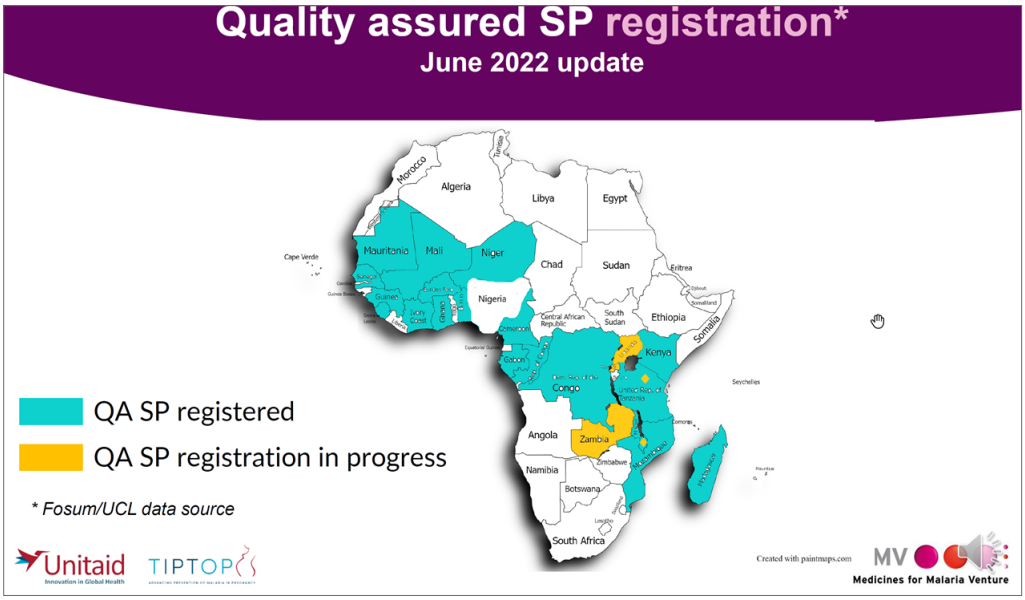
With regard to the SP resistance study, children were chosen as the study population because resistant strains of the parasite can be transmitted from pregnant women to the community, and it is easier to identify children with fever and malaria.

SESSION 8. QUALITY-ASSURED SP AND ADAPTED PACKAGING FOR IPTP

Presenter: **Maud Majeres**

Maud Majeres presented MMV's work to improve the supply of quality-assured SP, including the development of appropriately packaged SP. At the start of the project, only 50% of the available SP was quality assured. The lack of quality-assured SP and frequent stockouts contributed to low IPTp uptake. The main objectives of the Unitaid supply grant to MMV were to address this market failure by bringing at least two new manufacturers of SP finished products to WHO prequalification, and to develop new SP packaging to promote acceptance of, and adherence to, IPTp. SP is mainly procured with the national budget, from local manufacturing. In some countries, SP is on the import prohibition list to protect local manufacturing. The best option for MMV was to partner with local companies to apply for WHO prequalification based on locally produced, quality-assured SP (e.g. in Kenya, Uganda, Nigeria). Three manufacturers were selected through a robust bidding process. The UCL corporation in Kenya submitted the required paperwork to WHO in December 2019, and prequalification is expected in the second half of 2022. The dossier for SWIPHA (Nigeria) was submitted in December 2021 and for EMZOR (Nigeria) in May 2022; the WHO prequalification review process usually takes 18–24 months. The main delay between the Kenyan and the Nigerian submission was due to the COVID-19 pandemic, which delayed recruitment of participants in bio-equivalence studies. Although not part of the project, during the course of the project, three other companies received prequalification status for SP: Fosun Pharmaceuticals in China (2018), S Kant Healthcare in India (2021) and Macleods in India (2021).

MMV wanted to develop a map with the status of prequalified SP registration in Africa. So far, only data from Fosun and UCL could be used. This project is under development, and more data need to be obtained from other manufacturers.

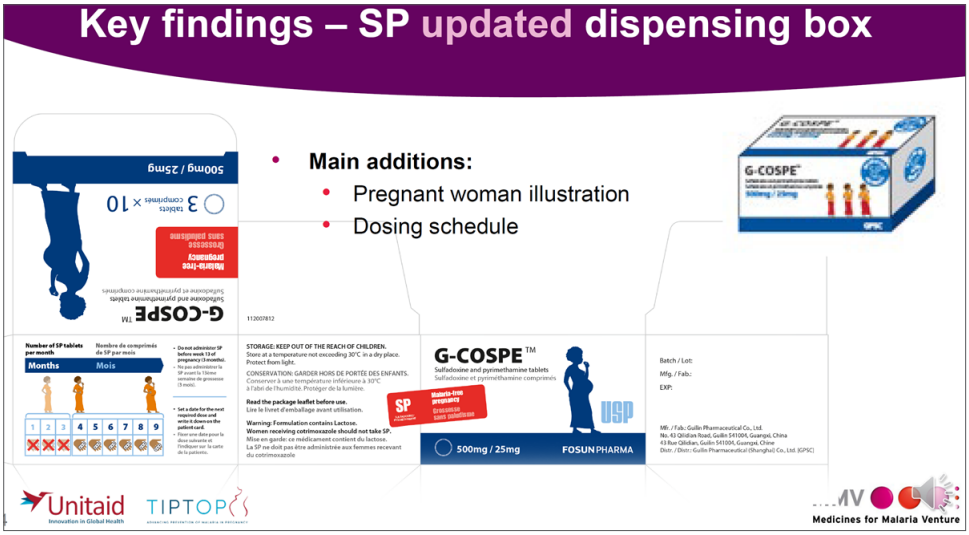


MMV worked on the development of quality-assured SP packaging that makes clear that the SP is for the prevention of malaria in pregnant women and not for treatment. Packaging should be user-friendly and facilitate IPTp delivery in the community. Some packaging of SP products currently on the market still provides an indication

for malaria treatment, despite the WHO recommendation that SP is only used for prevention. Inappropriate packaging may affect provider and patient trust in the medicine, contributing to low IPTp uptake.

Activities conducted during the project included the development of a prototype new packaging in 2017, field testing of the prototype in all TIPTOP countries (except Madagascar) in 2018, introduction of updated packaging in TIPTOP pilots in 2020–2021 and socio-anthropological research on end users' experience in 2021. During field testing in 2018, health workers' perception of SP was evaluated using participatory research. This revealed confusion between SP and paracetamol (the tablets look similar), and reluctance to recommend SP because of perceived side effects (e.g. nausea, vomiting). Other concerns included the indistinct white colour of the tablets, which made it hard to differentiate from other medicines; fear of counterfeit medicines; the use of SP for other interventions (e.g. seasonal malaria chemoprevention); and the absence of specificity, such as its own label *(12)*. SP usually is distributed from a large jar with no label, which gives health workers the perception that it is not safe to administer. From the perspective of pregnant women, IPTp-SP was negatively perceived because of side effects; the quality of SP (e.g. dispensing from a large jar with no label raises concern about hygiene measures and expiry date); the smell, shape and size of the SP tablet; the lack of identity (loose white tablets raising concern about counterfeits); doubt about the effectiveness of the intervention; and fear of harming their baby.

Existing blister packaging for three tablets of SP was updated with an image of a pregnant woman and the IPTp indication for use (G-COSPE; name given by the manufacturing company) on the blister pack. The box for the blister packages (10 per box) was updated. The old medication box had the brand name, the ingredients, the manufacturer's information, the batch number and the expiry date. The revised box had more colour, an image of a pregnant woman, and a dosing schedule indicating pregnancy months and when it is safe to swallow the tablets.



Next steps will be to have the manufacturers adopt the new packaging, support manufacturers with countries' registration of the quality-assured SP, and work with partners to increase access to quality-assured SP. Scale-up will be promoted in the "speed up IPTp scale up" campaign by Roll Back Malaria that MMV is championing.

Cristina Enguita presented the results of an exploratory qualitative study on end users' experiences and perceptions of the new SP packaging, which refers to the primary packaging (blister pack) and the secondary packaging (dispensing box). This was

ancillary to the anthropological research in TIPTOP. It was conducted in two sites in the Democratic Republic of the Congo and two sites in Nigeria, where the updated packages were introduced. In each site, two FGDs were conducted with pregnant women and one with CHWs, and two semi-structured interviews were conducted with facility-based health workers. There were a total of 73 participants in Nigeria and 55 in the Democratic Republic of the Congo. Participants who had experience with the old system and the new packaging were selected for the study.

The results showed that the new dispensing box (secondary packaging) and the blister package were easily identified by pregnant women as a medicine intended for pregnant women because of the image on the blister package and box, suggesting it was a safe medicine to use during pregnancy. CHWs noted that the new packaging eased their work because of the reduced box size and compact instructions, which were more practical. They also noted that the visual identification with the medicine reduced reluctance among pregnant women to take it. The attractive appearance enhanced trust in the quality of the medicine for pregnant women, in terms of potency, genuineness and fewer side effects. In Nigeria, the secondary packaging enhanced the legitimacy and credibility of CHWs as IPTp-SP providers among pregnant women and their relatives. Its appearance and the fact that this product could not be found at the drug vendors gave them trust that it could not be a fake medicine. As identified in the TIPTOP anthropological study, it should be taken into account that concerns about counterfeit medicines seem to be common in Nigeria, possibly as a consequence of a widespread, and often unregulated, informal market.

Overall, the updated SP packaging achieved its intended objective of increasing the acceptability of SP for IPTp. The imagery used had a successful communicative capacity: it indicates that it is for pregnant women and contributes to its perceived safety. An unexpected effect may be that pregnant women have a preference for SP with the updated packaging, which could affect the perception of SP with different or no packaging (e.g. at a health-care facility), or perceptions of, and confidence in, other medicines provided at ANC visits.

Questions and responses

- **Will the combined production capacity of these local manufacturers (to be prequalified) be sufficient for the IPTp programme in sub-Saharan Africa?**
  Response: (by MMV): About 120 million tablets were procured last year between PMI and the Global Fund. The demand for SP may increase because of other programmes using it (IPTi, seasonal malaria chemoprevention). The tenders for PMI and the Global Fund have just closed. In the next couple of months, it will be known if the supply by local prequalified manufacturers is sufficient.

- **Have there been environmental considerations for the material used for these blister packages of SP? Empty blister packages will end up in the communities and may be polluting when disposed of.**
  Response: There were no considerations for the environment when developing these blister packages. The product was chosen by the manufacturer, and MMV had no influence.

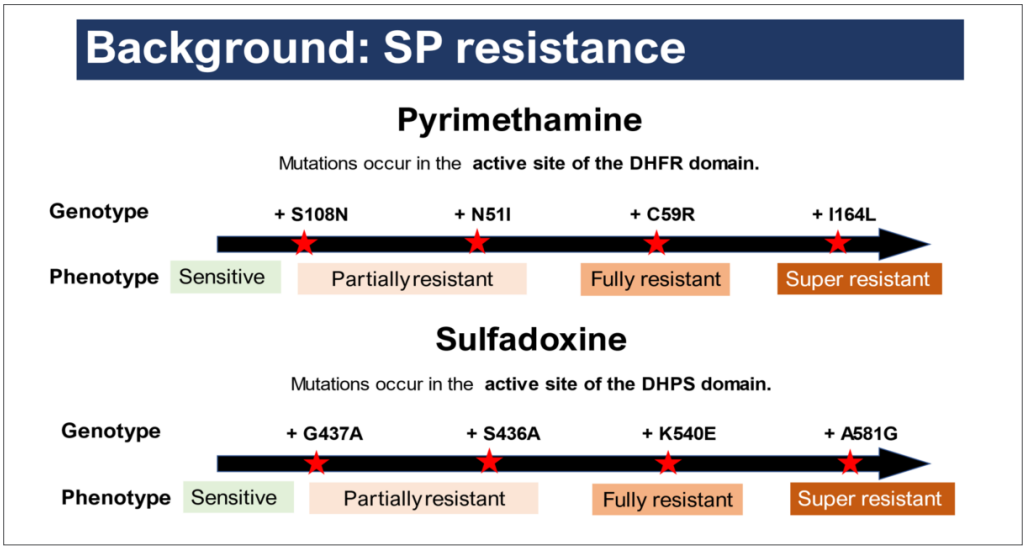
- **Counterfeit medicines are a big problem in African countries. How can you know what is a real or a fake one?**
  Response: MMV is exploring the possibility of adding a logo to identify the difference between quality-assured medicines and counterfeits.

SESSION 9. SP RESISTANCE MONITORING

Presenters: **Antia Figueroa, Didier Menard**

Antia Figueroa presented the design and methods of a study to assess the impact of c-IPTp on the prevalence of genetic markers related to resistance to SP in *Plasmodium falciparum*. Trends in SP resistance were monitored in the test area in each country and in a neighbouring area with similar epidemiological characteristics but with no c-IPTp (control area) at baseline (before project implementation), midline (after 18 months of intervention) and endline (after 3 years of intervention). Four health-care facilities were selected in each test and control area; selection was based on high attendance of children with fever and a high prevalence of *P. falciparum* infection. Children aged 6–59 months attending the selected health-care facilities with fever (≥37.5 °C) or a history of fever in the previous 24 hours were offered a malaria rapid diagnostic test. Those with uncomplicated clinical malaria who resided in the study area were eligible for this cross-sectional study. At enrolment, consent was obtained, a questionnaire was administered to the parent or caretaker, and a blood sample was collected. Samples were stored in the health-care facilities and then sent to country headquarters until they were sent to Paris for analysis. Survey rounds were conducted at baseline (Democratic Republic of the Congo, Nigeria and Madagascar: June–August 2018; Mozambique: September–October 2018), at midline (Madagascar and Democratic Republic of the Congo: February–April 2020; Nigeria and Mozambique: September–November 2020) and at endline (July–September 2021). In each survey, 75 children per health-care facility were enrolled; thus, in total, around 300 samples were collected during each survey from test areas and 300 from control areas. Children aged 6–59 months were selected as the study population because parasite strains resistant to SP in any population, including pregnant women, may be transferred by mosquitoes to the general population and are most easily detected in children. In addition, clinical malaria is more frequent in this age group, and *P. falciparum* parasites will be more easily detected. Samples from midline would only be considered if there were changes in the prevalence of molecular markers related to resistance to SP from baseline to endline.

Didier Menard presented on whether the implementation of c-IPTp with SP would lead to an increase in the prevalence of *Pfdhfr* and *Pfdhps* markers, which indicate SP resistance.



The parasite becomes resistant to SP through accumulation of mutations. The quintuple mutant – the triple mutant *dhfr* allele (N51I + C59R + S108N) combined with a double mutant *dhps* (G437A + K540E) – makes the malaria parasite resistant to SP when used as treatment in adults, but SP remains effective as IPTp in pregnant women. The additional *Pfdhps* A581G mutation reduces effectiveness of IPTp in pregnant women. Dry blood spots from the malarious children were send to the laboratory in France. The DNA was extracted, and a multiplex targeted amplicon sequencing procedure was developed that allowed processing of 384 samples per run, followed by Illumina sequencing and bio-informatics analysis. Around 600 samples per country were received. Of these, 100% of samples were processed for the Democratic Republic of the Congo and Nigeria, and about 85% for Madagascar; for Mozambique, only samples from the intervention area have been processed to date. More than 90% of samples were successfully sequenced.

- In the Democratic Republic of the Congo, the *Pfdhps* A581G and A613S mutations were not found, neither at baseline nor endline. There were low proportions of mutations in the *dhps* gene (<20%) and high proportions of mutations in the *Pfdhfr* gene (>60%; N51I, C59R and S108N), with a significant increase between baseline and endline in the proportion of *Pfdhfr* S108N. There were no significant differences in proportions of mutations between isolates from control and test areas.

- In Madagascar, the *Pfdhps* A581G mutation was not found. There was a high proportion of mutations in the *Pfdhfr* gene (>60%; N51I, C59R and S108N), with no differences between baseline and endline or between control and test areas. For S436A, differences were noted between control and test areas for the baseline samples but not for the endline samples. For *Pfdhps* G437A, the proportion at endline (30–50%) was lower than at baseline; a significant difference was noted with a higher proportion in the test area (49%) than in the control area (30%) at endline. The proportion of *Pfdhps* A613S was low, but with a significant higher proportion at endline in the control area (3%) than in the test area (1%).

- In Mozambique, only endline data for the test area were available. The *Pfdhps* A581G mutation was not found. There was a high proportion of mutations in the *Pfdhfr* gene (>60%; N51I, C59R and S108N), with no differences between baseline and endline. There was a high proportion of the *Pfdhps* K540E mutation (>60%), with no differences between baseline and endline.

- In Nigeria, the proportion of the *Pfdhps* A581G mutation was low (<10%), with no differences between test area and control area or baseline and endline. There was a high proportion of mutations in the *Pfdhfr* gene (>75%; N51I, C59R and S108N), with a significant difference at baseline for *Pfdhfr* N51I (74% in control area and 82% in test area), but no differences at endline. There were significant differences in the proportion of mutations between isolates from control and test areas at endline for *Pfdhps* I431V (47% in control area and 36% in test area) and G437A (13% in control area and 20% in test area), and at baseline for *Pfdhps* S436A (45% in control area and 53% in test area) and *Pfdhps* A613S (7% in control area and 13% in test area).

The analysis of haplotypes, to show physical groupings of genomic variants (or polymorphisms), showed that the triple haplotype was the most common in the Democratic Republic of the Congo. Only one sextuple and one septuple haplotype were identified, and there were no differences between baseline and endline. In Madagascar, the wild-type decreased, and the single, double and triple haplotypes increased compared with baseline. Some sextuples were identified but not from the test area at endline. In Mozambique, haplotype results were not yet available at endline. In Nigeria, there was no change in haplotypes between control and test areas at endline. The quintuple haplotype slightly increased compared with baseline. Some septuple haplotypes were identified in both control and test areas.

In conclusion, the analysis of the endline samples provided similar results to the baseline samples. Proportions of *Pfdhfr*/*Pfdhps* haplotypes differed significantly between each country. SP resistance was higher in Nigeria and Mozambique than in the Democratic Republic of the Congo and Madagascar. Some changes in proportions of *Pfdhfr* and *Pfdhps* mutants in the Democratic Republic of the Congo, Madagascar and Nigeria could be attributed to the intervention. In the Democratic Republic of the Congo, this may be for the *Pfdhfr 51I* mutant (96.4% at endline) and the *Pfdhps 613S* mutant (0.6% in the test area at endline). In Madagascar, it may be for the *Pfdhfr 108N* mutant (87.9% in the test area at endline). In Nigeria, it may be for the *Pfdhps 437A* mutant (20.0% in the test area at endline). The triple mutant *dhfr* allele (N51I + C59R + S108N) combined with a double mutant *dhps* (G437A + K540E) (known as the quintuple mutant) that is associated with clinical and parasitological SP treatment failure was not found in the baseline or endline samples. The *Pfdhps 581G* mutant was not detected in the Democratic Republic of the Congo or Madagascar. The frequency of this mutant remained low in Nigeria in the test areas (2.7%).

Questions and responses

- **Is there any assessment or information about use of other antifolate medicines in these areas that may be important for development of SP resistance in the community (e.g. IPT among infants or cotrimoxazole among HIV-infected people)?**
  Response: There is no information on that, but it can be assumed that this would contribute equally in control and test areas.

- **Do you have information on HIV infection prevalence in each country? For example, Mozambique has a higher HIV prevalence than the other TIPTOP countries, and HIV-infected people may use cotrimoxazole prophylaxis.**
  Response: The prevalence of HIV is very low in Madagascar and high in Mozambique. For the other countries, it would need to be checked.

- **Can you repeat the results in plain English? Are the changes that you noted between baseline and endline important for SP resistance development?**
  Response: No, the most important mutation for SP resistance development is the *Pfdhps 581G* mutant, and there were no signals of concern.

- **Was IPTp effective even in areas where the SP resistance is generally high?**
  Response: IPTp has been shown to be effective even if you have some mutations, but not when the sextuple haplotype is present. Even in areas of substantial SP resistance, IPTp continues to have a very good outcome on low birth weight, although the effect on *P. falciparum* infection (maternal or placental) is less. A recent review by Plowe showed that resistant mutants do not predict effectiveness of IPTp for prevention *(13)*. The association between SP effectiveness for prevention and the sextuple mutation has not really been established yet.

Comment: It should be noted that these results on IPTp resistance genes were obtained 2 years after the start of c-IPTp. It is possible that it takes more time for an increase in SP resistance to become clear. It should be recommended to continue monitoring the regular markers associated with SP resistance. However, in real life, it will be hard to ask countries to continue, as there are limited funds for regular monitoring of SP resistance. For example, in Sierra Leone, IPT in infants was implemented 4 years ago; although molecular markers of SP resistance were assessed in the first year, this has not been repeated. IPT in infants is expanding, and SP is also used for seasonal malaria chemoprevention, and may additionally be expanded among school children, so SP use may increase. However, there are financial challenges to regular monitoring of molecular markers of SP resistance.

SESSION 10. DISCUSSION ON DEVELOPMENT OF OPERATIONAL MANUAL

Presenter: **Emmanuel Otolorin**

Emmanuel Otolorin presented the outline of an operational manual for c-IPTp. A typical learning resource package has the following components: a reference manual (with need-to-know information), a facilitator's manual, a participant handbook and a series of training materials such as PowerPoint slides, handouts or job aids.

For the TIPTOP project, the generic c-IPTp learning resource package was shared with the countries. In place of a reference manual, TIPTOP adapted an existing implementation guide for community-directed interventions, which was later edited to become a specific c-IPTp implementation handbook at the request of WHO. Countries adapted the generic package as much as possible and translated key content to their local languages, as needed. Where the level of literacy was low, countries further adapted the content of the resource package to the literacy level of the health workers. The introduction section of the implementation handbook presents a rationale for c-IPTp, an explanation of why c-IPTp is needed to increase IPTp3+ coverage and a description of the TIPTOP project. Target audience, purpose and objectives of the handbook, and how to use it are also explained.

The next section presents the roles and responsibilities of different partners: the community, health facilities, and facilitation teams at national and district levels. The handbook then describes how to establish a c-IPTp programme, outlining the role of facility-based c-IPTp focal people in community entry, facilitation of community meetings, selection and training of CHWs, collection of quality-assured SP from health-care facilities, screening and administration of SP to eligible pregnant women, and supportive supervision.

Checklists are provided in a series of appendices. These included checklists for CHWs providing c-IPTp-SP to eligible pregnant women, learning objectives for c-IPTp training, patient education handouts, job aids for providing c-IPTp, monthly supportive supervision for CHWs, and supportive supervision for health workers in health-care facilities on prevention of malaria in pregnancy. At the end of the document are references.

When preparing an operational manual for c-IPTp, there should be a section that provides background on global and regional burden of malaria in pregnancy, highlighting the vulnerable group of pregnant women. There should be a review of WHO policy relevant to c-IPTp, including the WHO 2014 IPTp policy and WHO 2016 ANC guidelines, status and gaps in ANC and IPTp3+ coverage (drawing from the 2021 *World malaria report*) and a brief review of the WHO 2018 guidelines on CHW programmes. A section should be devoted to c-IPTp, describing about what it is, why it is needed, the current status of evidence, the medicine of choice, and any drug resistance and safety issues. Guidance should be provided for countries on how to include c-IPTp in national guidelines and policies, such as processes for including c-IPTp in the national malaria strategic plan and including malaria in pregnancy in policy-making.

A section on planning of implementation of c-IPTP is needed, including a situation analysis before the start of c-IPTp. The following components should be considered: the local burden of malaria in pregnancy, human resources available for malaria in pregnancy and c-IPTp, existing medicine logistics management systems, the existing HMIS, existing community health delivery systems in the context of the WHO 2016 ANC guidelines, mapping of health-care facilities and CHWs, current funding options, and availability of safe drinking water and cups to facilitate directly observed intake of SP. A section on planning to strengthen existing health systems is needed based on the findings of the situation analysis. The facility-based plans should pay attention to the

following components: training of frontline health-care workers (who, when, where and how); post-training supportive supervision (in TIPTOP, monthly meetings were held between CHWs and ANC staff); medicine management information systems, with regard to SP availability and storage (last-mile distribution); data management information systems, including scheduled data quality assessments during supportive supervision visits; and provision of safe drinking water and cups. At the community level, there need to be plans for the following components: community engagement (community entry and mobilization approaches, often in close collaboration with civil society organizations); selection of CHWs; training of CHWs; distribution of quality-assured SP to CHWs (storage conditions, child-safe storage); provision of incentives to CHWs; and supportive supervision plans for CHWs. There needs to be information on screening of pregnant women, provision of SP by directly observed intake, protocols for CHW home visits, identification and mapping of pregnant women in the community, screening of pregnant women for eligibility to receive SP, provision of monthly SP to eligible pregnant women by directly observed intake during home visits, recording of SP dose on ANC cards and records, and referral of pregnant women to ANC. To enable monitoring and evaluation, c-IPTp programme indicators need to be selected, and a description is needed of data sources and methods, data collection tools (revision, printing and dissemination), training of focal people for monitoring and evaluation, data collection and analysis, data use for decision-making and data qualitative assessments, and supportive supervision. Coordination and collaboration are very important; to facilitate this, technical working groups need to be established (or strengthened) at national and subnational levels. These groups should include representatives from government ministries, departments and agencies; partners; civil society organizations; and communities. They should have clear terms of reference and targeted advocacy. Materials for social and behaviour change communication need to be developed or adapted. Guidelines on approaches of health-care facilities, the community (through gatekeepers) and civil society organizations are needed, and health financing options need to be explored. The annexes can include a sample checklist for CHWs providing c-IPTp-SP to eligible pregnant women, sample patient c-IPTp education handouts, a checklist for monthly supportive supervision of CHWs, sample HMIS forms (e.g. ANC register, monthly summary form, CHW activity register, referral forms) and sample data use posters.

The following comments were made on the proceedings of the technical consultation.

- The suggestion was made that more guidance is needed on where and when c-IPTp is needed in malarious regions of sub-Saharan Africa. The most recent WHO recommendation, released on 3 June 2022, states that "antenatal care (ANC) contacts remain an important platform for delivering IPTp. Where inequities in ANC service and reach exist, other delivery methods (such as the use of community health workers) may be explored, ensuring that ANC attendance is maintained and underlying inequities in ANC delivery are addressed". An important consideration is the baseline level of IPTp coverage: if there is a low baseline level, c-IPTp may be more appropriate and effective, as found during the TIPTOP project. The manual should have information about these areas where c-IPTp can have maximal impact.
- WHO should be a strong advocate of IPTp in Africa, where there is strong evidence that it is useful, even in areas with a low intensity of malaria transmission. Countries need to consider the option of c-IPTp in relation to existing coverage of ANC and plans for strengthening ANC.
- If the involvement of CHWs is already institutionalized in a country (e.g. in Sierra Leone), it may be relatively easy to incorporate the training for c-IPTp into the existing manual for CHWs.

- There can be differences in regions within a country, as in Mozambique. The manual should provide some guidance on this, but policy needs to be considered at country level.
- A country should have a good view of other activities of CHWs, and how (and if) c-IPTp activities can be added. Ideally, CHWs should be paid and have their roles formalized in an institutional structure, as recommended by WHO; in reality, CHW are volunteers in many countries.
- WHO can develop global guidance documents; countries that are interested in the c-IPTp strategy can take elements from this guidance and adapt it to the country's situation, as necessary. However, there is still a need for countries to know if, where and when c-IPTp should be implemented.
- Community platforms and CHWs differ from country to country; the workloads of CHWs also differ, even within a country. In Mozambique, the community platform was not very successful in delivering c-IPTp. Being able to answer certain questions may help to assess where c-IPTp may work – for example, what are the characteristics of the current community health worker platform? What is the gender distribution of the CHWs? What is the ratio of CHW:population covered?
- The context of other preventive treatments for malaria (e.g. seasonal malaria chemoprevention, intermittent preventive treatment for infants, and perhaps for school children) is important. These strategies should also be considered for CHW programmes. CHWs should also encourage ITN use as part of visits to households.

The use of c-IPTp is not recommended everywhere, but only for settings with high missed opportunities, such as a large difference between ANC4 attendance and IPTp3 coverage. Adding c-IPTp can improve coverage in these settings. It is a low-cost and high-impact intervention. The operational manual should target those countries that want to increase IPTp3+ coverage and hopefully assist all countries that want to use this IPTp delivery method.

CLOSED SESSION: EXPERT PANEL AND WHO

In the closed session, the panel talked further about when it is appropriate to use c-IPTp, and the following comments were made. If ANC coverage is high but IPTp coverage is low, countries may consider improving ANC or trying c-IPTp. This decision should be made by countries. The c-IPTp strategy is valuable and does not affect ANC coverage negatively. The increase in IPTp3+ overall has been very slow; in the past 2 years, according to trends in the WHO *World malaria report*, IPTp3+ has even declined. Many programmes have tried to increase IPTp3+ coverage in a setting of high ANC attendance, with variable success. Although c-IPTp has the potential to rapidly increase IPTp coverage, there is a need to examine areas where it did not work. In west Africa, CHWs are involved in seasonal malaria chemoprevention, malnutrition and tuberculosis programmes. Adding c-IPTp would be another burden and may be difficult. In some countries, fees are charged for ANC; in these circumstances, c-IPTp may reduce attendance because of decreased costs for the pregnant woman. TIPTOP may have improved ANC functioning (e.g. with stable SP supply), and this may have contributed to the success of the project, apart from the impacts of c-IPTp. It will be important to assess how a programme can be successful when scaled up. CHWs are in a position between the ANC and the community; it is not always clear how TBAs can be involved (if they are not CHWs). There are many missed opportunities in ANC; c-IPTp may play a role in reducing the dropout rate from ANC and encourage early attendance. In a manual, aspects of poor-quality ANC, SP supply

and costs of SP need to be addressed. It will be important to monitor and evaluate progress in a c-IPTp programme. If the routine data are not of sufficient quality, extra investments in monitoring and evaluation are needed to ensure that any decrease in ANC visits is not missed.

Countries have to contribute funding to make c-IPTp work. Countries may need more information before deciding if they want to adopt c-IPTp, and need resource mobilization before they can start (e.g. by applying to the Global Fund). SP procurement needs to be of quality-assured medicines, but these may not be available in all countries. Malaria transmission intensity and local SP resistance levels should be considered before introducing a c-IPTp programme. When considering c-IPTp, all departments of the ministry of health should be involved, including the reproductive health department, and departments overseeing CHW programmes. Integration is important, because c-IPTp may be only one of the many tasks that a CHW may need to do.

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ANNEX 2. AGENDA OF THE TECHNICAL CONSULTATION

TUESDAY 21 JUNE 2022		
14:00–14:10	Welcome	Andrea Bosman
14:10–14:25	Short introduction of participating organizations **Meeting objectives and expected outcomes**	Silvia Schwarte
14:25–14:40	**Brief TIPTOP project overview and data sources** (10 min presentation, 5 min questions)	Elaine Roman
14:40–15:40	**Session 1: TIPTOP project – household survey results** (30 min presentation, 30 min discussion) • Democratic Republic of the Congo • Madagascar • Mozambique • Nigeria	Franco Pagnoni
15:50–16:50	**Session 2: TIPTOP project – routine monitoring** (30 min presentation, 30 min discussion) • Democratic Republic of the Congo • Madagascar • Mozambique • Nigeria	Christina Maly
16:50–17:10	Wrap-up and summary of key elements for Day 1 Closure for the day	Rapporteur WHO GMP
WEDNESDAY 22 JUNE 2022		
14:00–14:15	**Session 3: c-IPTp: literature review** Summary of key learnings from TIPTOP project household surveys and routine monitoring and pre-read overview	Rapporteur
14:15–15:15	**Session 4: Experiences from non-TIPTOP countries of impact of c-IPTp on IPTp3 coverage and ANC attendance, successes and challenges** (10 min presentation and 5 min discussion per country) • Burkina Faso • Malawi • Senegal • Sierra Leone	Nombre Yacouba, Gauthier Tougri John Munthali, Evance Kaunda, Seynabou Gaye Faye Kumba Wani Lahai, Ronald Carshon-Marsh
15:15–15:55	**Session 5: Anthropological study findings (TIPTOP)** (30 min presentation, 10 min discussion) *Includes community perceptions, lessons learned, and summary of key common elements of success and challenges across countries*	Cristina Enguita Yara Alonso
16:05–16:35	**Session 6: Cost and cost-effectiveness (TIPTOP)** (20 min presentation, 10 min discussion)	Laia Cirera
16:35–17:15	**Session 7: Considerations on methodological aspects and study design** (25 min presentation, 15 min discussion)	Lucy Paintain Issaka Sagara
17:15–17:30	Wrap-up and summary of key elements for Day 2 Closure for the day	Rapporteur WHO GMP

THURSDAY 23 JUNE 2022		
14:00–14:20	Summary of key learnings from non-TIPTOP countries and additional TIPTOP project studies, as discussed on Day 2	Rapporteur
14:20–14:50	**Session 8: Quality-assured SP and adapted packaging** (2 × 10 min presentations, 10 min discussion) • Improving availability of quality-assured and appropriately packaged SP • Qualitative study findings on end users' experience with SP updated packaging Discussion	Maud Lugand Majeres Cristina Enguita
14:50–15:20	**Session 9: Resistance monitoring** • Drug resistance study: Rationale, design and methodology (5 min) • TIPTOP resistance monitoring findings (15 min) Discussion: Impact on and implications for (c-)IPTp-SP (10 min)	Antia Figueroa Didier Menard
15:30–16:15	**Session 10: Discussion of conclusions for development of operational manual** (15 min presentation, 30 min discussion) • Suggested manual outline • Revision and discussion based on meeting conclusions	Emmanuel Otolorin Jhpiego, ISGlobal, Country representatives
16:15–16:30	Next steps and timelines Wrap-up and closure of meeting	Silvia Schwarte Andrea Bosman
CLOSED SESSION: EXPERT PANEL AND WHO		
16:30–18:00	• Common implementation aspects by rapporteur for field manual • Discussion of key recommendations and conclusions of the meeting in view of the development of field manual and implementation guidance (content, timelines, responsibilities)	Rapporteur Co-Chairs Technical Consultation Expert Members WHO GMP, country offices, regional office

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