Reply to Jones et al

Sudhir Venkatesan[1], Puja R. Myles[1], Ziad Memish[2,3] and Jonathan S. Nguyen-Van-Tam[1] on behalf of study authors.

1 Division of Epidemiology and Public Health, University of Nottingham, UK
2 Ministry of Health, Riyadh, Kingdom of Saudi Arabia
3 College of Medicine, Alfaisal University, Riyadh, Kingdom of Saudi Arabia

Corresponding author: Sudhir Venkatesan
Address: Room B104, Clinical Sciences Building, University of Nottingham, City Hospital, Nottingham NG5 1PB,
United Kingdom.
Telephone: +44 0115 823 1718
Email: Sudhir.Venkatesan@nottingham.ac.uk

Jones et al. assert that our conclusions hinge on exclusion of the 1,652 patients recorded as having received neuraminidase inhibitor (NAI) treatment on the day of hospitalization [1]. We did this after consultation with clinicians, on the grounds that, in such patients, the decision to hospitalize and treat with NAI was simultaneous; or, that these patients had deteriorated to a point where there was practically no window of opportunity for NAI treatment to impact on the need for hospitalization. Despite conceding that this "seems reasonable", these commentators present an alternative analysis which mistakenly considers such patients as treated, arriving at an odds ratio (OR) of 1.97 (95% CI not supplied) [2]. Placing all 1,652 patients into one group and assuming that all received pre-admission NAI treatment, is simply incorrect. We set out to investigate the impact of *preadmission* NAI use on hospitalization; our exposure variable was 'NAI treatment received in the community or in an outpatient setting' not 'NAI treatment at any time' as Jones and colleagues seem to imply with their alternative approach. If we had retained these 1,652 in our analysis, it would have been more reasonable to classify them as untreated, given that there was no time for the drug to have worked. This would have produced a crude OR 0.10 (0.08 to 0.12).

Jones et al. further state it is "misleading" to call our study an individual participant data (IPD) meta-analysis [2]. We make it very clear that our article is based on observational data and the Preferred Reporting Items for a Systematic Review and Meta-analysis of Individual Participant Data (PRISMA) statement acknowledges the legitimacy of the IPD approach for observational studies [3]. We have been clear about our inclusion and exclusion criteria and openly discuss the limitations of our approach [1]. It is claimed that we excluded 96% of patients because of missing data [2]. This a misleading assertion, which fails to recognize that the study was part of a cluster of studies, each with different objectives related to investigating the impact of NAI treatment on a range of public health outcomes in pandemic influenza patients. We therefore, requested raw data for all the studies together, recognising that not all centers would have data that could contribute on all outcomes. Therefore, while data relating to this study reflects only 2.6% of the total data obtained on pandemic influenza patients in any setting, we have included 67.1% data informative for this specific study question.

Finally, Jones et al. compare our findings to two studies that investigated the impact of NAI treatment on patients with relatively mild seasonal influenza. We have repeatedly emphasised that our findings are from a cohort of pandemic influenza patients at high risk of hospitalization, and may not be generalizable to a broader spectrum of community patients most of whom have mild influenza. Jones et al. appear to have overlooked the sensitivity analysis we performed in patients from centers with lower rates of hospitalization [1]; these finding are not dissimilar to ones that they cite [2].

Conflicts of Interest: JSN-V-T reports that a grant to the University of Nottingham from F. Hoffmann-La Roche funded the current study; he also reports grants to the University of Nottingham from GlaxoSmithKline for research in the area of influenza; and non-financial support from ESWI

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