# COVID-19 Vaccine Effectiveness by Vaccine Administration Schedule: A Canadian COVID-19 Emergency Department Research Network (CCEDRRN) Study

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## Introduction

Vaccines against SARS-Co-V-2 were licensed for widespread use in Canada in December, 2020.Their licensing was based on trials that demonstrated their safety and effectiveness in preventing symptomatic COVID-19 in healthy non-pregnant adults, and did not evaluate their real-world effectiveness.

Canada implemented delayed second dose administration to optimize population-level coverage. This may have changed the duration of vaccine protection.

## Objective

To ascertain the effectiveness of COVID-19 vaccines for preventing symptomatic COVID-19 requiring an emergency department (ED) visit for two-dose vaccination series with delayed second doses.

## Methods

We included consecutive eligible patients of all ages who presented to a CCEDRRN ED after January 1, 2021 and were tested for COVID-19 using a nucleic acid amplification test (NAAT).[1] We included anyone tested for SARS-CoV-2 in the ED or within 24h after their arrival. We received Research Ethics Board approvals to link our national cohort with provincial vaccination registries but have been unable to access vaccine registry data as of February 13, 2023. Therefore, we had to exclude patients for whom vaccination status could not been ascertained by chart review or by telephone follow-up, limiting our sample size.

We calculated estimates of vaccine effectiveness using the following formula: VE = (1 – OR) x 100%, where OR was the ratio of the odds of vaccination among study cases (SARS-CoV-2 NAAT positive) over the odds of vaccination among test negative controls (SARS-CoV-2 NAAT negative).[2] We defined fully vaccinated as having an ED presentation ≥7 days after having received the second dose of a two-dose vaccination series.

## Results

We included 2,432 patients in our vaccine effectiveness analyses all of whom had vaccination status either documented in their medical record or who consented to telephone follow-up. Of these, 411 (16.5%) were symptomatic test-positive cases, and 2,021 (83.5%) were test-negative controls.

A total of 2,129 eligible patients presented using the Delta dominant period, 91 patients presented during the Omicron BA1 dominant period, and 212 patients presented between the Delta and Omicron BA1 periods.

Among the 411 test-positive cases, 57 (13.9%) were fully vaccinated. Of the 2,021 test-negative controls, 1,371 (67.8%) were fully vaccinated. Vaccinated patients tended to be older than unvaccinated patients (median (IQR): 62 (34) compared to 45.5 (24), respectively). Nearly all vaccinated individuals (91.3%) received two doses of an mRNA vaccine.

We estimated the unadjusted and adjusted vaccine effectiveness against preventing a symptomatic COVID-19-related ED visit at 93% (95% CI: 89-95%) and 91% (95% CI: 87-93%), respectively. Unadjusted and adjusted vaccine effectiveness against preventing a COVID-19-related hospitalization were 92% (95% CI: 86-95%) and 91% (95% CI: 85-95%), respectively.

**Table 1.** Unadjusted and adjusted vaccine effectiveness estimates to prevent symptomatic COVID-19 requiring an ED visit for COVID evaluation among subgroups with time since 2nd dose

| Subgroup | Test-positive patients | Test-negative patients | Unadjusted VE (95% CI) | Adjusted VE (95% CI) |
|---|---|---|---|---|
| **Time since second dose, n (%)** | | | | |
| 14 or more days | 51 | 1256 | 0.93 (0.89-0.95) | 0.91 (0.87-0.93) |
| Unvaccinated | 354 | 650 | Reference | Reference |

VE=vaccine effectiveness;
COVID-related symptoms are any of the following: Cough, fever, chills, shortness of breath, dysgeusia, and myalgia;
Adjusted VE adjusted for age, sex, epidemiological week, and province

**Table 2.** Unadjusted and adjusted vaccine effectiveness estimates to prevent COVID-19 related hospitalization with COVID symptoms among subgroups with delays to full vaccination

| Subgroup | Test-positive patients | Test-negative patients | Unadjusted VE (95% CI) | Adjusted VE (95% CI) |
|---|---|---|---|---|
| **Time since second dose, n (%)** | | | | |
| 14 or more days | 21 | 1256 | 0.92 (0.86-0.95) | 0.91 (0.85-0.95) |
| Unvaccinated | 122 | 650 | Reference | Reference |

VE=vaccine effectiveness;
COVID-related symptoms are any of the following: Cough, fever, chills, shortness of breath, dysgeusia, and myalgia;
Adjusted VE adjusted for age, sex, epidemiological week, and province

## Conclusions

- Two doses of mRNA vaccines offered great protection against symptomatic COVID-19 infection requiring ED evaluation, and against COVID-19 hospitalizations.
- Processes need to be developed to facilitate timely and efficient access to vaccine registry data to accelerate national vaccine effectiveness studies.

## References

[1]Hohl et al. Development of the Development of the Canadian COVID-19 Emergency Department Rapid Response Network population-based registry: a methodology study. CMAJ Open 2021; 9(1): E261.

[2] Fukushima et al. Basic principles of test-negative design in evaluating influenza vaccine effectiveness. Vaccine 2017; 35: Basic principles of test-negative design in evaluating influenza vaccine effectiveness.

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