

Delta variant and mRNA Covid-19 vaccines effectiveness: higher odds of vaccine infection breakthroughs

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INTRODUCTION

Vaccination is the main pharmacological measure to control SARS-CoV-2 transmission and mitigate its complications.

Information on COVID-19 vaccines' effectiveness and viral loads in vaccine infection breakthrough cases are critical to inform decision-makers, particularly in the context of the emergence of novel variants of concern (VOC).

This study aimed:

- To compare effectiveness of mRNA vaccines (BNT162b2 - Comirnaty and mRNA-1273 - Moderna) against B.1.617.2 (Delta) versus B.1.1.7 (Alpha) VOC,
- To compare Ct values, as an indirect measure of viral load and thus transmissibility, between Alpha and Delta VOC by vaccination status.

METHODS

A case-case study was developed to compare mRNA vaccines' effectiveness against Delta vs. Alpha VOC using data on RT-PCR SARS-CoV-2 positive cases notified between 17th of May and 4th of July 2021.

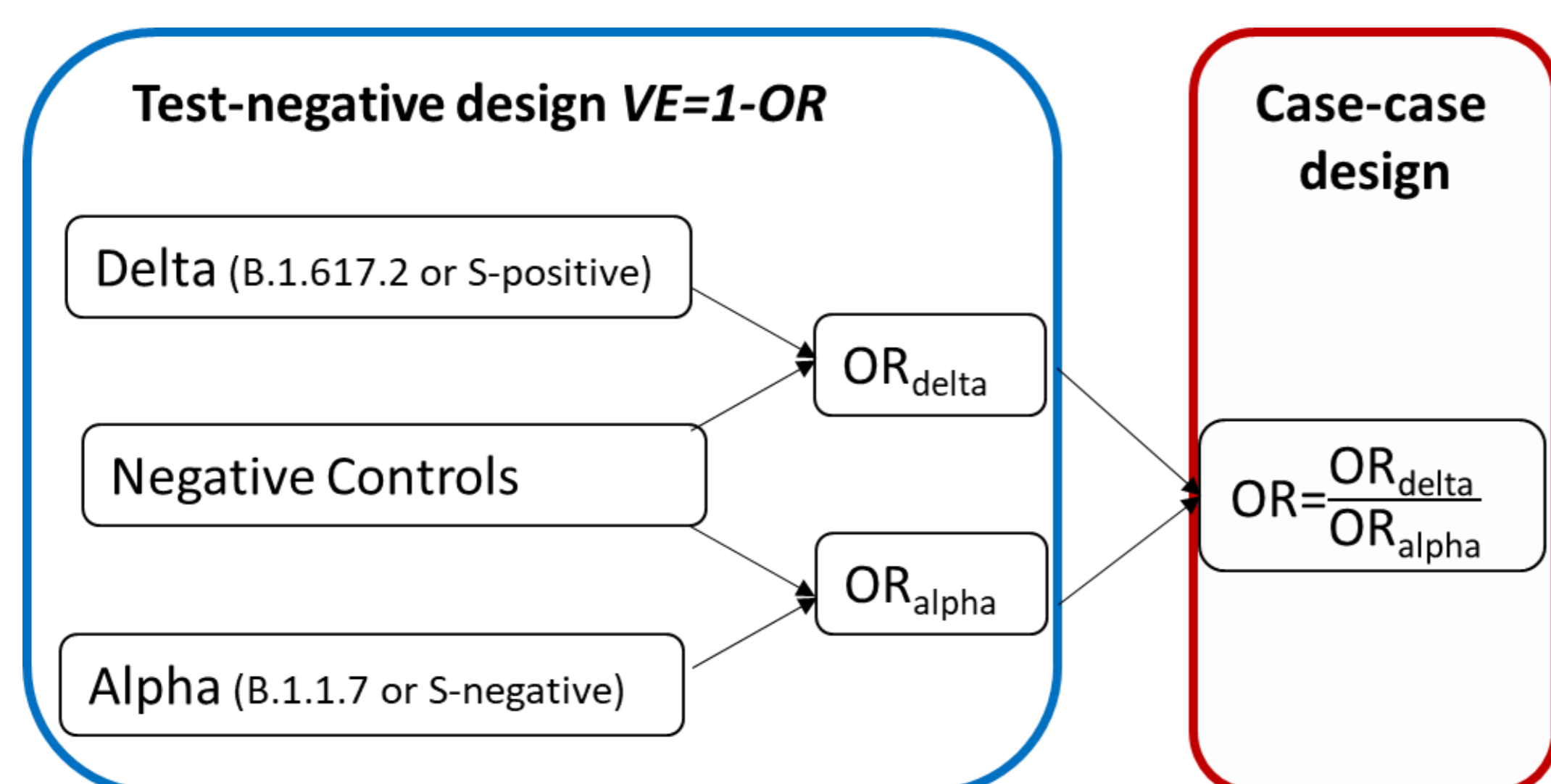


Figure 1 Comparison diagram between test-negative design and case-case design

Case definition: SARS-CoV-2 VOC were classified by whole-genome sequencing or inferred, for non-sequenced samples, based on amplification of S gene using the TaqPath™ Covid 19 CE IVD RT-PCR Kit.

Positive predictive value for Delta cases identification: 94.7%

Vaccination status:

Unvaccinated	Partial vaccination	Complete vaccination
<ul style="list-style-type: none"> • no register of vaccine administration (any brand) 	<ul style="list-style-type: none"> • 1 mRNA dose, more than 14 days or 2 mRNA doses, less than 14 days 	<ul style="list-style-type: none"> • 14 or more days after second dose

Statistical analysis:

- The odds of vaccine infection breakthrough in Delta compared to Alpha cases were estimated by conditional logistic regression adjusted for age group, sex, matched by the week of diagnosis.
- RT-PCR cycle threshold values (Ct values) were compared by vaccination status and variant as an indirect measure of viral load and infectiousness using linear regression.

RESULTS

Overall, 2 097 SARS-CoV-2 RT-PCR positive cases were included in the analysis, of these 65% were Delta VOC.

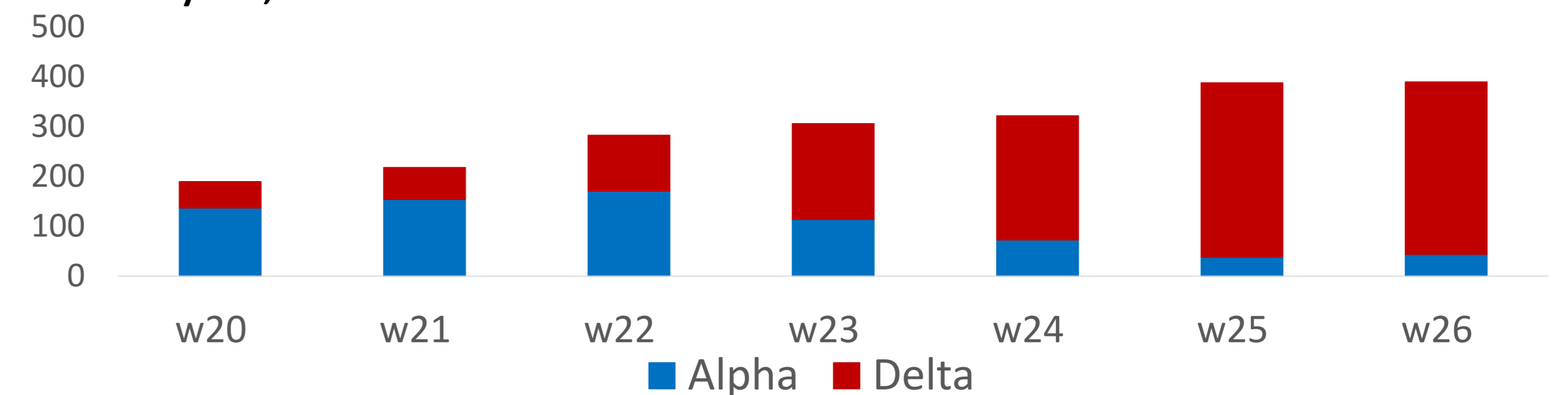


Figure 2. Weekly number of SARS-CoV-2 positive cases by VOC, Portugal 2021

Statistically significant higher odds of being partially vaccinated (OR=1.81) and completely vaccinated (OR=1.96) in the Delta cases compared to the Alpha cases. (Table 1)

Table 1. Confounder-adjusted odds ratio of being vaccinated (odds of vaccine infection breakthrough) in Delta cases compared to Alpha SARS-CoV-2 cases, Portugal, weeks 20-26 2021

Vaccination status	Delta n	Alpha n	Confounder-adjusted Odds Ratio (CI95%)
Unvaccinated	777	517	ref
Partial	198	49	1.81 (1.37 to 2.39)
Complete	162	38	1.96 (1.22 to 3.14)

Ct values were lower for the Delta VOC compared to Alpha, regardless the vaccination status (Figure 3).

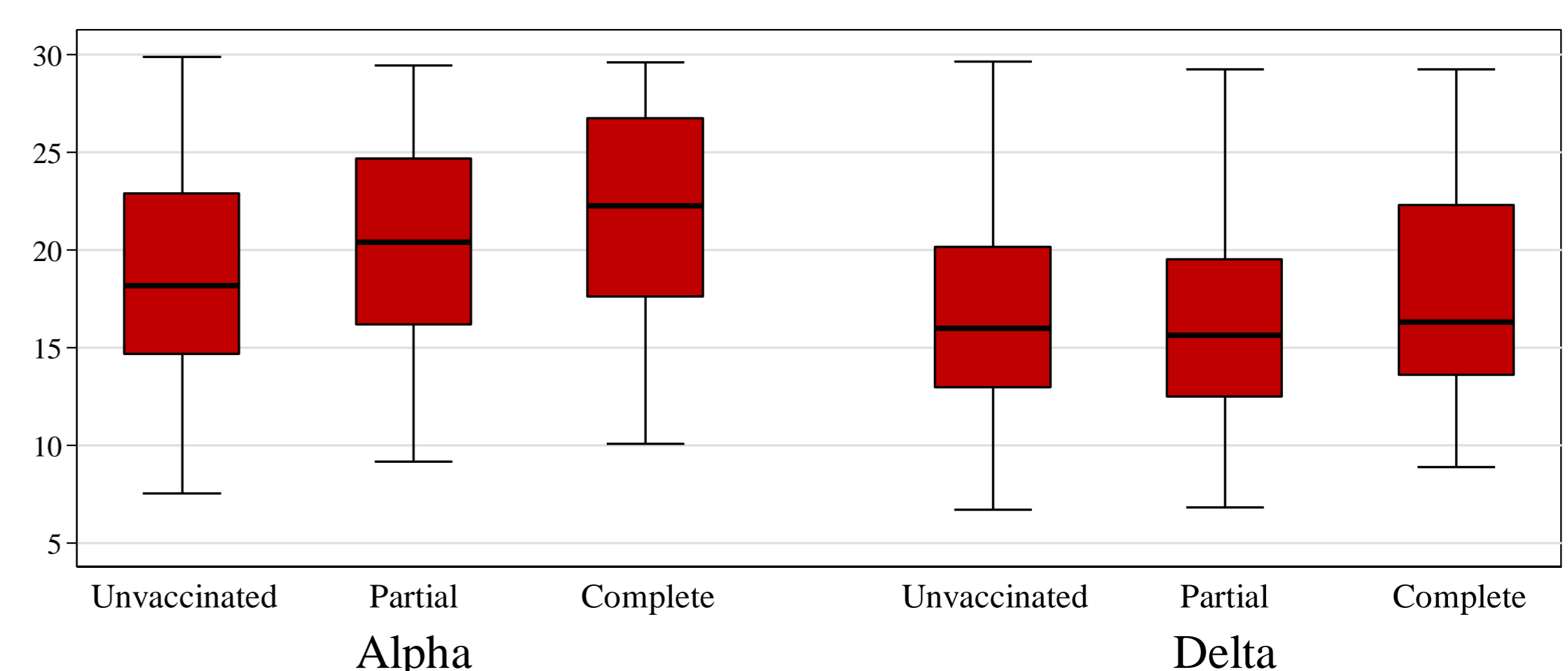


Figure 3. Distribution of Ct values by VOC and vaccination status, Portugal weeks 20-26 2021

The Delta cases revealed Ct-value mean difference of 2.24 (CI95%: 0.85 to 3.64) between unvaccinated and fully vaccinated contrasting with 4.49 (CI95%: 2.07 to 6.91) mean difference observed for the Alpha VOC.

CONCLUSIONS

- Case-case design has proven to be helpful to compare relative vaccine effectiveness between VOC in context of novel VOC emergence.
- Higher odds of vaccination in Delta cases compared to Alpha suggest lower effectiveness of the mRNA vaccines in preventing Delta VOC infections.
- Higher mean Ct values among fully vaccinated support the need to promptly complete vaccination schemes.
- These findings can help decision-makers weigh on the application of control measures and adjusting vaccine roll-out depending on VOC circulation and the coverage of partial and complete vaccination.