Risk of Myocarditis after Covid-19 mRNA Vaccination: Impact of Booster Dose and Dosing Interval

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Background

- Covid-19 mRNA vaccines associated with short-term increased risk of myocarditis
- Highest risk observed after the second dose relative to the first
- Risk associated with *more distant* booster doses is less clear
  - Lower incidence relative to the second dose [1]
  - Increase with every sequential doses [2]
- Extending the timing between first two doses could lower the risk [3]

[1] L. Friedensohn et al., JAMA. 327, 1611–1612 (2022); K. Goddard et al., Ann Intern Med. 175, 1169–1771 (2022).

[2] M. Patone et al., Circulation. 146, 743–754 (2022).

[3] S. A. Buchan et al., JAMA Network Open. 5, e2218505 (2022).

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mRNA vaccines in France

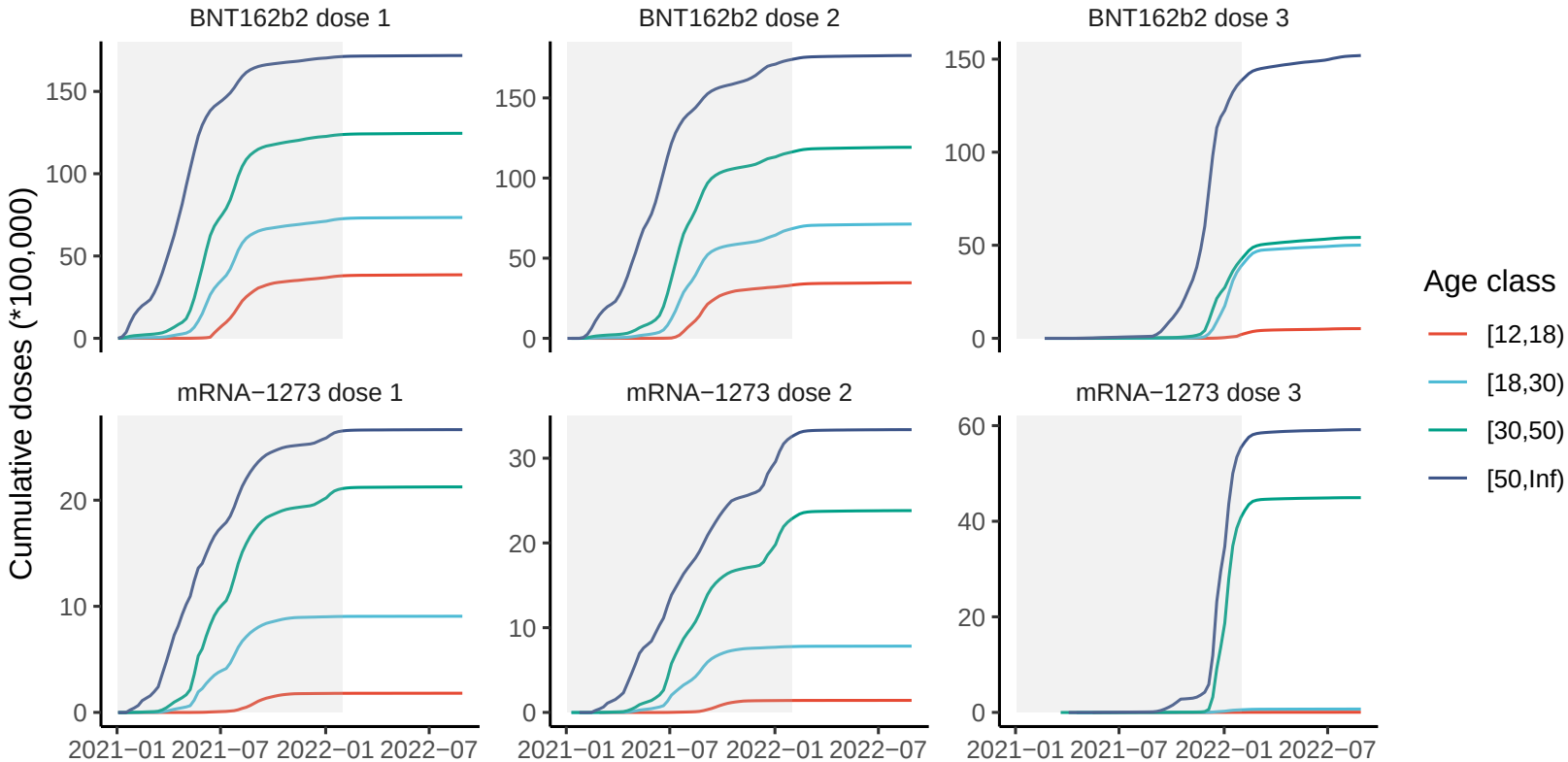

Figure 1: mRNA vaccines uptake

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Objective

To assess the association between dosing interval and the risk of myocarditis for both the two-dose primary series and the third dose (first booster).

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Data & Methods

Data

- National Health Data System [4]
  - French hospital discharge database
  - Covid-19 vaccination
  - Covid-19 testing
- Entire French population aged 12 or older.
- From December 27, 2020 to January 31, 2022.

[4] covers $\sim$ 99% of the French population (67 million inhabitants).

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Methods

- Matched case-control study.[5]
- Cases
  - ICD-10 codes for myocarditis (I40.x, I41.x, and I51.4)
- Controls
  - 10 individuals matched
  - at the date of hospital admission (*index date*),
  - and on age, gender and *departement* of residence
- Exposure
  - mRNA vaccine 0 to 7 days prior to the *index date*
- Covariates:
  - History of myocarditis in last 5 years
  - SARS-CoV-2 infection in past month
  - Antiobiotics use in past month
  - Deprivation Index from area of residence
  - Various myocarditis related comorbidities within 5 years
- Conditional logistic regression

[5] S. Le Vu et al., Nat Commun. 13, 3633 (2022).

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Findings

Overall association

- 4 890 cases of myocarditis
- 48 900 matched controls

Exposure	Dose	Case	Control	aOR	95%CI
Unexposed		4015	43933		
BNT162b2	1	76	556	1.7	1.3 to 2.2
	2	261	616	5.9	5.0 to 7.0
	3	59	252	3.1	2.3 to 4.3
mRNA-1273	1	14	91	1.9	1.1 to 3.5
	2	126	90	19	14 to 25
	3	24	102	4.1	2.5 to 6.6

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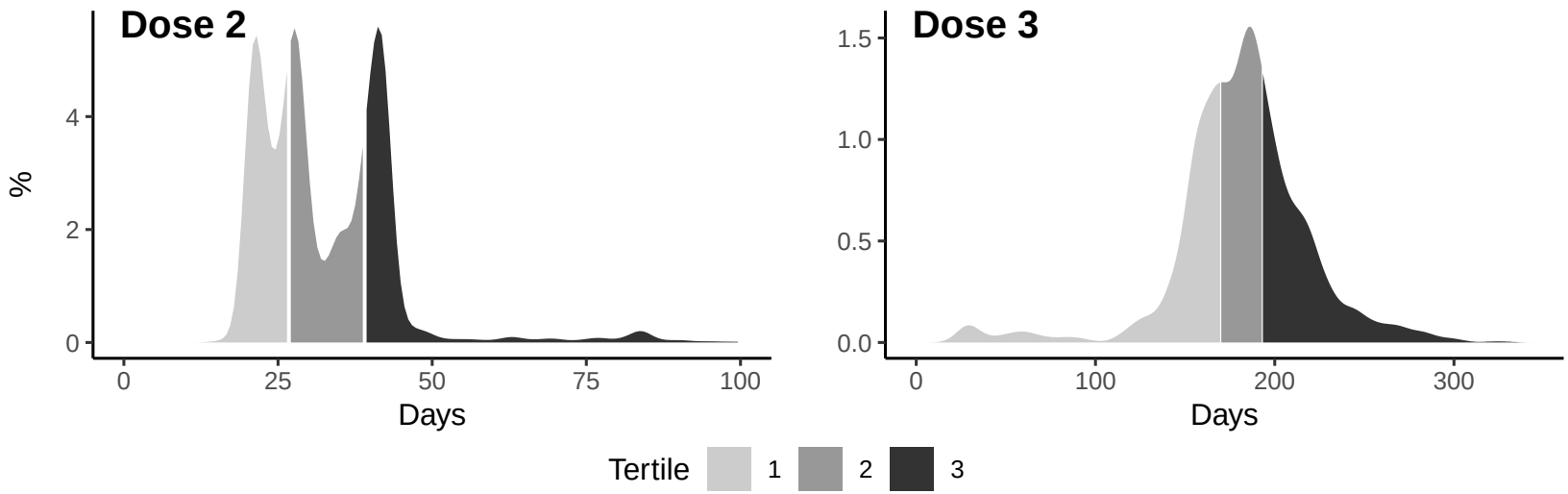
Dosing interval tertiles



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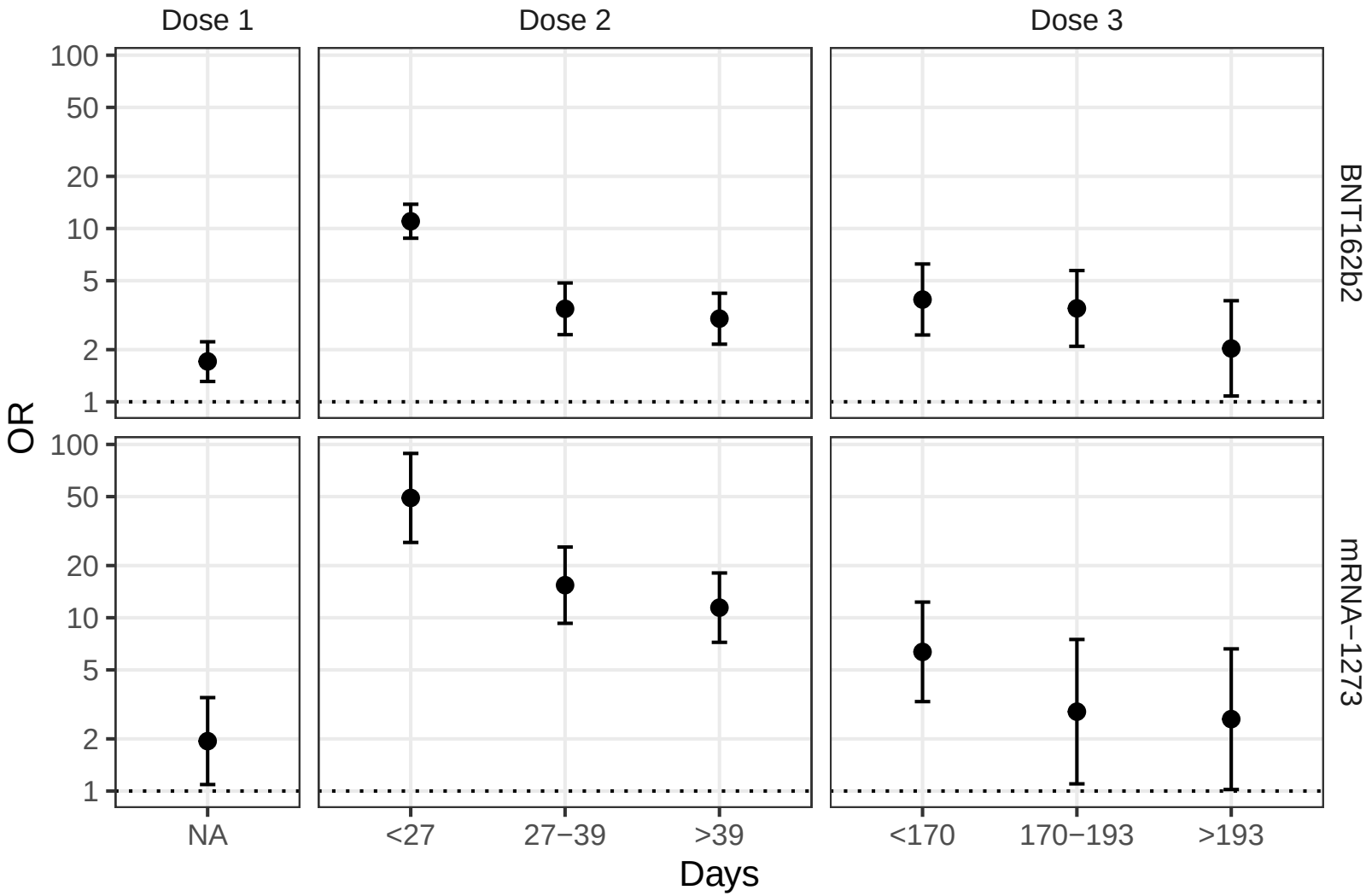
Odds ratio by dose/interval



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Discussion

- Risk of myocarditis remained elevated after the booster dose
- Longer intervals between each consecutive dose (including booster doses) may decrease the occurrence of vaccine-associated myocarditis
- Nationwide picture of mRNA vaccination up to dose 3
- Cases only detected in outpatient setting
- Under reporting of SARS-CoV-2 infections

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Thank you

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