



## When an “Active Call” can be a “Wake-up Call”

Stefania Maggi<sup>1</sup> · Jean-Pierre Michel<sup>2</sup>

Published online: 11 March 2019  
© Springer Nature Switzerland AG 2019

**Keywords** Vaccine co-administration · Hesitancy · Herpes zoster · Active call

Vaccine-preventable diseases are a major cause of morbidity and mortality around the world, with elderly patients being disproportionately affected. They pay a particularly heavy tribute to diseases such as influenza, pneumococcal disease and herpes zoster, which together account for hundreds of thousands of deaths in the elderly alone. The burden of infectious diseases in older subjects is such that their prevention is recognized as one of the main public health priorities of the World Health Organization (WHO), which has issued a Global Vaccine Action Plan for the period 2011–2020 intended as “a framework to prevent millions of deaths by 2020 through more equitable access to vaccines for people in all communities” [1]. Indeed, uptake of vaccines remains low, for variety of reasons, including lack of awareness of the disease among the general population, or lack of awareness of the vaccine—both among the public and by healthcare providers. Other factors also come into play such as access to healthcare, cost issues, and personal beliefs. However, increasing vaccine coverage rates are essential for ensuring adequate protection across the population, and in particular, among those at highest risk. For influenza, for example, despite the fact that annual vaccination is recommended for all adults over 65 years of age in most countries of the European Union, coverage rates range from 0.03 to 76.3% (median 34.4%), with only one country (Scotland) reaching the WHO and European Council goal of 75% in the 2014/2015 season [2].

In this regard, the article in this issue by Giuffrida et al. [3] provides important insights into the ways and means of improving uptake, especially among the elderly. In their report, Giuffrida et al. describe the innovative strategy employed with success in the Italian Region of Calabria to

increase awareness of herpes zoster among the population, and to improve uptake of herpes zoster vaccine. In this initiative, the Reggio Calabria Local Health Services sought to maximize the convenience of vaccination programmes and reduce the number of lost opportunities to vaccinate, by planning routine administration of the herpes zoster vaccine at the same time as scheduled pneumococcal vaccination (13-valent pneumococcal conjugate vaccine, PCV13). This approach was based on the principle that patients who are compliant with one vaccination will be more easily convinced to adhere to others, a phenomenon known as the “carry-on effect”. Over a period of almost 2 years, the authors sent 7490 detailed invitation letters to subjects aged 65 years and 6179 letters to subjects aged 70, an approach termed the “Active Call”. The two vaccines were successfully co-administered in a total of 2811 individuals, with no apparent safety issues, reaching higher vaccine coverage rates than usually observed in their setting.

There are several important take-home messages from this experience reported by Giuffrida et al. Firstly, it is clear that the “Active Call” is a key strategy to increasing vaccine coverage, because it reaches out directly to the intended target audience. It stimulates discussion, between the patient and their General Practitioner, or between patients themselves, or among families. It also provides a golden opportunity for General Practitioners to be informed or updated about the latest available vaccines, their modes of administration, target audience, and efficacy/safety profiles. The “Active Call” strategy is a starting point for a journey that may eventually lead that patient to the vaccination clinic to receive the vaccine. As such, its value as a simple, inexpensive, yet highly effective communication tool cannot and should not be underestimated.

The second important message to retain is that co-administration of vaccines should be more widely implemented, to take maximum advantage of opportunities for healthcare delivery. It has been shown that co-administration of the

✉ Stefania Maggi  
stefania.maggi@in.cnr.it

<sup>1</sup> CNR Aging Branch-NI, Padova, Italy

<sup>2</sup> University of Geneva, Geneva, Switzerland

herpes zoster live vaccine together with the quadrivalent inactivated influenza vaccine elicited varicella zoster virus-specific and influenza-specific antibody responses comparable to the administration of each vaccine separately, without safety concerns [4]. Concomitant administration of influenza vaccine with the 13-valent pneumococcal conjugate vaccine (PCV13) has also been shown to induce adequate antibody response, without interference and again with good safety profiles [5, 6]. Therefore, this combination could be widely co-administered with a view to increasing uptake of both vaccines. Regarding the co-administration of herpes zoster vaccine with the 23-valent pneumococcal polysaccharide vaccine (PPV23), there has been some controversy about this combination in the literature. Indeed, in 2009, the USA Food and Drug Administration included a note on the labeling of the zoster vaccine live stipulating that it should not be given together with PPV23, based on a study reporting that the co-administration of these two vaccines led to reduced immunogenicity of the zoster vaccine [7]. However, these results were based on geometric mean titers and short-term antibody response in a randomized controlled study among 473 subjects. Since then, real-world evidence has accumulated, assessed by actual disease incidence in a population of over 35,000 persons followed for over 9 years, indicating that the concomitant administration of zoster vaccine live with PPV23 does not seem to be associated with an increased risk of herpes zoster infection [8, 9]. Therefore, it would seem that previous concerns about the co-administration of herpes zoster vaccine and PPV23 may be moot, and opportunities to administer these two vaccines together should be seized whenever they present themselves.

Needless to say, the data presented by Giuffrida et al. in this issue are just a starting point. Further longitudinal studies are warranted to assess the safety of co-administration, and the actual incidence of disease, for all co-administration combinations and permutations among the available influenza, pneumococcal (PCV13, PPV23) and herpes zoster vaccines (zoster vaccine live, recombinant zoster vaccine). Only robust real-world evidence over the long-term will be able to confirm the safety and efficacy of co-administration as a useful strategy to improve vaccine uptake. In the meantime, the “Active Call” can be a wake-up call to healthcare providers everywhere to seize every opportunity to administer vaccines, thus contributing to reducing the burden of infectious diseases, especially in the elderly.

## Compliance with ethical standards

**Conflict of interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

## References

1. World Health Organization (2013) Global vaccine action plan 2011–2020. Geneva. [https://www.who.int/immunization/global\\_vaccine\\_action\\_plan/GVAP\\_doc\\_2011\\_2020/en/](https://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/). Accessed 1 Dec 2018
2. Jorgensen P, Mereckiene J, Cotter S et al (2018) How close are countries of the WHO European Region to achieving the goal of vaccinating 75% of key risk groups against influenza? Results from national surveys on seasonal influenza vaccination programmes, 2008/2009 to 2014/2015. *Vaccine* 36:442–452
3. Giuffrida S (2019) Calabria: a successful experience implementing Herpes Zoster vaccination strategies. *Aging Clin Exp Res*. <https://doi.org/10.1007/s40520-019-01145-2>
4. Levin MJ, Buchwald UK, Gardner J et al (2018) Immunogenicity and safety of zoster vaccine live administered with quadrivalent influenza virus vaccine. *Vaccine* 36:179–185
5. Seo YB, Choi WS, Lee J et al (2017) Comparison of immunogenicity and safety of an influenza vaccine administered concomitantly with a 13-valent pneumococcal conjugate vaccine or 23-valent polysaccharide pneumococcal vaccine in the elderly. *Clin Exp Vaccine Res* 6:38–44
6. Song JY, Cheong HJ, Hyun HJ et al (2017) Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine and an MF59-adjuvanted influenza vaccine after concomitant vaccination in 60-year-old adults. *Vaccine* 35:313–320
7. MacIntyre CR, Egerton T, McCaughey M et al (2010) Concomitant administration of zoster and pneumococcal vaccines in adults  $\geq 60$  years old. *Hum Vaccin* 6:894–902
8. Tseng HF, Smith N, Sy LS et al (2011) Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine. *Vaccine* 29:3628–3632
9. Bruxvoort K, Sy LS, Luo Y et al (2018) Real-world evidence for regulatory decisions: concomitant administration of zoster vaccine live and pneumococcal polysaccharide vaccine. *Am J Epidemiol* 187:1856–1862

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.