UK Health Security Agency

# SMART Release & Return Study

## Final Results: Confirming key messages of 26 Apr 22

## Testing Initiatives Evaluation Board: 5 Sep 22

NHS
Liverpool University Hospitals
NHS Foundation Trust

UNIVERSITY OF LIVERPOOL

# Thanks to the team


University of Liverpool with UKHSA

- Civic Data Cooperative
  - Claire Smith; Gary Leeming; Rachel Thompson
- Health Data Science
  - Chris Cheyne; David Hughes; Marta Garcia-Finana
- Psychology
  - Michael Humann
- Virology/Cultures
  - Lance Turtle; Chris Jones; Anna Smielewska; Rebekah Penrice-Randal; Catherine Hartley
- Public Health
  - Iain Buchan (CI); Tom Fowler (UKHSA)

Liverpool University Hospitals NHS Trust

- Tim Neal (PI); Diane Haddock; Liz Roden; Karl McIntyre; Julia West; Heather Rogers; Roger Hunt; Stephanie Ingram; Leon Williams

# Formation of this action-research

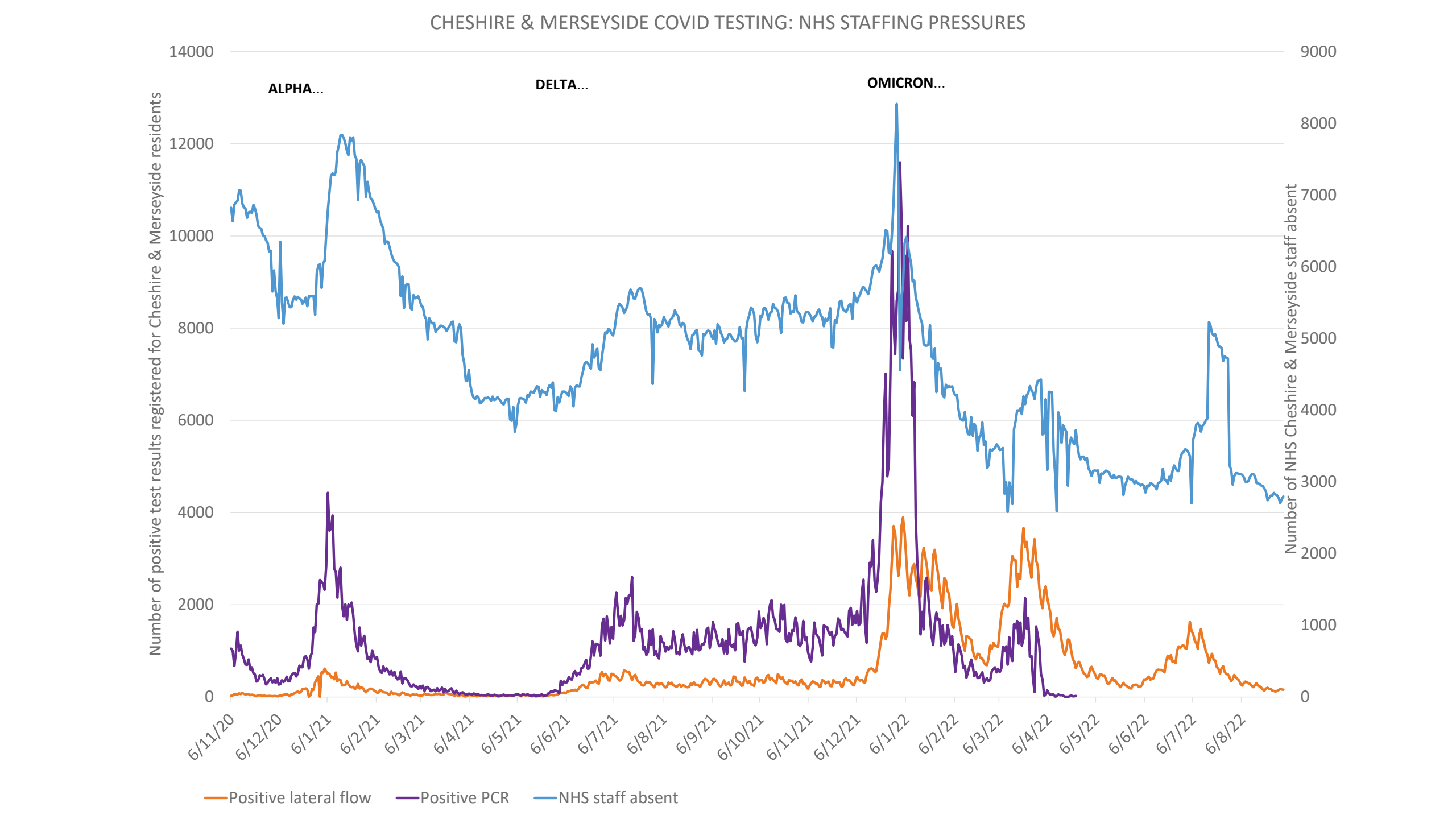
- NHS staffing crisis in Dec 21 as Omicron emerged
  - Over a quarter of staff off sick in some organisations including the main acute hospital
  - Merseyside Local Resilience Forum requested support

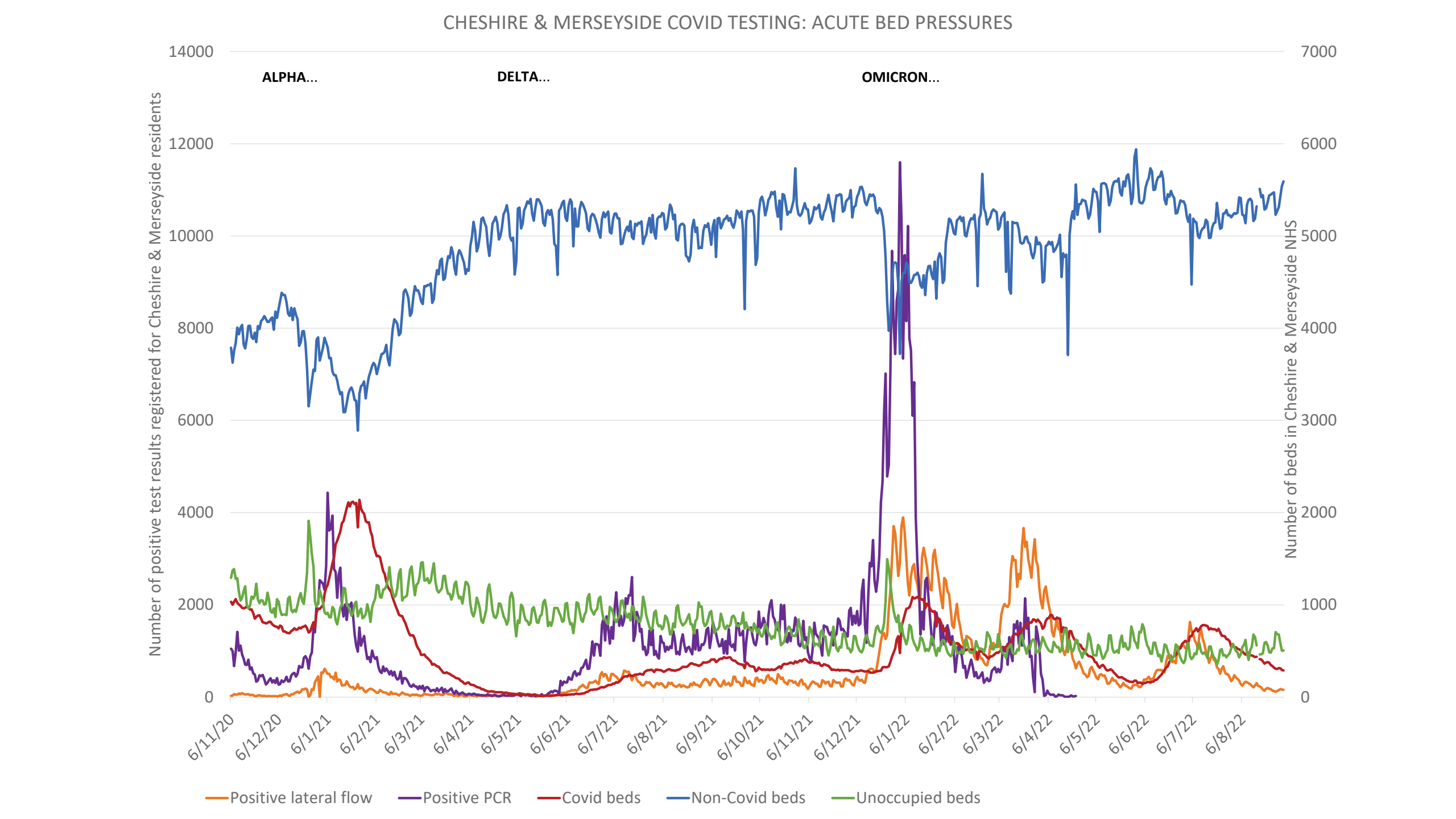
- Original research question
  - Could test-to-release from quarantine be adapted to test-to-return from isolation?

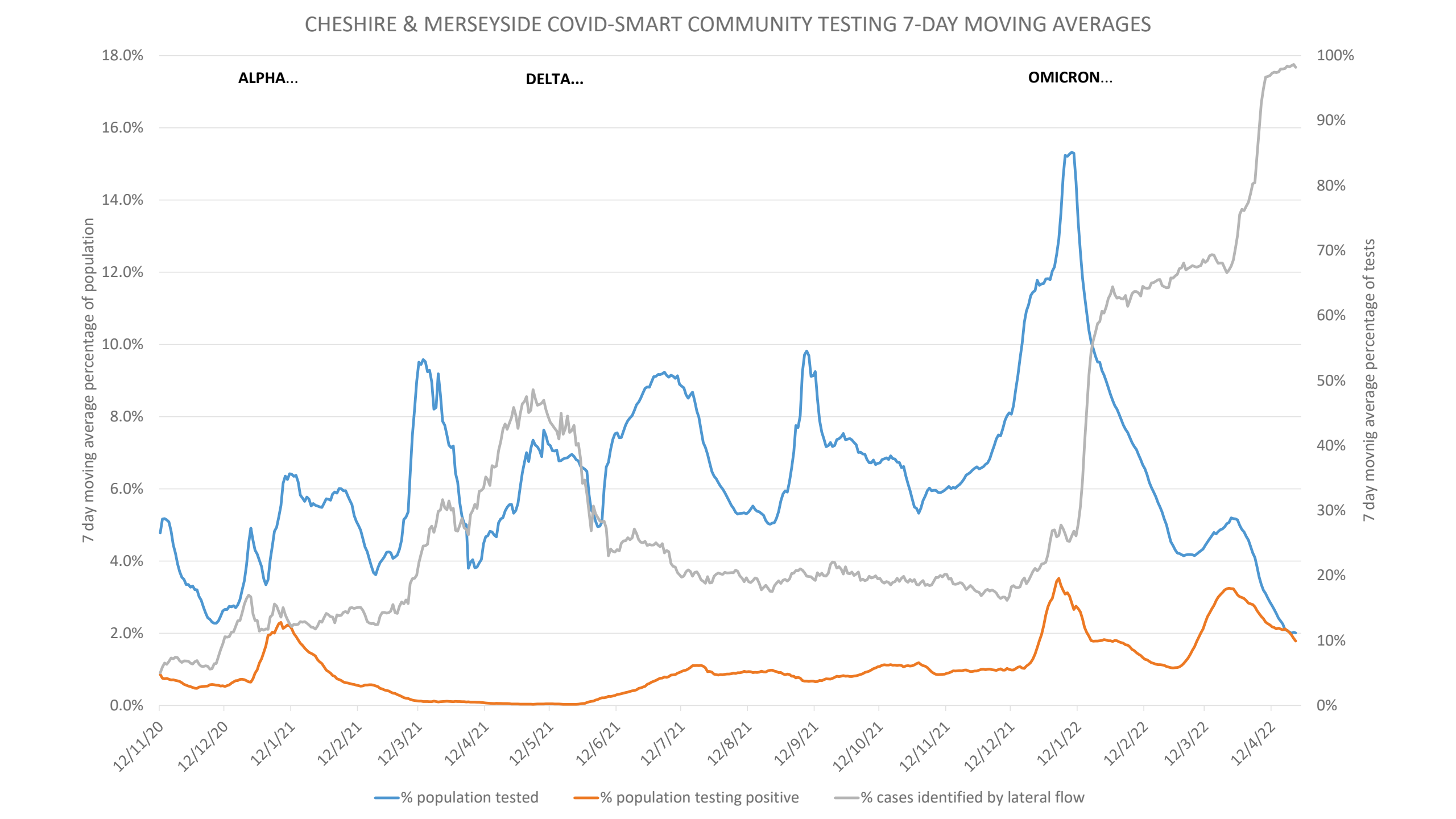
- Policy changes Dec 21 & Jan 22
  - NHS implemented return after 2 days of negative lateral flow tests from day 5
  - Policy questions arose over whether Omicron tropism affected the value of nasal swabbing
  - SMART Release & Return study protocol prepared from Dec 21

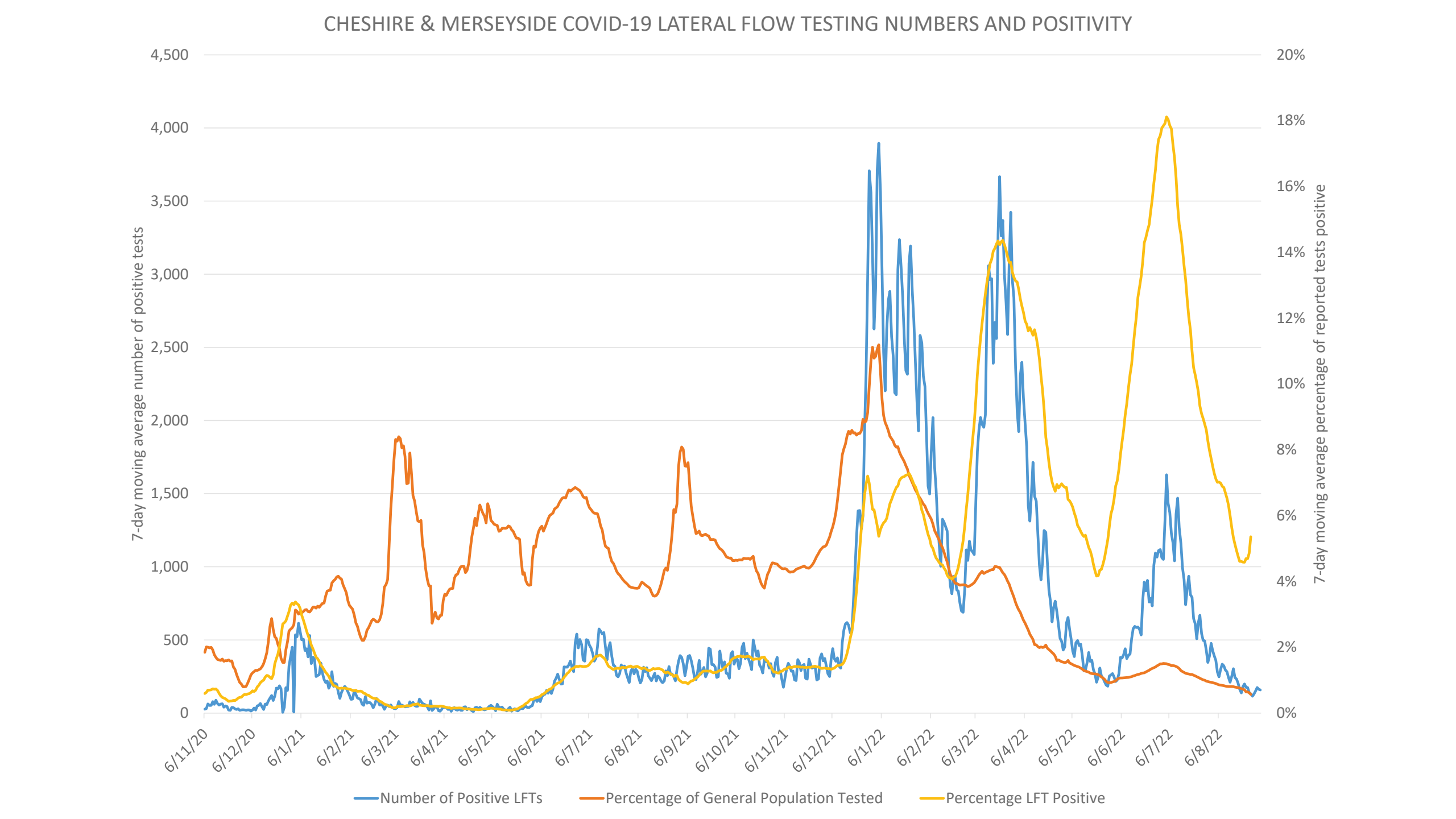
- Staffing crisis subsided from Feb 22
  - Policy change; decline of first Omicron wave; ?burnout rebound from end of year break

- SMART Release & Return study proceeded in Feb 22
  - Ready to run in Jan 21 but approvals took 6 weeks
  - Policy questions remained over value of dual lateral flow device testing and culturability from serial positive lateral flow subjects beyond day 7


CHESHIRE & MERSEYSIDE COVID TESTING: NHS STAFFING PRESSURES
ALPHA...
DELTA...
OMICRON...
Number of positive test results registered for Cheshire & Merseyside residents
Number of NHS Cheshire & Merseyside staff absent
14000
12000
10000
8000
6000
4000
2000
0
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
6/11/20
6/12/20
6/1/21
6/2/21
6/3/21
6/4/21
6/5/21
6/6/21
6/7/21
6/8/21
6/9/21
6/10/21
6/11/21
6/12/21
6/1/22
6/2/22
6/3/22
6/4/22
6/5/22
6/6/22
6/7/22
6/8/22
Positive lateral flow
Positive PCR
NHS staff absent


CHESHIRE & MERSEYSIDE COVID TESTING: ACUTE BED PRESSURES
ALPHA...
DELTA...
OMICRON...
Number of positive test results registered for Cheshire & Merseyside residents
Number of beds in Cheshire & Merseyside NHS
14000
12000
10000
8000
6000
4000
2000
0
7000
6000
5000
4000
3000
2000
1000
0
6/11/20
6/12/20
6/1/21
6/2/21
6/3/21
6/4/21
6/5/21
6/6/21
6/7/21
6/8/21
6/9/21
6/10/21
6/11/21
6/12/21
6/1/22
6/2/22
6/3/22
6/4/22
6/5/22
6/6/22
6/7/22
6/8/22
Positive lateral flow
Positive PCR
Covid beds
Non-Covid beds
Unoccupied beds


CHESHIRE & MERSEYSIDE COVID-SMART COMMUNITY TESTING 7-DAY MOVING AVERAGES
ALPHA...
DELTA...
OMICRON...
7 day moving average percentage of population
7 day movnig average percentage of tests
18.0%
16.0%
14.0%
12.0%
10.0%
8.0%
6.0%
4.0%
2.0%
0.0%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
12/11/20
12/12/20
12/1/21
12/2/21
12/3/21
12/4/21
12/5/21
12/6/21
12/7/21
12/8/21
12/9/21
12/10/21
12/11/21
12/12/21
12/1/22
12/2/22
12/3/22
12/4/22
% population tested
% population testing positive
% cases identified by lateral flow


CHESHIRE & MERSEYSIDE COVID-19 LATERAL FLOW TESTING NUMBERS AND POSITIVITY
7-day moving average number of positive tests
7-day moving average percentage of reported tests positive
4,500
4,000
3,500
3,000
2,500
2,000
1,500
1,000
500
0
20%
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
6/11/20
6/12/20
6/1/21
6/2/21
6/3/21
6/4/21
6/5/21
6/6/21
6/7/21
6/8/21
6/9/21
6/10/21
6/11/21
6/12/21
6/1/22
6/2/22
6/3/22
6/4/22
6/5/22
6/6/22
6/7/22
6/8/22
Number of Positive LFTs
Percentage of General Population Tested
Percentage LFT Positive

# SMART Release & Return Study

- New concern in Jan 22 over potential Omicron tropism reducing detection from nose-only c.f. nose and throat swabbing
- Effects on detection and usability from combining different manufacturers' lateral flow kits unknown
- Transmission risk from 'long shedders' (serial positive lateral flow test subjects beyond day ~5) unknown
- Study protocol approved by TIEB in Jan 22
- Recruitment after further approval starts in Feb 22

# Recruitment

- Liverpool University Hospitals NHS Foundation Trust agreed in Dec 21 to recruit staff from two hubs set up for swabbing for PCR testing of contacts and possible cases

- Recruitment began fully at the end of Feb 22, after decline of first Omicron wave

- Policy changes successively removed requirements for staff testing: around half of cases participated in Mar-Apr 22

Liverpool University Hospitals
NHS Foundation Trust

# COVID-SMART NHS Staff Testing

## Participant information

*IRAS Project ID: 311842*

LIVING OUR VALUES

CARING FAIR INNOVATIVE

## Journey for participant who becomes positive or enters as a case

**Day 0**
- Staff member becomes positive
- Feels well enough to work
- Consent to study
- Pick up 20+2 Multi-pack

**Days 1-4**
- Q-RT-PCR at home
- 2 (random order) LFTs any results
- Stay at home

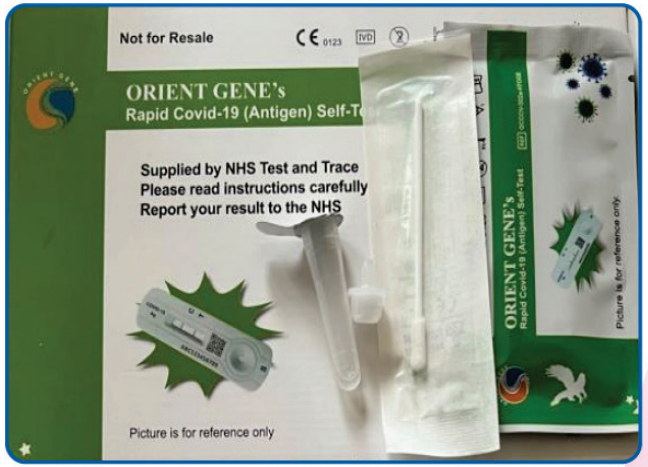
**Day 5**
- Q-RT-PCR at home
- 2 (random order) LFTs both negative
- Stay at home

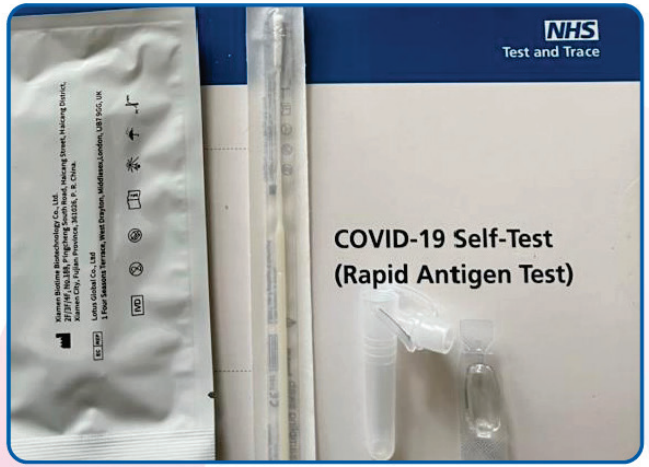
**Days 6**
- 2 (random order) LFTs both negative
- Proceed to work

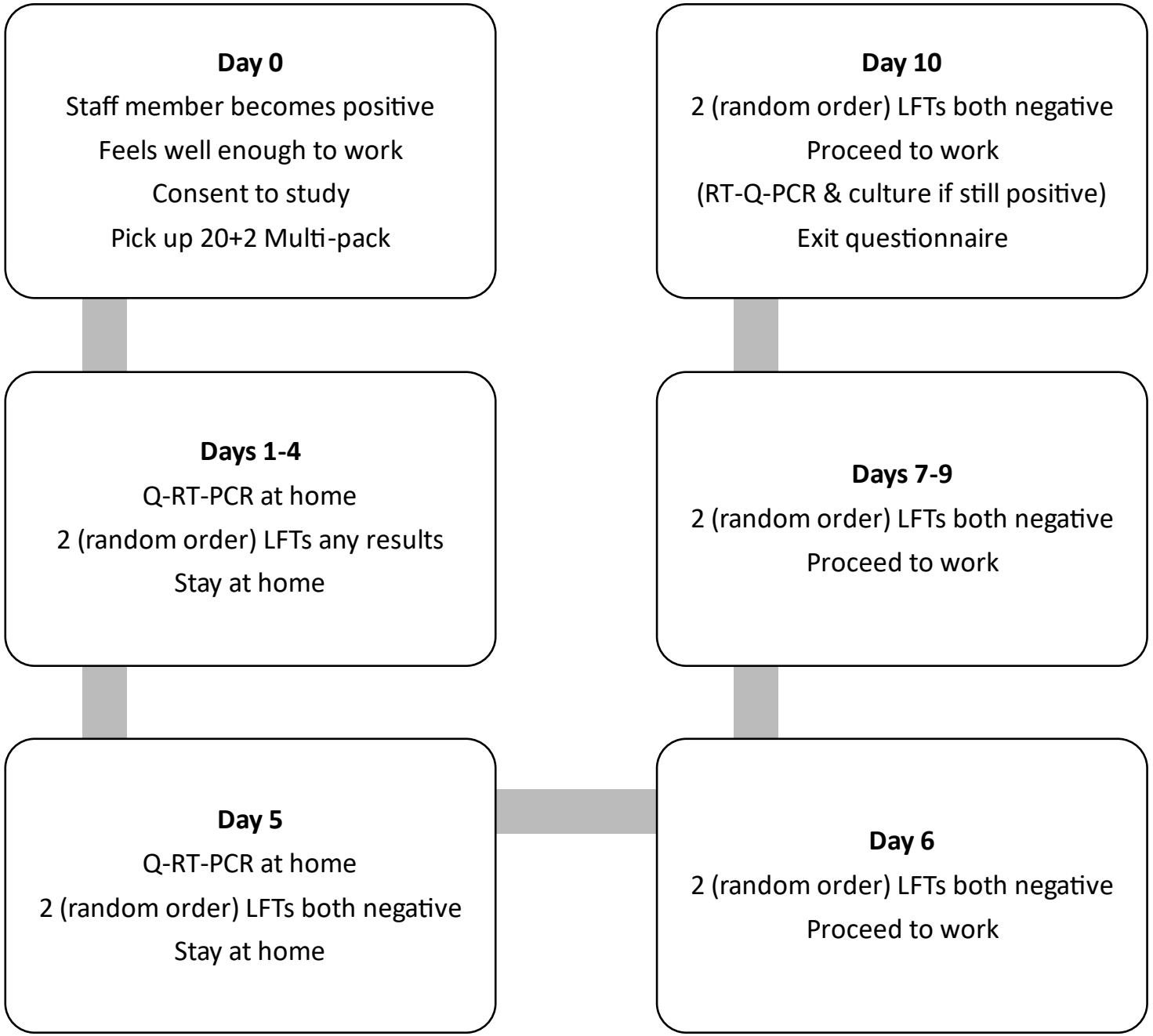
**Days 7-9**
- 2 (random order) LFTs both negative
- Proceed to work

**Day 10**
- 2 (random order) LFTs both negative
- Proceed to work
- (RT-Q-PCR & Culture if still positive)
- Exit questionnaire

The test kits in your pack will look like the ones below and will be labelled Test A or Test B on the box. The daily instruction sheet in your pack will tell you which order to take two tests on each day – some days that will be Test A first and other days it will be Test B first:



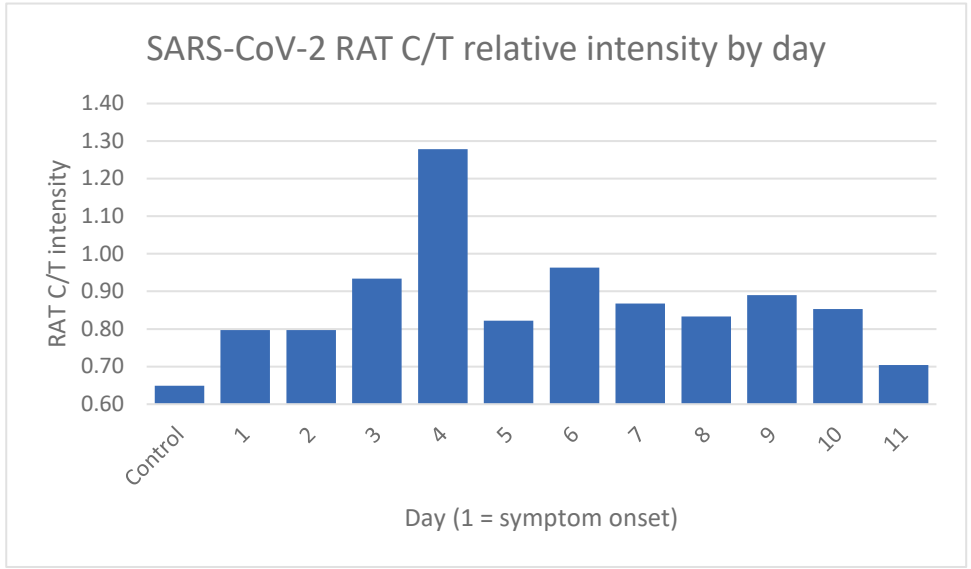





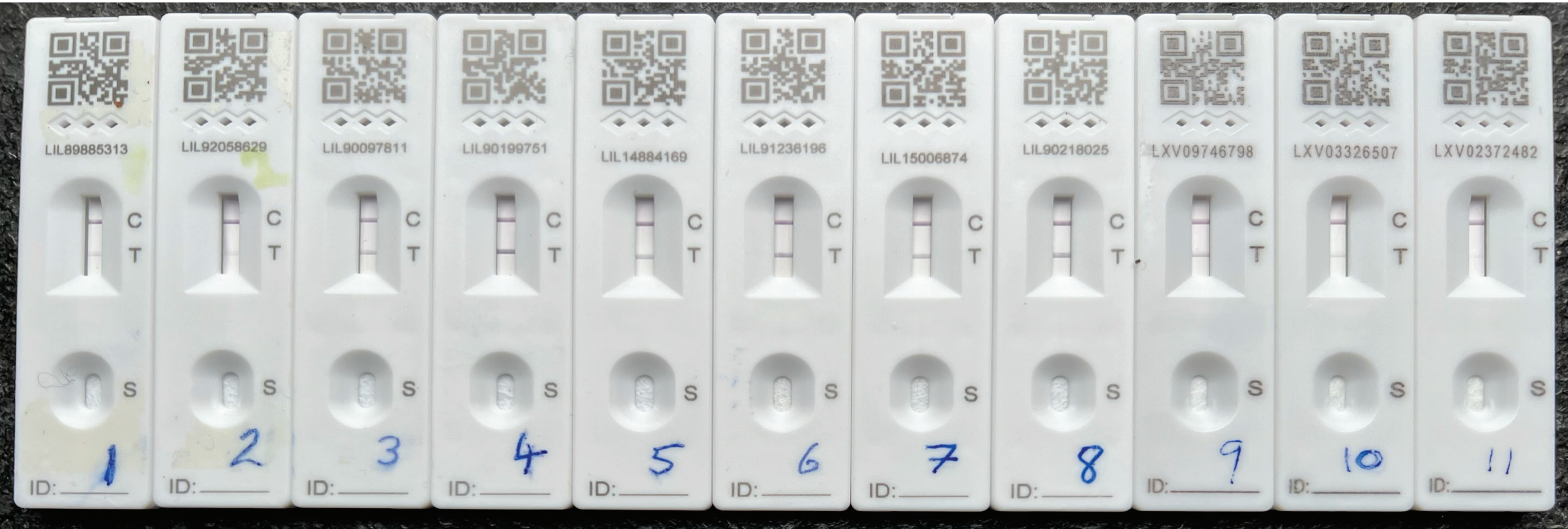

Typical recruit was a symptomatic case or asymptomatic contact who had become aware of status from universal access home testing

Participation with daily dual testing protocol was only practical among cases

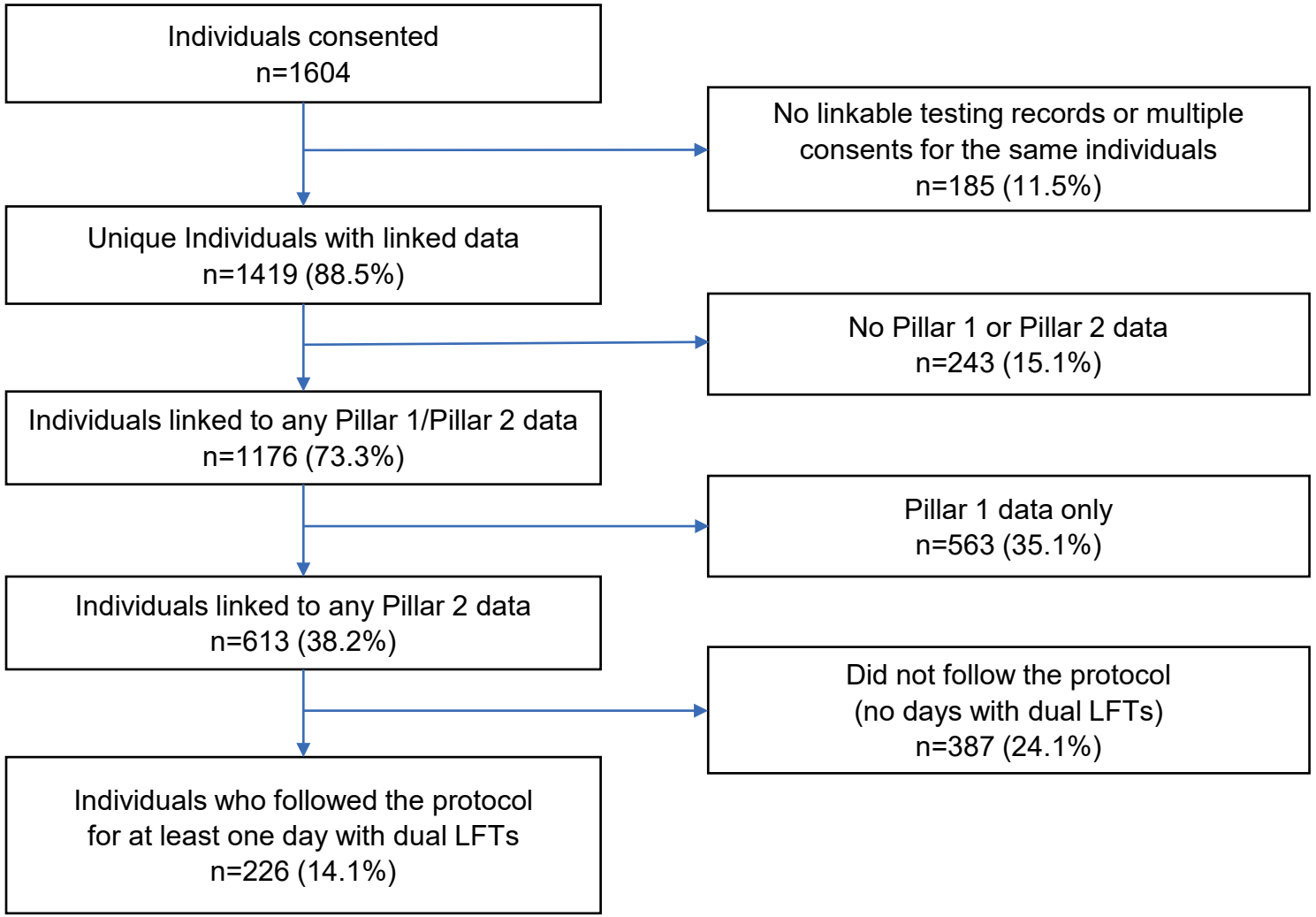
Subject: I. Buchan
22/2/22 – 3/3/22




Acculturation of self-testing of Omicron trajectories among the general public and commonly on social media



# Data yield and cleaning

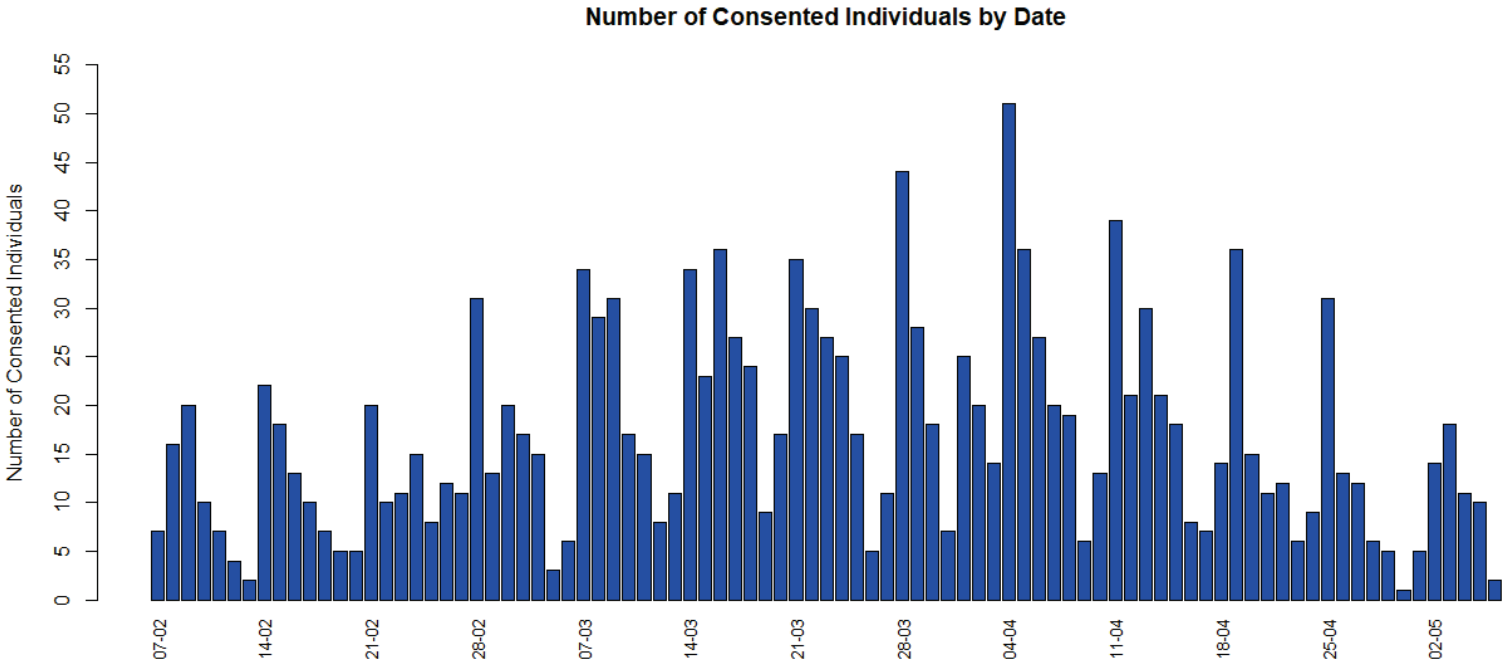



Low uptake and compliance with compared with previous community based studies

Concurrent with low NHS staff morale and multiple changes to testing policies nationally

Concurrent with reduced easy access to lateral flow test kits from community sources

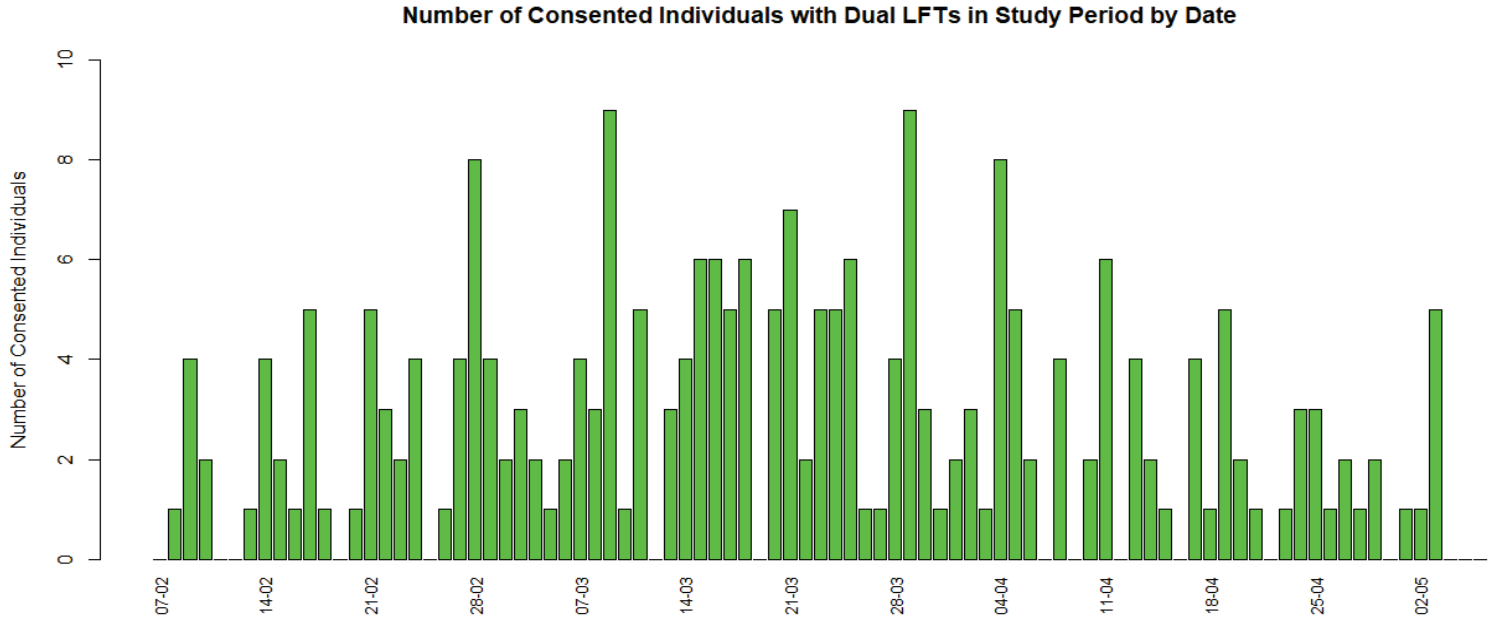
Sufficient data collected for internally controlled comparisons of dual swabbing and device results




Sponsor permission to proceed 4 Feb 22

Two swab hubs started recruiting 7 Feb 22

Storm damage took one hub out on 19 Feb 22




Lower returns of dual LFT results in Apr 22 with falling numbers and national policies moving away from testing

# Discordance in LFD results overall

Data captured from Pillar 2 test dataflows:

Total number of days with exactly two lateral flow device (LFD) results (one Orient Gene and one Innova) = 1488

Orient Gene involves a nose only swab, whereas Innova is a nose plus throat swab

Number of unique individuals with at least one day with exactly 2 LFD tests (one Orient Gene and one Innova) = 226

**Total disagreements between Orient Gene and Innova LFD results** = (49+79) = 128 (**8.6%**)

**Difference** between Orient Gene and Innova discordance = **2% (0.05% to 3.5%)**: **Orient Gene more likely to be positive**

| | | Innova | | | |
|---|---|---|---|---|---|
| | | Negative | Positive | Equivocal | TOTAL |
| Orient Gene | Negative | 602 (39.4%) | 49 (**3.2%**) | 3 (0.2%) | 654 |
| | Positive | 79 (**5.2%**) | 752 (49.2%) | 1 (0.1%) | 832 |
| | Equivocal | 2 (0.1%) | 0 (0.0%) | 0 (0.0%) | 2 |
| | TOTAL | 683 | 801 | 4 | 1488 (100%) |

# Discordance in LFD order

Discordance of Orient Gene and Innova LFD test results when **Orient Gene** test is **recorded first**

| | | Innova | | | |
|---|---|---|---|---|---|
| | | Negative | Positive | Equivocal | TOTAL |
| Orient Gene | Negative | 309 (40.1%) | 18 (**2.3%**) | 1 (0.1%) | 328 |
| | Positive | 48 (**6.2%**) | 393 (51.0%) | 0 (0%) | 441 |
| | Equivocal | 2 (0.3%) | 0 (0%) | 0 (0%) | 2 |
| | TOTAL | 359 | 411 | 1 | 771 (100%) |

**3.9% (1.8 to 6.0) more likely Orient Gene than Innova to be positive if the other is negative and Orient Gene swab was take first**

Discordance of Orient Gene and Innova LFD test results when **Innova** test is **recorded first**

| | | Innova | | | |
|---|---|---|---|---|---|
| | | Negative | Positive | Equivocal | TOTAL |
| Orient Gene | Negative | 293 (40.9%) | 31 (**4.3%**) | 2 (0.3%) | 326 |
| | Positive | 31 (**4.3%**) | 359 (50.1%) | 1 (0.1%) | 391 |
| | TOTAL | 324 | 390 | 3 | 717 (100%) |

**No significant difference between LFD type proportions discordant when Innova taken first**

# Discordance by day since presenting

Overall test disagreements (positive/negative only) by period since presenting for testing

| Orient Gene (Innova) Results | Days 1-3 | Days 4-6 | Days 7+ | Total |
|---|---|---|---|---|
| Positive (Negative) | 11 (2.1%) | 25 (5.3%) | 43 (8.9%) | 79 |
| Negative (Positive) | 15 (2.9%) | 15 (3.2%) | 19 (3.9%) | 49 |
| Concordant | 499 (95.0%) | 432 (91.5%) | 423 (87.2%) | 1354 |
| Total | 525 | 472 | 485 | 1482 |

$Chi^2$ trend = 23.3  $P < 0.0001$

$Chi^2$ trend = 1.1  $P = 0.25$

Overall test disagreements (positive/negative only) by day since first recorded positive test

| Orient Gene (Innova) Results | Days 0-3 | Days 4-6 | Days 7+ | Total |
|---|---|---|---|---|
| Positive (Negative) | 16 (3.5%) | 26 (6.9%) | 37 (11.7%) | 79 |
| Negative (Positive) | 20 (4.3%) | 14 (3.7%) | 15 (4.7%) | 49 |
| Concordant | 424 (92.2%) | 336 (89.4%) | 265 (83.6%) | 1025 |
| Total | 460 | 376 | 317 | 1153 |

$Chi^2$ trend = 16.9  $P = < .0001$

$Chi^2$ trend = 0.03  $P = 0.85$

**Orient Gene positive + Innova negative tended to occur more with longer time from presenting for testing**

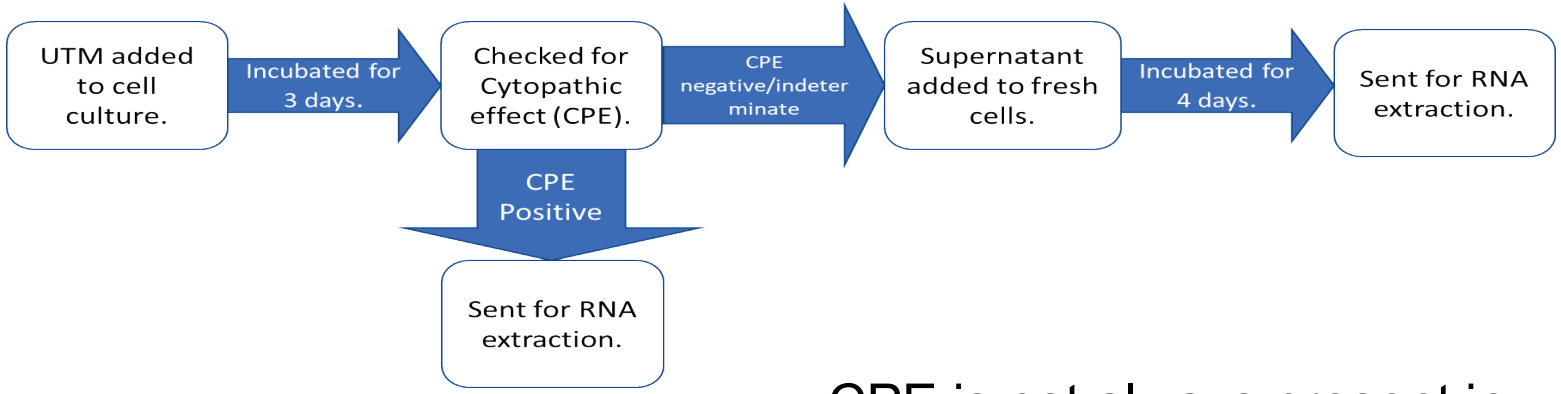
**Innova positive + Orient Gene negative showed no significant time trend in occurrence**

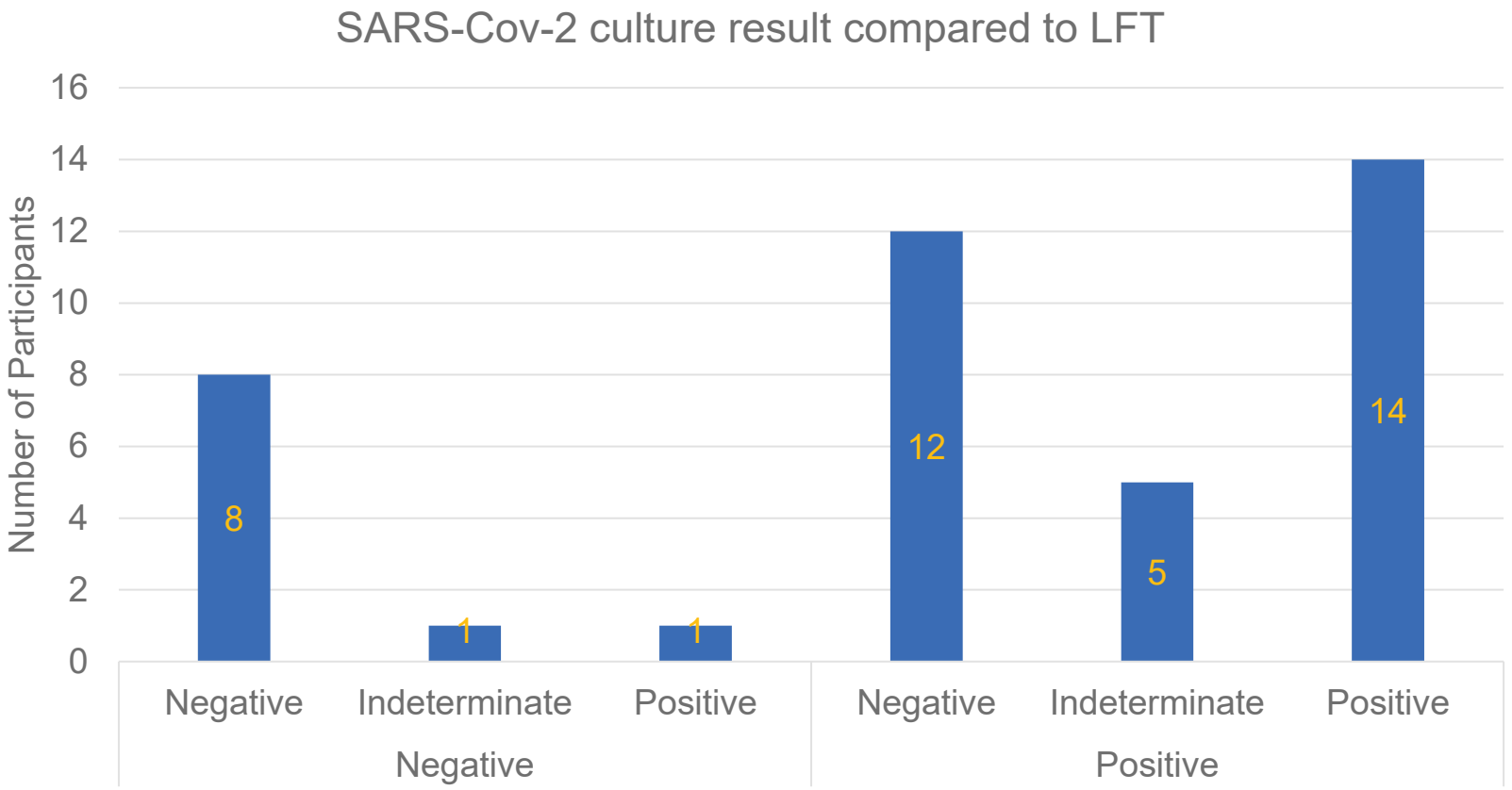
# Cultures among week-long shedders

- A sample of 41 participants had swabs taken for culture
- 31 came from those still testing LFT positive at day 5-7
- 10 came from those testing LFT negative at day 5-7

THE PANDEMIC INSTITUTE

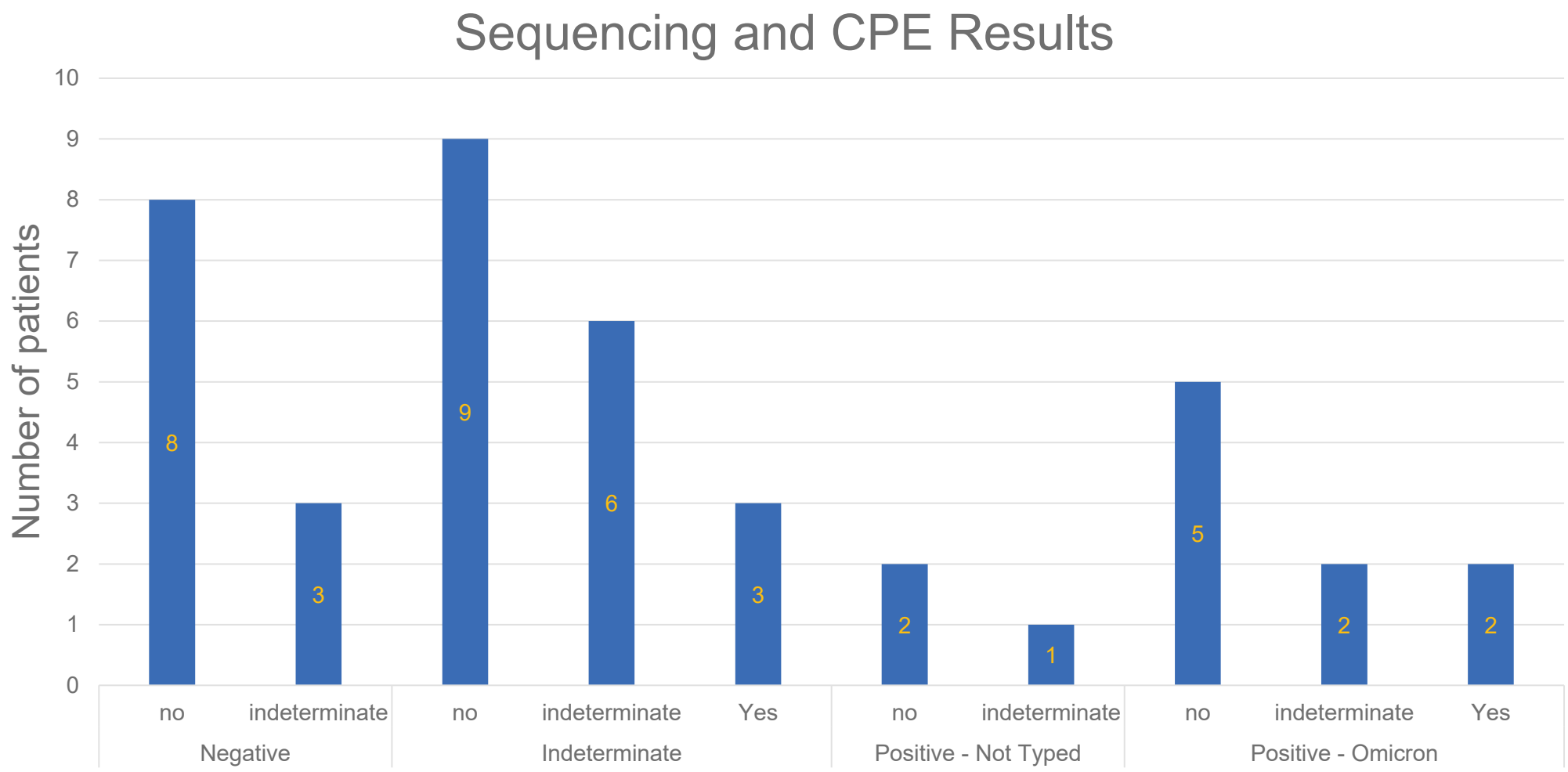
# Viral culture



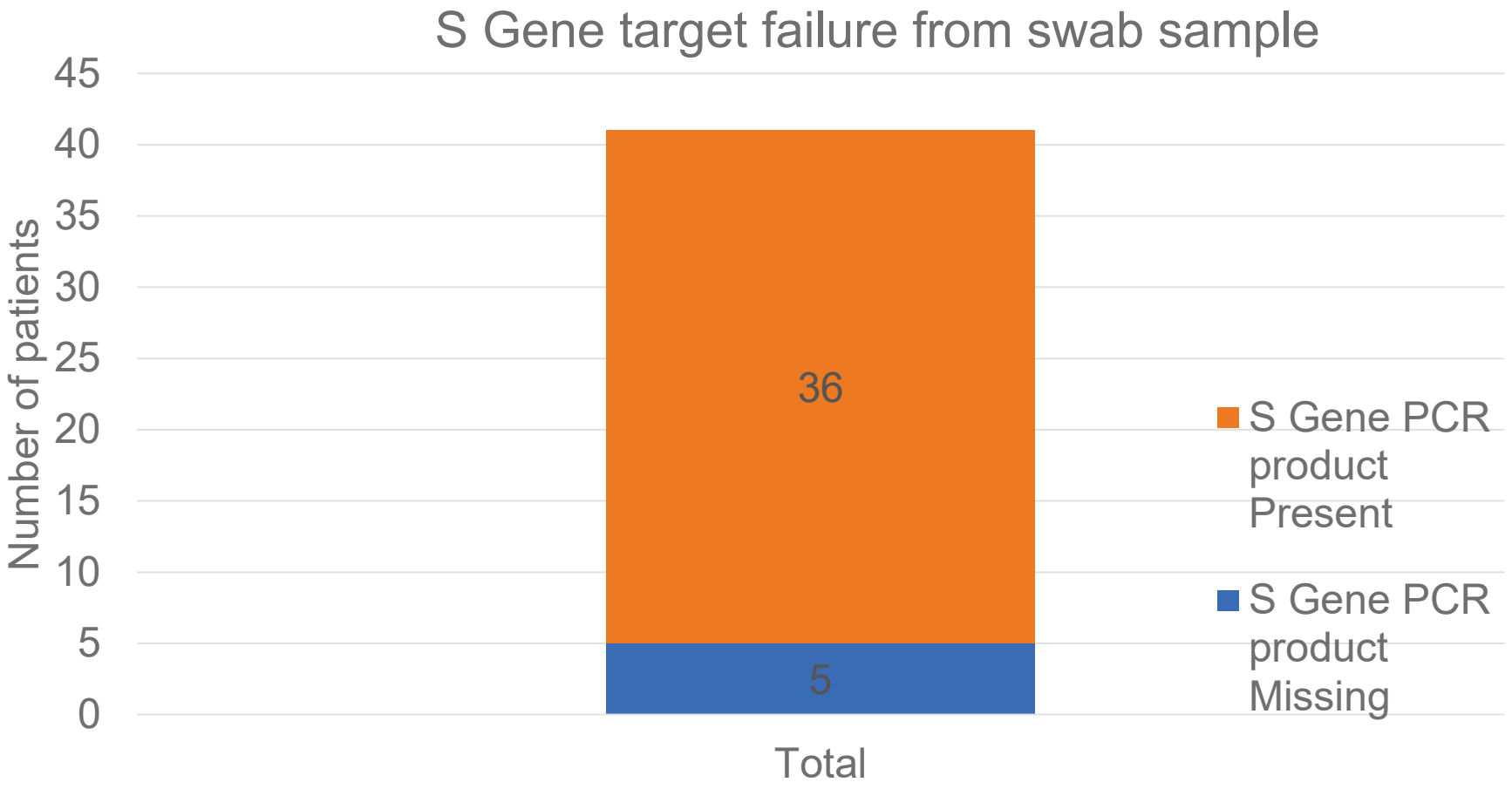




- CPE is not always present in viral cultures, especially with the omicron variant. Absence of classical CPE signs does not necessarily mean no virus is present.
- Cultures were therefore considered positive if either some evidence of SARS-CoV-2 was identified by sequencing, and CPE was present, or if SARS-CoV-2 sequence was unequivocally identified and CPE was present

# Culture RNA sequencing




- The indeterminate results are due to insufficient RNA when sequencing
- Omicron is the variant detected most which is to be expected given its prevalence at the time of sampling



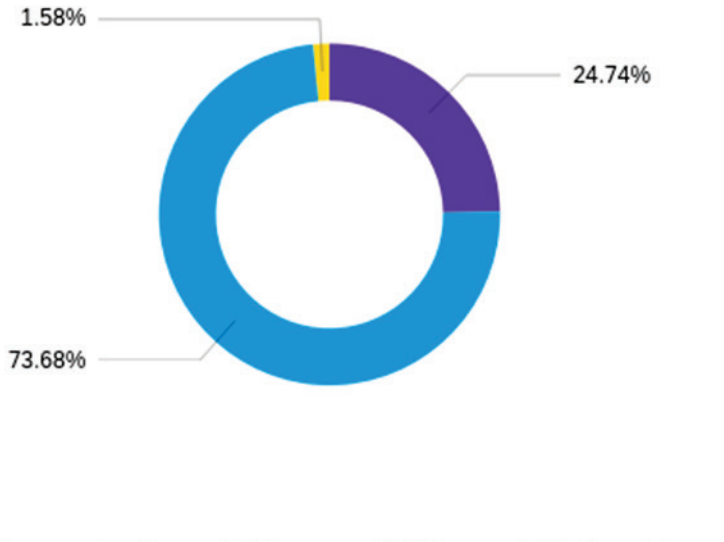

- PCR was carried out on original swab aliquots
- Every sample came back positive for SARS-CoV-2
- S gene drop out shows the presence of at least 2 variants with the sampled population:
  - S gene target negatives likely omicron BA.1
  - S gene target positives likely omicron BA.2

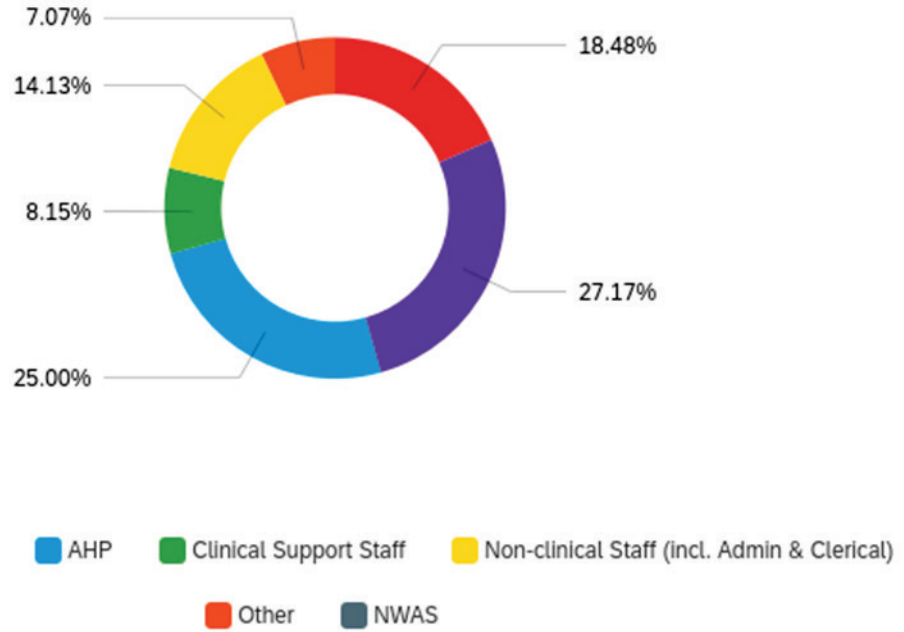
# Lessons learnt in culture sub-study

- Collection of additional material (another swab) would have allowed more work to be carried out in parallel while still having material to return to for any re-runs
- More detailed laboratory work such as diagnostic PCR tests and sequencing on swab samples, would allow us greater confidence that any isolates were SARS-CoV-2 and not another virus
- Overall excellent collaboration and communication between many different departments, including Liverpool NHS Trust and University of Liverpool
- Rapid pace of set up – Swab collection kits were quickly made and dispersed to participants for sample collection

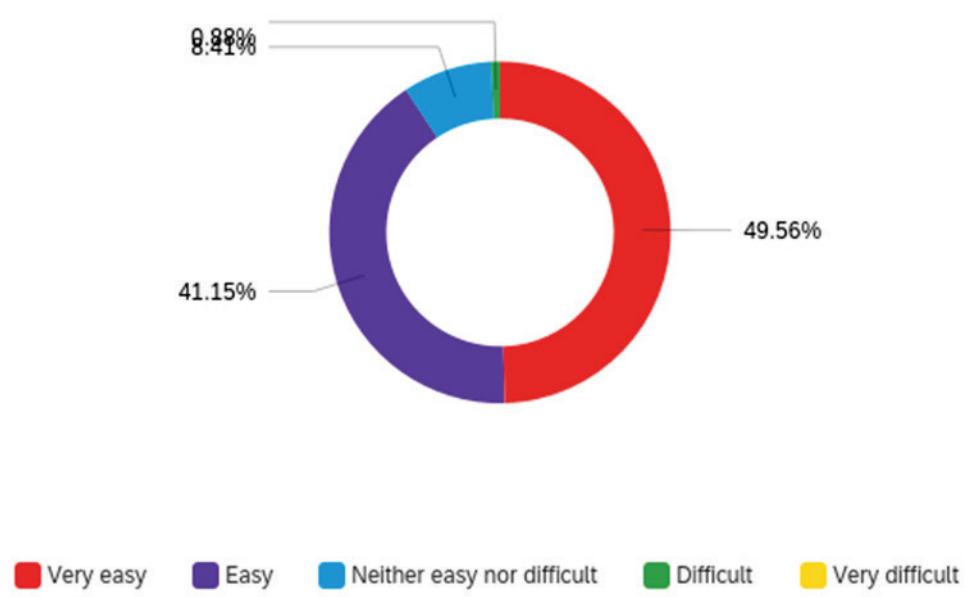
# Exit survey of participants on Day 10

- Total: 311 responses (10th February – 20th July 2022)
  - Three quarters female
  - Wide variety of roles within an NHS acute hospital trust



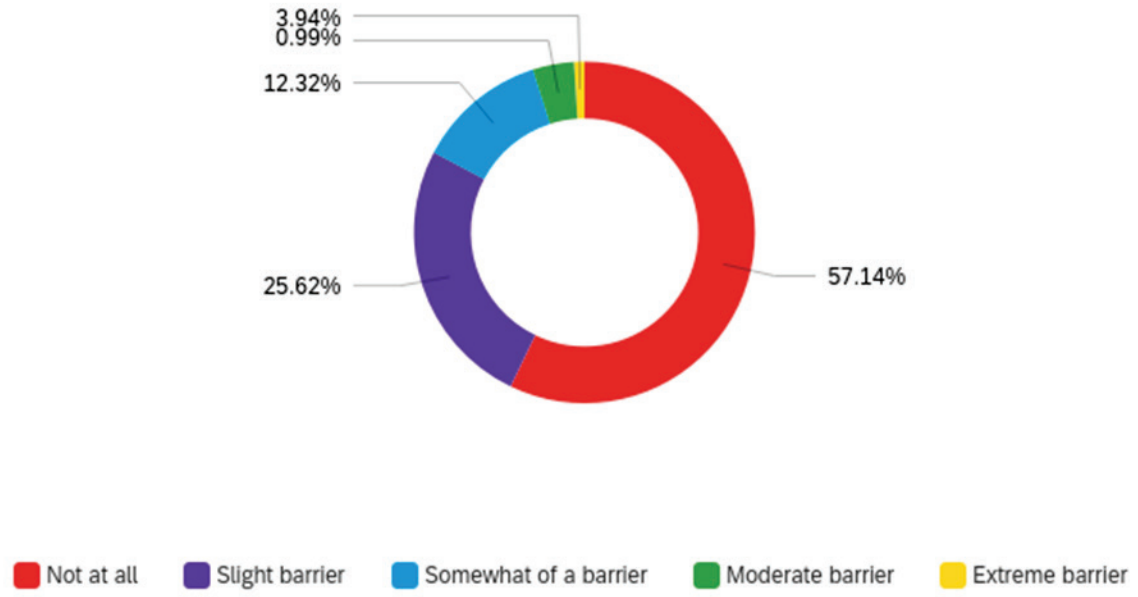



When asked to report on the ease of the swabbing process, nearly 90% participants stated that it was easy.



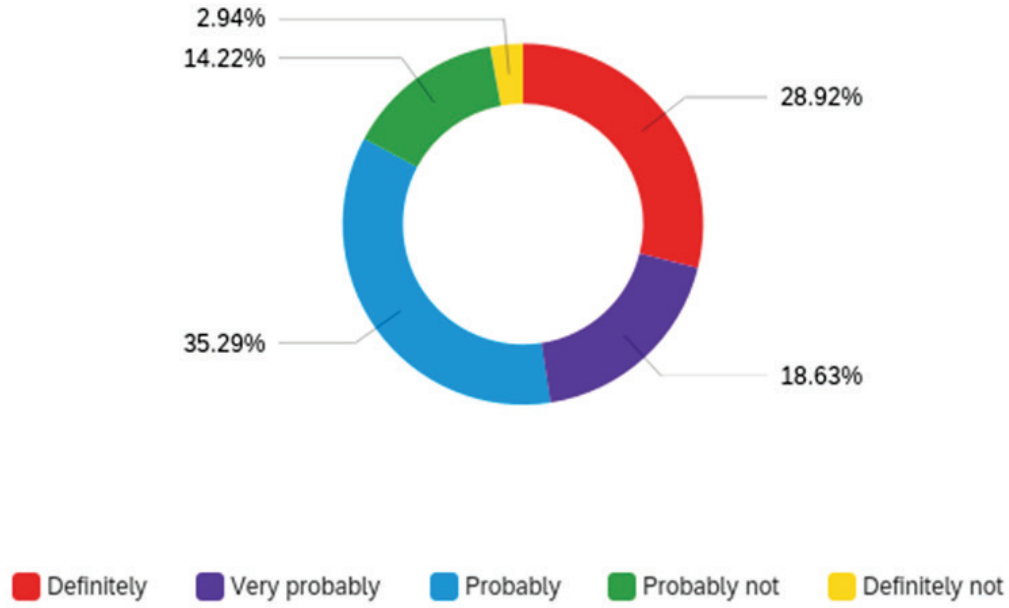

*How easy was the swabbing process?*

Over 57% of participants stated that the two-testing process represented no barrier to their daily routine, with 38% reporting it as some form of barrier:



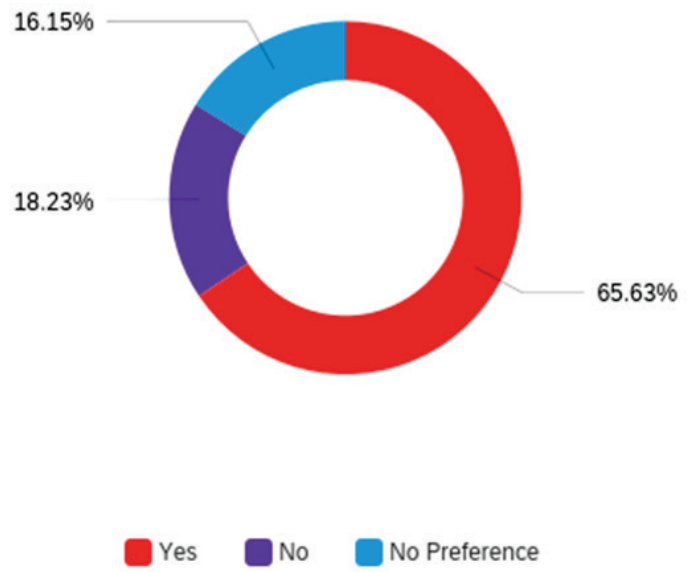

*How much of a barrier is having to take a throat as well as a nose swab for your daily rapid test?*

Asked to consider how testing requirements could fit into their daily routine, 29% of participants stated that they were definitely and 54% that they can probably fit two tests in within an hour of leaving for work.



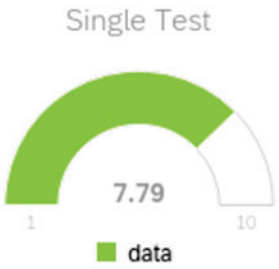

*Could you fit taking two rapid tests into your daily routine within an hour of leaving for work?*

Considering the potential requirement of carrying out two daily tests, 67% stated that they would do so and 16% noted no preference, against the remaining 18% reporting that they would not do so.



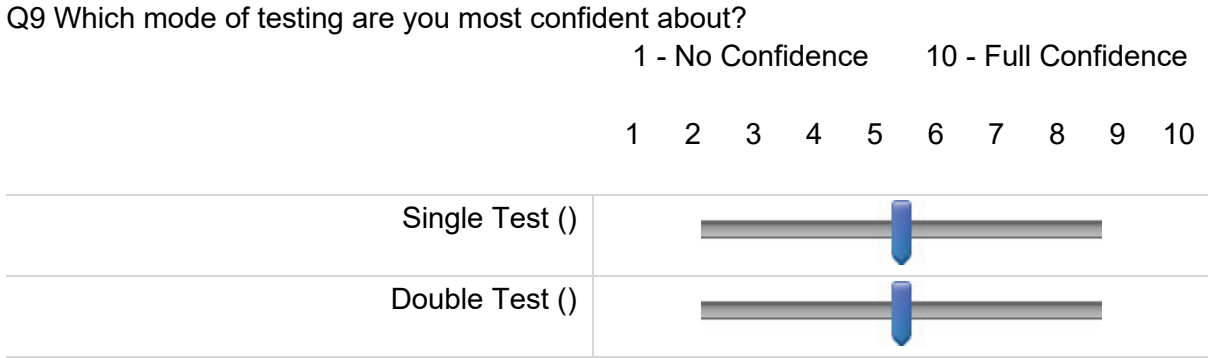

*If you were asked to continue to do two tests daily instead of one, would you?*

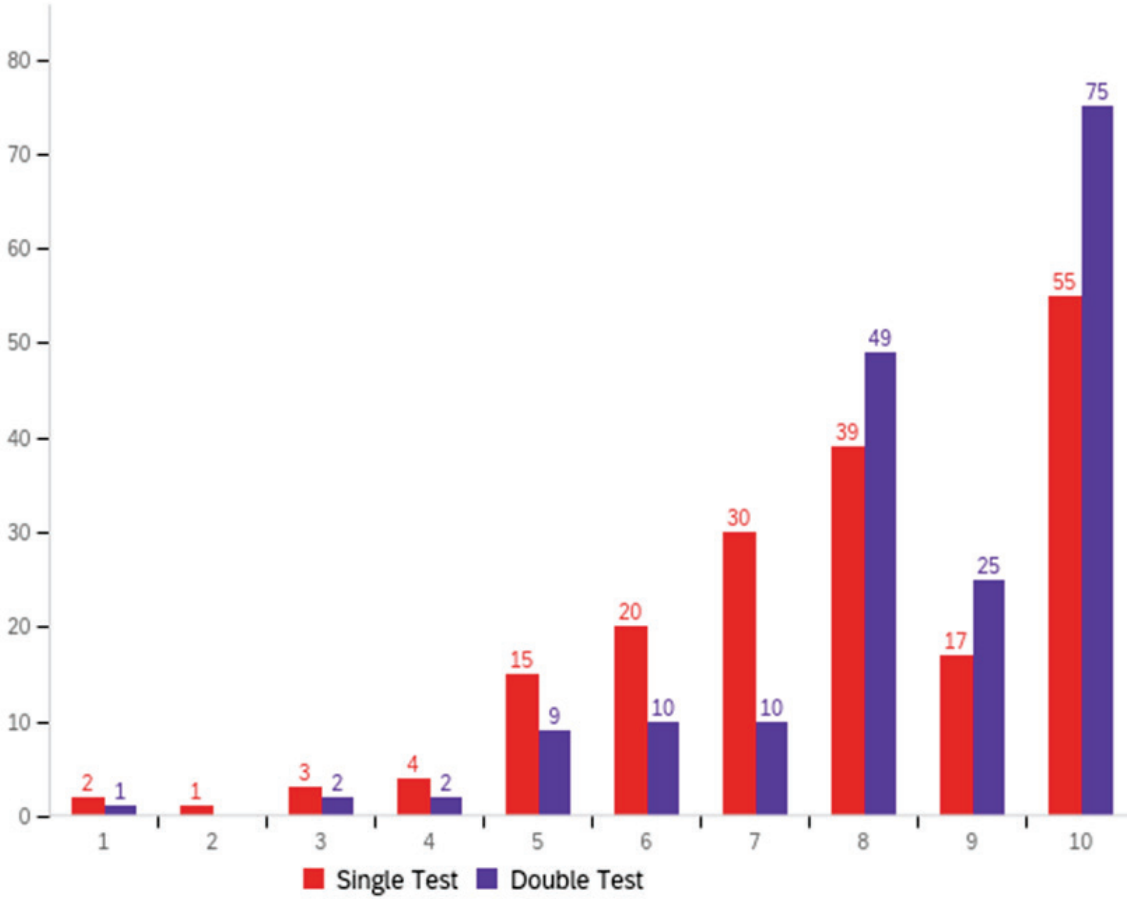
When asked about their confidence rating for each mode of testing, participants reported a higher level of confidence for the double testing (8.51) against the single test (7.79), although not at a significant margin:





This is further reflected in the distribution of confidence scores (1 – No Confidence to 10 – Full Confidence) with more of the difference driven by higher confidence levels:



# Conclusions

- Policymaker concern over nose only swabbing potentially missing a substantial proportion of Omicron cases was not supported, at least in the UK Feb-Apr 22 among NHS workers
- Orient-gene was more sensitive than the Innova device in terms of swab order in discordant results, and in later days of serial positive tests
- Almost two thirds of LFT positives at day 5-7 were culture +ve or intermediate
- Randomised order of testing and TIEB feedback on protocol was useful
- Longest delay to insight was due to approvals, for conventional research in an unconventional urgent public health context

# Further report and questions

This work will be reported in a manuscript that is in preparation.

Data and laboratory results are undergoing final checks.

If you have any questions, please do not hesitate to contact:

buchan@liverpool.ac.uk