Characterizing viral load dynamics in community SARS-CoV-2, Influenza, and RSV infections : the role of age, sex, and vaccination

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CONTEXT

- **Acute respiratory infections** (ARIs) represent a major public health burden, with the co-circulation of **SARS-CoV-2**, **influenza A virus** (IAV), **influenza B virus** (IBV), and **respiratory syncytial virus** (RSV)
- Each year, hundreds of thousands of individuals presenting **respiratory symptoms** undergo **PCR testing** in city laboratories to identify the etiological agent responsible for ARIs
- Most of these tests are **triplex assays** designed to maximize pathogen detection, and are collected through the **RELAB network** in France
- Beyond their primary diagnostic purpose, these tests generate **large-scale surveillance** datasets, including both binary diagnostic outcomes and **cycle threshold (Ct) values**
- Ct values are **inversely related to viral load** and may provide insights into transmission potential[1,2], disease severity[3], and vaccination impact
- However, while most viral load analyses rely on clinical trial data, Ct data derived from community-based PCR testing remain largely **underexplored**[4]

Community virological testing for ARI → Ct values (viral load) → Mathematical modeling → Population-level insights

Objective: Use community-based multiplex PCR Ct values to characterize viral dynamics of SARS-CoV-2, Influenza and RSV

→ Develop mechanistic within-host models

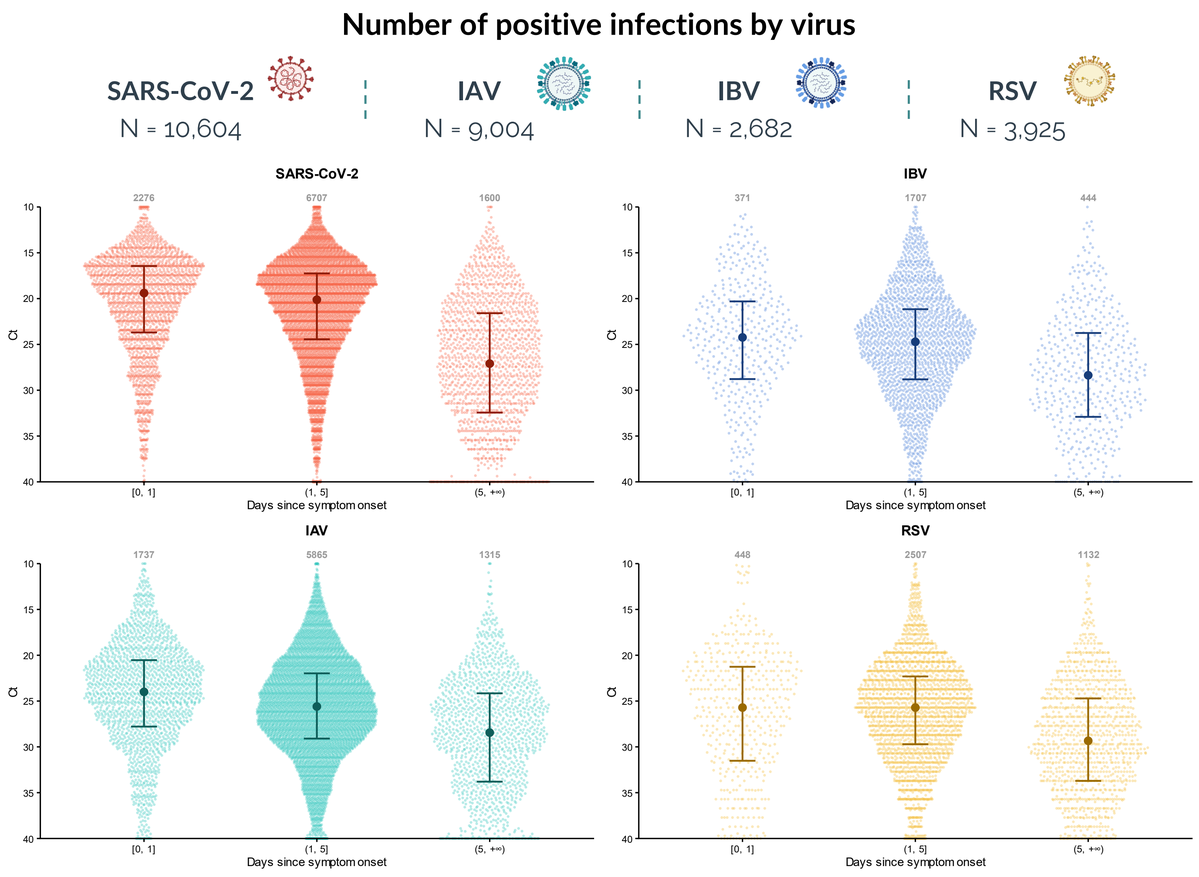
→ Assess covariate effects on viral dynamics (age, sex, epidemic period)

→ Evaluate vaccine effects on viral load

METHODS

Data

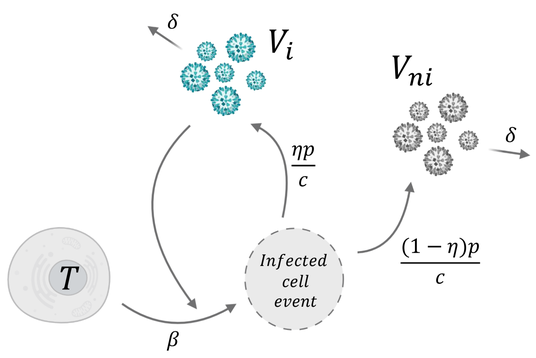
- **112,557 PCR tests** from 111,492 symptomatic individuals
- 2024/2025 & 2025/2026 winter seasons
- Age groups: **<18** (14.1%), **18-65** (57%), **>65** (29%)
- Vaccination coverage: **SARS-CoV-2** (4.4%), **IAV** (16%), **IBV** (3.1%)



Ct values distribution by reported time since symptoms onset intervals

Biological model

- Target-cell limited (**TCL**) model[5]
- Two virion populations: **infectious (V_i)** / non-infectious (V_{ni})



Within-host viral dynamics model

Quantities of interest

- Peak viral load
- Viral clearance duration
- **Covariate effects**: age, sex, vaccination status, epidemiological period, and season

Statistical framework

- Nonlinear mixed-effects modeling (*Monolix2024R1*)[6]
- A fixed **incubation period** was assumed
  - SARS-CoV-2 & RSV : $T_{incub} = 5$ days [7,8]
  - Influenza A/B : $T_{incub} = 2$ days[5]
- Fixed literature parameters[7,8]
  - **Virion clearance** : $c = 10\ days^{-1}$
  - **Fraction of infectious virions** : $\eta = 10^{-4}$

Model development workflow

Model reduction
- Model selection via ΔBIC_c[9]
- Random effects elimination : $\Delta BIC_c \geq 10$

→ **Covariate selection**

Forward inclusion: Add covariate if $\Delta BIC_c \geq 2$ → Backward elimination: Remove if $\Delta BIC_c < 2$

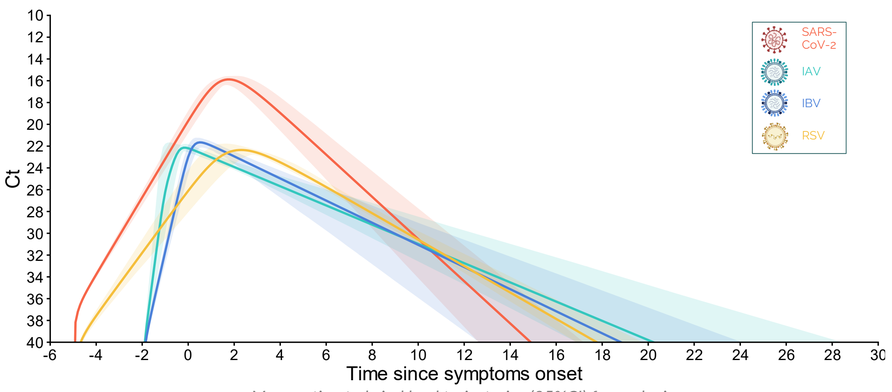
Effects tested on β, p, δ → non-significant categories merged

RESULTS

Estimated viral kinetics across pathogens

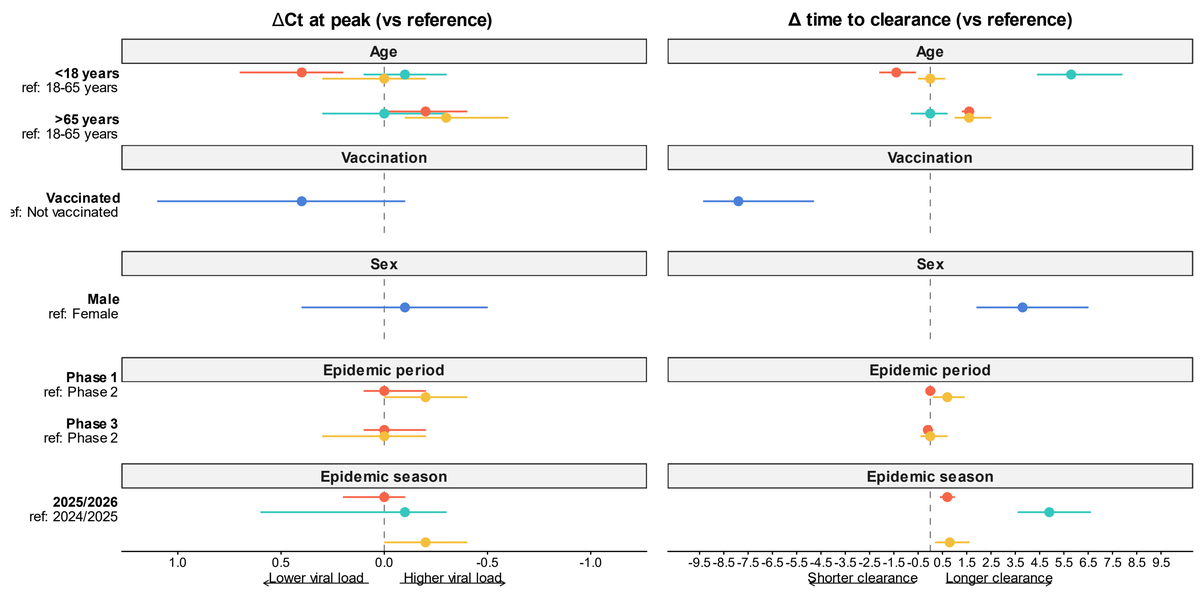
Estimated parameters sampled from a joint uncertainty distribution (MVN derived from the FIM)

- SARS-CoV-2 and RSV exhibited **longer times to peak viral load**
- Influenza viruses showed **slower viral clearance dynamics**
- SARS-CoV-2 had the **shortest mean positivity duration** (20 days) and RSV the longest (23 days)



Mean estimated viral load trajectories (95%CI) for each virus

Covariate effects



Estimated effect size on peak Ct differences and time to clearance with 95% confidence intervals

Age

- SARS-CoV-2: children showed **lower peak** viral load (+0.4 Ct) and **shorter clearance** time (-1.4 days)
- IAV: children had **longer viral clearance** (+5.8 days)
- RSV: older adults showed **higher peak** viral load (-0.3 Ct) and **longer clearance** (+1.6 days)

Sex

- IBV: men exhibited **longer viral clearance** (+3.8 days)

Vaccine status

- IBV: vaccinated individuals had **shorter viral clearance** (-7.9 days)

Epidemic season

- 2025/2026 season: **longer clearance** for
  - SARS-CoV-2: +0.7 days
  - IAV: +4.9 days
  - RSV: +0.8 days

CONCLUSION

- **Age-related effects** observed for SARS-CoV-2 and IAV, as well as **sex-related differences** for IBV, were consistent with previous findings[10,11,12]
- **Vaccine-related differences** were observed only for IBV, likely reflecting higher vaccine effectiveness[13]
- The influence of **epidemic periods** and **seasonal patterns** remained less clear, but may reflect shifts in circulating variants
- **Limitations** include the observational design, cross-sectional data structure, restriction to symptomatic infections, and potential confounding effects
- This framework could be used as an **early-warning surveillance tool** during epidemic surges by enabling near real-time characterization of viral dynamics and their key determinants

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