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, Armstrong, 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](https://doi.org/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 Edinburgh 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.

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

David. I. Rendle ^{a, b}, Susan. K. Armstrong ^{a, c}, Jane. Heller ^a, Kristopher. J. Hughes ^{a, *}

School of Animal and Veterinary Sciences, Charles Sturt University, Locked Bag 588, Boorooma Street, Wagga Wagga, NSW 2678 Australia.

^bCurrent address: Rainbow Equine Hospital, Old Malton, Malton, North Yorkshire, YO17 6SG UK.

^cCurrent address: Royal (Dick) School of Veterinary Studies and Roslin Institute, University of Edinburgh, Roslin, Midlothian, EH25 9RG UK.

* Corresponding author. Tel.: +61 69334253.

Email address: krhughes@csu.edu.au (K.J. Hughes).

Abstract

Point-of-care glucometry is used commonly in clinical and research settings; however, accuracy and precision of this method are concerns. The objectives of this study were to determine the accuracy of glucometry in adult horses and the precision of duplicate measurements. Blood samples were 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 were determined, in duplicate, by glucometry from the syringe (plain whole blood [WB] group), EDTA tube (EDTA group) and one FO tube (FO group). One FO sample was used to measure plasma glucose concentration by a laboratory chemistry analyser (LAB group) ≤ 1 h after collection. The third FO tube was used to measure plasma glucose concentration by glucometry after 3 h storage (FO3hr group).

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 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 for WB-LAB and ≤ 2.75 mmol/L for most other comparisons. For the glucometer used, performance is influenced by sample type: WB is unsuitable, while FO or EDTA samples result in adequate precision and accuracy, provided under-estimation of glucose concentrations is accounted for by using method-specific reference ranges. Glucometer performance and optimal sample type(s) should be determined prior to use in horses.

Keywords: Horse; Glucometry; Repeatability; Agreement; Equine

Introduction

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

There are few published studies of the accuracy and precision of glucometers in horses (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 influences of sample type, glucose concentration and delays in analysis on results in horses are largely unknown. In one equine study, glucometry with plasma had excellent agreement with a laboratory method, while measurements from whole blood did not (Hollis et al., 2008b). In some human and equine studies, glucometer performance was less reliable when marked hypoglycaemia or hyperglycaemia was present (Hollis et al., 2008b; Kanji et al., 2005; Khan et al., 2006). Bias in glucometer results may be important in critically-ill horses where performance at the extremes of blood glucose concentrations

may influence decision-making and accurate glycaemic control. The objectives of this study were to determine (1) the accuracy of glucometry in adult horses using blood and plasma samples in comparison to a laboratory standard method and (2) the precision of duplicate measurements.

Materials and methods

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

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.

For each horse, whole blood (WB) was collected from the jugular vein into a 3 mL syringe, one blood collection tube containing ethylenediaminetetraacetic acid (EDTA) (Vacutainer, Becton Dickinson) and 3 blood collection tubes containing fluoride oxalate (FO) (Vacutainer, Becton Dickinson). The tubes were filled to the manufacturer's designated level. Immediately after collection, the glucose concentration of WB in the syringe was determined using a human-specific POC glucometer (Accutrend Plus, Roche Diagnostics), according to the manufacturer's instructions (WB group). Within 5 min of 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 determination of plasma glucose concentration using the glucometer after storage of the sample for 3 h at 22 °C and separation of the plasma by centrifugation (10 min at 3000 rpm) immediately prior to analysis (FO3hr group). The third FO tube was used to measure plasma glucose concentration by a wet chemistry analyser using the hexokinase/glucocose-6-phosphate dehydrogenase method (Konelab 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 measurements were obtained using the same device. For the WB, EDTA, FO and FO3hr groups, the same lot number for the glucometer measurement strips and a single glucometer was used throughout 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.

Data analysis

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

Between groups, association of paired glucose measurements (first measurement for each sample) was determined using Spearman's correlation, and agreement was determined using Lin's concordance correlation (Lin, 1989) and the mean bias and 95% limits of agreement (LOA) (Bland and Altman, 1986). Concordance correlation coefficients (ρ_c) were interpreted using the criteria of >0.99: almost perfect, 0.95-0.99: substantial, 0.90-0.95: moderate, <0.90: poor concordance (Domori et al., 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 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 percentage of glucometer results that were within 5%, 10%, 15% or 20% of the LAB glucose concentration were calculated according to guidelines to describe glucometer performance (Krouwer 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 $P < 0.05$.

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.

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).

Between groups, r_s 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_s 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.

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

Discussion

The results of this study demonstrate that glucometer precision and accuracy can be influenced 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 glucometer repeatability and agreement with the laboratory standard, albeit with underestimation of glucose concentration. In addition, precision and accuracy varied across the glycaemic range, supporting the recommendation that glucometer performance should be assessed in clinically-relevant glucose ranges (hypo-, eu- and hyperglycaemia) (Gerber and Freeman, 2016). Determination of glucometer performance is important for patient care, particularly in intensive care settings. In both humans and horses, glycaemic abnormalities are associated with a worse prognosis for survival (Bochicchio et al., 2005; Hassel et al., 2009; Hollis et al., 2008a; Sung et al., 2005) and monitoring and 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-side decision making, poor accuracy and precision may lead to erroneous clinical assessment and management (Hoedemaekers et al., 2008; Kanji et al., 2005; Russell et al., 2007).

For all categories, WB had poor precision (CV: 5.5-9.4%, RC: 2.14-2.94 mmol/L). For euglycaemic animals, a difference of over 2.14 mmol/L may alter clinical interpretations, suggesting that WB is inappropriate for this glucometer. The reason for this poor precision is unknown; however, it may involve the interaction of horse erythrocytes with the test strip. The strips filter erythrocytes while plasma diffuses to the reagents and sensor for glucose measurement and differences in the sizes of human 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 concentrations between erythrocytes and plasma, and differences in glucose distribution between humans and horses are likely (Coldman and Good, 1967; Hackett and McCue, 2010). In one study (Hackett and McCue, 2010), a veterinary glucometer coded for equine use (and likely species-specific assumption of glucose distribution) accurately measured glucose concentrations in WB, while in other studies, plasma provided superior agreement with a laboratory method than WB when human-specific glucometers were used in horses (Hollis et al., 2008b) and alpacas (Tennent-Brown et al., 2011). These 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 influence decision-making.

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.

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

The mean bias and 95% LOA results revealed variable agreement between glucometer groups 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 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, good accuracy of veterinary-specific glucometers with WB has been demonstrated for horses (Hackett 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 acceptable LOA is a clinical, rather than a statistical decision, and for the current study, <1.7 mmol/L

(euglycaemic samples) and <2.8 mmol/L (hyperglycaemic samples) were chosen, based on glucometer 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) and LAB-FO, LAB-FO3hr and FO-FO3hr (hyperglycaemic samples). The FO and FO3hr groups had the smallest LOA ranges, which are unlikely to alter clinical interpretation, irrespective of glucose concentration. While acceptable agreement between the EDTA and LAB groups was present for euglycaemic samples, proportional bias with increasing glucose concentration was present, suggesting that EDTA is not suitable for interchangeable use with the laboratory method when hyperglycaemia is present. Proportional bias has occurred in previous studies of glucometer performance in veterinary species (Cohen et al., 2009; Tennent-Brown et al., 2011), indicating that assessment of glucometer accuracy over a wide glucose concentration range is necessary. In the current study, there was constant bias with underestimation of glucose concentrations by the glucometer for the EDTA, FO and FO3hr groups. For FO and EDTA, this may, in part, reflect higher glucose concentrations in plasma, which are 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 estimated difference of 10-15% between plasma (LAB) and blood (FO). Constant bias with glucometer use in horses and other species has been demonstrated previously (Beemer et al., 2013; Cohen et al., 2009; Russell et al., 2007; Tennent-Brown et al., 2011), although the direction of the bias varied between studies. Given the small size of the hyperglycaemic group in the current study, further investigation of the effects of hyperglycaemia on glucometer performance using larger numbers of hyperglycaemic and systemically-ill horses is warranted.

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 glucose concentrations in an individual animal. The results of the current and previous studies (Hollis et al., 2008b; Russell et al., 2007) suggest that human-specific glucometers may be inaccurate when used in horses (due to systematic bias), and careful consideration of appropriate sample type is necessary for specific glucometers. The poor agreement between WB and other groups, can be anticipated from the large RC for WB, as repeatability limits the amount of achievable agreement (Bland and Altman, 1986).

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 glucometer performance criteria include 95-100% of measurements within 5-20% of the laboratory method for acceptable accuracy (Tonyushkina and Nichols, 2009). While similar standards for glucometer accuracy in horses have not been established, our results, overall, reflected glucometer inaccuracy, irrespective of sample type. Similarly, glucometer performance often failed to achieve adequate accuracy in alpacas (Beemer et al., 2013) and dogs (Cohn et al., 2000). Glucometer inaccuracy may result in erroneous clinical decisions if glucose reference ranges for a reference laboratory method are used. However, systematic bias may not preclude individual glucometer use if a conversion factor is applied. Alternatively, for sample types with acceptable repeatability (e.g. EDTA, FO, FO3hr), establishing glucometer-specific reference ranges for each sample type would maximise the application of the glucometer and avoid errors in clinical-decision making.

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

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

(Paul et al., 2011; Tang et al., 2000; Tennent-Brown et al., 2011). In a previous equine study (Hollis et 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 the test strip filters cannot be discounted. In addition, other sources of analytic error from interference (e.g. lipaemia, bilirubin, pH, drugs) (Gerber and Freeman, 2016) were not recorded. To minimise methodological influences on glucometer performance (Beemer et al., 2013; Hollis et al., 2008b), measurements were made by a single operator using one glucometer, all test strips had the same lot number and were used within the expiry date and the glucometer and test strips were used according to the manufacturer's instructions, including calibration procedure, storage and operation temperature and humidity.

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.

Conflict of interest statement

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

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.

Appendix A: Supplementary material

Supplementary data associated with this article can be found, in the online version, at
<https://doi.org/...>

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.
- Domori, A., Sunahara, A., Tateno, M., Shimokawa Miyama, T., Setoguchi, A., Endo, Y., 2014. The clinical utility of two human portable blood glucose meters in canine and feline practice. *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.

402 Hollis, A.R., Furr, M.O., Magdesian, K.G., Axon, J.E., Ludlow, V., Boston, R.C., Corley, K.T.T., 2008a.
403 Blood glucose concentrations in critically ill neonatal foals. *Journal of Veterinary Internal*
404 *Medicine* 22, 1223-1227.

405 Hollis, A.R., Schaer, B.L.D., Boston, R.C., Wilkins, P.A., 2008b. Comparison of the accu-chek aviva
406 point-of-care glucometer with blood gas and laboratory methods of analysis of glucose
407 measurement in equine emergency patients. *Journal of Veterinary Internal Medicine* 22, 1189-
408 1195.

409 Hug, S.A., Riond, B., Schwarzwald, C.C., 2013. Evaluation of a continuous glucose monitoring system
410 compared with an in-house standard laboratory assay and a handheld point-of-care glucometer
411 in critically ill neonatal foals. *Journal of Veterinary Emergency and Critical Care* 23, 408-415.

412 Kanji, S., Buffie, J., Hutton, B., Bunting, P.S., Singh, A., McDonald, K., Fergusson, D., McIntyre, L.A.,
413 Hebert, P.C., 2005. Reliability of point-of-care testing for glucose measurement in critically ill
414 adults. *Critical Care Medicine* 33, 2778-2785.

415 Khan, A.I., Vasquez, Y., Gray, J., Wians, F.H., Kroll, M.H., 2006. The variability of results between point-
416 of-care testing glucose meters and the central laboratory analyzer. *Archives of Pathology and*
417 *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.

420 Lewis, K.S., Kane-Gill, S.L., Bobek, M.B., Dasta, J.F., 2004. Intensive insulin therapy for critically ill
421 patients. *Annals of Pharmacotherapy* 38, 1243-1251.

422 Lin, L.I., 1989. A Concordance Correlation-Coefficient to Evaluate Reproducibility. *Biometrics* 45, 255-
423 268.

424 Paul, A.E.H., Shiel, R.E., Juvet, F., Mooney, C.T., Mansfield, C.S., 2011. Effect of hematocrit on
425 accuracy of two point-of-care glucometers for use in dogs. *American Journal of Veterinary*
426 *Research* 72, 1204-1208.

427 Ray, J.G., Hamielec, C., Mastracci, T., 2001. Pilot study of the accuracy of bedside glucometry in the
428 intensive care unit. *Critical Care Medicine* 29, 2205-2207.

429 Russell, C., Palmer, J.E., Boston, R.C., Wilkins, P.A., 2007. Agreement between point-of-care
430 glucometry, blood gas and laboratory-based measurement of glucose in an equine neonatal
431 intensive care unit. *Journal of Veterinary Emergency and Critical Care* 17, 236-242.

432 Shi, R.Z., Seeley, E.S., Bowen, R., Faix, J.D., 2009. Rapid blood separation is superior to fluoride for
433 preventing in vitro reductions in measured blood glucose concentration. *Journal of Clinical*
434 *Pathology* 62, 752-753.

435 Sung, J., Bochicchio, G.V., Joshi, M., Bochicchio, K., Tracy, K., Scalea, T.M., 2005. Admission
436 hyperglycemia is predictive of outcome in critically ill trauma patients. *Journal of Trauma-Injury*
437 *Infection and Critical Care* 59, 80-83.

438 Tack, C., Pohlmeier, H., Behnke, T., Schmid, V., Grenningloh, M., Forst, T., Pfutzner, A., 2012.
439 Accuracy Evaluation of Five Blood Glucose Monitoring Systems Obtained from the Pharmacy:
440 A European Multicenter Study with 453 Subjects. *Diabetes Technology and Therapeutics* 14,
441 330-337.

442 Tang, Z.P., Lee, J.H., Louie, R.F., Kost, G.J., 2000. Effects of different hematocrit levels on glucose
443 measurements with handheld meters for point-of-care testing. *Archives of Pathology and*
444 *Laboratory Medicine* 124, 1135-1140.

445 Tennent-Brown, B.S., Koenig, A., Williamson, L.H., Boston, R.C., 2011. Comparison of three point-of-
446 care blood glucose meters for use in adult and juvenile alpacas. Journal of the American
447 Veterinary Medical Association 239, 380-386.

448 Tonyushkina, K., Nichols, J.H., 2009. Glucose meters: a review of technical challenges to obtaining
449 accurate results. Journal of Diabetes Science and Technology 3, 971-980.

450 Vogelzang, M., Nijboer, J.M., van der Horst, I.C., Zijlstra, F., ten Duis, H.J., Nijsten, M.W., 2006.
451 Hyperglycemia has a stronger relation with outcome in trauma patients than in other critically ill
452 patients. Journal of Trauma-Injury Infection and Critical Care 60, 873-879.

453

454

455

456

457

458

459

460

461

462

463

464

465

466

467

468

469

470

471

472

473

474

475

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).

Glucose concentration category	Group	RC (mmol/L)	CV (%)	Spearman's correlation	
				r_s	P
All samples (n=62)	WB	2.36	8.1 [3.3-14.6]	0.79	<0.001
	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 samples (n=49)	WB	2.14	9.4 [3.6-16.5]	0.60	<0.001
	EDTA	0.74	3.1 [1.6-5.9]	0.71	<0.001
	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
Hyperglycaemic samples (n=13)	WB	2.94	5.5 [2.5-9.0]	0.83	<0.001
	EDTA	1.24	1.9 [0.9-2.5]	0.93	<0.001
	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

Table 2: Lin's concordance (ρ) and Spearman's correlation coefficient (r_s) analysis of paired glucose measurements between groups for each glucose concentration category. (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 comparison	Glucose concentration category											
	All samples (n=62)				Euglycaemic samples (n=49)				Hyperglycaemic samples (n=13)			
	ρ	95% CI	r_s	P	ρ	95% CI	r_s	P	ρ	95% CI	r_s	P
WB-LAB	0.94	0.90-0.96	0.68	<0.001	0.31	0.13-0.46	0.37	0.01	0.89	0.68-0.97	0.8	<0.001
WB-EDTA	0.93	0.89-0.96	0.60	<0.001	0.18	0.03-0.33	0.20	0.17	0.94	0.83-0.98	0.9	<0.001
WB-FO	0.86	0.79-0.91	0.66	<0.001	0.11	0.01-0.22	0.33	0.01	0.77	0.48-0.91	0.8	<0.001
WB-FO3hr	0.88	0.81-0.92	0.68	<0.001	0.19	0.07-0.31	0.37	0.00	0.76	0.45-0.91	0.8	<0.001
EDTA-LAB	0.98	0.96-0.99	0.83	<0.001	0.49	0.33-0.63	0.66	<0.001	0.93	0.81-0.98	0.9	<0.001
EDTA-FO	0.94	0.92-0.96	0.79	<0.001	0.38	0.22-0.52	0.57	<0.001	0.79	0.55-0.91	0.9	<0.001
EDTA-FO3hr	0.95	0.93-0.97	0.73	<0.001	0.48	0.29-0.64	0.45	0.00	0.79	0.54-0.91	0.8	<0.001
FO-LAB	0.93	0.90-0.95	0.84	<0.001	0.23	0.14-0.32	0.67	<0.001	0.84	0.67-0.93	0.9	<0.001
FO-FO3hr	0.99	0.98-0.99	0.85	<0.001	0.66	0.48-0.78	0.69	<0.001	0.98	0.95-0.99	0.9	<0.001
FO3hr-LAB	0.94	0.92-0.96	0.76	<0.001	0.28	0.16-0.39	0.51	<0.001	0.86	0.69-0.94	0.9	<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 comparison	Glucose concentration category								
	All samples (n=62)			Euglycaemic samples (n=49)			Hyperglycaemic samples (n=13)		
	Mean bias	95% LOA (mmol/L)		Mean bias	95% LOA (mmol/L)		Mean bias	95% LOA (mmol/L)	
	(mmol/L)			(mmol/L)			(mmol/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