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Opinion Article

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Correlation between Increases of Covid-19 Cases and Percentage of Fully Vaccinated Population

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Introduction

In a correspondence paper published on the European Journal of Epidemiology [1], Subramanian and Kumar proposed an interesting correlation analysis between percentage of vaccinated population (PVP) and Covid-19 contagion incidence. The presented statistical analysis utilized a substantial dataset, encompassing demographic data from multiple countries worldwide and thousands of US counties. Nevertheless, the methodology may be improved, e.g., through multivariate regression analyses, to yield more reliable outcomes. While, as acknowledged by the authors, combining vaccines with other contagion containment measures is undoubtedly beneficial, the manuscript in its current form may risk being misleading and may lead readers to flawed conclusions. The univariate statistical analysis at the country level cannot adequately assess a correlation between contagion rate and vaccination coverage, whereas the county-level analysis, contrary to the authors' conclusions, reveals a risk reduction associated with high population vaccination rates.

Country Level Analysis

In the country-level analysis of COVID-19 infection spread, two primary variables play a crucial role: (i) The percentage of vaccinated population (PVP) and (ii) The intensity of Non-Pharmaceutical Interventions (NPIs) such as lockdown, social distancing, business closures, etc.

It is essential to emphasize that NPIs entail substantial economic and social costs, prompting governments to reduce their intensity as faster as possible. Consequently, these variables exhibit a strong stochastic dependence. Indeed, upon achieving a reasonable percentage of vaccinated individuals, governments tend to systematically weaken (or eliminate) NPIs.

Examining the combined effect of these two variables (PVP and NPI intensity) necessitates the employment of multivariate statistical analyses, which considers the contagion rate as dependent from both PVP and NPI. Otherwise, distinguishing the effect of one variable from the other is infeasible. As the cited study employed a univariate analysis, it cannot refute the evident hypothesis that any observed increase in infections in countries with high vaccination rates could be attributed to the relaxation of NPIs.

US County Level Analysis

The analysis of the US counties suffers from the same bias limitations described above, also necessitating the employment of multivariate statistics. However, within the specific analyzed time interval, near an epidemic peak, the differences in median weekly contagion values observed among several US counties (illustrated in Figures S2 and S3 of the aforementioned manuscript) are significant, contrary to the authors' claims. Figure 1 shows the relative risk reduction (RRR) values for the various percentage classes of PVP, highlighting, for instance, that a PVP greater than 70% leads to an infection risk reduction exceeding 70% compared to the case with PVP < 35%.

The analysis of the increase in contagion cases between two consecutive 7-day periods, proposed by the authors (Figure 3 in the cited manuscript), is irrelevant. Specifically, the period considered by the authors (late August 2021) coincides with an epidemic peak in the United States. In this

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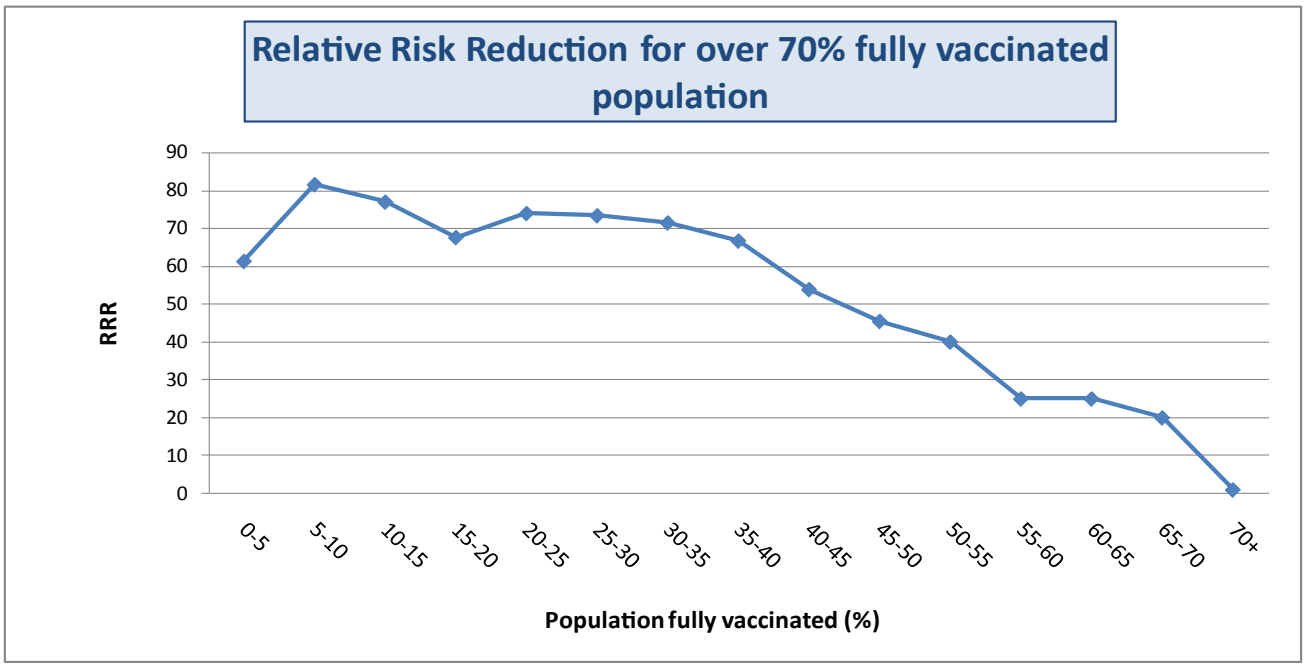

Figure 1: Relative risk reduction calculated between category 70% + (PVP > 70%) and all other PVP categories (data from Figure S2 in the original manuscript). RRR values are calculated by means of the usual formula: RRR = (IV% - I70+)/IV%, where IV% denotes the weekly incidence of infections, estimated through the median (Figure S2 within the original manuscript), for the generic PVP category and I70+ that relating to areas with over 70% of individuals vaccinated. By way of example, we can state that having a vaccinated population over 70% has lead to a reduction in the risk of infection of 71%, in the considered week, compared to the case in which this percentage was in the range of 30%-35%.

scenario, some regions peaked a few days or weeks earlier than others. The variation in infection rate between two consecutive weeks is not related to vaccine effectiveness but merely highlights whether a particular region was before (positive variation) or after (negative variation) the epidemic peak.

Cited Literature Data

- Vaccine effectiveness: The authors cited an Israeli government report [2] emphasizing a significant reduction in vaccine efficacy against SARS-CoV-2 infection. This decline was likely attributable to the combined effect of the lower efficacy of the vaccine version used at the time against the Delta variant and the natural waning of efficacy over time. However, Guerriero, et al., [3] highlighted the importance of quantifying the propensity of recovered individuals to vaccinate, especially in populations with high vaccination rates, to avoid underestimating vaccine efficacy.
- Increase in vaccinated individuals among hospitalized and deceased: The increase in the percentage of vaccinated individuals among hospitalized (from 0.01% to 9%) and deceased (from 0% to 15.1%), cited in a US CDC report [4], is an obvious consequence of the significant increase in the proportion of vaccinated individuals in the population between January and May 2021. The authors [1] erroneously refer to this data (percentage of vaccinated individuals among hospitalized) as "rates of hospitalizations and deaths amongst the fully vaccinated". The percentage reported by the US CDC [4] represents the ratio of vaccinated individuals to unvaccinated individuals within the hospitalized population. This ratio is fundamentally diverse from the hospitalization or death rate among vaccinated individuals. Confusing these two variables inevitably leads to a wrong interpretation of population data.

Concluding Remarks

The results of the country-level analysis conducted by [1] cannot be interpreted as a lack of correlation between vaccination percentage and infection rate. The observed increase in contagion rates in countries with high vaccination coverage could be attributed to the relaxation of non-pharmaceutical public health interventions (NPIs), which typically follow the achievement of high vaccination percentages.

The county-level analysis in the US demonstrates a significant reduction in contagion risk in counties with high vaccination coverage, contrary to the authors' [1] conclusions. On the other hand, the analysis of the increase in cases between two consecutive 7-day periods in US counties is irrelevant, as it provides no information regarding vaccine effectiveness.

Finally, the data reported by the US CDC [4] has been misinterpreted in the cited work [1] and does not provide information on vaccine efficacy.

Conflict of Interest

The author declares no role of the funding source and no conflict of interest. The author has no relevant financial or non-financial interests to disclose nor competing interests to declare that are relevant to the content of this article. The work has not been published elsewhere, either completely, in part, or in another form. The manuscript has not been submitted to another journal.

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