

# THE UNIVERSITY of EDINBURGH

# Edinburgh Research Explorer

## Precision and accuracy of a point-of-care glucometer in horses and the effects of sample type

#### Citation for published version:

Rendle, DI, Årmstrong, S, Heller, J & Hughes, KJ 2019, 'Precision and accuracy of a point-of-care glucometer in horses and the effects of sample type', *The Veterinary Journal*, vol. 252, 105359. https://doi.org/10.1016/j.tvjl.2019.105359

#### **Digital Object Identifier (DOI):**

10.1016/j.tvjl.2019.105359

#### Link: Link to publication record in Edinburgh Research Explorer

**Document Version:** Peer reviewed version

Published In: The Veterinary Journal

#### **General rights**

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

#### Take down policy

The University of Édinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



1	Precision and accuracy of a point-of-care glucometer in horses and the effects of sample type
2	David. I. Rendle <sup>a, b</sup> , Susan. K. Armstrong <sup>a, c</sup> , Jane. Heller <sup>a</sup> , Kristopher. J. Hughes <sup>a, *</sup>
3	
4	School of Animal and Veterinary Sciences, Charles Sturt University, Locked Bag 588, Boorooma Street,
5	Wagga Wagga, NSW 2678 Australia.
6	<sup>b</sup> Current address: Rainbow Equine Hospital, Old Malton, Malton, North Yorkshire, YO17 6SG UK.
7	°Current address: Royal (Dick) School of Veterinary Studies and Roslin Institute, University of
8	Edinburgh, Roslin, Midlothian, EH25 9RG UK.
9	
10	* Corresponding author. Tel.: +61 69334253.
11	Email address: krhughes@csu.edu.au (K.J. Hughes).
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27 20	
∠o 29	
30	
31	

32

#### 33 Abstract

34 Point-of-care glucometry is used commonly in clinical and research settings; however, accuracy 35 and precision of this method are concerns. The objectives of this study were to determine the accuracy 36 of glucometry in adult horses and the precision of duplicate measurements. Blood samples were 37 collected from 62 horses into one plain syringe, one ethylenediaminetetraacetic acid (EDTA) tube and three fluoride oxalate (FO) tubes. Immediately after collection, glucose concentrations in whole blood 38 39 were determined, in duplicate, by glucometry from the syringe (plain whole blood [WB] group), EDTA 40 tube (EDTA group) and one FO tube (FO group). One FO sample was used to measure plasma glucose 41 concentration by a laboratory chemistry analyser (LAB group) ≤1 h after collection. The third FO tube 42 was used to measure plasma glucose concentration by glucometry after 3 h storage (FO3hr group).

43

44 Adequate precision was present for all groups (coefficient of variation: 0.7-3.5%) except WB (5.5-9.4%). Between groups, correlations were significant (P < 0.05) (except WB-EDTA), varied with 45 46 group comparison and tended to be lowest for comparisons involving WB. Mean bias was lowest for WB-LAB and greatest for FO-LAB and FO3hr-LAB; however, the limits of agreement were ≥4.65 mmol/L 47 48 for WB-LAB and ≤2.75 mmol/L for most other comparisons. For the glucometer used, performance is 49 influenced by sample type: WB is unsuitable, while FO or EDTA samples result in adequate precision 50 and accuracy, provided under-estimation of glucose concentrations is accounted for by using method-51 specific reference ranges. Glucometer performance and optimal sample type(s) should be determined 52 prior to use in horses.

53

54 Keywords: Horse; Glucometry; Repeatability; Agreement; Equine

- 55
- 56
- 57
- 58
- 59 60
- -
- 61
- 62

63 64

#### 65 Introduction

66 Regulation of blood glucose concentrations is important in critically-ill horses, as derangements in glucose concentrations are associated with increased mortality (Hassel et al., 2009; Hollis et al., 67 68 2007; Hollis et al., 2008a). Hyperglycaemia is a negative prognostic indicator in critically-ill human 69 patients, supporting regulation of blood glucose concentration through monitoring and intervention 70 (Bochicchio et al., 2005; Sung et al., 2005; Vogelzang et al., 2006). Point-of-care glucometry has 71 become standard in human and equine intensive care settings and testing of insulin dysregulation, 72 given the ease of measurement, small blood volumes required, and ability for immediate decisionmaking (Hoedemaekers et al., 2008; Hollis et al., 2008b; Russell et al., 2007; Tack et al., 2012). 73 74 However, for optimal patient management, the precision and accuracy of individual glucometers needs 75 to be determined. Despite extensive use of glucometry in intensive care units and diabetes control in 76 human medicine, conflicting results of glucometer performance have been reported. In some studies, 77 glucometry was an accurate alternative to laboratory methods (Ray et al., 2001; Tack et al., 2012). 78 However, considerable glucometer inaccuracy was reported in other studies (Denfeld et al., 2011; 79 Hoedemaekers et al., 2008; Kanji et al., 2005), with implications for incorrect decision-making when 80 tight glycaemic control is necessary. Possible explanations for the disparity in glucometer performance 81 include haematocrit interference, sample type (whole blood/plasma, capillary/venous/arterial blood) and 82 analyser type (Gerber and Freeman, 2016; Kanji et al., 2005; Tang et al., 2000).

83

84 There are few published studies of the accuracy and precision of glucometers in horses 85 (Hackett and McCue, 2010; Hollis et al., 2008b; Hug et al., 2013; Russell et al., 2007) and only one veterinary-specific glucometer has been validated for horses (Hackett and McCue, 2010). The 86 87 influences of sample type, glucose concentration and delays in analysis on results in horses are largely 88 unknown. In one equine study, glucometry with plasma had excellent agreement with a laboratory 89 method, while measurements from whole blood did not (Hollis et al., 2008b). In some human and equine 90 studies, glucometer performance was less reliable when marked hypoglycaemia or hyperglycaemia 91 was present (Hollis et al., 2008b; Kanji et al., 2005; Khan et al., 2006). Bias in glucometer results may 92 be important in critically-ill horses where performance at the extremes of blood glucose concentrations 93 may influence decision-making and accurate glycaemic control. The objectives of this study were to 94 determine (1) the accuracy of glucometry in adult horses using blood and plasma samples in 95 comparison to a laboratory standard method and (2) the precision of duplicate measurements.

96

#### 97 Materials and methods

98 The study was granted approval by the Animal Care and Ethics Committee, Charles Sturt
99 University (Approval number 11/043; Approval date September 2011).

100 Sample collection

Blood samples were obtained from horses that were >1 year of age and from the research herd of Charles Sturt University (CSU) or presented to the Veterinary Clinical Centre, CSU, for clinical assessment.

104

105 For each horse, whole blood (WB) was collected from the jugular vein into a 3 mL syringe, one 106 blood collection tube containing ethylenediaminetetraacetic acid (EDTA) (Vacutainer, Becton 107 Dickinson) and 3 blood collection tubes containing fluoride oxalate (FO) (Vacutainer, Becton Dickinson). 108 The tubes were filled to the manufacturer's designated level. Immediately after collection, the glucose 109 concentration of WB in the syringe was determined using a human-specific POC glucometer (Accutrend 110 Plus, Roche Diagnostics), according to the manufacturer's instructions (WB group). Within 5 min of 111 blood collection, the blood glucose concentrations in the EDTA tube (EDTA group) and one of the FO tubes (FO group) was determined using the glucometer. The second FO sample was used for 112 determination of plasma glucose concentration using the glucometer after storage of the sample for 3 113 114 h at 22 °C and separation of the plasma by centrifugation (10 min at 3000 rpm) immediately prior to 115 analysis (FO3hr group). The third FO tube was used to measure plasma glucose concentration by a 116 wet chemistry analyser using the hexokinase/glucocose-6-phoshate dehydrogenase method (Konelab 117 30i, Thermo Fisher Scientific) as the reference method, within 1 h of blood collection and after centrifugation (10 min at 3000 rpm) (LAB group). For every sample, two glucose concentration 118 measurements were obtained using the same device. For the WB, EDTA, FO and FO3hr groups, the 119 120 same lot number for the glucometer measurement strips and a single glucometer was used throughout 121 the study. The glucose measurement strips were stored according to the manufacturer's instructions.

Using the LAB results, samples were categorised as euglycaemic (4.0-7.0 mmol/L) or hyperglycaemic
(>7.0 mmol/L). Raw glucose concentration data for all 62 horses are provided in Appendix A:
Supplementary material.

126

#### 127 Data analysis

128 Within groups, precision of glucose measurement was determined by calculation of the 129 repeatability coefficient (RC: 1.96 times the SD of the differences of paired measurements) (Bland and 130 Altman, 1986). The RC is expected to contain 95% of the differences, and values of <0.8 mmol/L and 131 <2.0 mmol/L were considered acceptable for euglycaemic and hyperglycaemic samples, respectively, 132 based on criteria for glucometer performance in humans (Tonyushkina and Nichols, 2009). Within each 133 group, the coefficient of variation (CV) for repeated glucose measurements was determined: a median 134 CV of <4% was considered adequate measurement precision (Carr et al., 1995; Chen et al., 2003). 135 Blood glucose measurements within each group were compared also using Spearman's correlation as 136 data were non-normally distributed (Shapiro-Wilk test). Spearman's correlation coefficients ( $r_s$ ) were 137 interpreted using the criteria of 0.90-1.00: very high, 0.70-0.89: high, 0.50-0.69: moderate, 0.30-0.49: 138 low and <0.30: little/no correlation (Domori et al., 2014).

139

140 Between groups, association of paired glucose measurements (first measurement for each 141 sample) was determined using Spearman's correlation, and agreement was determined using Lin's 142 concordance correlation (Lin, 1989) and the mean bias and 95% limits of agreement (LOA) (Bland and 143 Altman, 1986). Concordance correlation coefficients ( $\rho_c$ ) were interpreted using the criteria of >0.99: 144 almost perfect, 0.95-0.99: substantial, 0.90-0.95: moderate, <0.90: poor concordance (Domori et al., 145 2014). Based on criteria for glucometer accuracy for humans (Tonyushkina and Nichols, 2009), adequate agreement was considered with LOA <1.7 mmol/L and <2.8 mmol/L for euglycaemic and 146 147 hyperglycaemic samples, respectively. The relative difference between paired glucose measurements for each glucometer group and the LAB group was calculated (POC group-LAB/LAB x 100%) and the 148 percentage of glucometer results that were within 5%, 10%, 15% or 20% of the LAB glucose 149 150 concentration were calculated according to guidelines to describe glucometer performance (Krouwer 151 and Cembrowski, 2010; Tennent-Brown et al., 2011; Tonyushkina and Nichols, 2009).

All statistical analyses were performed using SPSS Statistics version 20 (IBM). Significance was set at
 *P* <0.05.</li>

155

156 Results

Blood samples were obtained from 62 horses (30 Thoroughbreds, 19 Standardbreds, 5 Quarter horses, 4 ponies, 3 Arabians, 1 Warmblood and 1 Clydesdale) with a median age of 9.5 years (range 1-23). The study population consisted of 33 geldings, 6 entire male horses and 23 mares. Forty-two animals were research horses, of which 10 underwent combined glucose and insulin testing performed for the investigation of insulin dysregulation and had hyperglycaemia. Twenty horses were client-owned animals that had blood collected for clinical assessment. Forty-nine and 13 horses were euglycaemic and hyperglycaemic, respectively. No horses were hypoglycaemic.

164

For euglycaemic and hyperglycaemic samples, RC and CV values indicated adequate repeatability for all groups with the exception of WB (Table 1). For all glucose concentration categories, the RC and CV values were smallest and largest for the LAB and WB groups, respectively. For all glucose measurements,  $r_s$  was significant and the strength of correlation was moderate to very high (Table 1).

170

Between groups, *r<sub>s</sub>* was significant for all comparisons, with the exception of WB-EDTA for euglycaemic samples (Table 2). Correlation and concordance of glucose measurements varied substantially with group comparison and glucose concentration (Table 2). For all categories, *r<sub>s</sub>* and concordance tended to be lowest for comparisons between WB and other groups. The bias and 95% LOA for agreements between groups are provided in Table 3. Bland-Altman plots are provided in Appendix A: Supplementary material.

177

178 No group had 95% of the glucose measurements within 5-20% of the LAB results, with the 179 exception of EDTA for hyperglycaemic samples (Table 4).

180

181 Discussion

182 The results of this study demonstrate that glucometer precision and accuracy can be influenced 183 by blood sample type and storage. Poor glucometer performance occurred with WB without anticoagulant, while anticoagulated blood (EDTA, FO) and plasma (FO3hr) resulted in improved 184 185 glucometer repeatability and agreement with the laboratory standard, albeit with underestimation of 186 glucose concentration. In addition, precision and accuracy varied across the glycaemic range, 187 supporting the recommendation that glucometer performance should be assessed in clinically-relevant 188 glucose ranges (hypo-, eu- and hyperglycaemia) (Gerber and Freeman, 2016). Determination of 189 glucometer performance is important for patient care, particularly in intensive care settings. In both 190 humans and horses, glycaemic abnormalities are associated with a worse prognosis for survival 191 (Bochicchio et al., 2005; Hassel et al., 2009; Hollis et al., 2008a; Sung et al., 2005) and monitoring and 192 regulation of blood glucose concentrations is associated with improved outcomes in critically-ill humans (Lewis et al., 2004; Sung et al., 2005). While glucometry provides rapid results for immediate patient-193 194 side decision making, poor accuracy and precision may lead to erroneous clinical assessment and 195 management (Hoedemaekers et al., 2008; Kanji et al., 2005; Russell et al., 2007).

196

For all categories, WB had poor precision (CV: 5.5-9.4%, RC: 2.14-2.94 mmol/L). For 197 198 euglycaemic animals, a difference of over 2.14 mmol/L may alter clinical interpretations, suggesting that 199 WB is inappropriate for this glucometer. The reason for this poor precision is unknown; however, it may 200 involve the interaction of horse erythrocytes with the test strip. The strips filter erythrocytes while plasma 201 diffuses to the reagents and sensor for glucose measurement and differences in the sizes of human 202 and horse erythrocytes and rouleaux formation may be sources of pre-analytic error when WB was used. Further, glucometers designed for humans assume a stable relationship of glucose 203 204 concentrations between erythrocytes and plasma, and differences in glucose distribution between 205 humans and horses are likely (Coldman and Good, 1967; Hackett and McCue, 2010). In one study 206 (Hackett and McCue, 2010), a veterinary glucometer coded for equine use (and likely species-specific 207 assumption of glucose distribution) accurately measured glucose concentrations in WB, while in other 208 studies, plasma provided superior agreement with a laboratory method than WB when human-specific 209 glucometers were used in horses (Hollis et al., 2008b) and alpacas (Tennent-Brown et al., 2011). These 210 findings indicate that the performance of individual glucometers, including influence of sample type,

should be assessed prior to use in horses, as discrepancies in accuracy and precision may influencedecision-making.

213

For both euglycaemic and hyperglycaemic samples, the RC and CV values for the EDTA, FO and FO3hr groups were consistent with acceptable precision. Glucometer precision in equine practice has been reported once previously, where the CV of a veterinary glucometer that uses WB was 1.3% (Hackett and McCue, 2010). Using described values (<3.5-4%) for glucometry in human medicine (Carr et al., 1995; Chen et al., 2003), the CVs for EDTA, FO and FO3hr in our study indicate that the precision of the glucometer with these sample types is adequate for horses, while WB resulted in poor precision.

221 When all samples were considered, all glucometer groups had moderate or high correlation 222 with LAB. However,  $r_s$  increases with a greater range of measured values (Bland and Altman, 1986) 223 and the strengths of association may have been artificially improved. Importantly, only low to moderate 224 correlations between groups and LAB were present for euglycaemic samples, emphasising the importance of determining glucometer performance within clinically-relevant glucose concentration 225 226 ranges. Similarly,  $\rho_c$  values were influenced by glucose concentration category, and demonstrated poor agreement of the glucometer with LAB for euglycaemic samples and often poor agreement between 227 228 glucometer groups for euglycaemic and hyperglycaemic samples, suggesting that results should not be 229 used interchangeably with reference laboratory methods or when different sample types are used. 230 However, the magnitude of the lack of agreement cannot be determined using this method.

231

232 The mean bias and 95% LOA results revealed variable agreement between glucometer groups 233 and LAB. Whole blood had the poorest agreement (LOA ≥4.7 mmol/L), representing differences with risk of clinical misinterpretation. Similarly, when used in human-specific glucometers, WB was 234 235 associated with poor agreement with a laboratory method in foals (Russell et al., 2007), adult horses (Hollis et al., 2008b), alpacas (Tennent-Brown et al., 2011) and dogs (Cohen et al., 2009). In contrast, 236 237 good accuracy of veterinary-specific glucometers with WB has been demonstrated for horses (Hackett 238 and McCue, 2010) and alpacas (Tennent-Brown et al., 2011), which may reflect more accurate programmed assumptions of glucose distribution between plasma and erythrocytes. The selection of 239 acceptable LOA is a clinical, rather than a statistical decision, and for the current study, <1.7 mmol/L 240

241 (euglycaemic samples) and <2.8 mmol/L (hyperglycaemic samples) were chosen, based on glucometer 242 performance criteria for humans (Tonyushkina and Nichols, 2009). Using these LOA values, acceptable agreement was present for LAB-EDTA, LAB-FO, LAB-FO3hr and FO-FO3hr (euglycaemic samples) 243 244 and LAB-FO, LAB-FO3hr and FO-FO3hr (hyperglycaemic samples). The FO and FO3hr groups had 245 the smallest LOA ranges, which are unlikely to alter clinical interpretation, irrespective of glucose 246 concentration. While acceptable agreement between the EDTA and LAB groups was present for 247 euglycaemic samples, proportional bias with increasing glucose concentration was present, suggesting 248 that EDTA is not suitable for interchangeable use with the laboratory method when hyperglycaemia is 249 present. Proportional bias has occurred in previous studies of glucometer performance in veterinary 250 species (Cohen et al., 2009; Tennent-Brown et al., 2011), indicating that assessment of glucometer 251 accuracy over a wide glucose concentration range is necessary. In the current study, there was constant 252 bias with underestimation of glucose concentrations by the glucometer for the EDTA, FO and FO3hr 253 groups. For FO and EDTA, this may, in part, reflect higher glucose concentrations in plasma, which are 254 approximately 10-15% higher than those in blood (Gerber and Freeman, 2016), emphasising that results are often not interchangeable. The mean bias for FO-LAB (-1.17 mmol/L) is similar to an 255 256 estimated difference of 10-15% between plasma (LAB) and blood (FO). Constant bias with glucometer 257 use in horses and other species has been demonstrated previously (Beemer et al., 2013; Cohen et al., 258 2009; Russell et al., 2007; Tennent-Brown et al., 2011), although the direction of the bias varied 259 between studies. Given the small size of the hyperglycaemic group in the current study, further 260 investigation of the effects of hyperglycaemia on glucometer performance using larger numbers of 261 hyperglycaemic and systemically-ill horses is warranted.

262

263 With the exception of FO-FO3hr, there was, at best, only moderate agreement between glucometer groups, demonstrating that different sample types should not be used for monitoring of 264 265 glucose concentrations in an individual animal. The results of the current and previous studies (Hollis 266 et al., 2008b; Russell et al., 2007) suggest that human-specific glucometers may be inaccurate when 267 used in horses (due to systematic bias), and careful consideration of appropriate sample type is 268 necessary for specific glucometers. The poor agreement between WB and other groups, can be 269 anticipated from the large RC for WB, as repeatability limits the amount of achievable agreement (Bland 270 and Altman, 1986).

272 No glucometer group had 95% of the measurements within 5-20% of the LAB results, with the exception of the EDTA group for hyperglycaemic samples. In human medicine, recommended 273 274 glucometer performance criteria include 95-100% of measurements within 5-20% of the laboratory 275 method for acceptable accuracy (Tonyushkina and Nichols, 2009). While similar standards for 276 glucometer accuracy in horses have not been established, our results, overall, reflected glucometer 277 inaccuracy, irrespective of sample type. Similarly, glucometer performance often failed to achieve 278 adequate accuracy in alpacas (Beemer et al., 2013) and dogs (Cohn et al., 2000). Glucometer 279 inaccuracy may result in erroneous clinical decisions if glucose reference ranges for a reference 280 laboratory method are used. However, systematic bias may not preclude individual glucometer use if a 281 conversion factor is applied. Alternatively, for sample types with acceptable repeatability (e.g. EDTA, 282 FO, FO3hr), establishing glucometer-specific reference ranges for each sample type would maximise 283 the application of the glucometer and avoid errors in clinical-decision making.

284

The accuracy of glucometry using FO3hr was lower than for the FO group. In blood, glucose 285 286 continues to be utilised by erythrocytes at a rate of approximately 5-7% per h (Chan et al., 1989), and 287 while FO prevents glycolysis through inhibition of enolase, enzymes 'upstream' of enolase are 288 unaffected and continue to metabolise glucose-6-phosphate (Shi et al., 2009). Consequently, glucose 289 concentrations in FO blood samples decrease over the first h after collection and immediate separation 290 of serum or plasma is recommended to preserve glucose concentrations (Chan et al., 1989). In humans, 291 glucose concentrations in FO blood decreased, on average, by 0.39 mmol/L during 4 h transit to the 292 laboratory (Shi et al., 2009). Glucose utilisation after blood collection may have, in part, reduced the 293 repeatability and agreement for the FO3hr group in comparison to the FO group.

294

A limitation of this study was the lack of hypoglycaemic samples. A hypoglycaemic group would have allowed determination of glucometer performance across a larger glycaemic range. However, the tendency of the glucometer to under-estimate glucose concentrations is less likely to result in erroneous treatment decisions in hypoglycaemic horses. Further, the effect of haematocrit on glucometer accuracy was not assessed. The haematocrit can influence glucometer accuracy in humans, alpacas and dogs, with decreased and increased haematocrit levels resulting in a positive and negative bias, respectively

301 (Paul et al., 2011; Tang et al., 2000; Tennent-Brown et al., 2011). In a previous equine study (Hollis et 302 al., 2008b), there was no influence of haematocrit on glucometer accuracy. While haematocrit was not assessed in our study, an influence of erythrocytes on glucometer performance due to interactions with 303 304 the test strip filters cannot be discounted. In addition, other sources of analytic error from interference 305 (e.g. lipaemia, bilirubin, pH, drugs) (Gerber and Freeman, 2016) were not recorded. To minimise 306 methodological influences on glucometer performance (Beemer et al., 2013; Hollis et al., 2008b), 307 measurements were made by a single operator using one glucometer, all test strips had the same lot 308 number and were used within the expiry date and the glucometer and test strips were used according 309 to the manufacturer's instructions, including calibration procedure, storage and operation temperature 310 and humidity.

311

#### 312 Conclusion

The precision and accuracy of the glucometer was influenced by sample type. Whole blood is unsuitable for glucometry using this equipment as inaccuracy has potential for erroneous clinical decisions. Glucometry using blood collected into FO or EDTA tubes results in precision and accuracy sufficient for clinical use, provided trends in under-estimation of blood glucose concentration are accounted for by determination of method-specific reference ranges. Given the lack of readily available validated equine-specific glucometers, these findings emphasise the importance of assessing individual glucometer performance and optimal sample type prior to use in horses.

320

#### 321 Conflict of interest statement

None of the authors have financial or personal relationships that could inappropriately influenceor bias the content of this paper.

324

#### 325 Acknowledgements

The authors are grateful for the assistance provided for this study by the staff and students at the Veterinary Clinical Centre and Veterinary Diagnostic Laboratory, Charles Sturt University. The glucometer test strips were provided by Roche Diagnostics. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### 331 Appendix A: Supplementary material

332	Supplementary	data	associated	with	this	article	can	be	found,	in	the	online	version,	at
333	https://doi.org/													
334														
335														
336														
337														
338														
339														
340														
341														
342														
343														
344														
345														
346														
347														
348														
349														
350														
351														
352														
353														
354														
355														
356														
357														
358														
359														
360														

#### 361 References

- Beemer, O., Byers, S., Bohn, A., 2013. Evaluation of four point-of-care glucose meters in alpacas.
   Journal of Veterinary Internal Medicine 27, 990-995.
- Bland, J.M., Altman, D.G., 1986. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1, 307-310.
- Bochicchio, G.V., Sung, J., Joshi, M., Bochicchio, K., Johnson, S.B., Meyer, W., Scalea, T.M., 2005.
   Persistent hyperglycemia is predictive of outcome in critically ill trauma patients. Journal of Trauma-Injury Infection and Critical Care 58, 921-924.
- Carr, S.R., Slocum, J., Tefft, L., Haydon, B., Carpenter, M., 1995. Precision of office-based blood
   glucose meters in screening for gestational diabetes. American Journal of Obstetrics and
   Gynecology 173, 1267-1272.
- Chan, A.Y., Swaminathan, R., Cockram, C.S., 1989. Effectiveness of sodium fluoride as a preservative
   of glucose in blood. Clinical Chemistry 35, 315-317.
- Chen, E.T., Nichols, J.H., Duh, S.H., Hortin, G., 2003. Performance evaluation of blood glucose
   monitoring devices. Diabetes Technology and Therapeutics 5, 749-768.
- Cohen, T.A., Nelson, R.W., Kass, P.H., Christopher, M.M., Feldman, E.C., 2009. Evaluation of six
   portable blood glucose meters for measuring blood glucose concentration in dogs. Journal of
   the American Veterinary Medical Association 235, 276-280.
- Cohn, L.A., McCaw, D.L., Tate, D.J., Johnson, J.C., 2000. Assessment of five portable blood glucose
   meters, a point-of-care analyzer, and color test strips for measuring blood glucose
   concentration in dogs. Journal of the American Veterinary Medical Association 216, 198-202.
- Coldman, M.F., Good, W., 1967. Distribution of Sodium Potassium and Glucose in Blood of Some
   Mammals. Comparative Biochemistry and Physiology 21, 201-206.
- Denfeld, Q.E., Goodell, T.T., Stafford, K.N., Kazmierczak, S., 2011. Precision and Accuracy
   Comparison of Point-of-Care and Laboratory Glucose Concentrations in Cardiothoracic
   Surgery Patients. Journal of Cardiovascular Nursing 26, 512-518.
- 387 Domori, A., Sunahara, A., Tateno, M., Shimokawa Miyama, T., Setoguchi, A., Endo, Y., 2014. The
   388 clinical utility of two human portable blood glucose meters in canine and feline practice.
   389 Veterinary Clinical Pathology 43, 55-62.
- Gerber, K.L., Freeman, K.P., 2016. ASVCP guidelines: quality assurance for portable blood glucose
   meter (glucometer) use in veterinary medicine. Veterinary Clinical Pathology 45, 10-27.
- Hackett, E.S., McCue, P.M., 2010. Evaluation of a veterinary glucometer for use in horses. Journal of
   Veterinary Internal Medicine 24, 617-621.
- Hassel, D.M., Hill, A.E., Rorabeck, R.A., 2009. Association between Hyperglycemia and Survival in 228
   Horses with Acute Gastrointestinal Disease. Journal of Veterinary Internal Medicine 23, 1261 1265.
- Hoedemaekers, C.W.E., Gunnewiek, J.M.T.K., Prinsen, M.A., Willems, J.L., Hoeven, J.G.D., 2008.
   Accuracy of bedside glucose measurement from three glucometers in critically ill patients.
   Critical Care Medicine 36, 3062-3066.
- Hollis, A.R., Boston, R.C., Corley, K.T.T., 2007. Blood glucose in horses with acute abdominal disease.
   Journal of Veterinary Internal Medicine 21, 1099-1103.

- Hollis, A.R., Furr, M.O., Magdesian, K.G., Axon, J.E., Ludlow, V., Boston, R.C., Corley, K.T.T., 2008a.
   Blood glucose concentrations in critically ill neonatal foals. Journal of Veterinary Internal
   Medicine 22, 1223-1227.
- Hollis, A.R., Schaer, B.L.D., Boston, R.C., Wilkins, P.A., 2008b. Comparison of the accu-chek aviva
   point-of-care glucometer with blood gas and laboratory methods of analysis of glucose
   measurement in equine emergency patients. Journal of Veterinary Internal Medicine 22, 1189 1195.
- Hug, S.A., Riond, B., Schwarzwald, C.C., 2013. Evaluation of a continuous glucose monitoring system
   compared with an in-house standard laboratory assay and a handheld point-of-care glucometer
   in critically ill neonatal foals. Journal of Veterinary Emergency and Critical Care 23, 408-415.
- Kanji, S., Buffie, J., Hutton, B., Bunting, P.S., Singh, A., McDonald, K., Fergusson, D., McIntyre, L.A.,
   Hebert, P.C., 2005. Reliability of point-of-care testing for glucose measurement in critically ill
   adults. Critical Care Medicine 33, 2778-2785.
- Khan, A.I., Vasquez, Y., Gray, J., Wians, F.H., Kroll, M.H., 2006. The variability of results between point of-care testing glucose meters and the central laboratory analyzer. Archives of Pathology and
   Laboratory Medicine 130, 1527-1532.
- 418 Krouwer, J.S., Cembrowski, G.S., 2010. A review of standards and statistics used to describe blood 419 glucose monitor performance. Journal of Diabetes Science and Technology 4, 75-83.
- Lewis, K.S., Kane-Gill, S.L., Bobek, M.B., Dasta, J.F., 2004. Intensive insulin therapy for critically ill patients. Annuals of Pharmacotherapy 38, 1243-1251.
- Lin, L.I., 1989. A Concordance Correlation-Coefficient to Evaluate Reproducibility. Biometrics 45, 255-268.
- Paul, A.E.H., Shiel, R.E., Juvet, F., Mooney, C.T., Mansfield, C.S., 2011. Effect of hematocrit on accuracy of two point-of-care glucometers for use in dogs. American Journal of Veterinary Research 72, 1204-1208.
- Ray, J.G., Hamielec, C., Mastracci, T., 2001. Pilot study of the accuracy of bedside glucometry in the
   intensive care unit. Critical Care Medicine 29, 2205-2207.
- Russell, C., Palmer, J.E., Boston, R.C., Wilkins, P.A., 2007. Agreement between point-of-care
   glucometry, blood gas and laboratory-based measurement of glucose in an equine neonatal
   intensive care unit. Journal of Veterinary Emergency and Critical Care 17, 236-242.
- Shi, R.Z., Seeley, E.S., Bowen, R., Faix, J.D., 2009. Rapid blood separation is superior to fluoride for
   preventing in vitro reductions in measured blood glucose concentration. Journal of Clinical
   Pathology 62, 752-753.
- Sung, J., Bochicchio, G.V., Joshi, M., Bochicchio, K., Tracy, K., Scalea, T.M., 2005. Admission
   hyperglycemia is predictive of outcome in critically ill trauma patients. Journal of Trauma-Injury
   Infection and Critical Care 59, 80-83.
- Tack, C., Pohlmeier, H., Behnke, T., Schmid, V., Grenningloh, M., Forst, T., Pfutzner, A., 2012.
  Accuracy Evaluation of Five Blood Glucose Monitoring Systems Obtained from the Pharmacy:
  A European Multicenter Study with 453 Subjects. Diabetes Technology and Therapeutics 14, 330-337.
- Tang, Z.P., Lee, J.H., Louie, R.F., Kost, G.J., 2000. Effects of different hematocrit levels on glucose
   measurements with handheld meters for point-of-care testing. Archives of Pathology and
   Laboratory Medicine 124, 1135-1140.

- Tennent-Brown, B.S., Koenig, A., Williamson, L.H., Boston, R.C., 2011. Comparison of three point-of care blood glucose meters for use in adult and juvenile alpacas. Journal of the American
   Veterinary Medical Association 239, 380-386.
- Tonyushkina, K., Nichols, J.H., 2009. Glucose meters: a review of technical challenges to obtaining
   accurate results. Journal of Diabetes Science and Technology 3, 971-980.
- Vogelzang, M., Nijboer, J.M., van der Horst, I.C., Zijlstra, F., ten Duis, H.J., Nijsten, M.W., 2006.
   Hyperglycemia has a stronger relation with outcome in trauma patients than in other critically ill patients. Journal of Trauma-Injury Infection and Critical Care 60, 873-879.

**Table 1:** Repeatability coefficient (RC), median [interquartile range] coefficient of variation (CV) and Spearman's correlation coefficient ( $r_s$ ) for paired measurements of glucose concentration for each group and for each category of glucose concentration. (EDTA = ethylenediaminetetraacetic acid, FO = fluoride oxalate, FO3hr = fluoride oxalate and 3 h of storage, LAB = fluoride oxalate and wet chemistry analyser at laboratory, WB = whole blood).

- 481
- 482

Glucose	Group	RC	CV	Spearman's c	orrelation
concentration		(mmol/L)	(%)	rs	Р
category					
All samples	WB	2.36	8.1 [3.3-14.6]	0.79	<0.001
(n=62)	EDTA	0.86	2.9 [1.5-5.3]	0.85	<0.001
	FO	0.61	2.2 [1.6-4.1]	0.92	<0.001
	FO3hr	0.82	3.5 [1.9-6.3]	0.92	<0.001
	LAB	0.34	1.4 [1.1-2.5]	0.95	<0.001
Euglycaemic	WB	2.14	9.4 [3.6-16.5]	0.60	<0.001
samples	EDTA	0.74	3.1 [1.6-5.9]	0.71	<0.001
(n=49)	FO	0.50	3.3 [1.7-4.1]	0.85	<0.001
	FO3hr	0.78	3.5 [1.9-7.3]	0.62	<0.001
	LAB	0.33	1.5 [1.3-2.8]	0.90	<0.001
Hypergylcaemic	WB	2.94	5.5 [2.5-9.0]	0.83	<0.001
samples	EDTA	1.24	1.9 [0.9-2.5]	0.93	<0.001
(n=13)	FO	0.93	2.0 [1.0-3.0]	0.98	<0.001
	FO3hr	0.94	2.1 [1.3-3.9]	0.99	<0.001
	LAB	0.39	0.7 [0.4-1.3]	1.00	<0.001

483

484

**Table 2:** Lin's concordance ( $\rho$ ) and Spearman's correlation coefficient ( $r_s$ ) analysis of paired glucose 487 measurements between groups for each glucose concentration category. (EDTA = 488 ethylenediaminetetraacetic acid, FO = fluoride oxalate, FO3hr = fluoride oxalate and 3 h of storage, 489 LAB = fluoride oxalate and wet chemistry analyser at laboratory, WB = whole blood).

Group				Gluco	se conce	entratior	category						
comparison	All samples			E	Euglycaemic samples				Hyperglycaemic samples				
	(n=62)					(n:	=49)		(n=13)				
	ρ	95% CI	r <sub>s</sub>	Ρ	ρ	95% Cl	r <sub>s</sub>	Р	ρ	95% Cl	r <sub>s</sub>	Р	
WB-LAB	0. 94	0.90- 0.96	0.68	<0.001	0.3 1	0.13- 0.46	0.37	0.01	0.89	0.68- 0.97	0.8 7	<0.001	
WB-EDTA	0. 93	0.89- 0.96	0.60	<0.001	0.1 8	0.03- 0.33	0.20	0.17 7	0.94	0.83- 0.98	0.9 4	<0.001	
WB-FO	0. 86	0.79- 0.91	0.66	<0.001	0.1 1	0.01- 0.22	0.33	0.01 9	0.77	0.48- 0.91	0.8 5	<0.001	
WB-FO3hr	0. 88	0.81- 0.92	0.68	<0.001	0.1 9	0.07- 0.31	0.37	0.00 8	0.76	0.45- 0.91	0.8 3	<0.001	
EDTA-LAB	0. 98	0.96- 0.99	0.83	<0.001	0.4 9	0.33- 0.63	0.66	<0.0 01	0.93	0.81- 0.98	0.9 2	<0.001	
EDTA-FO	0. 94	0.92- 0.96	0.79	<0.001	0.3 8	0.22- 0.52	0.57	<0.0 01	0.79	0.55- 0.91	0.9 0	<0.001	
EDTA- FO3hr	0. 95	0.93- 0.97	0.73	<0.001	0.4 8	0.29- 0.64	0.45	0.00 1	0.79	0.54- 0.91	0.8 6	<0.001	
FO-LAB	0. 93	0.90- 0.95	0.84	<0.001	0.2 3	0.14- 0.32	0.67	<0.0 01	0.84	0.67- 0.93	0.9 9	<0.001	
FO-FO3hr	0. 99	0.98- 0.99	0.85	<0.001	0.6 6	0.48- 0.78	0.69	<0.0 01	0.98	0.95- 0.99	0.9 7	<0.001	
FO3hr-LAB	0. 94	0.92- 0.96	0.76	<0.001	0.2 8	0.16- 0.39	0.51	<0.0 01	0.86	0.69- 0.94	0.9 7	<0.001	

Table 3: Summary of the Bland Altman analyses of agreement for glucose measurement between
groups for each category of glucose concentration. (EDTA = ethylenediaminetetraacetic acid, FO =
fluoride oxalate, FO3hr = fluoride oxalate and 3 h of storage, LAB = fluoride oxalate and wet chemistry
analyser at laboratory, WB = whole blood).

Group	Glucose concentration category												
comparison	All sam	iples (n:	=62)	Euglycae (	emic sai n=49)	mples	Hyperglycaemic samples (n=13)						
	Mean bias (mmol/L	95% (mm	LOA nol/L)	Mean bias (mmol/L	95% (mm	LOA iol/L)	Mean bias (mmol/L	95% (mm	LOA iol/L)				
WB-LAB	0.07	2.44	-2.31	0.11	2.44	-2.21	-0.12	2.53	-2.76				
WB-EDTA	0.44	2.91	-2.04	0.62	3.08	-1.84	-0.26	1.83	-2.35				
WB-FO	1.24	3.79	-1.30	1.18	3.67	-1.31	1.47	4.27	-1.33				
WB-FO3hr	1.04	3.56	-1.48	0.98	3.33	-1.37	1.26	4.40	-1.88				
EDTA-LAB	-0.37	0.94	-1.68	-0.51	0.25	-1.26	0.15	2.38	-2.09				
EDTA-FO	0.80	2.42	-0.81	0.56	1.40	-0.29	1.73	4.16	-0.69				
EDTA- FO3hr	0.60	2.32	-1.11	0.36	1.24	-0.52	1.52	4.25	-1.20				
FO-LAB	-1.17	-0.27	-2.07	-1.07	-0.36	-1.77	-1.58	-0.47	-2.70				
FO-FO3hr	-0.20	0.57	-0.97	-0.20	0.54	-0.93	-0.21	0.70	-1.12				
FO3hr-LAB	-0.97	0.05	-2.00	-0.87	-0.06	-1.67	-1.38	0.00	-2.75				

Table 4: Percentage of glucose measurements determined for each blood glucose category and each
glucometer group that were within 5, 10, 15 or 20% of the glucose measurement determined by the
laboratory reference method. (EDTA = ethylenediaminetetraacetic acid, FO = fluoride oxalate, FO3hr =
fluoride oxalate and 3 h of storage, LAB = fluoride oxalate and wet chemistry analyser at laboratory,
WB = whole blood).

Group	Category	Within 5%	Within 10%	Within 15%	Within 20%
WB	All samples (n=62)	24.2	41.9	56.5	67.7
	Euglycaemic samples (n=49)	20.4	36.7	51.0	61.2
	Hyperglycaemic samples (n=13)	38.5	61.5	76.9	92.3
EDTA	All samples (n=62)	22.6	56.7	83.3	93.3
	Euglycaemic samples (n=49)	14.3	51.0	81.6	91.8
	Hyperglycaemic samples (n=13)	53.8	76.9	84.6	100
FO	All samples (n=62)	1.6	8.3	26.7	56.7
	Euglycaemic samples (n=49)	2.0	4.1	14.3	44.9
	Hyperglycaemic samples (n=13)	0.0	23.1	69.2	92.3
FO3hr	All samples (n=62)	8.1	23.3	40.0	70.0
	Euglycaemic samples (n=49)	6.1	16.3	32.7	65.3
	Hyperglycaemic samples (n=13)	15.4	53.8	69.2	84.6