Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Fast COVID-19 vaccine effectiveness estimation on the basis of recovered individual propensity to be vaccinated

Since March 2020, the study of COVID-19 pandemic contagion data has been perceived as relevant by a wide audience composed not only of epidemiologists and specialized personnel but also of press offices, independent agencies, and ordinary people. There is therefore a strong need to provide clear information understandable to a wide unspecialized public. Vaccine efficacy, in terms of risk reducing of infection/hospitalization/death, is usually estimated by the Government Centers for Disease Control (CDC) through multivariate analysis (e.g. [1,2]); however, these statistical methods are often incomprehensible to the general public. To provide immediate information to the general (unqualified) public, the CDCs of different nations (e.g. [3–5]), as well as several prestigious press offices (e.g. [6]), have published epidemiological data and statistics on dedicated Web pages and dashboards.

The main purpose of this article is to point out to the CDCs of the various governments, as well as to independent agencies and press offices, the need and advantages of correcting incidence data of the infection, as well as to propose a practical equation to calculate vaccine effectiveness, based on the count of recovered subjects who have not yet been vaccinated. This equation can be used to accompany data on infection incidence aimed at the general public, as well as an "easy-to-access" formula to be used for the official and institutional communication of the CDCs.

Relative risk reduction (RRR) can be defined as follows:

$$\mathrm{RRR} = (\mathrm{Pn} - \mathrm{Pv})/\mathrm{Pn}; \tag{1}$$

where *Pn* and *Pv* denote the probability of SARS-CoV-2 infection in the subpopulations of unvaccinated and vaccinated individuals, respectively. Usually, *Pn* and *Pv* are estimated by the respective incidence values; nevertheless, this produces a bias in *RRR* estimation depending on various factors. Among these, a major bias source consists in the failure in excluding the recovered individuals from the count of unvaccinated population, whose consequence is a systematic underestimation of vaccine efficacy. In fact, if the vaccinated population were compared with the unvaccinated one, but inclusive of the healed subjects, the degree of susceptibility to infection would be biased because a part of the unvaccinated is instead immunized from the previous infection.

An unbiased vaccine efficacy estimate is provided by (Appendix 1):

$$RRR = 1 - \frac{N_V \cdot ((1 - V) - G \cdot E_G \cdot (1 - P_R))}{N_N \cdot V} \tag{2}$$

where RRR = vaccine efficacy, N_V = positive cases among vaccinated, N_N = positive cases among unvaccinated individuals; V = fraction of vaccinated population, G = fraction of recovered population, E_G = recovery immunization efficacy, P_R = propensity of the recovered individuals to vaccination, P_R = probability(vaccination | recovery), and N_V and N_N denote the numbers of detected positive individuals in a certain time interval (e.g. 128 positive in a certain day); all other variables represent probabilities or fractions of the unit; therefore, they are positive real numbers less than 1 (e.g. $E_G = 0.85$; $G = 0.1$, etc.).

Such equation allows to easily estimate vaccine effectiveness in terms of reducing the risk of diagnosing SARS-CoV-2 infection for different values of the propensity of the recovered individuals to vaccination. If we assume that E_G = RRR, then equation 2 becomes:

$$\mathrm{RRR} = (\mathrm{R} \cdot (1 - \mathrm{V}) - \mathrm{V})/(\mathrm{R} \cdot \mathrm{G} \cdot (1 - \mathrm{Pr}) - \mathrm{V}); \tag{3}$$

where R = Nv/Nn.

In the proposed equation, the contagion reduction risk (RRR in case of vaccine, E_G in case of recovery) may be defined as the value, averaged over the population and a time interval, of the relative reduction in the probability of contracting the infection at each contact or occasion of contagion.

The propensity of recovered individuals to undergo vaccination is affected by the technical time to vaccinate (of several months), as well as by postponing the decision or give up (propensity stricto sensu). We suggest to CDCs to provide updated *Pr* values to allow correcting effectiveness estimates according to Eq. (2) within the framework of a simplified analysis.

To illustrate the advantages related to the proposed correction, we have applied such method to simulated data whose solution is already known, according to the scenario illustrated in Fig. 1A, where likely values have been assigned to vaccine and recovery efficacy: $RRR = E_g = 0.8$.

By way of example, biased RRR values (Eq. (1)) and corrected ones, by means of Eq. (2), for each age class, have been compared (Fig. 1B).

For the week 4–10 October 2021, corrected and uncorrected SARS-CoV-2 contagion incidence values have been compared in Fig. 1C and 1D. This latter figure provides a valid example of diagram possibly aimed to a wide unspecialized audience to be published in dedicated Web pages or dashboards.

In summary, we point out to the CDCs of various nations the importance and the need of correcting contagion incidence data (e.g. tables, diagrams etc.), as well as risk reduction estimates by means of Eq. (2), on the basis of the propensity of recovered individuals to vaccination to disseminate immediate and explanatory information regarding COVID-19 vaccine effectiveness.

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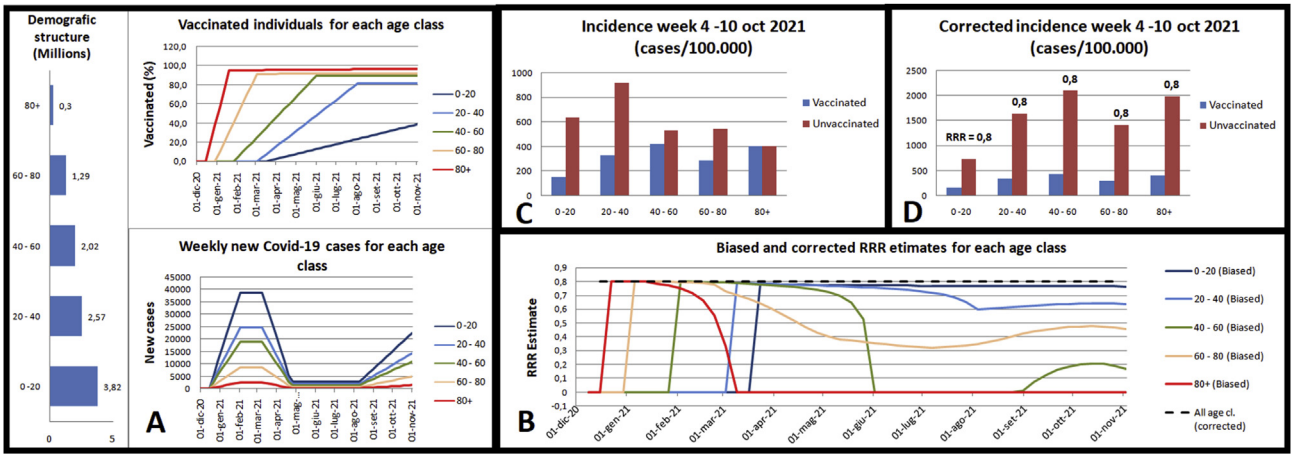

Fig. 1. **(A)** Simulated scenario of epidemic diffusion in population showing the illustrated demographic structure. Weekly new infected individuals and cumulative vaccinated ones are illustrated for several age classes. In this simulation, we have assumed that the propensity of infected people to vaccination is equal to zero within 5 months from positive diagnosis and then it increases according to a linear law for the successive 6 months. **(B)** Estimations of *RRR* calculated according to Eq. (1) (biased vales) and by means of Eq. (2) (corrected) for several age classes. Should be noted as, for some age class, the *RRR* estimates significantly decay after the first wave, whereas the corrected estimation is constant and equal to the true value (0.8). **(C)** Weekly incidence values detected during the simulated epidemic outbreak (week October 4–10, 2021), calculated without excluding recovered unvaccinated individuals from unvaccinated population and **(D)** by excluding them. Should be noted as, for age classes exhibiting highest vaccination ratios, the uncorrected incidence values for unvaccinated individuals approach that of vaccinated ones. Namely, in the age class of over 80, these assume the same value.

Appendix I. Derivation of Equation 2

Let denote by:

P_{op} = number of population individuals
S_V = number of susceptible vaccinated individuals
S_N = number of susceptible unvaccinated individuals

$$S_V = P_{op} \cdot V \cdot (1 - RRR). \tag{A1}$$

Here we have assumed that recovered and never-infected individuals, if vaccinated, exhibit the same degree of immunization.

$$S_N = P_{op}((1 - V) - G \cdot E_G \cdot (1 - P_R)). \tag{A2}$$

As when a population fraction is infected in a certain interval time, it results: $N_V/N_N = S_V/S_N$; therefore, after substitution of S_V and S_N with the terms in Eqs. A1 and A2, respectively, and after simple manipulations, Eqs. 2 and 3 are derived.

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