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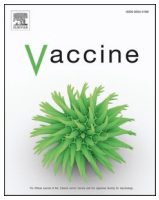

Short communication

Impact of the 2023/24 autumn-winter COVID-19 seasonal booster campaign in preventing severe COVID-19 cases in Italy (October 2023–March 2024)

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ABSTRACT

We assessed the impact of the 2023/2024 COVID-19 vaccination campaign in Italy by estimating the number of averted COVID-19 severe cases (i.e. COVID-19 associated hospitalisations or deaths) between October 2023 and March 2024, in those aged ≥60 years. We estimated that 565 (95 % CI: 497–625) cases, corresponding to 2.1 % (95 % CI: 1.8–2.3) of the expected cases without a vaccination campaign, were averted. We simulated three vaccination coverage scenarios: 50 %, 75 %, 90 % (versus the observed 10.7 %), finding that 9.7 % (95 % CI: 8.5–10.7); 14.5 % (95 % CI: 12.8–16.1); and 17.4 % (95 % CI: 15.3–19.3) of the expected cases would have been averted, respectively.

1. Introduction

By 2023, many countries shifted from universal COVID-19 vaccination campaigns to delivering booster doses to high-risk groups, aiming to prevent severe COVID-19 disease. In June 2023, the European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) recommended the use of monovalent XBB-adapted vaccines for the 2023/24 autumn-winter vaccination campaigns, based on surveillance and sequencing data showing the global predominance of XBB.1 descendent lineages [1].

The Italian 2023–2024 seasonal vaccination campaign started on 1st October 2023 targeting high risk groups (i.e. those aged ≥60 years and those with high-risk comorbidities (full list in Supplementary Table 1)) [2,3]. Vaccines administered included a single dose of a COVID-19 vaccine adapted to Omicron XBB 1.5 (i.e. Comirnaty Omicron XBB 1.5 and, since December, Nuvaxovid XBB 1.5) [3,4]. This additional dose was recommended to be administered at least 6 months after the last received dose of any COVID-19 vaccine or the last SARS-CoV-2 infection (i.e. date of positive diagnostic test) [3]. As of the beginning of the vaccination campaign, Sars-Cov-2 variant EG.5 was the most prevalent variant up until week 50 (2023), when JN.1 variant became dominant [5].

Generating evidence on the impact of the 2023/2024 seasonal vaccination campaign is crucial to support vaccination program evaluation and the planning of future vaccination programs. We aimed to estimate the number of COVID-19 associated hospitalizations and deaths prevented by the 2023/24 autumn-winter COVID-19 seasonal booster campaign in Italy, in those aged ≥60 years.

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2. Methods

2.1. Study design and data sources

We conducted a nationwide retrospective cohort analysis between October 2023–March 2024 among individuals ≥60 years of age, who were eligible to receive the seasonal vaccine on 1st October 2023 (i.e. had possible previous doses and SARS-CoV-2 infections more than 180 days before 1st October 2023) [3], from which we selected those who had previously received at least one booster dose, comprising the vast majority of the elderly population in Italy. We linked the Italian COVID-19 vaccination registry data, held by the Ministry of Health, containing individual information on each COVID-19 vaccination dose administered in the country [6], with data from the SARS-CoV-2 integrated surveillance system in Italy [7], including information on every laboratory confirmed case of SARS-CoV-2 followed up until recovery or death associated to COVID-19.

These databases were deterministically linked using a unique identifier (universal tax code).

We also used the latest available information on the levels of urbanization and socioeconomic deprivation (SED) of the Italian municipalities, which was linked to individual records through the municipality's code where the vaccination took place [8].

2.2. Estimation of relative vaccine effectiveness of the COVID-19 seasonal vaccination campaign

We compared the time to SARS-CoV-2 infection leading to severe COVID-19 (i.e. hospitalization or death occurring within 28 days since testing positive) between individuals who received a booster dose with XBB.1 adapted vaccines during the seasonal vaccination campaign and those who did not receive the booster.

We conducted a Cox proportional hazard regression analysis to estimate the adjusted hazard ratio (HR) of severe COVID-19 between the two groups, using calendar time measured in days as the underlying time scale and vaccination as a time-dependent exposure for different observation periods (i.e., two-month calendar intervals as of 1st October 2023). Individual follow-up started at the beginning of the vaccination campaign on the 1st October 2023 and ended on the first of the following dates: the date of testing positive for SARS-CoV-2 infection subsequently leading to severe COVID-19, the imputed date of death for causes unrelated to COVID-19 (Supplementary Method 2), the end of the study period on 31st March 2023 or the date of vaccination if any of the prior three events occurred within the first two weeks post vaccination.

Estimates were adjusted for sex, age (5-year age groups), country of birth (born in Italy or abroad), geographical area where the last vaccination took place (19 regions and two autonomous provinces of Italy), high-risk conditions (presence/absence of at least one condition among those listed in Supplementary Table 1), post-primary cycle number of booster doses received before the starting date of the study (1, 2, or ≥3), urbanization level (high, medium, low) and SED level (1st quintile-least deprived to 5th).

We then calculated relative vaccine effectiveness (rVE) against severe COVID-19 as [(1 − HR) * 100].

2.3. Estimation of severe events averted by the vaccination campaign

We estimated the number of averted severe cases by adapting the formula proposed by Machado et al. [9], using the bi-monthly adjusted rVE estimates, the weekly vaccine uptake and the weekly number of observed events. In addition, we estimated the expected number of averted cases based on scenarios in which the weekly rates of vaccine uptake were re-proportioned, following the observed weekly coverage curve, to simulate different cumulative vaccination coverage. We evaluated three scenarios with cumulative vaccination coverage rates of 50 %, 75 %, and 90 % at the study end.

3. Results

We included in the analysis 15,558,829 (99 %) of the 15,719,063 eligible individuals, who, at the starting date of the vaccination campaign, were alive (Supplementary Methods 2), had received a minimum of one booster dose, and had no prior infections nor had received booster doses in the previous 180 days. We excluded 160,234 (1 %) individuals through a set of selection criteria described in Supplementary Fig. 1.

3.1. Demographic and clinical characteristics of the study population

The demographic and clinical characteristics of persons included in the study are presented in Table 1. A total of 1,659,448 individuals (10.7 %) received a booster dose with XBB.1 adapted vaccines during the seasonal vaccination campaign (of which >99 % received a Comirnaty Omicron XBB 1.5 booster). A total of 13,899,381 individuals (89.3 %) did not receive a booster dose.

3.2. Trends in booster vaccination coverage and severe COVID-19 cases

The start of the vaccination campaign coincided with an increase in the trend of severe cases, which lasted until weeks 48–50 of 2023 (Fig. 1). Incidence decreased steeply afterwards until the end of the season, whilst cumulative vaccine coverage among those aged ≥60 years reached its maximum (10.7 %) at around week 7 of 2024.

3.3. Vaccine effectiveness of the COVID-19 vaccination campaign and severe events averted

We estimated that rVE peaked at 60 % (95 % CI, 51–67) in October–November and then progressively declined to 47 % (95 % CI, 43–51 %) in December–January, and 36 % (95 % CI, 21–47 %) in February–March.

We estimated that the 2023/24 autumn winter COVID-19 vaccination campaign averted 565 (95 % CI: 497–625) severe COVID-19 cases in Italy, corresponding to 2.1 % (95 % CI: 1.8–2.3) of those expected without a vaccination campaign. Based on our analysis, under scenarios with cumulative vaccination coverage rates of 50 %, 75 %, and 90 % at the study end, a total of 2636 (95 % CI: 2320–2914); 3953 (95 % CI: 3480–4371); and 4744 (95 % CI: 4176–5245) severe cases would have been averted respectively, accounting for 9.7 % (95 % CI: 8.5–10.7); 14.5 % (95 % CI: 12.8–16.1); and 17.4 % (95 % CI: 15.3–19.3) of the expected cases in each respective scenario (Table 2). Fig. 2 shows the number of averted severe cases by calendar month, both observed and under different scenarios, most of them estimated in December.

4. Discussion

We found that less than 3 % of expected severe COVID-19 events were averted by the 2023/24 seasonal booster campaign in Italy. The low number of severe averted events can be partially explained by the moderate rVE of XBB.1.5 vaccines we found, the overall low uptake of the booster, and the increasing incidence trend of severe cases preceding considerable vaccine uptake among the elderly population. Indicatively, our simulated scenarios suggested that increasing VC to 50 %, 75 %, and 90 % could have potentially averted a substantially larger proportion of severe COVID-19 cases.

Other countries have investigated VE of XBB.1.5 vaccines. Preliminary studies conducted in Denmark [10] and the Netherlands [11] in the first weeks of the campaign reported higher levels of protection compared to our study, with VE around 70 % against hospitalization in older adults. Later studies, with observation periods ending in the first weeks of January, estimated VE against severe COVID-19 comparable to our results [12,13], suggesting that the seasonal vaccines were moderately effective in preventing severe disease. One of the reasons could be

Table 1
Baseline characteristics of the individuals included in the analysis, as eligible to receive a seasonal booster at the beginning of the study. (Italy, 1st October 2023–31st March 2024).

	Did not receive seasonal booster[1] $n = 13,899,381$		Received seasonal booster[1] n = 1,659,448		Total $n = 15,558,829$	
	n	%	n	%	n	%
Sex						
Male	6,327,472	45.5	808,547	48.7	7,136,019	45.9
Female	7,571,909	54.5	850,901	51.3	8,422,810	54.1
Age Group						
60–64	3,142,155	22.6	155,235	9.4	3,297,390	21.2
65–69	2,679,721	19.3	241,075	14.5	2,920,796	18.8
70–74	2,381,214	17.1	298,131	18	2,679,345	17.2
75–79	2,155,305	15.5	325,341	19.6	2,480,646	15.9
80–84	1,670,828	12	291,944	17.6	1,962,772	12.6
85–89	1,156,928	8.3	213,334	12.9	1,370,262	8.8
90–94	540,212	3.9	102,511	6.2	642,723	4.1
95+	173,018	1.2	31,877	1.9	204,895	1.3
Country of birth						
Other	632,010	4.5	46,224	2.8	678,234	4.4
Italy	13,267,371	95.5	1,613,224	97.2	14,880,595	95.6
Geographical macroarea						
North-East (ITH)	2,619,488	18.8	430,869	26	3,050,357	19.6
North-West (ITC)	3,768,252	27.1	574,867	34.6	4,343,119	27.9
Centre (ITI)	2,822,147	20.3	441,327	26.6	3,263,474	21
Islands (ITG)	1,518,307	10.9	55,443	3.3	1,573,750	10.1
South (ITF)	3,171,187	22.8	156,942	9.5	3,328,129	21.4
High-risk group						
None reported	9,556,985	68.8	853,627	51.4	10,410,612	66.9
Immunocompromised	83,873	0.6	18,196	1.1	102,069	0.7
RLTCF	170,180	1.2	51,820	3.1	222,000	1.4
Other health-risk conditions	4,088,343	29.4	735,805	44.3	4,824,148	31
Number of prior booster doses						
1 dose	10,032,155	72.2	247,088	14.9	10,279,243	66.1
2 doses	3,613,929	26	1,207,762	72.8	4,821,691	31
3 or more doses	253,297	1.8	204,598	12.3	457,895	2.9
Urbanization level[2]						
High	4,713,466	33.9	723,011	43.6	5,436,477	34.9
Medium	6,606,213	47.5	712,401	42.9	7,318,614	47
Low	2,579,702	18.6	224,036	13.5	2,803,738	18
Deprivation level[2]						
1st quintile (least deprived)	5,899,252	42.4	611,410	36.8	6,510,662	41.8
2nd quintile	3,361,316	24.2	445,916	26.9	3,807,232	24.5
3rd quintile	2,068,653	14.9	254,600	15.3	2,323,253	14.9
4th quintile	1,657,280	11.9	220,213	13.3	1,877,493	12.1
5th quintile (most deprived)	912,880	6.6	127,309	7.7	1,040,189	6.7

RLTCF, resident in long term care facilities.
[1] Vaccination status: having received or not a booster dose of Comirnaty XBB or Novavax XBB during the seasonal COVID-19 vaccination campaign (1 October 2023 to 31 March 2024).
[2] Urbanization and socio-economic deprivation (SED) levels were based on the municipality where vaccination took place.

that, whilst these vaccines were designed to target the XBB 1.5 sub-variant, this was not the prevalent variant in Italy at any timepoint of the seasonal campaign [5].

Vaccine coverage of the 2023/24 seasonal booster in Italy in those aged ≥60 years (10.7 %) was slightly lower than the median coverage in the EU/EAA area (12.0 %; country range: 0.01–66.1 %) [14]. Several factors could explain the low booster coverage observed in Italy. General Practitioners (GP) played key roles in the management of the seasonal vaccination campaign and the co-administration of vaccination against influenza and COVID-19 in Italy [15]. However, as the mRNA XBB.1.5 vaccines require cold chain maintenance [16], vials are stored in authorized central pharmacies, and prepared and distributed on demand [17], likely negatively affecting GP participation in the vaccine program. Less effective vaccination communication strategies, fear of vaccination side effects and current low perception of risks associated with SARS-CoV-2 infection may also underlie the low booster coverage we found [18].

These barriers could partly explain why the uptake of COVID-19 boosters was significantly lower than the average seasonal influenza vaccine uptake in Italy, which tends to be between 50 and 60 % in those aged ≥65 years [19].

One strength of our work is that we used data from complete and accurate national databases. We also examined a longer period of observation compared to previous studies, allowing for a more thorough evaluation of the vaccination campaign. Our study has several limitations. Firstly, our estimates of rVE was adjusted for several variables, but could not evaluate unmeasured confounders, such as behavioral factors related to vaccine uptake and SARS-CoV-2 infection risk. In addition, high rates of self-diagnosis and consequent under-reporting of asymptomatic/mild cases likely led to an overestimation of eligible individuals at the start of the vaccination campaign, especially in those who did not uptake the seasonal booster, possibly causing an underestimation of rVE in the early months. Moreover, the surveillance system may have misclassified incidental positive admissions as severe cases, introducing a bias toward underestimating rVE [20]. Finally, we adjusted our estimates for the level of socioeconomic deprivation measured at the municipality level, which does not necessarily reflect the individual socioeconomic status, especially in large municipalities where heterogeneity between subareas is likely present.

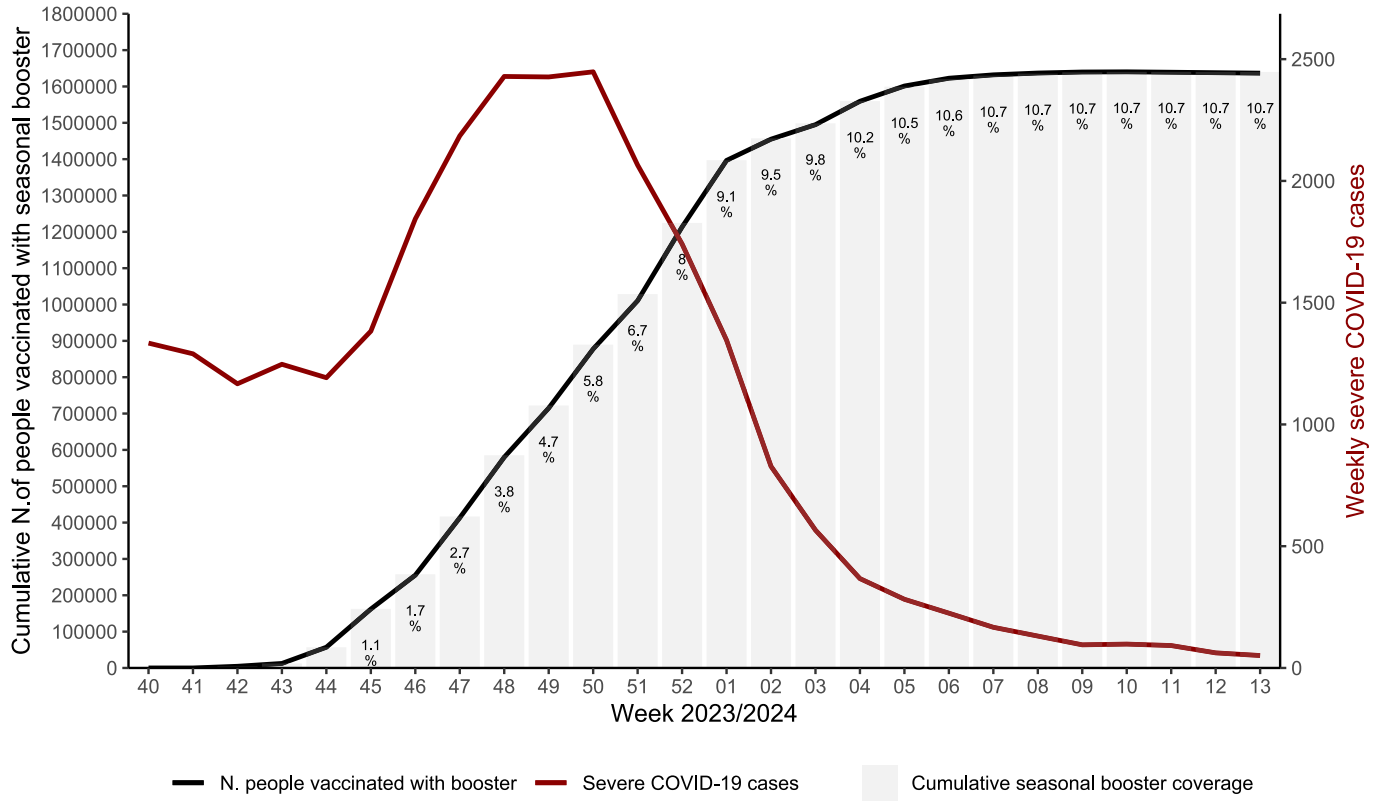

Fig. 1. Cumulative weekly number of people vaccinated with the seasonal booster by 14 days post vaccination calendar date (black line), corresponding vaccination coverage (grey bars), and number of severe COVID-19 cases by calendar week (red line), among those aged ≥60 years; Italy, 1st October 2023– 31st March 2024. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Cumulative number (and %) of severe COVID-19 cases averted by the seasonal vaccination campaign, also by scenarios with vaccine uptake set at different levels, in those aged ≥60; Italy, 1 October 2024–31 March 2024.

	VCmax = 10.7 % (observed)	VCmax = 50 % (simulated)	VCmax = 75 % (simulated)	VCmax = 90 % (simulated)
n. observed	27,062	–	–	–
n. adjusted[1] (95 % CI)	26,653 (26,593–26,721)	24,582 (24,304–24,898)	23,265 (22,847–23,738)	22,474 (21,973–23,042)
n. averted (95 % CI)	565 (497–625)	2636 (2320–2914)	3953 (3480–4371)	4744 (4176–5245)
% averted (95 % CI)	2.1 (1.8–2.3)	9.7 (8.5–10.7)	14.5 (12.8–16.1)	17.4 (15.3–19.3)
Adjusted incidence per 100,000 (95 % CI)	171.3 (170.9–171.7)	158.0 (156.2–160.0)	149.5 (146.8–152.6)	144.4 (141.2–148.1)
Expected[2] incidence per 100,000	174.9	174.9	174.9	174.9

VCmax: cumulative vaccination coverage at the end of the campaign.
[1] Estimates based on vaccine effectiveness adjusted for sex, age, region, deprivation, urbanization, number of previous boosters, risk-conditions and country of birth.
[2] Expected incidence of severe events without the 2023/24 seasonal vaccination campaign.

5. Conclusions

Our study found that the 2023/24 COVID-19 autumn winter campaign in Italy averted a low number of severe COVID-19 cases among those aged ≥60 years, mainly due to the low uptake of the booster dose in the eligible population. These findings can be used by public health authorities to aid decision-making and planning of future COVID-19 vaccination campaigns.

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Ethical statement

This study, based on routinely collected data, was not submitted for approval to an ethical committee because the dissemination of COVID-19 surveillance data was authorized by Law number 52 on 19 May 2022 (article 13). Because of the retrospective design and the large size of the population under study, in accordance with the Authorization n. 9 released by the Italian data protection authority on 15 December 2016, the individual informed consent was not requested for the conduction of this study.

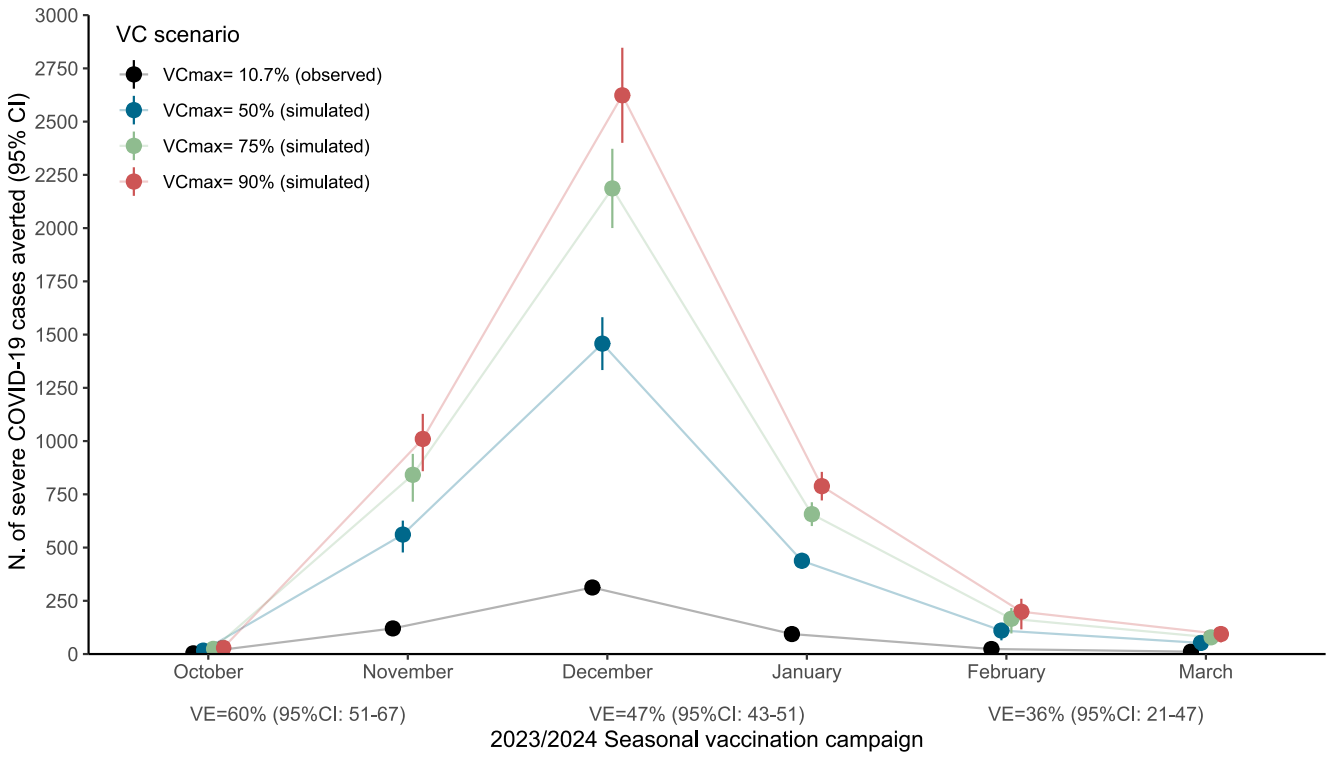

Fig. 2. Monthly number of severe COVID-19 cases averted through the seasonal vaccination campaign and according to scenarios with cumulative vaccine coverage (VC) at the end of the campaign set at different levels, in those aged ≥60; Italy, 1 October 2023–1 March 2024.

Disclaimer

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Authors' contributions

EAF, AM-U, EP, AO, MF and CS designed the study, which was further refined with the input of PP and DP. CS, AB, MDM, MT and AC extracted data from the different databases and linked them. EAF, AM-U, and EP reviewed the current epidemiological, immunological, and microbiological literature. EAF carried out the analysis. The first draft was written by EP, AM-U and MF, with the contribution of EAF and PP. The draft was then circulated, reviewed, and modified by all mentioned authors. All listed authors reviewed and approved the final version, and had final responsibility for the decision to submit for publication.

CRediT authorship contribution statement

E.A. Fotakis: Writing – review & editing, Visualization, Methodology, Investigation, Formal analysis, Conceptualization. **E. Picasso:** Writing – original draft, Methodology, Investigation, Conceptualization. **C. Sacco:** Writing – review & editing, Methodology, Data curation, Conceptualization. **D. Petrone:** Writing – review & editing, Methodology. **M. Del Manso:** Writing – review & editing, Data curation. **A. Bella:** Writing – review & editing, Data curation. **F. Riccardo:** Writing – review & editing. **A. Odone:** Writing – review & editing, Methodology. **A. Cannone:** Writing – review & editing, Data curation. **M. Tallon:** Writing – review & editing, Software, Data curation. **L. De Angelis:** Writing – review & editing. **A. Sciurti:** Writing – review & editing. **D. Cescutti:** Writing – review & editing. **P. Pezzotti:** Writing – review & editing, Supervision, Methodology. **M. Fabiani:** Writing – review & editing, Supervision, Methodology, Conceptualization. **A. Mateo-Urdiales:** Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization.

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During the preparation of this work no generative AI or AI-assisted technologies were used in the writing process.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2024.126375.

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