COVID-19 testing outcomes over time since exposure: a statistical model and implications for enhanced contact tracing

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How soon can I find out I'm infected?

You're likely to test positive by **qPCR** earlier in your course of infection than any other test: **median 3 days** post infection (range 1 – 5 days).

By **lateral flow test (LFT)** you might have to wait longer, with a median time to first positive test of **4 days** post infection and higher variability (range 2 – 8 days).

Note: how you take your sample might matter! Throat swabs have a median of 2 days (range 1 – 3) until first positive qPCR, which will give you a result sooner than taking a nasal swab (p=0.0056).

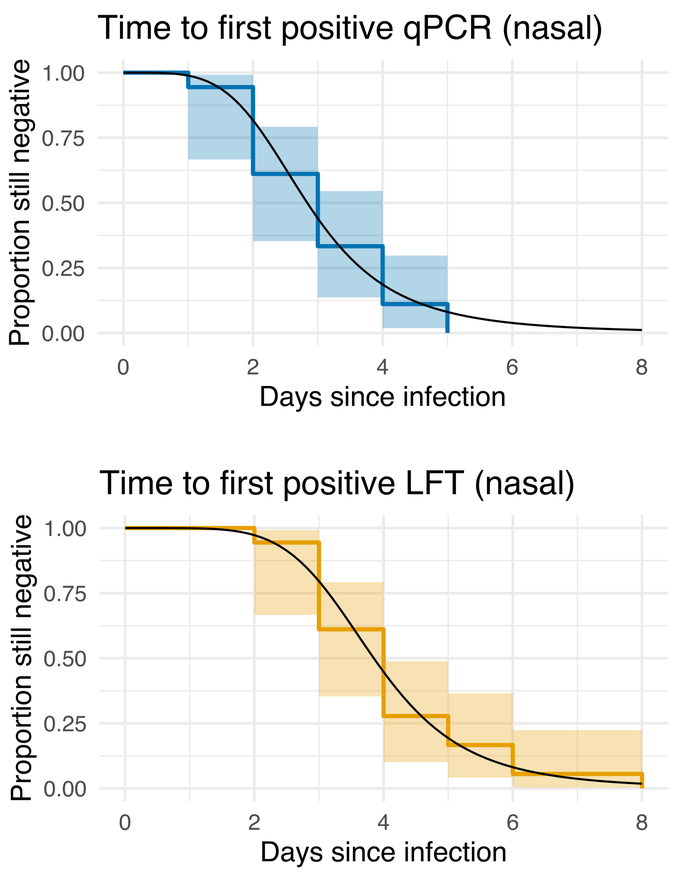


Figure 1: Survival curves for time from infection to first positive test. Top: qPCR. Bottom: Lateral flow (LFT).

How good are lateral flow tests really?

You might have heard people talking about lateral flow tests (LFTs) being "worse" than qPCR, or just generally that they are not very reliable. It turns out this is mainly because they have a **shorter window** of being able to pick up infection.

If well-timed, LFTs can be highly sensitive, and are able to detect **93.3%** (85.1% - 98.0%) of cases at around **day seven** post infection via nasal swab.

Throat swabs aren't quite as good, with a maximum sensitivity of **82.4%** (67.0% - 91.8%) on **day six** post infection. They also stop showing positive results 1-3 days sooner than nasal swabs.

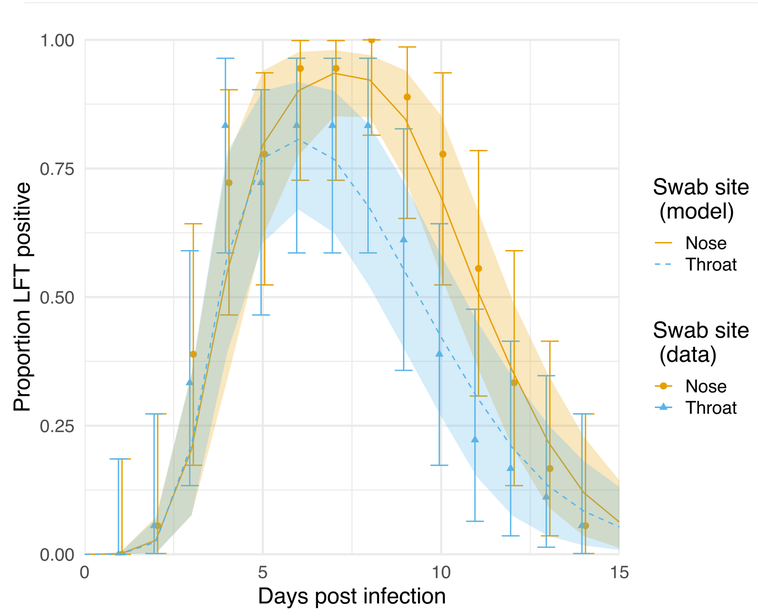


Figure 2: Model for LFT test positivity over time since infection for nose (orange) and throat (blue) swabs.

"What does my COVID-19 test result actually mean?"

How do I know if I'm infectious?

Testing for culturable virus by focus forming assay (FFA) gives a proxy for infectiousness – if virus can be cultured from a swab, then you might be able to transmit it to others.

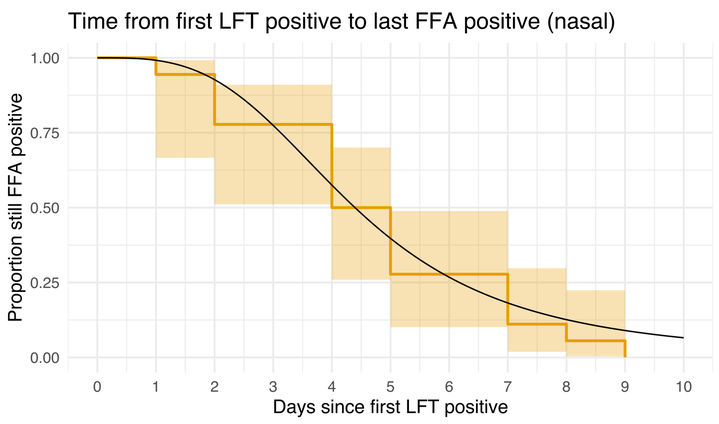


Figure 3: Time from first LFT positive to last positive by focus forming assay (FFA) – proxy for infectiousness.

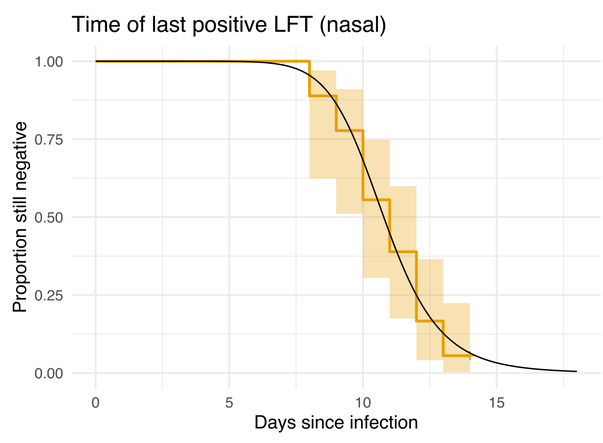
There is strong positive correlation between first positive lateral flow test (LFT) and first culturable FFA (nasal: p=0.00032; throat: p=0.00019).

↓

A positive LFT is likely to be a good indicator of infectiousness.

Figure 3 shows that if you've been testing regularly then **you could be infectious for a median of 5 days** (range 1 – 9 days) after you first test positive on a lateral flow, although some people might be infectious for longer so it may be best to wait until you test negative.

The last LFT positive occurs on **average one day** (range 0 – 1 .75 days) after the last FFA positive, so you probably stop being infectious just before, or when, you stop testing positive.



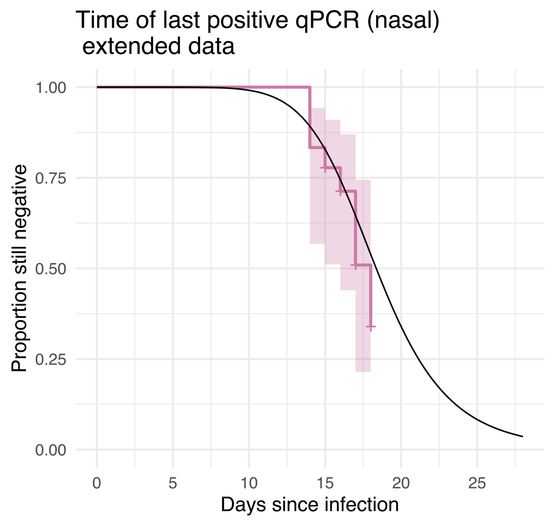


Figure 4: Timing of last positive result (from infection). Top: Lateral flow (LFT). Bottom: qPCR.

How long will I test positive for?

The median time from infection to last positive LFT is **11 days** (95% CI: 10 – 12 days) for nasal swabs and **9 days** (95% CI: 8 – 11 days) for throat swabs and the majority of people will be negative after two weeks.

By qPCR individuals test positive a lot longer, usually at least two weeks, with a median of **18 days** and 25% of people still testing positive three weeks after infection.

Because the study these models are based on only collected data for a limited period, we can only draw limited conclusions about the upper end of how long and individual might test qPCR positive for.

Methods

Data used is from a human challenge study with 18 infected participants aged 18-30 [1].

This analysis is based on two accelerated failure time (AFT) survival models: time from infection to first positive and time from infection to last positive, which are combined to consider the temporal positivity of tests over time [2].

$$S(t) = \frac{1}{1+\alpha t^{\gamma}}$$

And the probability of testing positive at time t after infection is given by:

$$P(t) = \mathbb{P}[X = t] + \phi\mathbb{P}[X < t < Z] + \mathbb{P}[Z = t], \text{ where } X < Z.$$

Where $\phi =$ maximum sensitivity of the test and:

$$\mathbb{P}[X = t] = S_X(t-1) - S_X(t),$$

$$\mathbb{P}[X < t < Z] = \sum_{n=1}^{t-1} \mathbb{P}[X = n]\frac{S_Z(t)}{S_Z(n)}, \text{ and}$$

$$\mathbb{P}[Z = t] = \sum_{n=1}^{t-1} \mathbb{P}[Z = t]\mathbb{P}[X = n].$$

Confidence intervals are calculated using a percentile bootstrapping case-resampling method and all models are fitted in R using the survival package.

Implications for enhanced contact tracing

Understanding when people are likely to test LFT positive or negative, and what testing positive on different types of test means, is useful when designing contact tracing interventions.

- **LFT testing could be targeted** 4 days after a known exposure, to allow earlier detection, or 7 days after, to maximize test sensitivity.
  - Useful for deciding when to test asymptomatic contacts
  - Minimize wasting testing resources
- When a contact tests positive could be used to determine the **direction of transmission**
  - E.g. Testing positive 1 day after contact → more likely to be a "backwards" contact (i.e. infector of index case)
  - Targeted backwards contact tracing could allow the identification of case **clusters**
- **Repeat testing** interventions could focus on 2 – 8 days after a known exposure (range of possible first positive) to ensure **early detection** and to **rule out infection**.
- Duration of infectiousness from first positive could be used to inform case isolation periods.

This model could also be used to inform population-level models of COVID-19 transmission, as well as guide health practitioners and individuals on interpretation of testing outcomes.

References
[1] Killingley, B. *et al.* Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge in young adults. *Nature Medicine* **28**, 1031–1041 (2022).
[2] Davis, E.L. and Hollingsworth T.D. Estimating LFT and qPCR sensitivity over time since infection from a human challenge study. [Pre-print] (2022).
[3] R code: https://github.com/emmalouisedavis/temporaltestsensitivity (DOI: 10.5281/zenodo.6977350)