Evaluation of anti-nucleocapsid level variation in frequent plasma donors to assess SARS-CoV-2 seroprevalence in a vaccinated population

Presented by :

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No conflict of interest to disclose
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Objectives

1. A brief history of SARS-CoV-2 **serosurveillance in blood donors** at Héma-Québec
   - The difficulty of serosurveilling in the context of mass vaccination
   - The limitations of cross-sectional anti-N testing
2. The **PlasCov Biobank**: a repository of samples obtained from frequent plasma donors
3. A method to evaluate recent COVID-19 infections using the **anti-N signal on serial samples** from the PlasCov Biobank
4. Applying this method to estimate the impact of the **Omicron wave** in the province of Quebec

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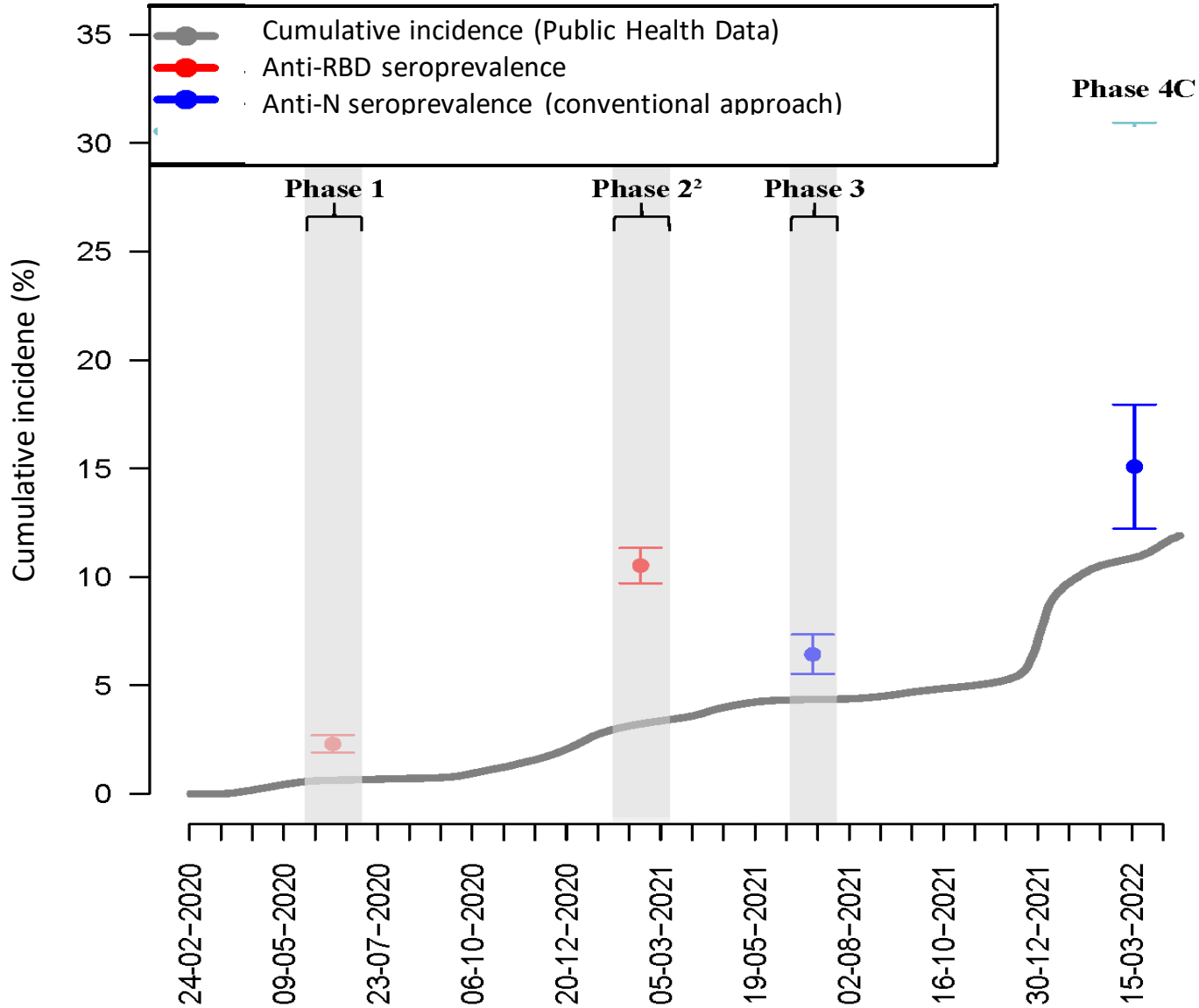
SARS-CoV-2 seroprevalence studies at Héma-Québec



The anti-N assay

- In-house anti-N ELISA, similar to a previously described anti-RBD assay, except:
- N antigen (0.25 µg/ml) was used (Centre National en Électrochimie et en Technologie Environnementales Inc., Shawinigan, Canada) in lieu of the RBD antigen (2.5 µg/ml).
- Sensitivity of **98.5%** and a specificity of **98.1%** among unvaccinated individuals using a **cut-off value of 0.350**
  - n=52 (recently) infected (convalescent plasma) donors (non-vaccinated)
  - n=66 non-infected (pre-pandemic) plasma donors

The anti-N assay – Its known limitations

- Anti-nucleocapsid (N) seroprevalence is more affected by seroreversion than anti-S or anti-RBD

  Bolotin S et al. J Infect Dis. 2021;223(8):1334-1338; Whitcombe AL et al. Clin Transl Immunol. 2021;10(3):e1261; Carreño JM et al. Iscience. 2021;24(9):102937; etc.

- Vaccination hinders the sensitivity of conventional anti-N assays.

  Allen N et al. J Infect. 2021;83(4):e9-e10

  - 4000 vaccinated health care workers:
  - 23 experienced a breakthrough infection, but only six (**26%**) were seropositive for anti-N.

  Follmann D et al. Ann Intern Med . 2022 Jul 5;M22-1300

  - A study of COVE (i.e., mRNA-1273 vs. placebo to prevent COVID-19) participants with a confirmed history of SARS-CoV-2 breakthrough infection
  - only **40.4%** of vaccine recipients were seropositive for anti-N, as compared with **93.4%** among placebo recipients

PLASMA DONOR BIOBANK (PLASCOV)

Context : Since the beginning of the COVID-19 pandemic, Héma-Québec has been playing a supportive role to the Québec and Canadian health care networks by conducting SARS-CoV-2 seroprevalence studies in blood donors. The biobank and the studies arising from it will be a continuation of this collaboration, by facilitating studies pertaining to the **evolution of the COVID-19 pandemic in the context of the deployment of the vaccination.**

Plasma Donor Biobank at Hema-Quebec was supported by funding from the **Public Health Agency of Canada (PHAC)**, through the **Vaccine Surveillance Reference group** and the **COVID-19 Immunity Task Force (CITF).**

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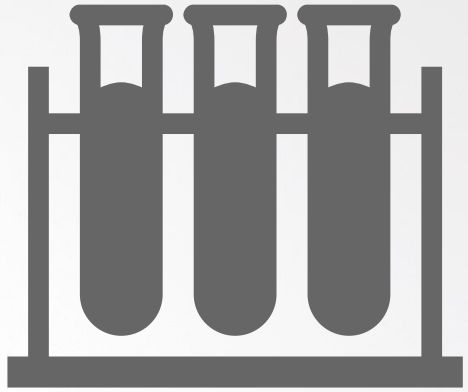
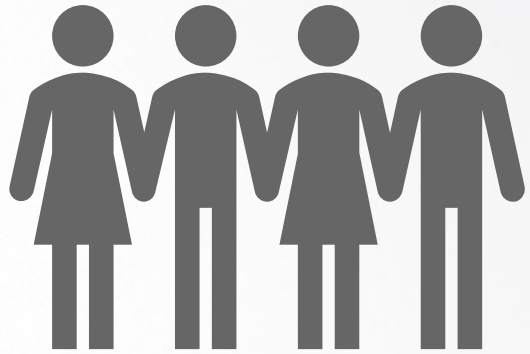
The ten (10) Centres that collect Biobank-dedicated Samples from plasma Donors are Héma-Québec's Donation Centres, namely: Saguenay, Lebourgneuf, Sainte-Foy, Trois-Rivières, Sherbrooke, Laval, Montreal, Kirkland, Brossard and Gatineau

Current picture of the cohort (January 2023)

- More than **175 000 samples** collected (since April 2021)
- More than **20 000 individual donors**
- 90 % participation rate
- More than 7600 donors with samples taken pre/post-infection and/or pre/post-vaccination





Data collected*

Variables	Baseline before vaccination/infection	After vaccination/infection questionnaire
Internal Data Collection		
Medical Questionnaire		
Demographics: Age/Sex/Area of living	✓	✓
Ethnicity	✓	✓
Height	✓	✓
Weight	✓	✓
BMI	✓	✓
Medication use	✓	✓
History of blood pressure	✓	✓
Diabetes profile and treatment	✓	✓
COVID-19 vaccination status	✓	✓
Type of vaccine received	✓	✓
Number of shots	✓	✓
Vaccine date	✓	✓
History of PCR-detected infection	✓	✓
PCR date	✓	✓
Laboratory tests		
Blood type (ABO *Rh* genotype/phenotype)	✓	✓
Ministry data (infection and vaccination registry)		
COVID-19 vaccination status	✓	✓
Type of vaccine received	✓	✓
Number of shots	✓	✓
Vaccine date	✓	✓
History of PCR-detected infection	✓	✓
PCR date	✓	✓

*** Data from the vaccination and infection register have been requested from the MSSS, still awaiting authorization**

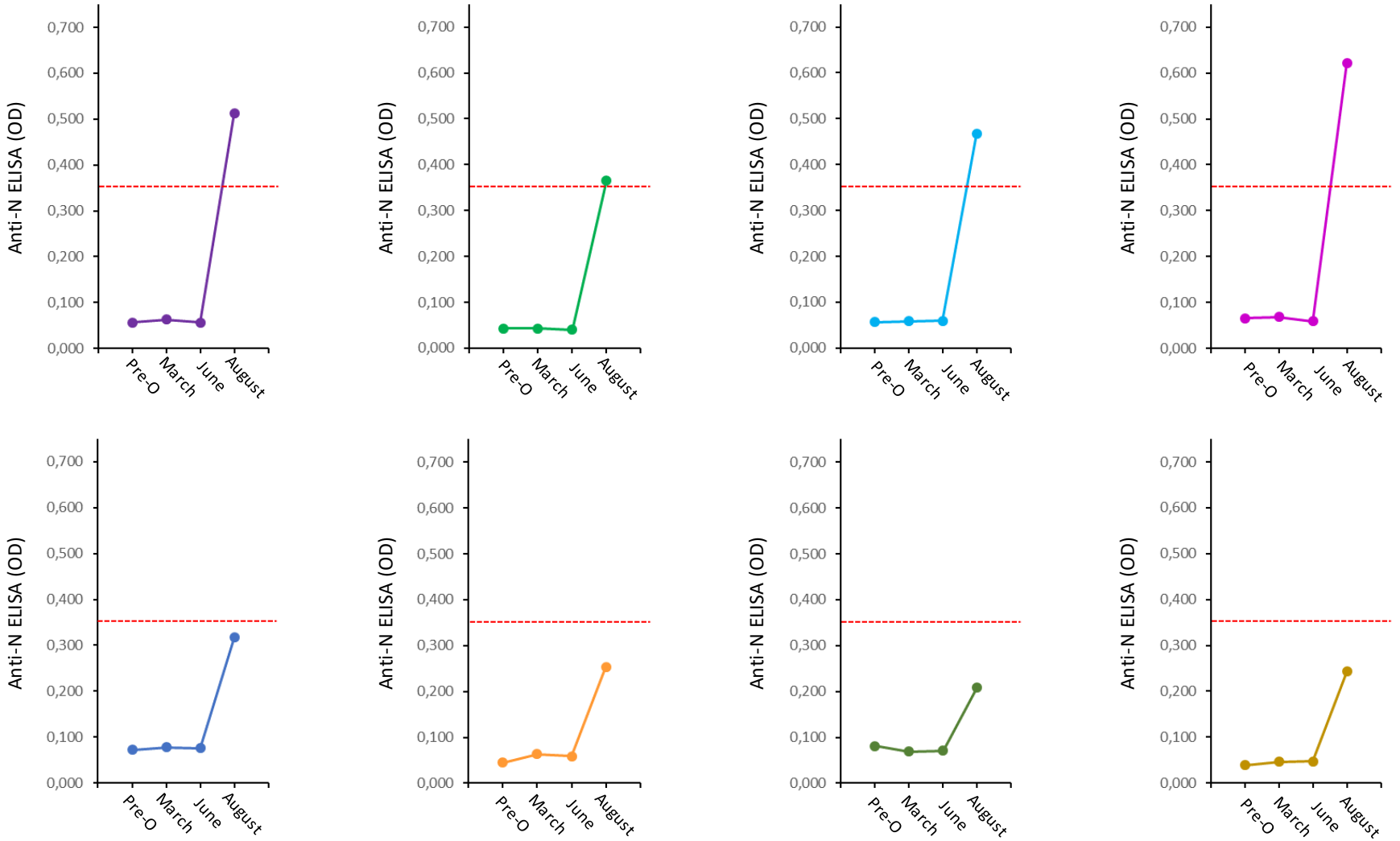
Validation of a ratio-based approach to identify acute Omicron infections

- **248 vaccinated Plascov donors with a PCR-confirmed infection** during the early phase of the Omicron wave
  - Mean age: 40.6 years;
  - Females: 48.3%;
  - 246 (99.2%) had received ≥2 vaccine doses before their infection;
  - Median interval between infection and sample collection was 31 days (range: 3-111)
- **Two samples**: one prior (but as close as possible) to December 15, 2021; second sample closest to, but after PCR-confirmed infection

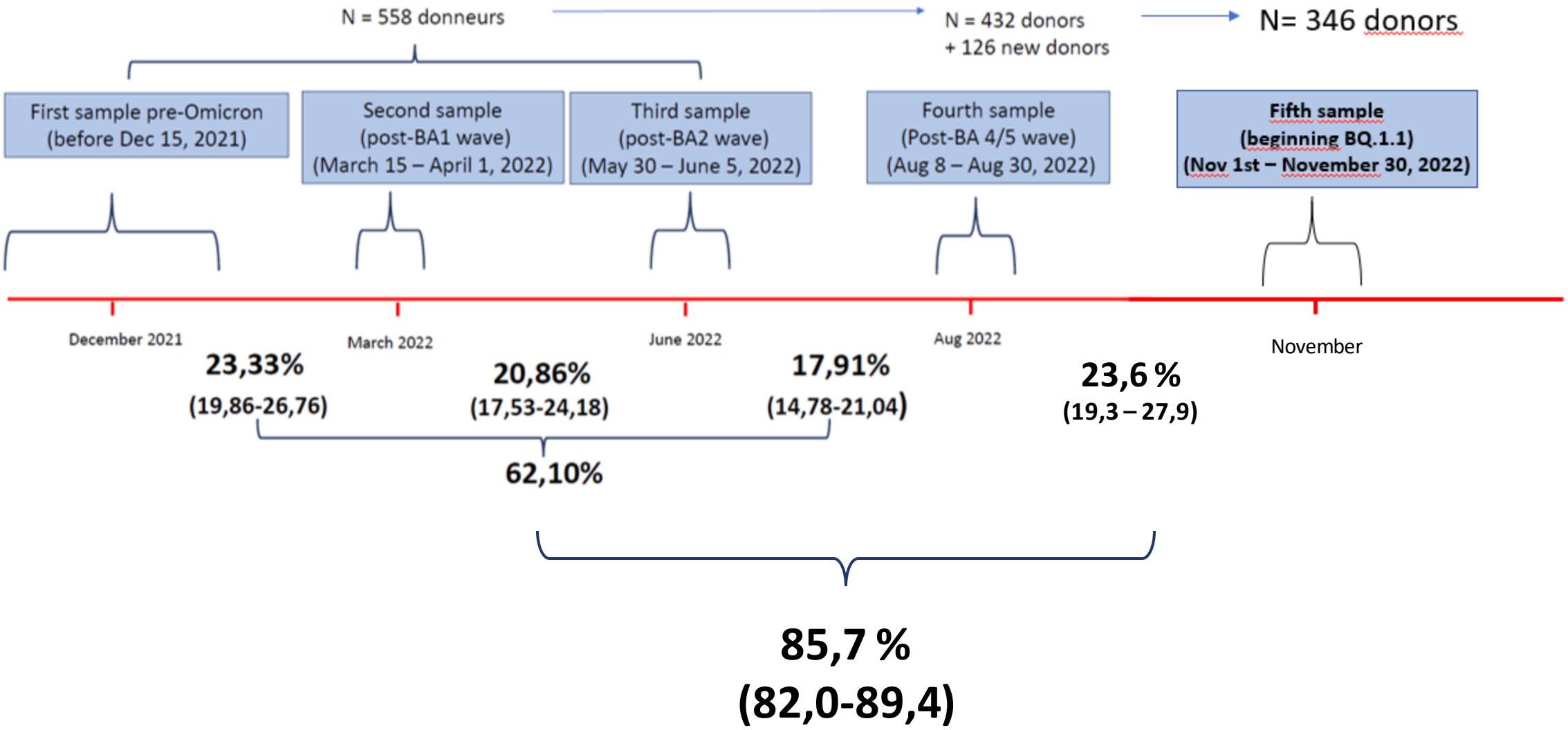
Validation of a ratio-based approach to identify acute Omicron infections

	n/N	Sensitivity (%)
'Conventional' approach (testing of post-infection sample, at the 0.35 OD threshold)	**157/248**	**63.3%**
'Ratio-based' approach (post-infection sample OD ≥ 1.5 times the OD of the pre-infection sample) Autres régions	**236/248**	**95.2%**

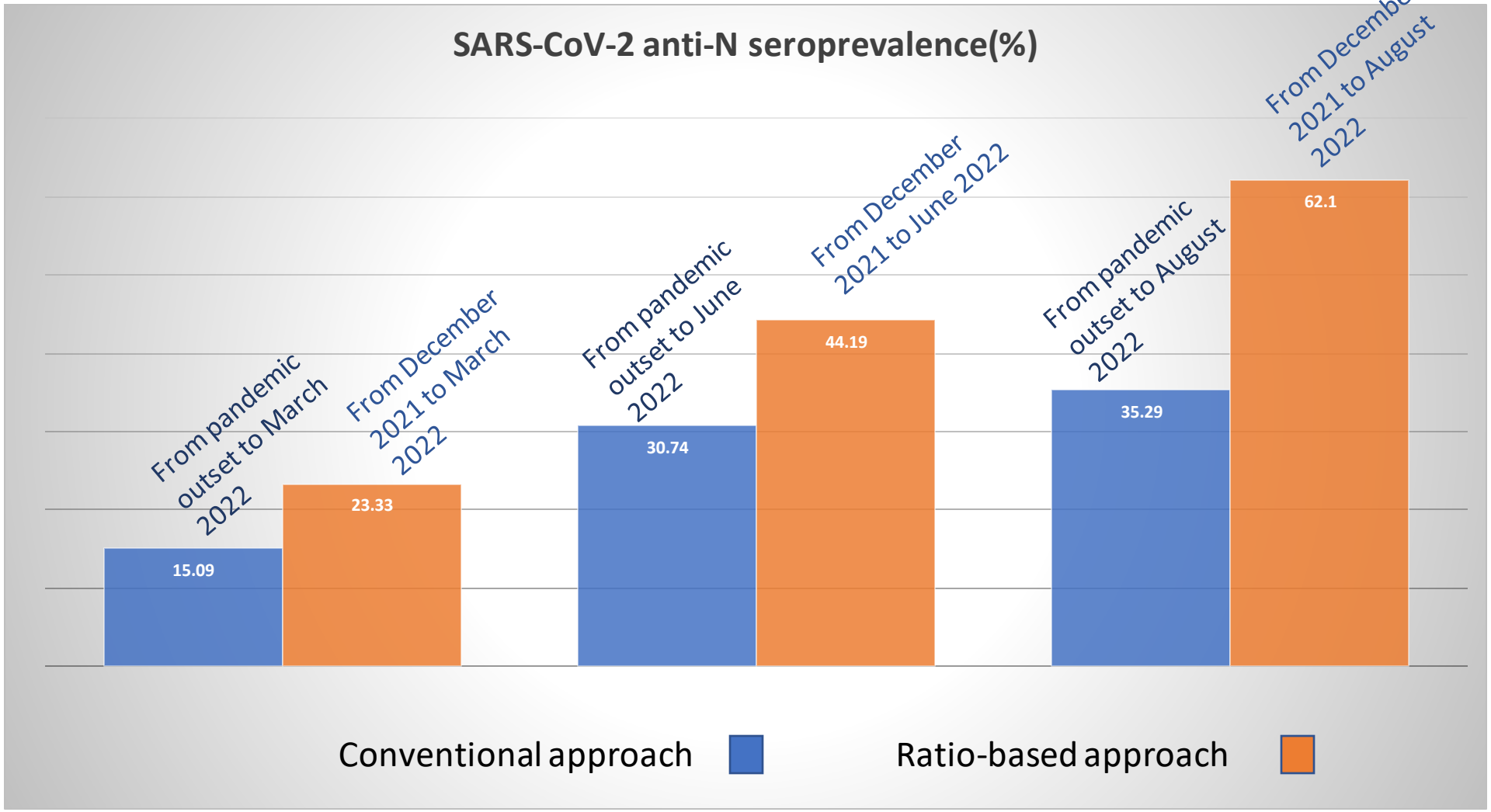
Stability of the ‘pre-infection’ anti-N signal



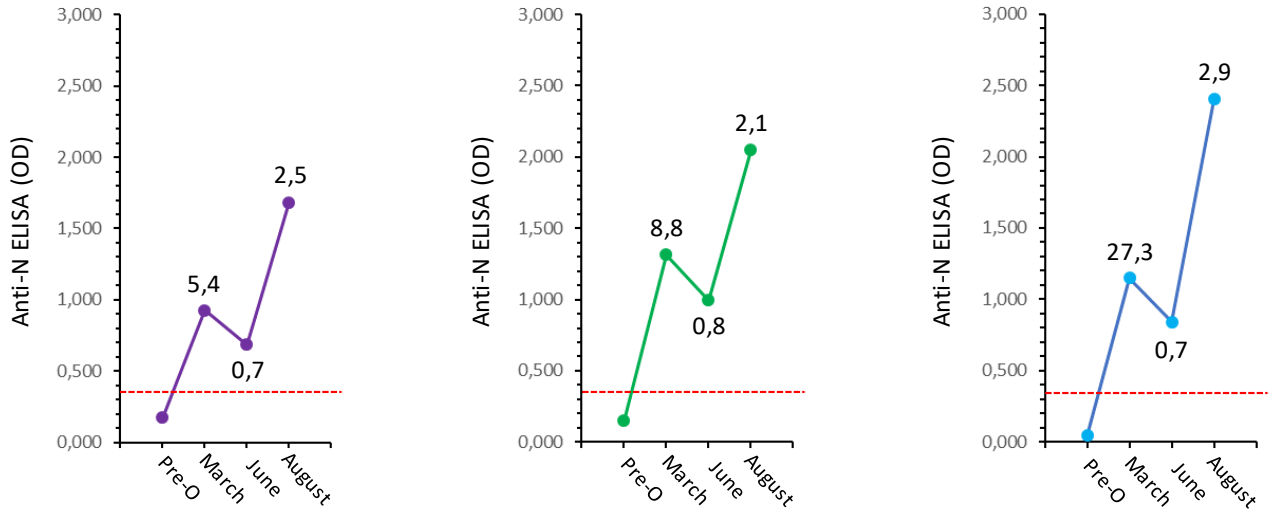
Ratio-based approach to identify acute Omicron infections – December 2021 to November 2022



Comparison between ‘conventional’ and ratio-based approach



Exemple of anti-N DO profiles with suspected reinfection



Conclusions

1. SARS-CoV-2 serosurveillance studies in blood donors have been very useful to public health authorities as a way to assess the progression of the COVID-19 pandemic in the general population
2. Cross-sectional seroprevalence studies can no longer present an accurate picture of the cumulative incidence of infection:
   - Seroreversion phenomenon (more so for anti-N than for anti-S)
   - Blunting of the anti-N response by previous vaccination
3. Access to serial samples obtained from sentinel populations such as blood donors can greatly improve our ability to identify recent infections
4. As of November 2022, the Omicron wave has struck about 85% of the Quebec population
5. Some remaining questions:
   - Specificity of the anti-N ratio-based approach?
   - Comparison of our in-house anti-N assay with commercial platforms (ongoing work)
6. This approach might be applicable to other emerging pathogens

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Thank you

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COVID-19 IMMUNITY TASK FORCE
GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

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