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Authors' reply

We would like to thank Andrew Lover for using our case-control study¹ (of the association between Zika virus infection in neonates and microcephaly) to discuss an alternative analytical approach, penalised logistic regression.² In that approach the odds ratio would have been higher (OR 86.5, 95%CI 4.9–1523.4) than the one estimate using exact logistical regression (OR 55.5, 95% CI 8.6–+∞). We note that the inferior limit is lower, but the association is still highly statistically significant.

Lover also did a sensitivity analysis (again using penalised logistical regression) to explore the potential effect of the refusal rate among control participants of about 25%. The observed laboratory positivity (the exposure under study) in cases was 41%. None of the 62 controls were laboratory confirmed for Zika virus. In his sensitivity analysis, Lover assumed that 10–50% of controls refusing to participate in the study were laboratory confirmed. Even in the clearly unrealistic assumption of 50% laboratory confirmation among controls refusing study participation (a higher positivity than in cases), the association is still statistically significant. Whatever the analytical approach used, the conclusion is the same: congenital Zika virus infection is the cause of microcephaly.

The next public health question is not the magnitude of the odds ratio, but what is the risk of microcephaly and others manifestation of the congenital Zika syndrome in babies of

women who have Zika infection during pregnancy. This estimation, and the effect of any cofactors of this risk, will not be established in a case-control study but in the ongoing cohort studies³ of pregnant women with Zika virus infection.

We declare no competing interests.

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Crimean-Congo haemorrhagic fever virus and Eid-UI-Adha festival in Pakistan

Crimean-Congo haemorrhagic fever (CCHF) has caused 20 deaths in Pakistan as of Aug 20, 2016.¹ These deaths might be attributable to Eid-ul-Adha, an annual religious festival observed by Muslims, during which nearly 8 million animals, including goats, sheep, cows, and camels are sacrificed.² Pakistan has experienced various nosocomial outbreaks of CCHF and Eid-UI-Adha is regarded as a vulnerable period for these outbreaks. In routine butchery for food, animals are slaughtered at designated facilities in the presence of veterinarians to

ensure the animal's health.³ However, during Eid-UI-Adha, the pattern of animal slaughter changes in accordance with religious beliefs. These changes include factors such as transport of animals for sale from endemic rural to urban areas, little regulation of animal sales, advanced purchase of animals, few health checks on purchased animals, freelance and non-professional butchers, slaughtering of animals in public areas, gathering of spectators around the butcher to watch the slaughter, absence of formal training among butchers, delayed disposal of blood and carcasses of sacrificed animals, and scarceness of appropriate methods for the disposal of the animal waste. These factors result in increased exposure of the general public to viraemic animals and enable animal-to-animal, animal-to-human, and human-to-human transmission of CCHF virus.

Despite efforts made by Government of Pakistan, the upsurge of CCHF remains uncontrolled.⁴ Moreover, the death of a senior surgeon who became infected while operating on a patient with CCHF has also raised serious concerns over biosafety measures at health facilities.⁵ The government has not taken a hard line and we believe that putting full effort into the control of the aforementioned factors could go a long way to combating CCHF in Pakistan.

In the next 10–15 years, Eid-UI-Adha will occur in summer when CCHF is more prevalent, suggesting a dire need to implement policies on the slaughter of sacrificial animals to prevent a potential health catastrophe. We believe that cattle farmers, shepherds, and butchers are unaware of the health hazards posed by CCHF virus, especially via the infected blood of slaughtered animals. Provision of appropriate and comprehensible training will be of paramount importance for reducing CCHF transmission.

We suggest that the Government of Pakistan should focus its efforts on vertical programmes for the control