

# Annual Meeting of the Roll Back Malaria (RBM) Malaria in Pregnancy (MiP) Working Group Meeting

# Commitment to Strengthening, Accelerating and Supporting MiP Programming

15-17 July 2014 Accra, Ghana



**MEETING MINUTES** 

\*All meeting presentations can be found at <u>http://www.rbm.who.int/mechanisms/mpwg.html</u>

# DAY 1: 15 July 2014

# **I. Opening Session**

Dr. Viviana Mangiaterra, MiP WG Co-Chair, welcomed all working group members and participants to the 16<sup>th</sup> Annual Malaria in Pregnancy Working Group Meeting. Dr. Mangiaterra also introduced the WHO Representative, Dr. Magda Robalo, who welcomed participants to Ghana and briefly highlighted the need to engage women earlier in ANC and increase IPTp uptake. Dr. Koki Agarwal, MiP WG Co-Chair, was unable to attend the meeting due to illness. Dr. Mangiaterra made general opening comments about the current global momentum surrounding MiP and the opportunity to use this meeting to identify strategies for MiP interventions and integration beyond the 2015 MDGs. Dr. Mangiaterra reviewed the following meeting objectives: 1) review and discuss country progress in terms of adoption and implementation of IPTp policy; 2) review and discuss new technical evidence and promising programming practices; 3) review and discuss how to better integrate MiP programming into RMNCH services; and 4) review and update MiP working group work plan.

Colleagues from our host country, Ghana, then welcomed all participants. Mr. Appiah, Director of Administration of the Ministry of Health, and Dr. Constance Bart-Plange, Malaria Control Program Manager, delivered a formal speech on behalf of the Minister of Health which emphasized and highlighted Ghana's historic and continued commitment to address maternal health, specifically malaria in pregnancy. Notably, Ghana has achieved one of the highest levels of IPTp coverage, 72.4% in Africa.

# II. Smart Integration: Reproductive, Maternal, Newborn and Child Health (RMNCH) & Infectious Diseases

### Addressing Infectious Diseases Across the RMNCH Platform Dr. Viviana Mangiaterra, The Global Fund

Dr. Mangiaterra started her presentation by highlighting the need to demonstrate the added value of integration and noting how evidence supporting integration will further facilitate efforts to scale-up MiP interventions. She reviewed current maternal mortality estimates and how HIV/AIDS, TB and malaria (ATM) specifically contribute to both morbidity and mortality. Dr. Mangiaterra noted that integrated service delivery, in particular, is an opportunity to improve the delivery of ATM interventions and gain efficiency in the health system. There are many opportunities for integration of ATM interventions across the RMNCH continuum of care, but in reality there is a "dipping in and out of care." Dr. Mangiaterra provided several country examples (Zambia, Mozambique, Rwanda, Kenya, South Africa, Uganda and Malawi) of the benefits of strengthening the integrated service platform. However, she asserted that integration is not without significant challenges. It requires a functional health system but unfortunately a major bottleneck remains historical use of a vertical system. Effective integration, therefore, requires: infrastructure development, HR strengthening and capacity building for RMNCH staff; commodities and supplies for malaria, HIV and TB control; and quality service delivery with well-equipped laboratories. Dr. Mangiaterra ended her presentation by suggesting that, given the benefits, integration be made a priority for the MiP WG moving forward. The MiP WG must explore how to interact and coordinate with other colleagues and WGs in RMNCH and set an agenda for operational research in this area.

### <u>Discussion</u>

Integration is essential across all levels (funding, policy developing, training) for maximum impact at facility level. The Ghana WR noted that we need to embrace a "patient-centered approach." Even by including ATM, we are leaving other infectious diseases behind. Dr. Valentina Buj from UNICEF further highlighted the need for political will and noted that many lessons have already arrived from iCCM. She also spoke about the "perils of integration" and danger of overworking the CHW, for example. There is a need to work with governments to make sure there is attention paid to the MoH pyramid. Several colleagues spoke passionately about the need to focus on health systems strengthening and noted that the problem of integration is not at the delivery of services, but higher. They advocated for the development of a new set of indicators and targets to document the impact of integration. Finally, Dr. Maurice Bucagu from WHO spoke about ANC as a "platform" and the challenges of the operational aspects. He made appeal to move beyond policy and think about implementation and quality of care.

# *Health Systems Strengthening (HSS) investments to maximize impact and to foster integration* Dr. Yoko Akachi, The Global Fund

Dr. Akachi noted that the mandate of the Global Fund continues to be on HIV/AIDS, TB and malaria, but HSS is a critical aspect of the work of Global Fund and serves to maximize the impact of investments in these three areas. HSS support develops the capacity of a single health system and addresses system-wide weaknesses. HSS benefits are across several disease outcomes and beyond. Dr. Akachi highlighted the five priority areas for the Global Fund: service delivery, procurement and supply chain, health workforce, health management information system and financial management/expenditures/resource tracking. She also discussed how Global Fund funding has been associated with reduced maternal mortality and a consistent positive relationship between the Global Fund disbursements and subsequent accelerated improvement in coverage of ART, PMTCT and ITNs. Dr. Akachi reviewed the RMNCH interventions included in the modular template in the New Funding Model (NFM) concept note. She also emphasized the importance of

strengthening ANC for the delivery of several of these key RMNCH interventions and highlighted Kenya as an example of a country that has maximized Global Fund support for RMNCH. Dr. Akachi closed her presentation by asking participants to think about two key questions: 1) Are we sufficiently supporting RMNCH interventions that directly address ATM and 2) What about the synergistic interventions highly relevant to ATM? How are they funded and implemented? Any potential complementarity?

### **Discussion**

Dr. Ambrose Talusina from the Case Management Working Group highlighted how the Global Fund has evolved but CSS/HSS may actually be eliminated by countries under the indicative funding model. He also commented how voluntary pooled procurement does not build the capacity of countries and asked if it will be phased out. Dr. Akachi responded by agreeing to the concerns raised but also pointed out that some countries that have shown reduction in allocation have still managed to prioritize and secure funding for HSS under the allocation as this is the time to invest in sustainability of the programs. Countries and PSM technical partners have been raising the same concern regarding VPP, and PSM is one of the HSS priority areas for the Global Fund. This includes the issue of, once the drugs have been purchased centrally (which is what VPP focuses on), how it gets to the hands of patients.

Dr. Akachi received several questions about (1) the review of concept notes and (2) measuring impact. She discussed how the disease-specific advisors, country teams and HSS/RMNCH team collectively review all concept notes which then go to the Technical Review Panel (TRP). Dr. Akachi noted that the most recent TRP review highlighted and criticized the lack of HSS and integration in the concept notes. She also explained how Global Fund will be using the SARA tool to assist with data collection and measuring HSS related indicators at facility-level. Dr. Akachi noted that the Global Fund has funding for country operational research but does not conduct disease/intervention specific (i.e., MiP) scientific research.

In response to a question about gender programming, Dr. Akachi also noted that HSS support has been used for GBV programming. There is a dedicated Gender Team providing technical support in this area.

Dr. Mangiaterra also provided additional comments from the Global Fund perspective. She highlighted that the National Strategy is the basis of the NFM and the TRP is really scrutinizing concept notes for the inclusion of HSS. She noted the importance of M&E earmarking HSS indicators to track impact and emphasized that MiP WG Meeting participants need to be at the table and encouraged them to "knock on the door of the CCM."

Finally, there was a fruitful discussion on CHWs. Several colleagues commented on the need to think about CHW and how they are overloaded. While they "support the health systems but are not part of the health system." Several colleagues asserted that we need to start thinking about how to move CHWs to part of the system, like in

Ethiopia. Dr. Akachi also gave an example of how this is being addressed in Burkina Faso with CHWs now receiving a salary under the just approved policy. Another colleague noted that there is a school for CHWs in Zambia, and they are also paid by the government.

### *Integration and Routine Support to Malaria Activities Including MIP* Dr. Valentina Buj, UNICEF

Dr. Buj opened her presentation by giving an overview of UNICEF and its four major areas of work: advocacy, technical assistance, leveraging and procurement. She highlighted UNICEF's activities in prevention (LLINs and IPTp) and emphasized the importance of routine net distribution given the ups and downs of campaigns which are often linked to funding. Dr. Bui discussed several key challenges related to ITNs: 1) routine vs campaign, 2) quantification (e.g., how many women will be coming to ANC), 3) logistics, 4) integration (e.g., how many interventions to integrate), and 4) communication (e.g., with less GF funding, demand creation down). She also highlighted IPTp as a missed opportunity even when ANC attendance is high. In a resource-constrained environment, she asserted that we must focus on scaling-up appropriately and utilizing a FANC package. In her presentation, Dr. Buj highlighted several opportunities for integrated support: child and maternal health days, integrated mass campaigns, EPI & ANC, outreach (CHW), harmonized funding and private sector. She also gave a summary of the current Global Fund – UNICEF MoU and entry points for UNICEF engagement. For iCCM, several building blocks are in place and highlighted several key considerations. Dr. Buj closed her presentation by provided the example of making use of complimentary resources – financing and technical – to address the febrile child in DRC.

### **Discussion**

Using iCCM as a model, a colleague asked what should be done at the community level for MiP? Dr. Clara Menendez from ISGlobal responded by suggesting that community should be seen as complimentary to health facility and noted that we need to find a way to reach women early in pregnancy. EPI is as possibility but it misses the primigravida population. Dr. Kwame Ankobea from PMI Ghana suggested that perhaps iCCM is just a new form of community IMCI. He asked if countries that failed in implementing the community aspect of ICMI initially would be able to succeed with iCCM.

Several colleagues also highlighted the importance of the "country-context." In response, Dr. Buj acknowledged that geographical variations are a reality and UNICEF using "monitoring for results" model. She emphasized the importance of developing indicators and the importance of nation investments in HSS. UNICEF has an equity agenda and separates out indicators.

### Integrating TB and PMTCT programming into RMNCH Platform Ms. Stacie Stender, Jhpiego

Ms. Stender started her presentation by highlighting the current and overlapping epidemiological situation of TB and HIV and then discussed the three delays model (delay in decision to seek care, delay in reaching care and delay in receiving care) and how it impacts access and treatment to TB and HIV. Ms. Stender reviewed a framework for integration necessitating advocacy, policy, education and training and facility-based implementation, and specifically mentioned Jhpiego's role in developing HIV and TB pre-service education interventions. Ms. Stender summarized a minimum package of services necessary to prevent, diagnose, care, treat and support women and children infected and affected by TB and HIV and highlighted key considerations for county programs. Ms. Stender also mentioned The Double Dividend and priority areas of "smart" opportunities (e.g., strengthening PNC, immunizations and HIV testing, nutrition and HIV and re-invigorating capacity for IMCI). Finally, in closing, she highlighted various tools developed by Jhpiego to promote integration and offered several practical recommendations.

### Trends in Maternal Anemia and Control Programs Ms. Rae Galloway, PATH

Ms. Rae Galloway opened her presentation with a series of slides documenting trends in anemia prevalence from 1995-2011 and noted there has not been much change in anemia prevalence in Asia and Africa. She highlighted the three major maternal anemia control interventions (i.e., ITN/IPTp, 90+iron-folic acid and deworming) and reviewed the evidence supporting the impact of these interventions. While there is evidence about the efficacy of these interventions, coverage remains low. The greatest progress made has been on insecticide-treated bednets (ITN/LLIN). Ms. Galloway discussed ways to improve programs and obtain at-scale coverage of at least 80% of women receiving these interventions including: get the dose and timing right, accurate forecasting, and delivery and monitoring of the integrated package. In addition, improving demand for these interventions by improving counseling messages on why and when to take these interventions and addressing women's concerns about taking medications during pregnancy. She emphasized the importance of getting the right dose of folic acid. Ms. Galloway reviewed how SP interferes with the malaria parasite's FA synthesis and why 5mg or more of FA increases the risk of treatment failure with SP in pregnant women. She closed by noting that most countries are giving a combined IFA supplement containing 60mg of iron and 400mcg of FA but some countries continue to give 5mg dose despite recommendation against this practice and it remains part of the UNICEF procurement catalog.

### **Discussion**

Dr. Peter Ouma from KEMRI noted that high-dose FA is not necessary in the African context given low prevalence of FA-deficiency in SSA. He also noted that would be a mute point if we no longer used SP. Ms. Galloway suggested that high-dose FA may be a vestige of previous beliefs that folic acid deficiency is prevalent and a major cause of maternal anemia. There also are misconceptions that folic acid taken during pregnancy prevents neural tube defects (NTDs) which is not the case because NTDs form within 20 days after conception, long before women would start taking IFA.

Dr. Menendez noted that she was surprised to see such low coverage of IFA, and in response Ms. Galloway said that there is very little data available and DHS surveys do not have specific questions on IFA.

Dr. Boi-Betty Udom from RBM Secretariat inquired whether there have been discussions in other fora with UNICEF on this issue for considering taking high-dose FA off the procurement list, and, in response, Dr. Buj noted that UNICEF procurement catalogue is developed from country's essential drug list – based on country demands.

Ms. Susan Youll from PMI asked for clarification on supplementation versus treatment of anemia, and Ms. Galloway noted that treatment for iron deficiency requires increased doses of iron but not FA.

Finally, there was a discussion on countries' various experiences moving from highdose to low-dose FA. PMI Ghana noted how they are working with the Ghana FDA to produce new low-dose FA. They are helping to generate demand creation with revised clinical guidelines and addressing the supply by working with manufactures. Dr. Ouma also noted that in Kenya change was pushed at policy level but because the supply agency was overstocked with high-dose FA, it has been a slow process to phase into low-dose.

# III. Prioritization of MIP: 2014 and Beyond

### MIP Implementation: Where are We? Dr. Morkor Newman-Owiredu, WHO AFRO

Dr. Newman-Owiredu reviewed the major causes of maternal deaths and the basic programme of FANC. She then reviewed the summary of various country policies on IPTp and provided a chart summarizing dosage in policy statements (versus actual practice in countries). Several issues were highlighted from this policy review: implementation of the 2<sup>nd</sup> and 3<sup>rd</sup> SP doses remains challenging, implementation of FANC remains patching and monitoring of update is focused mainly on IPTp1 and IPTp2. Dr. Newman-Owiredu reported that there has been significant variation in training and training material on MiP activities. She noted that there are many new

challenges due to stratification changes, and many countries are left wondering when to phase out of IPTp if there are different epidemiological zones in a single country. Other challenges noted by Dr. Newman-Owiredu include: stock-outs, inadequate monitoring, late ANC entry, absence of community strategy, financing of new policy and tools and overall reluctance of programmes to add another dose when IPTp2 already low. Finally, she ended her presentation with several issues for consideration: linkages with community based programmes of both malaria and RH, linkages with institutions to conduct research on efficacy of SP and how to use T3 approach.

### **Discussion**

Dr. Mangiaterra has asked for a more recent update from AFRO following the dissemination of the MiP WG Consensus Statement, IPTp Policy and IPTp Policy Brief.

Dr. Udom noted the importance of creating demand and engaging the community. She stated that despite the policies in place and all the efforts made by several organizations, we are still not making progress in IPTp coverage/implementation. The solution may therefore not be with the technical partners, but the community. The question then is how can this working group move the agenda forward.

Dr. Menendez remarked about the low coverage of IPTp2+ and stated that we need to know why women don't have continuity of care. Ms. Emily Ricotta from JHU highlighted a recent study in Uganda on ANC attendance and noted that many women didn't attend because they didn't want to reveal their early pregnancy and didn't want to take medications during pregnancy. Ms. Stender also noted that the M&E system perhaps is not capturing the full picture (e.g., prohibitive and fractured).

Finally, there was a discussion about the efficacy and effectiveness of SP. Dr. Menendez commented that effectiveness is difficult to determine but multiple studies demonstrated SP efficacy. Dr. Ouma further emphasized that the WHO policy on IPTp-SP is based on clear data supporting continued IPTp use with SP, despite growing resistance. However, he also noted that data on IPTp monitoring is currently being evaluated and will be made available by the WHO-ERG to support the continued use of IPTp. Dr. Mangiaterra noted that the IPTp Policy and Policy Brief clearly outline the policy, provide guidance on the implementation of the policy and summarize the current evidence available supporting continued SP use.

### President's Malaria Initiative Update Ms. Susan Youll, PMI

Ms. Susan Youll opened her presentation noting that PMI is implemented by USAID together with U.S. Centers for Disease Control (CDC) and works in 19 countries in SAA, and one regional program in the Mekong Subregion. PMI supports a three-pronged approach to MiP: LLINs, IPTp (17/19 countries implement IPTp-SP) and case management. Ms. Youll reported that in PMI countries the median for ITN use

increased from 17% to 43% in 8 years while for IPTp2 increased from 13% to 25%. She highlighted barriers to achieving high coverage of IPTp and presented data from a PMI review of national MiP documents to assess for consistency of NMCP and RH documents. Key findings document that all had inconsistencies about IPTp timing and none provided correct MiP treatment. Ms. Youll noted that IPTp policy is implemented in 17 of 19 PMI countries. 5 countries have updated policies and 8 additional countries are actively updating their policy. She outlined PMI support for MiP on the global level and country level, as well as operational research and areas of work moving forward.

#### <u>Discussion</u>

In Nigeria, SP is procured by DELIVER for PMI focus states. There was a question about if there are any plans to strengthen government capacity for procurement and distribution? In general, procurement by the centrally-managed USAID DELIVER Project is done in collaboration with NMCP. The example of Angola, which is actively going through transition of transferring PSM responsibilities to country-level, was shared by our colleague.

Dr. Talusina commented that changing context from stable to unstable malaria within a country has presented new challenges. WHO needs to address countries concerns through the provision of updated policy recommendations.

### *Bill and Melinda Gates Foundation Update* Mr. Lee Pyne-Mercier, Gates Foundation

Mr. Pyne-Mercier opened his presentation discussing the relationship between malaria and MNCH teams at the Gates Foundation. He reviewed how the Malaria Analytic Framework of the Gates Found is organized with three strategic goals: Accelerate to Zero Now (eliminate), Prepare for the Future (infection detection, achieve radical cure, prevent transmission and last mile) and Sustain Progress (mobilize), while the MNCH strategy is grounded in a Model of Impact. He reviewed the current and past investments in MiP and summarized future directions.

#### <u>Discussion</u>

The Gates Foundation currently supporting UNICEF and Vector Control WG activities as well. "Integrated Delivery" is another team at Gates Foundation doing important work related to iCCM. The teams are working together to address malaria from different perspectives. Future investments include collaboration with partners for "single encounter radical cure." Once products are available, is Gates investing in innovative ways of delivery? Gates has historically focused on new product development but is beginning to think more about systems (i.e., how to use these new products).

# **IV. Closing**

At the close of Day1, Dr. Mangiaterra urged participants to think about two issues: 1) how can/should the MiP WG move the integration agenda forward, and 2) in an environment of limited resources, where should we place our efforts?

# DAY 2: 16 July 2014

# I. Opening Session

Dr. Mangiaterra opened the day by reminding everyone that the WHO Policy and Policy Brief still support the continued use of SP for IPTp and stated that she would make these documents available for all participants. Dr. Erin Ferenchick. Independent Consultant, reviewed the major themes from the presentations and discussions yesterday: (1) smart integration (need for political will and commitment, importance of integration across all levels, role of HSS and challenges of operationalization/implementation of integration) and (2) prioritization of MiP (importance of engaging the community, understanding that current evidence supports continued use of SP but acknowledgement that the changing context from stable to unstable transmission is presenting new challenges). Dr. Ouma also emphasized the importance of early ANC attendance and the need for HSS to support and be prepared for early attendance. Ms. Chantelle Allen from Inpiego Ghana highlighted the importance of thinking about strategies for integrated service delivery at ANC, and Dr. Mangiaterra also mentioned the important role of CHWs and the need to strengthen the platform for integrated child health.

# II. Country Level Implementation

# Collaboration between RH and Malaria Control to Improve Outcomes for MiP Ghana, Ms. Naa-Korkor Allotey (National Malaria Control Programme)

MiP interventions are integrated into all levels of maternal health services in Ghana, and interventions include IPTp through DOT, LLIN distribution (currently using continuous distribution) and case management (usually handled by OPD/IPD). Coordination of MiP is done through MiP Sub-Committee and IPTp and LLINs indicators have been incorporated into primary data collection tools and district health reporting forms. ANC attendance throughout pregnancy is high in Ghana (with ANC4 at 72.5% in 2013) so there are many opportunities for MiP. In addition, pregnant women are increasingly registering early at ANC which gives increased opportunity for early access MiP interventions. In Ghana, ITN use by pregnant women has been steadily increasing since 2003 but the team noted a recent stock-out of SP which likely contributed to a spike in OPD cases in 2012-2013. Overall, however, there has been a plateauing of the proportion of stillbirths; this is likely

related to non-MiP health issues. Finally, the challenges highlighted included: documentation, SP stock-out, inconsistent supply of LLINs, linking interventions given during ANC with pregnancy outcomes and non-inclusion of MiP medications on National Health Insurance List.

### Making Improvements in IPTp Uptake Nigeria, Dr. Grace Julius (National Malaria Elimination Programme)

Dr. Julius opened the presentation by giving background epidemiological information about Nigeria. Malaria accounts for 11% of maternal mortality in Nigeria. The trend of IPTp uptake in Nigeria from 2003-2013 increased from 1% to 15% (though skilled ANC attendance was steady at approximately 60% during this same period). Dr. Julius summarized strategies for improving IPTp intake in Nigeria which included the following: integration, community involvement, effective commodity logistic management, capacity development of health workers, high level advocacy and effective M&E. Several challenges and opportunities for improving uptake in Nigeria were highlighted. Dr. Julius concluded by noting that there is a slow but progressive increase in the uptake of IPTp in Nigeria but aggressive integration and advocacy is still needed.

### Fostering National Level Partnerships Between RH and Malaria Control Uganda, Dr. Okui Albert Peter (National Malaria Control Programme)

Background information was provided about the context of malaria in Uganda, and the presenters noted that the country has recently prepared a concept note for the GF NFM and finalized a new Malaria Reduction Strategic Plan (2014 – 2020). In Uganda, the roles of RH (lead in planning and implementation of MiP as part of FANC) and the NMCP (TA to ensure quality implementation) in MiP programming are clearly defined. The presenters gave an overview of MiP progress. In 2006, IPTp2 was 16% (UMIS) but in 2013 was estimated at 50% (HMIS). The proportion of pregnant women who slept under an ITN the previous night was 44% in 2010, and 47% in 2011 (UDHS). Uganda has been working to strengthen MiP programming and MiP activities are integrated within FANC policy and procedures. A MiP Task Force (also called MiP Working Group) has been established and Uganda is working to enhance partner coordination and stakeholder engagement. Uganda is now in the process of updating policy and materials in accordance with the latest WHO policy guidelines.

### IPTp in Pregnant Women in DRC DRC, Dr. Charles Longoso (National Malaria Control Programme)

The presentation opened with a description of the context of MiP in DRC. It was noted that the IPTp policy in DCR was adopted in 2002 and updated in 2013 to the recommended 4 doses of SP (5 for HIV+ women). The MiP strategy in DRC was reviewed and updated data was presented. In 2007, IPTp uptake was 5-18% and in 2010 21-50%. Low IPTp coverage is still a serious problem in the DRC despite good coverage with IPTp1 88% (DHS 2013) and IPTp 275%. Several challenges of IPTp uptake were highlighted as well as future plans to: improve access to services by increasing mass awareness for pregnant women, their partners and the community to promote the rapid and complete use of IPTp; to strengthen the capacity of providers at the ANC; to strengthen the capacity of health facility managers; to reproduce and disseminate guidelines and educational materials; and to engage in regular monitoring and supervision.

### Integrating MiP Programming into RMNCH Platform Ms. Elaine Roman, Jhpiego

Ms. Roman opened her presentation by reminding participants that MiP is a maternal and newborn health issue and highlighted that because ANC care attendance is high in many countries, it is an opportunity to maximize synergies that can help improve outcomes. She outlined key health systems strengthening interventions for MiP and specifically highlighted: policy and guidance harmonization, community involvement and M&E. Ms. Roman provided case examples from Zambia (developed national integrated training package) and Nigeria (bridged the link between facility and community through CDI with results that demonstrated 3-fold increase in IPTp without detraction from ANC attendance). In conclusion, Ms. Roman outlined challenges and consideration, specifically highlighting the current environment of vertical and disproportionate funding streams as well as the forgotten prong of case management.

### <u>Discussion</u>

The team from Ghana further discussed the relationship between RH and NMCP and noted how the programs are well integrated. They further highlighted the importance of developing good relationships and the importance of RH taking the lead. The team from Nigeria then presented their experiences trying to harmonize documents with support from Jhpiego and discussed the working relationship between RH and NMCP in Nigeria. In addition, the team from Ghana discussed routine distribution versus mass campaigns ("Hang Up" campaign every 3 years). They noted slow uptake with routine distribution and stated that active involvement of helping families hang the nets during the campaigns has been a successful intervention. Dr. Mangiaterra asked DRC about program financing. The team spoke about their process of performing a gap analysis and identifying other funding sources but identified not having enough partners as a problem.

The Uganda team was asked about MiP data and responded that there are many challenges and issues related to HMIS data.

*Ms. Galloway reminded the team about the importance of including the nutrition team, as well as including MiP messages as part of nutrition counseling and materials.* 

Dr. Menendez asked DRC about guidelines for IPTp for HIV+ women. The team responded stating that the medical conditions of the patient are taken into consideration before giving IPTp.

# **III. RBM Working Group Panel**

### Case Management Working Group Dr. Ambrose Talusina, KEMRI

Dr. Talusina reported that the CMWG is a dynamic group with four workstreams: 1) scaling-up diagnostics (particularly with lessons learned from private sector), 2) strategies to improve access to treatment (improve prompt and effective treatment), 3) drug resistance management and 4) pharmacovigilance.

### Malaria Advocacy Working Group Dr. Valentina Buj, UNICEF

Dr. Buj opened her presentation by defining advocacy and giving an overview of the strategic advocacy cycle. She emphasized that given the changing landscape of development and resource mobilization, key advocacy work must be done at country-level. The MAWG has three major workstreams: 1) advocacy resource mobilization, 2) messaging, and 3) donor resource mobilization. The MAWG has asked for the MiP WG to contribute to the document "Evidence for advocacy" and to nominate a FP from MiP to work with the MAWG. Finally, Dr. Buj gave an overview of the African Resource Mobilization for Malaria (ARMM) toolkit which can be used at country level for resource mobilization and advocacy.

### *Communication Community of Practice (CCoP) Vector Control Working Group Dr. Matt Lynch, JHU*

The CCoP ensures that the tools the malaria community has are used for maximum impact. It brings rigor and quality to social and behavior change communication (SBCC) programs. Mr. Lynch outlined the CCoP objectives and reminded the MiP WG to call upon the CCoP for technical assistance. He outlined the five key actions of CCoP and highlighted the importance of evidence-based communication.

Mr. Lynch also briefly spoke about the VCWG and noted it has 8 workstreams. The continuous distribution workstream is most closely linked to MiP and focused on distribution through ANC and EPI. Historically it also worked on reallocation of nets from ANC to campaigns but this is no longer the recommendation. He emphasized that continuous distribution should continue before, during and after mass campaigns. It is important for women to get an ITN at the right time, and Mr. Lynch suggested that the MiP WG issue consensus statement on this issue.

### **Discussion**

Ms. Roman opened the discussion by stating that there are real opportunities for collaboration with other WGs (i.e., participation on MAWG, consensus statement on ITNs, consensus statement on CTXp and IPTp).

Ms. Youll asked specifically about MiP case management and suggested that MiP WG participation in the CMWG. She also asked WHO for an update on ACT use in the first trimester. Dr. Talusina responded by noting that the CMWG workstreams are across all groups and include pregnant women. Dr. Talusina noted that there is documentation discussing how women in first trimester have inadvertently received ACTs. Evidence seems to suggest ACTs are ok in first trimester but we need to wait for formal recommendations from WHO.

Ms. Stender asked if there is cross-coordination between CMWG with other infectious disease working groups (e.g., procurement, training). Dr. Buj noted that there are current efforts to support integration from multiple departments at WHO. UNICEF is also looking at integration around RDTs, PSM strengthening and integrated training. There are opportunities for Global Fund support in this area.

The P&I Series on MiP has been promoted by RMB while MAWG has focused on messaging to go to country-level and national strategies.

Dr. Zandra Andre from the CDC noted that during a recent MOPs activity she observed ITN redistribution from ANCs to campaigns. She asked what else could be done to advocate for continued ANC distribution? Mr. Lynch emphasized the importance of proper quantification before procurement. He suggested using 1.65 people per net for a mass campaign. He noted that if you are going to run out and need to prioritize nets, a program should spread nets across biologically vulnerable populations rather than spreading them geographically. He noted that this recommendation is based on modeling, but has not been supported by the MPAC as WHO technical guidance. Future work will focus on guidance for net distribution during periods of scarcity.

# IV. A Closer Look at Net Prioritization, Use and Distribution

### Are pregnant women prioritized for nets? An assessment of net use by pregnant women using survey date from 10 African countries Ms. Emily Ricotta, JHU

Ms. Ricotta reminded participants that the current LLIN policy has moved away from prioritizing vulnerable populations to a universal coverage campaign. Her presentation focused on determining whether and to what extent pregnant women are prioritized for ITN use within the household. Using data from 10 DHS/MIS, results from the study suggested that there is a discrepancy in usage rates between having a net and having enough nets (i.e., partial net coverage) which impacts the coverage of pregnant women. In households with enough nets, pregnant women are more likely to use nets suggesting that access is essential. Ms. Ricotta also noted that here was no difference in the prioritization of pregnant women and women of reproductive age for net us, indicating that there is an opportunity to reach more women in first trimester. She concluded by positing that ITN use is more of an issue of access, than behavior.

### <u>Discussion</u>

Dr. Azcucena Bardaji from ISGlobal asked if study results were impacted by timing of campaigns and if other age groups were examined in the study. Ms. Ricotta noted that both children under 5 and pregnant women were prioritized for nets. There is no question about where a woman obtained her net in most countries, but the inclusion of such a question would open door on use, funding and access. Colleagues from Nigeria did note that this question is part of their DHS.

### Improving routine LLIN distribution Dr. Matt Lynch, JHU

Dr. Lynch gave an overview of a four country rapid assessment of LLIN distribution through ANC and EPI. In all four countries, policies for routine ANC and EPI distribution exist but training and supervision were noted to be not as strong as they could be. LLIN logistics and supply chain were separate from other supply chains in all four countries, and there was also a mix of push- and pull-systems across the countries. He noted that in terms of service delivery, health facilities identified limited staff and high staff turnover as key problems. Dr. Lynch also highlighted the challenges of data collection and usage in his presentation. He noted that health staff consistently reported over-burden with reporting forms and datacollection registers. Most of the data available comes from DHS data. As a group, he suggest that we need to do a much better job of demonstrating value for money for donors with improved data collection at ANC. Dr. Lynch highlighted key challenges and made clear recommendations (e.g., prioritize funding for supervision, strengthen EPI distribution, include health facilities in supply distribution planning, streamlining registers, and assess options for LLINS in health center wards) and emphasized the importance of RH ownership of MiP programming. He closed his presentation suggesting there is an urgent need to improve data for more efficient program planning and evaluation with stronger HMIS with streamlined reporting and gave two examples of new survey questions to included.

### <u>Discussion</u>

Ms. Katherine Wolf from DELIVER asked for further clarification on populations prioritized for ITN use, particularly mothers with young children. Ms. Ricotta said that she does not think that having a child sleeping in the same bed with the mother was a driving factor in the use by pregnant women.

Ms. Mary Nell Wegner from the MHTF asked about the condition of the nets seen during the survey. Ms. Ricotta spoke about a study in Uganda that assessed the quality of nets but remarked that is something they would like to investigate further. Other colleagues are working on durability. Dr. Lynch noted that the VCWG recommends that immediately after campaign, continuous channels (EPI, ANC, school distribution, etc.) also be pumped-up.

# V. The Role of the Community in Improving MiP Outcomes

### Increasing IPTp Coverage in Western Kenya by Combining "Memo" and Community Engagement Dr. Peter Ouma, KEMRI/CDC

Dr. Ouma opened his presentation by reaffirming the recommendation for IPTp-SP but noted that Kenya has had low IPTp2 coverage (5-20%) between 2000-2009. In 2009, KEMRI/CDC piloted a simplified "memo" and subsequently made recommendations to ensure that national guidelines and job aids are made accessible at point of care. In 2011, Jhpiego engaged in community activities to increase uptake. Subsequently, a survey was conducted to see if IPTp and ANC uptake improved after both these "memo" and community activities. Dr. Ouma reported that survey data demonstrated that IPTp2 coverage increased to 63% (recall) – 68.3% (ANC cards) in 2013 following these interventions. The coverage surpassed the KNMS targets of attaining 50% by 2013 and 80% in 2016.

# Increased Update of IPTp-SP in Kisumu, Kenya through community-based distribution Dr. Michel Pacque, PATH

Dr. Pacque gave an overview of a pilot project to strengthen ANC and increase coverage of IPTp and demonstrated the feasibility of improving IPTp uptake through community distribution. The aim of the study was to facilitate community dialogue. Dr. Pacque reviewed the qualitative results of the study and shared many direct quotes from study participants on the reasons for ANC attendance, barriers to ANC attendance and attitudes toward IPTp-SP. Dr. Pacque then discussed how PATH trained CHWs and launched activities for the community distribution of IPTp. He presented a series of graphs based on the data available but expressed concerns about data quality. Interestingly, ANC4 attendance increased in the intervention arm compared to the control suggesting that community-based distribution did not detract from ANC attendance. Overall community-based administration of IPTp-SP was well-accepted by CHW and pregnant women, and Dr. Pacque concluded that CHWs can play a key role in increasing IPTp-uptake without decreasing ANC attendance and IPTp uptake at facility level.

### Linking Communities and Health Facilities to Improve MiP Coverage: Community Based Health Planning and Services (CHPS) Ms. Chantelle Allen, Jhpiego

Ms. Allen gave an overview of the CHPS program and noted that community health nurses (CHN) and community health volunteers (CHV) have a key role to play in this program. Malaria is a cross-cutting theme in CHPS, and the MiP strategy at CHPS level takes services to the community. Ms. Allen noted that anecdotally the results have been good but, unfortunately, the impact is not being seen at the "big picture" level. She highlighted specific challenges facing the program including issues with volunteers, first dose of SP, national health insurance scheme, drugs and RDTs and DHIMS II data, and she offered specific recommendations for their program moving forward.

#### **Discussion**

Ms. Roman raised concerns about countries still using 16 weeks/quickening as the marker to start IPTp. Dr. Ouma noted that in the updated 2012 guidelines mentioned quickening, not a specific number of weeks. The specific language states: "Administer IPTp with each scheduled visit after quickening to ensure women receive a minimum of 2 doses." Ms. Roman noted that because quickening can vary significantly, using this can mean late IPTp1 and suggested that this be an issue addressed by the MiP WG.

The team from PMI Ghana asked about what experiences have been reported by women about reluctance to take SP. Dr. Ouma noted that refusal to take IPTp is not a key contributor to low IPTp uptake; he was not aware of a single study examining the refusal of women to take IPTp as an obstacle to uptake. Dr. Pacque conquered.

Several colleagues spoke about the importance of the quality of FANC. Dr. Pacque said that the PATH study did not specifically examine this factor but acknowledged quality of care is important.

In additional, several colleagues pondered how we reconcile 4 ANC visits with the recommendation of SP throughout the entire pregnancy. She also asked about CHW fatigue. Dr. Pacque responded by stating that the current WHO policy recommends IPTp at every ANC visit which, in theory, would give women an opportunity to receive at least three does. If she came more frequently, she would have the opportunity to receive more doses as long as the doses are given one month apart. Many colleagues acknowledged the issue of CHW fatigue as a real concern.

# VI. Technical Evidence and Programmatic Considerations

### Evaluation of the Safety and Efficacy of Mefloquine for IPTp (MiPPAD Trials) Dr. Clara Menendez, ISGlobal

Dr. Menendez noted that the efficacy of IPTp-SP has been threatened by the development of parasite resistance. Additionally, she noted the growing challenges related HIV and malaria co-infection. Dr. Menendez reviewed that all pregnant women should be on cotrimoxazole prophylaxis (CTXp) in high HIV areas with limited health resources but started that SP is not recommended in women receiving daily CTXp. As such, there is a need to identify other antimalarials. Mefloquine (MQ) offers advantages for use as IPTp (long half-life, single dose, acceptable safety profile) but there are issues around tolerability. Dr. Menendez discussed the MiPPD Trial 1 which compared the safety, tolerability and efficacy of MQ to SP as IPTp in HIV negative women. Efficacy results demonstrated that there was no difference between the SP and MQ in terms of impact on LBW however there were slight differences in malaria related outcomes in the pregnant women favoring MQ, as well as a decrease in incidence of clinical malaria in women receiving MQ (particularly after the second dose). In terms of tolerability, there were more women reporting vomiting with MQ (both full dose and splitting the dose). Safety results demonstrated that there was no difference in frequency of stillbirths between the groups. Dr. Menendez reported that MQ has a better prophylactic antimalarial effective compared to SP, and MQ is safe in terms of adverse outcomes. However, MQ at 15mg/kg has worse tolerability than SP for IPTp. Splitting the MQ dose not seem to confer benefits in terms of tolerability. She asserted that MQ at the dose used in the study is not an alternative to SP for IPT and stated that the results do not support a change in the current WHO policy on IPTp.

Dr. Menendez then discussed MiPPAD Trial 2 which focused on evaluating the efficacy of IPTp-MQ in HIV-infected women receiving CTXp. She noted that in the IPTp-MO group (compared to the IPTp-placebo group), there was a reduced rate of maternal parasitemia at delivery, placental infection and hospital admissions. There were no differences in frequency of adverse pregnancy outcomes and no maternal SAEs related to medication. She also noted that in IPTp-MQ group, there was higher frequency of vomiting and dizziness, higher viral load and higher PMTCT. Dr. Menendez suggested that the data demonstrating increased in MTCT of HIV highlights the need for specifically designed studies to fully understand the effects of antimalarials and ARV co-administration. These results may have implications regarding the antimalarial drug combinations containing MO currently recommended for malaria treatment. Dr. Menendez noted that an effective antimalarial added to CTXp and LLINs in HIV-infected pregnant women can improve malaria prevention, as well as maternal health through reduced hospital admissions. She concluded by noting that the search for improved malaria prevention in the most vulnerable group of women should be research and public health priority.

#### **Discussion**

Dr. Ambrose Talisuna asked about safety profile. Dr. Menendez clarified that the study looked at both tolerability and adverse pregnancy but noted that to power a study for safety outcomes is very difficult. Ms. Stender then asked about disaggregation by ARVs. Dr. Menendez noted that there was no difference in terms of regimen and compliance

A colleague highlighted that there was a difference in infant follow-up. Dr. Menendez stated that infants born to HIV negative mothers were followed for one year and those born to HIV-infected women only two months. This was the recommendation from the institutional review committee. Dr. Menendez said that follow-up of the infants at one year included passive case detection.

Dr. Bucagu then asked about the relationship between the last dose of MQ and time of HIV testing in the child. Dr. Menendez noted that HIV PCR was done at 6 weeks and last dose of MQ was given 2 months before delivery.

### Establishing the causes of maternal deaths to reduce its burden Dr. Clara Menendez, ISGlobal

Dr. Menendez introduced a descriptive cross-sectional study conducted at the Maputo Central Hospital examining maternal deaths through complete autopsy with macroscopic examination and histology. Obstetrical complications accounted for 38.2% of deaths and non-obstetrical conditions contributed to 56.1% of deaths (84% infection diseases). The results of this study suggest that the widely accepted assumption that maternal deaths directly attributable to malaria occur only in areas

of unstable malaria transmission needs to be revised. The percentage of the population living in urban areas with low transmission but surrounded by highly endemic areas is increasing in many African countries. This change together with the overall reduction in malaria transmission as part of a global elimination agenda may lead to increased deaths due to malaria in adults, especially pregnant women.

This study specifically evaluated clinic-pathological discrepancies in the diagnosis of causes of death in SSA. Dr. Menendez noted that clinical errors were present in 62% of maternal deaths and 40% had a major clinical error detected. Interestingly, eclampsia was the main source of false positive diagnoses (57.1%). Dr. Menendez noted that this study revealed that infectious disease are a significant cause of MM in Mozambique, there is an urgent need to implement effective and available tools, and deaths due to obstetric causes represent a failure of the health care system and require urgent improvements. She asserted that knowing which are the main causes of death is invaluable for health planning, priority setting , designing effective health programs and evaluating their impact, and introduced the possibility of minimally invasive autopsies (MIAs) based on targeted key organ biopsies in many countries.

### <u>Discussion</u>

Ms. Wolf asked for clarification on classification of death if co-infection (with HIV, for example) is present. Dr. Menendez commented that it is often difficult to give a final diagnosis. She explained that when more than one pathological diagnosis was identified, the main disease causing the death was classified as the cause of death. For example, cerebral toxoplasmosis in a patient with HIV/AIDS, the cause of death was classified as AIDS.

Dr. Pacque noted that he was surprised by the absence of maternal deaths from abortion. Dr. Menendez noted that likely these women were not accessing care a tertiary facility.

Dr. Marie-Thérèse Kyungu from DRC asked how can you be sure if the parasite identified in the brain is the cause of death and asked about the feasibility of lab services in developing countries like DRC. Dr. Menendez stated that it is difficult to attribute COD to malaria in many cases. She further explained that if the women had symptoms of severe malaria and sequestered parasites in the central nervous system, it was classified as malaria being a necessary cause of death. Recognizing the fact that limited lab services for the validation of minimally invasive autopsies was a challenge right now, it may not be so in the near future.

Dr. Bucagu noted he was surprised by the false diagnosis of eclampsia, given the diagnostic criteria. He noted WHO has recently published a maternal death surveillance tool to assist with correct diagnosis and COD. Several colleagues agreed that developing protocols is essential.

At the close of the session, Ms. Roman asked Dr. Menendez to quickly give an overview of the work of the MiP Consortium (MiPc). The MiPc works in four areas (treatment, prevention in Africa, prevention in Asia & Latin America and public health impact), as well as cross-cutting activities. It works with 41 institutions in 29 countries.

### Malaria in Pregnancy in the Americas Dr. Azucena Bardaji, ISGlobal

Dr. Bardaji introduced her presentation by providing a historical background on malaria in the Americas. Currently there are 21 countries with malaria transmission in the Americas. It is low and unstable transmission with P. falciparum and P. vivax (the latter which is responsible for 65% of reported cases). Brazil, Columbia and Venezuela contribute to <sup>3</sup>/<sub>4</sub> of reported cases. Dr. Bardaji noted that PAHO recommendations for malaria control during pregnancy rely on: active detection of infection at each ANC visit, promote diagnosis and effective treatment and ITN use.

Dr. Bardaji then summarized a non-systematic review of available data between 1990 until May 2014. The estimated number of pregnancies at risk in the Americas is 2.9 million and 3 million pregnancies at risk of Pv and Pf, respectively. The evidence on the burden of MiP in the Americas suggests that there is a higher risk of malaria in younger women with an unclear parity pattern. The impact of MiP in the America influences maternal and newborn health. Maternal anemia is the most common complication among infection women, which is frequently associated with thrombocytopenia. Dr. Bardaji noted that there have been 13 maternal death reports associated with Pf but no maternal death report associated with Pv. She also noted that MiP in the Americas is associated with higher risk of LBW. Dr. Bardaji highlighted that the region has contributed to the understanding of the pathophysiology of MiP.

In terms of MiP control recommendations, Dr. Bardaji stated that each country has different treatment regimen for prevention and cure (e.g., selection of first choice drugs, approach for prevention and relapses and radical cure) and recommendations are non-specific according to malaria transmission. The epidemiology of MiP in the region mirrors global trends in the region over the last decade. In conclusion, there are important lessons learned. In the context of decreased malaria transmission, MiP is still associated with harmful effects. As malaria transmission diminished, the approach in the detected may change from ACD to PCD.

### <u>Discussions</u>

Dr. Udom asked about the number of recommended and rate of ANC visits in the Americas. Dr. Bardaji noted that ANC attendance is quite high but noted she did not have exact figures available (likely >90% for ANC1 and >50% for ANC4). There are no specific incentives to attend ANC.

Dr. Mangiaterra asked about trends across the period studied and analyzing why these changes are happening. She also commented that change in transmission still poses risks to women and children. Dr. Bardaji noted that she will keep this in consideration in revising the final report, and the next first step will be dissemination with countries and stakeholders and need to think about other ways it can be useful (perhaps a technical consultation in-country).

Dr. Ouma asked for clarification on prevalence and which countries are actively moving toward elimination. Dr. Bardaji stated that a high proportion is due to Pv but varies across countries. Countries in the pre-elimination phase include: Costa Rica, El Salvador, Ecuador, Mexico, Belize, Paraguay and Argentina.

Dr. Peter Okui from Uganda requested clarification about terminology, noting the use of "malaria" and "malaria with danger signs." Dr. Baradji noted that it was a "homemade" classification used in one particular study in Columbia.

# DAY 3: 17 July 2014

# I. Opening Session

Dr. Mangiaterra opened Day 3 by noting that today's focus will be on workplanning. She highlighted key areas that have emerged during the meeting: integration, HSS, BCC. IPTp, CM, LLINs, Advocacy and Research. In addition, Dr. Ferenchick briefly summarized the main themes emerging from the presentation on Day 1.

# II. Additional Updates

### Providing Antenatal Care: updates Dr. Maurice Bucagu, WHO

Dr. Bucagu highlighted three main areas (evidence, new interventions, HSS) that have influenced the development of updated ANC guidelines. The guidelines are currently being updated and a FANC training package and ANC e-learning package have also been developed. The training manual has been finalized and field-tested; it will be available online in the near future. Additionally, there is implementation research on compliance with FANC guidelines in Uganda currently being undertaken. Dr. Bucagu concluded that ANC is an appropriate platform for MiP and updated guidelines are critical to include new evidence.

#### <u>Discussion</u>

*Ms.* Roman asked for the link for the materials. This will be circulated once available.

There was a specific question asking for clarification about the flu vaccine in pregnancy. Dr. Bucagu said that he included this example to demonstrate that colleagues in other areas are looking at ANC as a potential platform and that we must strengthen the platform to host all necessary intervention. Several colleagues also emphasized the importance of nutrition during pregnancy. Dr. Bucagu agreed that nutrition is very important but we also need treatment of infectious diseases.

Ms. Roman asked for more information how the training package is being rolled out. Dr. Bucagu reported that it was field tested in three countries (Ghana, Zambia, Malawi) and is now being disseminated at country-level. Countries are preparing for roll-out activities. Dr. Mangiaterra reported that members from the MiP WG provided input during the development but requested the opportunity to review a final version. She requested that WHO AFRO be informed that the MiP WG is ready and able to assist with the dissemination at country-level. Ms. Youll suggested that countries see how to incorporate roll-out activities into their workplans. Ms. Youll also suggested that Dr. Josephine Namboze serve as the link between MiP WG, AFRO and HQ.

Dr. Bucagu confirmed that the updated ANC Guidelines will be ready in 2015. Ms. Stender inquired as to whether or not a landscape analysis was done prior to development of training since many counties already have integrated packages. Dr. Bucagu said that this was developed in response to country requests and will assist many countries (such as South Sudan and Namibia) update existing training packages based on new evidence.

# EARN Update Policy Updates and Implementation Dr. Ambrose Talusina, KEMRI

Dr. Talusina highlighted MiP policy updates presented during the last EARN ARPM. Most of the EARN countries have MiP policy but may require support for updating policies. Rwanda does not have an IPTp policy, and Burundi is currently developing a policy to reintroduced IPTp. Sudan is contemplating introducing seasonal IPTp along Sahel belt.

### <u>Discussion</u>

Dr. Udom noted that RH and NMCP were invited to participate in all SRN APRMs last year and there was a side-session for MiP. SRN FPs were tasked to develop a list of TA needs and see how countries can be supported. Ms. Youll asked if workplans that came from these meetings could be shared. Dr. Mangiaterra asked Dr. Udom to follow-up on this last point and facilitate a TC for information sharing.

# **III. Work Planning**

### Identifying Priority Areas of Work for the MiP Working Group

Dr. Mangiaterra and Ms. Roman identified nine priority areas (integration, HSS, advocacy, BCC, research, case management, IPTp, LLINs and M&E) for the MiP WG moving forward. Participants were asked to work in small groups to identify specific needs in each of these categorizes. A spokesperson then reported back to plenary on the list generated for each area. Please see **Annex 1** for a chart summarizing the inputs of working group members.

### <u>Discussion</u>

Integration

- Several colleagues emphasized the need to educate the TRP on MiP and provide stronger technical support at country-level for MiP. Participants agreed that partners should be involved at the national level; a clear entry-point is assistance with the development of National Strategy.
- *Ms. Stender noted that there is a real opportunity for integration on diagnosis of infectious-diseases at ANC.*

Case Management

• Several questions regarding treatment of malaria in pregnancy (specifically the use of quinine) were raised. Dr. Bucagu confirmed that quinine is the recommended treatment and current evidence used by WHO supports this practice; use is not a risk factor for abortion.

IPTp

- Colleagues requested evidence on the self-administration of SP.
- There were several requests to follow-up with the MERG on the development of IPTp indicators and clarify what is being officially recommended by WHO.
- *Ms. Wolf highlighted longer lead times for SP procurement. Several colleagues reminded us that PSM is a cross-cutting issue.*

Other recommendations for possible MiP WG activities included the following: briefing note on quinine, guidance on how to address diversion of SP, consensus statement supporting continuous distribution of ITNs, push for inclusion of MiP in DHIS (consider a official letter from RBM on behalf of all the WGs)

### RBM Secretariat Work Planning Process & Election Dr. Betty Udom, RBM

Dr. Udom reviewed the work planning process and noted that given tight resources the MiP WG needs to actively think about resource mobilization. She also noted that the Secretariat will be downsizing over the coming months. Dr. Udom introduced participants to a new tool for development and tracking ("Roadmap") at countrylevel, and noted that the Secretariat will likely be using a similar tool for WGs as well.

Dr. Udom also reviewed the election process and noted that the MiP WG would begin the process of elections following this meeting. Both Dr. Agarwal and Dr. Mangiaterra have come to the end of their second two-year term but in the absence of any other identified candidate, should the WG want to re-elect the current cochairs, it is a possibility. Dr. Lynch noted that another WG faced a similar situation and re-elected one co-chair for a two-year term and extended the mandate of another by one year until another candidate was identified.

Elections will be held virtually over the coming weeks. Dr. Udom will facilitate.

# Review of the 2014-2015 Workplan Dr. Viviana Mangiaterra, The Global Fund

Dr. Mangiaterra reviewed the current workplan with participants. It is summarized by priority area in **Annex 2**. Several deliverables that have already been completed and links to these documents are listed below:

Progress and Impact Series: The contribution of malaria control to maternal and newborn health <u>http://www.rbm.who.int/ProgressImpactSeries/report17.html</u>

*PMI/MCHIP Review of National Level MiP Documents in 19 Countries* <u>http://www.mchip.net/sites/default/files/mchipfiles/19%20Country%20Review</u> <u>%20of%20MIP.pdf</u>

# Closing

Dr. Mangiaterra and Ms. Roman closed the meeting by noting that it was a very productive three days. They thanked participants for their valuable contributions, and also specifically thanked Dr. Udom and Ms. Shantell'e Baker from Jhpiego for their administrative support throughout the meeting preparations. They stated that all presentations would be made available on the RBM website and minutes would be circulated in the coming weeks. A follow-up teleconference will be scheduled for August 2014.

# ANNEX 1: POTENTIAL AREAS OF WORK FOR THE MIP WG

| Priority Area | Needs Identified in Each Priority Area   |
|---------------|--|
| INTEGRATION   | <ol> <li>Ensure coordinated planning         <ul> <li>Make a conjoint plan with defined joint activities</li> <li>Procure at the same time</li> </ul> </li> <li>Include MIP directly into training curricula (especially RN, midwives and CHWs)         <ul> <li>Ensure the during re-trainings that the newest guidance is being communicated and that supervisors directly ask about ANC and IPTp outreach</li> </ul> </li> <li>Strengthen M&amp;E and data collection         <ul> <li>Improve the quality of service provision</li> <li>Ensure WHO/GF/RBM/Stop TB guidance clearly mention and encourage integration in the TA they provide</li> <li>Use high-level advocacy platforms, (e.g. ALMA, AU, etc.)</li> <li>Use newly launched platforms (e.g., Global Action Plan on Newborns, Prevention of Stillbirth Initiatives) to pass the message about health pregnancies</li> <li>Produce an evidence package (e.g., literature review, Cochrane review, lessons learned documents, etc.)</li> <li>Develop consensus statement promoting correct use of folic acid; specific to WHO recommendations.</li> </ul> </li> </ol> |
| HSS           | <ul> <li>1. Development of resource materials for countries on HSS<br/>investment guidance in the context of Malaria in Pregnancy         <ul> <li>Development of PowerPoint slides specifically<br/>addressing Global Fund malaria/HSS Concept Note and<br/>grant making opportunities</li> <li>Brown Bag session on MIP at the Global Fund for the<br/>Secretariat (other opportunities?)</li> <li>Highlighting MIP and related issues such as anemia in<br/>Global Fund Information Notes (e.g. malaria, HSS,<br/>RMNCH)</li> <li>Contribute to HSS Conference in South Africa satellite<br/>session on service integration to highlight MIP</li> </ul> </li> <li>Lab strengthening         <ul> <li>If not done yet, the first step would be to conduct<br/>mapping for commodities and human resources in<br/>country</li> <li>Focus on microscopy (malaria, TB and HIV)</li> </ul> </li> </ul>   |

|          | Training of health service providers   |
|----------|--|
|          | 3. Procurement and supply chain (PSM)  |
|          |  |
|          | <ul> <li>If not done yet, the first step would be to conduct</li> </ul>                      |
|          | mapping of health commodities distribution (RDTs, SP,  |
|          | other key medicines) in country (e.g. being done for   |
|          | malaria commodities in Nigeria)  |
|          | <ul> <li>Countries developing integrated PSM system as a</li> </ul>                          |
|          | longer term objective  |
|          | 4. M&E and health information systems  |
|          | <ul> <li>Data generation (less reliance on DHS and MIS? More</li> </ul>                      |
|          | in routinely collected data such as DHIS)  |
|          | Harmonization of routinely collected data across   |
|          | diseases   |
|          | 5. Integrated training at primary care level   |
|          | • This relates to lab strengthening, PSM, and M&E as   |
|          | well as on the range of conditions (e.g. malaria &   |
|          | pneumonia)   |
|          | • The content of the training matters as well and needs                                      |
|          | to be innovative. Class-room type one time training  |
|          | has shown to be ineffective, providers need to actively                                      |
|          | gain skills from the training->what is a good training                                       |
|          | material for MIP that could be developed by the WG?  |
|          | 6. Leadership and accountability   |
|          | <ul> <li>Leadership and accountability by disease programs are</li> </ul>                    |
|          | strong while those in HSS is lacking as they often cut                                       |
|          | across several departments within MoH. Address   |
|          | structural issues such as collaboration between  |
|          | national malaria programs and RMNCH departments?   |
|          | (e.g. Nigeria has a department of health planning and  |
|          | statistics that is responsible for HMIS and ensures data                                     |
|          | integration of all diseases)   |
|          | integration of an alseasesy  |
| ADVOCACY | 1. Increase investments for MIP interventions by key funding                                 |
|          | institutions   |
|          | Review country concept notes to check level of MIP   |
|          | investment, technical appropriateness and adequacy   |
|          | of commodity support included;   |
|          | Promote the new Progress & Impact report to key  |
|          | target audiences to raise awareness of the value of  |
|          | MIP investments;<br>Identify key global level target audiences for MIP                       |
|          | <ul> <li>Identify key global level target audiences for MIP messaging, including:</li> </ul> |
| L        |  |

|          | <ul> <li>TRP</li> <li>Global Business Council</li> </ul>   |
|----------|--|
|          | <ul> <li>National malaria/RBM partner/ coordinating</li> </ul>   |
|          | groups,  |
|          | <ul> <li>CCMs</li> </ul>   |
|          | <ul> <li>Businesses with large numbers of employees</li> </ul>   |
|          | in endemic countries   |
|          | 2. Build national level advocacy capacity for MIP  |
|          | Develop national-level coalitions of   |
|          | stakeholders/partners in MIP who can advocate for  |
|          |  |
|          | system strengthening related to MIP interventions  |
|          | 3. Increase competencies in delivery of MIP services   |
|          | Identify key HSS issues  |
|          | <ul> <li>Prioritize actions, particularly funding</li> </ul>   |
|          | <ul> <li>Sequence actions, based on risk of success/failure</li> </ul>   |
|          | 4. Find cost-effectiveness data to strengthen the evidence base and  |
|          | provide messages for Ministers of Finance, Business leaders and  |
|          | others   |
|          |  |
| BCC      | 1. Increase community involvement in MIP interventions   |
|          | <ul> <li>Change policy to allow CHWs to do IPTp and LLIN</li> </ul>  |
|          | distribution   |
|          | <ul> <li>Document experiences, assemble evidence base and</li> </ul>   |
|          | then use MIP WG to disseminate Best Practices  |
|          | Assess additional potential communication channels in  |
|          | communities and disseminate these (including mother  |
|          | support groups)  |
|          | 2. Harmonize and standardize messaging on key MIP interventions  |
|          | for communities  |
|          | 3. Provide input into general malaria BCC campaigns relevant to MiP  |
|          | (act as a resource)  |
|          | 4. Integrated MiP into in-service and pre-service training   |
|          | 5. M&E/measurement of BCC for MiP  |
|          | 6. Improve technical quality of BCC  |
|          | 7. Share best practices in MiP BCC between countries   |
|          | 8. Develop core set of BCC messages for adaptation and use (policy,  |
|          | provider, public)  |
| DESEADOU | <ul> <li>9. Integrated MiP messages into other areas such as nutrition</li> <li>1. Need for epidemiological data to tailor MIP interventions in the</li> </ul> |
| RESEARCH | face of changing transmission dynamics [Objective: To collect  |
|          | regular epidemiological data to inform MIP activities]   |
|          | <ol> <li>Continued efficacy of SP – ongoing monitoring of IPTp (efficacy,</li> </ol>   |
|          | measuring actual use in the community) [Objective: To continue   |
|          | monitoring IPTp efficacy to inform MIP programming]  |
|          | 3. Include LLIN questions in core malaria module for the DHS/etc   |
|          | questionnaire [Objective: To acquire data on net source, continued   |
|          |  |

| Γ               | use and assess to inform policy!   |
|-----------------|--|
|                 | <ul> <li>use, and access to inform policy]</li> <li>Streamline paper registers and ensure column for LLINs in the ANC register, and the routine HMIS reports [Objective: To ensure more accurate documentation of LLIN receipt at ANC]</li> <li>The role of the CHW? How much burden can we place on them going forward – specifically for MIP (IPTp, LLINs, Fe+) [Objective: to assess the role of CHWs in providing MIP interventions (IPTp, LLINs – in addition to everything else)]</li> <li>Strategies to improve quality of care to increase ANC attendance [Objective: To assess the quality of ANC care across malaria endemic countries and to devise strategies to improve them in an attempt to increase ANC attendance]</li> <li>Integration of care topics at first ANC attendance and centralization of information [Objective: To assess ANC service integration and better understand how to reach women at the beginning of their pregnancy and harmonize services]</li> <li>Design and roll out electronic health records to make service documentation easier, faster, and more accurate [Objective: Pilot studies on the design and implementation of EHRs]</li> <li>OR research on adherence to standard treatment guidelines for MIP across countries (Case Management) [Objective: Observational study to assess current MIP treatment practices across countries]</li> <li>Research to identify the key factors affecting the use of Quinne in the first trimester and come up with mitigation initiatives. [Objective: To determine which antimalarial, if any is preservice across countries]</li> </ul> |
|                 | initiatives [Objective: To determine which antimalarial, if any, is  |
|                 | safe for use in the first trimester]   |
| CASE MANAGEMENT | 1. Translate/re-enforce WHO guidelines for case management   |
|                 | (diagnosis & treatment) in pregnancy for severe and  |
|                 | uncomplicated (WG)   |
|                 | 2. Evidence for safety of ACTs in 1 <sup>st</sup> Trimester and general pharmaco   |
|                 | in pregnancy: Guidelines & Tools (WG)  |
|                 | 3. Support improvement of quality of case management in  |
|                 | pregnancy (tools and guidelines) M&E indicators  |
|                 | Pre-service training & supportive supervision -  |
|                 | engagement of countries (malaria and anaemia)  |
|                 | (SRNS)   |
|                 | Reluctance to change to new policies   |
|                 | 4. RDTs vs microscopy in pregnancy (WG)  |
|                 | Update evidence base : Desk Review   |
|                 | 5. Acceptability of AA –QS for treatment in pregnancy (WARN &  |
|                 | CARN) SRNs)  |
|                 | 6. PSM-malaria commodities (SRNs)  |
| 1               |  |

|       | 7. Screening and treatment during ANC visits – integrated             |
|-------|---|
|       | 8. Integrated symptom screening at ANC: Assessment of service         |
|       | availability (SRNs and countries)                                     |
|       | 9. Provider perceptions about quinine in 1 <sup>st</sup> trimester WG |
|       | Alternative treatment   |
|       | Drug surveillance/PV Quinine  |
| ІРТр  | 1. Further clarify the date for the first SP dose.                    |
|       | 2. Clear understanding of the # & schedule of ANC visits (this is     |
|       | expected to be addressed by WHO as part of the ANC guidelines to      |
|       | be updated by 2015)   |
|       | 3. M&E: How to adjust the IPTp coverage rate at country level, taking |
|       | into account the number of HIV – infected mothers on CTX (not to      |
|       | be given SP and therefore not to be included in the denominator)      |
| LLINS | 1. Provide guidance on the role of continuous distribution in         |
|       | sustainable net supply  |
|       | Consensus statement promoting LLINs availability                      |
|       | at ANC  |
|       | 2. Provide guidance on use of additional channels outside ANC/EPI to  |
|       | increase net supply   |
|       | 3. Strategies to ensure regular supply of LLINs                       |
|       | Voucher system  |
|       | House-to-house distribution   |
|       | Subsidization of sale of LLINs @ GHC1.50                              |
|       | 4. Improve supply chain process                                       |
|       | Funding   |
|       | Forecasting   |
|       | Procurement process   |
|       | Documentation   |
|       | 5. Improve reporting at all levels (community, district, regional and |
|       | national)   |
|       | 6. Continuous public education to promote acceptability               |
|       | 7. Data at community level to be harmonized with mainstream MOH data  |
| M&E   | 1. Harmonize indicators   |
|       | 2. Longitudinal national ANC registers with clear reporting systems   |
|       | 3. Tools to collect data at community level                           |

#### ANNEX 2: 2014-2015 MIP WG WORKPLAN UPDATE

# **Priority Area: Funding**

Sustain current level of funding for malaria and to close the funding gap by 2015, including through improved coordination among multilateral, bi-lateral, and domestic funders

- MiP interventions included in H4+ (Every Woman, Every Child) annual workplan and highlighted as a key component of RMNCH programming in all H4+ grant applications
  - Coordination with H4+ Technical Team and Inter-Agency Task Teams through regular MiP WG representation at meetings to mobilize resources for MiP

Funding secured annually for MiP interventions and integrated programming through strong partnership with RMNCH leaders.

- Representation of MIP WG at key maternal and newborn health meetings (e.g. Global Maternal Health Meeting, Women Deliver) to coordinate resource mobilization for MiP
- Increased funding for MiP interventions mobilized annually through collaboration with key donors
  - Continued coordination with PMI, UNICEF, BMGF for resource mobilization
  - Support partners (e.g. Jhpiego, Abt, PATH) to prioritize MiP through RMNCH platforms

Improve country access to, absorption, and efficient use of available funds

- Countries reprogramming GF grants through the end of 2015 include strategies for scaling-up MiP actvitives and are aligned with prinicples of integration
  - Coordination with Harmonization WG of GF related activities through regular MiP WG representation at meetings
  - Preparation of updated guidance on integration of malaria and RMNCH to assist countries in leveraging additional resources for MiP
  - Resolution of MiP bottlenecks and successful scaling-up of MiP activities in 6 priority countries
  - Facilitation of partner-supported technical assistance as indentified by RMNCH and NMCP representatives during SRN APRMs in 2013

# **Priority Area: Disease Control**

Improve acceptance and use of malaria control/ elimination interventions.

- Documentation and dissemination of best practices in Ghana to close the gap between IPTp1 & IPTp2 and scaling-up efforts by mid-2015 Technical Review of Ghana MiP success story brief
- Package of MiP guidance (i.e., policies, BCC & IEC messages) developed and disseminated at countrylevel by end of 2014
  - Preparation of MiP messages with support from Malaria Advocacy Working Group Dissemination of MiP guidance at global meetings (e.g.
  - MIM, ASTMH, Women Deliver, Maternal Health)
  - Review and udapte current MiP documents as necessary and appropriate.
    - Link existing and new materials to MHTF website
- Systematic review summarizing what is being done at country level for case management during pregnancy in three countries published by mid-2014
  - A systematic review and meta-analysis of what we know about women's access and provider practices for the case management of malaria during pregnancy
- Mechanism plans and progress reviewed annually Bi-annual Review and planning meeting convened

Strengthen routine surveillance for malaria, and the use of those data for evidence-based decision making.

- Three reports documenting country-level MiP coverage, M&E MIP indicators and successes/ challenges by program area developed, reviewed and disseminated by mid-2014
  - Develop MiP Synthesis of Best Practices and Lessons Learned
  - Technical review of document highlighting MiP M&E Indicators in 6 countries
  - Technical review of document reviewing MiP national level documents in 19 PMI countries

# **Priority Area: Advocacy**

Position the control and elimination of malaria as an integral part of the post-2015 development agenda at global regional, and country levels.

- RBM's Progress and Impact Series Report published in early 2014 and biannual contributions to the Maternal Health Health Task Force publication through the end of 2015 both demonstrate MiP progress and impact to build strong case for future investment and action in MiP
  - Publish article on MiP interventions in Progress and Impact Series
  - Publish biannually on MiP progress in MHTF publication
- Article advocating for continued MiP programming in Latin American countries (LAC) published by September 2014
  - Publish article on key issues, epidemiology and barriers to MiP interventions in LAC

Continue galvanizing political and financial commitment and technical engagement at global, regional, country, district and community levels.

- RBM MiP WG website functioning as main platform and repository for MiP materials and tools by mid-2014
  - Update website, with possible independent MiP page for general audience, as outlined in Global MiP Communications Strategy

# **Priority Area: Procurement/Supply Systems**

Improve global, country and local availability of affordable, quality commodities for the control and elimination of malaria.

- MiP included as part of dialogue on essential drugs and commodities for maternal, infant and child health through the end of 2015
  - Representation of MiP WG Co-Chairs or representatives at global and regional-level meetings on priority medicines and life saving commodities for women and children

# **Priority Area: Program Coordination**

Strengthen programmatic and management capacity at all levels, and in countries, controlling, eliminating, and preventing the re-introduction of malaria

- Managerial quality assurance tool for monitoring of MiP coverage and identifying and addressing impediments developed in 2 African countries by end of 2014
  - Facility assessments and bottleneck analyses in two African countries to identify factors impeding IPTp delivery and uptake from the perspective of managers, provides and clients

Maximize use of malaria investments to strengthen health systems and delivery of routine health services.

- Improved harmonization of RMCNH and NMCP to ensure consistency in country-level MiP guidance and integrated service delivery
  - Work with partner organizations to promote harmonization by encouraging inclusion of RMNCH and NMCP representatives at all meetings

# **Priority Area: Research & Development**

Promote Operational Research to support evidence-based, efficient Programme implementation and the use of existing tools.

- Report that provides evidence-base for communitybased distribution of IPTp without detracting from ANC published by the end of 2014
  - Review IPTp uptake and outcomes of community distribution programs in Kenya for MiP

#### Annex 3: Evidence-Based Q&A

Several important questions arose during the meeting. This Q&A summarizes key themes and provides a list of resources for further reading.

#### 1. What evidence is available on self-administered SP?

Namusoke F, Ntale M, Wahlgren M, Kironde F, Mirembe F: Validity of self-reported use of sulphadoxine-pyrimethamine intermittent presumptive treatment during pregnancy (IPTp): a cross-sectional study. *Malar J* 2012, 11:310.

Offianan, A., Penali, L., Coulibaly, MA., Tiacoh, N., Ako, A., Adji, E., Coulibaly, B., Koffi, D., Sarr, D., Jambou, R., Kone, M. Comparative efficacy of uncontrolled and controlled intermittent preventive treatment during pregnancy (IPTp) with combined use of LLTNs in high resistance area to sulfadoxine-pyrimethamine in Côte d'Ivoire. Infect Drug Resist. 2012; 5: 53-63.

# 2. What evidence is available to support continued use of quinine in the first trimester?

Dellicour, S., Desai, M., Mason, L., Odidi, B., Aol, G., Phillips-Howard, P. A., Laserson, K. F., Ter Kuile, F. O. Exploring risk perception and attitudes to miscarriage and congenital anomaly in rural Western Kenya. *PLoS One*, 2013, 8(11): e80551 <u>http://dx.doi.org/10.1371/journal.pone.0080551</u>

Jones KL, Donegan S, Lalloo DG: Artesunate versus quinine for treating severe malaria. *Cochrane Database Syst Rev* 2007, (4):CD005967.

Piola P, Nabasumba C, Turyakira E, Dhorda M, Lindegardh N, Nyehangane D, Snounou G, Ashley EA, McGready R, Nosten F, Guerin PJ: Efficacy and safety of artemetherlumefantrine compared with quinine in pregnant women with uncomplicated Plasmodium falciparum malaria: an open-label, randomised, non-inferiority trial. *Lancet Infect Dis* 2010, 10(11):762-769.

Ward SA, Sevene E, Hastings I, Nosten F, McGready R. Antimalarial drugs and pregnancy; safety, pharmacokinetics and pharmacovigilance. *Lancet Infect Dis.* 2007, 7(2), pp. 136-144. <u>http://dx.doi.org/10.1016/S1473-3099(07)70025-7</u>

Yeka A, Achan J, D'Alessandro U, Talisuna A: Quinine monotherapy for treating uncomplicated malaria in the era of artemisinin-based combination therapy: an appropriate public health policy? *Lancet Infect Dis* 2009, 9:448-452

### 3. What evidence is available on the use of ACTs in first trimester?

Dellicour, S., Brasseur, P., Thorn, P., Gaye, O., Olliaro, P., Badiane, M., Stergachis, A., ter Kuile, F.O. Probabilistic record linkage for monitoring the safety of artemisinin-based combination therapy in the first trimester of pregnancy in Senegal. *Drug Saf*, 2013, 36(7): 505-513, <u>http://dx.doi.org/10.1007/s40264-013-0059-1</u>

Manyando C, Mkandawire R, Puma L, Sinkala M, Mpabalwani E, Njunju E, Gomes M, Ribeiro I, Walter V, Virtanen M, Schlienger R, Cousin M, Chipimo M, Sullivan FM: Safety of artemether-lumefantrine in pregnant women with malaria: results of a prospective cohort study in Zambia. *Malar J* 2010, 9:249.

# 4. What data is available to support continued IPTp-SP use despite increasing resistance?

Kayentao, K., Garner, P., van Eijk, A.M., Naidoo, I., Roper, C., Mulokozi, A., MacArthur, J.R., Luntamo, M., Ashorn, P., Ogobara, K. D., ter Kuile, F.O. Intermittent Preventive Therapy for Malaria During Pregnancy Using 2 vs 3 or More Doses of Sulfadoxine-Pyrimethamine - and Risk of Low analysis. JAMA, 2013, 309(6), pp. 594-604, <u>http://dx.doi.org/</u>10.1001/jama.2012.216231

Taylor, S.M., Antoni,a A.L., Chaluluka, E., Mwapasa, V., Feng, G., Molyneux, M.E., ter Kuile, F.O., Meshnick, S.R., Rogerson, S.J. Antenatal receipt of sulfadoxinepyrimethamine does not exacerbate pregnancy-associated malaria despite the expansion of drug-resistant Plasmodium falciparum: clinical outcomes from the QuEERPAM study. *Clin Infect Dis.* 2012, Jul; 55(1):42-50, http://dx.doi.org/10.1093/cid/cis301

#### 5. What studies demonstrate how quality of ANC affects MiP interventions?

Hill J., Hoyt J., van Eijk A.M., D'Mello-Guyett L., ter Kuile F.O., Steketee, R., Smith, H., Webster, J. Factors Affecting the Delivery, Access, and Use of Interventions to Prevent Malaria in Pregnancy in Sub-Saharan Africa: A Systematic Review and Meta-Analysis. *PLoS Med*, *2013*, 10(7): e1001488, <u>http://dx.doi.org/10.1371/journal.pmed.1001488</u>

Menaca, A,, Pell, C., Manda-Taylor, L., Chatio, S., Afrah, N.A., Were, F., Hodgson, A., Ouma, P., Kalilani, L., Tagbor, H., Pool, R. Local illness concepts and their relevance for the prevention and control of malaria during pregnancy in Ghana, Kenya and Malawi:

findings from a comparative qualitative study. *Malar J*, 2013, 12(257), <u>http://dx.doi.org/10.1186/1475-2875-12-257</u>

Pell, C., Menaca, A., Were, F., Afrah, N,. Chatio, S., Manda-Taylor, L., Hamel, M., Hodgson, A., Tagbor, H., Kalilani, L., Ouma, P., Pool, R. Factors Affecting Anenatal Care Attendance: Results from Qualitative Studies in Ghana, Kenya and Malawi. *PLoS ONE*, 2013, 8(1): e53747, http://dx.doi.org/10.1371/journal.pone.0053747

Pell, C., Straus, L., Andrew, E.V.W., Menaca, A., Pool, R. Social and Cultural Factors Affecting Uptake of Interventions for Malaria in Pregnancy in Africa: A Systematic Review of the Qualitative Research. *PLoS ONE* 2011, 6(7): e22452. http://dx.doi.org/10.1371/journal.pone.0022452