

Serosurveillance of SARS-CoV-2 in Frequent Plasma Donors

Presented by :

Dr. Marc Germain Vice-president, Medical
Affairs and innovation, Héma-Québec



**IPFA/PEI 28th International Workshop on Surveillance and Screening of Blood-borne Pathogens
Porto, September 21-22, 2022**

No conflict of interest to disclose



HÉMA-QUÉBEC

Contents

1. A brief history of SARS-CoV-2 serosurveillance in blood donors at Héma-Québec
 - The difficulty of serosurveillance in the context of mass vaccination
 - The limitations of cross-sectional anti-N testing
2. Setting up a repository of plasma samples obtained from frequent plasma donors (PlasCov Biobank)
3. Establishing 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



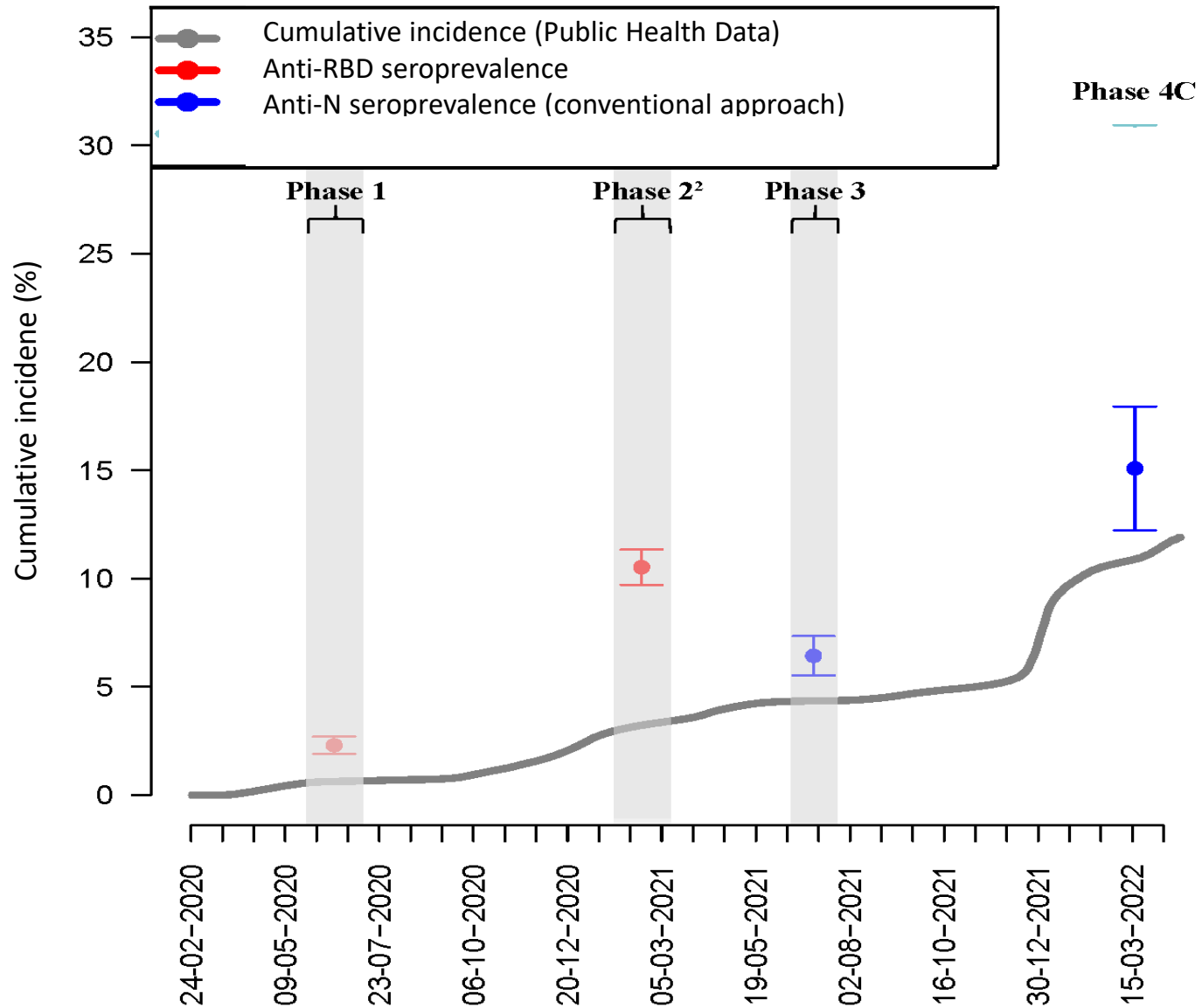
HÉMA-QUÉBEC

1. Serosurveillance of COVID-19 in
Quebec blood donors



HÉMA-QUÉBEC

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

2. The Plascov Biobank – serial
samples from regular plasma donors



HÉMA-QUÉBEC

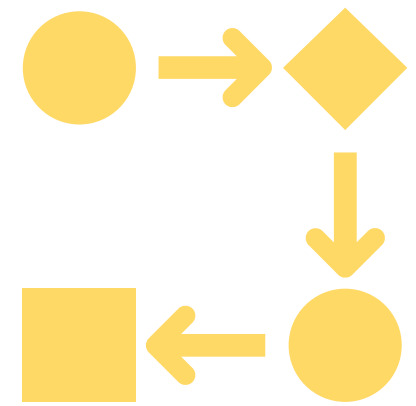
PLASMA DONOR BIOBANK (PLASCOV)

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)**.



HÉMA-QUÉBEC



Process flow: from consent to banking of samples

Who: All plasma donors

Where: In all fixed centers in the province

When: At each donation since April 2021 (donors can give once a week if they wish)

How:

- The donor agrees to participate in the study during the selection interview (consent valid for all subsequent donations)
- Data collection on the donor during the medical questionnaire + socio-demographic and health data
- An additional 3 ml tube of plasma is collected directly from the plasma bag at the end of the donation
- The tubes are sent to the R&D laboratories in Quebec and then banked
- Management of refusals in R&D upon receipt of tubes

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

- 📍 Établissement
- 📍 Centre des donneurs de sang GLOBULE
- 📍 Service régional des collectes mobiles
- 📍 Salon des donneurs de plasma PLASMAVIE
- 📍 PLASMAVIE incluant un espace dédié au don de sang
- 📍 Point de dépôt pour le lait maternel



En plus de milliers de collectes mobiles à travers la province!



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 <i>Rh</i> 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

1. Current picture of the cohort (July 2022)

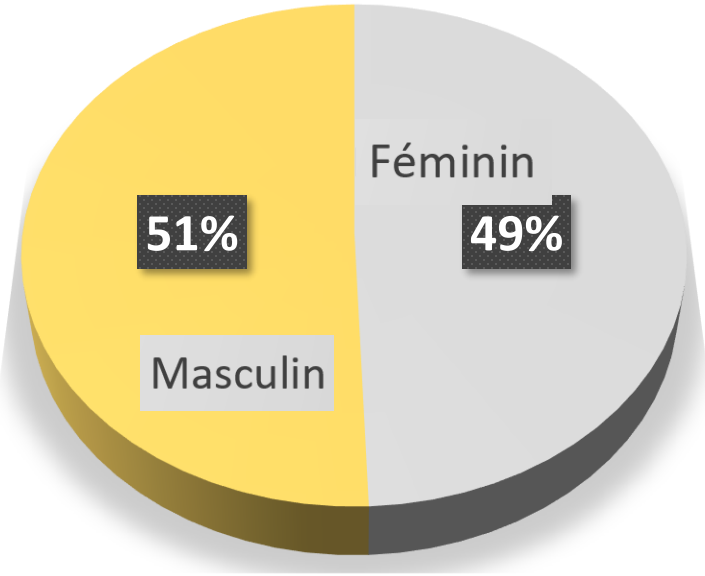
- ❑ More than **140 000 samples** collected (since April 2021)
- ❑ More than **15 000 individual donors**
- ❑ 90 % participation rate
- ❑ More than 7600 donors with samples taken pre/post-infection and/or pre/post-vaccination



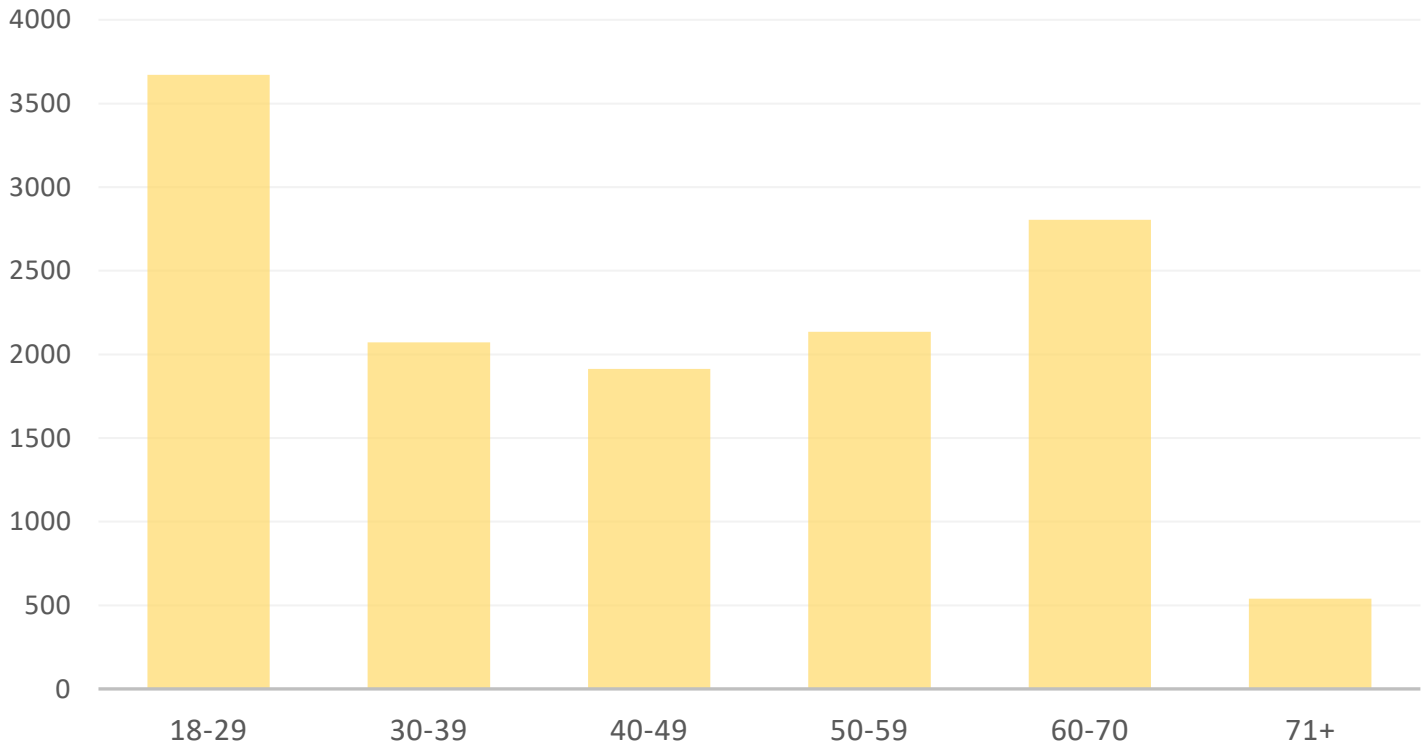
Sociodemographic Profile of the Cohort



Gender Distribution



Number of frequent donors by age group



3- Optimizing the detection of recent infections using anti-N seroconversion



HÉMA-QUÉBEC

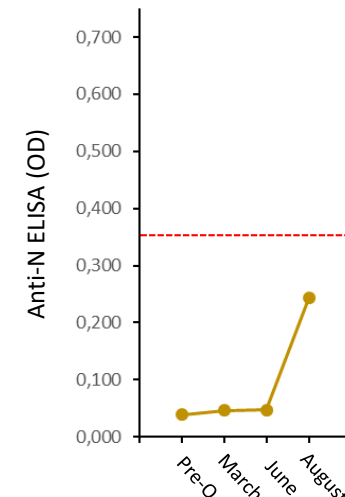
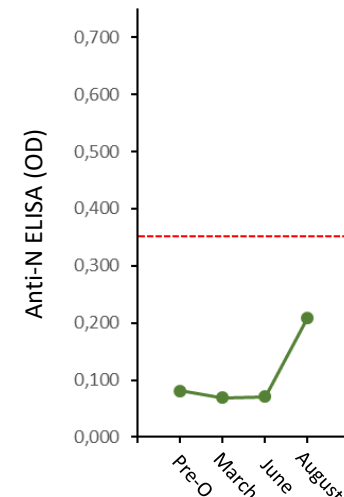
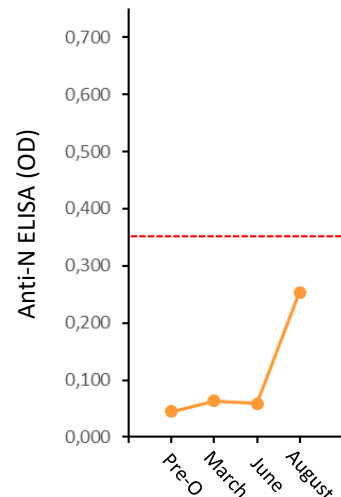
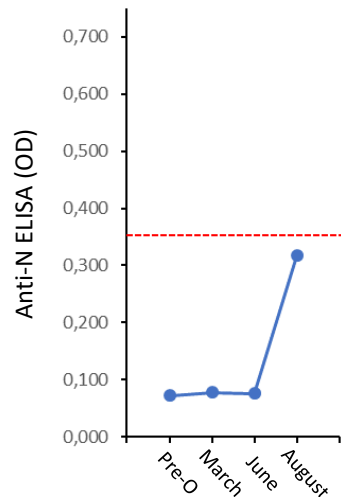
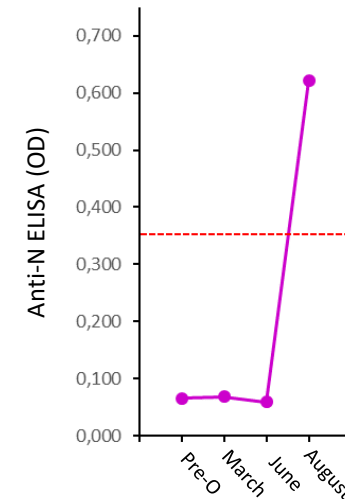
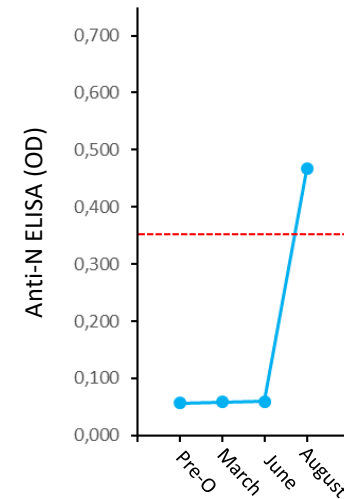
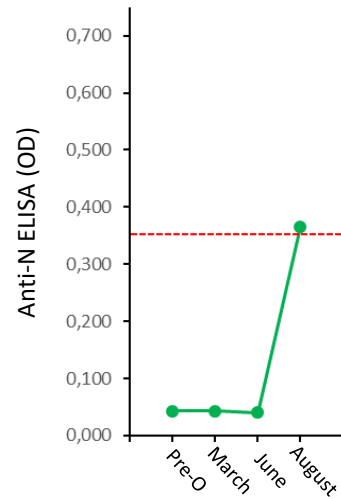
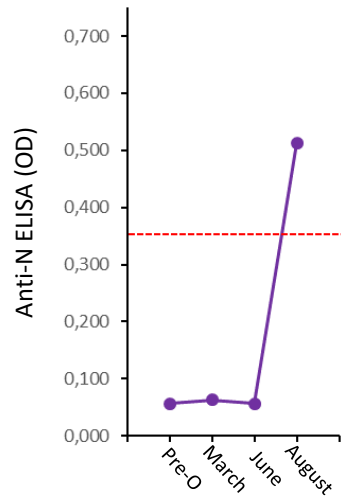
Validation of a ratio-based approach to identify acute Omicron infections

- **248 vaccinated Plascov donors with a PCR-confirmed infection** during 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 $\geq$ 1.5 times the OD of the pre-infection sample) Autres régions	236/248	95.2%

Stability of the 'pre-infection' anti-N signal



Measuring the impact of the Omicron wave in
Quebec – December 2021 to June 2022



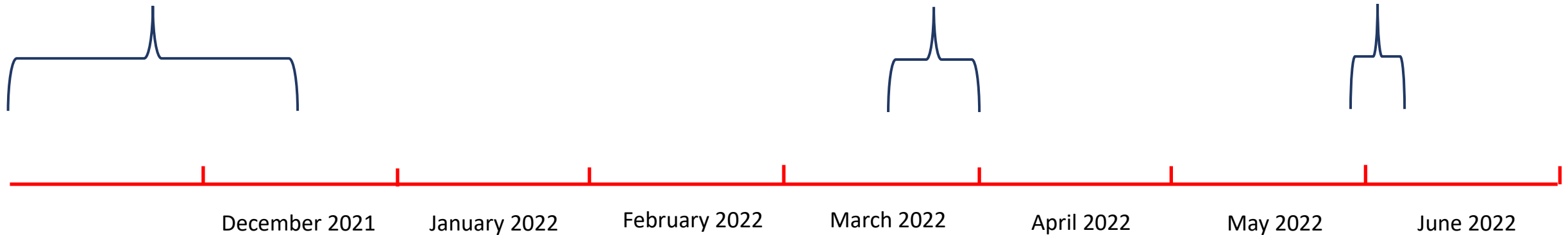
HÉMA-QUÉBEC

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

First (pre-Omicron) sample
(before December 15, 2021)

Second (post-B1 wave) sample
(March 15 – April 1, 2022)

Third (post-B2 wave) sample
(March 30 – June 5, 2022)



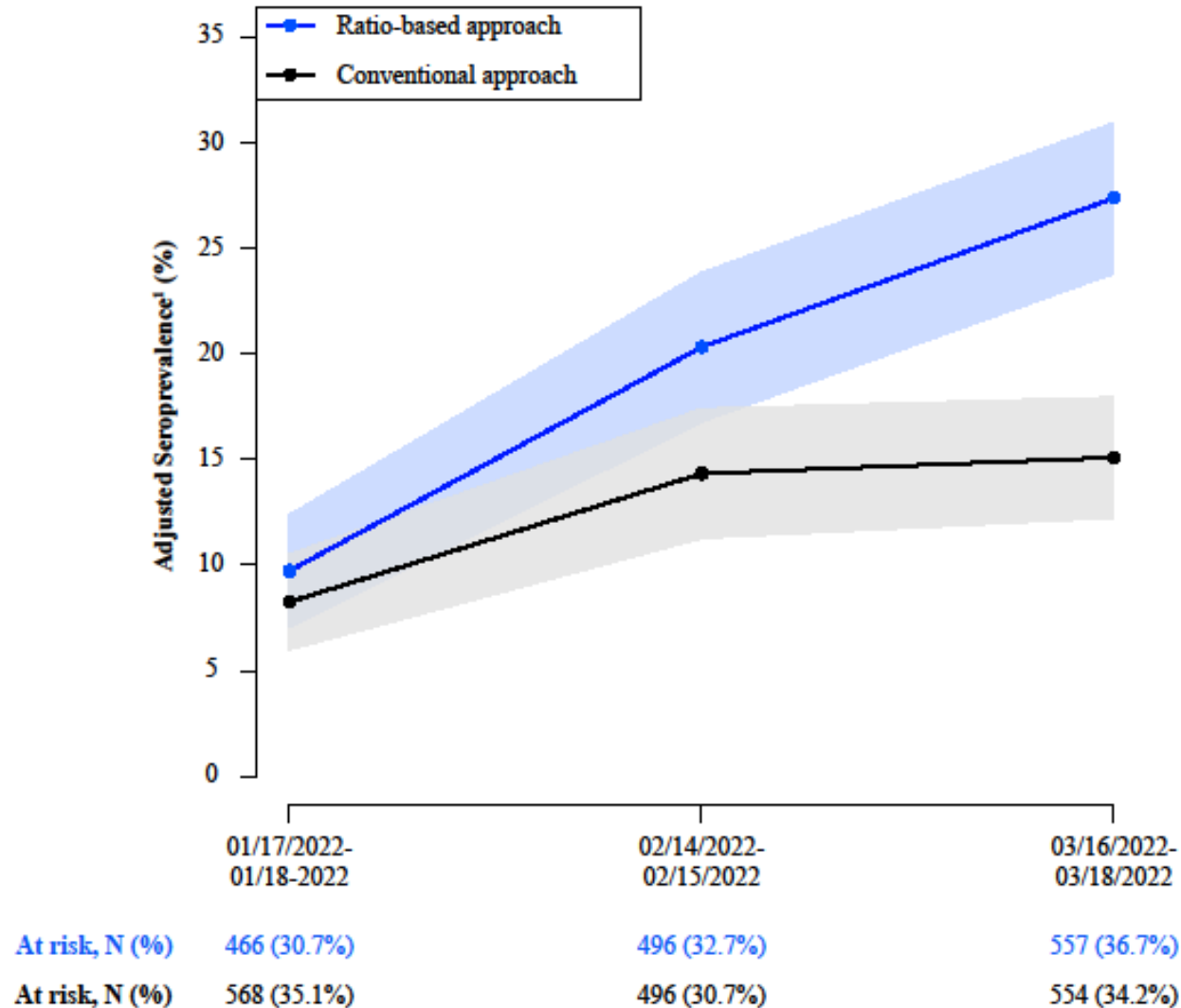
Ratio-based approach to identify acute Omicron infections – December 2021 to June 2022

	N=568
Age, mean $\pm$ SD	55,87 $\pm$ 14,34
Women, n (%)	134 (24,01%)
Greater Montreal region, n (%)	74 (13,26%)
Caucasians, n (%)	544 (97,49%)
Material deprivation index (Q5), n (%)	91 (17,11%)
Social deprivation index (Q5), n (%)	41 (7,70%)

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

	June (Conventional approach)		December – June (Ratio-based approach)	
	n/N	Seroprevalence (%) (95% CI)	n/N	Seroprevalence (%) (95% CI)
Geographical region				
Greater Montreal	20/74	28,65 (21,13 – 36,16)	29/74	41,60 (33,40 – 49,79)
Other regions	135/484	31,41 (27,04 – 35,78)	206/484	46,51 (41,82 – 51,21)
Total	155/558	30,74 (26,96 – 34,52)	235/558	45,32 (41,24 – 49,40)

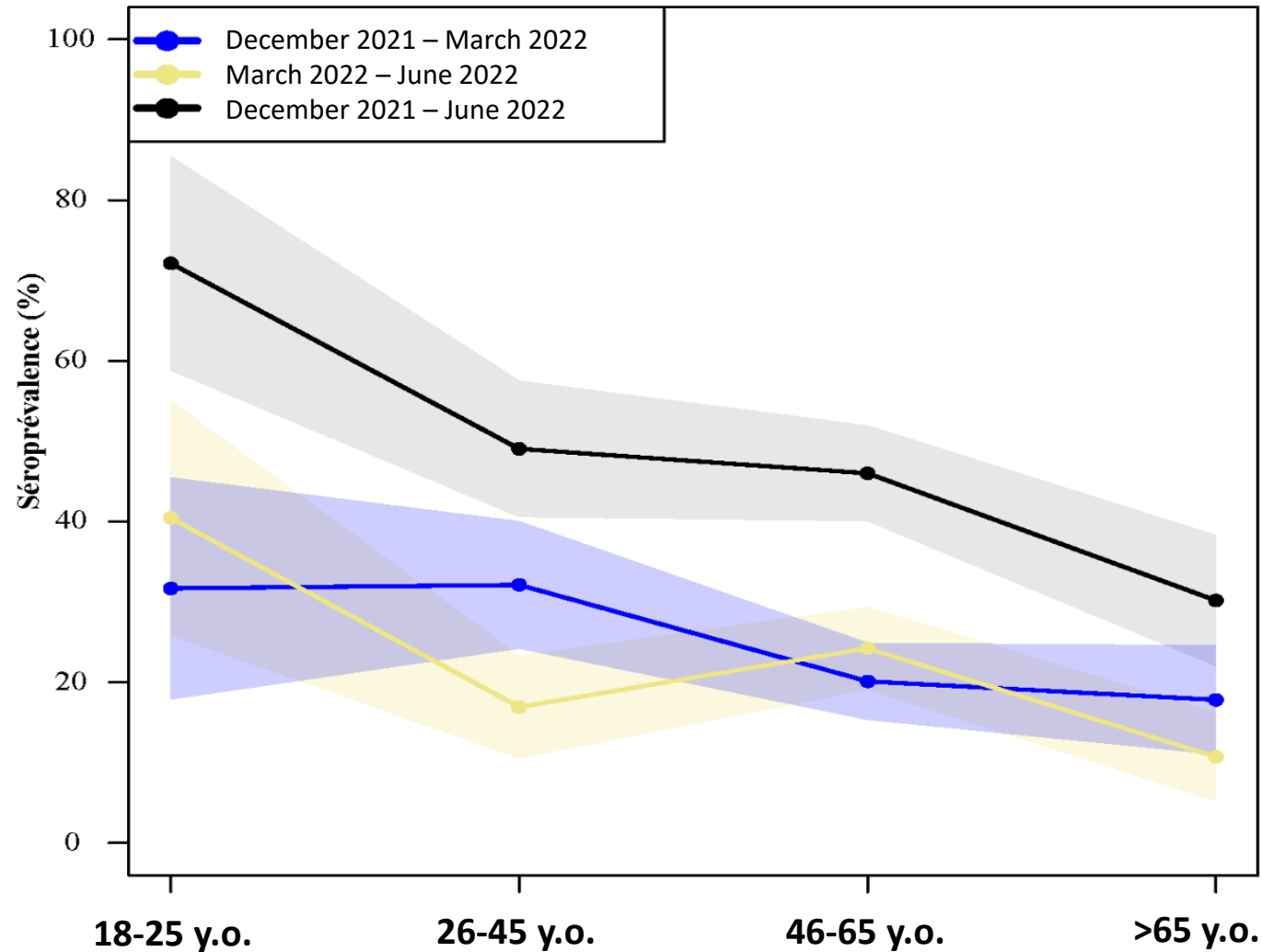
Ratio-based approach to identify acute Omicron infections – December 2021 to March 2022



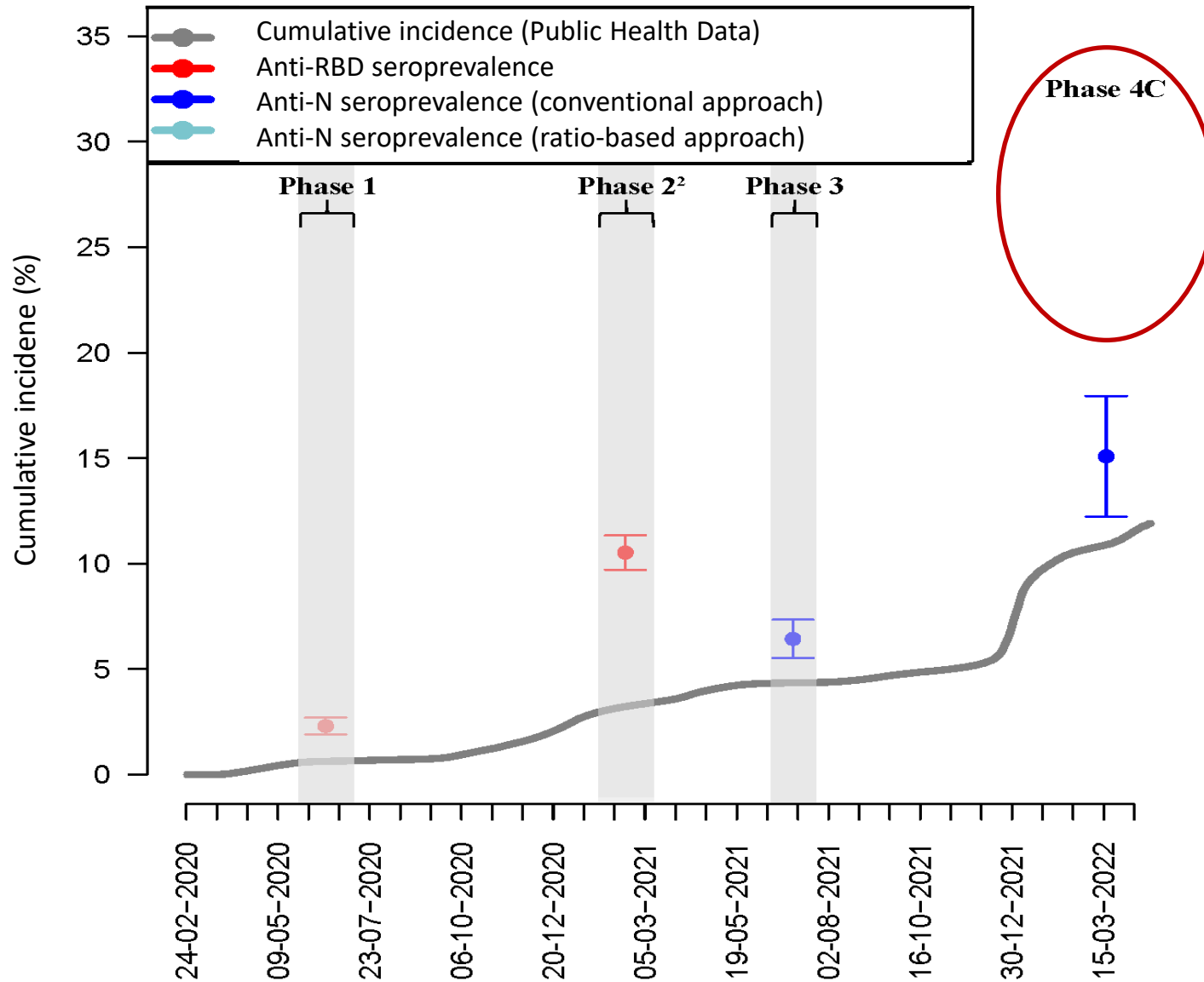
Ratio-based approach to identify acute Omicron infections – December 2021 to June 2022

	December to March				March to June				December to June			
	Men		Women		Men		Women		Men		Women	
	n/N	Seroprevalence (%), (IC 95%)	n/N	Seroprevalence (%), (IC 95%)	n/N	Seroprevalence (%), (IC 95%)	n/N	Seroprevalence (%), (IC 95%)	n/N	Seroprevalence (%), (IC 95%)	n/N	Seroprevalence (%), (IC 95%)
Greater Montreal	11/50	24,18 (15,38 – 32,97)	3/24	12,50 (3,14 – 21,86)	9/50	19,58 (11,43 – 27,73)	3/24	12,50 (3,14 – 21,86)	21/50	45,95 (35,71 – 56,19)	8/24	33,33 (20,00 – 46,67)
Other regions	88/374	24,31 (19,40 – 29,22)	23/110	24,43 (17,32 – 31,53)	67/374	22,27 (17,50 – 27,03)	27/110	21,59 (14,79 – 28,39)	156/374	46,75 (41,04 – 52,46)	50/110	46,02 (37,78 – 54,26)
Total	99/424	24,28 (19,99 – 28,57)	26/134	21,39 (15,54 – 27,24)	76/424	21,63 (17,51 – 25,75)	30/134	19,28 (13,65 – 24,91)	177/424	46,56 (41,57 – 51,55)	58/134	42,79 (35,73 – 49,85)

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

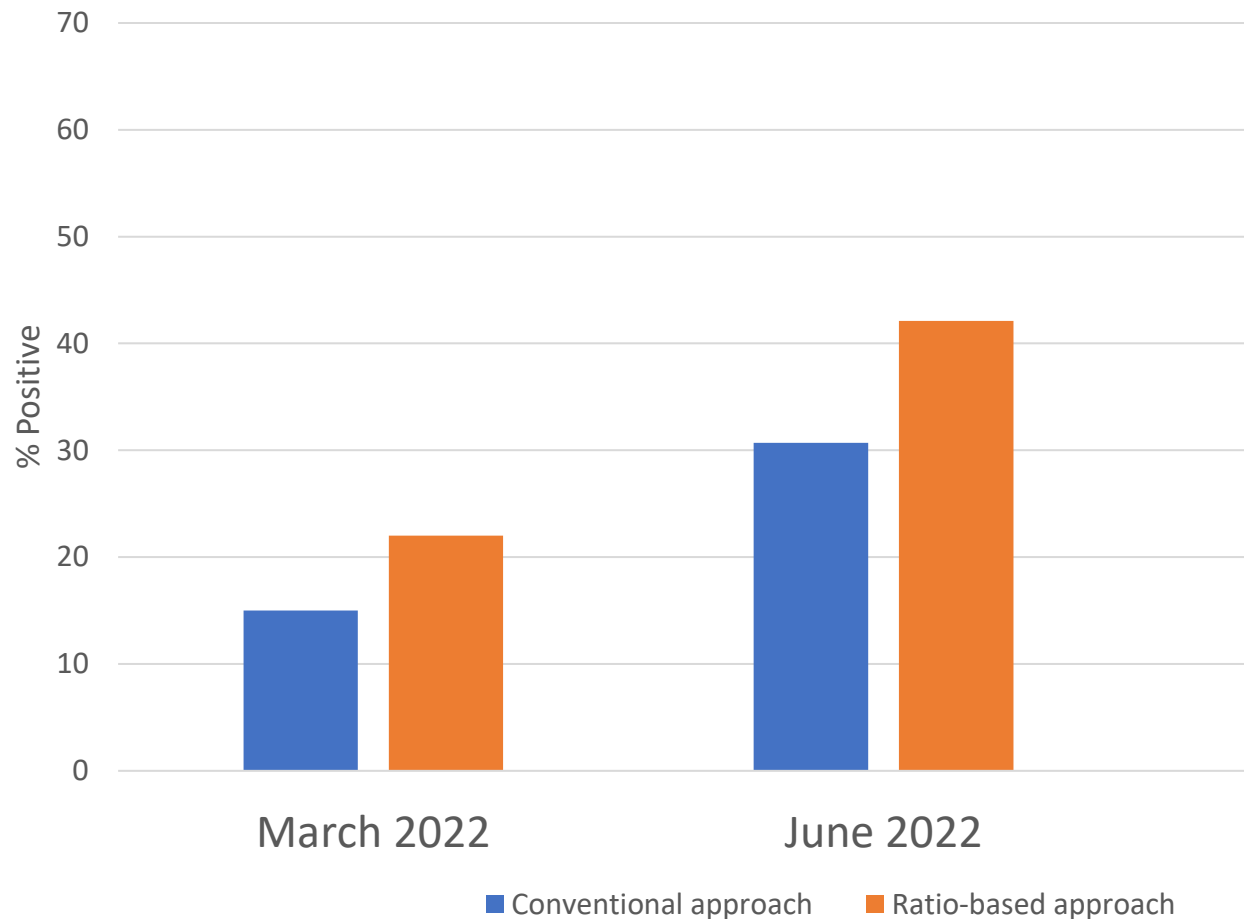


SARS-CoV-2 seroprevalence studies at Héma-Québec



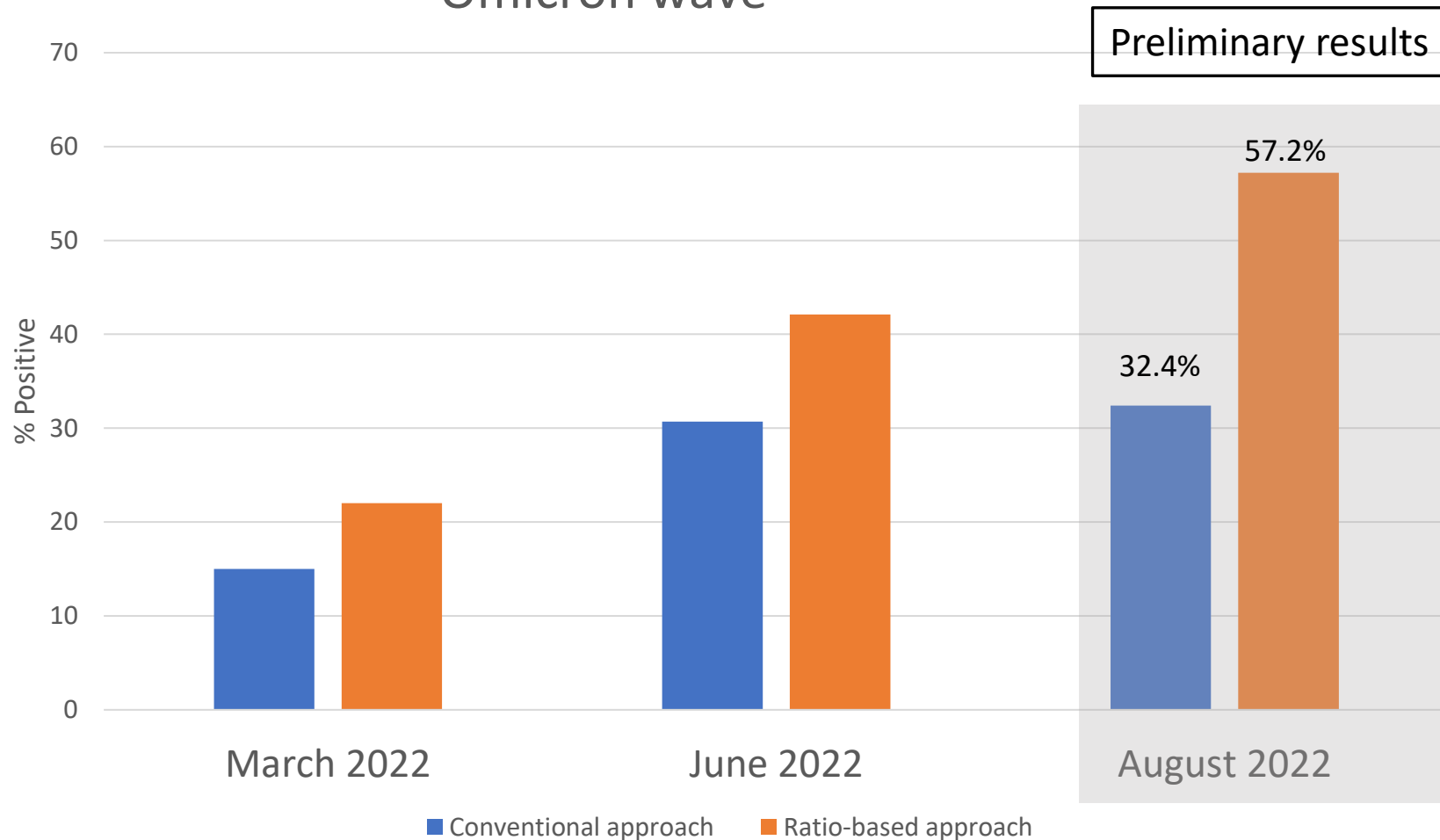
SARS-CoV-2 seroprevalence studies at Héma-Québec

Evolution of anti-N seroprevalence during the
Omicron wave



SARS-CoV-2 seroprevalence studies at Héma-Québec

Evolution of anti-N seroprevalence during the
Omicron wave



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 can greatly improve our ability to identify recent infections, by following the anti-N response
4. As of August 2022, the Omicron wave has struck close to 60% 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)
 - What happened to never-vaccinated donors?



HÉMA-QUÉBEC

Thank you

Those who did the actual work :

Renée Bazin, PhD.

Christian Renaud, M.D.

Antoine Lewin, Ph.D.

Yves Grégoire, M.Sc

Amélie Boivin, M.Sc., MBA

Gaston DeSerres, M.D. (MSSS)

And many others...



COVID-19
IMMUNITY
TASK FORCE

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



Gouvernement
du Canada

Government
of Canada

Québec 

Ministère de la Santé et des Services sociaux