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Comparative Accuracy Evaluation of a Blood Glucose Meter with novel Haematocrit Correction Technology, with three currently used commercially available Blood Glucose Monitoring Systems

Authors list: Gareth J Dunseath, Dominic Bright, Stephen D Luzio

Author details:

Dr Gareth J Dunseath (PhD)
Diabetes Research Unit Cymru
Grove Building
Swansea University
Singleton Park
Swansea
SA2 8PP
G.J.Dunseath@swansea.ac.uk

Dominic Bright (BSc)
Diabetes Research Unit Cymru
Grove Building
Swansea University
Singleton Park
Swansea
SA2 8PP
D.J.Bright@swansea.ac.uk

Professor Stephen D Luzio (PhD)
Diabetes Research Unit Cymru
Grove Building
Swansea University
Singleton Park
Swansea
SA2 8PP
S.luzio@Swansea.ac.uk

Corresponding Author: Gareth Dunseath, Diabetes Research Unit Cymru, Grove Building, Swansea University, Singleton Park, Swansea. SA28PP.
email address: G.J.Dunseath@swansea.ac.uk

Abbreviations:

(BGM) Blood Glucose Meter, (CEG) Consensus Error Grid, (ISO) International Organization for Standardization, (SEG) Surveillance Error Grid, (SMBG) Self-monitoring of Blood Glucose

Keywords:

accuracy, blood glucose meter, haematocrit

Figures/Tables:

5 figures / 2 tables

Abstract

Haematocrit is known to influence glucose values obtained on some blood glucose meters, with bias observed especially at low and high haematocrit levels. We evaluated the performance of a meter with haematocrit correction technology alongside 3 other commercially available meters. Capillary blood samples from 100 subjects were analysed in duplicate and compared to the plasma values obtained by reference laboratory analyser. Bias, error grid and sensitivity to haematocrit analyses were performed for each meter. Average percentage bias was similar for all meters, however the evaluated meter performed best with respect to error grid analysis, with 100% of values falling within the 'no effect on clinical action' and 'no risk' categories and did not display any haematocrit associated bias.

Introduction

Diabetes is a chronic condition, affecting approximately 425 million people globally [1]. Achieving tight glucose control in people with diabetes has been shown to reduce the development of a number of diabetes-associated complications [2]. Self-monitoring of blood glucose (SMBG) provides a means to improve the glycaemic control of a person with diabetes, in addition to identifying hypoglycaemic events in those on insulin therapy [3].

The guidelines for determining system accuracy on blood glucose meters (BS EN ISO 15197:2015) [4] state that accuracy should be determined from at least 100 different subjects, and evaluated under actual conditions of use to include the effects of both systematic error (measurement bias) and random error (measurement imprecision). The system accuracy evaluation should be performed on fresh blood samples, at least in duplicate and compared to reference laboratory glucose concentrations, both pre- and post-measurement with the glucose meter.

Haematocrit has previously been shown to demonstrate considerable influence on the glucose readings obtained from certain blood glucose monitors, even when tested within the manufacturer's recommended haematocrit range [5, 6]. Typically, a positive bias is observed at low haematocrit levels and a negative bias at higher haematocrit levels [7 - 9]. In this study, the system accuracy of the evaluated blood glucose meter, the GlucoRx HCT meter (GlucoRx, Surrey, UK), that utilises a novel haematocrit correction technology, was compared to 3 other blood glucose meters used in the UK across a wide range of blood glucose concentrations, similar to that specified in Section 8 BS ISO 15197:2015 [4].

Methods

This study was performed between March and April 2018 at the Joint Clinical Research Facility, ILS2, Swansea University, Swansea, UK, in compliance with Good Clinical Practice and was approved by Wales REC 6 (18/WA/0023) prior to commencement of the study.

Subjects

A total of 114 participants were recruited to achieve 100 full, evaluable datasets. Subjects with diabetes mellitus (type 1 and type 2) and without diabetes were included in the study, and on entry were all aged $\geq$ 18 years old. Informed, signed consent was received from all participants.

Blood Glucose Monitoring Systems

The evaluated meter (Meter A) is a multiparameter meter, capable of measuring blood glucose, ketones and haematocrit. The meter uses advanced GDH-FAD enzyme technology with an AC signal which provides the haematocrit result, and DC signal which calculates glucose. The meter then modulates the glucose level according to the haematocrit value allowing enhanced accuracy in measurement of glucose. Meter A was compared to three other meters (Meters B, C and D - in no particular order); these included the Roche Accu-chek Aviva (Roche Diagnostics Ltd., West Sussex, UK) which measures blood glucose only, and two dual glucose and ketone meters;

Caresens Dual BGM System (distributed by Spirit Healthcare, Leicester, UK) and Menarini GlucoMen Areo 2K (A Menrini Diagnostics, Berkshire, UK). Meters B, C and D were selected for this study due to their availability and current use within the UK. For this study, the ketone function was not used on the dual systems. All meters and strips were purchased directly by the research team and were not provided by the manufacturers.

Study Procedure

Procedures performed were similar to those outlined in EN ISO 15197:2015. Briefly, eligible subjects had a fingerprick performed using a high flow lancet. Capillary blood (approximately 100ul) was collected into lithium heparin anticoagulant (Microvette, Sarstedt, Leicester, UK), with the sample used for determination of plasma glucose on the reference laboratory glucose analyser. Following this, duplicate blood glucose measurements were performed on the 4 blood glucose meters in a random order, before a second reference glucose sample was collected. Finally, haematocrit was determined. For the reference YSI measurement, the Microvette tubes were centrifuged within 5 minutes of collection and the plasma glucose determined. A total of approximately 250ul was collected from each participant.

Of the 100 eligible samples, a total of 20 modified samples were included to allow determination of sufficient numbers of low (by glycolysis) and high (by addition of glucose solution) glucose concentrations.

Laboratory Measurements

The reference laboratory plasma glucose was determined using a YSI 2300 Stat Plus (Yellow Springs Instruments, Fleet, UK). Daily internal quality control was performed before any study samples were run (Assayed Chemistry Control Plus, levels 2 and 3, Randox, UK). Microvette tubes were centrifuged within 5 minutes of collection and the plasma component used for glucose determination.

Haematocrit was determined using a HemoControl analyser (EKF Diagnostics, Cardiff, UK)

Data Analysis

Data were excluded from analysis if the reference laboratory measurements differed by >4% at glucose concentrations <100mg/dL or >4mg/dL at glucose concentrations ≥100mg/dL, if valid glucose readings were not obtained on all meters or if insufficient sample volume was available for all measurements to be performed.

Accuracy for each meter was assessed according to the number of readings within 5, 10 and 15mg/dL (glucose <100 mg/dL) or 5, 10 and 15% (glucose ≥mg/dL) of the reference glucose value and the accuracy for each individual meter compared using the Cochran-Mantel-Haenszel test. Bias plots, Parkes Consensus Error Grids (CEG) [10] and Surveillance Error Grids (SEG) [11] were performed for each meter. In addition, sensitivity of the individual meters to haematocrit was assessed by regression analysis of the relative glucose differences (meter and reference glucose) versus haematocrit.

Results

The batches of meters and strips used were:

Meters 4279317350041211 / 4279317350041299; Strips TD17G110-BHF

Meters 45900007291 / 45900013602 / 45900019971; Strips 497275

Meters F024073F0910 / F024073F0906; Strips PJ25CAQ1B

Meters GT168145 / GT168206; Strips HS170705.

For the 100 evaluated samples, the observed glucose range determined on the reference analyser was 33 to 581mg/dL and haematocrit was 28 – 50%.

The average percentage bias between the meters and reference glucose measurement were 5.3, 5.0, 5.9 and 6.6%; meters A to D respectively (Figure 1).

For meters A to D respectively, 99.5, 98.0, 96.0 and 96.0% of the meter values were within ±15mg/dL (glucose <100mg/dL) or ±15% (glucose ≥100mg/dL) of the reference glucose value (Table 1), with meter A displaying significantly greater accuracy when compared to both meters C and D (P=0.044 and 0.043 respectively).

Error Grid Analysis

For meter A, 100% of glucose values fell within Zone A (no effect on clinical action) and were classed as 'no risk' on the CEG and SEG plots respectively. For the remainder of the meters, the corresponding values were 100% and 97.5%

(meter B), 99.5% and 98.5% (meter C) and 98.0% and 96.5% (meter D) (Table 2 and Figures 2 and 3).

Sensitivity to Haematocrit

The haematocrit values of the samples tested were within the accepted ranges for all meters. Across an increasing haematocrit range, the magnitude of spread of relative glucose differences (reference and meter) remained relatively constant for meters A, B and C, however greater variation was observed for meter D (Figures 4 and 5). Neither the slope nor intercept of the calculated regression lines differed from zero for meters A or D but were significantly different for both meters B and C (all $P<0.01$).

Discussion

In this study, the performance of a blood glucose meter with novel haematocrit correction technology (meter A) was evaluated and compared to the performance of three commercially available blood glucose monitoring systems across a wide glucose concentration range, based on the guidelines stated in Section 8 BS ISO 15197:2015. One of the limitations of this study is that while the latest ISO guidelines were followed in terms of number of samples and glucose concentration range tested, only a single batch of test strips was employed. The three comparator meters (B to D) were selected due to their availability and usage within the UK.

The accuracy of readings generated by blood glucose meters is essential to ensure both tight glucose control and patient safety, as such the International

Organisation for Standardisation (ISO) has published guidelines to evaluate blood glucose meters. According to the most recent recommendations (ISO 15197:2015), 95% of meter readings should be within ±15mg/dL (for glucose concentrations <100mg/dL) or ±15% (glucose concentrations ≥100mg/dL) of the reference glucose concentrations. In this study, all meters were found to achieve these targets, ranging from 99.5% (meter A) to 96.0% (meters C and D).

With respect to the CEG and SEG scores the evaluated meter (meter A) performed the best with all results in zone A (no effect on clinical outcome - CEG) or 'no risk' (SEG). Meter D was more variable with 1 % of values falling in Zone C (leading to unnecessary treatment –CEG) and 'moderate, lower risk' (SEG).

The magnitude of the relative glucose differences between meter and reference glucose was similar across the tested haematocrit range for meters A, B and C, but showed greater variation for meter D. However, despite this similarity in magnitude of spread for meters A, B and C, the meter A was the only one that did not display haematocrit associated bias.

Conclusions

In this study, the performance of all the blood glucose meters was within ISO 15197:2015 guidelines, meter A had the best performance due to the haematocrit correction technology employed within this meter.

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Disclosures: None

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Tables and table legends:

Table 1 Accuracy results

	Glucose <100mg/dL			Glucose ≥100mg/dL			Combined
	±5mg/dL	±10mg/dL	±15mg/dL	±5%	±10%	±15%	±15mg/Dl OR ±15%
Meter A	48/60 80.0%	56/60 93.3%	59/60 98.3%	72/140 51.4%	129/140 92.1%	140/140 100.0%	199/200 99.5%
Meter B	38/60 63.3%	56/60 93.3%	58/60 96.7%	90/140 64.3%	129/140 92.1%	138/140 98.6%	196/200 98.0%
Meter C	35/60 58.3%	56/60 93.3%	58/60 96.7%	74/140 52.9%	118/140 84.3%	134/140 95.7%	192/200 96.0%
Meter D	21/60 35.0%	45/60 75.0%	55/60 91.7%	77/140 55.0%	122/140 87.1%	137/140 97.9%	192/200 96.0%

Table 2 Error Grid analysis

	Consensus Error Grid (CEG) Zone					Surveillance Error Grid Degree of Risk					
	A	B	C	D	E	None	Slight, Lower	Slight, Higher	Moderate, Lower	Moderate, Higher	Great, Lower
Meter A	200 100.0%	-	-	-	-	200 100.0%	-	-	-	-	-
Meter B	200 100.0%	-	-	-	-	195 97.5%	5 2.50%	-	-	-	-
Meter C	199 99.5%	1 0.5%	-	-	-	197 98.5%	3 1.5%	-	-	-	-
Meter D	194 98.0%	2 1.0%	2 1.0%	-	-	193 96.5%	5 2.5%	-	2 1.0%	-	-

Figures and figure legends:

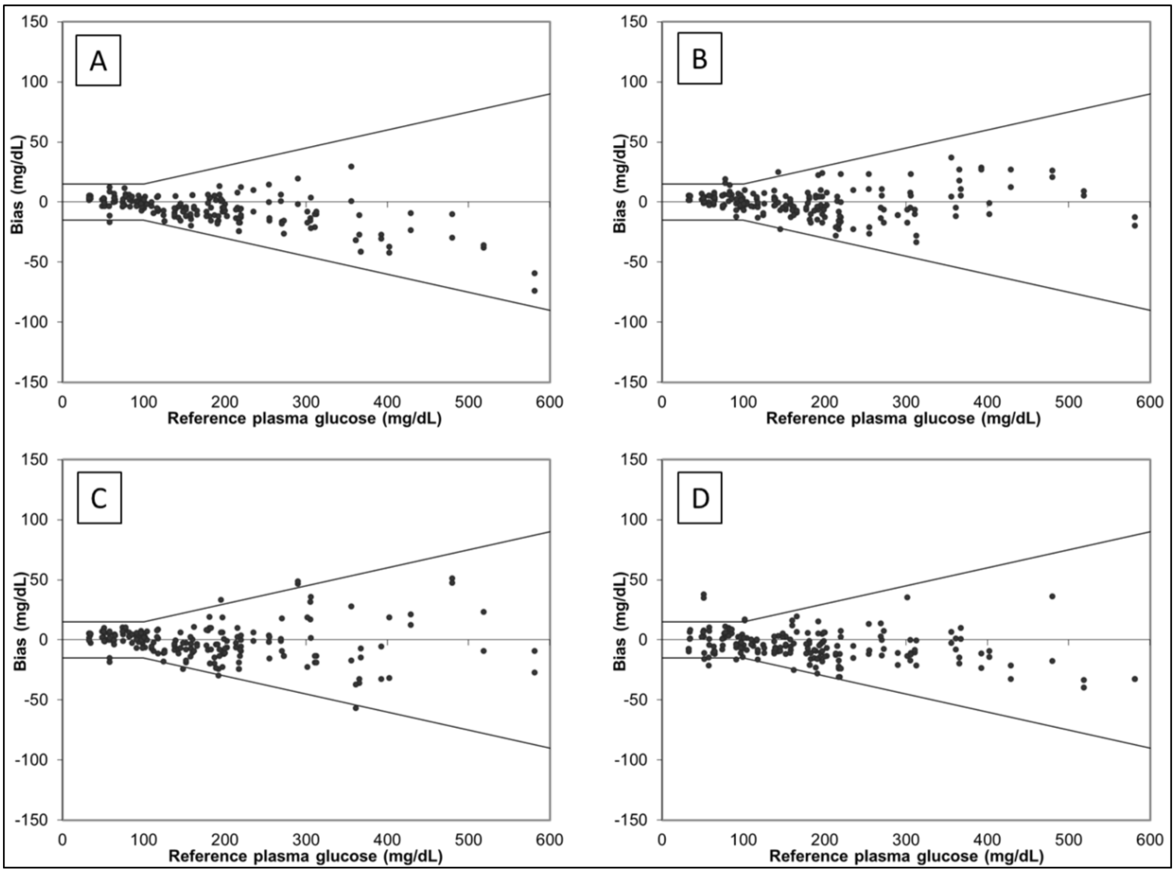

Figure 1 Bias plots; Meter A, B, C and D

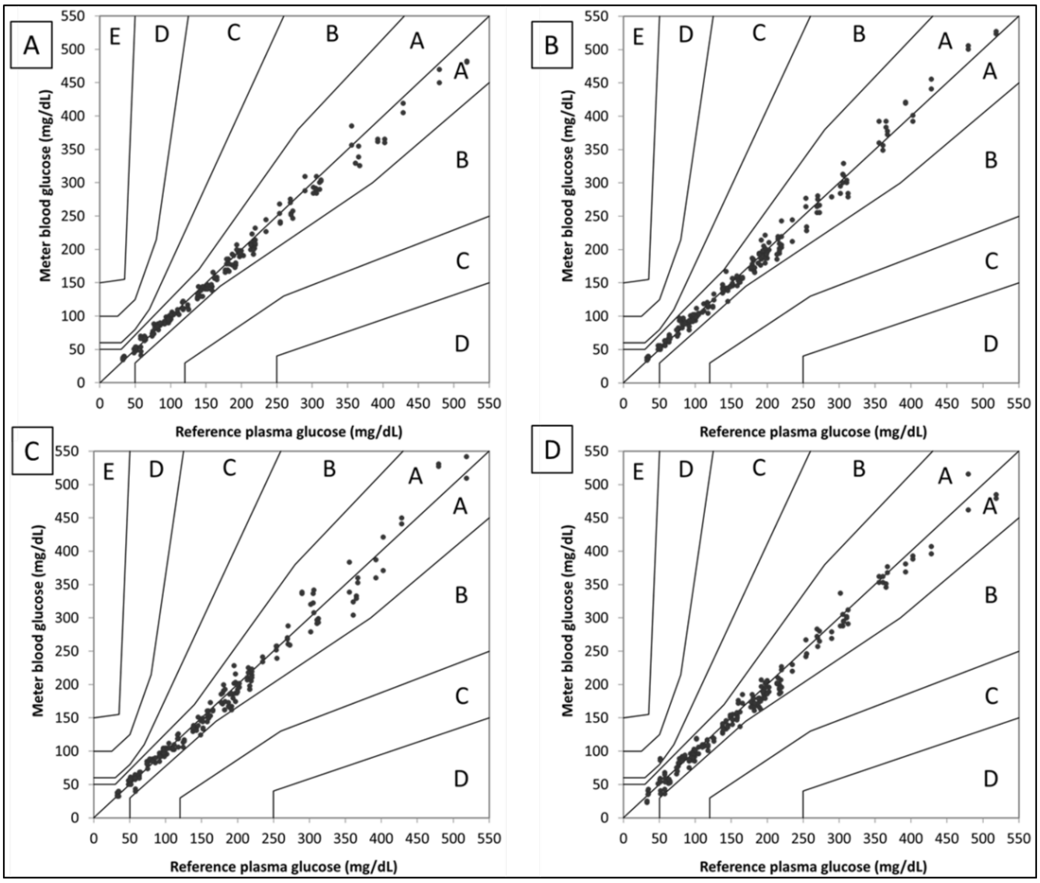

Figure 2 Consensus Error Grids; Meter A, B, C and D

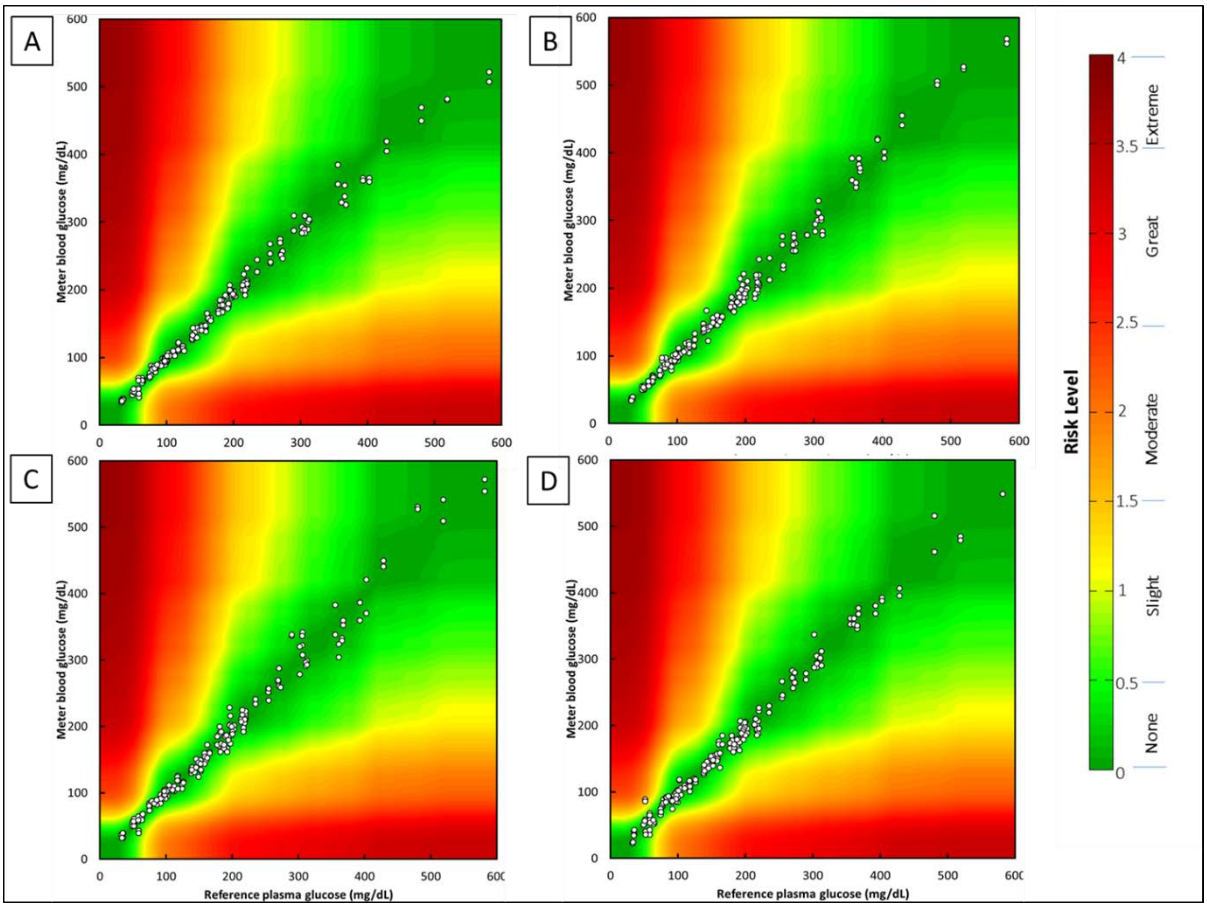

Figure 3 Surveillance Error Grids; Meter A, B, C and D

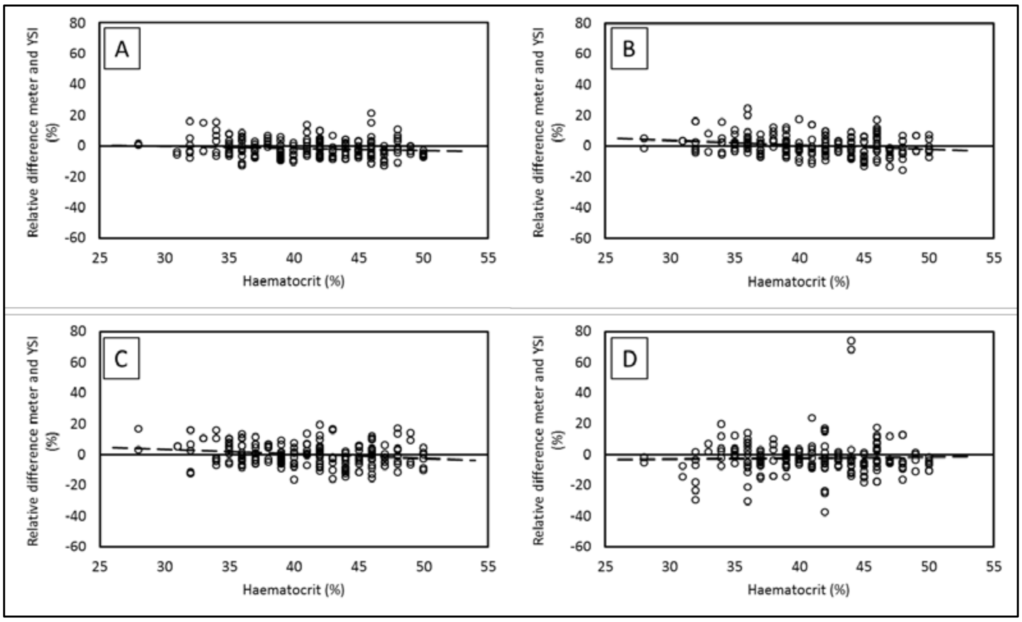

Figure 4 Relative difference between meter and YSI according to haematocrit; Meter A, B, C and D

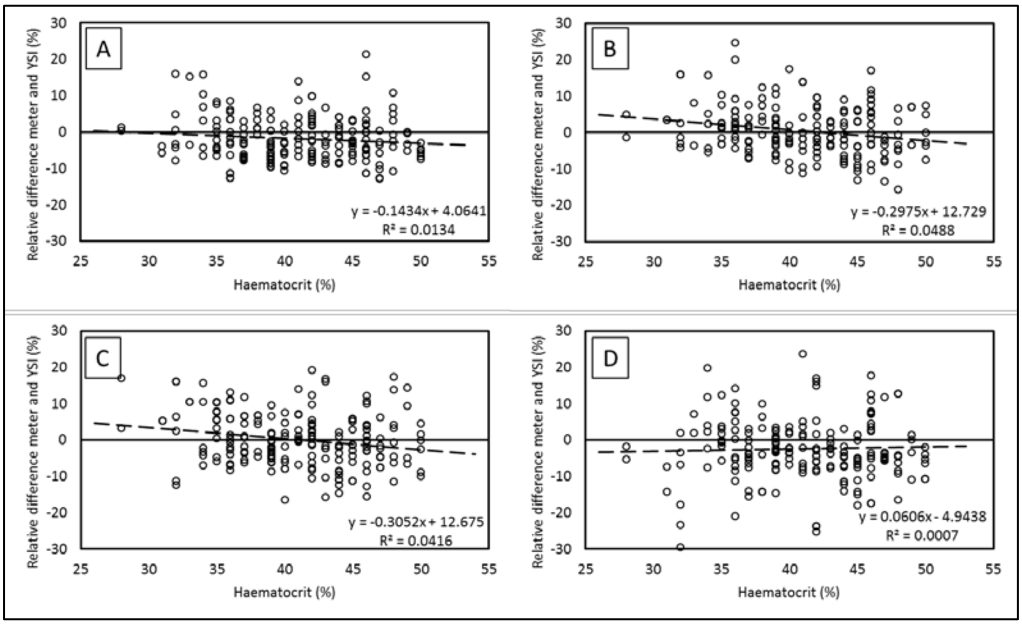

Figure 5 Expanded view of the relative difference between meter and YSI according to haematocrit; Meter A, B, C and D