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Routine molecular point-of-care testing for SARS-CoV-2 reduces hospital-acquired COVID-19

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Abstract:	Objectives Risk of hospital-acquired COVID-19 (HA-COVID-19) infection is increased by cohorting infected and non-infected patients together in assessment areas, whist awaiting laboratory PCR results. Molecular point-of-care tests (mPOCT) reduce time to results and improve patient flow but the impact on HA-COVID-19 is unknown. Methods In this pre and post implementation study patients were evaluated across two time periods: March 1st to August 13th 2020, prior to the introduction of mPOCT in medical admissions areas, and 14th August 2020 to 1st April 2021, after mPOCT introduction. The primary outcome was proportion of HA-COVID-19 infection among all COVID-19 positive patients. Secondary outcome measures included time to SARS-CoV-2 results, length of time spent in the medical assessment area and comparison of local, regional and national proportions of HA-COVID-19. Results 1988 patients were admitted through the acute medicine admission cohorting area and tested for SARS-CoV-2 prior to introducing mPOCT and 4640 afterwards. Median (IQR) time to SARS-CoV-2 result was 6.5 (2.1-17.9) hours prior to introducing mPOCT and 1.0 (0.8-1.3) hours afterwards (p<0.0001). Median (IQR) duration in the assessment cohort area was 12.0 (4.8-20.6) hours prior to introduction of POCT and 3.2 (2.0-5.6) hours afterwards (p<0.0001). The proportion of hospital-acquired COVID-19 cases was 108 (16.5%) of 654 prior to introducing mPOCT compared with 168 (9.4%) of 1782 afterwards, (HR 0.55, 95%CI 0.43-0.70; p<0.0001). In the period following the introduction of mPOCT up to 1st April 2021 the median proportion of HA-COVID-19 was 13.6% (95% CI 8.2% - 18.9%) locally, compared with 43.8% (95% CI 37.8%-49.9%) for all acute NHS trusts regionally and 30.9% (95% CI 28.4%-33.5%) for all NHS trusts nationally.

	Conclusions Routine mPOCT for SARS-CoV-2 was associated with reduced time to results, time spent in admission cohort areas, and hospital-acquired COVID-19, compared to laboratory PCR.

19th November 2021

Dear Professor Read,

Many thanks for considering our article "Routine molecular point-of-care testing for SARS-CoV-2 reduces hospital-acquired COVID-19" for consideration of publication in the *Journal of Infection*.

In this paper we describe the impact of introducing molecular point of care testing (mPOCT) for SARS-CoV-2 on the rate of hospital acquired COVID-19 (HA-COVID-19) infections at a large tertiary teaching hospital in the South of England. This pre and post implementation study shows that mPOCT reduced the proportion of HA-COVID-19 by around 50% and we estimate that this intervention prevented over 100 cases of hospital acquired COVID-19 and saved around 35 lives at our trust, which serves about 1% of the UK population. We feel that the study is significantly novel with findings that are relevant to patient care across the NHS and as such would be of interest to a large readership and is likely to be highly cited.

The manuscript, including related data, figures and tables is original work which has not been previously published and is not under consideration elsewhere. All authors have made substantial contributions to either the design of the study, acquisition and analysis of data or drafting/revision of the main text.

Thank you for considering this manuscript for publication.

Yours sincerely,

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On behalf of all authors

16th January 2022

Dear Professor Read,

Many thanks for your comments on our article “Routine molecular point-of-care testing for SARS-CoV-2 reduces hospital-acquired COVID-19”.

We provide the following responses to your comments:

Comment 1

I am happy to accept this more or less as it is, but the abstract could be improved (the last line of the methods paragraph is incomplete and the comparison to regional data could be included)

Response 1

We have clarified and expanded upon the methods section of the abstract, and defined our primary and secondary outcomes. We have also commented upon our comparison to regional and national data in the methods and results section of the abstract.

Yours sincerely,

Dr Rob Livingstone
University Hospital Southampton

Routine molecular point-of-care testing for SARS-CoV-2 reduces hospital-acquired COVID-19

Running Title: Point-of-care testing reduces hospital-acquired COVID

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Summary

Objectives Risk of hospital-acquired COVID-19 (HA-COVID-19) infection is increased by cohorting infected and non-infected patients together in assessment areas, whist awaiting laboratory PCR results. Molecular point-of-care tests (mPOCT) reduce time to results and improve patient flow but the impact on HA-COVID-19 is unknown.

Methods In this pre and post implementation study patients were evaluated across two time periods: March 1st to August 13th 2020, prior to the introduction of mPOCT in medical admissions areas, and 14th August 2020 to 1st April 2021, after mPOCT introduction. The primary outcome was proportion of HA-COVID-19 infection among all COVID-19 positive patients. Secondary outcome measures included time to SARS-CoV-2 results, length of time spent in the medical assessment area and comparison of local, regional and national proportions of HA-COVID-19.

Results 1988 patients were admitted through the acute medicine admission cohorting area and tested for SARS-CoV-2 prior to introducing mPOCT and 4640 afterwards. Median (IQR) time to SARS-CoV-2 result was 6.5 (2.1-17.9) hours prior to introducing mPOCT and 1.0 (0.8-1.3) hours afterwards (p<0.0001). Median (IQR) duration in the assessment cohort area was 12.0 (4.8-20.6) hours prior to introduction of POCT and 3.2 (2.0-5.6) hours afterwards (p<0.0001). The proportion of hospital-acquired COVID-19 cases was 108 (16.5%) of 654 prior to introducing mPOCT compared with 168 (9.4%) of 1782 afterwards, (HR 0.55, 95%CI 0.43-0.70; p<0.0001). In the period following the introduction of mPOCT up to 1st April 2021 the median proportion of HA-COVID-19 was 13.6% (95% CI 8.2% - 18.9%) locally, compared

with 43.8% (95% CI 37.8%-49.9%) for all acute NHS trusts regionally and 30.9% (95% CI 28.4%-33.5%) for all NHS trusts nationally,

Conclusions Routine mPOCT for SARS-CoV-2 was associated with reduced time to results, time spent in admission cohort areas, and hospital-acquired COVID-19, compared to laboratory PCR.

Keywords - Point-of-Care Testing; Hospital acquired infection; COVID-19; SARS-CoV-2

Highlights

- Cohorting of patients at admission increases the risk of hospital-acquired COVID-19
- Point-of-care testing (POCT) reduced time to results compared with laboratory PCR
- POCT reduced the time that patients spent in cohort areas
- POCT was associated with a reduction in the risk of hospital-acquired COVID-19

Introduction

Timely recognition and management of COVID-19, caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is critical in preventing onward transmission to other patients in hospital [1]. NHS data suggests that by May 2021 over 32,000 hospital-acquired COVID-19 cases had occurred with nearly 9000 associated deaths [2]. A recent nationwide study has estimated that during the first wave of the pandemic 11.3% of patient with COVID-19 in UK hospitals had acquired their infection in hospital [3]. In addition, genome sequencing-based studies from the UK suggest that the vast majority of hospital-acquired COVID-19 (HA-COVID-19) originates from patient-to-patient transmission [4].

Although multiple factors are implicated in hospital transmission of SARS-CoV-2, delays in SARS-CoV-2 test results have been recognised as being among the leading causes [1,5]. The risk of patient-to-patient transmission is increased when single room capacity is exceeded by the number of suspected cases with an unconfirmed COVID-19 status as this leads to the practice of cohorting of acute hospital admissions in assessment wards whilst awaiting SARS-CoV-2 results, inadvertently leading to co-location of infected and non-infected patients in shared bay areas. Reducing the amount of time that patients spend in assessment cohort areas is therefore key to reducing both patient-to-patient transmission. Rapid downstream flow of SARS-CoV-2 positive patients to designated COVID-19 wards allows optimal use of facilities providing patient isolation, adequate ventilation, and clinical care from designated staff with appropriate personal protective equipment [1].

Centralised laboratory SARS-CoV-2 polymerase chain reaction (PCR) testing is associated with long delays in returning results, representing the rate-limiting step in effective patient flow through the hospital [6]. Molecular point-of-care testing (mPOCT) has been shown to significantly reduce the time from admission to test results for SARS-CoV-2 and to reduce the length of time spent in assessment cohort areas, however its effect on HA-COVID-19 is unknown [6].

Methods

Study design and patients

We performed a single centre, pre and post implementation study in a tertiary hospital in the UK. We analysed the records of all medical admissions tested for SARS-CoV-2 with laboratory PCR or mPOCT, and all positive cases across specialities, between 1st March 2020 and 1st April 2021 at University Hospital Southampton Foundation Trust (UHSFT), a large acute teaching hospital in the South of England serving a population of 1.9 million [7].

Following local R&D governance review formal application for ethical approval was deemed unnecessary, as only routinely collected, pseudo-anonymised data was used, this study was prospectively approved by senior trust governance. Ref No: SEV/0320.

Point of care testing for SARS-CoV-2

Routine molecular point-of-care testing for SARS-CoV-2 and other respiratory viruses was introduced on the 13th August 2020 for patients admitted under the department of medicine via the acute medical admission pathway. Following device validation and a period of staff training all patients admitted to the Acute Medical Unit (AMU) had a nose and throat swab taken at arrival and tested using the BioFire (Salt Lake City, USA) FilmArray Respiratory PCR Panel 2.1 plus which includes targets for SARS-CoV-2 and 17 other respiratory viruses and atypical bacteria (for full details of the panel targets see supplementary material). The FilmArray SARS-CoV-2 Respiratory Panel 2.1 plus SARS-CoV-2 assay contains gene targets for the S gene and M gene. Patient swabs were collected directly into guanidine thiocyanate containing media tubes (Medical Wire molecular medium) to inactivate viruses and then tested on the FilmArray Torch platform located

within a dedicated testing hub within the AMU. Nursing staff wearing appropriate personal protective equipment performed the testing and the run time of the test was around 45 minutes. The FilmArray systems were integrated with the hospitals Laboratory Information Management System (LIMS) and the electronic patient records so that results were available to clinical and infection control teams as soon as the run was completed.

Pre and post implementation time periods

Patients were analysed over two time periods: from March 1st, 2020 to August 13th, 2020, prior to introducing routine use of mPOCT in the AMU, when medical patients were tested for SARS-CoV-2 using laboratory testing within the on-site PHE microbiology laboratory, and August 14th 2020 to April 1st 2021, after the introduction of routine mPOCT in the AMU. For both periods, patients admitted outside of the acute medical admissions pathway were tested with laboratory PCR.

Outcomes

The primary outcome measure was the proportion of hospital-acquired COVID-19 infection among all COVID-19 positive patients. HA-COVID-19 infection was defined in two ways, firstly as detection of SARS-CoV-2 RNA at any time point after 48 hours of admission and secondly where patients had previously tested negative as detection of SARS-CoV-2 RNA at any time point after 7 days of admission, in keeping with the NHS England definition of probable hospital-acquired infection [8].

Secondary outcome measures included time to results (defined as time from SARS-CoV-2 test request to time result was available to the clinical teams, in hours) and length of time

spent in the AMU assessment area (in hours), the proportion of HA-COVID-19 cases in patients tested with mPOCT and laboratory PCR, the proportions of HA-COVID-19 at UHSFT, across the southern region and nationally (calculated from routinely collected data from acute NHS trusts).

Patients and pathways

For the primary outcome, analysis of proportion of HA-COVID-19 infection was undertaken in all hospitalised COVID-19 patients at UHSFT. This included all patients over the study period admitted under any hospital speciality, testing positive for SARS-CoV-2. Patients who were admitted directly to the intensive care unit or not admitted to a downstream hospital ward were excluded.

For the secondary outcomes, analyses of time to results and time spent in the AMU assessment area were undertaken in all patients admitted under the department of medicine via the acute medical admission pathway and tested for SARS-CoV-2 with laboratory PCR or mPOCT.

Data collection and preparation

Baseline characteristic data was collected for all patients including age, gender, ethnicity, comorbidities and body mass index (BMI). Binary variables were derived for comorbidities from the casemix database using the appropriate codes for: previous myocardial infarction, congestive cardiac failure, peripheral vascular disease, previous stroke or TIA, dementia, COPD, connective tissue disease, peptic ulcer disease, liver disease, diabetes, hemiplegia,

chronic kidney disease, cancer (solid/lymphoma/metastatic) and HIV/AIDS. These were used to calculate the Charlson Comorbidity Index (CCI) for each patient.

Data was retrieved to flag use of mPOCT at admission and those patients on a non-medical admission pathway as defined by specialty destination ward code to exclude this as a potential confounder.

Data were extracted from structured and/or unstructured components of the electronic health record (EHR) at our institution. All data was handled securely on-site using python 3.7 and associated packages. Further details regarding data processing including pseudonymisation are presented in the supplementary materials – Supplement A.

Statistical Analysis

Analysis was done using Prism version 9.2 (GraphPad Software Inc; La Jolla, California), and Python version 3.7 + packages. All continuous parameters were summarised using either mean or median and interquartile range (IQR) as appropriate. Proportions and confidence intervals were used for categorical data. The Mann-Whitney U test was used to compare medians and mean differences and corresponding CIs were calculated with the Hodges-Lehmann estimate. Groups were compared using chi-square tests or Fishers exact test for equality of proportions, as appropriate based on group size.

Multivariate model

We evaluated time from hospital admission to hospital-acquired infection amongst the COVID-19 positive patients accounting for competing risks and right-censored data (i.e.

patients still in hospital at the time of censoring) using the Nelson-Aelen and Kaplan-Meier estimators, respectively. We used adjusted and unadjusted cox proportional hazards regression to assess predictors of risk for hospital-acquired COVID-19 infection and their impact compared to our primary covariate – mPOCT. Variables with a *p* value below 0.05 in adjusted regression were considered significant. Variables such as BMI with a greater than 20% rate of missingness were excluded from regression analysis. The proportional hazards assumptions were evaluated using Schoenfeld's residuals [9]. The Ljung-Box and Box-Pierce tests were used to prove that the residuals were not autocorrelated.

Role of funding source

The funders of the study had no role in the study conception, design, conduct, data analysis, or manuscript preparation. The corresponding author had full access to all data and the final responsibility to submit for publication.

Results

We identified 6944 patients admitted and tested for SARS-CoV-2 through the acute medical admissions pathway with laboratory PCR or mPOCT during the study period from 1st March 2020 to 1st April 2021. Full data on time to results was available for 6628 patients: 1988 prior to introduction of routine mPOCT (1st March 2020 to 13th August 2020) and 4640 after the introduction of routine mPOCT (14th August 2020 to 1 April 2021), shown in Figure 1.

Median (IQR) age in the pre mPOCT period was 75 years (57-85) and was 74 (54-85) years in the post mPOCT period. 1023 (51.5%) of 1099 patients were male in the pre-mPOCT period compared with 2527 (54.5%) of 2527 in the post mPOCT period. Overall, a higher proportion of patients had co-morbidities in the pre- mPOCT group compared to the post mPOCT group. Baseline characteristics for the patients admitted through the acute medical admission pathway are shown in Table 1.

The median (IQR) time from admission to SARS-CoV-2 result was 6.5 (2.1-17.9) hours prior to introducing mPOCT and 1.0 (0.8-1.3) hours afterwards (difference of 5.5 hours, 95%CI (5.2 to 5.8); p<0.0001), shown in Figure 2a. Median (IQR) length of stay in the assessment cohort area was 12.0 (4.8 to 20.6) hours prior to the introduction of POCT and 3.2 (2.0 – 5.6) hours afterwards (difference of 8.8 hours, 95%CI 8.5 to 9.1; p<0.0001), shown in Figure 2b. This is equivalent to 367 COVID-19 assessment area bed-days saved for every 1000 patient cohort area journeys. Given that there were 9878 patient journeys through the cohorting area after the introduction of mPOCT this is equivalent to 3,625 bed days saved in the assessment cohort area in total.

2436 individuals were admitted with COVID-19 or were diagnosed whilst in hospital, during the study period; 654 prior to the introduction of routine mPOCT and 1782 afterwards, shown in Figure 3. Baseline characteristics for both groups are shown in Table 2.

Following the introduction of routine mPOCT, the proportion of HA-COVID-19 fell from 178 (27.2%) of 654 to 317 (17.8%) of 1782 (HR 0.63, 95%CI 0.52-0.75; p<0.0001), when defined as a SARS-CoV-2 PCR positivity after 48 hours of admission, and from 108 (16.5%) of 654 to 168 (9.4%) of 1782 (HR 0.55, 95%CI 0.43-0.70; p<0.0001), when defined as SARS-CoV-2 PCR positively after 7 days of admission, shown in Figure 4a and b.

Following the introduction of mPOCT, the proportion of HA-COVID-19 across the hospital was lower in the patients who were tested with mPOCT compared with laboratory testing, both when defined as SARS-CoV-2 PCR positivity after 48 hours of admission; 139 (12.3%) of 1133 vs 178 (27.4%) of 649 (HR 0.41, 95% CI 0.33-0.52; p<0.0001) and after 7 days 69 (6.1%) of 1133 Vs 99 (15.3%) of 649 (HR 0.38, 95%CI 0.28-0.52; p<0.0001), shown in Figure 5a and 5b. Multivariate time series regression, adjusting for age, gender and CCI demonstrated a similar reduction in HA-COVID-19 infection (HR 0.30, 95% CI 0.22-0.41; p<0.0001) with comorbidity (CCI) also associated with the risk of HA-COVID-19 (HR 1.13, 95% CI 1.07-1.21; p<0.0001), shown in Figure 6.

74/1782 (4.2%) of patients in this time period were admitted via a surgical admission pathway. The proportion of HA-COVID-19 was 32 (43.2%) of 74 patients in this patient group (HR 3.82, 95% CI 2.54 – 5.74; p<0.0001, compared with 136 (8.0%) of 1708 amongst patients admitted via medical and other pathways (HR 0.38, 95% CI 0.27 – 0.52; p<0.0001), shown in

Figure S1. Schoenfeld residual testing revealed no autocorrelation within the model with the Ljung-box test and Box Peirce tests confirming this (p=0.989 and 0.999 respectively) suggesting that the variables in our time series analysis are independent of each other. 527 (29.5%) of 1782 patients lacked either a usable height or weight thus BMI could not be used for regression. 226 (12.7%) of 1782 patients had their ethnicity recorded as 'other' or 'unknown'. The addition of this variable had no significant impact on the model, p=0.111.

Across the entire study period 417 (17.0%) of 2436 COVID-19 patients died whilst in hospital. 68 (24.6%) of 276 patients with HA-COVID-19 died compared with 349 (16.2%) of 2160 with community-acquired infection (RR 1.75 ,95%CI: 1.40 - 2.19; p<0.0001). mPOCT was associated with a reduced risk of HA-COVID-19 (RR of 0.34, 95%CI 0.26 – 0.43; p<0.0001) with a number needed to test (NNT) of 8.8 (95%CI: 7.2 – 11.3) to prevent a single HA-COVID-19 infection. This suggests that around 140 HA-COVID-19 episodes were prevented at UHSFT after the introduction of mPOCT, resulting in around 35 fewer deaths.

In the period following the introduction of mPOCT up to 1st April 2021 the median proportion of HA-COVID-19, defined as PCR positivity >7 days after admission to hospital, was 13.6% (95% CI 8.2% - 18.9%) at UHSFT compared with 43.8% (95% CI 37.8%-49.9%) for all acute NHS trusts in the South of England and 30.9% (95% CI 28.4%-33.5%) for all NHS trusts nationally, shown in Figure 7.

Discussion

To our knowledge, this real-world study is the first to assess the impact of routine use of mPOCT in an admission pathway, upon HA-COVID-19 infection rates. Consistent with the results of our previous trials, we have demonstrated in that routine use of mPOCT in acute hospital admissions significantly reduced the time to SARS-CoV-2 results and the time that patients spent in assessment cohort areas [6]. In addition, we have also demonstrated in this study that that the introduction of mPOCT in our institution was associated with a large reduction in the rate of HA-COVID-19. Molecular point-of-care testing is likely to reduce HA-COVID-19 by providing a rapid accurate result, allowing patients with SARS-CoV-2 infection to be identified early and transferred to definitive care areas before they are able to transmit infection to other patients in the assessment areas. According to nationally available data [10] 280,737 patients were admitted to hospital or diagnosed with COVID-19 whilst in hospital in England during our study period. Based on these data 86,832 of these patients are likely to have contracted COVID-19 in hospital. Extrapolating from our data around 52,100 of these infections could have been prevented by nationally deploying mPOCT for acute admissions, potentially resulting in 13,025 fewer COVID-19 related deaths. Although the availability of mPOCT test platforms for SARS-CoV-2 was severely limited during the early part of the pandemic, there are now several widely available test platforms with high levels of accuracy demonstrated though national validation [11] that can be deployed in hospitals at the point-of-care or in near-patient settings.

The strengths of the study include its real-world nature. We have performed a pre and post implementation study in a typical acute NHS setting with a large number of patients over a prolonged period of time, suggesting that our results are generalisable to similar UK and

international centres. Our study also has a number of potential weaknesses. It was observational, not interventional, and outside the setting of a randomised control interventional trial we are unable to definitively attribute the observed reduction in hospital-acquired COVID-19 infection rates to the introduction of routine mPOCT. There were potential confounding variables within our study as it took place during a period of time with a rapidly changing landscape as the United Kingdom responded to the COVID-19 pandemic. Following the first waves of the pandemic there were a number of changes introduced during the study period in addition to mPOCT that could have influenced HA-COVID-19 rates including staff screening, changes to PPE and infection control practices and staff and community vaccination programmes. We have attempted to control for these by comparing HA-COVID-19 with mPOCT and laboratory testing after the introduction of mPOCT and also by including regional and including national data. As most of these interventions were introduced nationally and at the same time, the lack of a fall in HA-COVID-19 either regionally or nationally over the study period suggests that the changes seen at UHSFT were the result of mPOCT rather than other interventions.

At the end of December 2020, the SARS-CoV-2 lineage B.1.1.7 (VOC 202012/01, 'alpha variant') became the dominant SARS-CoV-2 lineage in the UK [12]. This may also be a confounding factor as altered strain dynamics may impact upon likelihood of nosocomial transmission. Notably, this variant has been associated with increased transmissibility [13] when compared with prior lineages, and therefore are unlikely to be associated with a reduction in hospital-acquired cases. We did not routinely analyse sequencing data from cases within this study, but the local prevalence of the alpha variant was already >50% by December 2020.

NHSE defines probable hospital-acquired COVID-19 as a positive test for SARS-CoV-2 after 7 days of hospital admission [8] to account for the incubation period of SARS-CoV-2, although for other infections hospital-acquired infection is conventionally defined as an infection occurring greater than 48 hours after hospital admission [14] and therefore, use of NHSE definition may significantly underestimate the true rates of HA-COVID-19 infection. Our results show a similar impact of mPOCT upon HA-COVID-19 infection when defined as infection occurring after either 48 hours or after 7 days.

In conclusion, the use of mPOCT as part of the medical admission pathway for COVID-19 significantly reduced the time to results, the time spent on assessment cohort wards and the proportion of HA-COVID-19 infection. Routine use of mPOCT should therefore become the standard of care in hospital admission pathways.

Author contributions

RL – **Drafted and wrote the manuscript.**

LH – **Drafted and wrote the manuscript.**

NJB - **Critical review of manuscript and implemented mPOCT**

SP – **Critical review of manuscript and implemented mPOCT**

ART - **Critical review of manuscript and implemented mPOCT**

FB - **Obtained raw data, helped prepare the data and performed statistical analysis of the data**

TS – **Critical review of manuscript and implemented mPOCT**

MS – **Obtained raw data, transformed the data and performed statistical analysis of the data. Drafted and wrote the manuscript.**

TWC - **Reviewed the medical literature, conceived of and designed the study, participated in the interpretation or data, drafted and wrote the manuscript.**

Declaration of interests

RL – None

LH – None

NJB – None

SP – None

ART - None

FB – None

TS – None

MS – None

TWC has received speaker fees, honoraria, consultancy fees, travel reimbursement, and equipment and consumables free of charge for the purposes of research outside of this submitted study, from BioFire diagnostics and BioMerieux. He has received speaker fees and discounted equipment and consumables from QIAGEN. He has received consultancy fees from Shionogi, Synairgen research,

Randox laboratories and Cidara therapeutics. He has been a member of advisory boards for Roche, Janssen and Cepheid. He is a member of two independent data monitoring committees for trials sponsored by Roche. He has acted as the UK chief investigator for a trial sponsored by Janssen

Data sharing

The data analysed and presented in this study are available from the corresponding author on reasonable request, providing this meets local ethical and research governance criteria.

Acknowledgments

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This study was funded by University Hospital Southampton NHS Foundation Trust.

Figure legends

Figure 1. Patient flow through the study - patients admitted and tested for SARS-CoV-2 through the acute medical admissions pathway

Figure 2a. Median (IQR) time from admission to results, hours

Figure 2b. Median (IQR) length of stay in assessment area, hours

Figure 3. Patient flow through the study - patients testing positive for COVID-19

Figure 4a. Proportion of HA-COVID-19 before and after introduction of mPOCT, when defined as a positive PCR after 48 hours of admission

Figure 4b. Proportion of HA-COVID-19 before and after introduction of mPOCT, when defined as a positive PCR after 7 days of admission

Figure 5a. Proportion of HA-COVID-19 when tested with mPOCT or laboratory testing, when defined as a positive PCR after 48 hours of admission

Figure 5b. Proportion of HA-COVID-19 when tested with mPOCT or laboratory testing, when defined as a positive PCR after 7 days of admission

Figure 6. Multivariate model for HA-COVID-19 when tested with mPOCT or laboratory testing

Figure 7. Median proportions of HA-COVID-19 for UHSFT, the South of England and all of England

Supplementary Appendix

Supplement A: Data Processing and Transformation Steps

Figure S1. Multivariate model for HA-COVID-19 when tested with mPOCT or laboratory testing including surgical admission pathway covariate

References

1. HSIB. COVID-19 transmission in hospitals: management of the risk - a prospective safety investigation [Internet]. HSIB. [cited 2021 Sep 5]. Available from: https://www.hsib.org.uk/investigations-and-reports/covid-19-transmission-in-hospitals-management-of-the-risk/.

2. Up to 8,700 patients died after catching Covid in English hospitals [Internet]. The Guardian. 2021 [cited 2021 Sep 5]. Available from: http://www.theguardian.com/world/2021/may/24/up-to-8700-patients-died-after-catching-covid-in-english-hospitals.

3. Read JM, Green CA, Harrison EM, Docherty AB, Funk S, Harrison J, et al. Hospital-acquired SARS-CoV-2 infection in the UK's first COVID-19 pandemic wave. The Lancet. 2021 Sep;398(10305):1037–8.

4. Illingworth CJ, Hamilton WL, Warne B, Routledge M, Popay A, Jackson C, et al. Superspreaders drive the largest outbreaks of hospital onset COVID-19 infections. Walczak AM, Ogbunugafor CB, Cobey SE, editors. eLife. 2021 Aug 24;10:e67308.

5. David Oliver: Could we do better on hospital-acquired covid-19 in a future wave? BMJ. 2021 Jan 13;372:n70.

6. Brendish NJ, Poole S, Naidu VV, Mansbridge CT, Norton NJ, Wheeler H, et al. Clinical impact of molecular point-of-care testing for suspected COVID-19 in hospital (COV-19POC): a prospective, interventional, non-randomised, controlled study. The Lancet Respiratory Medicine. 2020 Dec 1;8(12):1192–200.

7. Chief Inspector praises 'impatience to improve' at University Hospitals Southampton NHS Foundation Trust | Care Quality Commission [Internet]. [cited 2021 Jul 13]. Available from: https://www.cqc.org.uk/news/releases/chief-inspector-praises-%E2%80%98impatience-improve%E2%80%99-university-hospitals-southampton-nhs.

8. Healthcare associated COVID-19 infections –further actions [Internet]. NHS England and NHS Improvement. 2020 [cited 2021 Sep 5]. Available from: https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/06/Healthcare-associated-COVID-19-infections--further-action-24-June-2020.pdf.

9. Schoenfeld D. Partial Residuals for The Proportional Hazards Regression Model. Biometrika. 1982;69(1):239–41.

10. Statistics » COVID-19 Hospital Activity [Internet]. [cited 2021 Aug 20]. Available from: https://www.england.nhs.uk/statistics/statistical-work-areas/covid-19-hospital-activity.

11. National technical validation process for manufacturers of SARS-CoV-2 (COVID-19) tests [Internet]. GOV.UK. [cited 2021 Sep 5]. Available from: https://www.gov.uk/government/publications/assessment-and-procurement-of-coronavirus-covid-19-tests/coronavirus-covid-19-serology-and-viral-detection-testing-uk-procurement-overview.

12. COVID-19 Infection Survey: estimates of COVID-19 cases to 23 December for England, regions of England and by cases compatible with the new variant - Office for National Statistics [Internet]. [cited 2021 Jun 17]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseas

es/adhocs/12716covid19infectionsurveyestimatesofcovid19casesto23decemberforenglandregionsofenglandandbycasescompatiblewiththenewvariant.

13. Volz E, Mishra S, Chand M, Barrett JC, Johnson R, Geidelberg L, et al. Assessing transmissibility of SARS-CoV-2 lineage B.1.1.7 in England. Nature. 2021 May;593(7858):266–9.

14. World Health Organization. Prevention of hospital-acquired infections : a practical guide [Internet]. World Health Organization; 2002 [cited 2021 Nov 13]. Report No.: WHO/CDS/CSR/EPH/2002.12. Available from: https://apps.who.int/iris/handle/10665/67350

Table 1: Baseline patient characteristics for medical admissions pre and post introduction of molecular point-of-care testing (mPOCT).

	Pre mPOCT group n=1988	**Post mPOCT group n=4640**	**Difference (95%CI)**	**p value[a]**
Age, years	75.2 [57.5-85.3]	73.9 [54.0-84.8]	1.4 (1.1-1.6)	0.0019
Male Sex	1023 (51.5%)	2527 (54.5%)	3% (2.2 – 3.8)	0.0265
BMI[b]	26.0 [22.28-30.06]	26.1 [22.49-30.27]	0.2 (0.1-0.3)	0.2799
BAME[c]	87 (4.6%)	220 (5.1%)	0.5% (0.2-0.8)	0.4611
Asthma	280 (14.1%)	478 (10.3%)	3.8% (3.1–4.4)	<0.0001
COPD	332 (16.7%)	477 (10.3%)	6.4% (5.7-7.2)	<0.0001
CKD	15 (0.8%)	27 (0.6%)	0.2% (0.0-0.4)	0.5204
Diabetes	198 (10.0%)	340 (7.3%)	2.6% (2.1-3.2)	0.0004
Dementia	48 (2.4%)	61 (1.3%)	1.1% (0.8-1.5)	0.0018
Hypertension	861 (43.3%)	1354 (29.2%)	14.1% (13.3 15.0)	<0.0001
IHD	272 (13.7%)	417 (9.0%)	4.7% (4.0-5.4)	<0.0001
CCF	170 (8.6%)	211 (4.6%)	4.0% (3.4-4.6)	<0.0001
Cirrhosis	101 (5.1%)	123 (2.7%)	2.4% (1.9-2.9)	<0.0001
CCI	3.7 (1.7-5.7)	3.1 (1.2-5.0)	0.54 (0.5-0.6)	<0.0001

All data are presented as n (%), median [interquartile range] or mean (SD). CI, confidence interval. BMI, body mass index. BAME, black and minority ethic. COPD, chronic obstructive airways disease. CKD, chronic kidney disease. IHD, ischaemic heart disease. CCF, congestive cardiac failure. CCI, Charlson comorbidity index. [a]Mann Whitney U Test, Chi squared or Fisher's Exact Test. [b]Assessed in 1561 and 1946 patients in the pre and post implementation groups respectively. [c]Assessed in 1902 and 4357 patients in the pre and post implementation groups respectively

Table 2: Baseline patient characteristics for hospitalised patients with COVID-19, pre and post introduction of molecular point-of-care testing (mPOCT).

	Pre mPOCT group n=654	**Post mPOCT group n=1782**	**Difference (95%CI)**	**p value[a]**
Age, years	72.6 [55.9-83.4]	64.8 [49.7-79.4]	7.8 (7.3-8.4)	<0.0001
Male Sex	280 (42.8%)	832 (46.7%)	3.9% (2.4-5.4)	0.0977
BMI[b]	26.9 [23.8-31.1]	27.9 [23.9-32.9]	1 (0.8-1.2)	0.0039
BAME[c]	59 (10.2%)	156 (10.1%)	0.1% (0.1–0.1)	1.0000
Asthma	115 (17.6%)	298 (16.7%)	0.9% (0.3-2.1)	0.6591
COPD	123 (18.8%)	261 (14.6%)	4.2% (2.8-5.5)	0.0149
CKD	123 (18.8%)	228 (12.8%)	6.0% (4.6-7.5)	0.0002
Diabetes	179 (27.4%)	407 (22.8%)	4.5% (3.1-6)	0.0235
Dementia	75 (11.5%)	145 (8.1%)	3.3% (2.15-4.5)	0.0138
Hypertension	256 (39.1%)	526 (29.5%)	9.6% (8-11.3)	<0.0001
IHD	166 (25.4%)	400 (22.4%)	2.9% (1.5-4.3)	0.1426
CCF	154 (23.5%)	322 (18.1%)	5.5% (4.0-7.0)	0.0030
Cirrhosis	41 (6.3%)	126 (7.1%)	0.8% (0.1-1.5)	0.5463
CCI	5.2 (1.8-8.7)	4.2 (0.75-7.6)	1 (0.9-1.1)	<0.0001

All data are presented as n (%), median [interquartile range] or mean (SD). CI, confidence interval. BMI, body mass index. BAME, black and minority ethic. COPD, chronic obstructive airways disease. CKD, chronic kidney disease. IHD, ischaemic heart disease. CCF, congestive cardiac failure. CCI, Charlson comorbidity index. [a]Mann Whitney U Test, Chi squared or Fisher's Exact Test. [b]Assessed in 494 and 1255 patients in the pre and post implementation groups respectively. [c]Assessed in 581 and 1551 patients in the pre and post implementation groups respectively.

Figure 1 - Patient flow through the study - patients admitted and tested through the acute medical admissions pathway

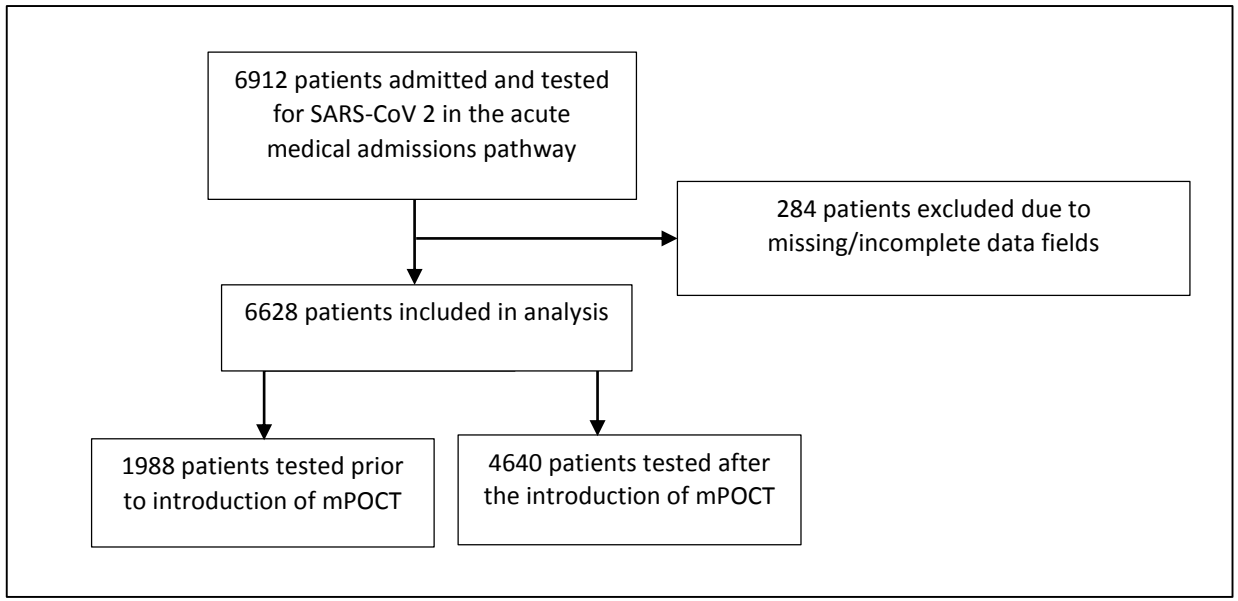

Figure 2 - Turnaround times for tests and cohorting areas

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Figure 2a

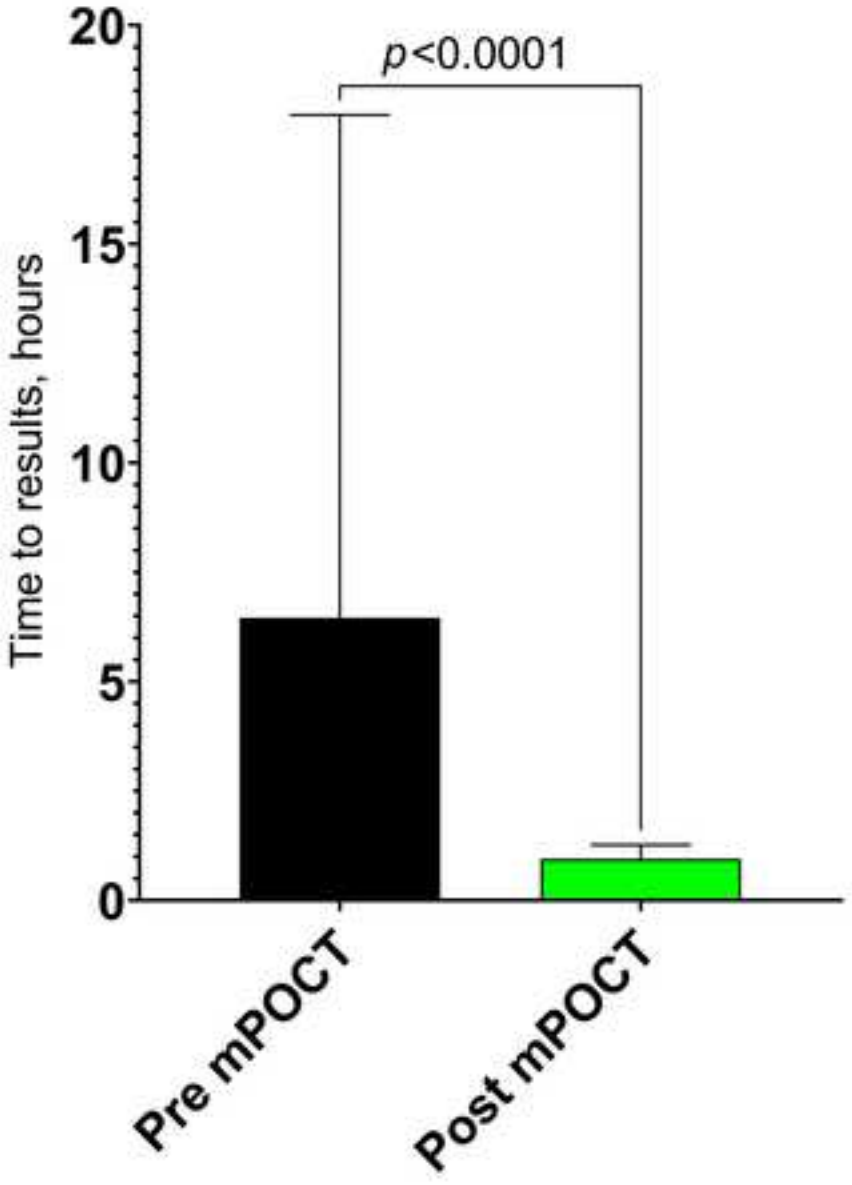

Figure 2b

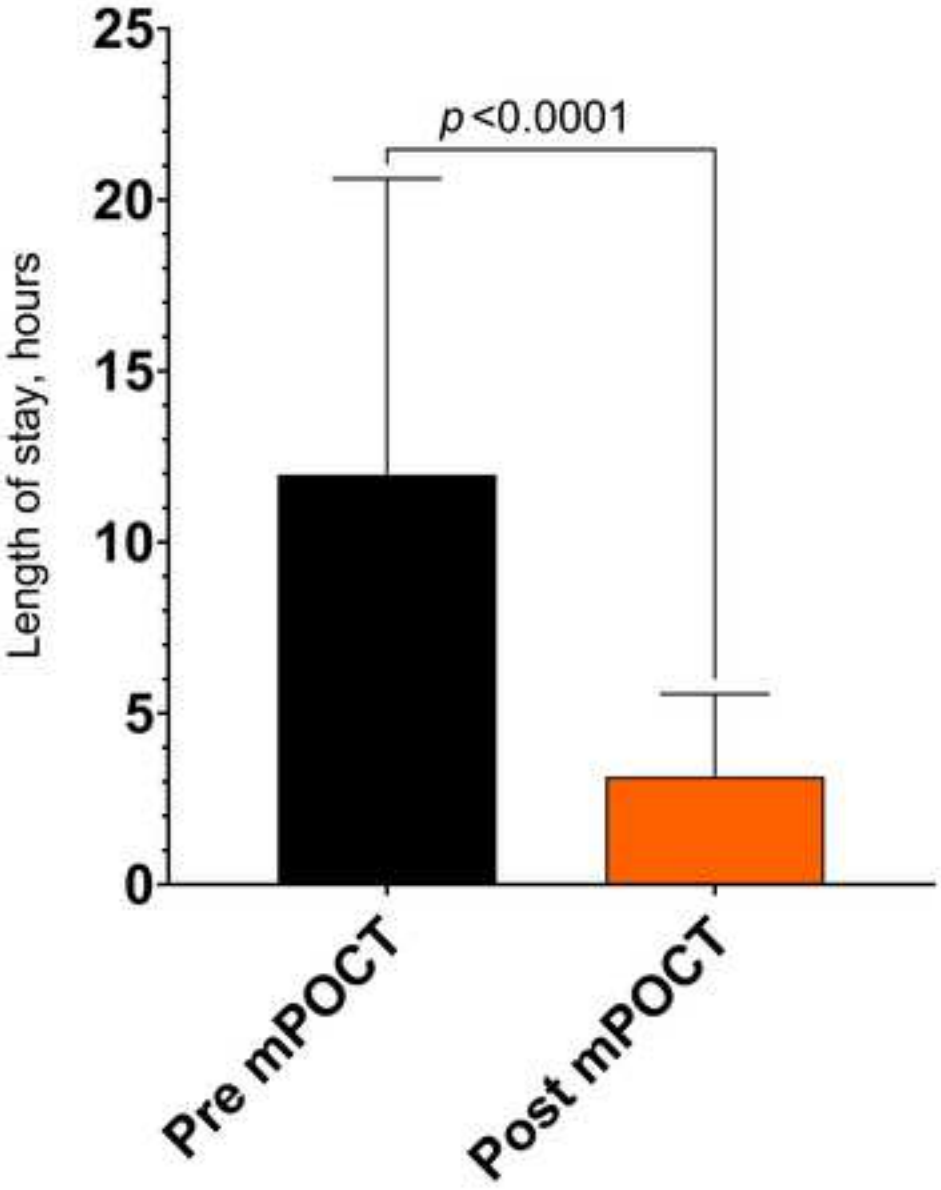

Figure 3 - Patient flow through the study - patients testing positive for COVID-19

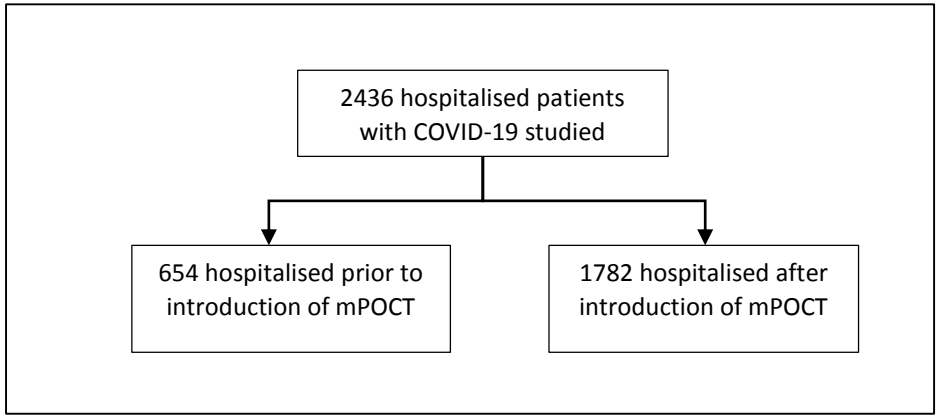

Figure 4 - Proportion of patients with hospital acquired COVID-19 before and after implementation of mPOCT

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Figure 4a

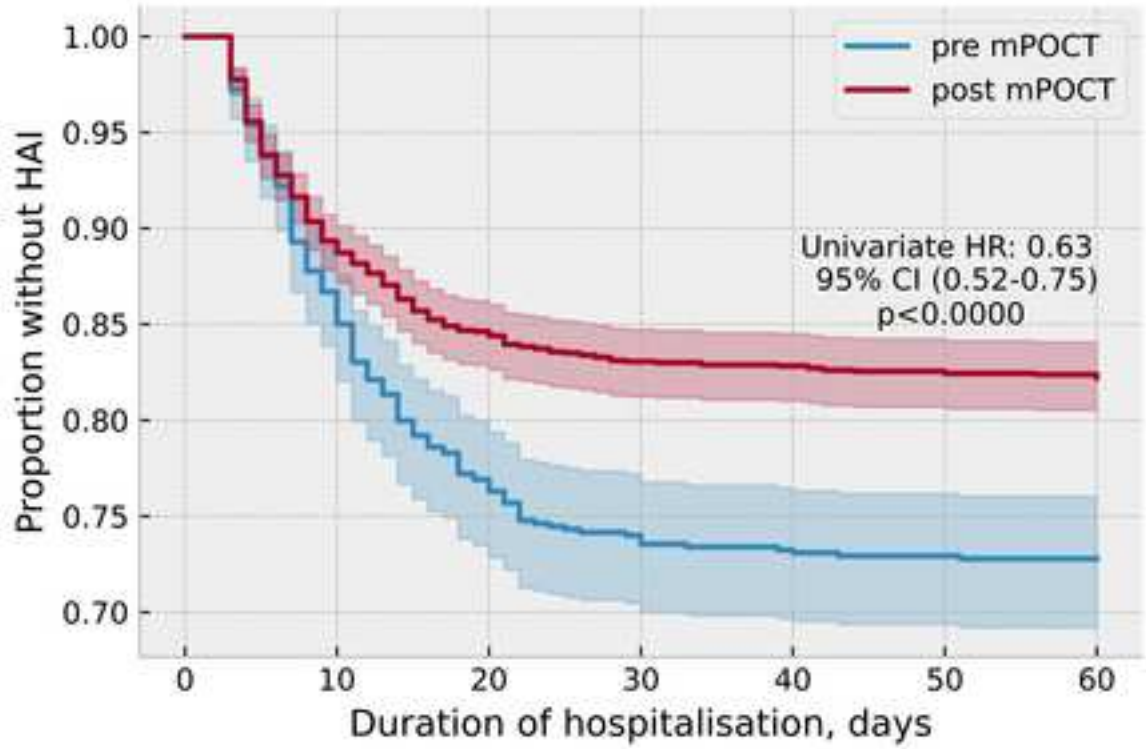

Figure 4b

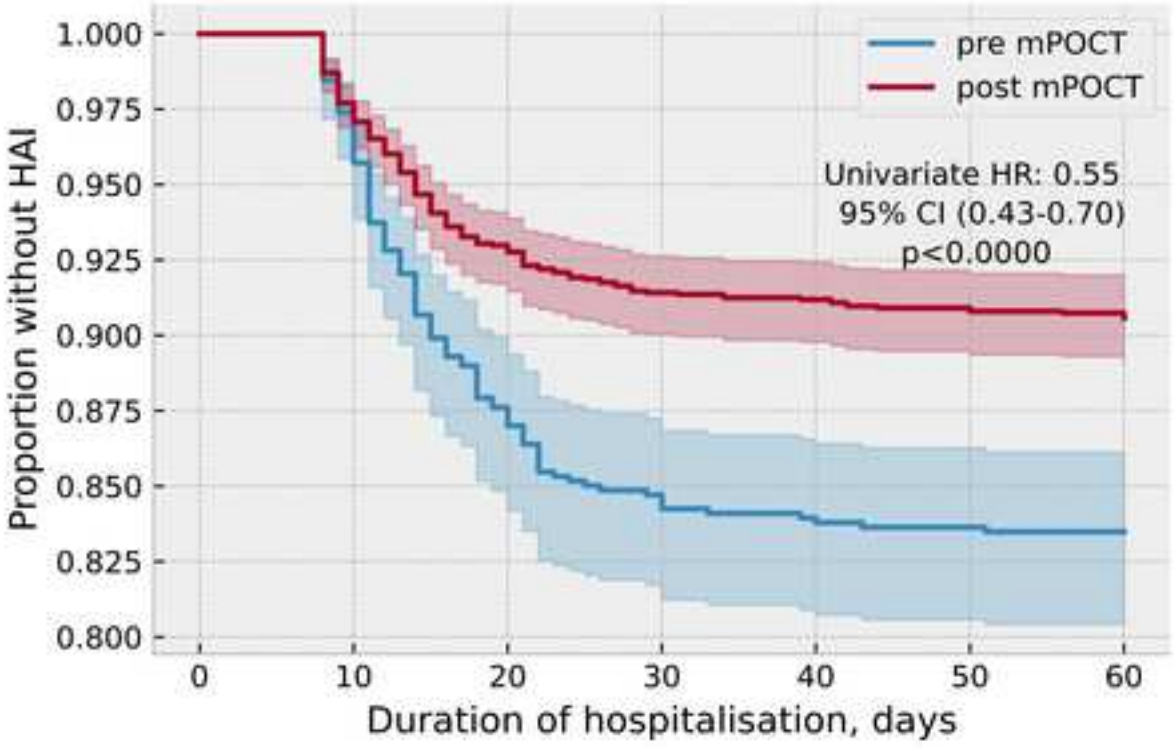

Figure 5 - Proportion of patients with hospital acquired COVID-19 by diagnostic modality after mPOCT introduction

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Figure 5a

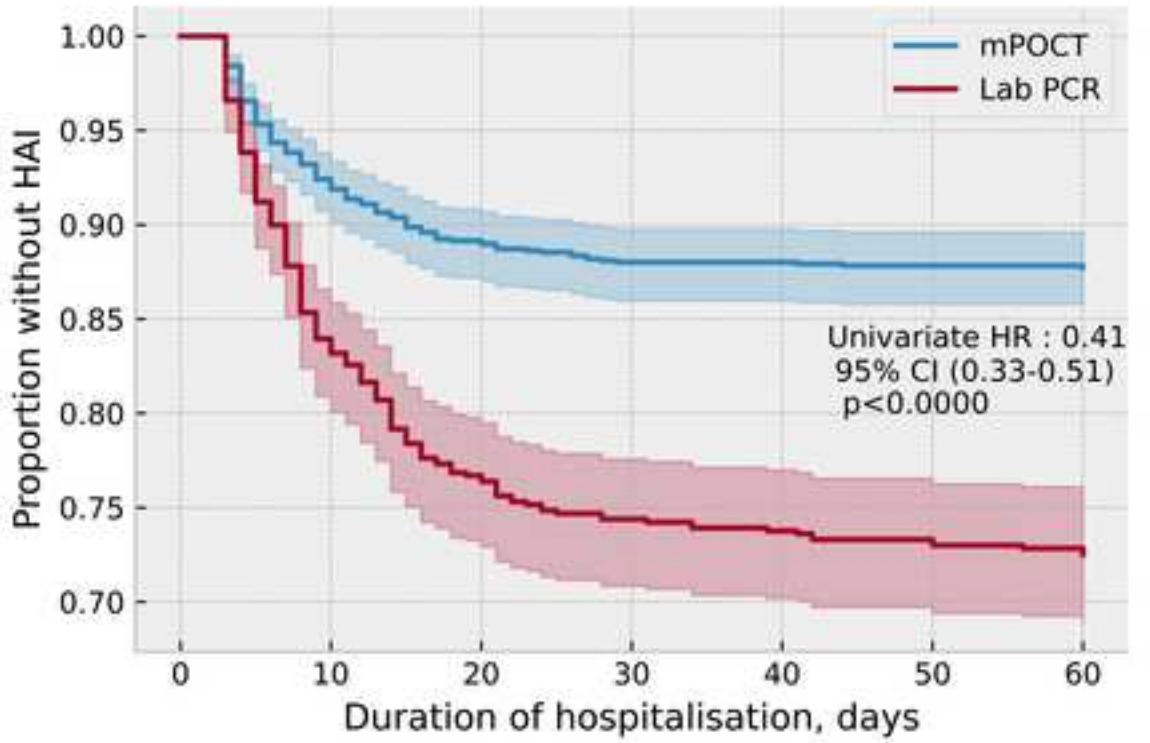

Figure 5b

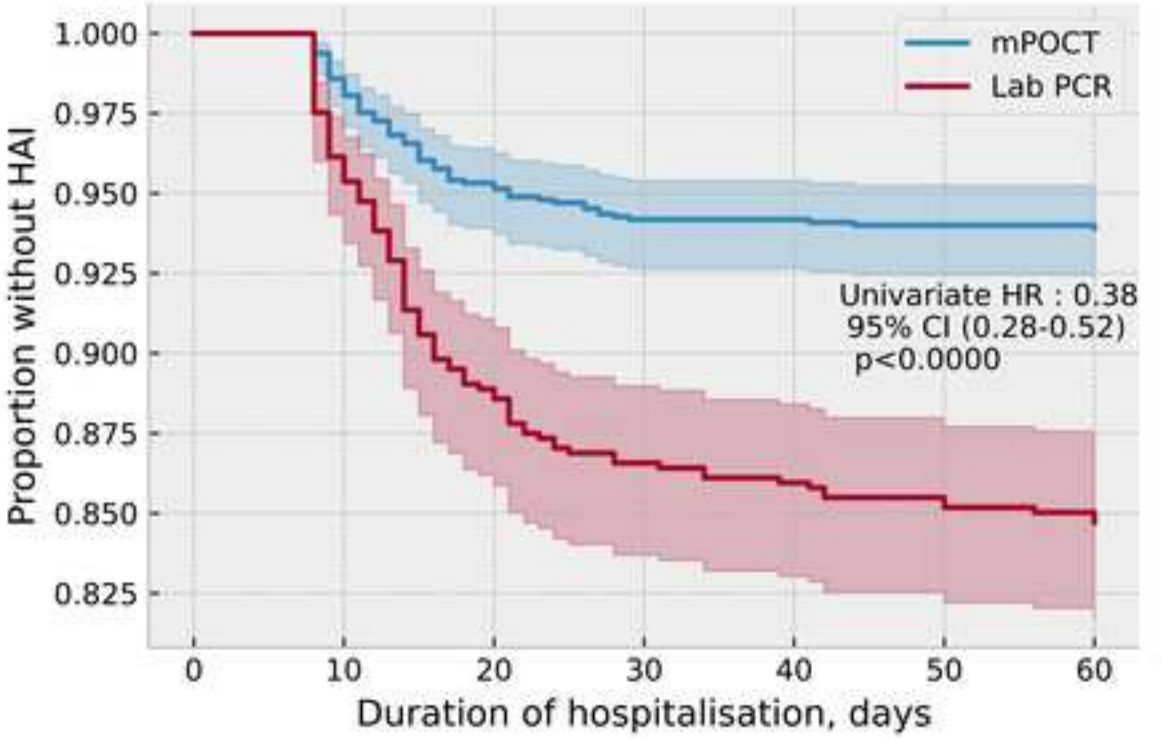

Figure 6 - Multivariate model for HA-COVID-19 when tested with mPOCT or laboratory testing

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Figure 6

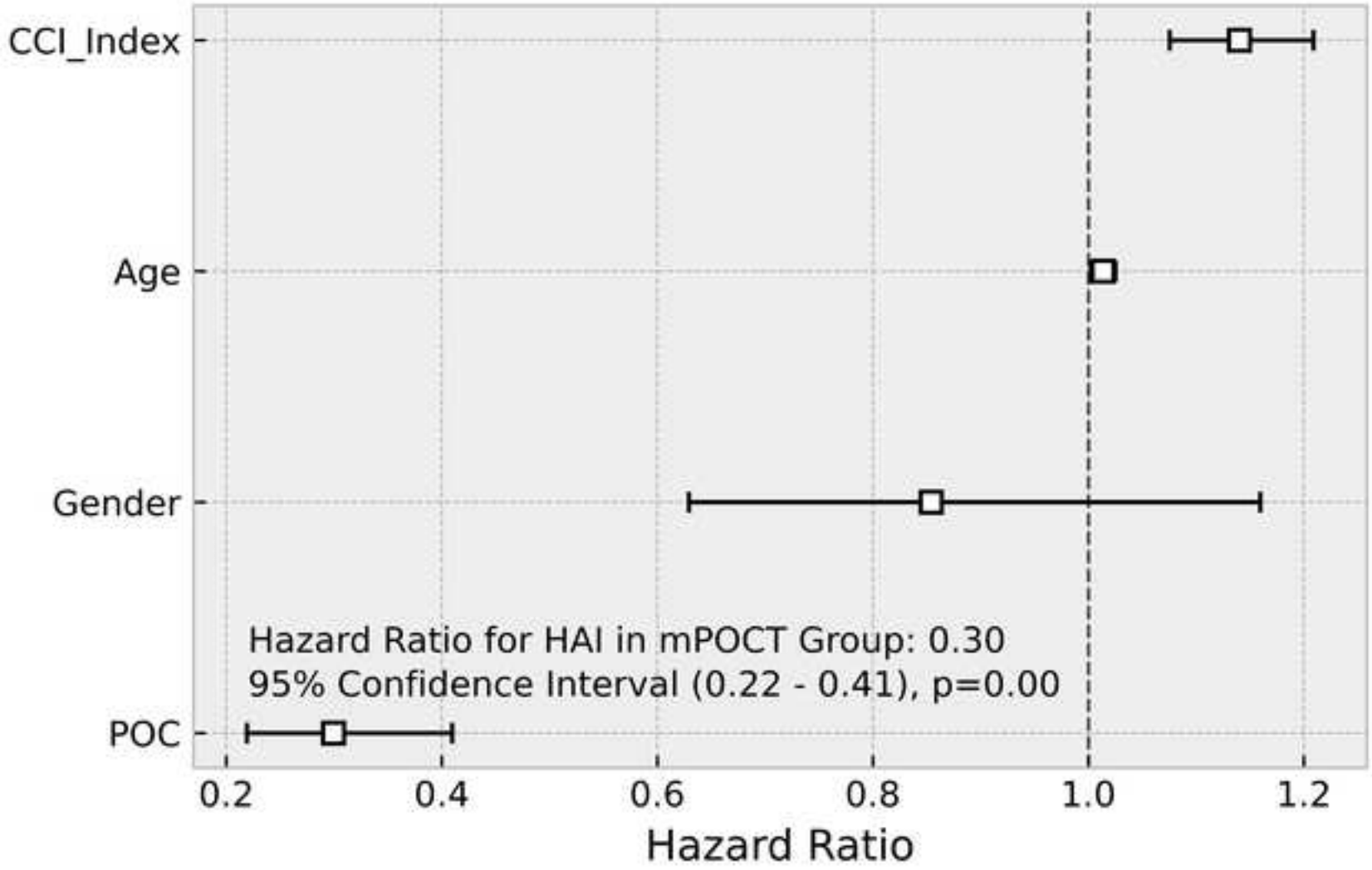

Figure 7 - Median proportions of HA-COVID-19 for UHSFT, the South of England and all of England

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