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Washington, D.C. Community Consensus on the Earlier Inclusion of Pregnant Women and Persons in TB Research

We, sixteen representatives of communities affected by tuberculosis (TB) and with experience related to TB in pregnancy, met in Washington, D.C., on October 25–28, 2023, to develop a consensus on the inclusion of pregnant and breastfeeding women and persons in TB treatment and vaccines research. The community meeting was part of a larger convening hosted by the Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination (SMART4TB) Consortium, the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network, and the World Health Organization (WHO) Global TB Program (*Tuberculosis and pregnancy: Laying the groundwork for consensus on inclusion in research*).

* We have elected to use the phrase “pregnant women and persons” in acknowledgement that not all who become pregnant identify as women. We chose this approach as it underscores the experiences of women and the ongoing fight for gender equality and human rights, including those related to health and science, while being inclusive of other identities that share in these struggles. As we are all cisgendered women and men, we cannot speak for persons of childbearing potential that do not identify as women. But we hope this statement and our advocacy for the inclusion of pregnant women and persons in research benefits all individuals who can become pregnant, in all their diversity. We hope our statement catalyzes additional input from affected communities, especially community members that represent broader gender identities.

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What follows is our consensus positions on how pregnant and breastfeeding women and persons should be included in TB research. These positions were informed by discussions held with scientists and clinicians and shaped by our lived experiences and the work we do in communities affected by TB. We end with a call to action and a commitment on our part to work together and with our communities to see these calls come to fruition.

It is our intention that these positions influence the discussions and recommendations that emerge from an ongoing scientific consensus process expected to inform a future WHO consensus statement on the earlier inclusion of pregnant women and persons in TB research.

1 *TB remains a significant global health challenge, affecting hundreds of thousands of pregnant, postpartum, and breastfeeding women and persons. We demand nothing less than equitable health care that ensures the well-being of pregnant and breastfeeding women and persons affected by TB.*

2 Pregnant and breastfeeding women and persons have been historically excluded from clinical trials due to concerns about potential risks to the developing fetus or infant. We raise with concern that this exclusion has resulted in few evidence-based guidelines and treatment options available to pregnant and breastfeeding women and persons.

AND

3 We strongly believe that the exclusion of pregnant and breastfeeding women and persons from TB clinical research is not only a missed opportunity to improve the health outcomes of pregnant women and persons, the health outcomes of their infants, and public health as a whole, but it is also a violation of their basic human right to appropriate medical care and to enjoy the advancements of science. We argue this exclusion is rooted in misogyny and a form of sex-based discrimination.

4 We acknowledge that respecting ethics and human rights is paramount when involving pregnant and breastfeeding women and persons in research, and we see pregnant and breastfeeding women and persons as key authorities in how ethics and human rights are maintained in the research setting. We agree that the following principles must be upheld:

- A commitment to **equity and reciprocity** in research is needed to overcome power imbalances between researchers, clinicians, and pregnant women and persons. Researchers must create equitable, mutually beneficial, and bidirectional relationships with pregnant and breastfeeding women and persons and their communities throughout research and beyond.
- **Participatory decision making** requires the direct and meaningful engagement of pregnant and breastfeeding women and persons in research decisions, especially those concerning their own exclusion from trials. Pregnant and breastfeeding women and persons are uniquely qualified to weigh the risks and benefits of research and enhance the relevance, acceptability, and impact of research through their contributions.
- **Intersectionality and cultural sensitivity** must inform all future research. Even between neighbors, experience, knowledge, and relationships with TB will differ. Researchers must build trials and programs that acknowledge, embrace, and address the unique needs, experiences, and realities of local communities and individuals.
- **Accessibility and flexibility** must be foundational to all research efforts to support pregnant and breastfeeding women and persons participation in their own care and in research. Researchers must consider the entire process of service delivery to communities participating in trials and integrate research with existing service delivery systems — meeting pregnant and breastfeeding women and persons where they are.
- The well-being, safety, privacy, and confidentiality of pregnant and breastfeeding women and persons and their choices must be prioritized and upheld through **integrity and robust informed consent** in research.
- The **autonomy** of individuals must be respected, with pregnant and breastfeeding women and persons centered as active collaborators in their own care and recognized as equal stakeholders in decision making.
- **Human rights** must be upheld and respected at each stage of the research process.

TREATMENT

5 We are discontented with the reality that pregnant and breastfeeding women and persons are burdened with making decisions regarding the health and safety of themselves and their child in the complete absence of data. Pregnant women and persons are denied their autonomy and the right to choose their own inclusion in clinical trials to generate data — infringing on their right to health and right to science.

6 We are in unanimous agreement that the potential benefits of including pregnant and breastfeeding women and persons in trials to identify better, safer treatment regimens often outweigh the potential risks.

VACCINES

7 We unanimously agree that the potential benefits of vaccination to prevent infection or disease demand the inclusion of pregnant women and persons in vaccine clinical trials. We also acknowledge that the risks of each vaccine candidate require individualized assessment to weigh the risks and benefits for pregnant women and persons.

8 We recognize that vaccines are critical tools in TB prevention. The current failure to investigate vaccine safety in pregnancy during efficacy trials represents a missed opportunity to identify safe and effective vaccines to protect women and persons during pregnancy, the postpartum period, and/or beyond.

9 We believe that the risks to pregnant women and persons in vaccine clinical trials can be mitigated through earlier preclinical developmental and reproductive toxicology studies and clinical trial design that prioritize the safety of parent and child.

10 We strongly believe in each pregnant woman's and person's ability to gauge the risk of participating in clinical trials for vaccines when provided with necessary and complete information in an accessible and culturally appropriate form.

11 We recognize that pregnant and breastfeeding women and persons share experiences. But we believe that there is little justification for excluding breastfeeding women and persons from TB vaccine studies, even those in which the exclusion of pregnant women and persons is supported by evidence-based rationale.

CALL TO ACTION

12 Continued failure to include pregnant and breastfeeding women and persons in the research agenda leaves pregnant and breastfeeding women and persons to shoulder the risks of older, untested treatments and without the prospect of protective immunity during pregnancy and the postpartum period through vaccination. We call on the following stakeholders to take immediate action:

- ➔ Policymakers, funding agencies, and regulatory bodies **must actively promote and support the inclusion of pregnant and breastfeeding women and persons in TB research.** This requires providing adequate resources, guidance, and training to researchers and product sponsors to address the specific needs and concerns of pregnant and breastfeeding women and persons.
- ➔ Researchers and product sponsors **must start with the assumed inclusion of pregnant and breastfeeding women and persons in clinical trials and justify any exclusions.** Exclusions should be based on clear rationale developed in consultation with pregnant women and persons and with their explicit support.
- ➔ Researchers and product sponsors **must protect pregnant and breastfeeding women and persons by normalizing their inclusion in phase III studies. Preclinical developmental and reproductive toxicology studies must be conducted earlier in the research process** (no later than Phase IIb) to achieve this.
- ➔ National programs **must collect and analyze data on TB in women and persons who are pregnant.** Multiple approaches, including sentinel sites, prospective cohorts, and birth outcomes surveillance studies are urgently needed to understand the safety of existing and future TB drugs in pregnancy.
- ➔ Researchers, product sponsors, and policymakers **must recognize that safety concerns differ for pregnant versus breastfeeding women and persons. Research inclusion, data, and policies should therefore be considered separately.**
- ➔ Research and product sponsors and other relevant stakeholders **must involve pregnant and breastfeeding women and persons and communities directly affected by TB in the entire research process, from preclinical to clinical studies, to design and distribution of innovations.** Pregnant and breastfeeding women and persons are uniquely situated to assess the risks and benefits of research that will affect them and can provide integral feedback to support the success of the trial and resulting policies.
- ➔ Research and product sponsors and national programs **must share information about treatments, vaccines, and the research process with the community before research begins and throughout the research process** in an accessible, simplified language so they can provide input into the research process and make informed decisions about their health and participation.
- ➔ **Acting on these recommendations will accelerate progress toward developing evidence-based interventions for and improved health outcomes among pregnant, postpartum, and breastfeeding women and persons that are affected by TB. We invite you to join us in rejecting the status quo and building a future in which pregnant women and persons have access to the full suite of scientific and health advancements.**