

## Vaccination in patients with COPD: COVID has raised the bar

Patients with chronic lung disease, including chronic obstructive pulmonary disease (COPD), are recommended to have vaccination for influenza and pneumococcus both because of their higher risk of adverse outcomes from these infections, but also to reduce healthcare costs from hospital admissions with pneumonia and/or acute exacerbations. While there is good evidence to support this practice, much greater awareness of vaccine efficacy, and vaccine side effects, driven by medical and community experience with coronavirus disease 2019 (COVID-19), has raised expectations and scrutiny of the efficacy of our current vaccines for respiratory infections.

Assessing the efficacy of vaccines in the setting of COPD is not straightforward because there is significant season-to-season and year-to-year variation in the prevalence of common respiratory pathogens, especially viral pathogens like influenza (and almost certainly COVID-19 in coming years). Observational studies must therefore be carefully interpreted if they do not encompass at least several years including multiple winter seasons. Equally, in observational studies, there are potential biases in that those vaccinated may be more likely to have access to health care and may be more motivated to utilize other protective measures such as adherence with medications, cessation and avoidance of tobacco smoke and other environmental irritants, avoidance of others with active respiratory infections and use of personal protective strategies such as masks and regular hand washing.

In a recent publication in *Respirology*, Li et al.<sup>1</sup> present data from a 1-year observational study of the impact of 23-valent pneumococcal vaccine and influenza vaccine on hospitalizations in patients with COPD in Hebei province in China. In an attempt to adjust for seasonal variation in pathogens, they recorded exacerbations in the 3 years prior to vaccination and compared them in the 1 year following. Of 474 patients enrolled in the study, 109 received trivalent influenza vaccine (TIV), 69 received 23-valent polysaccharide pneumococcal vaccine (PSV-23) and 296 received both with the choice of vaccine strategy determined by individual patient preference. Vaccine effectiveness for exacerbations was calculated to be 70% for influenza vaccine, 54% for PSV-23 and 72% for the combination. For pneumonia, the corresponding effectiveness was 59%, 53% and 73% while for hospitalization it was 58%, 46% and 69%.

The estimates of effect by Li et al.<sup>1</sup> for the efficacy of PSV-23 are not that much larger than suggested by meta-analyses of randomized controlled trials and a similar recent observational study in Hungary.<sup>2</sup> Walters et al.<sup>3</sup> in the last

Cochrane analysis of pneumococcal vaccines in COPD found a 41% reduction in pneumonia and a 40% reduction in exacerbations for PSV-23, but no difference in hospitalizations or death. One issue with Li et al.<sup>1</sup> is the use of PSV-23, rather than a newer conjugate vaccine. The 13-valent conjugate vaccine is clearly more efficacious in preventing pneumonia.<sup>4</sup> Equally, conjugate vaccines lead to longer lasting antibody responses in patients with COPD,<sup>5</sup> which is consistent with their greater efficacy after the first year and over 5 years compared to PSV-23 in a small observations study.<sup>6</sup> For these reasons, conjugate pneumococcal vaccines have generally supplanted PSV-23 in high-risk groups like the elderly and those with COPD.<sup>7</sup>

The impact of influenza vaccine in patients with COPD has not been as well studied as PSV-23. A recent Canadian study<sup>8</sup> estimated that influenza vaccine was associated with only a 22% reduction in hospitalizations in patients with COPD; however, a number of small randomized trials have had estimates in excess of 50%.<sup>9</sup> It was interesting that the combination of TIV and PSV-23 was not observed to be as effective by Li et al.<sup>1</sup> as has been suggested by other groups.<sup>10</sup> One critical factor may be that the efficacy of influenza vaccine can vary considerably year by year,<sup>11,12</sup> probably due to both the relative match to circulating strains as well as innate immunogenicity of the vaccine.

While the study by Li et al.<sup>13</sup> adds further weight to the recommendations for both influenza and pneumococcal vaccination in patients with COPD, their efficacy is well short of that for which we have come to expect (and publicly debate) with COVID-19. Given the enormous health and economic cost of these pathogens, especially in COPD, governments need to provide the proper inducements for the development of a new generation of vaccines for pneumococcus and influenza so that we can achieve 90% or greater reductions in all clinical endpoints for these endemic and problematic pathogens. COVID-19 has not only provided new tools and pathways for vaccine development, but we have also been shown what can be done when there is sufficient support and resourcing, and we now need to make sure we leverage this new-found capacity and capability to full effect.

### KEYWORDS

chronic obstructive pulmonary disease, COPD, coronavirus disease, COVID-19, influenza and pneumococcal vaccination, pneumonia

### CONFLICT OF INTEREST

None declared.

**ORCID**

Grant Waterer  <https://orcid.org/0000-0002-7222-8018>

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Grant Waterer MD, PhD 

*School of Medicine, University of Western Australia, Royal Perth Hospital, Perth, Western Australia, Australia*

**Correspondence**

Grant Waterer

Email: [grant.waterer@uwa.edu.au](mailto:grant.waterer@uwa.edu.au)

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