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Personal view

Agreeing Language in Veterinary Endocrinology (ALIVE): Diabetes mellitus - a modified Delphi-method-based system to create consensus disease definitions

Stijn J.M. Niessen [a,b,*,1], Charlotte Bjornvad [c,2], David B. Church [a,2], Lucy Davison [a,2], Diego Esteban-Saltiveri [d,2], Linda M. Fleeman [e,2], Yaiza Forcada [a,b,2], Federico Fracassi [f,2], Chen Gilor [g,2], Jeanette Hanson [h,2], Michael Herrtage [i,2], Patty Lathan [j,2], Rodolfo O. Leal [k,2], Araceli Loste [l,2], Claudia Reusch [m,2], Thomas Schermerhorn [n,2], Christiane Stengel [o,2], Stein Thoresen [p,2], Julianna Thuroczy [q,2], ESVE/SCE membership[3]

[a] Royal Veterinary College, NW1 0TU London, UK
[b] Veterinary Specialist Consultations, 1215JX Hilversum, the Netherlands
[c] Department of Veterinary Clinical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, 1870 Copenhagen, Denmark
[d] Clínica Felina Barcelona, 08015 Barcelona, Spain
[e] Animal Diabetes Australia, 3066 Melbourne, Australia
[f] Department of Veterinary Medical Sciences, University of Bologna, 1088 Bologna, Italy
[g] Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL 32608, USA
[h] Swedish University of Agricultural Sciences, Department of Clinical Sciences, SE-750 07 Uppsala, Sweden
[i] Cambridge University, Faculty of Veterinary Medicine, CB3 0ES Cambridge, UK
[j] Mississippi State University, College of Veterinary Medicine, Starkville, MS 39762, USA
[k] CIISA - Centro de Investigação Interdisciplinar em Sanidade Animal, Faculdade de Medicina Veterinária, Universidade de Lisboa, 1300–477 Lisbon, Portugal
[l] Departamento de Patología Animal, Instituto Agroalimentario de Aragón-IA2, Universidad de Zaragoza-CITA, Facultad de Veterinaria, 50013 Zaragoza, Spain
[m] Clinic for Small Animal Internal Medicine, Vetsuisse faculty of the University of Zurich, CH-8057 Zurich, Switzerland
[n] Dept Clinical Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, KS 66502, USA
[o] Tierklinik Hoffheim, 65719 Hoffheim, Germany
[p] Faculty of Veterinary Medicine, Norwegian University of Life Sciences, N-1433 Ås, Norway
[q] Animal Health Center Budafok, 1221 Budapest, Hungary

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Introduction

Progress in clinical practice, research and teaching is facilitated when communication takes place based on a common language. With the increased appreciation of the value of evidence based medicine and systematic reviews and meta-analyses being considered to provide one

* Corresponding author at: Veterinary Specialist Consultations, 1215JX Hilversum, the Netherlands.
E-mail address: info@veterinaryspecialistconsultations.com (S.J.M. Niessen).

[1] Stijn.J.M. Niessen is founding chair and facilitator of the ALIVE program

[2] Authors who took part in the first ALIVE cycle dealing with diabetes mellitus associated terminology; all authors had equal contribution and are shown in alphabetical order

[3] The memberships of the European Society of Veterinary Endocrinology (ESVE) and Society of Comparative Endocrinology (SCE) participated in the endorsement phase of the process, validating the ALIVE definitions.

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of the highest levels of evidence, comes the increased realisation that often studies cannot be compared easily due to the use of varying disease definitions (Murad et al., 2016). An agreed set of common disease definitions and classifications can aid in the early phases of study design, eventually leading to increased comparability of study results and therefore also increased feasibility of such systematic reviews and meta-analyses. Creating consensus definitions would also aid in other areas. This could include offering a language framework for educational professionals and resources, including journals, authors and reviewers during the review and publication process. It could also enhance transparency and efficiency, as well as help avoid confusion among those studying the field and thus consulting different (online or offline) texts. Finally, agreement over clinical definitions is expected to be beneficial to clinical standards. The agreed staging system for renal disease recommended by the International Renal Interest Society [4] is a good example of this (Boyd et al., 2008).

It is the above reasoning that stimulated the birth of a definition setting program in the field of veterinary endocrinology, based on a modified Delphi method of achieving consensus (Hsu and Sandford, 2007; Boulkedid et al., 2011; Darling et al., 2014; Bleijlevens et al., 2016; Rioja-Lang et al., 2019; Barrett and Heale, 2020; Rioja-Lang et al., 2020). It is hoped that this program will aid the development of veterinary endocrinology, as well as stimulate other fields across medicine (veterinary, human and comparative) to consider following a similar approach.

Project ALIVE - methodology

Project Agreeing Language in Veterinary Endocrinology (ALIVE) was founded in 2016 as a project of the European Society of Veterinary Endocrinology (ESVE) [5] and endorsed by the Society of Comparative Endocrinology (SCE) ,[6] the two largest independent veterinary endocrinology interest groups in the world (total annual membership numbers fluctuating between 200 and 400 endocrinology experts and endocrinology-interested veterinarians, originating from more than 40 countries worldwide). The methodology of project ALIVE was based on a modified Delphi Method of achieving consensus (Hsu and Sandford, 2007; Boulkedid et al., 2011; Darling et al., 2014; Bleijlevens et al., 2016; Rioja-Lang et al., 2019; Barrett and Heale, 2020; Rioja-Lang et al., 2020) (Fig. 1). The Delphi method assumes that group judgments are more valid than individual judgments. Group agreement is attempted to be achieved among a group of several experts through ongoing cycles or rounds of meetings. During each round, findings of the previous rounds are shared among the group and reflected upon. The strength of the methodology is that, over time, agreement is fostered and achieved. Rounds or cycles are usually led by a facilitator. Anonymity is often, though not always part of the process (Boulkedid et al., 2011; Bleijlevens et al., 2016; Rioja-Lang et al., 2019). Modifications which relinquish anonymity in the procedure (sometimes referred to as 'conference Delphi') have been suggested to result in a higher probability of reaching agreement than anonymised 'classical' Delphi approaches (Rioja-Lang et al., 2016).

This first ALIVE cycle consisted of ESVE issuing several call outs for volunteers to participate as experts in the process; call outs took place at their annual meeting, social media and through email.

The overall chair ensured a mixed panel (the ESVE-panel) of a maximum of 10 panellists was formed from these volunteers, with all chosen volunteers being active (clinically – meaning being a person who colleagues refer diabetes mellitus cases to - and/or in research – meaning a person who publishes in this topic) in veterinary diabetes mellitus in a variety of settings (university as well as private practice) and from diverse geographic locations (aiming to have representatives of as many continents as feasible). Volunteers were not considered anymore after the maximum number was reached.

This panel, aided by the chair, initially divided itself into 2 sub-panels according to individuals' professional interest area and each appointed a chair (the sub-chair) (Fig. 1; step 1). This sub-division into two smaller groups was thought to aid the efficiency of initial discussions.

The sub-panels held a series of virtual meetings (pre-meetings) prior to the physical meetings to identify, study and create draft definitions relevant to a specified area within the topic of canine and feline diabetes mellitus (Fig. 1; step 2). The draft definitions were then presented by the sub-chairs to the entire group at the start of a series of physical meetings over a two-day period where all panellists met in-person. The draft definitions were then discussed, as well as amended, on the basis of the feedback provided by the rest of the group (Fig. 1; step 3). Definitions which could not be finalised during the physical meeting, due to time constraints or lingering disagreement, were further discussed and refined in email exchanges and virtual after-meetings (Fig. 1; step 4). A second series of two-day in-person meetings was then held as soon as SCE-members had approved its participation in the overall project during their annual society meeting. For these meetings a second set of volunteer experts from the SCE (the SCE-panel) was invited by the chair, following a call-out among its membership. Eight volunteers came forward and the SCE-panel discussed all definitions proposed by the initial ESVE-panel during these meetings and made amendments if deemed necessary (Fig. 1; step 5). The resulting next versions of the definitions were then sent electronically by the chair to the members of the original ESVE-panel for final approval (Fig. 1; step 6). Arbitrarily, an agreement of at least 75% of panellists was set to be sufficient for creation of a definition (though 100% agreement was sought).

Finally, panel-agreed definitions were put forward by the chair for endorsement by the entire current membership of both ESVE and SCE through an anonymous online survey sent to all email addresses available through the societies' secretaries (Fig. 1; step 7). Members were contacted on a minimum of three occasions through this route and participation encouraged through social media channels as well as during physical society meetings. Possible survey responses offered to members were: 'I endorse this definition' or 'I absolutely cannot endorse this definition' (Fig. 1; step 8).; all respondents were provided the opportunity to comment on the proposed definitions at the end of the survey. Comments have been stored digitally and will be presented to the panel members of the next cycle. This could lead to future panel members proposing an adaptation to the definitions of this current cycle during a next cycle (Fig. 1; step 9). A simple majority endorsement (>50% of respondents) qualified the definitions to become official ALIVE-approved terminology for subsequent use in research, education and clinical practice. The process aimed for a minimum of 20% of memberships to participate in the endorsement phase (survey phase) of the process. The entire process had been officially approved, and continues to be given a mandate of approval by the memberships of both societies through the process of annual membership meetings. Costs associated with the project were covered by the funds of ESVE, which in turn stem from membership fees, as well as external sponsoring. Influence of external sponsors on the content of the process was and will be prohibited. The process is summarised in Fig. 1.

Cycle 1: agreed definitions diabetes mellitus

This cycle took place in 2016–2018. The ESVE panel consisted of 12 and the SCE panel of 5 expert veterinarians leading to 16 definitions being proposed to the memberships of both societies. All definitions were accepted by all panellists (100%) and a simple majority of

[4] See: International Renal Interest Society. http://www.iris-kidney.com (Accessed 27 September 2022).

[5] See: European Society of Veterinary Endocrinology. www.esve.org (Accessed 27 September 2022).

[6] See: Society of Comparative Endocrinology. www.veterinaryendocrinology.org (Accessed 27 September 2022).

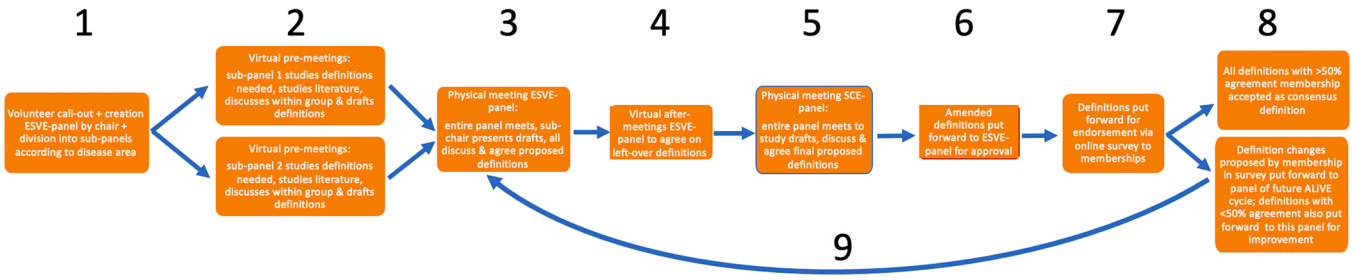

Fig. 1. Diagram showing the order of events in Project ALIVE (Agreeing Language in Veterinary Endocrinology), a modified Delphi-method definition consensus finding process. Numbers are used to help identify the steps.

respondents (n = 110–117 for each definition; 34.4–36.6% of total memberships). Below are the ALIVE consensus definitions resulting from this cycle with membership endorsement numbers shown in between brackets.

Definition: diabetes mellitus (endorsement 115/117)

Diabetes mellitus (DM) is a heterogeneous group of diseases with multiple aetiologies characterized by hyperglycaemia resulting from inadequate insulin secretion, inadequate insulin action or both.

ALIVE criteria for diagnosing DM in dogs (endorsement 105/110)

DM in dogs is diagnosed:

1. In a canine patient with a random (fasted or unfasted) blood glucose (BG) > = 11.1 mmol/L (>=200 mg/dL) with classic clinical signs of hyperglycaemia (with no other plausible cause) or hyperglycaemic crisis

   ○ In some cases clinical signs may not have been reported by the owner
   ○ In cases with uncertainty over presence/absence of clinical signs diagnosis should be confirmed by repeat BG measurement and/or documentation of alternative glycaemic parameters such as increased glycated proteins and/or glucosuria.

2. In some canine patients with fasting BG > 7 mmol/L (126 mg/dL) < = 11.1 mmol/L (200 mg/dL) with or without clinical signs of hyperglycaemia or hyperglycaemic crisis, DM is differentiated from stress hyperglycaemia by documentation of persistent fasting hyperglycaemia for more than 24 h or increased glycated proteins.

Comments:

- Fasting is defined by a period of a minimum of 8 h withholding food, not water (fasting should only be considered when it is safe for the canine patient).
- The definition implies use of a species-validated method to measure glucose as well as glycated protein, and conditions other than DM that specifically affect the concentration of glycated protein are excluded. Glycated blood proteins should be measured by a methodology with relevant, internally established reference interval, and regular quality assurance.
- Variations in protein concentration and metabolism can affect glycated protein concentrations.
- The diagnosis of DM is more likely than stress hyperglycaemia in dogs when contributing factors are present (e.g. Cushing's syndrome, diabetogenic treatment, dioestrus, pancreatitis).

ALIVE criteria for diagnosing DM in cats (endorsement 109/110)

The potential for stress hyperglycaemia warrants caution in interpretation of hyperglycaemia of any magnitude in cats.

DM in cats is diagnosed:

1. In a feline patient with a random (fasted or unfasted) BG> = 15 mmol/L (270 mg/dL) with classic clinical signs of hyperglycaemia (with no other plausible cause) or hyperglycaemic crisis AND **at least one** of the following criteria:
   ○ increased glycated proteins
   ○ glucosuria on more than one occasion on a naturally voided sample acquired in a home environment at least 2 days after any stressful events.
   ○ In some cases clinical signs may not have been reported by the owner
2. In a feline patient with random (fasted or unfasted) BG > 7 mmol/L (126 mg/dL) and < = 15 mmol/L (270 mg/dL) and **at least two** of the following:
   ○ classic clinical signs of hyperglycaemia (with no other plausible cause) or hyperglycaemic crisis
   ○ increased glycated proteins
   ○ glucosuria on more than one occasion on a naturally voided sample acquired in a home environment at least 2 days after any stressful events.

Applying the above ALIVE criteria permits the possible existence of a subpopulation of cats where DM or stress hyperglycaemia cannot be confidently confirmed or excluded; if concerns over presence of DM persist, periodic re-evaluation is warranted.

Comments:

- The definition implies use of a species-validated method to measure glucose as well as glycated protein, and conditions other than DM that specifically affect the concentration of glycated protein are excluded. Glycated blood proteins should be measured by a methodology with relevant, internally established reference interval, and regular quality assurance.
- Variations in protein concentration and metabolism can affect glycated protein concentrations.
- DM is more likely when DM-contributing factors are present (e.g. diabetogenic treatment, hypersomatotropism).

Definition: Subclinical diabetes mellitus in dogs and cats (endorsement 110/117)

Diabetes mellitus in a dog or cat is defined as subclinical if they meet the ALIVE definition of DM, without the presence of classic clinical signs compatible with DM. Differentiation of subclinical DM and stress-induced hyperglycaemia is challenging, particularly in cats.

Definition: Clinical diabetes mellitus in dogs and cats (endorsement 114/116)

Clinical diabetes mellitus in dogs and cats that meet the ALIVE

definition and criteria for diagnosing diabetes mellitus, WITH classic clinical signs compatible with DM, (e.g., polyuria, polydipsia, polyphagia, weight loss) with no other plausible cause.

Definition: Prediabetes (endorsement 110/113)

Prediabetes in human medicine is defined as hyperglycaemia below the cut-off for diabetes mellitus and/or impaired glucose tolerance. This definition may also be applicable for dogs and cats with hyperglycaemia below cut-off for DM. However, there is a lack of information/evidence on the topic e.g., validated glucose tolerance tests, to make this condition clinically relevant for dogs and cats.

Definition: Aetiologic classification of diabetes mellitus (endorsement 109/114)

Disease complex in dogs and cats as defined by the ALIVE project (Fig. 2).

1. Insulin deficient DM (beta-cell-related disorders)
    - Reduced insulin secretion
        - Beta-cell dysfunction
        - Beta-cell destruction
            1. Immune-mediated
            2. Beta-cell loss associated with exocrine pancreatic disease
                - Pancreatitis
                - Neoplasia
                - Idiopathic
            3. Toxicity (diazoxide)
            4. Infection
            5. Idiopathic
        - Beta-cell death (apoptosis)
            1. Glucotoxicity
            2. Lipotoxicity
            3. Idiopathic
        - Beta-cell aplasia/abiotrophy/hypoplasia
    - Production of defective insulin
2. Insulin resistant DM (target-organ disorders)
    - Endocrine influence
        - Growth hormone
            1. Endogenous hypersecretion
                - Pituitary origin
                - Mammary origin
            2. Exogenous GH
        - Steroids
            1. Glucocorticoids
                - Endogenous hypersecretion
                - Exogenous glucocorticoids
            2. Progesterone/ progestins
                - Luteal phase
                    - Pregnancy
                    - Diestrus (dog)
                - Exogenous progestins
            3. Other
        - Catecholamines
        - Thyroid hormone
            1. Hyperthyroidism
    - Obesity
    - Drugs
        - Thiazide diuretics
        - Beta adrenergic agonists
    - Inflammatory mediators
    - Disorders of receptor and intracellular signaling

Comments:

- An individual can concurrently have more than one underlying cause.

Fig. 2. Disease complex in dogs and cats as defined by the Agreeing Language in Veterinary Endocrinology (ALIVE) project. GH, growth hormone.

Definition: ALIVE diabetes mellitus characterisation checklists (Endorsement 109/114)

The ALIVE diabetes mellitus characterisation checklists (Tables 1 and 2) are designed to assist in classification and to alert clinicians and researchers to veterinary patient-related factors that might impact on the management of the canine or feline patient. ALIVE recommends completing the checklist at time of diagnosis. Several factors are also relevant for ongoing management, though this list does not represent a comprehensive checklist for evaluation of complicated veterinary patients.

The extent to which the items on the checklist are being evaluated will vary according to circumstances (clinical versus research scenario). The steps do not imply whether or how tests need to be carried out.

The ALIVE guidelines recognise existing challenges surrounding definitive diagnosis of several conditions listed, as well as the limited availability of C-peptide and autoantibody assays.

Definition: Diabetic ketoacidosis (DKA) (Endorsement 113/113)

Diabetic ketoacidosis is a potentially fatal metabolic complication of diabetes mellitus. Diabetic ketoacidosis consists of the biochemical triad of hyperglycaemia, ketonemia or ketonuria and metabolic acidosis.

ALIVE criteria for diagnosing DKA (Endorsement 112/112)

- Diagnosis of DM according to ALIVE criteria
- Demonstration of ketonaemia defined as increased beta-hydroxybutyrate concentration AND/OR ketonuria or ketonaemia defined as detectable ketones using nitroprusside test strips for ketonuria or ketonaemia
- Demonstration of metabolic acidosis defined as a venous/arterial blood pH < 7.35 and decreased bicarbonate.

When blood gas analysis is unavailable, a canine/ feline patient that is unwell and meeting the above remaining criteria should be suspected of suffering from DKA.

Definition: Diabetic remission (Endorsement 113/116)

A canine/ feline patient previously diagnosed with DM using ALIVE criteria, which ceases to receive exogenous insulin therapy and shows no evidence of DM according to ALIVE criteria after 4 weeks.

Table 1
Agreeing Language in Veterinary Endocrinology (ALIVE) diabetes mellitus (DM) characterisation checklist for dogs.

Date of diagnosis:			
Date of evaluation:			
	Yes	No	Unknown
Female entire			
Pregnant			
Dioestrus			
Onset of signs < 12 months of age			
History of exogenous diabetogenic drug therapy			
Overweight / obese			
Underweight			
Current Pancreatitis			
Historic Pancreatitis			
Cushing's syndrome			
Exocrine pancreatic insufficiency			
Ketoacidosis			
Ketonuria			
Ketonaemia			
Additional (unlisted above) comorbidity			
Additional research steps			
Insulin (or C-peptide) present at diagnosis			
Pancreatic autoantibody positive			

Table 2
Agreeing Language in Veterinary Endocrinology (ALIVE) diabetes mellitus (DM) characterisation checklist for cats.

Date of diagnosis:			
Date of evaluation:			
	Yes	No	Unknown
History of exogenous diabetogenic drug therapy			
Overweight / obese			
Underweight			
Hypersomatotropism + /- acromegaly			
Current Pancreatitis			
Historic Pancreatitis			
Exocrine pancreatic insufficiency			
Hyperthyroidism			
Cushing's syndrome			
Ketoacidosis			
Ketonuria			
Ketonaemia			
Additional (unlisted above) comorbidity			
Additional research steps			
Insulin (or C-peptide) present at diagnosis			
Pancreatic autoantibody positive			

Definition: Treatment goals of diabetes mellitus (Endorsement 108/113)

The ALIVE consensus recommends the following goals to be considered:

1. Good quality of life for pet and owner
2. Resolution of the classic clinical signs of diabetes mellitus
3. Avoidance of hypoglycaemia and DKA
4. Normalisation of body conditions score

The physiological mechanisms through which these aims are achieved include the following goals (Endorsement 115/116):

1. Decreasing hepatic glucose output
2. Improving insulin sensitivity
3. Ensuring appropriate insulin availability
4. Reducing post-prandial hyperglycaemia
5. Attending underlying causes or co-morbidities

The success of the therapy can be evaluated through the following assessments (Endorsement 108/112):

1. Systematic and standardised assessment of classic clinical signs of DM ideally incorporating a scoring system (see: ALIVE Diabetic Clinical Score scoring system, Table 3).
2. Assessment of glycaemic parameters in blood, interstitium and/or urine.
3. There is no prospective high level evidence that setting a specific glycaemic goal is correlated with a specific treatment outcome, including remission.
4. Glycaemic parameters within the reference interval of non-diabetic animals commonly indicates diabetic remission or insulin overdosing and therefore implies possibility of episodes of hypoglycaemia in a treated diabetic canine/ feline patient.

The ALIVE consensus emphasises the need for appreciation of the following factors (Endorsement 111/112):

- Serial glucose assessment shows substantial day to day variation.
- Fructosamine evaluation suffers from reliability problems and the use of the same validated assay in the same veterinary patient is recommended if this parameter is chosen to be used.

Table 3
Agreeing Language in Veterinary Endocrinology (ALIVE) Diabetic Clinical Score to be used for clinical assessment of diabetic veterinary patients. The range of the total score is 0–12. Treatment aim is to achieve the lowest score possible without unacceptably high risk of hypoglycaemia.

Factor	Score
Unintended Weight Loss	
0 = None, or gained since last examined	
1 = Mild (<5% loss)	
2 = Moderate (5–10% loss)	
3 = Severe (>10% loss)	
Polyuria and polydipsia	
0 = Normal	
1 = Mild (some increase noted by owner)	
2 = Moderate (increased filling of water bowl)	
3 = Severe (constantly at bowl)	
Appetite	
0 = Normal or decreased appetite (if decreased appetite exclude DKA or concurrent disease)	
1 = Mild polyphagia (finishes eagerly)	
2 = Moderate polyphagia (finishes eagerly and begs for more)	
3 = Severe polyphagia (obsessed with food)	
Attitude/activity	
0 = Normal	
1 = Mild decrease (a bit less running and jumping)	
2 = Moderate decrease (a lot less running and jumping)	
3 = Severe decrease (lying about all the time)[a]	
TOTAL SCORE	.....

DKA, Diabetic ketoacidosis. [a] Consider DKA in the ill veterinary patient with diabetes mellitus

- Negative urine glucose can indicate periods of hypoglycaemia in a treated diabetic veterinary patient.
- Co-morbidities are common and should especially be considered when there are clinical signs which are not classic clinical signs of DM.
- Specific blood glucose targets are not a goal.

Definition: Hypoglycaemia (Endorsement 113/113)

Hypoglycaemia is defined as a blood glucose measurement of less than 3.3 mmol/L (60 mg/dL). This may or may not be associated with clinical signs. Clinical signs of hypoglycaemia are diverse and can include lethargy, weakness, tremor, ataxia, collapse and seizures, among others, usually related to neuroglycopenia and/or autonomic activation.

Definition: Insulin resistance (Endorsement 110/112)

The ALIVE recommendation is to use the term 'insulin resistance' to describe the presence of varying degrees of interference of insulin action on target cells. The term is not defined by the exogenous insulin dose required or by the change of blood glucose following insulin injection. However, when there is concern over the need for a high insulin dose, the presence of insulin resistance should be considered among other potential causes.

Definition: ALIVE Diabetic Clinical Score (Endorsement 110/112)

A standardised scoring system to help describe and communicate the clinical signs of diabetes mellitus in a veterinary patient in clinical practice and research (Table 3).

Considerations

The current work represents the first successful attempt for the field of veterinary endocrinology to seek broad consensus on disease definitions. The ALIVE process proved effective in creating a body of terminology in companion animal diabetes mellitus, which met overall approval of a majority of those participating in the endorsement phase, achieving its aim. Whether it also achieves its ultimate aims, improved standards in research, education and clinics, depends on subsequent use of the agreed terminology in those areas.

Project ALIVE used a *modified* Delphi-based method. Traditional Delphi-methodology has developed over time and is frequently adapted according to investigators' specific needs. Three main facets are often associated with Delphi-based methodology (Barrett and Heale, 2020). Firstly, the methodology tends to include a series of 'rounds'; after the initial round, each time, feedback is requested to be provided to the output of the previous round, allowing output to develop over time. Secondly, participants are able to see the results of previous rounds, allowing reflection, feedback, as well as adapting their own opinion. Finally, the findings of each round are often shared with the broader group anonymously.

In project ALIVE, the first two characteristics were preserved, whereas the third, anonymity, was not maintained throughout the whole process. Anonymity helps reduce the dominance of the opinion of one person over the opinion of others ('halo-effect') or the tendency that opinions are adapted through peer pressure ('bandwagon-effect') (Barrett and Heale, 2020). Nevertheless, relinquishing strict anonymity enabled experts to directly and unimpededly exchange thoughts with each other. This led to more effective conceptulization of ideas in a positive atmosphere, especially during live online video-conferencing and face-to-face meetings. For this reason, other researchers have previously also abandoned anonymity in their modified-Delphi approaches (Boulkedid et al., 2011; Bleijlevens et al., 2016; Rioja-Lang et al., 2019). The role of the chair and sub-panel chairs was also focussed on reducing both 'halo' and 'bandwagon' effect. Additionally, a degree of anonymity was still provided through the fact that results of the first round (sub-panel sessions, step 2, Fig. 1) were presented by each sub-panel chair to the entire group as one single sub-panel opinion (step 3, Fig. 1). This enabled initial thought development in the smaller sub-panel group, as well as ensured it not being known to the wider group whose opinion led to which part of the definition set. The same level of anonymity applied to the presentation of the ESVE-panel draft definitions to the SCE-panel (step 5, Fig. 1). Moreover, step 7 of the ALIVE methodology, seeking endorsement and feedback from members of both endocrinology societies, was completely anonymous. This latter step was also aimed at creating truly global general consensus definitions, as well as stimulate endorsement and usage of the created definitions by peers.

The current set-up purposely involved representatives from diverse areas of the field (academia, private referral practice, private general practitioner), as well as diverse areas of the world. This proved particularly useful, since it ensured generated definitions could also be applied under diverse circumstances (e.g. diverse economic and cultural landscapes). The endorsement by the two largest veterinary endocrinology societies' memberships (ESVE and SCE) added real value to the generated definitions and will hopefully also encourage the subsequent use of the new terminology by the same memberships. Although only a subpopulation of the membership chose to respond to the survey, despite several call-outs, the minimal requirement of 20% was met. Not all respondents provided an answer to all endorsement questions, leading to a varying number of total respondents per proposed definition. It remains uncertain why respondents chose not to answer. It could be considered to make answering all questions mandatory in future and/ or to increase possibilities of open text feedback. A higher percentage participation would have added to the quality of the process and the certainty that the endorsement is actually carried by the entire membership. Nevertheless, higher participation rates in such survey are likely difficult to attain among a group of busy professionals, given the required time to go through the various definitions in detail. Given that endorsement levels of the individual definitions were all particularly high (>94%), it is expected that this endorsement would also reflect the opinion of the wider membership if more had responded to the survey call-out. In the literature, Delphi study methodology shows a varied interpretation of

what is meant by 'consensus'; arbitrary cut-offs are decided upon by study initiators themselves and often range from 51% to 100% (Keeney et al., 2006). In addition, the identification of an objective level consensus is easier when gathering quantifiable data, rather than qualitative concepts like the definitions in this project. The authors of this study therefore decided arbitrarily on the use of 75% of panel agreement, a simple majority for the survey stage, as well as 20% participation of membership in this survey. Finally, members could choose between the two options 'I endorse this definition' or 'I absolutely cannot endorse this definition'; the stronger wording of the latter option (instead of the more neutral 'I do not endorse this definition') was purposely chosen in order to stimulate agreement. Given the fact that this wording could have influenced the results, consideration will be given towards a more neutral wording for future cycles.

This publication represents agreed definitions from the original ALIVE cycle. It was not possible to amend any definitions during the manuscript review process. Nevertheless, the results of the ALIVE process should not be regarded as perfect, definitive, final or permanent. In fact, this first cycle represents a starting point which aims to stimulate discussion, as well as a pathway towards better definition setting in the future. The process already contains a feedback mechanism in its original design. Several potential improvements to the process and definitions have been highlighted by reviewers. These considerations for improved agreed language will be automatically forwarded for consideration by the panel of the next cycles. This will include for instance inclusion of definitions of ketosis without acidosis and hyperglycaemic crisis, as well as further clarifications around the expected day-to-day variability of glucose, reliability of glucose measurement, specific diabetogenic drugs, the exact meaning or appropriateness of the term 'subclinical diabetes mellitus' and the importance of avoiding hypoglycaemia. As a further improvement to the process, ESVE has now also set up a dedicated email address to facilitate with ongoing cataloguing topics for consideration during the next ALIVE cycles from all readers of this report (ALIVE@ESVE.org). All readers are encouraged to use this communication channel to help improve the agreed language depicted in this manuscript and to use only the latest versions of the definitions displayed on the continuously updated website[2].

Finally, given the positive experience using the ALIVE system to create consensus definitions within veterinary endocrinology using the specified modified Delphi-method, other professional societies are encouraged to consider using a similar system to achieve a consensus language in their respective fields. This would be envisioned to have a greatly positive impact in veterinary medicine at large. A common language would foster the common goal of improved animal welfare.

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