International Alliance for Biological Standardization

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Workshop on Assessing Consequences of Maternal Immunization on Foetal Outcomes
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Title: Assessing the Safety of Maternal Immunization in Observational and Real-World Data: Lessons Learned from a Global Study

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Background:
Findings from observational studies of maternal immunisation and preterm birth have been heterogeneous, raising questions about the extent to which variability reflects true effects versus differences in study design, analysis, and data structure. As observational, real-world data are essential for post-licensure safety evaluation, there is a need to better understand how these factors influence signal detection, comparability, and interpretation across settings.

Methods:
Global Vaccine Data Network (GVDN) conducted a harmonised, multi-country retrospective cohort study using linked electronic medical records and registries. COVID-19 vaccination during pregnancy was modelled as a time-varying exposure within a distributed analysis framework, with site-specific estimates combined via meta-analysis. Analyses addressed methodological considerations, including fixed cohort bias, gestational age estimation, and cross-site heterogeneity in outcome and covariate definitions and availability.

Results:
Estimates for preterm birth were broadly consistent with no increased risk following COVID-19 vaccination during pregnancy, although effect sizes varied across sites and analytic models. Across selected outcomes—including haemorrhage during pregnancy, postpartum haemorrhage, and hypertensive disorders—estimates were sensitive to analytic specification and differed between sites. For some outcomes, substantial heterogeneity persisted despite harmonised methods, highlighting the influence of confounding, outcome ascertainment, gestational age measurement, and site-specific data structures.

Conclusion:
In this multi-database study, no safety signal is evident for preterm birth; however, complementary analyses across multiple outcomes demonstrate that observational estimates are sensitive to analytic choices and between-site heterogeneity. Careful interpretation of real-world evidence and continued methodological refinement is critical to improving signal detection, supporting benefit–risk assessment, and strengthening confidence in maternal immunisation programmes globally.