

Consensus Statement

ASKING THE RIGHT QUESTIONS: Advancing an HIV Research Agenda for Women and Children



Photo: UNAIDS/A. Gutman

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Substantial progress has been made in expanding access to antiretroviral therapy (ART) for adults and children living with HIV and preventing vertical transmission.¹ However, the scale-up of ART programmes has also drawn attention to a number of knowledge gaps related to clinical management and ART programme delivery for women and children. Issues such as the development of weight-adjusted dosage recommendations and paediatric formulations, the impact of antiretroviral prophylaxis to prevent vertical transmission on future treatment options for women, and optimal ART delivery models to maximize access and minimize loss to follow-up are some of the questions which continue to challenge health care providers, programme managers and the populations they serve.

Through a 10-month consultative process involving investigators, clinicians, civil society and UN agencies, the International AIDS Society (IAS) and its international partners have identified 20 priority research questions to address these critical knowledge gaps. The undersigned organizations affirm their support for the proposed research agenda for women and children and call for increased investment and concrete action in pursuit of these recommendations. While the focus of this agenda is treatment research, it is also critical to recognize the importance of linking treatment and prevention research for women and children, a topic explored in other documents and by other groups.

A Priority Research Agenda

The Expert Reference Group convened for this initiative identified high-priority research questions within four broad categories: 1) clinical research on prevention of mother-to-child transmission (PMTCT) and paediatric treatment; 2) clinical research on treatment issues for women; 3) operations research on treatment for women; and 4) operations and implementation research related to PMTCT, including paediatric care, treatment and support.

Questions in the fourth research category in this consensus statement – operations/implementation research related to PMTCT, including paediatric care, treatment and support – were addressed by a parallel consultative process led by UNICEF. That initiative involved a high-level consultation with

¹ The IAS has been advised, in particular by networks of women living with HIV, that the term "prevention of vertical transmission" should be used instead of "preventing mother-to-child transmission (PMTCT)". Some women with HIV find the term PMTCT stigmatising. The term PMTCT is used by several organizations, in particular UN agencies, and is understood to describe four 'pillars' of preventing vertical transmission: primary prevention for women; prevention of unintended pregnancies; prevention of vertical transmission using ARV prophylaxis; and diagnosis, treatment and care for children and their families. Both terms are used in this statement according to the context.

The Consultative Process

In February 2009, the International AIDS Society - Industry Liaison Forum (IAS-ILF) began *Mapping and Building Consensus on Clinical and Operations Research Priorities for Women and Children*. This initiative was designed to develop a research agenda, based on the most current scientific evidence and expert advice, which would answer outstanding priority knowledge gaps in clinical and programme management relevant to the unique needs of women and children. The IAS established an Expert Reference Group to provide advice and strategic direction to the initiative, which included experts from the IAS, National Institutes of Health, Elizabeth Glaser Pediatric AIDS Foundation, UNAIDS, UNICEF, WHO and others. Additional detail on the iterative process used to develop, validate and prioritize the research questions identified in this consensus statement is available online at www.iasociety.org/ilf.aspx.

the Interagency Task Team for PMTCT including the WHO, UNAIDS and U.S. agencies in collaboration with George Washington University (GWU) and the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF). Information on this related initiative, including the final list of operations/ implementation research recommendations from a September 2009 technical consultation held in Washington, DC are available online at www.unicef.org and www.pedaids.org. The two initiatives worked closely to avoid duplication and to collaborate on areas of shared interest. Both sets of recommendations represent a collaborative effort among the IAS and its partners to strengthen research needed to inform the global response to AIDS.

OVERARCHING RECOMMENDATIONS TO IMPROVE RESEARCH FOR WOMEN AND CHILDREN

Three overarching recommendations provide guidance to all planned or current clinical and operations research trials across the first three categories. These principles speak to the need for better data sharing and for strategic investments in trial designs required to support the hypotheses and data analyses needed to address key knowledge gaps for women and children.

- RECOMMENDATION 1:** Invest in studies (e.g., prospective, retrospective and longitudinal) identified as optimal ways to answer the research questions outlined in this report.
- RECOMMENDATION 2:** Data from existing operations research studies, programme evaluations and clinical trials should be more broadly shared, reviewed and analyzed to answer some of the specific knowledge gaps identified in this report.
- RECOMMENDATION 3:** Research data should be disaggregated by sex to ensure opportunities for gender-based analysis using a variety of indicators, such as retention in ART programmes, morbidity and mortality, loss to follow-up, and pharmacokinetic and pharmacodynamic parameters.



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CLINICAL RESEARCH: PMTCT AND PAEDIATRIC TREATMENT

- RECOMMENDATION 4:** Invest in innovative drug manufacturing and delivery systems (e.g., dissolvable films, microtablets) to address the need for appropriate paediatric formulations.
- RECOMMENDATION 5:** Evaluate a range of weight-adjusted dosage recommendations and fixed-dose combinations (FDCs) for children.
- RECOMMENDATION 6:** Invest in innovative TB and HIV diagnostics and monitoring to facilitate paediatric and early infant diagnosis and treatment.
- RECOMMENDATION 7:** Review currently enrolled clinical trials and conduct necessary clinical studies to evaluate the impact of comorbid conditions and their treatment on drug dosage and toxicity, with priority given to TB, malaria and malnutrition.
- RECOMMENDATION 8:** Ensure a more comprehensive pharmacovigilance system by expanding the existing antiretroviral pregnancy registry to include low- and middle-income country cohorts/pilots and establishing an appropriate follow-up registry to evaluate the impact of ARV exposure *in utero* or during extended infant prophylaxis on uninfected children in resource-limited settings.
- RECOMMENDATION 9:** Review existing data and currently enrolled trials to establish optimal treatment strategies for children.

CLINICAL RESEARCH: TREATMENT FOR WOMEN AND GIRLS

- RECOMMENDATION 10:** Ensure clinical cohorts and clinical trial data are disaggregated by sex, ethnicity and race to support ongoing analysis of potential differences in pharmacokinetics and pharmacodynamics, treatment outcomes and adverse events in these populations.
- RECOMMENDATION 11:** Establish appropriate studies to answer the questions about the impact and interactions of endogenous and exogenous hormones and ART on health outcomes for girls and women.
- RECOMMENDATION 12:** Assess the impact of ARV prophylaxis to prevent inter-, peri- and post-partum HIV transmission on future ART options and health outcomes for women.

OPERATIONS RESEARCH: TREATMENT FOR WOMEN AND GIRLS

- RECOMMENDATION 13:** Conduct retrospective and prospective, context-specific studies to identify how to leverage health care systems (including primary care, sexual and reproductive health services, PMTCT, and harm reduction/opioid substitution programmes) to improve women's access to and retention in health care.
- RECOMMENDATION 14:** Conduct operations research, including programme evaluations, to improve ART access, remove barriers to access and ensure long-term follow-up for sub-populations of adolescent and adult women (e.g., women living in rural settings, single women, sex workers, women who use drugs, transgender individuals and women from different ethnic and socio-economic populations).
- RECOMMENDATION 15:** Conduct operations research, including programme evaluations, to identify nutritional supplementation interventions (micronutrient and macronutrient) for women that can be integrated into care, treatment and support programmes.

OPERATIONS RESEARCH: PMTCT AND PAEDIATRIC CARE, TREATMENT AND SUPPORT (from the UNICEF-led initiative)

- RECOMMENDATION 16:** Review existing data and conduct studies to determine the most effective strategies for providing and monitoring CD4 testing and ART for treatment-eligible pregnant and breastfeeding women.
- RECOMMENDATION 17:** Review existing data and conduct studies to determine the most effective implementation strategies for prophylaxis during breastfeeding and the comparative effectiveness of infant versus maternal prophylaxis
- RECOMMENDATION 18:** Review existing data and conduct studies to determine the feasibility and impact of providing ART for eligible pregnant women within routine maternal and child health services in antenatal clinics.
- RECOMMENDATION 19:** Review existing data and conduct studies to determine the effect and impact of task-shifting on PMTCT and paediatric care, support and treatment scale-up in various settings, at various levels of the health care system and among different cadres of health workers.
- RECOMMENDATION 20:** Review existing data and conduct studies to determine what interventions at the programme, facility, community and household levels have the greatest impact on retention in paediatric HIV care, especially in the first 12 months of life.

Conclusion

Advocating for the funding and implementation of this research agenda will necessarily require collaboration involving research-granting agencies, investigators, industry, health care providers, UN agencies and civil society, including women living with HIV. Some of the recommendations above provide strategic guidance on the design and analysis of clinical and operations research studies, seeking to optimize research investments and leverage the number and type of analyses

that can be conducted on a specific trial (or trials). Others identify a clear direction for exploring urgent issues with research-granting agencies in the near future.

The priority research questions outlined in this consensus statement offer a unique opportunity for stakeholders involved in HIV clinical and operations research to work collaboratively to close some of the most important knowledge gaps affecting women and children today. The organizations endorsing this agenda commit to working together on its implementation. We invite others to join us to help ensure that the overall AIDS research agenda works for women and children, too.

Endorsers

Joining the International AIDS Society in endorsing this research agenda for women and children are:

amfAR, The Foundation for AIDS Research
AVAC, Global Advocacy for HIV Prevention
Boehringer Ingelheim
Clinton Health Access Initiative
Coalition on Children Affected by AIDS
Elizabeth Glaser Pediatric AIDS Foundation
European AIDS Treatment Group
International Community of Women
Living with HIV/AIDS

International Treatment Preparedness Coalition
Merck
Treatment Action Group
UNAIDS
UNICEF
ViiV Healthcare
World Health Organization



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