2nd July 2019

Dear Dr Donnelly,

It is our great pleasure to submit our manuscript to JAC entitled “*Prevalence of and risk factors for gut mucosal colonisation with extended-spectrum beta lactamase producing Enterobacteriaceae in sub-Saharan Africa: a systematic review and meta-analysis”* for consideration for publication.

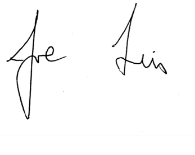
Antimicrobial resistance (AMR) and in particular extended-spectrum beta-lactamase producing *Enterobacteriaceae* (ESBL-E) pose a significant threat to human health in sub-Saharan Africa (sSA). Low-resource regions face distinct challenges in curbing the spread of ESBL-E, including; poor water sanitation and hygiene (WASH) infrastructure; a high burden of infectious diseases and lack of diagnostic capability all of which result in huge usage of 3rd generation cephalosporins.

Reduction in gut mucosal ESBL-E colonisation is an attractive target for intervention to reduce ESBL-E infection, as it is thought to precede invasive infection. However, the basic epidemiology of ESBL-E in sSA is poorly described. A 2016 systematic review examined community ESBL-E carriage world-wide and found only 4 studies in sSA, with no assessment of risk factors. We therefore present the results of a new systematic review and meta-analysis of 32 studies of ESBL-E in sSA.

We show that in many countries in sSA, the prevalence of carriage of ESBL-E is comparable to the highest in the world, and that hospitalisation, antimicrobial exposure and possible water hygiene practices are likely drivers of carriage. Moreover, we highlight numerous data gaps that must be filled to design interventions to interrupt ESBL-E transmission in sSA; long term longitudinal studies are lacking, the role of HIV in driving ESBL-E carriage is poorly defined, many studies introduce bias by selective recruitment of populations, and there is widespread unexplained heterogeneity in time and space across the continent.

Our study therefore not only provides estimates of ESBL-E carriage in sSA, but can serve as a first step to informing intervention studies designed to interrupt ESBL-E transmission in sSA.

Yours sincerely,



Dr Joseph Lewis