To the editors of *The Lancet Infectious Diseases*:

We submit the manuscript “Risks of Type 2 Oral Polio Vaccine use in post-cessation outbreak response”, for consideration for publication in *The Lancet Infectious Diseases*. The coordinated removal of Type 2 oral polio vaccine (OPV2) from immunization activities worldwide took place in April 2016, and presents an unprecedented situation in global health – the intentional cessation of a vaccine that, while critical to the eradication of natural Type 2 poliovirus, is known to itself have the ability to establish circulation in low-immunity populations and revert to the neurovirulent phenotype over time. The success of the second global eradication of a human pathogen hinges on removing all oral polio vaccine from use, but this cessation is not without its attendant risks.

This manuscript describes a modeling study of what we consider to be the primary risk to the success of Type 2 cessation – the continued persistence of vaccine-derived Type 2 poliovirus circulation, triggering outbreak response activities with OPV2 upon discovery, thereby seeding the circulation of new vaccine-derived polioviruses. We built a model of polio transmission on a realistic population network representing 16 countries in West Africa. This model is applied to estimate the risk of long-term circulation of vaccine-derived poliovirus following an outbreak response conducted according to current Global Polio Eradication Initiative protocol within northern Nigeria, a region historically susceptible to the emergence and persistence of vaccine-derived polioviruses. This risk is projected over a 5-year horizon under a wide range of assumptions about population immunity levels at and after vaccine cessation, migration rates, and vaccine transmission properties.

The results of the study indicate that once the cohort of immunologically naïve children born post-cessation grows to sufficient levels to support transmission, use of OPV2 in outbreak response presents a high risk of exportation from the response region and long-term circulation in the importing regions. Under all but the most optimistic assumptions, this risk presents in the immediate future, within 1-3 years from today. The manuscript concludes with a series of suggested actions that could mitigate this risk by accelerating the detection of and response to existing vaccine-derived poliovirus lineages.

The results of this study will be of interest to public health researchers, infectious disease modelers, and policymakers both within the polio program and in other global vaccine-preventable disease control and elimination efforts. Due to the historical significance of the potentially imminent eradication of a second human pathogen, we believe that the results are of broad interest to health practitioners.

This manuscript describes original work of the authors and has not been submitted to any other journal. The authors declare no competing interests. Thank you for considering this manuscript, and we look forward to your response.

Thank you,

Dr. Kevin McCarthy

Senior Research Scientist

Institute for Disease Modeling, 3150 139th Ave SE, Bellevue, WA, 98005, USA