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LETTER

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Cost-effectiveness analysis has to consider all available evidence when informing inputs

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Dear Dr. Ellis,

We read with interest the recent cost-effectiveness analysis (CEA) published by Ruiz-Aragón et al., 2020,[1] concluding: "QIVc [Flucelvax] offers a cost-effective alternative to QIVe [egg-manufactured influenza vaccine] and should be considered as an alternative vaccine to QIVe for people aged 9–64 at high risk of influenza complications in Spain".

As a cost-effectiveness analysis (CEA) measures the incremental health gains and costs of interventions, results are highly sensitive to assumptions of benefit. For this reason, WHO recommends vaccine effectiveness (VE) estimates should be based upon systematic reviews or meta-analyses; or use a range of values, subject to sensitivity analyses representative of extreme circumstances.[2] ISPOR guidelines insist on a comprehensive and transparent approach to select input data from the best available, evidence-based source.[3] Husereau *et al.* state that if single study effectiveness source is used, the design features must be fully explained and justified.[4]

This analysis by Ruiz-Aragón *et al.* is based on a single point relative vaccine effectiveness (rVE) from Boikos et al., 2019,[5] and therefore met none of these criteria above. While we focus here on health economic guidelines, the study from Boikos *et al.* is also flawed from a design perspective for several reasons (nonspecific outcomes; single season; unclear methods) and is notable mainly for the very high rVE reported. Indeed, to further support our position that the health economic model is flawed and is driven by bias toward high rVE estimates, the vaccine effectiveness used for 18–65 year old (26.8%) has been applied to those aged 9–18 years, yet the Boikos study referred to in their model reports only 18.8% for 4–17 year olds, and this did not reach statistical significance.

These limitations were avoidable as at least five other studies describing effectiveness of cell-manufactured vs. egg-manufactured vaccines have been completed, and four of these have been published in peer-reviewed journals.[6–10] These studies demonstrate no consistent trend in results favoring cell-manufactured over egg-manufactured vaccines.

The omission by Ruiz-Aragón *et al.* of these data points in favor of a single rVE estimate does not fit the minimal standards for CEA analysis,[2–4] provides a distorted view of the relative health economic attributes of the vaccines under analysis and prevents readers from taking an unbiased view of the relative health economic merits of egg- and cell-manufactured influenza vaccines.

Sincerely yours,

Disclosure of potential conflicts of interest

AP, FA, JN, RH, and JLLB work for Sanofi Pasteur, a company which makes influenza vaccines.

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