Written responses to open questions of the webinar 'Saving childrens' lives – treating neonatal sepsis' by Hanan Balkhy, Manica Balasegaram, Dhanya Dharmapalan and Borna Nyaoke, originally broadcast on 20 November 2020. See webinar recording here: https://revive.gardp.org/saving-childrens-lives-treating-neonatal-sepsis/

Question asked	Response from the speakers
Thank you for an interesting discussion. In many settings it is difficult to stop antibiotics in newborns with suspected sepsis and many times newborns received unnecessary long antibiotics treatments. Is there any role of biomarkers such as CRP in low resource settings to shorten antibiotic treatment, if blood cultures are not available? Any experience in your settings?	Borna Nyaoke: CRP is particularly useful for monitoring the response to treatment and for ruling out an infection. A repeated determination of CRP 24–48 h after the initiation of antibiotic therapy has been reported to carry a 99% negative predictive value in accurately identifying uninfected neonates, though nothing replaces a clinical impression and the gold standard (i.e. culture results). CRP has the best diagnostic accuracy when combined with another infection marker that compensates for its diagnostic weakness and provides reliable sensitivity during the early phases of sepsis. Suitable markers include but are not limited to PCT, IL-6, and IL-8. Many further parameters may provide similar good results, but are not yet sufficiently examined to be applied in clinical practice. (Hofer. N et al, 2012) Dhanya Dharmapalan: CRP is best used for monitoring response to treatment. However, it a nonspecific inflammatory marker. CRP may be falsely elevated due to non-infective factors which can give an erroneous impression of ongoing sepsis or new onset sepsis, therefore clinical correlation is important. On the other hand, CRP will take at least 8 to 10 hours to elevate and might be normal if checked very early in sepsis. However serial negative CRP would help point towards a non-septic condition.
Some local labs are reporting wrong antibiogram in developing and underdeveloped countries. This is due to the weak government steps and failure of good licence system among lab staff. What are the preventive measures we can take to stop this?	Borna Nyaoke: Regular antimicrobial audits and reviews of laboratory data (surveillance). Dhanya Dharmapalan: A standard operating procedure for reporting AMR was launched by ICMR. This guideline was recently updated in 2019. There are considerable efforts being taken for standardisation.

Remaining audience questions from the webinar 'Saving childrens' lives – treating neonatal sepsis', broadcast on 20 November 2020.

Question asked	Response from the speakers
It is often reported that sepsis diagnosis suffers from discrepancies within medical coding (As reported in the KE Rudd paper from Lancet on global burden of sepsis). Can neonatal sepsis treatment benefit from standardizing diagnosis to treatment protocols?	The present situation is that there is lack of global consensus regarding even the definition of neonatal sepsis. Standardising treatment protocols is extremely challenging as the causative organisms and resistance pattern differ in various settings. It is important to improve diagnostic facilities, facilitate development of local data on resistance with a continued surveillance and help develop local recommendations.
Why are you focusing on a treatment (antibiotics) with known resistance problems and not on preventing these infections through maternal vaccination?	Vaccines are indeed an alternative approach. WHO will review and publish the bacterial vaccine pipeline in 2021.
I would like to know what support is in place for Sepsis research in Nigeria? A multidisciplinary group of researchers in Kano are championing multi-center study on Sepsis Incidence, determinants and outcome in Kano (SIDOK). Main challenge is lack of funding. How can you support their work?	In Africa, GARDP is currently conducting clinical trials and studies on neonatal sepsis in Eastern Africa (Kenya and Uganda) and South Africa. Countries like Nigeria in West Africa with high incidences of neonatal sepsis would be good collaborating partners in our AMR work as the programmes expand.
There was a study from a rural part of India on Home Based Neonatal Care and use of Inj Gentamycin +/- Cotrimoxazole which brought down the neonatal sepsis incidence. Any similar data from Kenya?	No data has been published on this in Kenya but as has been shown with low rates of acceptance of referral advice from healthcare givers especially in rural and less educated populations then a simplified treatment regimen, administered at home may assist reduce neonatal sepsis incidence.
For Dr. Dharmapalan, in addition to blood culture, what other method do you use to isolate bacteria from sepsis patients?	In addition to blood cultures, bacteria can be isolated from CSF and urine samples of septic babies. Time to identification of bacteria can be reduced by using multiplex PCR on the bacterial isolates.

Question asked	Response from the speakers
Many thanks for this informative seminar. My question is to Dr. Dharmapalan- 1) Is it known how neonatal sepsis incidence differs between urban vs rural settings in India? Or the mode of delivery of the babies predisposes babies to sepsis or not? 2) The three Gram-negative bacteria mentioned to cause neonatal sepsis in India are also well-known nosocomial infection (hospital borne). What measures are in place or constituted to prevent nosocomial infection associated neonatal sepsis in India? 3) Is it possible that economic disparities affect accessibility of correct treatment to babies in India and are there findings to constitute optimal public health policies to prevent that?	1) The neonatal sepsis incidence differs between urban and rural settings. We do not have an exact data. Hospital based studies report neonatal sepsis of 30 per 1000 live births while various (limited) studies in community have reported sepsis incidence of 2.7% to 17% of all live births. It is not proven that any particular mode of delivery predisposes to sepsis. A recent meta-analysis and systemic review published in PLoS showed that the risk factors for neonatal sepsis in India were male neonates, outborn admissions, gestational age less than 37 weeks, need for artificial ventilation and premature rupture of membranes. 2) Yes, the three leading Gram-negatives are well known to cause nosocomial infection. Education and training regarding infection control measures are being undertaken to prevent nosocomial infection. Breastfeeding is being promoted across the country. But more needs to be done including avoiding overcrowding in NICU, improving nurse to baby ratio, implementing a good antibiotic policy, etc. 3) Economic disparities do affect accessibility of correct treatment. A field trial of homebased newborn care done in a tribal village of Gadchiroli in India (published in 2005 by Bang et al.) proved that newborn deaths can be significantly averted by home based care in regions where either facilities are not available or parents refuse for admission in higher centres. National health programmes like Janani Shishu Suraksha Karuakram (JSSK) started in 2011 entitles all pregnant delivery to deliver in institution at a completely free cost. Newborn services are also offered free including for sick newborns. LaQshya was launched in 2017 under a National scheme which is labour room quality improvement initiative to improve maternal and neonatal quality of care during labour. A lot of efforts are ongoing to bridge the gaps that might arise due to economic disparities.

Question asked	Response from the speakers
Congratulations to all the speakers for the excellent presentations. Question to Dr Dharmapalan - can you extrapolate the AMR data from big cities in India to the smaller places or rural areas given the lack of studies in those settings?	Unfortunately most of the studies are hospital based and mostly in the urban settings. It wouldn't be correct to extrapolate the AMR data to rural places as sepsis rates vary from place to place. We certainly need more studies.
Given the low yield of blood cultures, do you think we need more sensitive diagnostic tools for neonatal sepsis, and if yes, how can these be best deployed to protect existing and new antibiotics?	Yes, a diagnostic tool which is highly sensitive will be able to provide confidence in stopping empirically started antibiotics in culture-negative sepsis. We need more research in this area. With advancing molecular technology, if in future, we are able to detect the causative organisms easily; targeted treatment can be given rather than continuing empirically started broad spectrum antibiotics. Rational treatment will improve judicious use of antibiotics and help to protect both existing and new antibiotics.