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Author reply: RE:"Reassessing the global mortality burden of the 1918 influenza pandemic"

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We thank Dr. Chandra and Christensen for giving their letter (1) regarding our paper on the 1918 pandemic mortality burden (2). In our paper we assessed the distribution of country excess mortality rates due to the pandemic , based on observed age specific population mortality rates and, critical, use knowledge from other influenza pandemics and how variation in mortality can be expected between and within countries. The average of this distribution is taken as the excess rate for the world and used to calculate the total worldwide mortality given the world population of 1.92 billion.

Incomplete registries are not problematic as long as the methodology did not change in the six years we used. As long as there is a good representativeness, the excess mortality rate due to the pandemic would be the same for incomplete and complete registries. We didn't want to make an assessment of the pandemic burden in India, which in our view is extremely challenging (see our remarks paper about the India data in our paper (2)), we used India to have a country with an excess at the very high end of the distribution. It is important to note that Chandra and Christensen have misread table 2 (1,2). The difference between the two total death counts is not the mortality estimate for British India, but the difference between the total Global estimates, if the British India data are present or absent from the sample of countries used to make the Global estimations.

We stressed that the validity of the estimation should be studied extensively. Early twentieth century yearly mortality rates can vary strongly between adjacent years and countries (famine, war, outbreak of infectious diseases), we tried to control for this by using a short reference period, age specific mortality rates, three estimation scenario's, and control for a few factors. Most importantly, one should use bio-medical knowledge and experience with pandemic influenza to validate the findings (see the paper's extensive web-material(2)).

The second point made by Chandra and Christensen is that some parts of the world (colonial Asia and Africa) would have looked more like India then Europe. This needs to be carefully validated, China was hit mildly by the 1918 influenza pandemic (3). Another example of a high population country in Asia is Indonesia, where estimates range from 402,163 (4) to 4.3 million (5). If presented as an excess rate per 100,000 it varies from 1,159 to 12,464. The first rate is based on weekly registry mortality rates (4) for Java (34 million population) in the second wave. The second value of 4.3 Million, several times India's excess, would imply that 12.5% of the total population of Java would have died in 1918-1919. The

1918 pandemic age signature places the highest excess mortality rate in the 20-49 age group and the lowest in 5-19 and over 50 years old age groups (6). Steenis (7), compared Magelang in Indonesia with Amsterdam. For, Amsterdam, 33% of the deaths were in the under 20; 51.9% in the 20-50; and 15.1% in the over 50. For Magelang, 53.5% under 20; 32.2% were 20-50; and 14.3% over 50. This clearly indicates that most of the 1918 excess was among the young in Magelang, which suggests that other factors played a role in Indonesia. Furthermore, one would expect such a high mortality to lead to a significant decline in the population size, taking several years before to recover. The population registry (8), however, does not show such a decline. In comparison, in Sweden in 1773 , 5.2% of the total population died (the highest mortality found in the HMD database (9)), resulting in a population decline and requiring recovery of about 4 years.
The second point of Chandra implies a mortality distribution with two peaks: one 'European' peak with an excess mortality rate of around 500 per 100,000 and an 'India' peak with 3,000 as excess rate. For the experiment purposes, assuming there were 200 countries and total deaths of 50 million, the world rate would be around 2,750. This requires 20 'European-like' and 180 'India-like' countries. 100 million deaths would mean that just over 5% of the world population died due to the pandemic, which would mean that in most countries the population would decline and would need several years to recover. This is contrary to what was observed and to how influenza pandemics behave and lead to excess mortality.

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