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Prospect for a GBS vaccine and the pathway to licensure, including considerations for LMICs

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Despite over 50 years of research, there is still no vaccine against Group B Streptococcal disease (GBS) and GBS remains the leading cause of meningitis in neonates and early infancy. Several vaccine manufacturers have progressed maternal vaccines against different targets as far as Phase II clinical trials. However, GBS disease incidence means that a classical phase III efficacy trial would be extremely large and therefore costly. Thus, it is widely accepted that developing serocorrelates of protection against the main GBS disease-causing serotypes might be a useful tool to progress a vaccine to licensure. Such a serocorrelate would be predicted in natural immunity studies, comparing antibodies in infants with GBS disease to healthy controls. It is important to consider that any antibodies measured in both GBS disease cases and healthy controls must have been generated following exposure of the pregnant (or pre-pregnancy) woman and passed to the infant via the placenta. Thus, the protective mechanism is predominantly from IgG, as this is the only immunoglobulin that crosses the placenta. This makes the protection conferred from a maternal GBS vaccine different to that of vaccines designed for the infant vaccine schedule, where immunity is conferred by both IgG and IgM. It is therefore likely that a serocorrelate would be based on quantitative IgG concentrations correlated to in vitro function.

Several issues remain unresolved before such a serocorrelate can be finalised. Firstly, any seroepidemiology study will still be large, because of the need to prospectively collect cord blood from large numbers of women in anticipation of an infant going on to develop disease. Investigating whether maternal, cord and infant serum antibodies are comparable is critical to logistical and cost planning of such studies. Secondly, there remains a need to understand whether antibody-mediated protection is similar in countries with high burdens of malaria, HIV and syphilis in pregnancy. These factors, and potentially others such as maternal under-nutrition in pregnancy, are vital in understanding if protection via maternal vaccination will be effective in low and middle income countries. Finally, we need to explore whether antibodies generated following exposure to GBS via colonisation in the pregnant woman function in the same way as vaccine-induced antibodies. All these steps need to be explored as a matter of urgency if we are ever to see a maternal GBS vaccine licensed and available for those countries with the highest burden of disease.