

Point of Care testing in Haemostasis – INR and DDimer

Steve Kitchen

UK NEQAS Blood Coagulation, Sheffield

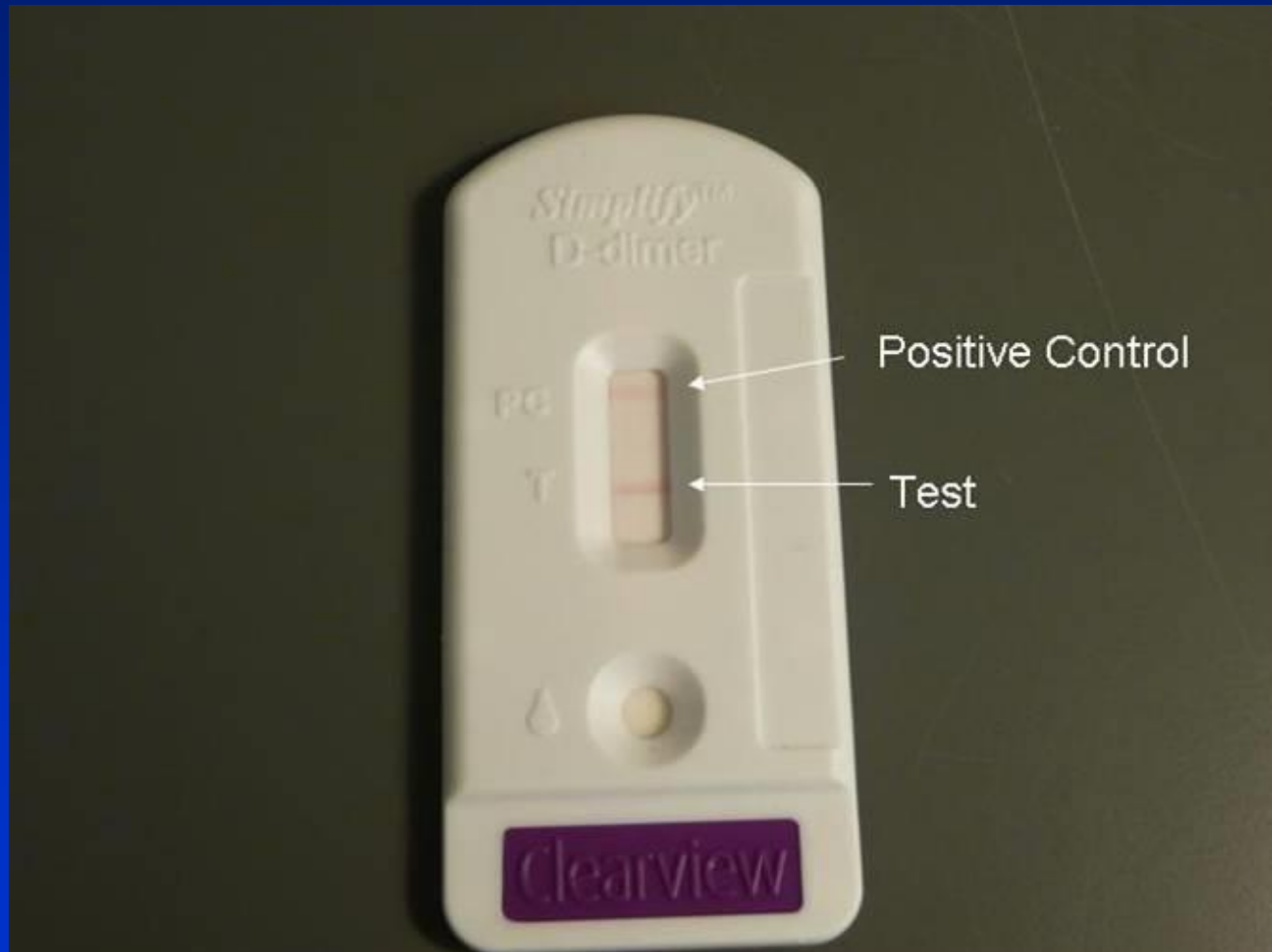


Automated POC Devices for INR

Currently in use in the UK are

- CoaguChek XS
- CoaguChek XS Plus
- CoaguChek XS Pro
- CoaguChek XS Pro II (launching soon in UK)
- Hemochron Signature Series
- i-STAT
- INRatio
- Protime
- MicroINR
- CoagMax
- Xprecia Stride

Qualitative POC D-Dimer (pos/neg)



Bridging the Gap between Point-of-Care Testing and Laboratory Testing in Hemostasis

Dianne P. Kitchen, FIBMS¹ Ian Jennings, PhD, CSci, FIBMS¹ Steve Kitchen, FIBMS, PhD¹
Timothy A. L. Woods, MBA, CSci, FIBMS¹ Isobel D. Walker, MD, MPhil¹

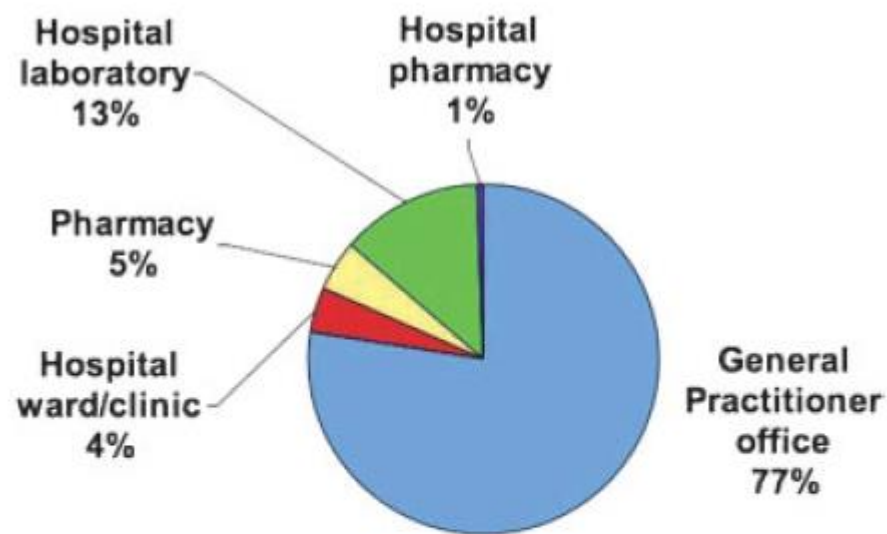


Fig. 1 Data showing sites of users in UK National External Quality Assessment Scheme for Blood Coagulation international normalized ratio point-of-care program.

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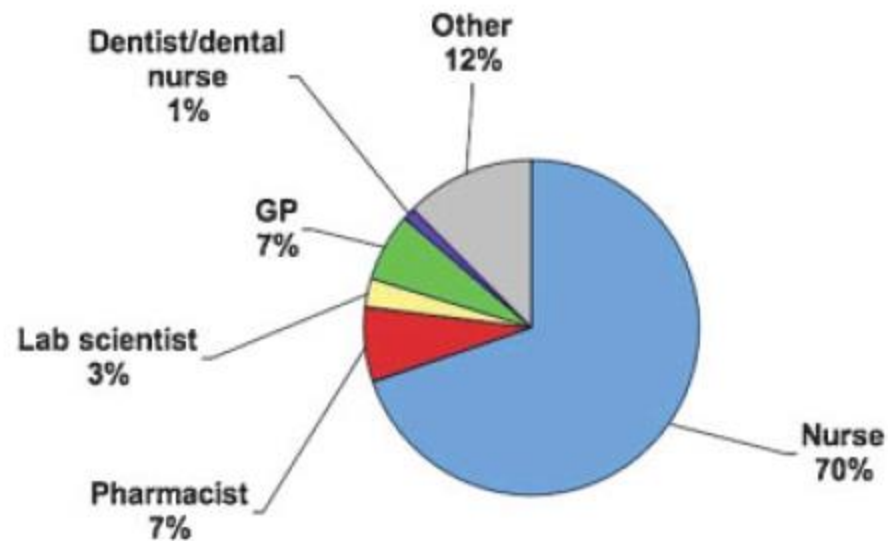


Fig. 2 Data from 2014 UK National External Quality Assessment Scheme for Blood Coagulation user's questionnaire showing types of staff performing point of care international normalized ratio testing.

Quality issues and quality management

POC INRs – Importance of quality assurance

- BMJ “ Rivaroxaban – Can we trust the evidence? (Cohen D. BMJ 2016: 352;179-80).
- Rocket AF study warfarin arm – INRs determined by INRatio
- INRatio – recall notice by FDA 2014 – clinically significantly lower readings”
- False low INR – more warfarin- more bleeding
- Rivaroxaban non inferior to poorly controlled warfarin?

POC INRs – Importance of quality assurance

- BMJ Cohen D. BMJ 2016: 352;179-80.
- INRatio
- Problems with accuracy reported to MHRA in UK
- UK NEQAS assessed and unable to develop a suitably stable EQA material
- No wet IQC test sample
- No EQA from other organizations

Urgent Field Safety Notice

Medical Device Recall of gabControl D-Dimer rapid test (M09DD02) from the market

Cologne, October 18, 2016

This Urgent Field Safety Notice of the gabmed GmbH concerns the gabControl D-Dimer rapid test (Product-ID: M09DD02).

Description of the problem:

Due to weakly visible test lines in the said batches, it came to an increased amount of false-negative results.

Although the potential risk is considered to be minor with a test considered to be a pre diagnostic test, the product is being recalled from the European market by the gabmed GmbH as a precautionary measure to prevent false negative results. As the test is used as an aid in diagnosis, there is residual risk that additional tests such as an ultrasound are not performed, particularly for patients considered to be at low risk. If you have performed this test recently consider the need to recall and retest patients with a laboratory based test. Production of new batches has been halted until further notice. **Please immediately discontinue use of the above-mentioned product; fill out the attached fax confirmation form and dispose of any remaining stocks in accordance with local regulations.**

Guidelines for point-of-care testing: haematology

British Journal of Haematology, 142, 904–915

2007

Key recommendations

- 1 The purpose, nature and potential benefits of POCT at a particular site should be defined before initiating the service.
- 2 An NHS Trust POCT committee should be established and take responsibility for all POCT and ensure it is appropriate and accreditable. The committee should involve laboratory staff and other relevant staff as appropriate. Where necessary, there should also be a local point-of-care committee to oversee the service when it is in a non-hospital setting.
- 3 The advice and involvement of an accredited clinical laboratory should be sought in order to achieve optimum quality and cost-effectiveness. This is also the recommendation for non-NHS sites (pharmacies for example). The haematology laboratory should play a key part in maintaining standards for patients in their catchment area.

Guidelines for point-of-care testing: haematology

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- 7 Documentation must include the name of the operator, date, patient identity details, results, lot number of calibrant, reagents and quality control materials. This must be recorded at the time of analysis. A record of any maintenance and repairs and should also be kept. It is advisable to keep an 'error log' to assist any investigation of potential incidents.
- 8 POCT raises the possibilities of litigation ensuing from erroneous results. Who bears legal responsibility locally should be established, as should the need for appropriate insurance cover.
- 9 All staff must recognise that only trained operators may use the equipment. An up-to-date list of trained operators and competency training should be maintained.

Guidelines for point-of-care testing: haematology

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- 11 Internal quality control (IQC) and EQA programmes must be established.

Quality Control for POCT INRs- Recommendations

- **Briggs et al 2007 (general haematology guidelines)**
- Results validated by IQC and EQA
- **Jennings, D Kitchen et al 2014 (patients guidelines)**
- Electronic QC each time monitor used
- IQC
- EQA – 2 options, either compare to a clinic device or compare to lab (both clinic device or lab should be in an EQA programme)
- **Perry et al 2010 (POCT in Haemostasis review)**
- Both IQC and EQA required if available

Venous samples to laboratory

- Sometimes venous samples are sent to the laboratory to check the result
- Points to consider
 - Quality of sample (haemolysed, under-filled)
 - Storage of sample until testing
 - How long between sample taken and testing
 - Transport of samples

What to do if POC INR is High

- Repeat on POC- if same –treat as per clinical requirements
- if >8.0 send venous sample to lab (or patient to hospital)

What to do if comparison studies with lab are not in agreement

- Look for consistent bias in results
- Review all samples tested
- Select patients carefully
- Ask Lab about any recent changes and their Quality control

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Table 3 Frequency of internal quality control testing for point of care^a

When do you test your IQC samples?	%
With a new batch of test strips	29
Other	26
With each clinic	15
Not available for our device	13
If unexpected results occurs	9
Monthly	3
Weekly	3
Never	2

Abbreviations: IQC, internal quality control.

^aData from questionnaire to UK National External Quality Assessment Scheme for Blood Coagulation users.

ISO 15189 2012

Medical Laboratories - Requirements for quality and competence

- Interlaboratory comparison programmes
CHOSEN BY THE LAB shall as far as possible provide clinically relevant challenges that mimic patient samples and have the effect of checking the entire examination process, including the pre analytical procedures, and post examination procedures, where possible

ISO 15189 2012

Medical Laboratories - Requirements for quality and competence

- Note : the lab should participate in interlaboratory comparison programmes that substantially fulfil the relevant requirements' of ISO 17043.

General requirements for proficiency testing

ISO 17043

- Have access to relevant expertise (eg advisory group)
- Provide advice in evaluating performance
- Items should match in terms of matrix , measurands and concentration as closely as practicable the type encountered in routine practice
- Sufficiently stable throughout the conduct of proficiency testing

UK NEQAS for Blood Coagulation

N ational

E xternal

Q uality

A sssessment

S cheme

- Part of UK National Health Service
- Role is to improve quality of testing and ultimately patient care

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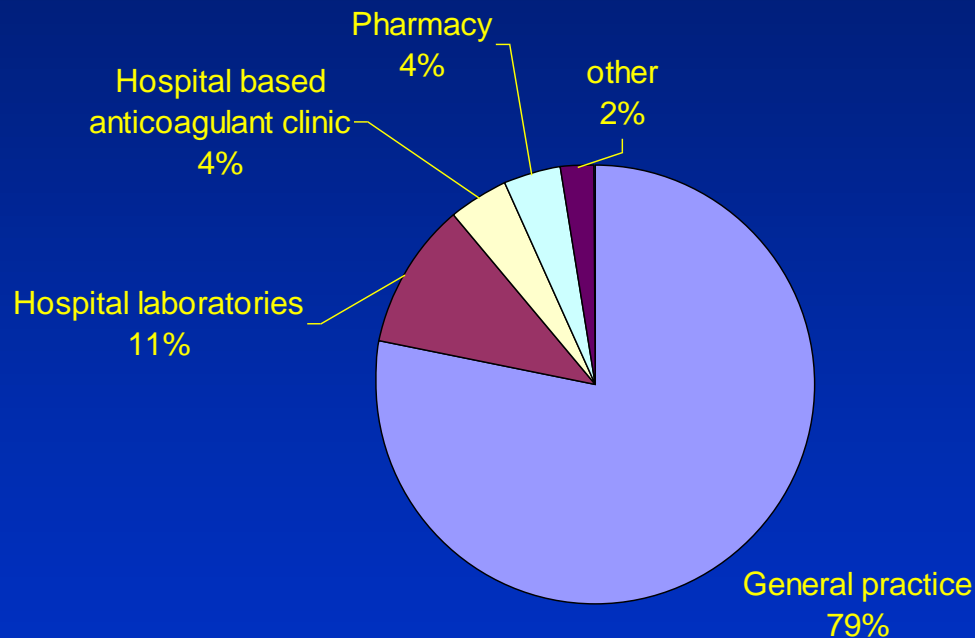
Seminars Thrombosis Haemostasis 2015

Table 1 Point-of-care programs provided by the UK NEQAS BC

	Year introduced	Number registered	Number of samples per year	Target acceptance criteria
INR for CoaguChek XS series users	April 2007	4,160	8	15% deviation around median
INR for Hemochron series users	June 2007	34	8	15% deviation around median
INR for i-STAT users	October 2012	82	8	15% deviation around median
ACT + for Hemochron users	August 2010	97	6	20% deviation around median
Thromboelastography for TEG users	September 2014	33	3	Central 80% of results
Rotational thromboelastometry for ROTEM users	September 2014	24	3	Central 80% of results
D-dimer	April 2014	115	4	Central 80% of results

Abbreviations: ACT, activated clotting time; INR, international normalized ratio, TEG, thromboelastography; UK NEQAS BC, UK National External Quality Assessment Scheme for Blood Coagulation.

Placement of POC INR users in UK NEQAS BC Programme



We have centres in:-

New Zealand

Ireland

Portugal

Italy

Denmark

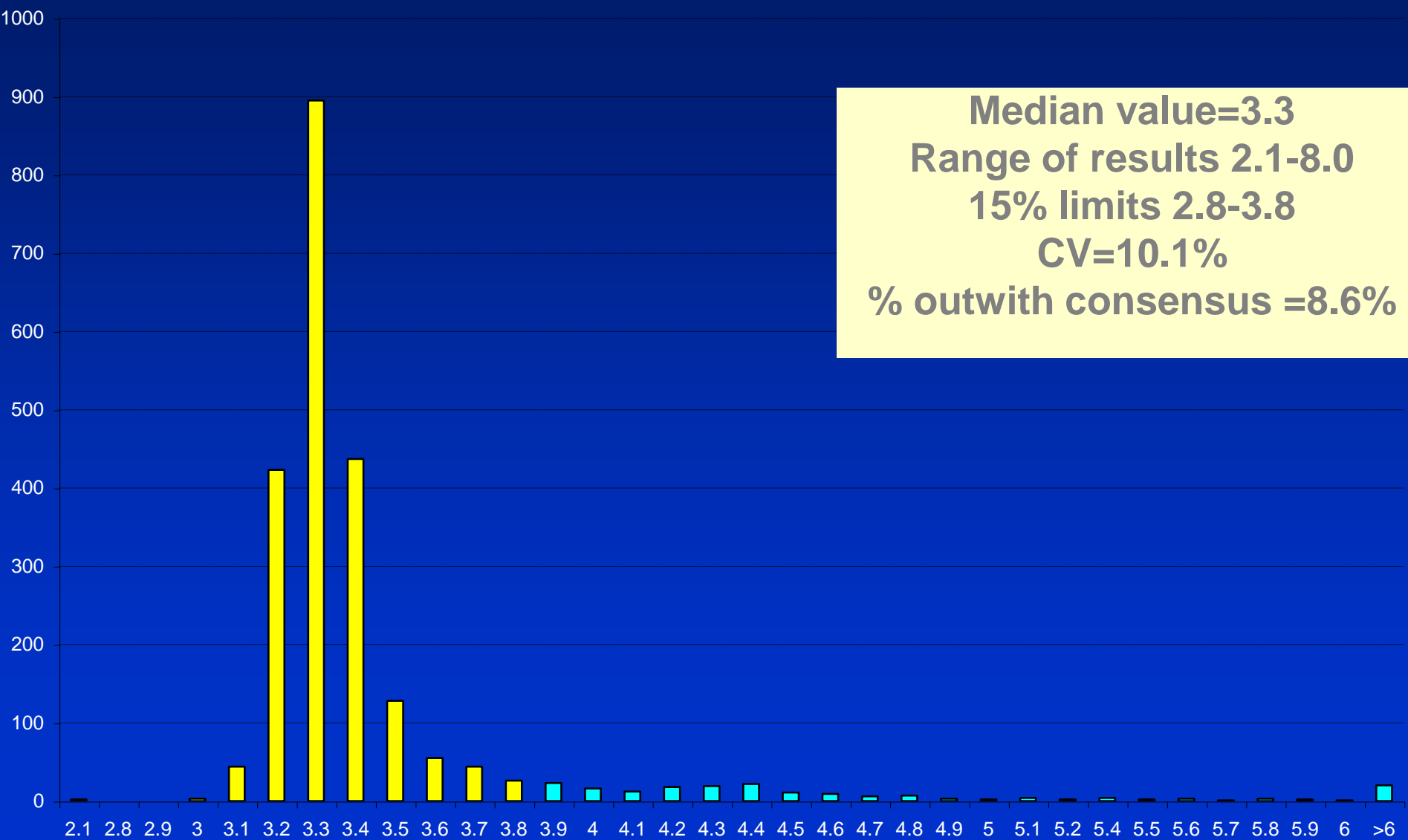
Greece

Hungary

Croatia

Brazil

POC EQA results for sample XS12:07 for Coaguchek XS Plus devices



Outwith consensus rate in INR POC

- An average of 10.2% of participants fail to return results each survey (3.6% in the lab INR programme)
- The majority of centres that receive a persistent outwith consensus letter (3 or more consecutive surveys) have not returned all their results.
- In a recent 2 year period only 6 Centres have had testing problems for 5 or more surveys(0.15%).

One centres persistent problems

Participant had 9 previous surveys all samples within consensus

Sample	INR	Acceptable range	Performance	Test strip batch
Oct 2012/1	4.6	2.8-3.8	Outwith	424
Oct 2012/2	5.5	3.7-4.9	Outwith	424
Repeat Oct 2012/1	4.1	2.8-3.8	Outwith	153
Repeat Oct 2012/2	5.0	3.7-4.9	Outwith	153
July 2012/1	3.8	2.9-3.9	Within	153
July 2012/2	6.1	3.5-4.7	Outwith	153

Advice and outcome

- NEQAS POC Co-ordinator advised contact with manufacturer and to consider stopping patient testing
- Manufacturer provided a loan machine
- Manufacturer found electrical corrosion
- Device replaced free of charge
- Following surveys results within consensus

Sensitivity and specificity of a quantitative point of care D-dimer assay using heparinized whole blood, in patients with clinically suspected deep vein thrombosis

Carl-Erik Dempfle¹, Wolfgang Korte², Michael Schwab³, Rainer Zerback³, Menno V. Huisman⁴; on behalf of the CARDIM study group

Thromb Haemost 2006; 95: 79–83

- 560 patients with ?VTE
- Exclusions – old event, warfarin, > 24 hr heparin, etc
- 223 DVT by ultrasound
- Roche cardiac reader, Tinaquant, VIDAS

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	POC	Tinaquant	VIDAS
cutoff	0.5 µg/ml		
Sensitivity	96.9 %	94.9 %	98.2%
Specificity	60.8 %	64.8 %	40.2 %

The new whole blood POC

D-dimer assay is a reliable tool for exclusion of DVT in symptomatic outpatients, displaying a comparable diagnostic performance as VIDAS D-dimer and Tina-quant D-dimer assays.

D-dimer POC programme

- Currently 120+ users
- 71% in general practice offices
- Used for suspected DVT patients' to determine whether further investigations are required.

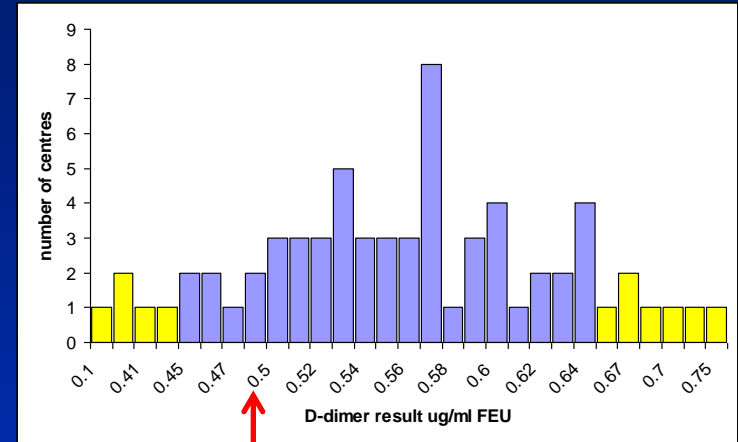
POC D-dimer survey 1,2 and 4 Cobas h232

	S1	S2	S4
Number taking part	61	48	81
Median $\mu\text{g/ml}$ FEU	0.29	0.35	0.1
Range of results returned	0.1-0.44	0.1-0.43	0.1-0.32
%CV	18%	12%	12%
DVT excluded/unlikely	94%	87%	96%
% outwith consensus for result	15%	15%	6%

All results for surveys 1,2 and 4 were less than cut off value (0.5 $\mu\text{g/ml}$ FEU) but some centres stated DVT not excluded .

POC D-dimer survey 3 Cobas h232

Number taking part	66
Median $\mu\text{g/ml}$ FEU	0.56
Range of results returned	0.1-0.75
%CV	17%
DVT not excluded	82%
% outwith consensus for result	18%



manufacturers
stated cut off

10.6% centres had discrepant interpretations and results.

5 centres with results above the cut off gave DVT excluded/unlikely with results of 0.5, 0.51, 0.51, 0.63 and 0.67 $\mu\text{g/ml}$ FEU.

2 centres with results below the cut off stated DVT not excluded

Conclusion for D-dimer POC

- POC D-dimer methods show higher percent CVs than laboratory systems with EQA samples
- Lack of understanding for the interpretations is a concern

EQA for POC haemostasis tests

- QA is required to ensure reliable results are produced from POC devices.
- Even though test not performed in a lab we still need the results to be of the same standard as a lab test.
- Education and support (manufacturer? Lab staff?) is required to get the best service possible.

Acknowledgments

- UK NEQAS Point of care co-ordinator Dianne Kitchen
- Other NEQAS staff
- NEQAS Participants
- dianne.kitchen@coageqa.org.uk

Contacting UK NEQAS

» www.ukneqasbc.org

» Tel 0114 2673300

» dianne.kitchen@coageqa.org.uk

» Tel 0114 2673302