CURIAL

Rapid screening for Covid-19 in Emergency Departments

NHS
Oxford University Hospitals
NHS Foundation Trust

UNIVERSITY OF OXFORD

Hospitals are struggling with Covid Testing

Patient Journey

- Arrive at hospital
- Routine clinical data
  vital signs & blood tests at front door (results 1h)
- PCR swab test ←
  (+/- Lateral Flow test)

Intermediate Precautions

1-2x / week

- Transfer to ward

8-24 hours

Time from arriving in hospital to PCR result

£50 Cost of each PCR test
(Excluding. PPE/staff time)

Swabbing uncomfortable
Nursing time & PPE
Difficulty allocating beds
Emergency care delayed
Strain on emergency departments
Missed COVID-19 cases

Rapid Antigen Testing

The OUH experience:

43 missed cases per 100

s

U.S. FOOD & DRUG ADMINISTRATION

Search | Menu

Home / Medical Devices / Medical Device Safety / Safety Communications / Stop Using Innova Medical Group SARS-CoV-2 Antigen Rapid Qualitative Test: FDA Safety Communication

Stop Using Innova Medical Group SARS-CoV-2 Antigen Rapid Qualitative Test: FDA Safety Communication

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Safety Communications

2021 Safety Communications

2020 Safety Communications

2019 Safety Communications

Date Issued: June 10, 2021

The U.S. Food and Drug Administration (FDA) is warning the public to stop using the Innova Medical Group SARS-CoV-2 Antigen Rapid Qualitative Test for diagnostic use. The FDA has significant concerns that the performance of the test has not been adequately established, presenting a risk to health. In addition, labeling distributed with certain configurations of the test includes performance claims that did not accurately reflect the performance estimates observed during the clinical studies of the tests. Finally, the test has not been authorized, cleared, or approved by the FDA for commercial distribution or use in the United States, as required by law.

Content current as of:
06/10/2021

Regulated Product(s)
Medical Devices

Health Topic(s)
Coronavirus

– Mar 2021

Sohan et al 2022, Lancet Digital Health

CURIAL

>$105bn

Total Global COVID-19 Testing Market

£1.06 bn UK NHS hospital inpatient only

$7.4 bn USA hospital inpatient market

Estimated NHS Savings

155,000 acute NHS hospital beds
~96-100% bed occupancy @ 6 day mean length of stay

Typical testing:
PCR + LFT on admission + 1-2x/PCR week = **£131/bed/week**

= 155,000 beds x 1.0 occupancy x £200 testing/week x 52 weeks
= ~£1.06bn annual UK COVID-19 inpatient testing

NHS
Oxford University Hospitals
NHS Foundation Trust

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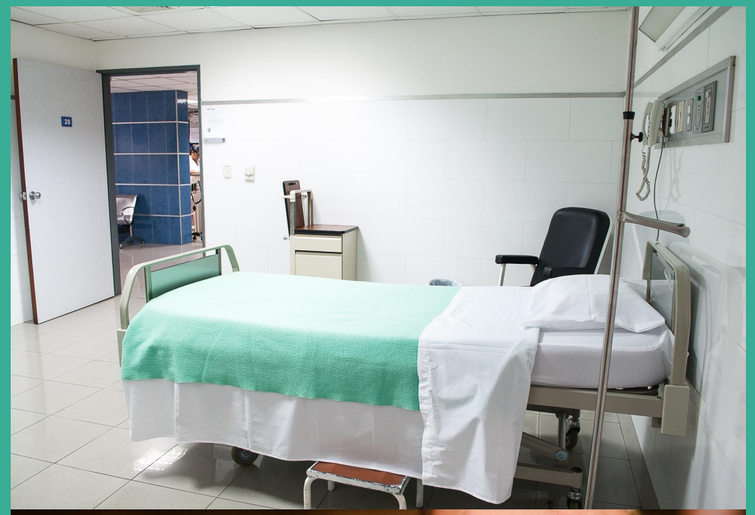
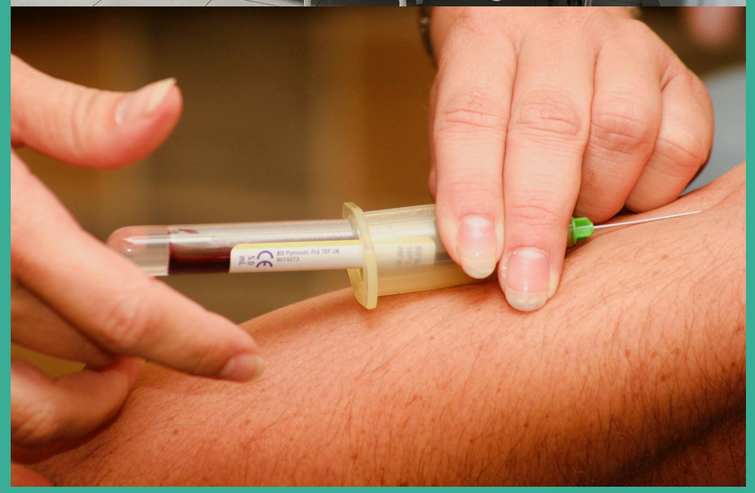
A high-confidence test of exclusion is needed

With results in minutes…

Feb 2020:
Can we use routinely collected data in Emergency Depts to predict who will test positive for COVID-19?



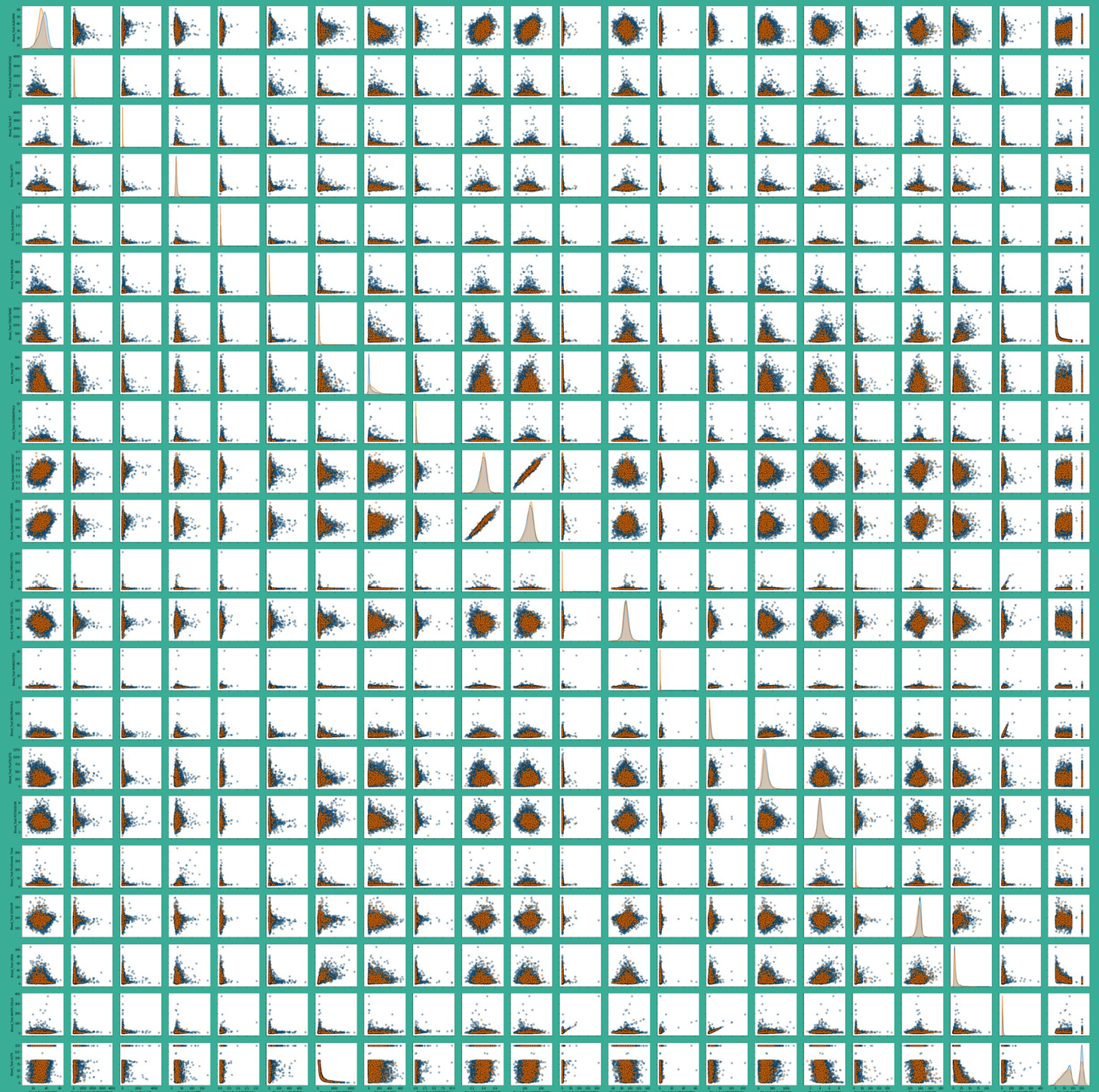


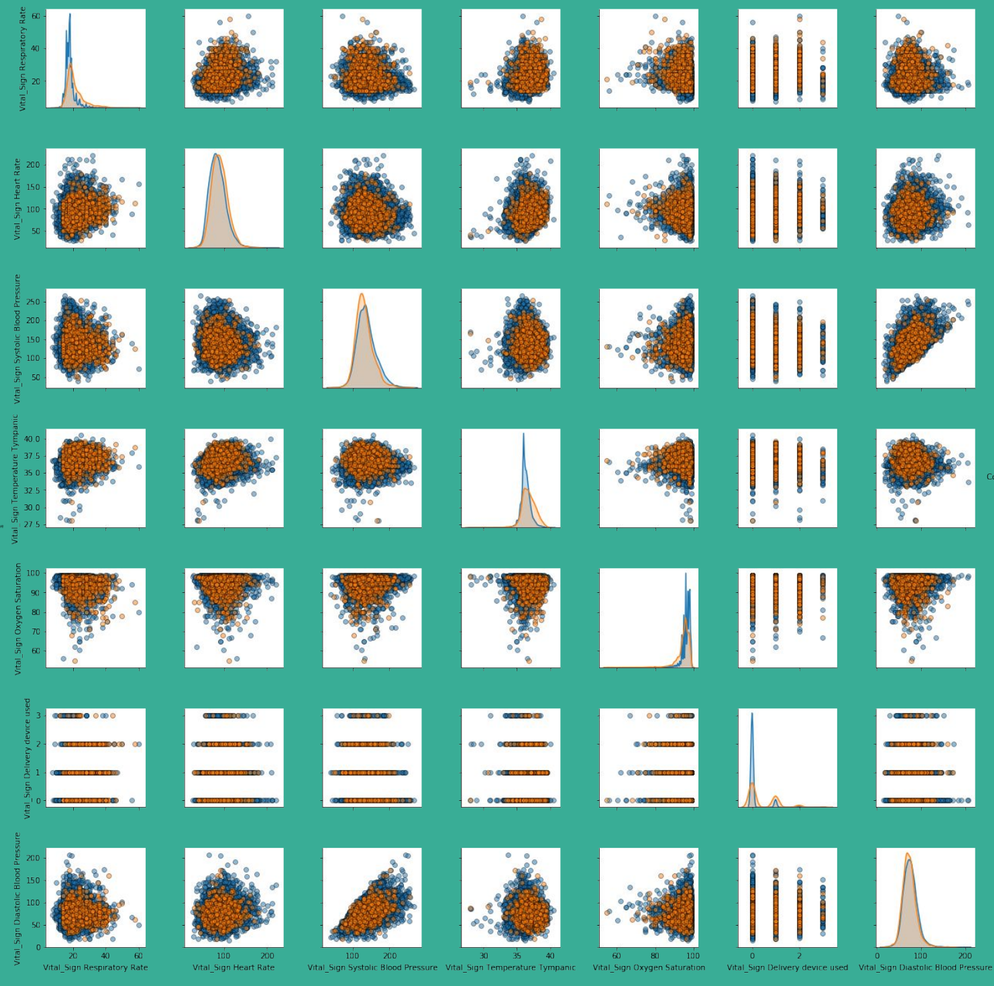
Patient arrives in emergency department

Routine data collected within existing pathways – vital signs, routine bloods

Blood tests & vital signs already available within 1h of arrival (10 mins with point-of-care)

CURIAL




Vital_Sign Respiratory Rate
Vital_Sign Heart Rate
Vital_Sign Systolic Blood Pressure
Vital_Sign Temperature Tympanic
Vital_Sign Oxygen Saturation
Vital_Sign Delivery device used
Vital_Sign Diastolic Blood Pressure
Covid-19 Positive
0.0
1.0

	Independent feature sets				Sets routinely performed on presentation			Sets integrating previous health data	
	Presentation blood tests	Blood gas results	Vital signs	Δ blood tests	Presentation blood tests	Presentation blood tests plus blood gas results	Presentation blood tests plus blood gas results plus vital signs	Sets performed on presentation plus Δ blood tests	Sets performed on presentation plus Δ blood tests plus CCI
Logistic regression	0·897 (0·003)	0·730 (0·001)	0·810 (0·003)	0·805 (0·008)	0·897 (0·003)	0·898 (0·003)	0·919 (0·002)	0·920 (0·004)	0·920 (0·004)
Random forest	0·901 (0·004)	0·780 (0·000)	0·815 (0·005)	0·835 (0·006)	0·901 (0·004)	0·907 (0·003)	0·922 (0·002)	0·941 (0·004)	0·937 (0·002)
XGBoost	0·904 (0·000)	0·770 (0·000)	0·823 (0·005)	0·808 (0·050)	0·904 (0·000)	0·916 (0·003)	0·929 (0·003)	0·942 (0·002)	0·942 (0·002)

Data are AUROC (SD). Δ=change in results from baseline. AUROC=area under the receiver operating characteristic curve. CCI=Charlson comorbidity index.

Table 3: **AUROCs achieved for each independent feature set and for increasing feature sets using stratified 10-fold cross-validation during training**

Soltan et al 2020, Lancet Digital Health

Timeline

CURIAL

March 2020:
Emergency NHS HRA approval for CURIAL programme

NHS Partnerships begin

April-May 2020:
Prospective evaluation of CURIAL at Oxford University Hospitals

April 2020:
Data sharing Partnership with **Oxford University Hospitals NHS Trust**

NHS Oxford University Hospitals NHS Foundation Trust

July 2020:
First publication showing development and efficacy of CURIAL algorithm

August 2020:
Awarded £82,000 non-dilutory funding

August 2020:
Partnership with **University Hospitals Birmingham NHS Foundation Trust**

NHS University Hospitals Birmingham NHS Foundation Trust

NHS Portsmouth Hospitals University NHS Trust

September 2020:
Partnership with **Portsmouth Hospitals University NHS Trust**

March 2021:
Partnership with **Bedfordshire Hospitals NHS Foundation Trust**

NHS Bedfordshire Hospitals NHS Foundation Trust

THE LANCET Digital Health

December 2020:
CURIAL paper published in **The Lancet Digital Health**

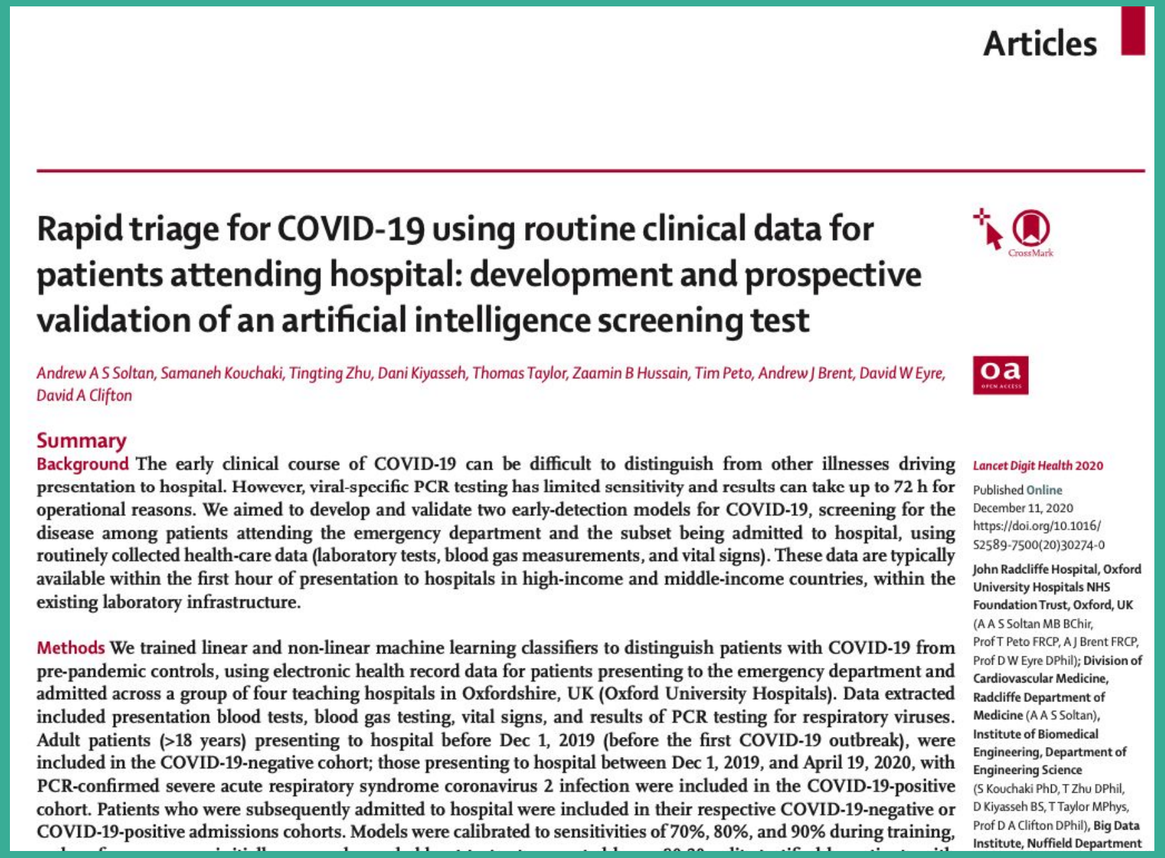
May 2021:
Deployment at **Oxford University Hospitals**

THE LANCET Digital Health

March 2022:
Results of large evaluation published **The Lancet Digital Health**

THE LANCET Digital Health

2020: Development & initial validation



Articles

Rapid triage for COVID-19 using routine clinical data for patients attending hospital: development and prospective validation of an artificial intelligence screening test

Andrew A S Soltan, Samaneh Kouchaki, Tingting Zhu, Dani Kiyasseh, Thomas Taylor, Zaamin B Hussain, Tim Peto, Andrew J Brent, David W Eyre, David A Clifton

Summary

Background The early clinical course of COVID-19 can be difficult to distinguish from other illnesses driving presentation to hospital. However, viral-specific PCR testing has limited sensitivity and results can take up to 72 h for operational reasons. We aimed to develop and validate two early-detection models for COVID-19, screening for the disease among patients attending the emergency department and the subset being admitted to hospital, using routinely collected health-care data (laboratory tests, blood gas measurements, and vital signs). These data are typically available within the first hour of presentation to hospitals in high-income and middle-income countries, within the existing laboratory infrastructure.

Methods We trained linear and non-linear machine learning classifiers to distinguish patients with COVID-19 from pre-pandemic controls, using electronic health record data for patients presenting to the emergency department and admitted across a group of four teaching hospitals in Oxfordshire, UK (Oxford University Hospitals). Data extracted included presentation blood tests, blood gas testing, vital signs, and results of PCR testing for respiratory viruses. Adult patients (>18 years) presenting to hospital before Dec 1, 2019 (before the first COVID-19 outbreak), were included in the COVID-19-negative cohort; those presenting to hospital between Dec 1, 2019, and April 19, 2020, with PCR-confirmed severe acute respiratory syndrome coronavirus 2 infection were included in the COVID-19-positive cohort. Patients who were subsequently admitted to hospital were included in their respective COVID-19-negative or COVID-19-positive admissions cohorts. Models were calibrated to sensitivities of 70%, 80%, and 90% during training,

Lancet Digit Health 2020

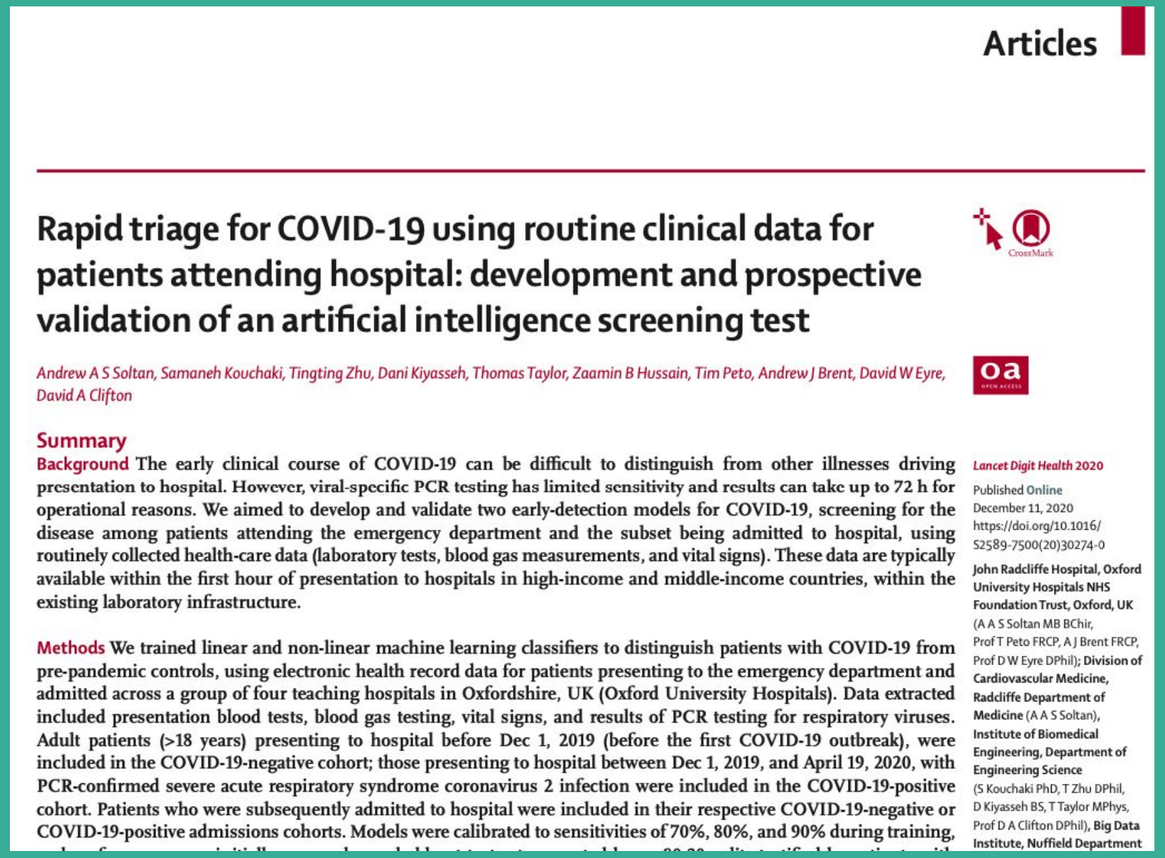
Published Online December 11, 2020 https://doi.org/10.1016/S2589-7500(20)30274-0

John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UK (A A S Soltan MB BChir, Prof T Peto FRCP, A J Brent FRCP, Prof D W Eyre DPhil); **Division of Cardiovascular Medicine, Radcliffe Department of Medicine** (A A S Soltan), **Institute of Biomedical Engineering, Department of Engineering Science** (S Kouchaki PhD, T Zhu DPhil, D Kiyasseh BS, T Taylor MPhys, Prof D A Clifton DPhil), **Big Data Institute, Nuffield Department**

We prospectively validated our ED and admissions models, calibrated during training to 80% sensitivity, for all patients presenting or admitted to Oxford University Hospitals between April 20 and May 6, 2020. 3326 patients presented to hospital and 1715 were admitted during the validation period. Prevalences of COVID-19 were 3·2% (107 of 3326) in patients presenting to hospital and 5·3% (91 of 1715) in those admitted to hospital. Our ED model performed with 92·3% accuracy (AUROC 0·881) and the admission model performed with 92·5% accuracy (0·871) on the validation set, assessed against results of laboratory PCR testing. PPVs were 46·7% (ED model) and 40·0% (admissions model) and NPVs were 97·6% (ED) and 97·7% (admissions).

THE LANCET
Digital Health

2020: Development & initial validation



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Can you trust it?

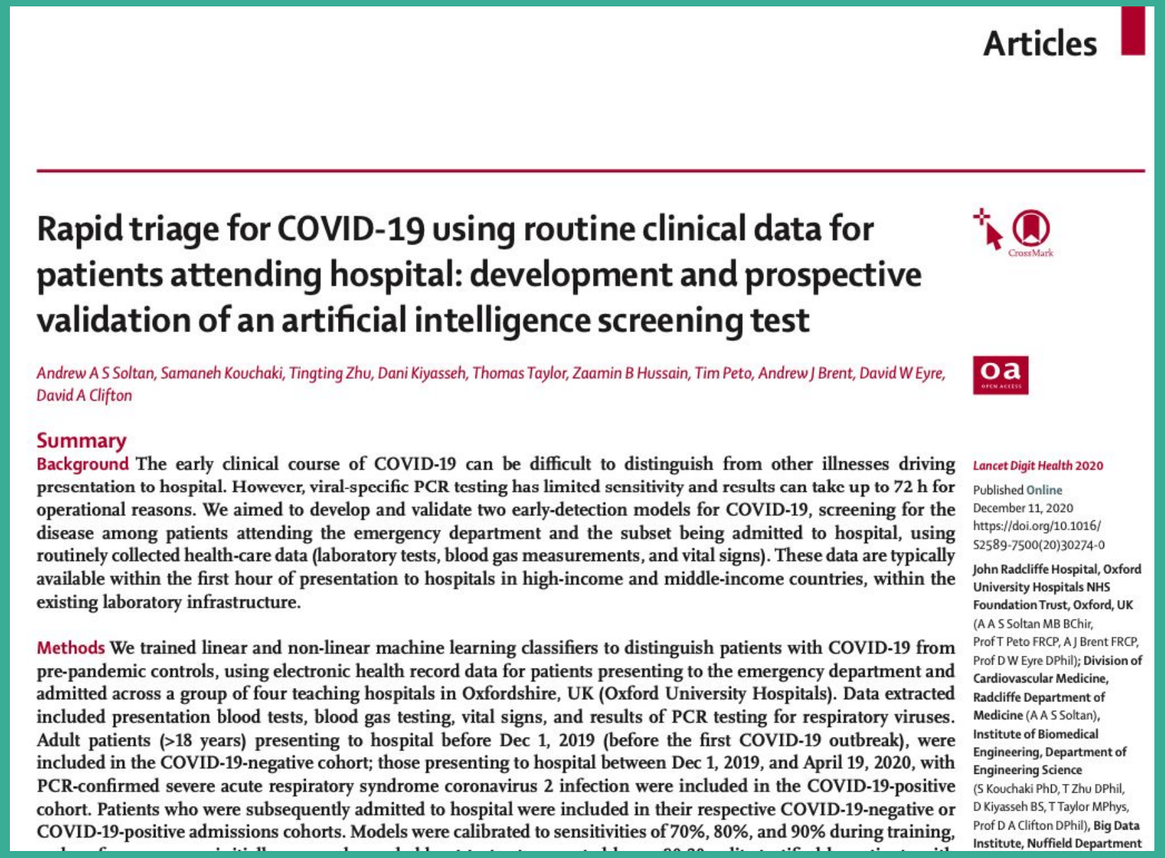
1. Does CURIAL generalize?
2. Are there biases?

What are the real world benefits?

1. Does CURIAL improve care in the age of lateral flow testing?
2. Is CURIAL faster than PCR/LFD?
3. How does CURIAL compare to clinicians?

THE LANCET
Digital Health

2020: Development & initial validation



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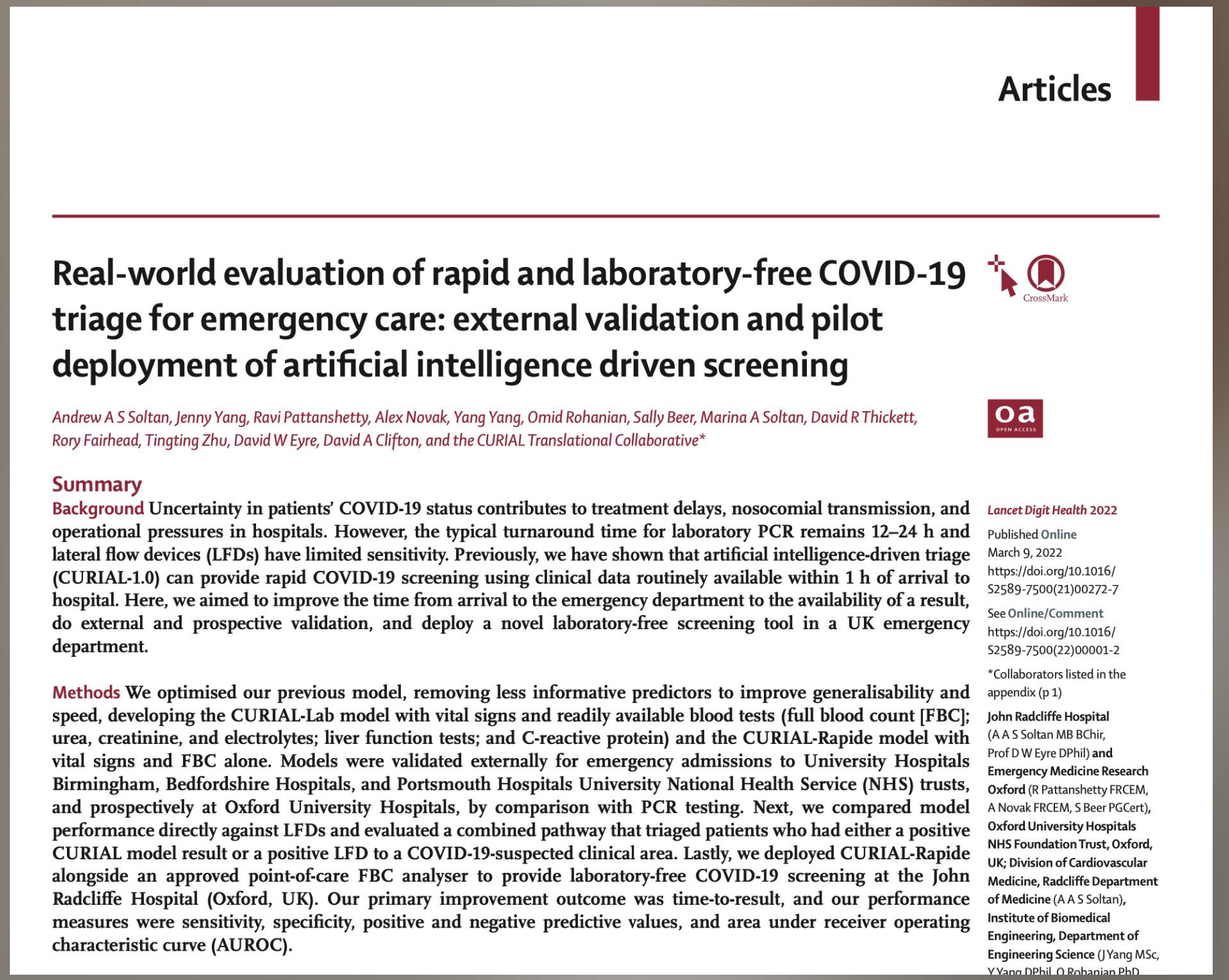
March 2022 – Real-world evaluation of CURIAL:

Extensive real-world evaluation – 72k patients
Direct Comparison with LFTs
Pilot deployment @ Oxford's John Radcliffe Hospital



Articles

Real-world evaluation of rapid and laboratory-free COVID-19 triage for emergency care: external validation and pilot deployment of artificial intelligence driven screening

*Andrew A S Soltan, Jenny Yang, Ravi Pattanshetty, Alex Novak, Yang Yang, Omid Rohanian, Sally Beer, Marina A Soltan, David R Thickett, Rory Fairhead, Tingting Zhu, David W Eyre, David A Clifton, and the CURIAL Translational Collaborative**

Summary

Background Uncertainty in patients' COVID-19 status contributes to treatment delays, nosocomial transmission, and operational pressures in hospitals. However, the typical turnaround time for laboratory PCR remains 12–24 h and lateral flow devices (LFDs) have limited sensitivity. Previously, we have shown that artificial intelligence-driven triage (CURIAL-1.0) can provide rapid COVID-19 screening using clinical data routinely available within 1 h of arrival to hospital. Here, we aimed to improve the time from arrival to the emergency department to the availability of a result, do external and prospective validation, and deploy a novel laboratory-free screening tool in a UK emergency department.

Methods We optimised our previous model, removing less informative predictors to improve generalisability and speed, developing the CURIAL-Lab model with vital signs and readily available blood tests (full blood count [FBC]; urea, creatinine, and electrolytes; liver function tests; and C-reactive protein) and the CURIAL-Rapide model with vital signs and FBC alone. Models were validated externally for emergency admissions to University Hospitals Birmingham, Bedfordshire Hospitals, and Portsmouth Hospitals University National Health Service (NHS) trusts, and prospectively at Oxford University Hospitals, by comparison with PCR testing. Next, we compared model performance directly against LFDs and evaluated a combined pathway that triaged patients who had either a positive CURIAL model result or a positive LFD to a COVID-19-suspected clinical area. Lastly, we deployed CURIAL-Rapide alongside an approved point-of-care FBC analyser to provide laboratory-free COVID-19 screening at the John Radcliffe Hospital (Oxford, UK). Our primary improvement outcome was time-to-result, and our performance measures were sensitivity, specificity, positive and negative predictive values, and area under receiver operating characteristic curve (AUROC).

Lancet Digit Health 2022

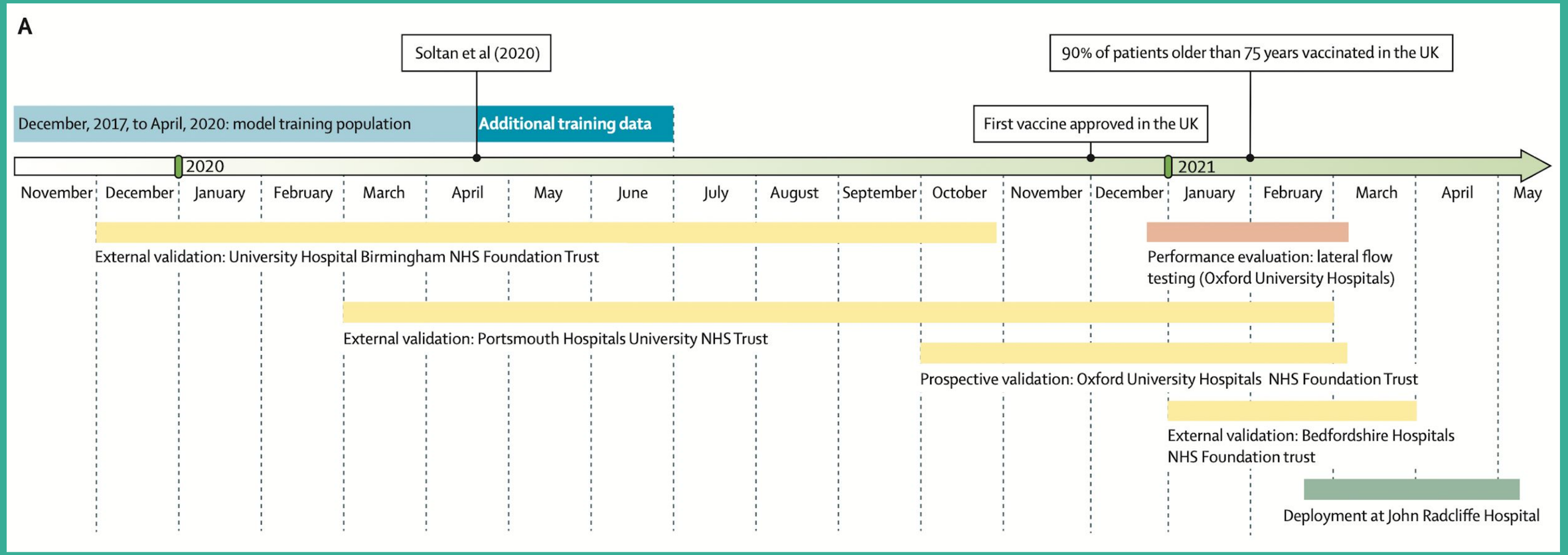
Published Online March 9, 2022 https://doi.org/10.1016/S2589-7500(21)00272-7

See Online/Comment https://doi.org/10.1016/S2589-7500(22)00001-2

*Collaborators listed in the appendix (p 1)

John Radcliffe Hospital (A A S Soltan MB BChir, Prof D W Eyre DPhil) **and Emergency Medicine Research Oxford** (R Pattanshetty FRCEM, A Novak FRCEM, S Beer PGCert), **Oxford University Hospitals NHS Foundation Trust, Oxford, UK; Division of Cardiovascular Medicine, Radcliffe Department of Medicine** (A A S Soltan), **Institute of Biomedical Engineering, Department of Engineering Science** (J Yang MSc, Y Yang DPhil, O Rohanian PhD

Timeline



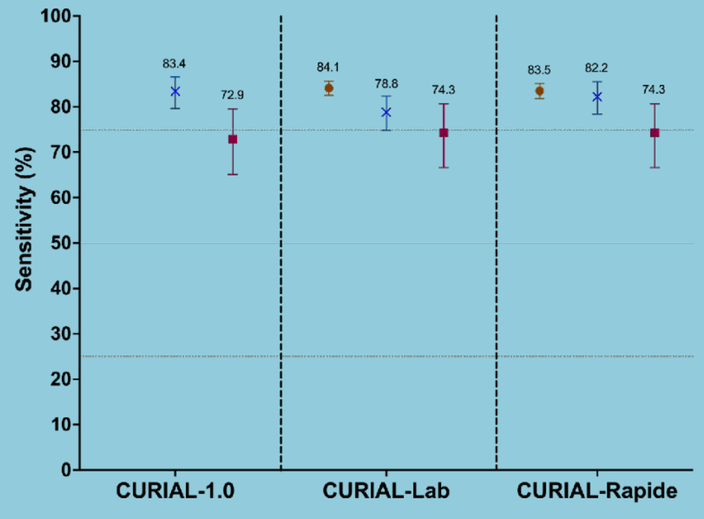
Soltan et al 2022, Lancet Digital Health

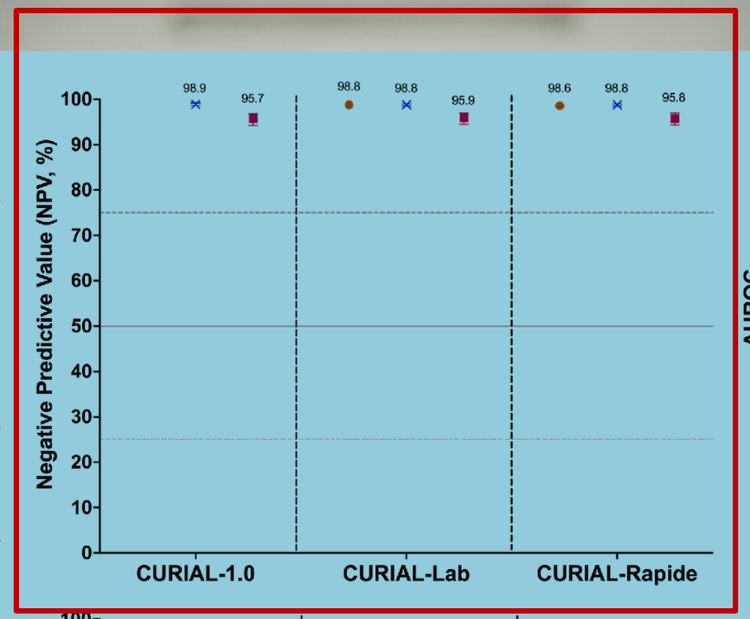
Evaluated at multiple NHS Trusts

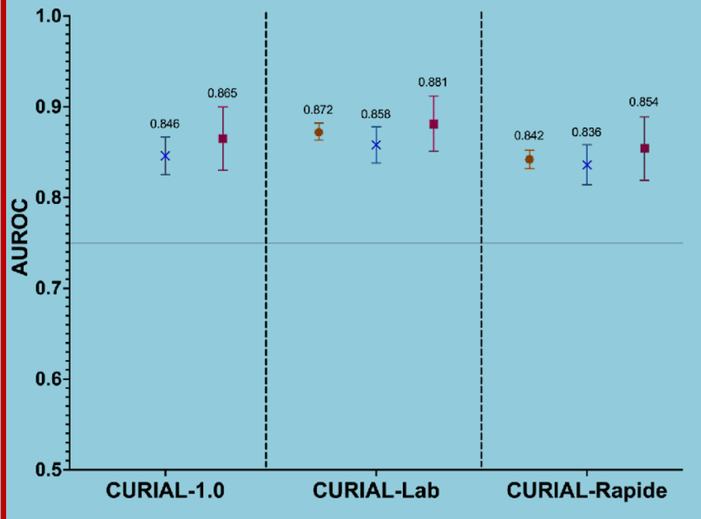
Bedfordshire Hospitals NHS Trust

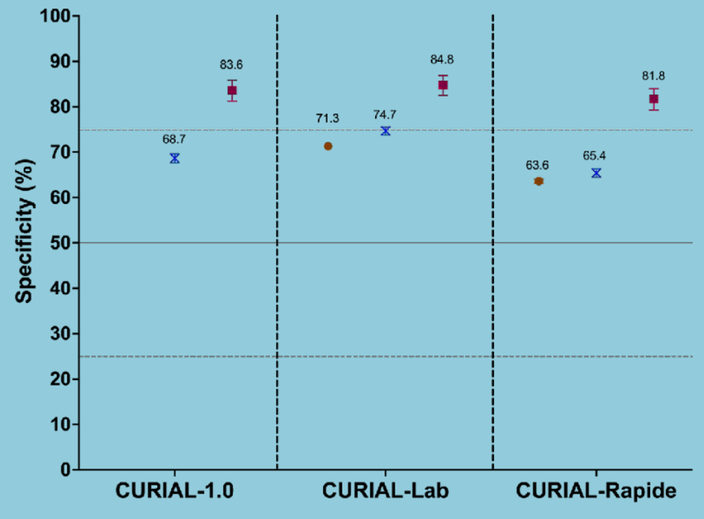
University Hospitals Birmingham NHS Trust

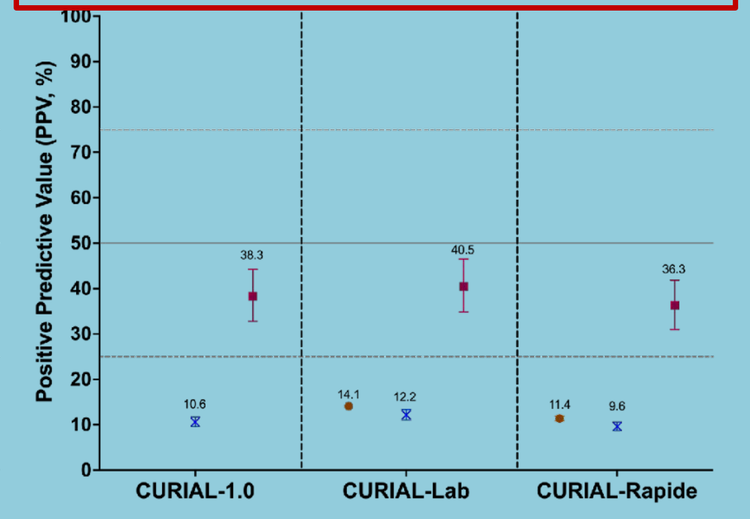
Portsmouth Hospitals NHS Trust











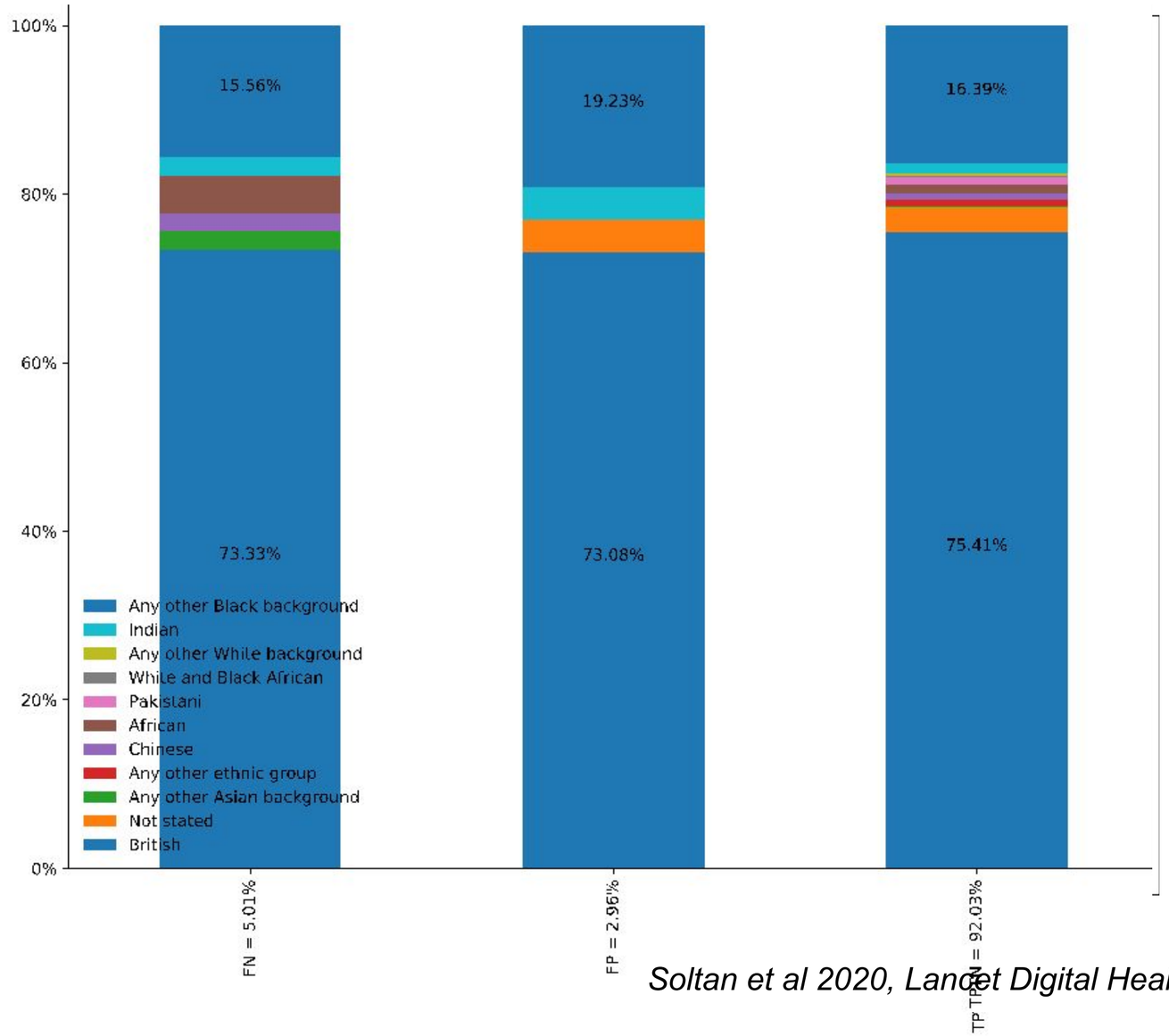
- Portsmouth University Hospitals NHS Trust
  n= 37,896, prevalence = 5.29%
- University Hospitals Birmingham NHS Foundation Trust
  n=10,293; prevalence = 4.27%
- Bedfordshire Hospitals NHS Foundation Trust
  n=1,177; prevalence = 12.2%

High NPV - Reproducible across four NHS trusts

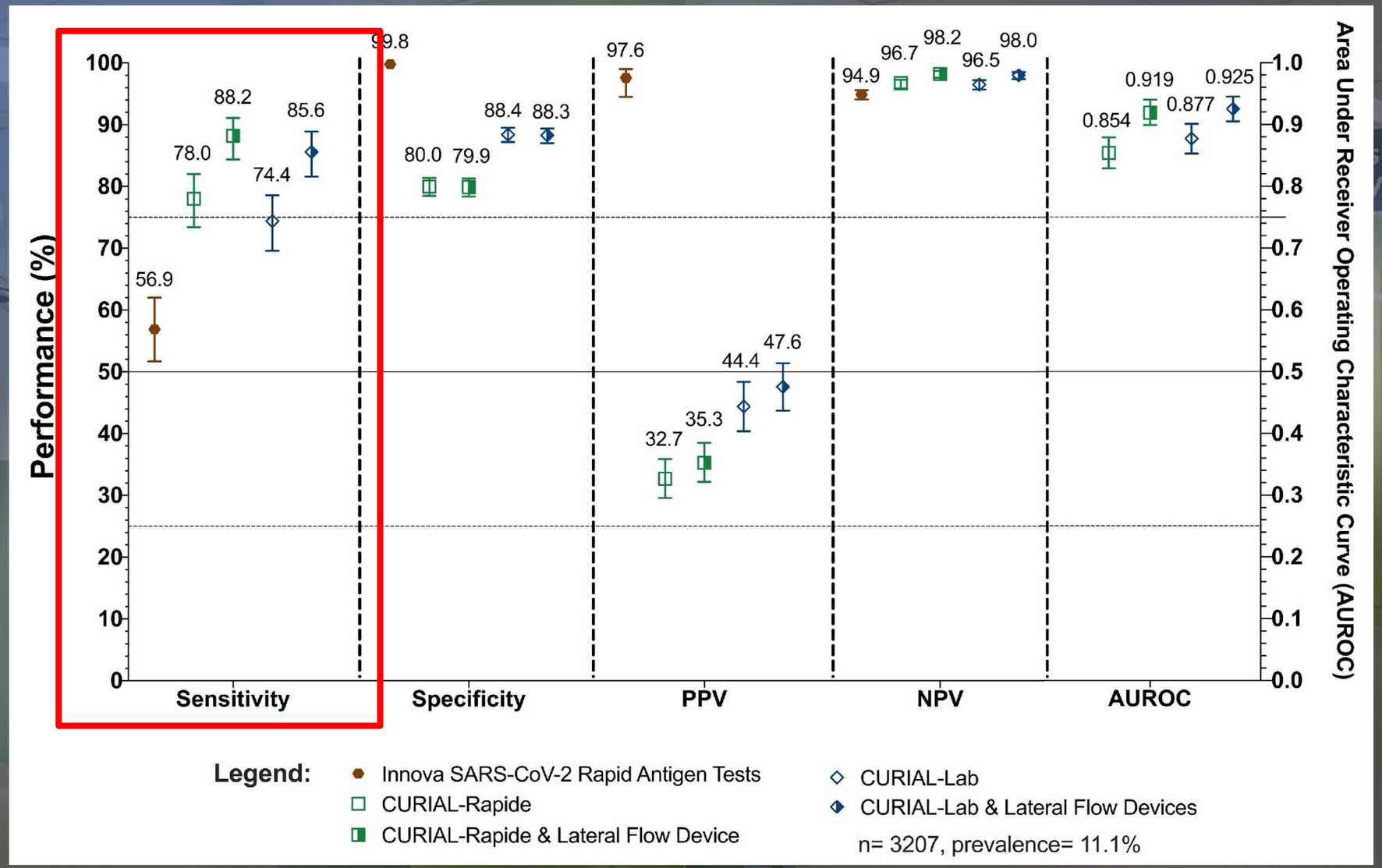
"A D-dimer for COVID"

Misclassification & Equality Analysis

- No significant difference in rates of misclassification between:
  - Over 60s VS Under 60s
    (p=0.187 & 0.191)
  - White British and BAME groups
    (Fishers' Exact test p= 0.374 & 0.358)
  - Men & Women
    (p=0.147 & 0.091)



Soltan et al 2020, Lancet Digital Health



21% more sensitive than LFTs –
In combination, reduces missed COVID-19 cases by 72%


Resus
Bay 7
71%
About 3 minutes remaining
PARAFILM M IS
PM-996
EMERGENCY AMBULANCE
Ambulance Entrance

Pilot deployment

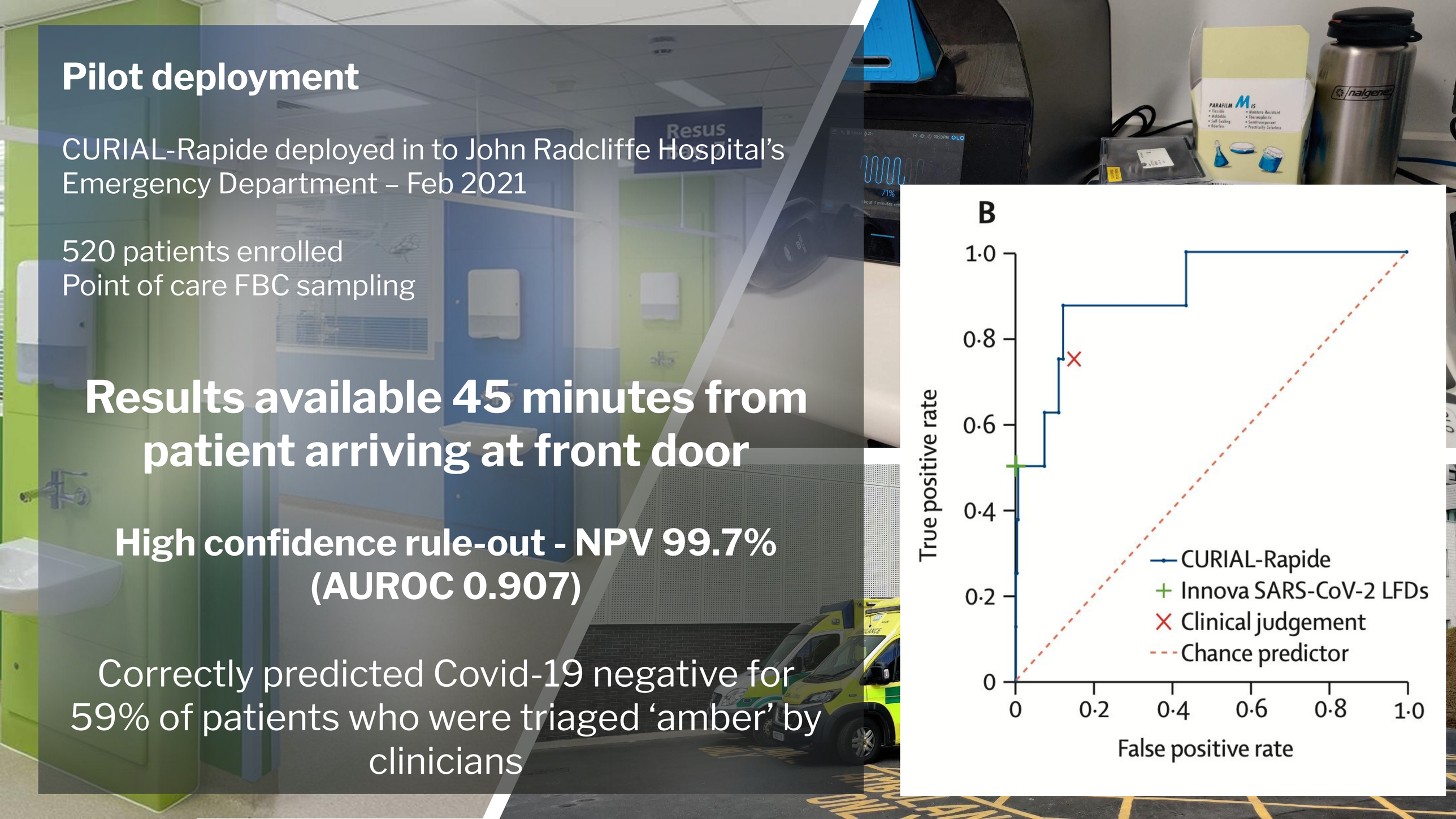
CURIAL-Rapide deployed in to John Radcliffe Hospital's Emergency Department – Feb 2021

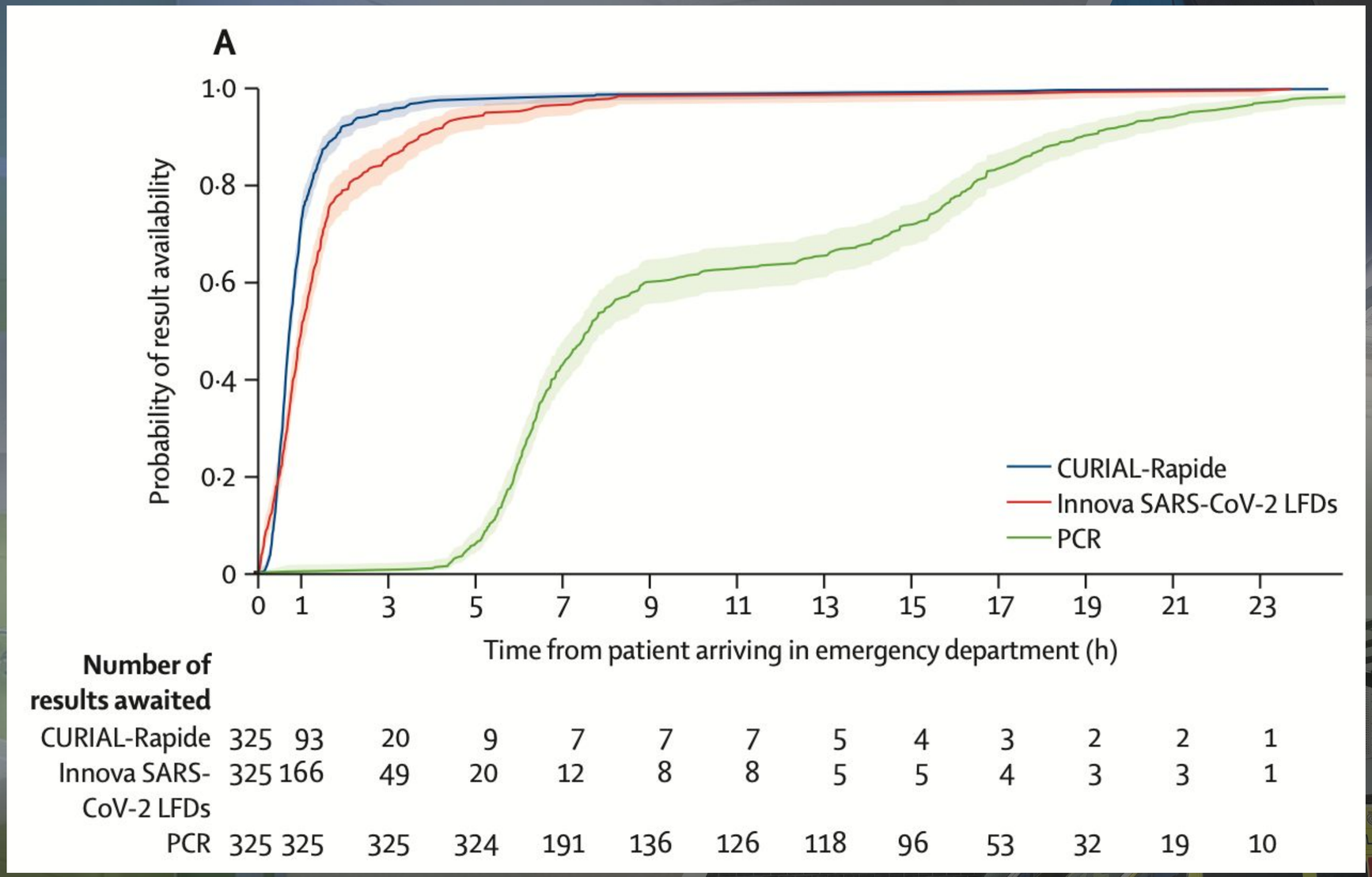
520 patients enrolled
Point of care FBC sampling

Results available 45 minutes from patient arriving at front door

High confidence rule-out - NPV 99.7% (AUROC 0.907)

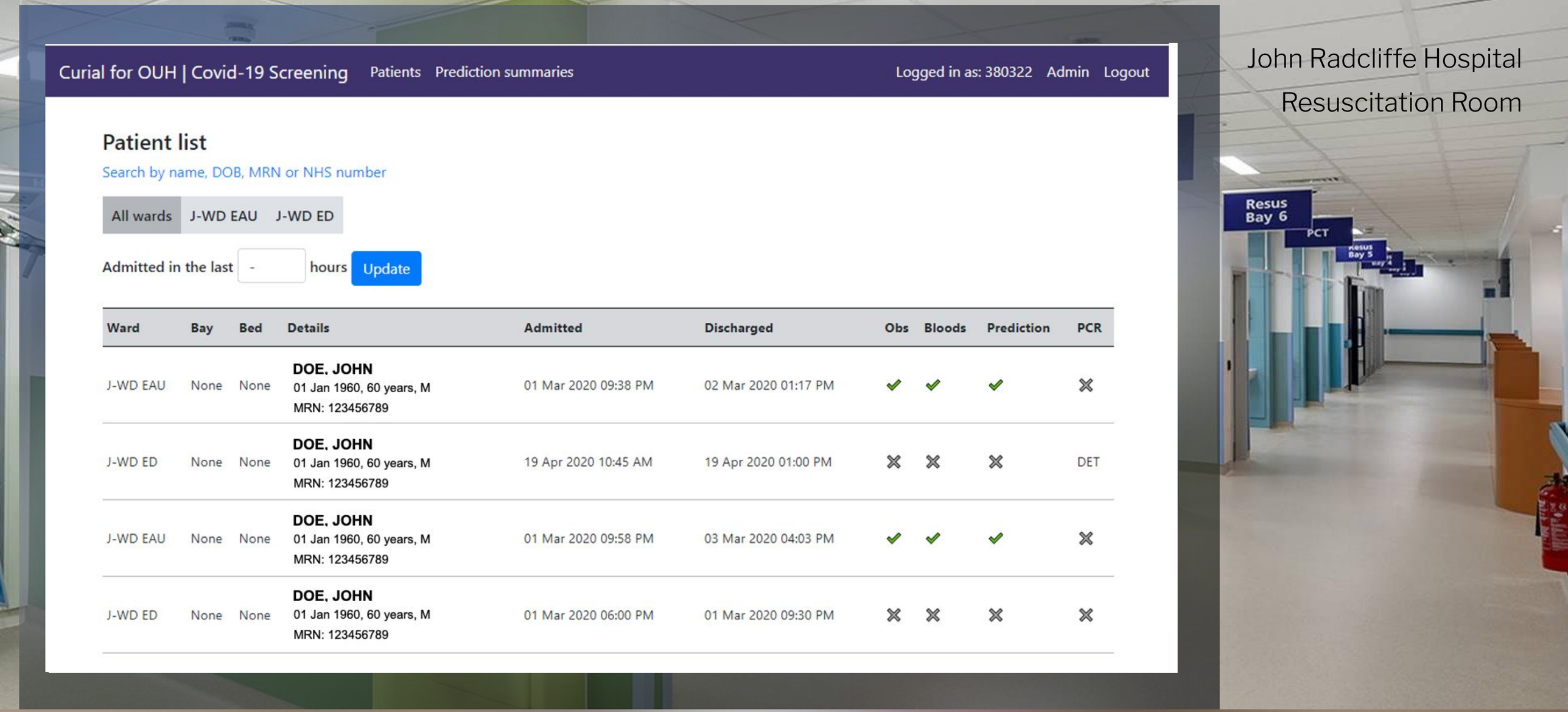
Correctly predicted Covid-19 negative for 59% of patients who were triaged 'amber' by clinicians





Number of results awaited													
CURIAL-Rapide	325	93	20	9	7	7	7	5	4	3	2	2	1
Innova SARS-CoV-2 LFDs	325	166	49	20	12	8	8	5	5	4	3	3	1
PCR	325	325	325	324	191	136	126	118	96	53	32	19	10

45-mins from front-door to COVID rule-out - 16 minutes faster than LFT
91% faster (6.5 hours) than PCR at OUH



John Radcliffe Hospital
Resuscitation Room

An AI test to rule out COVID-19 in real-time
No additional sample

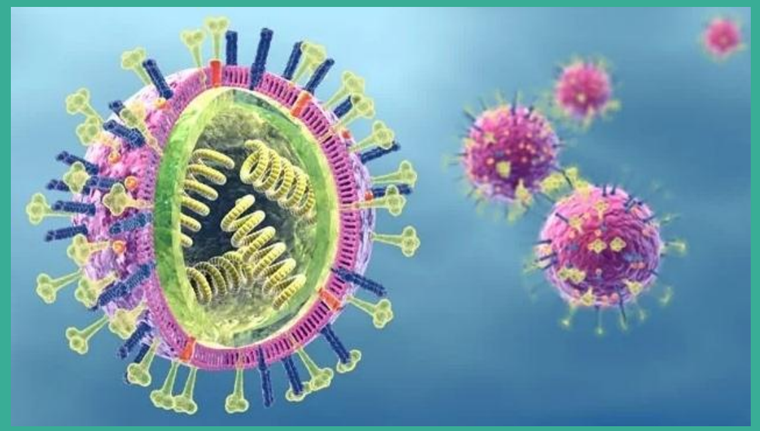
CURIAL

R&D

A platform approach

Universal screening on admission,

using data that is already routinely collected



Influenza screening
- Rapid screening at front door
- Judicial use of PPE
- Reduced nosocomial transmission
- Improved use of antivirals

Sepsis –
'for **every hour** treatment is delayed, odds of a patient's survival **reduced by 4 percent'**
New England Journal of Medicine, 2014

Media

BBC SOUTH

GOV.UK

theguardian

Centre for Data Ethics and Innovation

i inews

NIHR | National Institute for Health Research

THE LANCET Digital Health

MailOnline

RE·WORK

IET The Institution of Engineering and Technology

Technology Networks

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Blog

Centre for Data Ethics and Innovation Blog

Organisations: Centre for Data Ethics and Innovation

Explainer: Case study: AI-driven testing for COVID-19

Emily Jarratt, 5 August 2020 - Artificial intelligence, Covid-19, Data-driven technology

Set up by the government in 2018, the CDEI has a unique remit: to help the UK navigate the ethical challenges presented by AI and data-driven technology. We are led by an independent board of experts from across industry, civil society, academia and government. CDEI publications do not represent government policy or advice.

As part of the CDEI's series of introductory blogs, we will also be highlightin specific use-cases of data-driven technologies that we have uncovered through our COVID-19 repository and are currently being implemented. Thi week we're looking at an Oxford-based study of a new diagnostic tool, whic uses machine learning to predict whether a patient has coronavirus within a hour of them entering a hospital.

i News Politics Opinion Culture Money Sport Lifestyle Features

News

AI screening test could help hospitals manage Covid-19 risk

It accurately predicted the Covid-19 status of 92.3 per cent of patients coming to emergency departments at two UK hospitals

The test was carried out at John Radcliffe Hospital in Oxford (Photo : Finnbarr Webster/Getty)

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Alert

Artificial intelligence tool rules out COVID-19 within an hour in emergency departments

Published on 3 September 2021

doi: 10.3310/alert_47487

Researchers have developed an artificial intelligence (AI) tool for rapidly detecting COVID-19 in people arriving at a hospital's emergency department. The tool can accurately rule out infection within an hour of a patient arriving at hospital, significantly faster than the PCR (polymerase chain reaction) test that has a turnaround time of typically 24 hours.

NIHR | Oxford Biomedical Research Centre

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AI test identifies COVID-19 within an hour in emergency departments

30 July 2020 · Listed under Antimicrobial Resistance and Modernising Microbiology, Clinical Informatics and Big Data, COVID-19

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University of Oxford scientists specialising in infectious disease and clinical machine learning have developed an artificial intelligence test that can rapidly screen for COVID-19 in patients arriving in emergency departments.

The initial findings of the 'CURIAL' AI test, which has been supported by the NIHR Oxford Biomedical Research Centre (BRC), appeared in a preprint paper.

The test assesses data routinely collected during the first hour in

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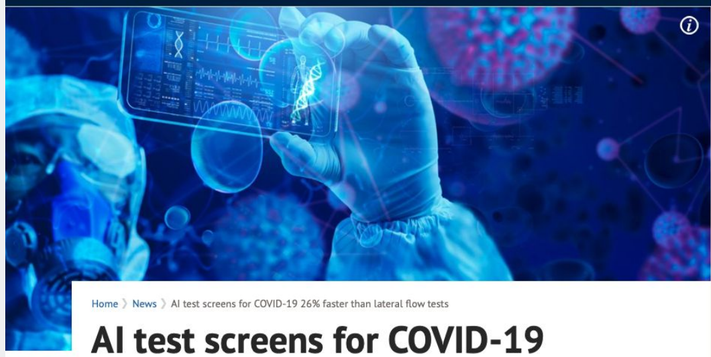

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AI test screens for COVID-19 26% faster than lateral flow tests

PUBLISHED 1 SEP 2021

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CORONAVIRUS HEALTH MEDICAL SCIENCES RESEARCH SCIENCE TECHNOLOGY

An Artificial Intelligence (AI) test performed by the bedside in 10 minutes quickly and safely triages patients coming to hospital for COVID-19, a University of Oxford-led study has shown.

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New AI test identifies COVID-19 within one hour in emergency departments

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Dawn Hinsley | 27 Jul 2020


BBC

CURIAL

Compliments

Accompanying commentary piece –

The Lancet Digital Health

April 2022 *(Gilbert at al 2022)*

"CURIAL devices represent an elegant breakthrough to enhance the clinical decision-making process in the age of AI."

"As we are now facing the COVID-19 fourth wave, we are confident that AI-driven triage will meet the challenge of optimizing the early detection of infected patients and limiting the spread of ED and in-hospital contamination."

CURIAL

Rule-out results
Up to 90% faster
At near-zero cost

CURIAL rules out COVID-19, using data available within 10 min-1 h of a patient arriving in ED

Real-world benefits
Missed cases reduced 72%

In a head-to-head comparison CURIAL cut false-negative results by 72% when compared to Lateral Flow Tests

Clinically Validated with Diverse training and validation sets

CURIAL is trained using rich datasets of 115,000 patients & validated for 72,000 patients across 4 NHS hospital groups serving ~3.5m patients. No consistent evidence of bias

Evidence based

The evidence for CURIAL is published in the world leading digital health journal - *The Lancet Digital Health*.

CURIAL Team

Many thanks to:

CHI lab

Prof David Clifton

Dr Jenny Yang
Dr Samaneh Kouchaki
Thomas Taylor
Dani Kiyaseh
Dr Tingting Zhu

OUH ID/Microbiology:

Prof David Eyre

Prof Tim Peto
Dr Andrew Brent

OUH Emergency Department:

Dr Alex Novak

Dr Ravi Pattanshetty
Sally Beer

OU Translational Research Office
Oxford University Hospitals NHS FT
University Hospitals Birmingham NHS FT
Portsmouth Hospitals University NHS T
Bedfordshire Hospitals NHS FT

To all patients & colleagues across Oxford University Hospitals

***Funding**:* Wellcome Trust/University of Oxford Medical & Life Sciences Translational Fund

Ethics: NHS HRA IRAS ID 281832

Dr Andrew Soltan, MB BChir

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CURIAL

Supplementary Information

NHS
Oxford University Hospitals
NHS Foundation Trust

UNIVERSITY OF OXFORD

Above (left): Professor David Eyre. *Centre:* Dr Andrew Soltan. *Right:* Professor David Clifton (© Oxford University/Joby Sessions)

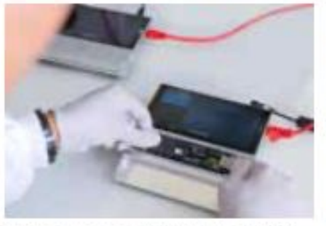
TESTING TIMES

Oxford contributed three rapid test technologies for COVID-19.

Oxford has long championed collaborative work across departmental boundaries. Take the leading clinician Dr Andrew Soltan and the two professors, respectively of Artificial Intelligence and Big Data, David Clifton and David Eyre. Out of their discussions came an algorithm to detect COVID-19, 'trained' on the real data of 115,000 emergency hospital visits by patients. The astonishing result was a tool that had over 90% accuracy in screening patients for COVID-19. It was also fast and cheap, showcasing what AI might be able to do for health care in the future.

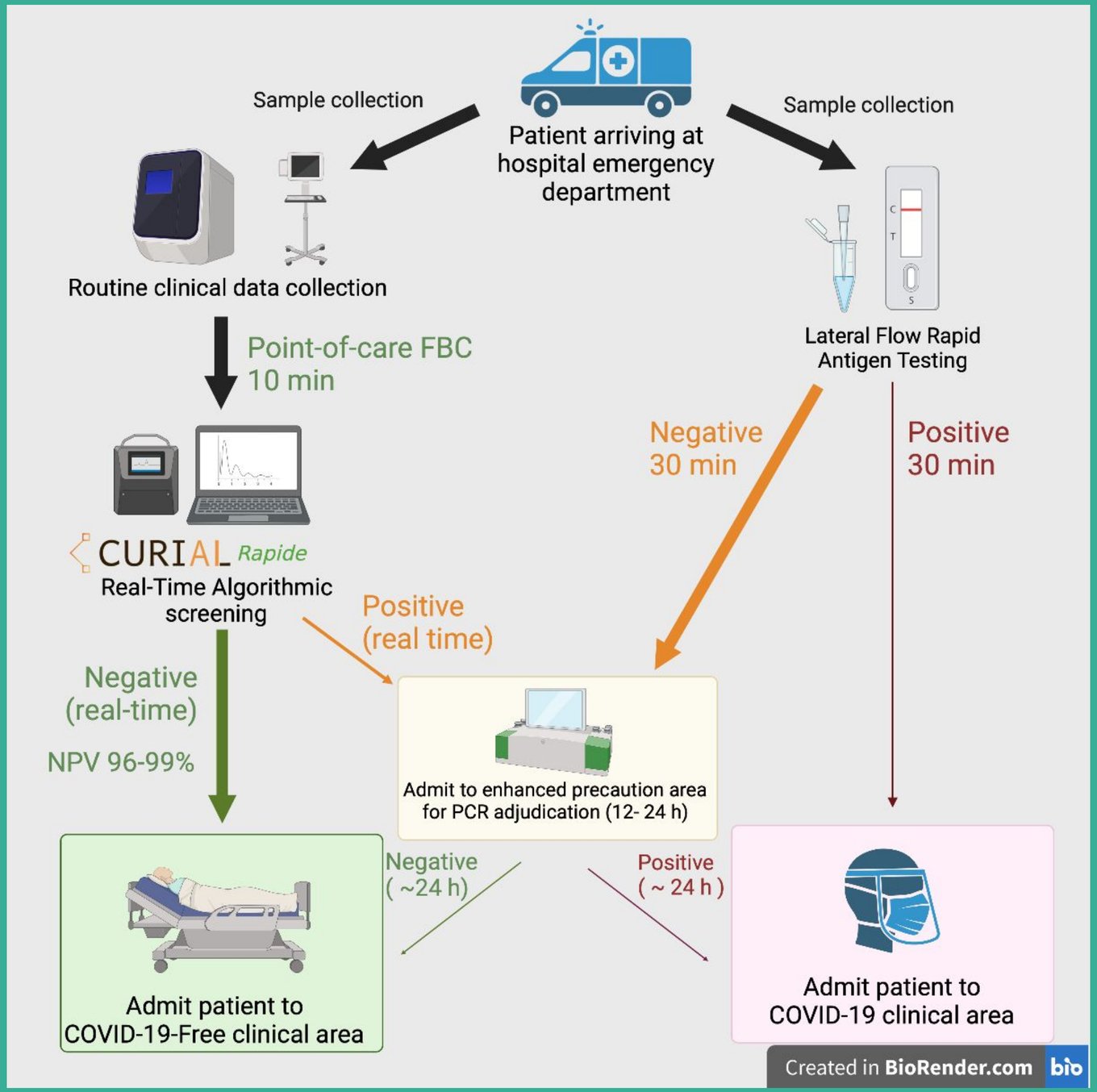
Further development of the AI test since 2020 has created a 'lab-free' screening solution, collecting all the data needed to screen a patient for COVID-19 in minutes, at the bedside. With faster results, better triage at the front door of hospitals can help curb the spread and reduce delays to care. Looking to the future, the researchers are investigating how these AI-driven approaches can improve early diagnostics and triage for other conditions.

speeding up the process. Led by Professor Derrick Crook, Oxford's expertise in clinical microbiology and pathogen sequencing was once again evident in this project, but so too is its broader ability to collaborate with industry.



Scientist inserting a flow cell into MinION Mk1C (© Oxford Nanopore)

A rapid COVID-19 test developed at Oxford University was the basis of a spinout company named Oxsed Ltd. By November its rapid test was being used in both London Heathrow Airport and Hong Kong International Airport. It was duly acquired by DNAFit Life Sciences, part of Hong Kong-based


Patient arriving at hospital emergency department
Sample collection
Sample collection
Routine clinical data collection
Point-of-care FBC
10 min
CURIAL Rapide
Real-Time Algorithmic screening
Lateral Flow Rapid Antigen Testing
Negative
30 min
Positive
30 min
Positive
(real time)
Negative
(real-time)
NPV 96-99%
Admit to enhanced precaution area for PCR adjudication (12- 24 h)
Negative
(~24 h)
Positive
(~ 24 h)
Admit patient to COVID-19-Free clinical area
Admit patient to COVID-19 clinical area
Created in BioRender.com

B

		Model:		
Feature set	**Constituents**	**CURIAL-1.0**	**CURIAL-Lab**	**CURIAL-Rapide**
Vital signs	Heart rate, respiratory rate, oxygen saturations, blood pressure, temperature, oxygen delivery device	√	√	√
Full blood count	Haemoglobin, haematocrit, mean cell volume, white cell count, neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count, platelets	√	√	√
Urea and electrolytes	Sodium, potassium, creatinine, urea, eGFR	√	√	
Liver function tests and CRP	Albumin, alkaline phosphatase, ALT, bilirubin, CRP	√	√	
Coagulation	Prothrombin time, INR, APTT	√		
Blood gas	Base excess, bicarbonate, calcium, chloride, estimated osmolality, fraction carboxyhaemoglobin, glucose, haemoglobin, haematocrit, potassium, methaemoglobin, sodium, oxygen saturation, calculated lactate, calculated p50, partial pressure carbon dioxide, pH, partial pressure oxygen	√		

CURIAL

Why Curial?

	CURIAL	Lateral Flow
No extra tests Fits immediately in to today's clinical pathway	✓	✗
Minimal staff time	✓ seconds	✗ 10 minutes
High confidence Covid rule-out	✓	✗
Rapid scale up to site-capacity	✓	✗
Unit consumable cost	Server costs <1p/unit	£8-£10 ex. staff time & PPE

CURIAL

CURIAL

R&D

Algorithmic Fairness and Bias Mitigation for Clinical Machine Learning: Insights from Rapid COVID-19 Diagnosis by Adversarial Learning

Jenny Yang, Andrew A. S. Soltan, Yang Yang, and David A. Clifton

***Abstract*— Machine learning is becoming increasingly prominent in healthcare. Although its benefits are clear, growing attention is being given to how machine learning may exacerbate existing biases and disparities. In this study, we introduce an adversarial training framework that is capable of mitigating biases that may have been acquired through data collection or magnified during model development. For example, if one class is over-presented or errors/inconsistencies in practice are reflected in the training data, then a model can be biased by these. To evaluate our adversarial training framework, we used the statistical definition of equalized odds. We evaluated our model for the task of rapidly predicting COVID-19 for patients presenting to hospital emergency departments, and aimed to mitigate regional (hospital) and ethnic biases present. We trained our framework on a large, real-world COVID-19 dataset and demonstrated that adversarial training demonstrably improves outcome fairness (with respect to equalized odds), while still achieving clinically-effective screening performances (NPV>0.98). We compared our method to the benchmark set by related previous work, and performed prospective and external validation on four independent hospital cohorts. Our method can be generalized to any outcomes, models, and definitions of fairness.**

***Index Terms*— machine learning, diagnosis, bias mitigation, algorithmic fairness, covid-19, adversarial learning**

across hospitals in different regions. This heterogeneity has been acknowledged worldwide and has been examined for a range of medical conditions and diseases [2]-[4], as well as different drivers of healthcare quality [2], [5]. If these types of biases become reflected in a model's decisions, then certain hospitals could be unintentionally isolated for exhibiting poorer outcomes, further widening interregional and interhospital inequality gaps, and also adversely affect model performance.

Health inequalities related to demographic biases such as sex, gender, age, and ethnicity, can also exist. For example, in terms of gender bias, physicians have been found to have an unconscious bias for ascribing the symptoms of coronary heart disease (CHD) among women to some other disorder [6]; and when the same proportion of women and men presented with chest pain, an observational study found that women were 2.5 times less likely to be referred to a cardiologist for management [7]. Similarly, it was shown that physicians tended to ask fewer diagnostic questions and prescribe the fewest CHD-related medications to middle-aged women [8]. In terms of ethnic bias, a systematic review of USA-based studies found that in the emergency room, black patients were 40% less likely to receive pain medication than white patients [9]. When such biases

Machine Learning Generalizability Across Healthcare Settings: Insights from multi-site COVID-19 screening

Jenny Yang, Andrew A. S. Soltan, David A. Clifton

doi: https://doi.org/10.1101/2022.02.09.22269744

Abstract

As patient health information is highly regulated due to privacy concerns, the majority of machine learning (ML)-based healthcare studies are unable to test on external patient cohorts, resulting in a gap between locally reported model performance and cross-site generalizability. Different approaches have been introduced for developing models across

PRIVACY-AWARE EARLY DETECTION OF COVID-19 THROUGH ADVERSARIAL TRAINING

Omid Rohanian[*1] **Samaneh Kouchaki**[1, 2, 3] **Andrew Soltan**[4, 5] **Jenny Yang**[1]

Morteza Rohanian[6] **Yang Yang**[1, 7] **David Clifton**[1, 7]

[1] Department of Engineering Science, University of Oxford, Oxford, UK
[2] CVSSP, University of Surrey, Surrey, UK
[3]UK Dementia Research Institute Care Research and Technology Centre, Imperial College London and the University of Surrey, UK
[6] Queen Mary University of London, London, UK
[7] Oxford-Suzhou Centre for Advanced Research, Suzhou, China
[5] John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, UK
4 RDM Division of Cardiovascular Medicine, University of Oxford, UK

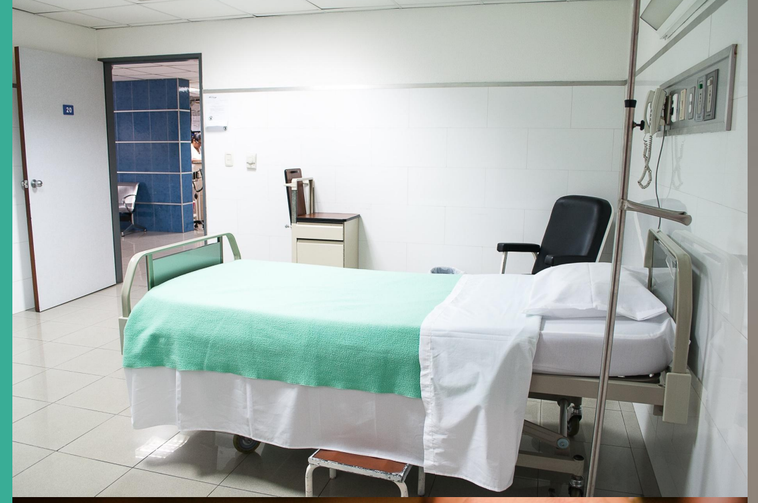
ABSTRACT

Early detection of COVID-19 is an ongoing area of research that can help with triage, monitoring and general health assessment of potential patients and may reduce operational strain on hospitals that cope with the coronavirus pandemic. Different machine learning techniques have been used in the literature to detect potential cases of coronavirus using routine clinical data (blood tests, and vital signs measurements). Data breaches and information leakage when using these models can bring reputational damage and cause legal issues for hospitals. In spite of this, protecting healthcare models against leakage of potentially sensitive information is an understudied research area. In this work, we examine two machine learning approaches, intended to predict a patient's COVID-19 status using routinely collected and readily available clinical data. We employ adversarial training to explore robust deep learning architectures that protect attributes related to demographic information about the patients. The two models we examine in this work are intended to preserve sensitive information against adversarial attacks and information leakage. In a series of experiments using datasets from the Oxford University Hospitals (OUH), Bedfordshire Hospitals NHS Foundation Trust (BH), University Hospitals Birmingham NHS Foundation Trust (UHB), and Portsmouth Hospitals University NHS Trust (PUH) we train and test two neural networks that predict PCR test results using information from basic laboratory blood tests, and vital signs performed on a patients' arrival to hospital. We assess the level of privacy each one of the models can provide and show the efficacy and robustness of our proposed architectures against a comparable baseline. One of our main contributions is that we specifically target the development of effective COVID-19 detection models with built-in mechanisms in order to selectively protect sensitive attributes against adversarial attacks.

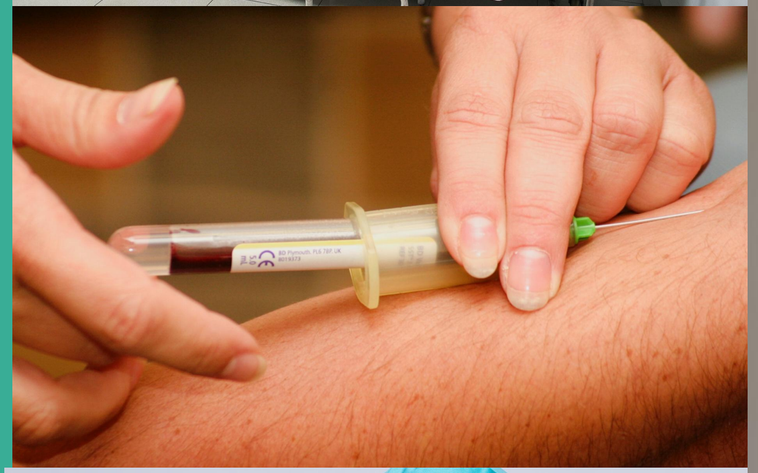
A high-confidence test of exclusion is needed

With results in minutes...

CURIAL



Patient arrives in emergency department



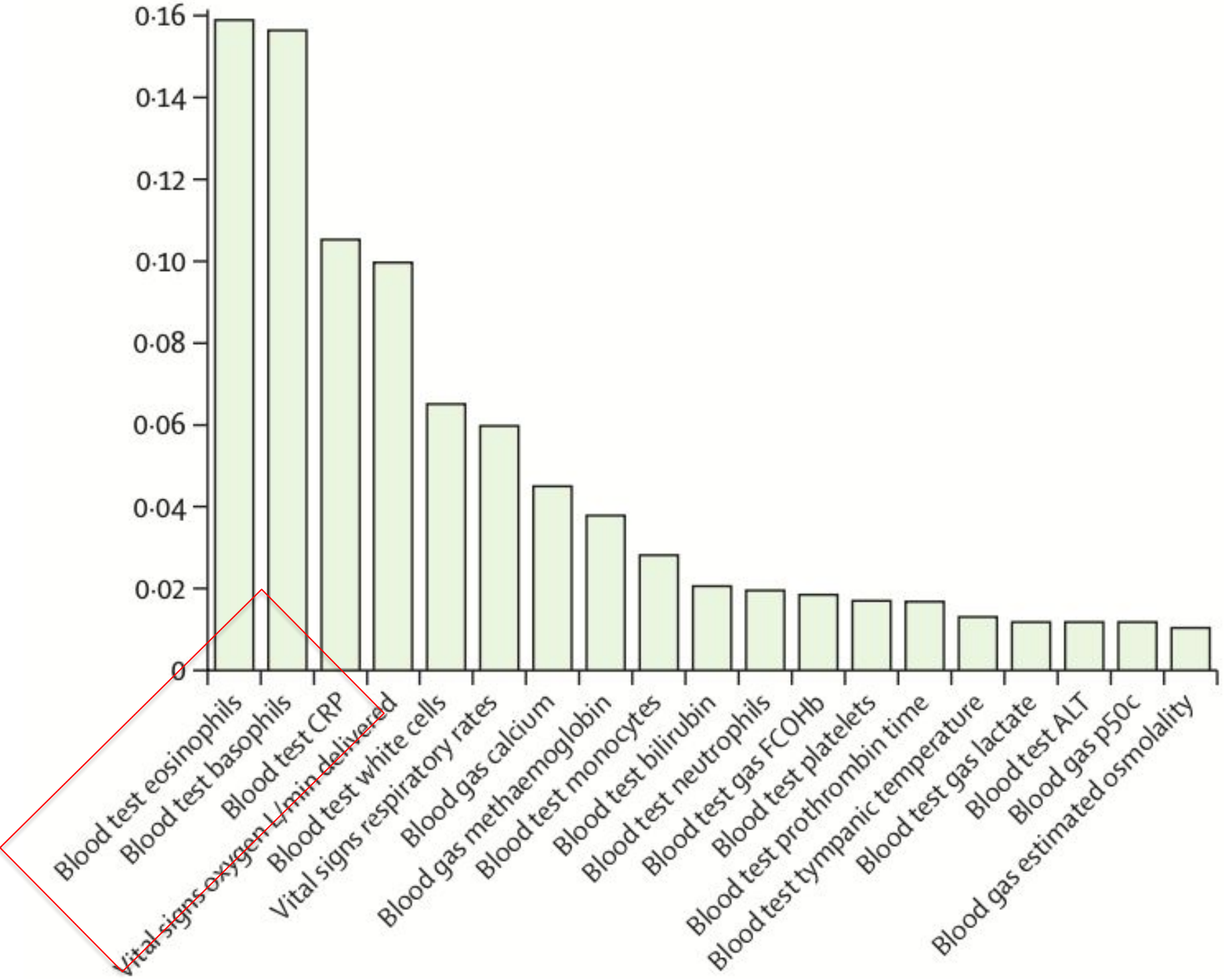
Routine data collected within existing pathways

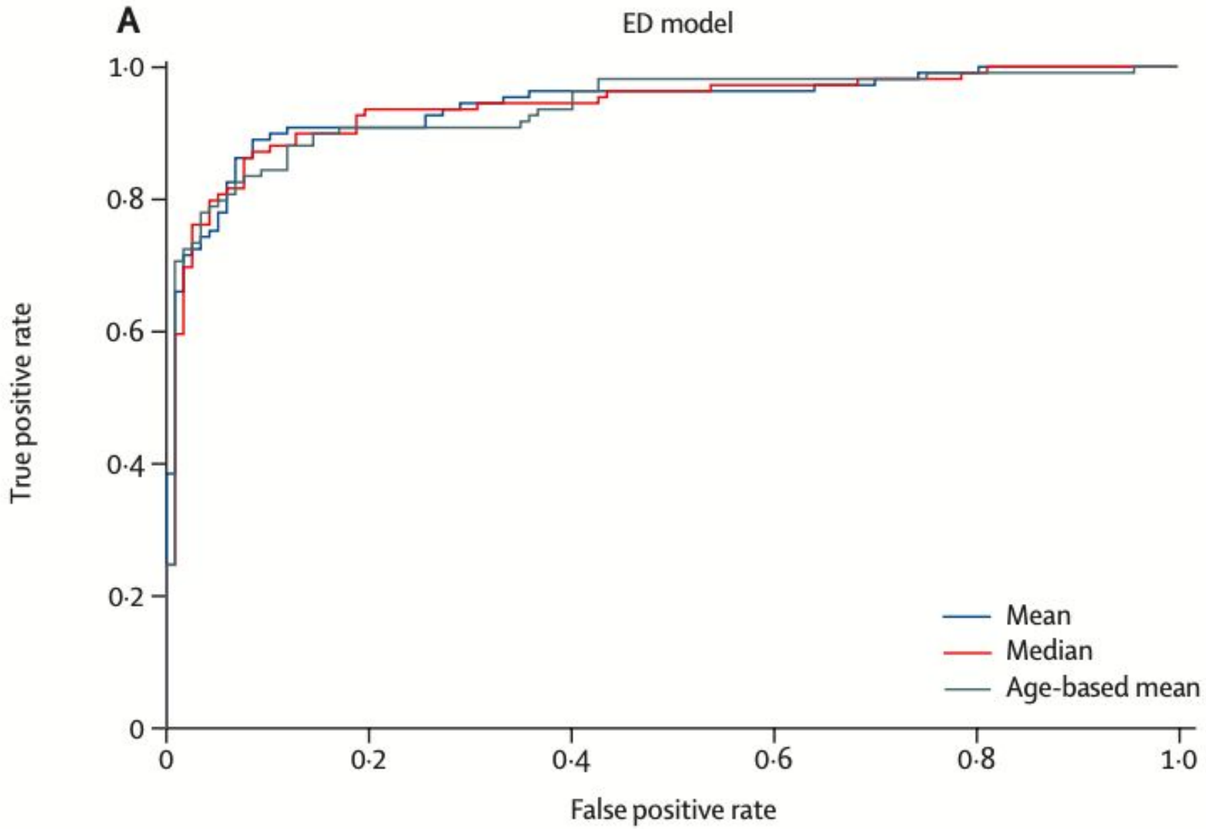
Blood tests & vital signs already available within 1h of arrival (& 10 mins with point-of-care)
Daily or bi-daily blood testing for inpatients

High confidence rule-out test performed in real time

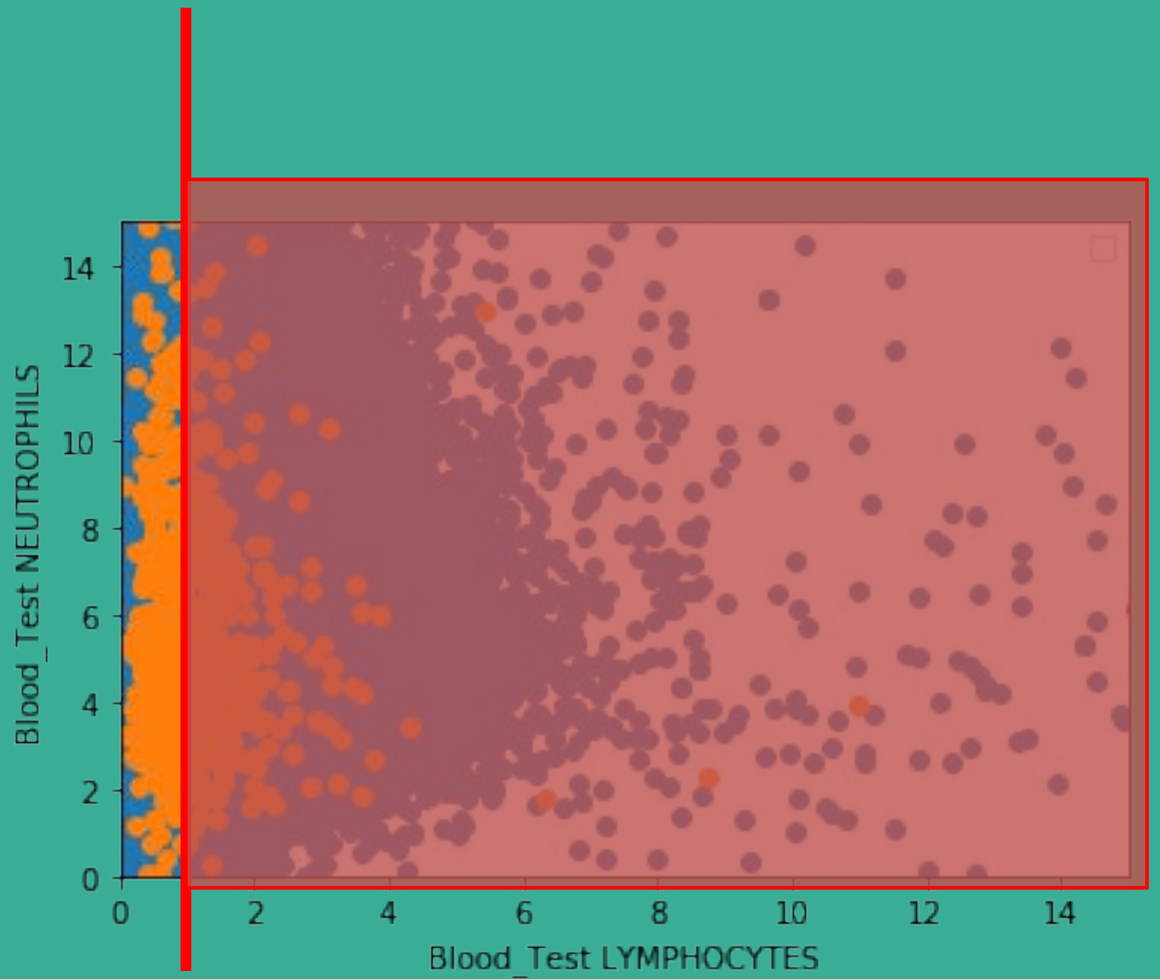
CURIAL result available immediately and gives clinicians high confidence that a patient does not have COVID-19

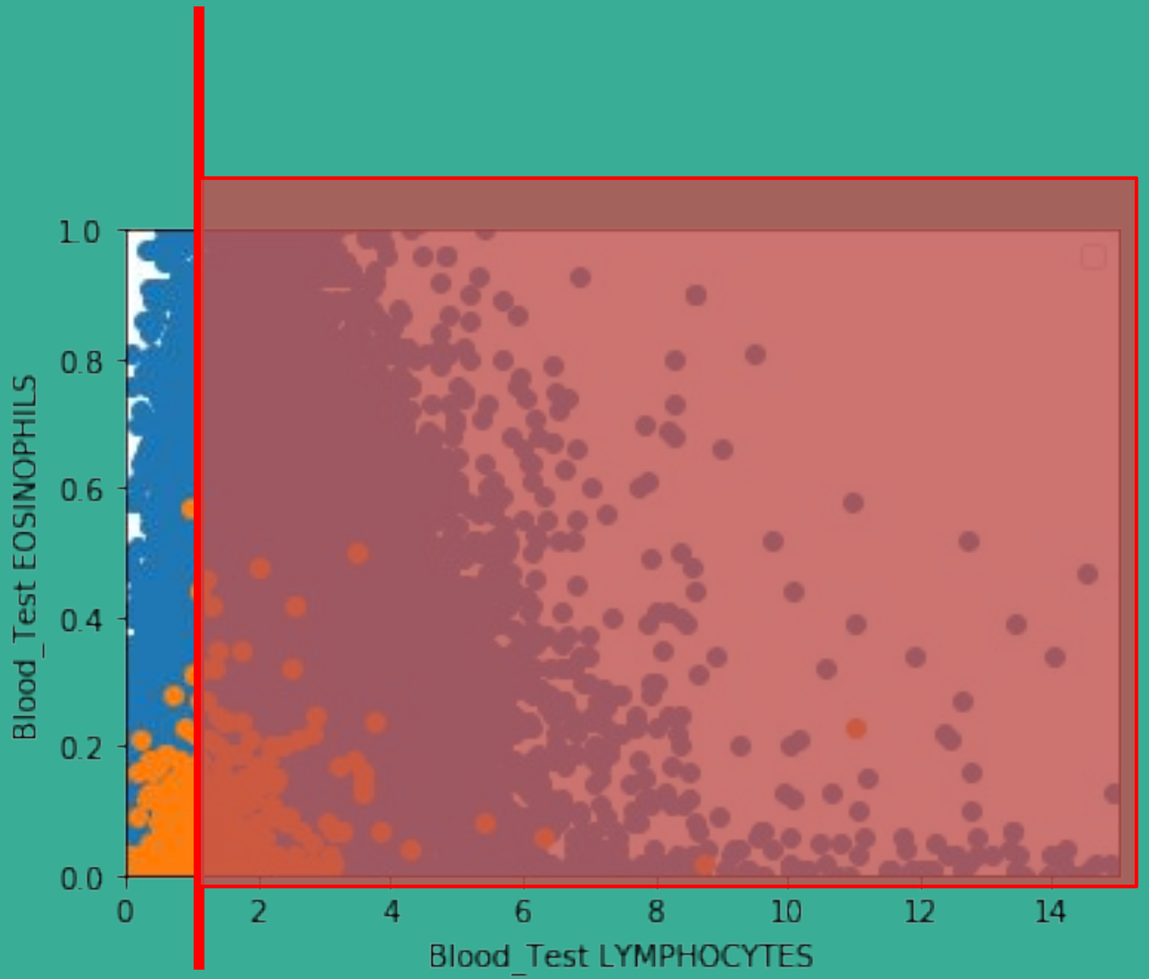
Which features are most important?





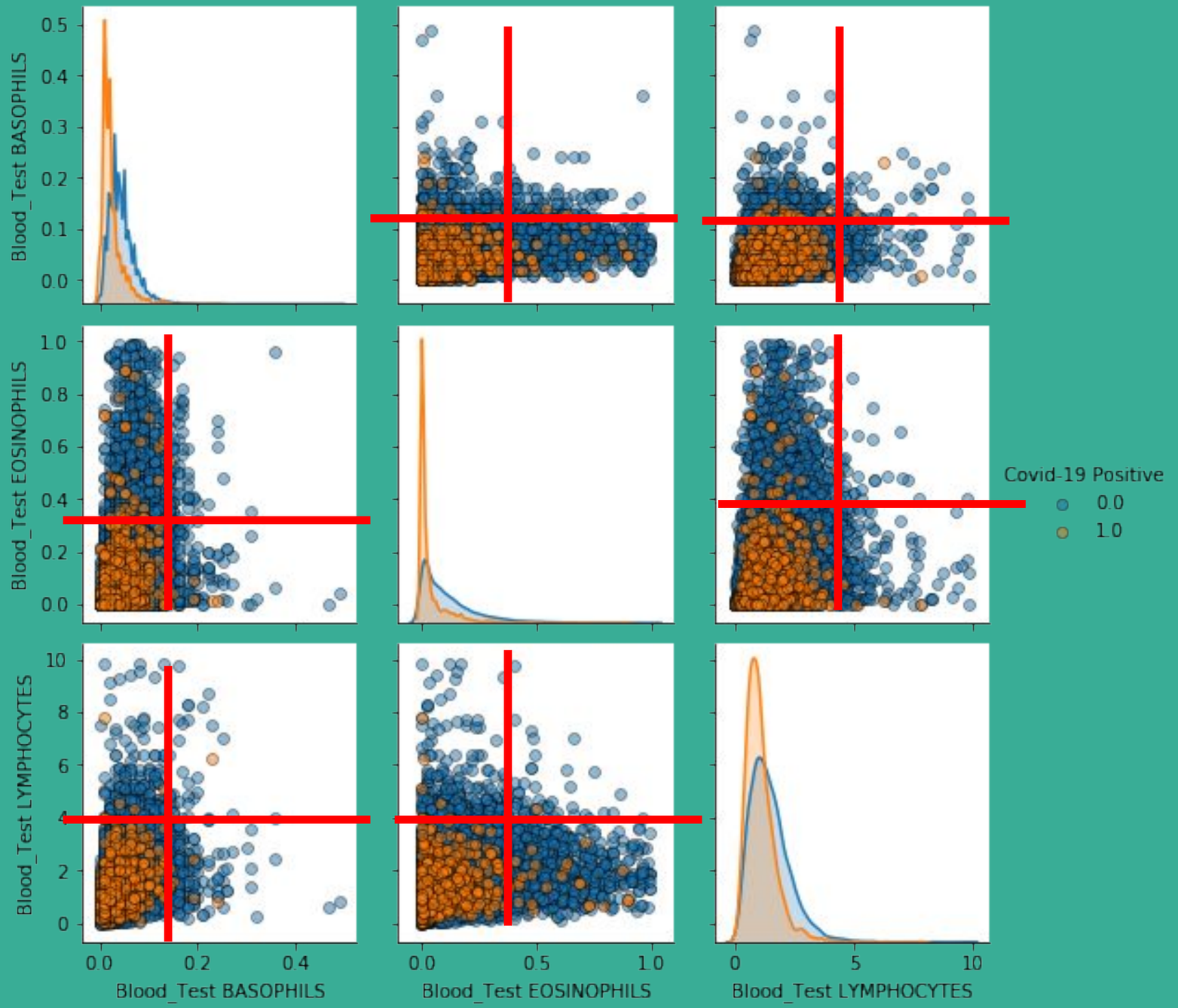
Soltan et al 2020, Lancet Digital Health

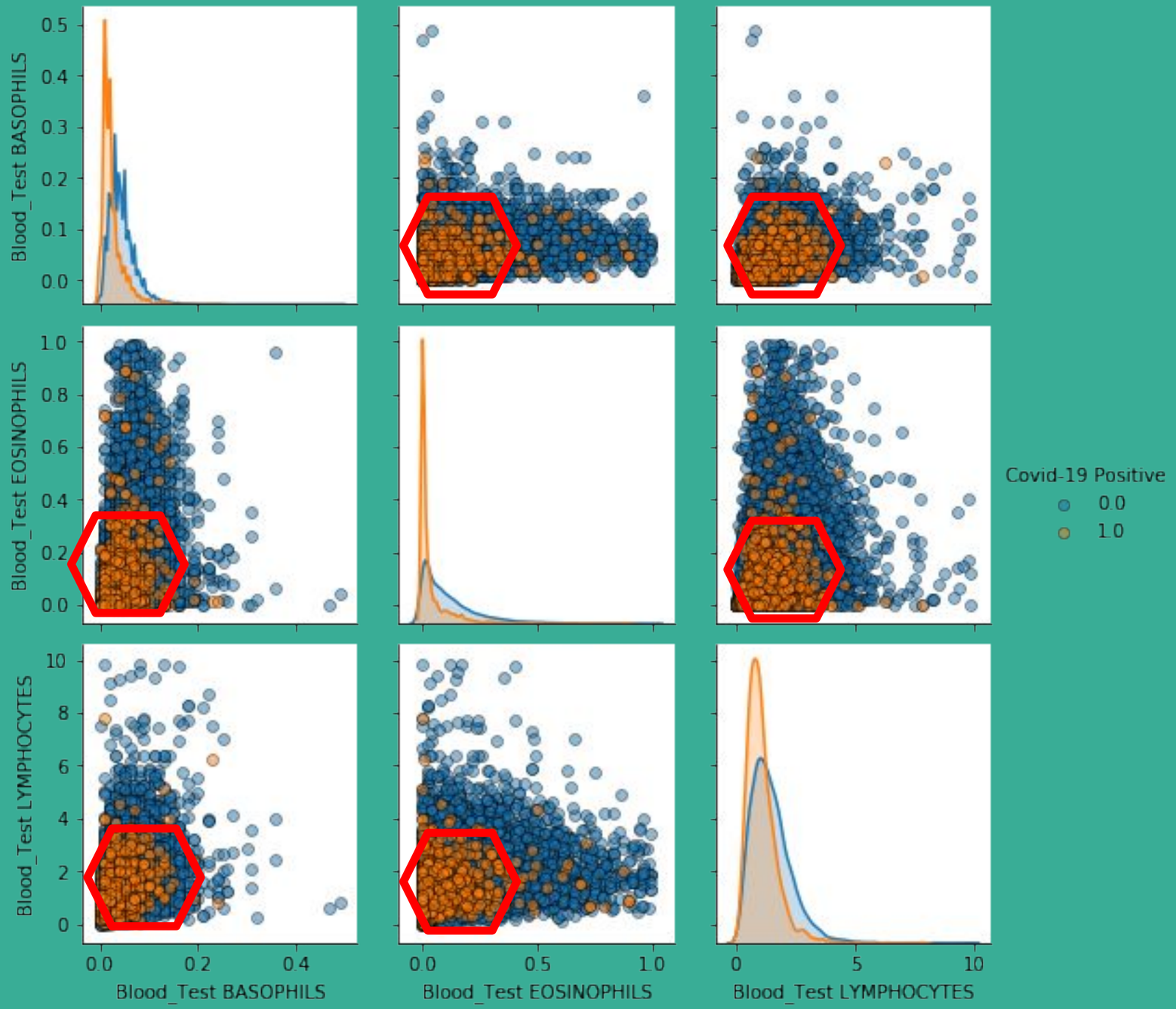


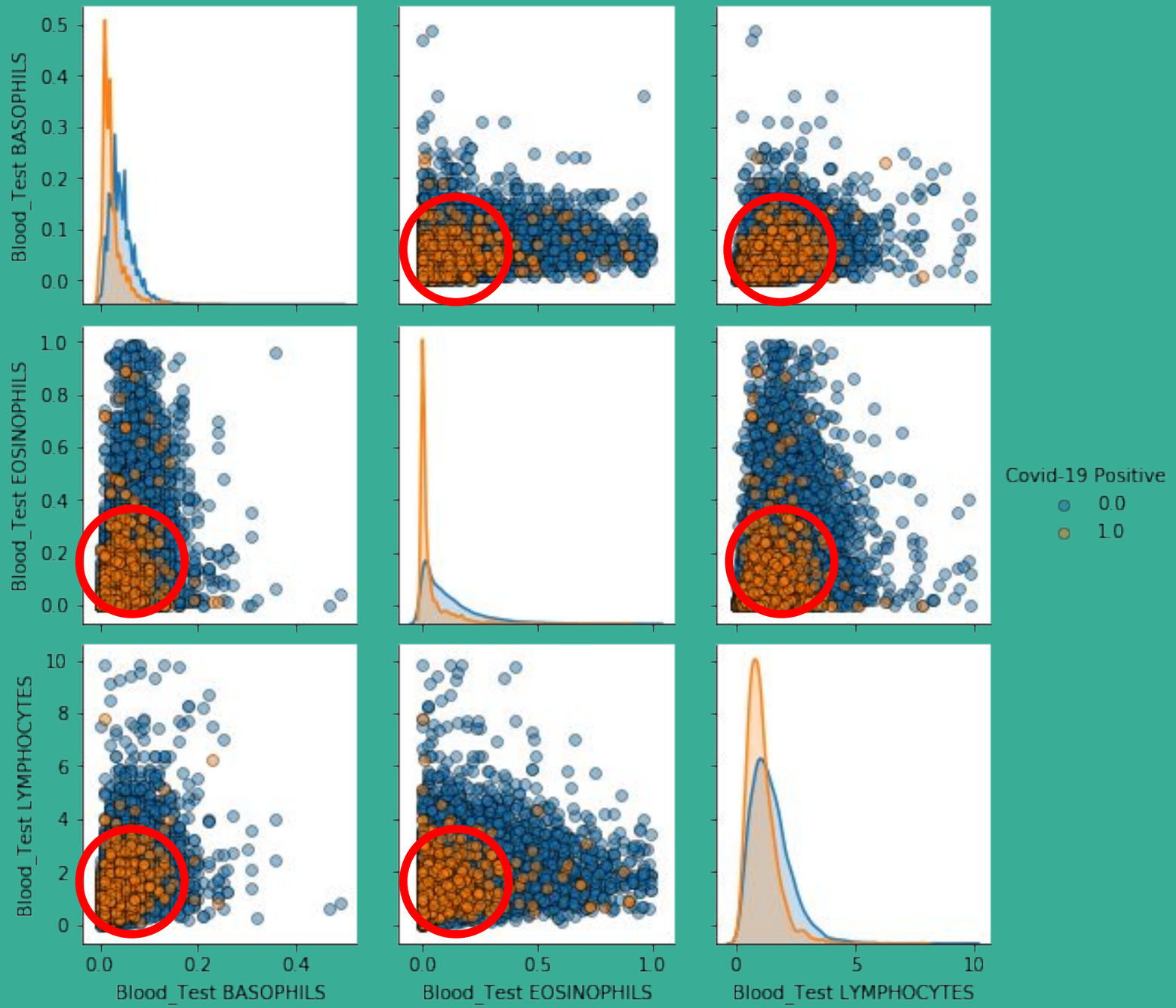


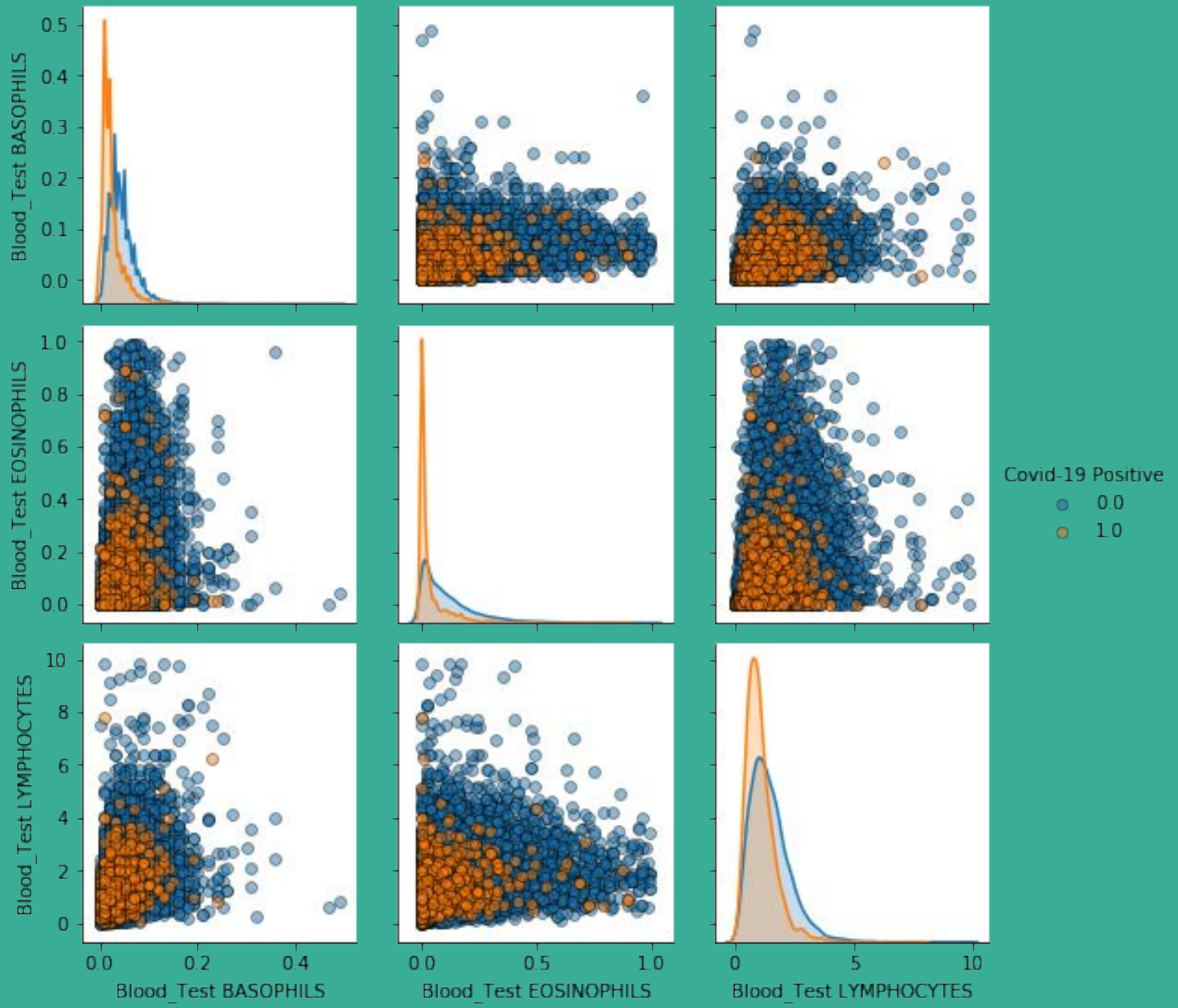
Lymphopenia?

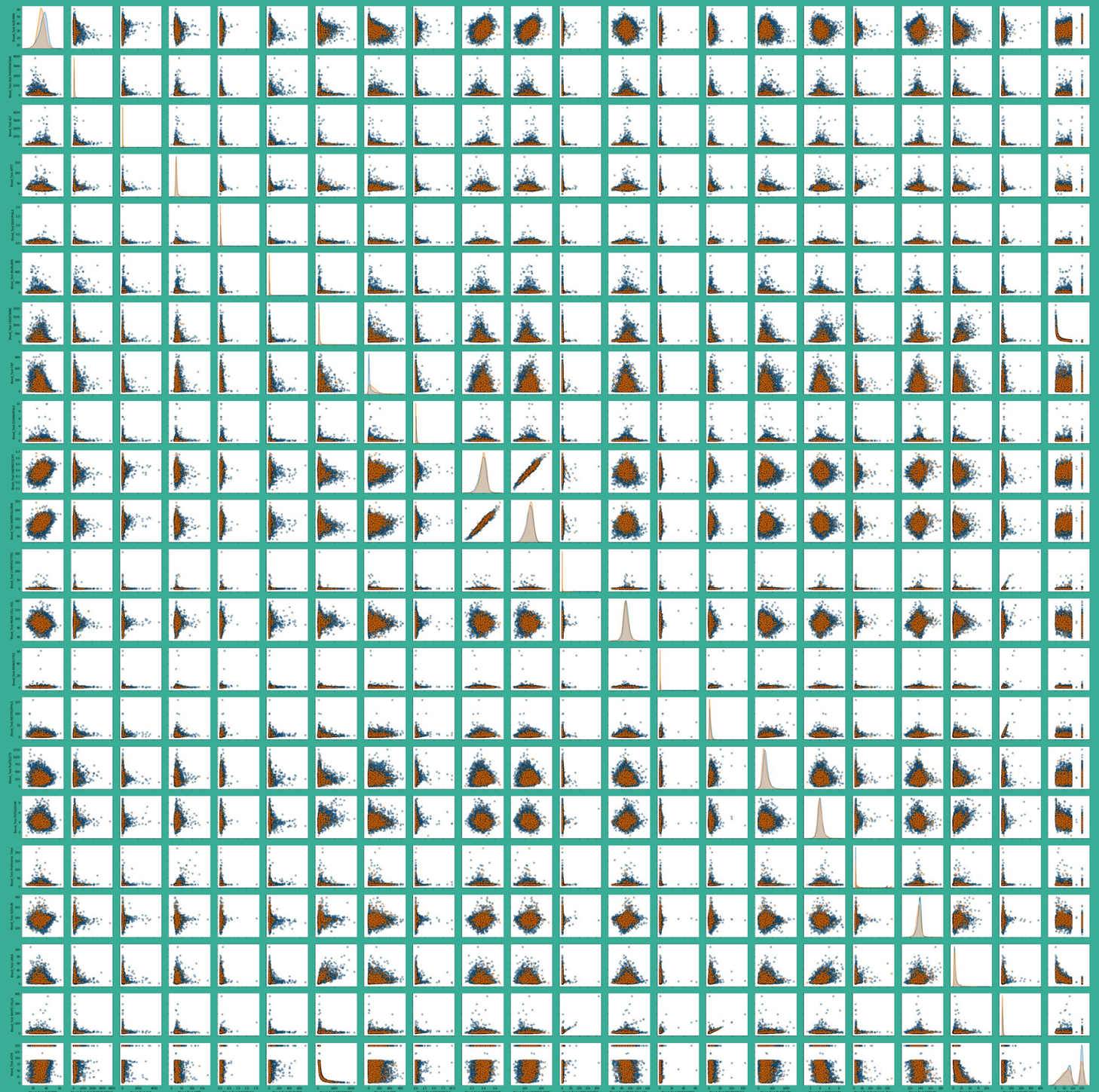
Unpublished analyses, All OUH ED visits

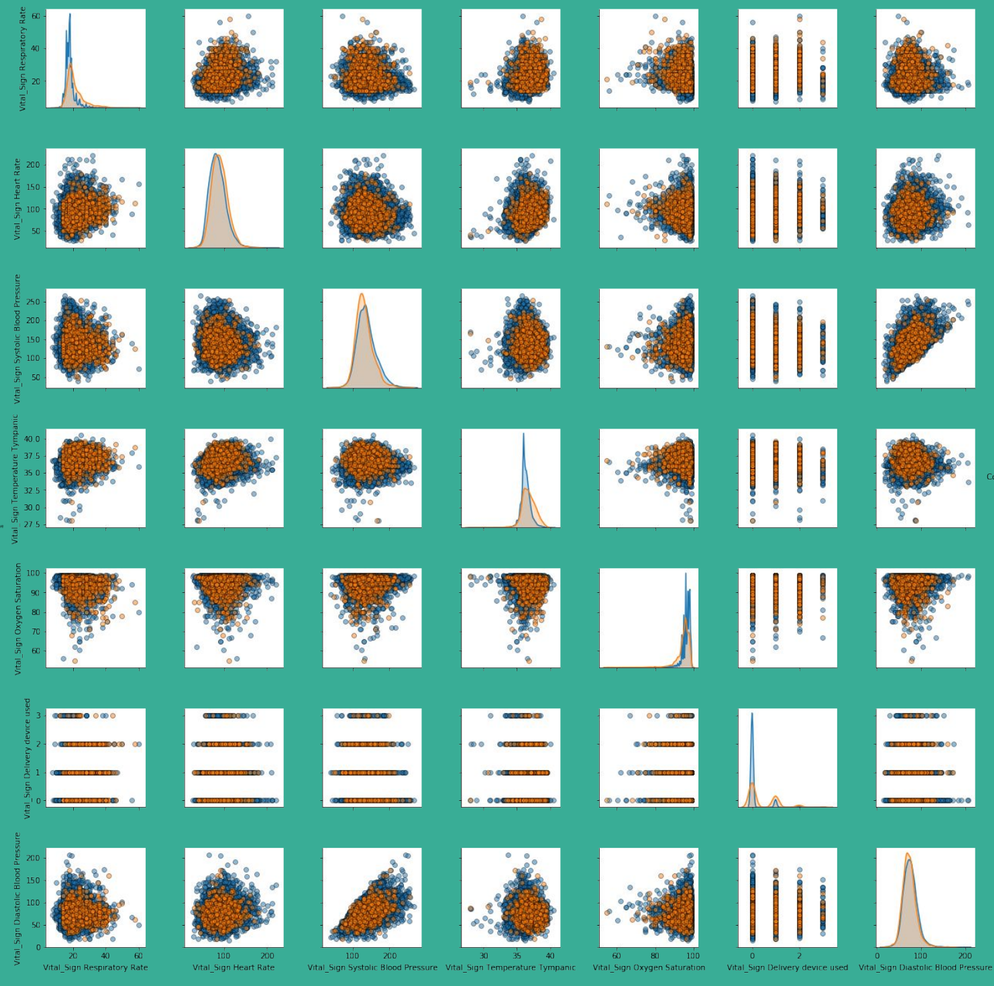

Blood_Test BASOPHILS
Blood_Test EOSINOPHILS
Blood_Test LYMPHOCYTES
Covid-19 Positive
0.0
1.0


Blood_Test BASOPHILS
Blood_Test EOSINOPHILS
Blood_Test LYMPHOCYTES
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.8
1.0
2
4
6
8
10
0.0
0.2
0.4
0.5
1.0
0
5
10
Covid-19 Positive
0.0
1.0


Blood_Test BASOPHILS
Blood_Test EOSINOPHILS
Blood_Test LYMPHOCYTES
Covid-19 Positive
0.0
1.0


Blood_Test BASOPHILS
Blood_Test EOSINOPHILS
Blood_Test LYMPHOCYTES
Covid-19 Positive
0.0
1.0




Vital_Sign Respiratory Rate
Vital_Sign Heart Rate
Vital_Sign Systolic Blood Pressure
Vital_Sign Temperature Tympanic
Vital_Sign Oxygen Saturation
Vital_Sign Delivery device used
Vital_Sign Diastolic Blood Pressure
Covid-19 Positive
0.0
1.0

CURIAL

>$105bn

Total Global COVID-19 Testing Market

£1.77bn UK NHS hospital inpatient only

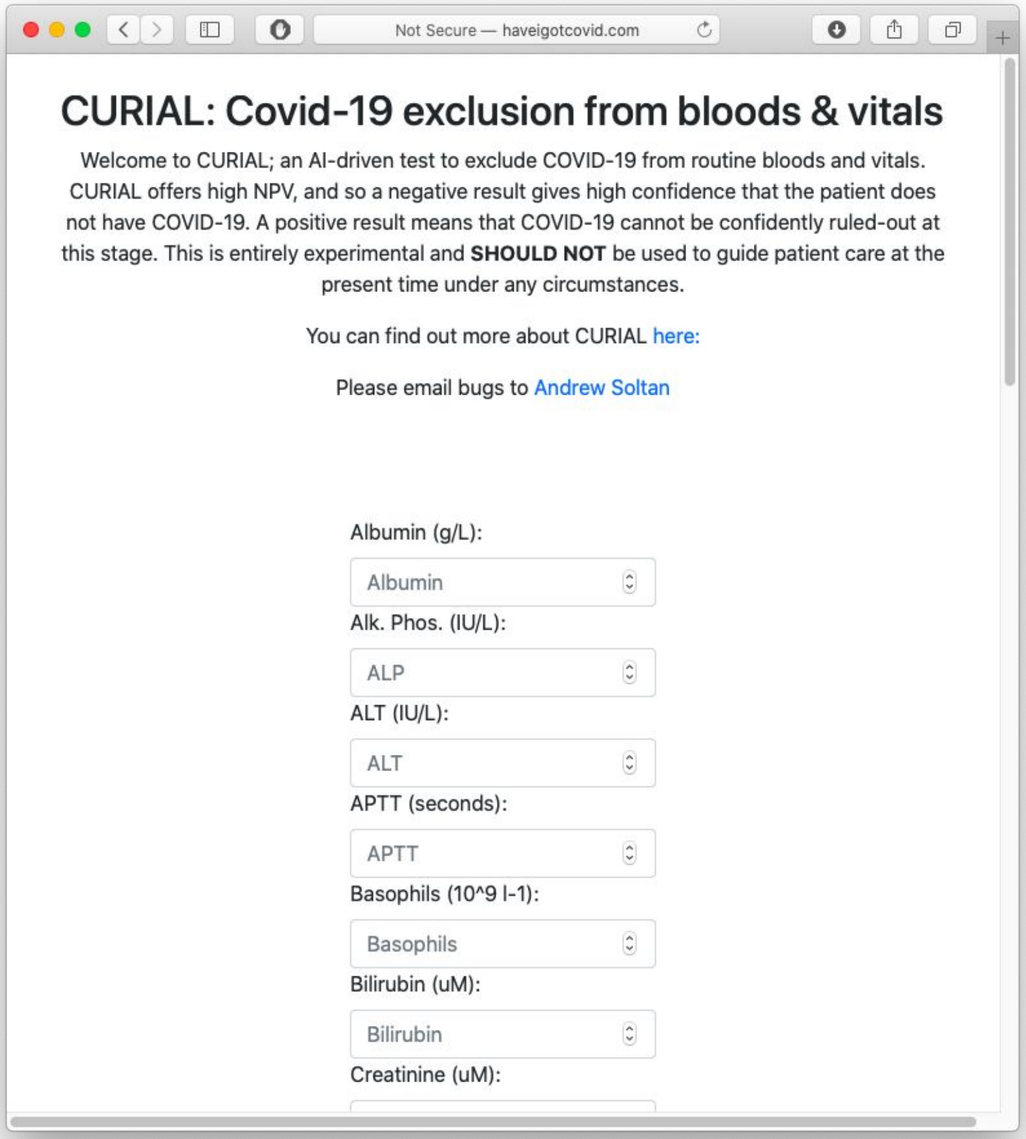
$9.94bn USA hospital inpatient market

NICE Health Technologies Approval Requirements

Evidence standards framework for digital health technologies (ECD7)

Evidence category	Minimum evidence standard	Best practice standard
Demonstrating effectiveness for treat, active monitoring, calculate or diagnose functions	High-quality intervention study (experimental or quasi-experimental design) showing improvements in relevant outcomes, such as: • diagnostic accuracy • patient-reported outcomes (preferably using validated tools) including symptom severity or quality of life • other clinical measures of disease severity or disability • healthy behaviours • physiological measures • user satisfaction and engagement. Generic outcome measures may also be useful when reported alongside condition-specific outcomes. The comparator should be a care option that is reflective of the current care pathway, such as a commonly used active intervention.	High-quality randomised controlled study or studies done in a setting relevant to the UK health and social care system, comparing the digital health technology (DHT) with a relevant comparator and demonstrating consistent benefit including in clinical outcomes in the target population, using validated condition-specific outcome measures. Alternatively, a well-conducted meta-analysis of randomised controlled studies if there are enough available studies on the DHT.

Evidence category	Minimum evidence standard	Best practice standard
Credibility with UK health and social care professionals	Be able to show that the DHT has a plausible mode of action that is viewed as useful and relevant by professional experts or expert groups in the relevant field. Show that relevant clinical or social care professionals working in the UK health and social care system have either been involved in designing, developing or testing the DHT, or given their informed approval.	Published or publicly available evidence documenting that the DHT has a plausible mode of action that is viewed as useful and relevant by professional experts or expert groups in the relevant field. Show that relevant clinical or social care professionals working in the UK health and social care system have either been involved in designing, developing or testing the DHT, or given their informed approval.
Relevance to current care pathways in the UK health and social care system	Evidence to show that the DHT has been successfully piloted in the UK health and social care system, showing that it is relevant to current care pathways and service provision in the UK. Also evidence that the DHT is able to perform its intended function to the scale needed (for example, having servers that can scale to manage the expected number of users).	Evidence to show successful implementation of the DHT in the UK health and social care system.
Acceptability with users	Be able to show that representatives from intended user groups were involved in the design, development or testing of the DHT. Provide data to show user satisfaction with the DHT.	Published or publicly available evidence to show that representatives from intended user groups were involved in the design, development or testing of the DHT, and to show that users are satisfied with the DHT.



Early access ‘MDCalc-style’ version available online today:
http://haveigotcovid.com

<u>Results:</u>
‘Not-Covid’: High NPV rule-out of Covid-19
‘Covid-19 Not excluded’: Threshold to confidently exclude Covid-19 not met, await swab

CURIAL