



The use of whole blood capillary samples to measure 15 analytes for a home-collect biochemistry service during the SARS-CoV-2 pandemic: A proposed model from North West London Pathology

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Abstract

Background: The COVID-19 pandemic has drastically changed the delivery of secondary care services. Self-collection of capillary blood at home can facilitate the monitoring of patients with chronic disease to support virtual clinics while mitigating the risk of SARS-CoV-2 infection and transmission.

Objective: To investigate the comparability of whole blood capillary and plasma venous samples for 15 routinely used biochemical analytes and to develop and pilot a user-friendly home-collection kit to support virtual outpatient clinical services.

Methods: To investigate the comparability of whole blood capillary and plasma venous samples for 15 routinely requested biochemical analytes, simultaneous samples of venous and capillary blood were collected in EDTA and lithium-heparin plasma separation tubes that were of 4–6 mL and 400–600 μ L draw volume, respectively. Venous samples were analysed within 4 h of collection while capillary samples were kept at ambient temperature for three days until centrifugation and analysis. Analyte results that were comparable between the matrices were then piloted in a feasibility study in three outpatient clinical services.

Results: HbA1c, lipid profile and liver function tests were considered comparable and piloted in the patient feasibility study. The home-collect kit demonstrated good patient usability.

Conclusion: Home collection of capillary blood could be a clinically-useful tool to deliver virtual care to patients with chronic disease.

Keywords

Laboratory methods, evaluation of new methods, laboratory management

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Introduction

The COVID-19 pandemic has changed the delivery of phlebotomy services and consultations in primary and secondary care.¹ In order to support physical

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distancing and reduce the transmission of SARS-CoV-2 between patients and staff, routine phlebotomy services have, in most cases, stopped offering a walk-in facility for patients, and face-to-face outpatient clinic appointments have been replaced by remote virtual consultations. There is a clinical need to develop a blood collection service that can support virtual clinics while mitigating the risk of SARS-CoV-2 infection and transmission, and to allay patient anxiety about attending health-care facilities during the pandemic.

To our knowledge, home collection of capillary blood samples has not been used routinely in NHS pathology services, but has been employed in the private sector in a direct-to-consumer model.²⁻⁴ This type of service would assist in the management of patients with chronic disease some of whom are at high-risk of SARS-CoV-2 infection. Home collection may also prove more convenient for patients in full-time employment and offer an alternative when venepuncture is difficult.

Before this service can be implemented, preanalytical variables associated with self-collection of capillary blood need to be optimized and standardized to limit measurement variability. Furthermore, given the likely shipping time between self-collection of capillary blood at home and laboratory analysis, the results of relevant analytes within posted capillary blood need to be assessed for clinical acceptability.^{5,6}

We aimed to ascertain (a) which biochemical analytes in whole blood capillary samples were comparable to plasma venous samples, (b) whether this service could be delivered from a busy NHS laboratory and (c) whether this service was acceptable to patients. In this study, we describe the development of a self-collection home capillary blood kit and service at hospitals served by North West London Pathology. We investigated routinely used biochemical analytes in capillary whole blood stored at ambient temperature for 72 h and developed a user-friendly home-collection capillary blood kit for patients which was piloted in three clinical outpatient services.

Methods and materials

Study 1: Comparability of whole blood capillary samples to plasma venous samples

Twenty-eight volunteers (12 males and 16 females aged between 27 and 56 years old) from the Biochemistry Department at Charing Cross Hospital, London, UK were involved in this service evaluation. All volunteers declared no significant medical history except for one participant who had a diagnosis of type 2 diabetes mellitus treated with metformin. A selection of clinically relevant analytes to support virtual clinics was chosen (Table 1).

Non-fasting venous samples were collected from each volunteer into one 4 mL ethylenediaminetetraacetic acid (EDTA) and one 6 mL lithium heparin-plasma separation (PST) Vacutainer Tubes (Becton Dickson, BD Diagnostics, Plymouth UK) between 10 am and 1 pm. Samples were centrifuged and analysed within 4 h of collection (T4h). Blood tubes remained closed during venous collection and each tube was inverted five times following collection. All samples were kept between 20 and 22°C and were protected from natural or artificial light until analysis. All samples were analysed in the same batch on the same analyser. Venous blood sampling was done in compliance with the EFLM-COLABIOCLI recommendations for venous blood sampling.⁷

Each volunteer self-collected a capillary sample into one 600 µL EDTA and one 600 µL PST Microtainer Microtubes (Becton Dickson, BD Diagnostics, Plymouth, UK) at the same time as the venous samples (T0h). Blood tubes were opened by participants prior to fingerprick, and each tube was inverted five times following capillary blood collection and capping. Capillary samples were kept in the biochemistry laboratory between 20 and 22°C and were protected from light until centrifugation and analysis, 72 h after collection (T72h). All samples were analysed in a single batch on the same analyser.

Each sample analysed at T4h and T72h was measured once, and therefore there were no duplicate analyses of the same sample. The start and end date of the comparability study was 10 and 13 June 2020, respectively.

The Tosoh G8 HLC-723G11 and Abbot Alinity (ci-series) were all traceable to international standards.

Temperature control. The temperature of the laboratory was monitored in a daily logbook using a minimum–maximum thermometer which reads between +15 and +30°C. The mean temperature during the three-day experiment was 21°C with a minimum of 20°C and maximum of 22°C.

Centrifugation. The 4–6 mL and 400–600 µL EDTA and PST samples were spun at 3000 g for 10 min.

Quality control. All analytes were analysed according to the manufacturer's recommendations. All analytes passed quality control testing at the relevant levels on the same day as analysis. Intermediate precision (%) data were obtained from in-house replication studies performed in July and August 2020. Samples were excluded based on the haemolytic, icterus and lipaemia (HIL) indices as reported by the analyser (Abbot Diagnostics).

Table 1. Clinically relevant biochemistry tests and analytes that were selected for the comparability study.

Biochemistry test	Analytes chosen for the comparability study	Method
Lipid profile	Total cholesterol	Enzymatic
	HDL-cholesterol	Enzymatic (Acceleration selective detergent)
	Triglycerides	Enzymatic (Glycerol phosphate oxidase)
	LDL-cholesterol	Friedewald equation
Liver function test	Bilirubin	Diazo
	ALT ^a	Enzymatic (IFCC).
	AST ^a	Enzymatic (NADH)
	GGT	Enzymatic (L-gamma-glutamyl-3-carboxy-4-nitroaniline substrate)
	ALP	Enzymatic (para-nitrophenyl phosphate)
Renal function test	Urea	Enzymatic (Urease)
	Creatinine	Jaffe
Bone profile	Calcium	Colorimetric (Arsenazo III)
	Albumin	Colorimetric (Bromocresol Purple)
	Magnesium	Enzymatic (Isocitrate dehydrogenase)
HbA1c		Anion exchange high-performance liquid chromatography

Note: All analytes were analysed on Abbott Alinity ci-series (Abbott Diagnostics) except for HbA1c which was analysed on Tosoh G8 HLC-723G II both of which are traceable to international standards.

HDL: high-density lipoprotein; LDL: low-density lipoprotein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma glutamyl transferase; ALP: alkaline phosphatase; IFCC: International Federation of Clinical Chemistry.

^aALT and AST assay contain pyridoxal phosphate monohydrate.

Development of home-collect biochemistry blood kit and service. Study 1 provided important volunteer feedback that helped improve capillary blood collection and contributed to the development of a home-collection capillary blood kit which includes instructions for blood collection, preprinted patient labels, prepaid postage labels and feedback forms. The components of the home-collection biochemistry blood kit are detailed in Supplemental Figure 1(a) and (b). A video was also created to assist patients when self-collecting capillary blood at home.

(<http://pathology.imperial.nhs.uk/uploads/images/2020/NHS%20MASTER%203.mp4>)

Calculations. The mean venous and capillary result of each analyte was calculated from the sum of individual analyte data. The absolute difference and bias (%) between the venous result at T4h and capillary result at T72h were calculated only for paired samples from the same patient.

$$\text{Absolute difference} = C - V$$

$$\text{Bias (\%)} = \left(\frac{C - V}{V} \right) 100$$

Where *C* = capillary analyte result (T72h), *V* = venous analyte result (T4h).

The reference change value⁸ was used to define a maximum permitted difference which was calculated using within-subject biological coefficient of variation data from the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)⁹ and intermediate precision (coefficient of variation) from in-house replication studies performed in July and August 2020.

$$2.77 \times \sqrt{\text{intermediate precision}^2 + \text{within subject biological variation}^2}$$

A maximum permitted concentration difference was also calculated using the maximum permitted difference (%) and baseline venous result (concentration).

$$\frac{\text{maximum permitted difference} \times \text{baseline venous result}}{100}$$

Calculations were performed in Microsoft Office Excel 2016 and GraphPad Prism version 8.0 was used for Bland-Altman plots.

Clinical acceptability. Clinical acceptability between venous and capillary results was firstly assessed by comparing the difference to the maximum permitted difference and secondly based on the clinical utility of the test. A two-step assessment was used because differences based on statistical calculations may not necessarily be clinically significant.

The clinical utility of the test was assessed by a panel of five experts who judged whether the difference between venous and capillary result was clinically-significant for the intended use¹⁰ in a virtual outpatient clinic during the current COVID-19 pandemic. If the observed difference between results was small enough to be deemed clinically insignificant by the expert panel, then the analyte passed comparability assessment and could be used in the patient feasibility study; however, if the observed difference was large enough to be considered clinically important by the panel, then the analyte failed comparability assessment and would not be trialled in the patient feasibility study.¹⁰

Each member of the panel independently decided to pass or fail an analyte. If a unanimous decision could not be made, then the decision was determined by consensus and if there was no consensus, then the analyte would not be considered for the feasibility study. This approach is similar to studies using B-type natriuretic peptide to predict heart failure, the diagnosis of which is based on clinical features that are reviewed by experts to reach a decision.^{11,12}

Adherence to guidelines. Although the present investigation was not a stability study, we used the Checklist for Reporting Stability Studies (CRESS) produced by the European Federation for Clinical Chemistry and Laboratory Medicine Working Group for the Pre-analytical Phase⁹ as a framework for the reporting of results.

Study 2: Patient feasibility study

Three outpatient clinical services took part in the feasibility study for the home-collect capillary blood service in a busy NHS laboratory: the Tuberculosis Clinic ($n=9$), the Lipid Clinic ($n=20$) and the Diabetes Clinic ($n=9$). Patients who were unable to attend primary or secondary care for routine venous blood collection for their respective clinics were offered a home testing kit. Postal kits were sent out one week before clinic visits so that results would be available for review during the virtual consultation. Clinicians were asked if the results of the capillary tests were clinically consistent with the patient's status. This was assessed by asking clinicians to provide feedback on the following

1. Whether the result was clinically significantly different from previous results
2. Whether the result was consistent with the patient's clinical features, for example, was the HbA1c in keeping with home blood glucose monitoring result? Was the lipid profile in keeping with a change in therapy? Were the LFTs in keeping with symptoms of jaundice or raised liver enzymes due to liver disease?
3. Whether they would like the result to be confirmed with a venous blood draw.

The number of returned kits and patient feedback was also recorded.

Patient feedback form. A feedback form with answers based on a three-level Likert scale is included within each capillary blood collection kit, which patients are asked to complete (Figure 1).

Results

Venous and capillary blood

Table 2 shows the number of paired venous and capillary samples that were of sufficient volume to quantify the comparability of 15 biochemical analytes in capillary whole blood that was stored between 20 and 22°C. Each venous and capillary sample was centrifuged and analysed at 4 and 72 h after collection, respectively. The raw data from our study are included in Supplemental file 2.

Individual comparability data for each analyte are presented on Bland-Altman plots in Figure 2. Analytes that passed comparability assessment were used in the patient feasibility study (total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, HbA1c, bilirubin, ALT, AST, GGT and ALP).

Calcium, creatinine and albumin failed comparability assessment because the mean difference between venous and capillary results was greater than the maximum permitted difference and the large observed difference between results was considered clinically meaningful. These analytes were not used in the patient feasibility study.

Urea and magnesium passed comparability assessment but were not trialled in the patient feasibility study because these tests require complementary analytes such as creatinine, potassium and calcium to offer complete clinical utility.

Patient feasibility study

The feasibility of the home-collect service was trialled in three outpatient services: the Tuberculosis Clinic

HOME TESTING FEEDBACK FORM

Chelsea and Westminster Hospital Imperial College Healthcare The Hillingdon Hospitals

NHS
North West London Pathology

1) How easy did you find this method for blood collection?

Very Easy ☺ ☹ ☹ Very Difficult

2) How easy did you find the kit to use in terms of packing and postage?

Very Easy ☺ ☹ ☹ Very Difficult

3) Would you recommend this Postal Service to family and friends?

Yes ☺ ☹ ☹ No

Please provide any additional comments:

Figure 1. The feedback form within each capillary blood collection kit that patients are asked to complete.

($n = 9$), the Lipid Clinic ($n = 20$) and the Diabetes Clinic ($n = 9$). Self-collect kits were sent out to 38 patients in total and returned by 31 patients (82%) (Table 3), all of whom provided user feedback (Table 4). All patients were advised to self-collect finger capillary samples on Monday and all kits were received within 72 h. We did not collect information from patients relating to the environmental conditions during self-collection of capillary blood because we felt that it would not be patient friendly and self-reporting from patients can be inconsistent.¹⁴ Postal kits were transported back to our laboratory via the national postal system that serves London, UK. Home-collect kits were sent out to follow-up patients rather than new patients because clinicians would be more alert to discrepant results in patients well known to the service with historical test results. This service could therefore have clinical utility in the management of patients with chronic disease who require longitudinal biochemical monitoring.

Discussion

The current article describes the development of a home collection kit and service that enables patients to self-collect capillary blood before sending the sample to our laboratory for analysis with the test result being interpreted by the requesting clinician. To identify which biochemistry tests were clinically acceptable to support virtual clinics, the results of 15 analytes in capillary whole blood collected by fingerprick and stored at ambient temperature for three days were compared with plasma venous samples analysed 4 h after venepuncture.

Clinical acceptability was assessed using two criteria. Firstly, a maximum permitted difference was

calculated using the equation for the reference change value⁸ and secondly, anticipated clinical need. The latter was included for several reasons. Firstly, observed differences between venous and capillary results that exceed a calculated statistical threshold (i.e. maximum permitted difference) may not be clinically important. This was the case for HDL-C, AST and ALP (Figure 2). The increased HDL-C result is unlikely to impact patient management and did not clinically impact the calculated LDL-C result. Equally, the AST and ALP results in our population of healthy volunteers were predominantly within the reference range despite a few results exceeding the maximum permitted difference.

Secondly, fingerprick capillary blood collection is influenced by preanalytical variables that are not accounted for by analytical and biological variation such as patient preparation to collect a sufficient volume of capillary blood and the method of collection,¹⁵ both of which were optimized in study 1 by creating an instruction sheet, a video demonstration and using BD MicrotainerTM Contact-Activated Lancet.

Thirdly, there is a risk of SARS-CoV-2 transmission and infection, among patients and staff, during venous blood collection, and equally, there are clinical risks with not having blood tests to monitor chronic disease and treatment. Both of these factors were considered when evaluating if the observed difference between venous and capillary results would clinically impact patient care.

We felt that it was not appropriate to use solely biological variation data and imprecision data to solely define acceptable comparability for the intended use of capillary testing to support virtual clinics during

Table 2. Comparability of 15 analytes in capillary whole blood stored between 20 and 22°C until centrifugation and analysis 72 h after collection.

Analyte	Paired venous and capillary result (n)	Mean \pm SD venous result (T4h)	Mean \pm SD capillary result (T72h)	Mean \pm SD of individual differences (capillary - venous)	Mean \pm SD of individual bias (%)	Intermediate precision (%)	Within subject biological variation (%)	Maximum permitted difference (%) ^a	Maximum permitted difference (conc)	Passed Comparability Testing ^b (Yes/No)
Total cholesterol (mmol/L)	20	5.1 \pm 0.9	5.5 \pm 0.9	0.4 \pm 0.2	7.3 \pm 4.5	1.4	6.4	15.2	0.8	Yes
Triglyceride (mmol/L)	18	1.4 \pm 1.3	1.3 \pm 1.3	-0.1 \pm 0.2	-3.7 \pm 18.0	3.2	15.9	56.1	0.8	Yes
HDL-cholesterol (mmol/L)	19	1.7 \pm 0.7	1.9 \pm 0.7	0.2 \pm 0.1	14.4 \pm 7.9	2.9	9.5	18.0	0.3	Yes
LDL-cholesterol (mmol/L)	18	2.7 \pm 0.7	2.9 \pm 0.6	0.2 \pm 0.2	7.0 \pm 7.6	-	10.3	23.0	0.6	Yes
Bilirubin (μ mol/L)	20	10 \pm 5	10 \pm 5	0 \pm 1	4 \pm 17	3.7	9.0	38.5	3.9	Yes
ALT (IU/L)	19	30 \pm 17	27 \pm 17	-2.9 \pm 2.9	-3.2 \pm 16.4	5.4	11.6	31.7	9.5	Yes
AST (IU/L)	19	32 \pm 7	37 \pm 9	5.0 \pm 5.1	16.3 \pm 18.3	2.5	8.4	27.5	8.8	Yes
GGT (IU/L)	19	24 \pm 22	25 \pm 24	0.7 \pm 2.1	1.6 \pm 16.2	3.9	15.8	27.4	6.6	Yes
ALP (IU/L)	19	58 \pm 18	51 \pm 16	-7.0 \pm 4.0	-11.9 \pm 21.0	2.7	9.2	16.5	9.6	Yes
Albumin (g/L)	20	44 \pm 2	48 \pm 3	4 \pm 2	8.6 \pm 3.7	1.4	2.2	8.2	3.6	No
HbA1C (mmol/mol)	28	36 \pm 3	36 \pm 3	-0 \pm 0.7	-1.3 \pm 1.4	1.6	1.5	6.3	2.3	Yes
Urea (mmol/L)	20	4.7 \pm 0.9	5.7 \pm 1.0	1.0 \pm 0.4	21.2 \pm 10.6	3.3	9.2	39.6	1.9	No
Creatinine (μ mol/L)	20	75 \pm 11	96 \pm 15	21 \pm 9	29.3 \pm 13.9	2.4	5.6	14.1	10.6	No
Magnesium (mmol/L)	20	0.8 \pm 0.1	0.9 \pm 0.1	0.1 \pm 0.0	10.6 \pm 4.3	3.0	1.6 ^c	13.0	0.1	No
Calcium (mmol/L)	20	2.4 \pm 0.1	2.7 \pm 0.2	0.3 \pm 0.1	13.0 \pm 4.9	1.4	0.8 ^c	7.0	0.2	No

Note: Allowable bias (%) is taken from the minimum desirable bias goal based on the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) biological variation database.

HDL: high-density lipoprotein; LDL: low-density lipoprotein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma glutamyl transferase; ALP: alkaline phosphatase; T4h: centrifuged and analysed 4 hours after collection; T72h: centrifuged and analysed 72 hours after collection.

^aA maximum permitted difference (%) was calculated using the following equation: $2.77 ((\text{intermediate precision}) + (\text{within-subject biological variation}^2))$.

^bAnalyses passed comparability testing based on two criteria (1) the maximum permitted difference and (2) based on the clinical use of the test from the independent assessment of a panel of five experts.

^cMagnesium and calcium within-subject biological variation data taken from Ricos et al.¹³

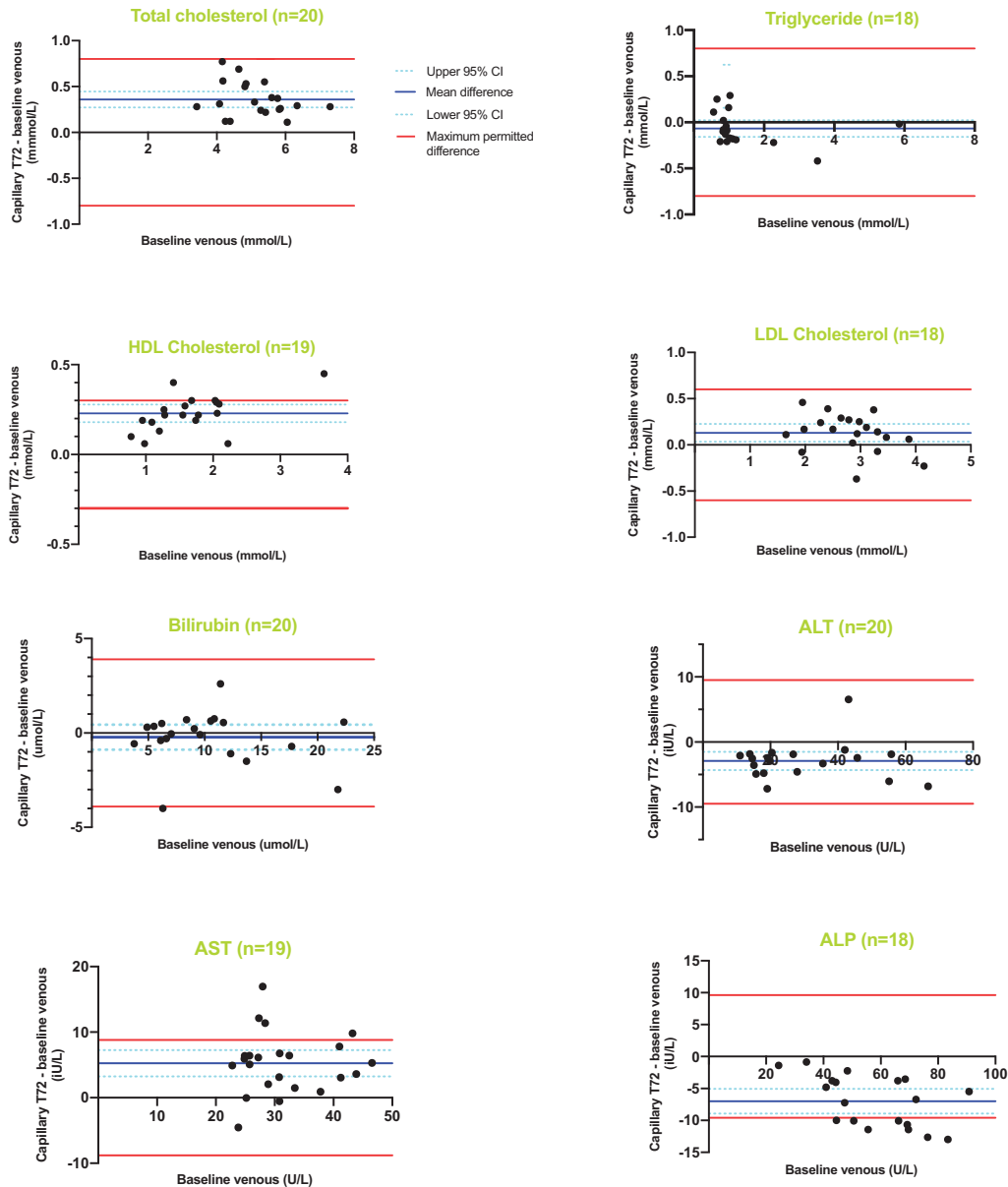


Figure 2. Bland-Altman plots of individual baseline T4h venous results (x-axis) plotted against the difference between the T72h capillary and venous result (y-axis). On each figure, *n* represents the number of paired venous and capillary samples for that analyte. The blue solid line represents the mean difference between capillary and venous results. The dashed light blue lines represent the upper and lower 95% confidence intervals (CI). The red line represents the maximum permitted concentration difference between venous and capillary results. Analytes written in green are considered acceptable for clinical use and analytes written in yellow and orange are not recommended for clinical use. T72h: centrifuged and analysed 72 h after collection; T4h: centrifuged and analysed 4 h after collection.

the COVID-19 pandemic. Clinicians requesting finger-prick capillary blood testing for their patients would need to consider the accuracy of this method vs. the risks of venous blood collection or avoiding venous blood collection during the COVID-19 pandemic on a case-by-case basis.

Lipid profile, HbA1c and liver function tests passed comparability assessment and were trialed in a patient

feasibility study, whereby self-collect capillary blood kits were sent out to patients in the lipid, diabetic and tuberculosis clinic. All capillary samples were sent out one week before the clinic appointment so that results were available for review in time for the virtual consultation. Clinicians were asked if the capillary results were in keeping with the patient's clinical features at the time of the virtual consultation and this

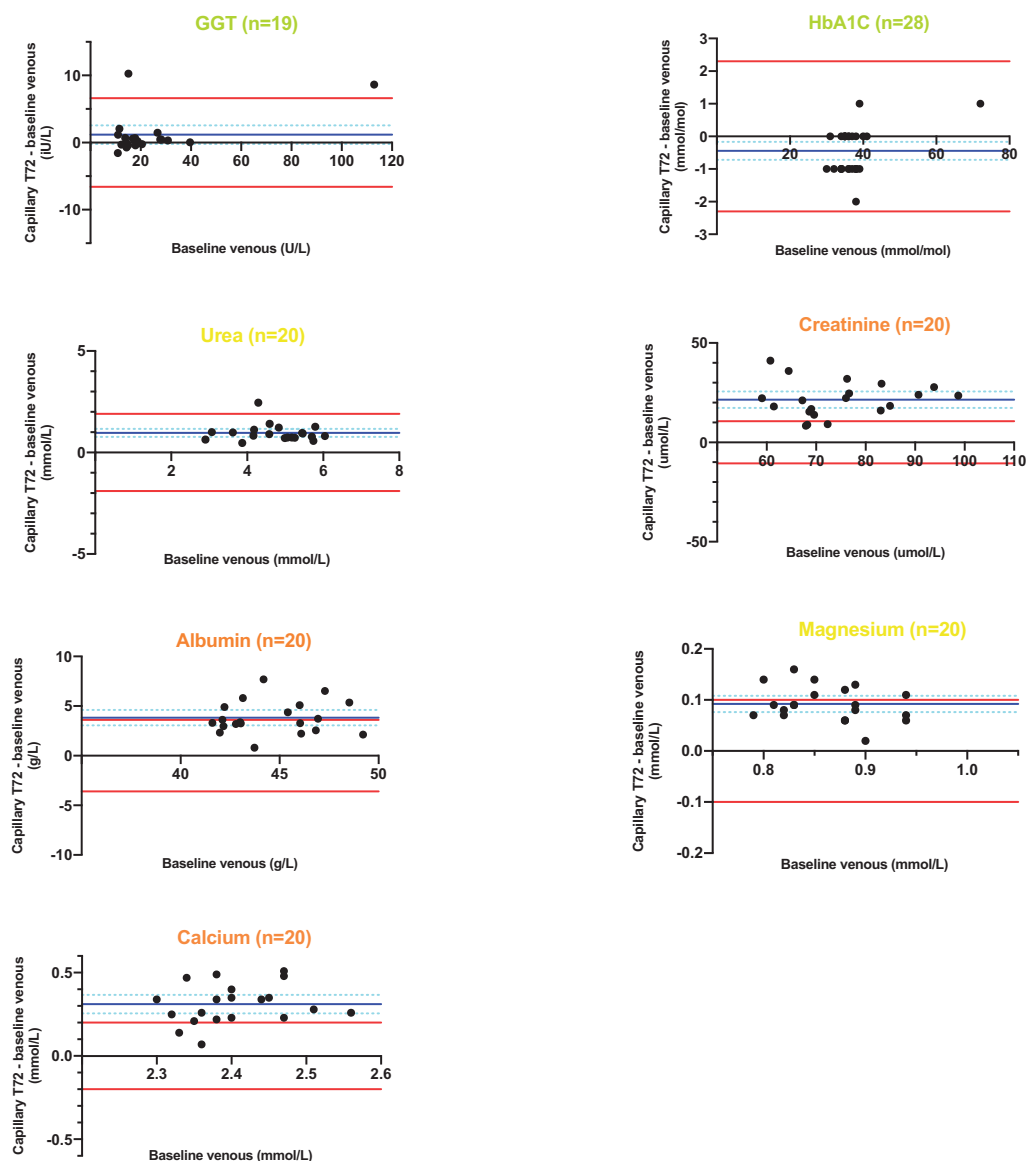


Figure 2. Continued

was assessed by history taking, reviewing historical results and asking clinicians if they would like the result to be confirmed with a venous blood drawer. In the diabetic clinic, the capillary HbA1c result was in keeping with home blood glucose monitoring and the lipid profile in the lipid clinic was in keeping with the patient's current treatment. In the tuberculosis clinic, no patients reported symptoms of jaundice or elevated liver enzymes and this was in keeping with normal capillary LFT results at the time of virtual consultation. None of the clinicians requested to confirm the capillary result with a venous blood drawer. We fully acknowledge that the feasibility study does not provide information about the comparability of

analytes in capillary whole blood and plasma venous samples in patients with the aforementioned chronic diseases but instead it suggests that the concept of using fingerprick capillary samples analysed in a busy NHS laboratory can be used to support virtual clinics.

A positive bias was observed for analytes within the lipid profile (except for triglycerides) and liver function tests (except for bilirubin). Communicating this bias to clinicians by adding a comment to capillary results would highlight the expected difference when compared with a venous matrix. This will be an important postanalytical precaution to allow an appropriate comparison to be made with previous venous results. Discrepant capillary results should be ideally managed

Table 3. Patient feasibility study characteristics and outcome.

Clinic	Number of Participants	Postal kits returned	Postal kits not returned ^a	Tests performed	Clinically consistent results ^b
Tuberculosis clinic	9	6	3	LFTs	6/6
Lipid clinic	20	16	4	Lipid profile LFTs HbA1c	16/16
Diabetic clinic	9	9	0	HbA1c	9/9

LFTs: liver function tests.

^aReasons cited for postal kits not being returned were: not received, bloods taken at general practitioner surgery, unable to perform test.

^bThis was assessed by history taking at the time of consultation, reviewing historical results and asking clinicians if they would like the result to be confirmed with a venous blood drawer.

Table 4. Patient feasibility study feedback form outcomes.

	Very difficult	Intermediate	Very easy
How easy did you find this method of blood collection? (<i>n</i> = 31)	3%	10%	87%
How easy did you find the kit to use in terms of packaging and postage? (<i>n</i> = 31)	10%	20%	70%
	No	Maybe	Yes
Would you recommend this postal service to family and friend? (<i>n</i> = 31)	7%	23%	70%

by performing a venous blood test, but this decision needs to be carefully considered by clinicians on case-by-case basis due to the current COVID-19 pandemic.

Previous studies have reported a positive bias for lipid profile in whole blood collected in LH tubes stored at room temperature for 8 h⁶ and 72 h.¹⁶ The negative bias observed in capillary ALT has been previously reported in a heparinized plasma venous samples (*n* = 10) stored at room temperature until analysis 56 h after collection.¹⁵ The same study also found that venous whole blood AST was stable, whereas a positive bias was observed in our study, which may be due to red blood cell membrane damage associated with fingerprick capillary blood collection;¹⁶ however, all of these studies were performed in venous blood using LH tubes, which is different to the present study. There is a lack of data on lipid profile and liver function tests in whole capillary blood compared with plasma venous blood and this warrants further investigation.

Study 1 highlighted that the difference between venous and capillary results for creatinine, calcium and albumin was clinically unacceptable and therefore they were not trialled in the patient feasibility study. The finger squeezing associated with capillary blood collection may explain the higher calcium results in this matrix

because there is a higher amount of calcium in interstitial fluid compared with plasma.¹⁷ The relatively increased concentration of creatinine in capillary samples is likely due to the formation of pseudochromogens which interfere with creatinine measurement by the Jaffe method.¹⁸ To overcome pseudochromogen interference, we plan to undertake further studies to measure creatinine using an enzymatic assay in a cohort of patients with chronic kidney disease.

Two quality indicators were implemented into the patient feasibility study so that the preanalytical phase of the self-collect capillary blood service could be monitored. Patient feedback forms were provided to improve the patient experience and optimize our service, and our laboratory kept a record of all samples that are sent and received which enables missing samples to be investigated.

The results of our feasibility study suggest that home collection of capillary blood can support virtual clinics during the COVID-19 pandemic, but our work has further implications. This model for delivering biochemistry services can be used in the remote management of patients with chronic disease who require specialist care at a remote centre, such as patients with cystic fibrosis who routinely require HbA1c, LFTs and vitamin D testing¹⁹ or patients with rare tumours such as gestational

trophoblastic disease who require surveillance with human chorionic gonadotrophin.²⁰ A recent study developed and validated a liquid chromatography-tandem mass spectrometry assay for capillary tacrolimus and creatinine which were collected using a Mitra micro-sampling device by research nurses. This assay and blood collection method could allow remote monitoring of renal transplant recipients.²¹

There are several limitations of the present study. Firstly, the results of the analytes were from two different matrices and it is possible that this may have contributed to some of the observed difference between venous and analyte concentrations, which have been reported in a previous study.²² Ideally, a capillary sample would have been analysed at the same time as the venous sample at T4h and this would have helped quantify the difference between venous and capillary results due to (in)stability and different matrices; however, volunteers were unable to self-collect a sufficient volume of capillary blood. Each volunteer self-collected 500–600 μ L of capillary blood which meant there was ~250–300 μ L plasma for the analysis of 15 analytes, HIL indices and troubleshooting. Consequently, capillary samples were not analysed in duplicate or triplicate, and to maintain consistent experimental conditions, venous samples were handled in the same way.

Secondly, the comparability study was conducted in mostly healthy volunteers with results predominantly within the reference range. This limits the generalizability of our findings for our intended population of patients with chronic disease who are likely to have abnormal results. Indeed, concentration-dependent differences outside of the reference range between venous and capillary results may exist, but this was not investigated in the comparability or feasibility study.

Another limitation affecting the generalizability of our findings is that self-collected capillary samples from volunteers were not posted to our laboratory during study 1, instead the capillary samples were kept in the laboratory at a temperature of 20–22°C protected from light until centrifugation and analysis three days after collection. The results of study 1 should therefore be interpreted in the context of our experimental conditions using healthy volunteers. Environmental factors such as temperature are known to affect the comparability of analytes in venous whole blood.^{5,17}

Based on the limitations of the present study, future work should aim to compare baseline venous and capillary sample to capillary samples that are analysed at specified daily intervals. If it is feasible, each capillary sample would be posted to the laboratory and analysed in duplicate or triplicate. The intended study

population would be patients with chronic disease with results spanning the measuring interval.

After discussion with clinicians at our Trust, potential areas of future work include capillary thyroid function testing, tacrolimus, enzymatic creatinine and eGFR calculated by the Chronic Kidney Disease Epidemiology Collaboration equation.

Conclusion

Fingerprick collection of capillary blood which can be performed at home by patients could be a feasible alternative to venous blood collection for a select number of analytes, but further work is needed to verify this in patients with abnormal values. This model of delivering biochemistry services received excellent user-feedback. Home collection could be a clinically-useful facet of delivering virtual care to facilitate remote chronic-disease management during the SARS-CoV-2 outbreak but also has implications for the longer term provision of pathology services.

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Guarantor

JC.

Contributorship

All authors conceived the study. SA was involved in data analysis. SA wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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Supplemental material

Supplemental material for this article is available online.

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