Clinical Reliability of point-of-care tests to support community based acute ambulatory care

Jan Y Verbakel[1], PhD, Charlotte Richardson[2], MBBS, Tania Elias[3], MBBS MSc, Jordan Bowen[3], MBBS, Roya Hassanzadeh[4], MBBS, Brian Shine[5], MD, Ian Smith[5], BSc, Gail Hayward[1], DPhil, Ann Van den Bruel[1], PhD, Sarah Pendlebury[3,6], DPhil, Daniel Lasserson[7,8,9*], MD

Running title: *Reliability of point-of-care tests for ambulatory care*

[1]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom
[2] Department of Infectious Diseases, Royal Free Hospital, London, UK
[3]Department of Geratology, Oxford University Hospitals NHS Foundation Trust
[4]Department of Primary Care and Public Health, Imperial College London, UK
[5]Department of Clinical Biochemistry, Oxford University Hospitals NHS Trust, Oxford, UK
[6]Nuffield Department of Clinical Neurosciences, Oxford University, Oxford, UK
[7]Nuffield Department of Medicine, Oxford University, Oxford, UK
[8]Institute of Applied Health Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK.
[9]Department of Acute Medicine, City Hospital, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK.

[*]Corresponding author: Professor Dr Jan Verbakel, jan.verbakel@phc.ox.ac.uk, Nuffield Department of Primary Care Health Sciences, University of Oxford, Woodstock Road, OX26GG Oxford, UK, +44(0)1865617946.

NUMBER OF REFERENCES: 26

NUMBER OF TABLES: 4

NUMBER OF FIGURES: 3

WORD COUNT: 2580

ABSTRACT

Objective: To ensure clinicians can rely on point-of-care testing results, we assessed agreement between point-of-care tests for creatinine, urea, sodium, potassium, calcium, Hb, INR, CRP and subsequent corresponding laboratory tests.

Participants: Community-dwelling adults referred to a community-based acute ambulatory care unit

Interventions: The Abbott iSTAT™ (Hb, clinical chemistry, INR) and the Afinion™ Analyser (CRP) and corresponding laboratory analyses.

Outcomes: Agreement (Bland Altman) and bias (Passing-Bablok regression).

Results: Among 462 adults we found an absolute mean difference between point-of-care and central laboratory analyses of 6.4g/L (95%LOA -7.9 to +20.6) for haemoglobin, -0.5mmol/L (95%LOA -4.5 to +3.5) for sodium, 0.2mmol/L (95%LOA -0.6 to +0.9) for potassium, 0.0mmol/L (95%LOA -0.3 to +0.3) for calcium, 9.0 µmol/L (95%LOA -18.5 to +36.4) for creatinine, 0.0mmol/L (95%LOA -2.7 to +2.6) for urea, -0.2 (95%LOA -2.4 to +2.0) for INR, -5.0 mg/L (95%LOA -24.4 to +14.4) for CRP.

Conclusions: There was acceptable agreement and bias for these analytes, except for haemoglobin and creatinine.

KEYWORDS: POINT-OF-CARE TESTING, AMBULATORY CARE, ACUTE CARE, CLINICAL ACCURACY, SERVICE EVALUATION

KEY POINTS

- Undertaking clinical validations of POC tests is essential to understand how they can be best used in practice.

- POC test performance can vary with patient population and clinical environment.

- Further research is needed to assess the impact of POC tests on clinically relevant outcomes.

INTRODUCTION

The delivery of acute ambulatory care is a national priority. Both the NHS England Five Year Forward View and the Royal College of Physicians' Future Hospital Commission set out the need for safely managing the rising demand for acute care with less reliance on the fixed capacity of hospital resources.[1 2]

Delivering acute ambulatory care requires rapid access to diagnostic tests.[1] For acute assessment units in community settings, designed to deliver care closer to home, the need for this rapid access for diagnostics can only be met with point-of-care (POC) diagnostic technology as there is no co-located laboratory. For example, diagnosing a patient with stage 1 acute kidney injury due to dehydration and interacting medications in acute ambulatory care can avoid the need for transfer to hospital for testing as the necessary interventions can be delivered from a community setting on an ambulatory pathway. However, clinicians have previously raised issues of quality assurance, costs and standardisation of sample collection and testing.[3] In addition, the sampling and analytical processes need to be robust to variations in technique that occur in the context of an acute assessment unit,[4] performed by busy clinicians rather than laboratory staff.

Previously, we embedded POC testing in an Emergency Multidisciplinary Unit (EMU), utilising the Abbott I-Stat™ and Alere Afinion™ systems, with the selection of tests that were available in the cartridges for those diagnostic platforms. This unit aims to facilitate the provision of acute assessment and treatment for adults where referring general practitioners (GPs) and ambulance paramedics consider that an out of hospital treatment pathway may be appropriate.[5] In particular, the EMU delivers acute multidisciplinary assessment to determine the optimal management for acute frailty syndromes (e.g. confusion, falls, general functional decline). The medical team are provided by an acute hospital trust and identify patients for whom transfer to an acute hospital would be the next appropriate step in care or whether they can continue on an ambulatory care pathway.

The EMU therefore provides an alternative to an acute hospital-based assessment with the flexibility to provide on-going care at home (through a hospital at home nursing team), daily visits to the unit or overnight care in a community hospital bed. Wider adoption of acute ambulatory care, delivered through units such as the EMU, is dependent on demonstrating a robust POC testing platform, including implementing appropriate quality control mechanisms in the POCT management process, so that treating clinicians can have confidence in making decisions based on the rapid outputs from POC devices.

We set out to study the agreement and bias between POC tests for electrolytes, haemoglobin (Hb), International Normalised Ratio (INR) and C-reactive Protein (CRP) and subsequent laboratory tests for creatinine, urea, sodium, potassium, calcium, Hb, INR, and CRP in a community-based acute care unit.

METHODS

Setting
Community based acute ambulatory care unit utilising POC testing and central laboratory testing of samples transported by road to a neighbouring acute hospital. The unit is equipped with POC blood testing using the Abbott iSTAT™ and Alere Afinion™ platforms.

Population
Community-dwelling adults (>18 years) referred for same-day assessment and treatment of a suspected acute medical illness where ambulatory care is considered possible by the referring healthcare professional.

Point-of-care test users
The POC tests were performed by clinical staff (nurse practitioners) who were trained by the device manufacturer to handle and prepare the samples and perform the POC test. Apart from an internal quality control during every device start up, regular quality control checks on the different POC devices were performed according to the manufacturer's instructions, by means of a liquid quality control. Users who had not been registered to use the device or whose registration to use it had expired and were not revalidated could not use the i-Stat™ or Alere Afinion™ devices.

Quality Management
I-Stat™ and Alere Afinion™ devices are connected to middleware (Siemens POCcelerator™ Data Management System). This enables result transfer and positive patient identification if the patient is known to the electronic patient record (EPR). POCcelerator™ also facilitates user registration. Users are trained and given an operator expiry. i-Stat™ and Alere Afinion™ devices are registered on an external quality assurance programme and results are monitored by the Department of Clinical Biochemistry at Oxford University Hospitals NHS Foundation Trust, who verified the assays in accordance with ISO 15189:2012 Medical laboratories - Requirements for quality and competence, clause 5.5.1.2 Verification of examination procedures. I-Stat™ and Alere Afinion™ cartridges are acceptance tested by the laboratory prior to issuing to the EMU.

Index tests
POC tests, on whole blood samples taken by venous puncture, with Abbott iSTAT™ clinical chemistry (creatinine, urea, sodium, potassium, calcium (all measured potentiometrically), haematology (haemoglobin, INR (both measured amperometrically), and Alere Afinion™ for C-reactive protein (immunometrically). Both these testing platforms are whole blood cartridge-based systems where no pipetting or sample dilution is required and results are produced automatically. The Afinion™ C-reactive protein has been shown to have a within-day variation of 7.4% (coefficient of variation (CV)) and a between-day CV of 4.6%,[6] while the iStat™ system has a within-run CV ranging from 0.1 to 9.5% and a between-run CV of 0.7 to 5.9% for the different analytes.[7]

Reference tests
Paired venous whole blood samples taken at the same time as those used for POC testing were sent the same day to biochemistry and haematology laboratories via a standard central lab sample transport service at the John Radcliffe Hospital for processing and analysis on arrival. Central laboratory biochemical testing on blood transported in lithium/heparin tubes for creatinine, urea, sodium, potassium and calcium was undertaken using an Abbott c16000 analyser (via potentiometry, CVs ranging from 0.4 to 2.9 for the different analytes)[8] and C-reactive protein using an Abbott Architect Analyser (via immunometry with CV of 1.8%)[8]. Central haematology laboratory testing on blood transported in EDTA for haemoglobin and citrate for INR, was undertaken using a Sysmex SN series analyser (turbo-densitometric and optomechanical detection with CV of 6.6% for haemoglobin and 1.9% for INR).[9 10] Mean reporting time for samples in the central laboratory is 330 minutes from collection.

Recruitment
The primary cohort for analysis were consecutive patients referred for acute assessment between 12th August 2015 and 8th December 2015, where we examined agreement between POC tests and paired laboratory samples for all analyses.

Outcomes
We aim to assess the agreement with limits of agreement and estimate relative bias between POC tests and the central laboratory. We report the bias for each analyte for a set of clinically relevant thresholds, based on clinical consensus among clinicians from a range of clinical backgrounds such as chemical pathology (BS), acute and geriatric medicine (SP, JSTB, TNCE, CR), acute ambulatory medicine (DSL), and primary care (JV, AvdB, GNH), as well as compare the observed total error to pre-specified specifications of allowable total error, whenever available.[11-13]

Statistical Analysis
Agreement between POC and laboratory tests was analysed using the Bland-Altman method[14] (both absolute and relative difference plots) and estimated relative bias was analysed and plotted using Passing–Bablok regression.[15] Limits of agreement (LOA) were calculated (mean bias +/- 2 standard deviations (SD) of the results obtained in this study) and plotted on the Bland-Altman plots so that 95% of differences are within these limits.
As the POC tests report ionised calcium, we multiplied ionised calcium by 2 to compare with the calcium test results measured at the central laboratory.[16 17] Observed total error was calculated as the sum of mean percentage bias and 1.65 the standard deviation (imprecision for each analyte obtained the central lab verification data).
All analyses were performed using the statistical program R version 3.3.3 with the mcr package (R foundation, Vienna, Austria).

RESULTS

Baseline characteristics

Blood samples from 462 patients were analysed, with a median age of 81 years (IQR 69-87) with 59.3% women. **(Table 1)** 82.1% were referred by their treating GP. As POC testing was performed as part of routine clinical care, the number of patients with parallel laboratory and POC testing varied across tests, with a range from 391 patients for haemoglobin estimation to 31 patients for INR testing (**Table 1**).

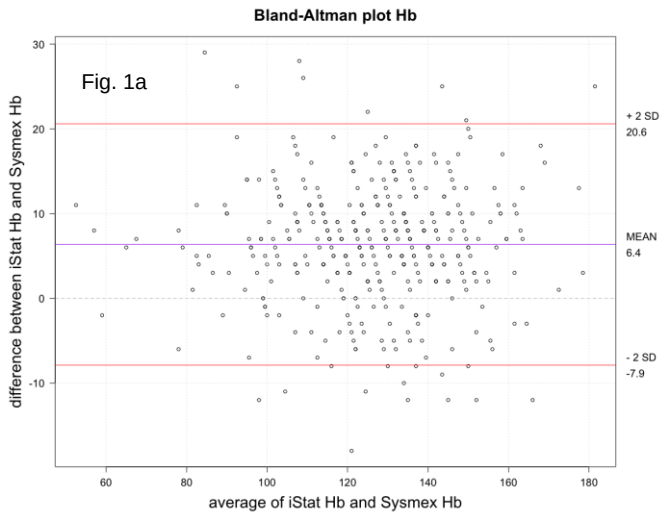
Table 1: Baseline characteristics

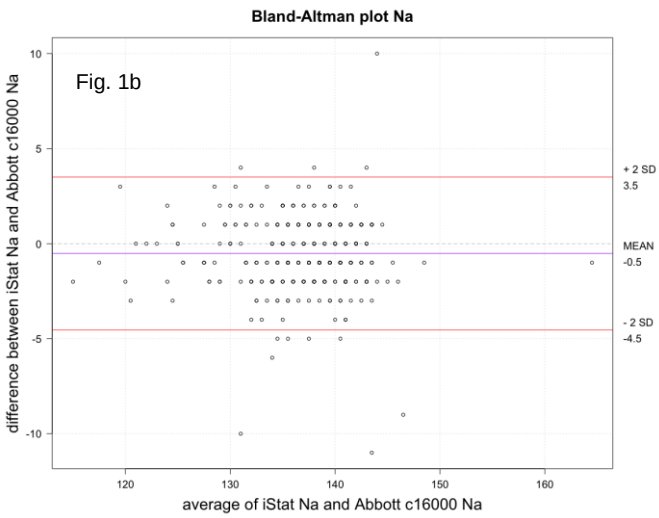
	n = 462
median age in years (IQR)	81 (69-87)
men (%)	188 (40.7%)
referred by GP (%)	379 (82.1%)
number of paired (POC & LAB) tests for:	
haemoglobin	391 (84.6%)
sodium (Na)	332 (71.9%)
potassium (K)	332 (71.9%)
calcium (Ca)	186 (40.3%)
creatinine	335 (72.5%)
urea	323 (69.9%)
C-reactive Protein (CRP)	247 (53.5%)
International Normalised Ratio (INR)	31 (6.7%)

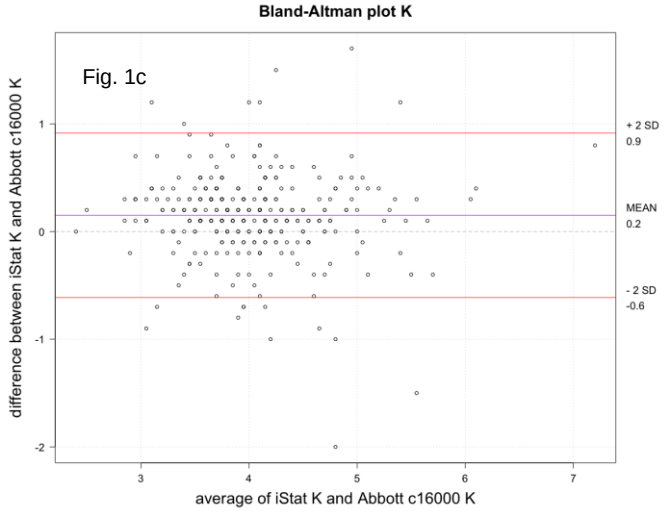
IQR: interquartile range; GP: General Practitioner; POC: point-of-care; LAB: central clinical laboratory

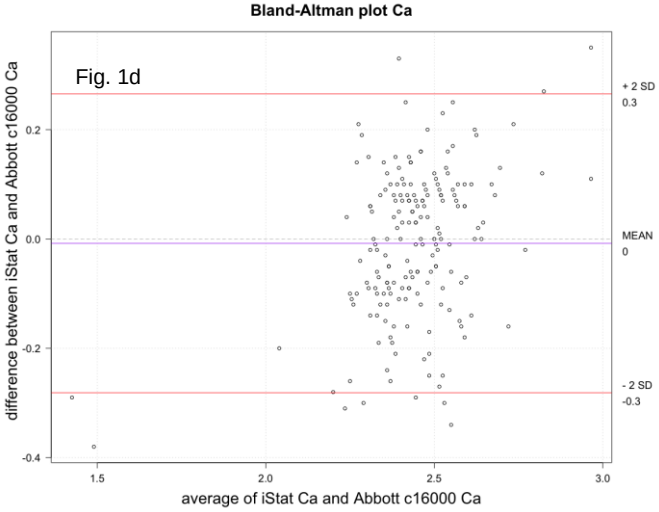
Agreement between POC tests and central lab tests

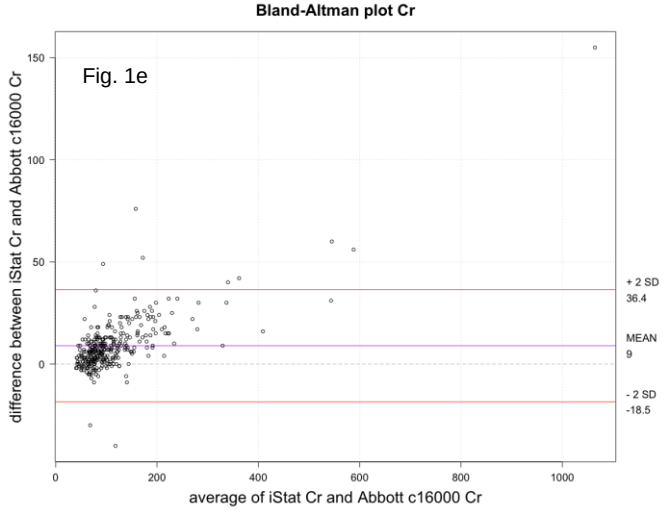
The agreement in the primary cohort between the results from POC tests and the central laboratory analyses are shown with Bland-Altman graphs in **Figure 1**, with the absolute mean difference and limits of agreement whenever both POC and laboratory testing were undertaken.

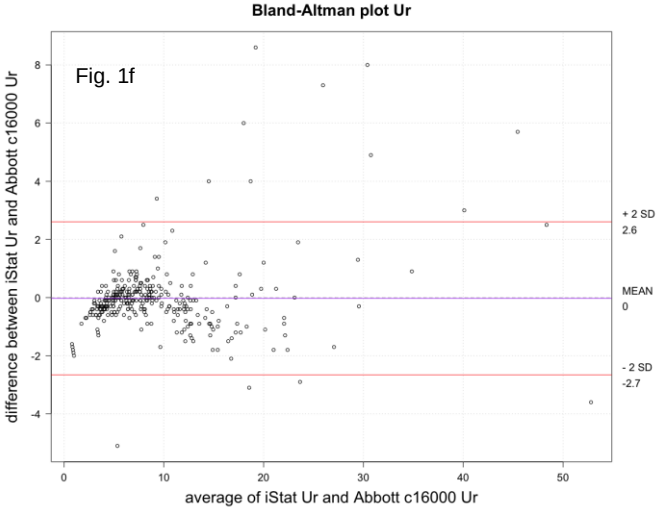


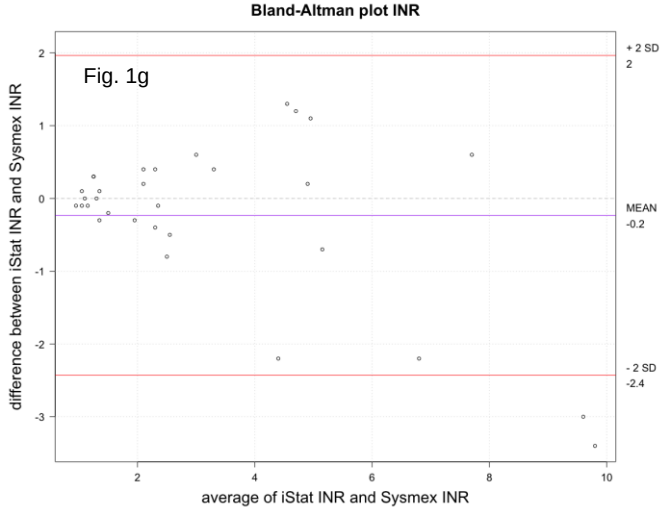












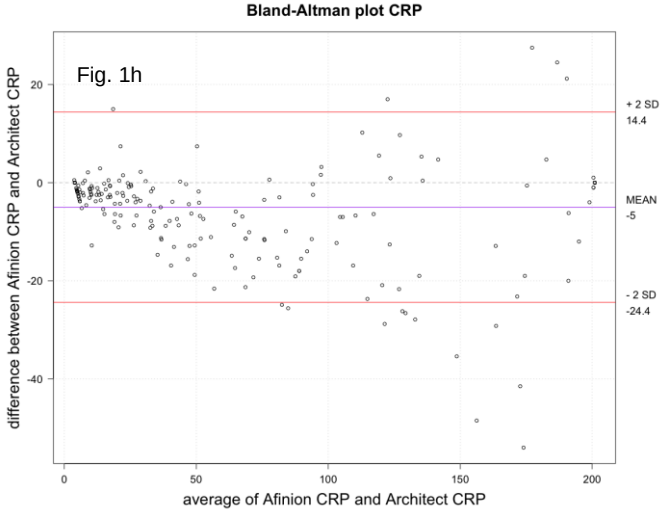


Figure 1a-h: Bland Altman absolute difference plots for haemoglobin (Hb), sodium (Na), potassium (K), calcium (Ca), creatinine (Cr), urea (Ur), INR, CRP dots: scatter; red lines: 95% limits of agreement; purple line: mean difference between point-of-care and central laboratory method; a positive mean difference indicates a positive bias for the point-of-care method

There was evidence of a positive bias for creatinine, haemoglobin and potassium and a negative bias for sodium, calcium, CRP and INR. **(Table 2)**

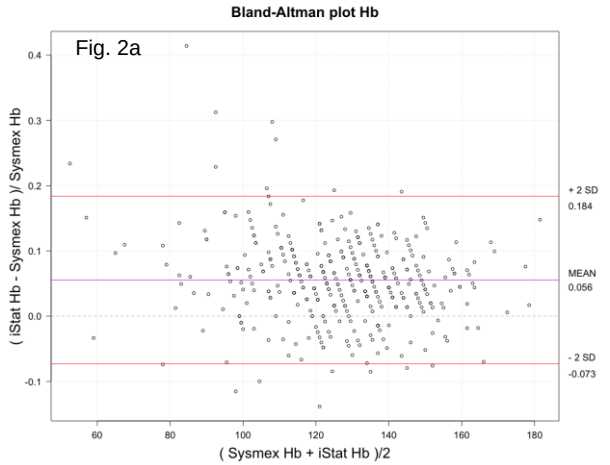
Table 2: Agreement between point-of-care test and central lab test for the different analytes

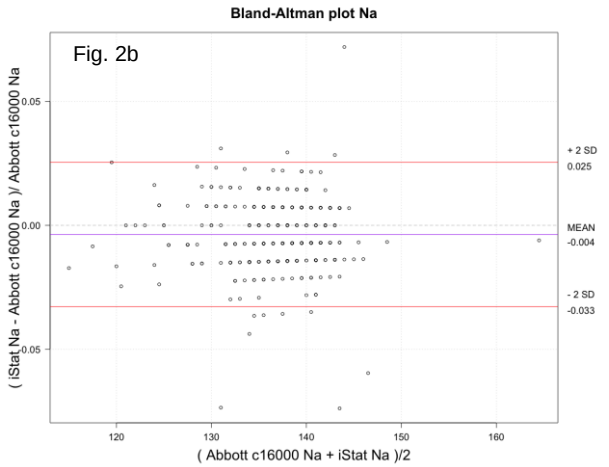
Analyte	Absolute mean difference 95% LOA	Relative mean difference 95% LOA	Correlation coefficient 95% CI
Haemoglobin	6.4 g/L	5.6%	0.94
	-7.9 to +20.6 g/L	-7.3 to 18.4%	0.93-0.95
Sodium	-0.5 mmol/L	0.4%	0.93
	-4.5 to +3.5 mmol/L	-3.3 to 2.5%	0.92-0.95
Potassium	0.2 mmol/L	4.5%	0.82
	-0.6 to +0.9 mmol/L	-15.1 to 24.1%	0.78-0.85
Calcium ionised	0.0 mmol/L	0.3%	0.74
	-0.3 to +0.3 mmol/L	-11.9 to 11.2%	0.66-0.80
Creatinine	9.0 µmol/L	7.7%	0.99
	-18.5 to +36.4 µmol/L	-12.3 to 27.7%	0.99-1.00
Urea	0.0 mmol/L	2.6%	0.98
	-2.7 to +2.6 mmol/L	-36.2 to 31.0%	0.98-0.99
INR	-0.2	0.6%	0.93
	-2.4 to +2.0	-41.3 to 40.0%	0.86-0.97
C-Reactive Protein	-5.0 mg/L	9.8%	0.99
	-24.4 to +14.4 mg/L	44.1 to 24.5%	0.99-0.99

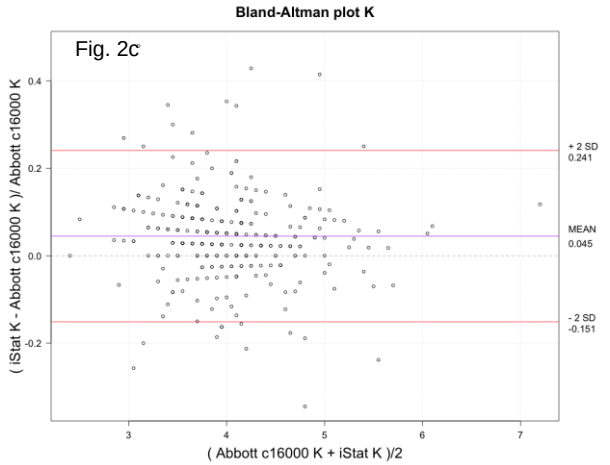
95% CI: 95% confidence intervals

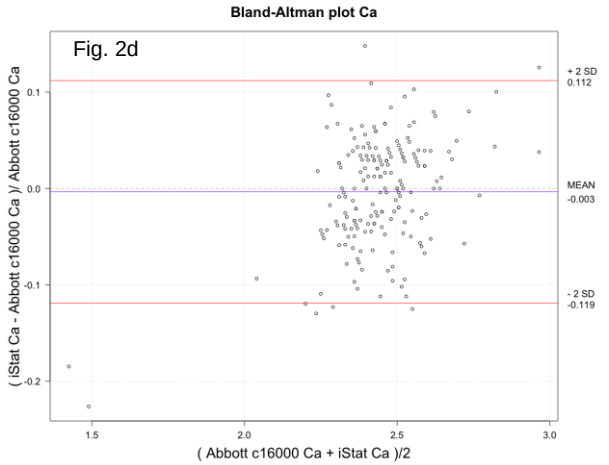
The relative limits of agreement indicated a much wider interval for some analytes, such as haemoglobin (-7.3 to +18.4%) versus other analytes, such as serum sodium -3.3 to +2.5%). The positive bias for POC creatinine appeared to increase with the average of POC and laboratory results, such that at very high levels the bias was higher (**Figure 1e**).

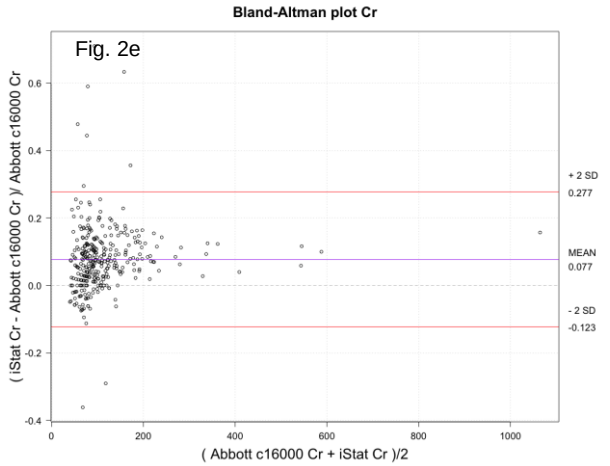
The relative difference plots are shown in **Figure 2** and **Table 2.**

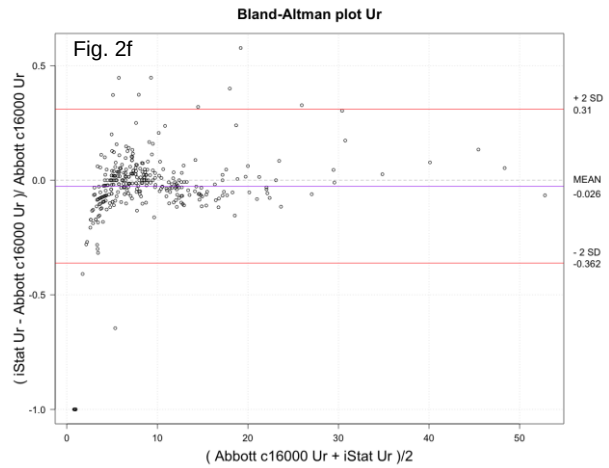


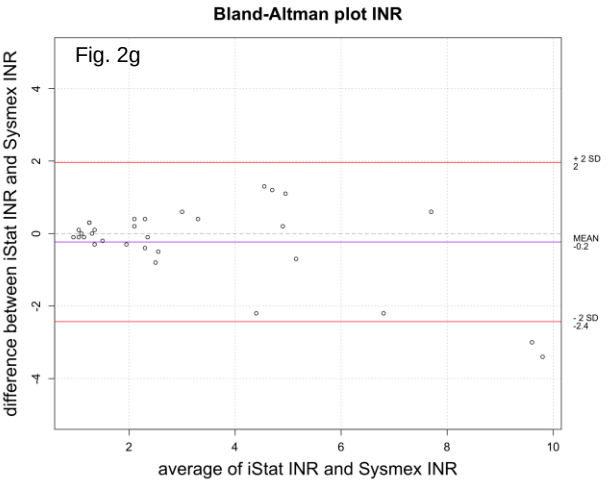












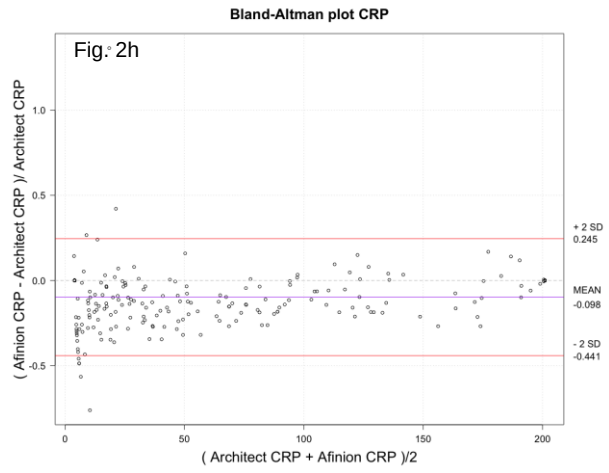


Figure 2a-h: Bland Altman relative difference plots for haemoglobin (Hb), sodium (Na), potassium (K), calcium (Ca), creatinine (Cr), urea (Ur), INR, CRP dots: scatter; purple line: mean difference between point-of-care and central laboratory method; red lines: 95% limits of agreements; a positive mean difference indicates a positive bias for the point-of-care method

Estimated bias between POC tests and central lab tests

The estimated bias between the POC test results and central laboratory tests is shown in **Figure 3** with 95% confidence regions.

Fig. 3a

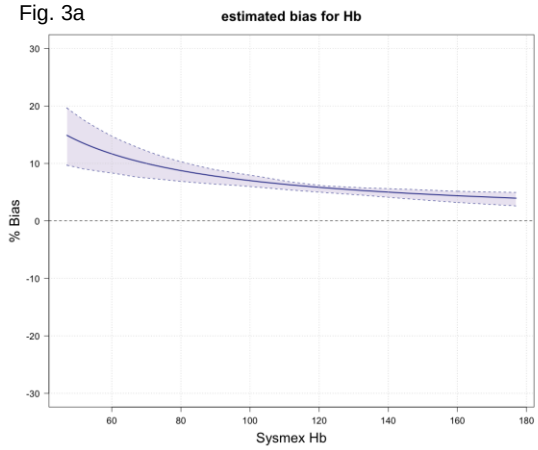


Fig. 3b

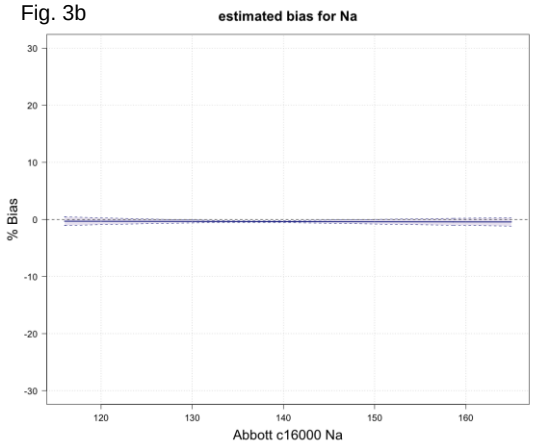


Fig. 3c

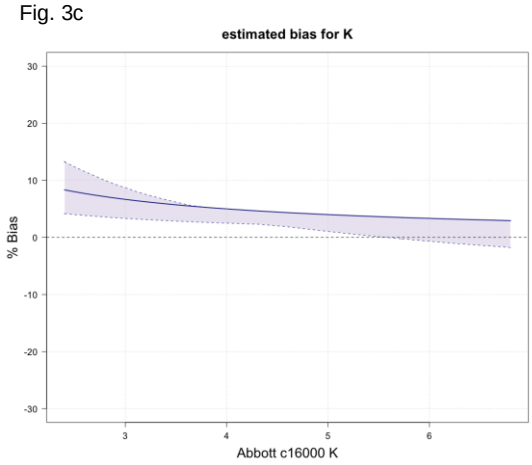


Fig. 3d

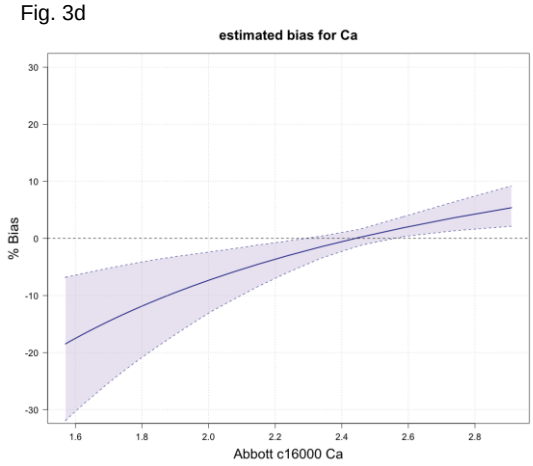


Fig. 3e

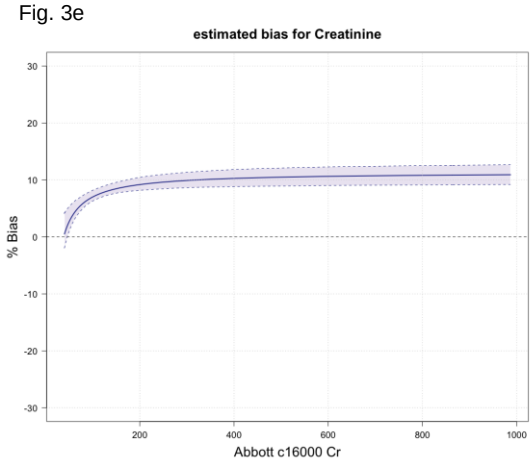


Fig. 3f

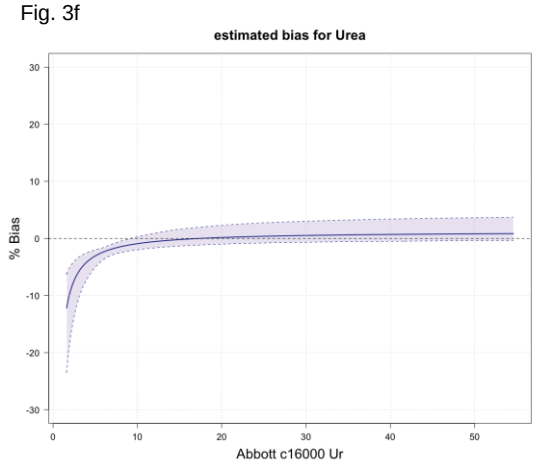


Fig. 3g

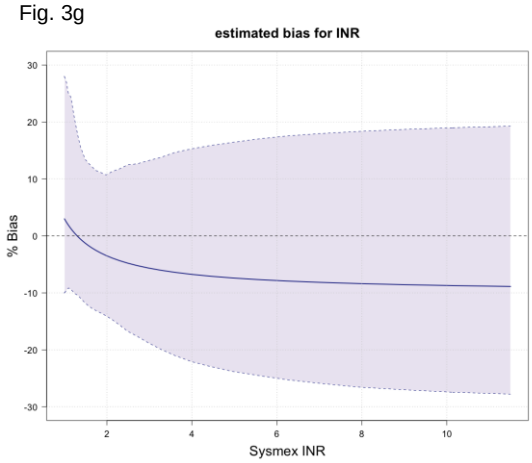


Fig. 3h

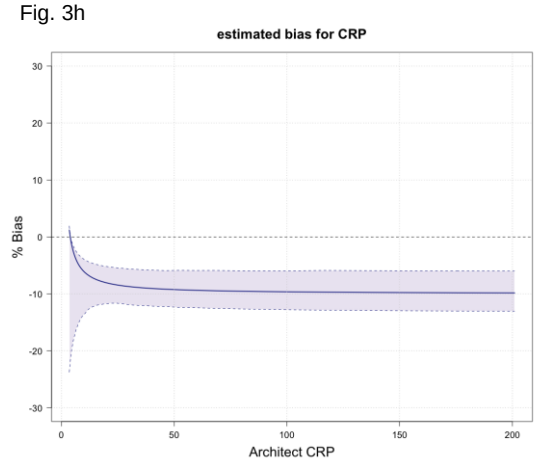


Figure 3a-h: Estimated bias (%) curves for haemoglobin, sodium, potassium, calcium, creatinine, urea, INR, CRP

Blue line: regression line of estimated bias; blue area: confidence area scatter

At pre-specified clinically relevant thresholds, there was acceptable bias for most analytes, apart from haemoglobin (7g/L (95%CI 5.3 to 8.2) at a threshold of 80 g/L and creatinine at a threshold of 150 µmol/L (bias of 12.7 µmol/L (95%CI 11.6 to 14.5)) (**Table 3)**.

Table 3: Bias between point-of-care test and central lab test at clinically relevant thresholds for the different analytes

Analyte	Threshold	Bias	95% confidence interval	
Haemoglobin (g/L)	80	+7.0	+5.3	+8.2
	110	+7.0	+6.0	+7.5
Sodium (mmol/L)	125	-0.3	-0.8	+0.1
	145	-0.4	-0.7	-0.1
Potassium (mmol/L)	3.5	+0.2	+0.1	+0.2
	6	+0.2	-0.1	+0.2
Calcium ionised (mmol/L)	1.15	-0.4	-0.8	-0.2
	1.4	-0.3	-0.6	-0.1
Creatinine (µmol/L)	50	+1.3	+0.5	+2.5
	150	+12.7	+11.6	+14.5
Urea (mmol/L)	2.9	-0.2	-0.3	-0.1
	8.2	-0.1	-0.2	-0.0
INR	2.0	-0.1	-0.3	+0.2
	3.5	-0.2	-0.7	+0.5
C-Reactive Protein (mg/L)	5	-0.1	-0.9	-0.1
	75	-7.1	-9.5	-4.5

When compared to pre-specified allowable total error specifications[11], sodium, potassium, calcium, urea, INR and CRP met these criteria (**Table 4).**

Table 4 (or Appendix table 1): Comparison between observed and allowable total error for the different analytes

	Analytical variation	Observed specification		Desirable specification[11-13]		
	Imprecision (%)	Bias (%)	Total error (%)	Imprecision (%)	Bias (%)	Total error (%)
Haemoglobin	3.2	5.6	10.9	1.4	1.8	4.2
Sodium	0.5	0.4	**1.3***	0.9	3.1	4.6
Potassium	0.5	4.5	**5.3***	2.3	1.8	5.6
Calcium ionised	0.6	0.3	**1.3***	0.9	0.6	2.0
Creatinine	6.4	7.7	18.3	3.0	4.0	8.9
Urea	1.0	2.6	**4.2***	6.1	5.6	15.6
INR	7.5	0.6	**13.0***	-	-	24.0
C-Reactive Protein	6.4	9.8	**20.4***	21.1	21.8	56.6

*within allowable total error; INR: International Normalised Ratio

DISCUSSION

We have shown that in an acute ambulatory care setting, POC results for some commonly requested tests as part of an acute medical assessment correlate reasonably well to those undertaken with paired central laboratory testing. The mean bias was acceptable at clinically relevant thresholds for most analytes, apart from haemoglobin and creatinine. POC results for sodium, potassium, calcium, urea, INR and C-reactive protein met the pre-specified allowable total error specifications.

Our use of different measures of agreement and correlation reveal some limitations of practice when clinically applying the results of POC testing. In the clinical environment of a community based acute ambulatory care unit, POC testing is used to screen for significantly disturbed physiology and to prompt a targeted diagnostic search for causative conditions – this may need additional scheduled investigations at an acute centre with a broader range of support services such as cross-sectional imaging. The iStat™ over-reads the Hb and the upper limit of agreement shows this positive bias could be up to 20 g/L. This may miss significant anaemia in a clinical setting unless the treating clinician is aware of the limitations of the POC test performance. Similarly, whilst the INR POC results, although only measured on a very small sample of patients, show a small average bias of 0.2, the limits of agreement are very wide, from -2 to +2 and significant under- or over-anticoagulation will be missed or mis-diagnosed and inappropriately treated.

In addition, this analysis has shown that some bias in results may have either no clinical impact or cause false-positive alerts leading to more conservative care. The Bland-Altman plots shows that the POC creatinine values are higher than the laboratory values particularly when the creatinine level is raised. Although acute kidney injury may be missed due to the lack of comparison to previous results, even if there is an over-reading at very high levels this will not affect clinical decision making as acute kidney injury stage 3 will be clearly diagnosed in the setting of acute illness. A positive bias for creatinine would be expected to yield false positive acute kidney injury warnings, especially if the baseline values largely or entirely comprised laboratory values. Where acute kidney injury was clinically likely and the POC creatinine was raised, additional central laboratory testing may be required to give an accurate acute kidney injury warning stage alert.

Strengths and limitations

The strengths of this study are that it has assessed the agreement between paired POC and laboratory tests under clinical conditions. In busy clinical units, POC testing is undertaken by staff who are not laboratory trained and the needs of patients are also competing for time and attention whilst they are carrying out POC tests. This analysis demonstrates the accuracy of the sampling and analytical methods in the context of day to day acute care in a setting without a co-located hospital laboratory. The time delay between the point-of-care test and the central lab test, inherent to routine clinical care, could have introduced bias in our results, although previous research has shown that these tests did not show deviations of clinical importance even after 10 hours storage and transport at 21ºC.[8]

Nevertheless, this analysis does have some limitations. As this is an evaluation of routinely delivered healthcare, there is a variation in the number of samples for the different tests. The smallest sample size was for INR and the results may be unrepresentative of true POC test performance. However, the largest sized sample was for haemoglobin estimation and therefore we can be more confident about the mean bias that was detected. The performance of the POC tests in our study generalises only to acute ambulatory settings rather than emergency departments or general practice populations. The device manufacturer delivered training sessions using the device, which may have had an impact on the content of the training although we believe the training was fair and transparent, focusing on how to use the device without giving any clinical recommendations. Furthermore, revalidation requirements were not imposed on clinical staff to maintain POCT use certification. We did not use pre-defined care pathways to protocolise diagnostic testing, and instead used clinical judgement as is routine practice in the UK.

Comparison with existing literature

The accuracy of the POC platforms used in this study has been assessed in other patient populations with differing results, suggesting an important link between the clinical context of POC testing and performance of POC tests. In patients with critical illness, the bias of the I-STAT Hb estimation has been found to be small and not clinically relevant.[18] A negative bias for Hb estimation was found in one small sample of intra-operative tests in surgical patients with repeatability affected by blood loss.[19] Further studies of Hb estimation in different critical illness populations have also shown that the bias of iSTAT™ varies with clinical context and that users of POC tests should interpret accuracy according to clinical setting to optimise decision making.[20]

Although potassium levels are known to be susceptible to ambient temperature during transport,[21] we found an acceptable bias at clinically relevant thresholds between the POC and central lab test.

Among stable patients being monitored for anticoagulation with samples taken by phlebotomists, the iSTAT™ INR shows comparable accuracy to central laboratory methods,[22] and in a prospective study in an emergency department, the bias of iSTAT™ INR was not clinically significant in patients with acute stroke and urgent requirement for coagulation assays in preparation for thrombolysis.[23] The difference we observed may be due to the need for immediate testing after appropriate sample mixing as there is no anticoagulant in the sample collection devices for INR testing, and as a result this may be easier in a scheduled clinic environment, or within a set stroke protocol, rather than a busy acute ambulatory care unit. Studies of clinical chemistry using the iSTAT™ have shown a similar small, but clinically insignificant, bias of creatinine[24] and a similar acceptable agreement for electrolytes.[25] We have not found reports of iSTAT™ agreement with laboratory results specifically in an adult acute ambulatory care population.

Our findings of an acceptable mean difference for CRP are consistent with published data from evaluations comparing the Alere device with other POC testing platforms.[6 26]

Implications for clinicians

In keeping with other reports of clinical accuracy from routinely collected data in acute settings,[16] our results imply that clinicians should be confident in making clinical decisions based on specific POC results. However, understanding where there are biases in agreement between POC and laboratory measures in different patient populations is essential to appropriately interpret results. Considering the POC test can over-read the Hb by up to 20g/L, clinicians might choose to use it as a test that indicates a range within which the Hb lies, with a guide as to the likely lowest value.

Implications for research

Further research is needed to assess the impact of POC tests on clinically relevant outcomes to support decision making in different clinical contexts and methods to allow clinical teams, in partnership with their supporting diagnostic services, to understand how POC tests perform in their patient populations.

ACKNOWLEDGEMENTS

- **CONTRIBUTORS:** DSL conceived the study, supervised data collection and analysis and clinically interpreted data. BS and IS supported the use of POC testing on the clinical unit and facilitated laboratory data collection. SP co-designed data analysis methods and provided clinical interpretation of results CR, JB, TE and RH performed data follow up and data cleaning and provided critical comments on manuscripts. JV performed the analyses and drafted the initial report. All authors had full access to all of the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. DSL affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted. All authors have provided critical comments on manuscript drafts and approved the final manuscript. We would like to thank Dr Tim James, Clinical Biochemistry Department, John Radcliffe Hospital, Oxford.
- **FUNDING:** This study represents independent work funded by the NIHR Oxford Diagnostic Evidence Cooperative, NIHR Oxford CLAHRC and NIHR Oxford Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the NIHR, the Department of Health, or the NHS.

COMPETING INTEREST

Competing interest: none declared.

ETHICAL APPROVAL

The use of routine healthcare data collected by the clinical treating team for the purposes of informing future service development using POC testing was prospectively approved as a service evaluation by Oxford University Hospitals NHS Foundation Trust (providers of the medical care on EMU), with audit Datix reference number 3812, and permission to publish was granted by Oxford Health NHS Foundation Trust R&D Department (provider trust for the EMU).

REFERENCES

1. Future Hospital Commission. Future hospital : caring for medical patients. London: Royal College of Physicians 2013.
2. Maruthappu M, Sood HS, Keogh B. The NHS Five Year Forward View: implications for clinicians. *BMJ* 2014;349:g6518. doi: 10.1136/bmj.g6518
3. Jones CH, Howick J, Roberts NW, et al. Primary care clinicians' attitudes towards point-of-care blood testing: a systematic review of qualitative studies. *BMC Fam Pract* 2013;14(1):117. doi: 10.1186/1471-2296-14-117
4. Turner PJ, Van den Bruel A, Jones CH, et al. Point-of-care testing in UK primary care: a survey to establish clinical needs. *Fam Pract* 2016;33(4):388-94. doi: 10.1093/fampra/cmw018
5. Jones CH, Glogowska M, Locock L, et al. Embedding new technologies in practice - a normalization process theory study of point of care testing. *BMC health services research* 2016;16(1):591. doi: 10.1186/s12913-016-1834-3 [published Online First: 2016/10/21]
6. Minnaard MC, van de Pol AC, Broekhuizen BD, et al. Analytical performance, agreement and user-friendliness of five C-reactive protein point-of-care tests. *Scand J Clin Lab Invest* 2013;73(8):627-34. doi: 10.3109/00365513.2013.841985
7. Yeo CP, Ngo A, Ng WY, et al. Assessing Performance of i-STAT at the Point of Care in the Emergency Room. *Proceedings of Singapore Healthcare* 2011;20(3):157-61. doi: 10.1177/201010581102000304
8. Henriksen LO, Faber NR, Moller MF, et al. Stability of 35 biochemical and immunological routine tests after 10 hours storage and transport of human whole blood at 21 degrees C. *Scandinavian journal of clinical and laboratory investigation* 2014;74(7):603-10. doi: 10.3109/00365513.2014.928940 [published Online First: 2014/07/06]
9. Geens T, Vertessen F, Malfait R, et al. Validation of the Sysmex CS5100 coagulation analyzer and comparison to the Stago STA-R analyzer for routine coagulation parameters. *Int J Lab Hematol* 2015;37(3):372-81. doi: 10.1111/ijlh.12295 [published Online First: 2014/09/23]
10. Coskun A, Carobene A, Kilercik M, et al. Within-subject and between-subject biological variation estimates of 21 hematological parameters in 30 healthy subjects. *Clin Chem Lab Med* 2018;56(8):1309-18. doi: 10.1515/cclm-2017-1155 [published Online First: 2018/04/02]
11. Ricos C AV, Cava F, Garcia-Lario JV, Hernandez A, Jimenez CV, Minchinela J, Perich C, Simon M. Desirable specifications for total error, imprecision, and bias, derived from intra- and inter-individual biologic variation. 2017 [Available from: http://www.westgard.com/biodatabase1.htm accessed 8th October 2017.
12. Westgard JO, Westgard SA. Measuring Analytical Quality: Total Analytical Error Versus Measurement Uncertainty. *Clin Lab Med* 2017;37(1):1-13. doi: 10.1016/j.cll.2016.09.001
13. Westgard JO. Useful measures and models for analytical quality management in medical laboratories. *Clin Chem Lab Med* 2016;54(2):223-33. doi: 10.1515/cclm-2015-0710

14. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1(8476):307-10. [published Online First: 1986/02/08]
15. Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. *Journal of clinical chemistry and clinical biochemistry Zeitschrift fur klinische Chemie und klinische Biochemie* 1988;26(11):783-90. [published Online First: 1988/11/01]
16. Mirzazadeh M, Morovat A, James T, et al. Point-of-care testing of electrolytes and calcium using blood gas analysers: it is time we trusted the results. *Emergency medicine journal : EMJ* 2016;33(3):181-6. doi: 10.1136/emermed-2015-204669 [published Online First: 2015/09/24]
17. Calvi LM, Bushinsky DA. When Is It Appropriate to Order an Ionized Calcium? *Journal of the American Society of Nephrology* 2008;19:1257-60.
18. Rudolf J, Douglass J, Baron J, et al. Evaluation of the i-STAT point-of-care capillary whole blood hematocrit and hemoglobin: Comparison to the Siemens RAPIDLab 1200, Sysmex XE5000, and manual spun hematocrit. *Clinica chimica acta; international journal of clinical chemistry* 2015;446:37-42. doi: 10.1016/j.cca.2015.03.035 [published Online First: 2015/04/12]
19. Ng WL, Short TG, Gunn KN, et al. Accuracy and reliability of the i-STAT point-of-care device for the determination of haemoglobin concentration before and after major blood loss. *Anaesth Intensive Care* 2014;42(4):495-9.
20. Steinfelder-Visscher J, Teerenstra S, Gunnewiek JM, et al. Evaluation of the i-STAT point-of-care analyzer in critically ill adult patients. *The journal of extra-corporeal technology* 2008;40(1):57-60. [published Online First: 2008/04/09]
21. Seamark D, Backhouse S, Barber P, et al. Transport and temperature effects on measurement of serum and plasma potassium. *J R Soc Med* 1999;92(7):339-41.
22. Pena JA, Lewandrowski KB, Lewandrowski EL, et al. Evaluation of the i-STAT point-of-care capillary whole blood prothrombin time and international normalized ratio: comparison to the Tcoag MDAII coagulation analyzer in the central laboratory. *Clin Chim Acta* 2012;413(11-12):955-9. doi: 10.1016/j.cca.2012.01.035 [published Online First: 2012/02/15]
23. Drescher MJ, Spence A, Rockwell D, et al. Point-of-care testing for coagulation studies in a stroke protocol: a time-saving innovation. *The American journal of emergency medicine* 2011;29(1):82-5. doi: 10.1016/j.ajem.2009.09.020 [published Online First: 2010/09/10]
24. Dimeski G, Tilley V, Jones BW, et al. Which point-of-care creatinine analyser for radiology: direct comparison of the i-Stat and StatStrip creatinine methods with different sample types. *Annals of clinical biochemistry* 2013;50(Pt 1):47-52. doi: 10.1258/acb.2012.012081 [published Online First: 2012/10/31]
25. Veldhoen ES, de Vooght KM, Slieker MG, et al. Analysis of bloodgas, electrolytes and glucose from intraosseous samples using an i-STAT((R)) point-of-care analyser. *Resuscitation* 2014;85(3):359-63. doi: 10.1016/j.resuscitation.2013.12.002 [published Online First: 2014/01/07]

26. Verbakel JY, Aertgeerts B, Lemiengre M, et al. Analytical accuracy and user-friendliness of the Afinion point-of-care CRP test. *J Clin Pathol* 2014;67(1):83-6. doi: 10.1136/jclinpath-2013-201654 [published Online First: 2013/09/13]