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Definition of low birth weight in domestic mammals: a scoping review

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Review Article

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Abstract

In people and animals, low birth weight (LBW) is recognized as highly predictive of health trajectory from the neonatal period to elderly ages. Regarding the neonatal period, although LBW is recognized as a major risk factor for neonatal mortality, there does not appear to be a clear definition of ‘when a birth weight should be considered low’ in all species. The aim of this work was to use the scientific literature available to map the various thresholds proposed to define LBW in domestic mammals. Using a standardized methodology, a scoping review was conducted through a literature search in three different bibliographic databases. After a two-step screening of 1729 abstracts and full-text publications by two independent reviewers, eleven studies met the inclusion criteria. Selected publications represented six mammalian species (rat, mouse, dog, pig, cow, and rabbit). Birth weight thresholds were identified through six different methods. In addition to the scarcity of scientific literature about the definition of LBW, this scoping review revealed the lack of standardization for the description, evaluation or the pertinence these definitions. Because the health consequences of LBW could be preventable, providing early identification of at-risk neonates, a consensus for the standardized definition of LBW is required.

Introduction

Birth weight is one variable of intrauterine life with a theoretical optimum for each mammalian species (Scales *et al.*, 1986; Wilcox, 2001; Gardner *et al.*, 2007). In the case of preterm birth and/or restricted intrauterine growth (WHO, 2004; Cutland *et al.*, 2017), birth weight can be pathologically lowered with lifelong health implications. First, the most obvious impact of low birth weight (LBW) is its strong deleterious effect on short-term survival, as demonstrated in many species (Wilcox and Russell, 1983; Wu *et al.*, 2006). Human LBW newborns have a 10 times greater risk of neonatal death compared with heavier babies (McIntire *et al.*, 1999). In domestic mammals, neonatal mortality rates are also increased when birth weight is low (Wu *et al.*, 2006; Fix, 2010; Mugnier *et al.*, 2019b), with economic consequences for breeders and major impact on animal welfare. Later in life, LBW has been demonstrated to be associated with a range of health outcomes (Reyes and Manalich, 2005; Risnes *et al.*, 2011), including impaired growth (Quiniou *et al.*, 2002; Panzardi *et al.*, 2013), metabolic syndrome (Barker, 1998) and being overweight (Ravelli *et al.*, 1976; Gondret *et al.*, 2006; Mugnier *et al.*, 2020b).

The major short- and long-term impacts of LBW make its early and accurate identification important for appropriate monitoring and care. For human beings, a variety of definitions for LBW have been and are still being used with reference to a raw value (birth weight under 2.5 kg) or by comparison to a reference population at country, continent or species level (under 10th percentile or themean – 2 standard deviations) (Malin *et al.*, 2014). Since 1976, human LBW has been defined officially by the World Health Organization as a weight at birth of less than 2500 g (WHO, 2004; Hughes *et al.*, 2017). Guidelines could then be developed by experts (Vayssière *et al.*, 2015; World Health Organization, 2017) to provide special care to LBW newborns identified through this consensus definition.

There have been numerous studies on LBW individuals among domestic mammals. Nevertheless, it is unclear whether there has been any consensus for the definition for LBW for domestic animals. The aim of this scoping review was to inventory existing literature in order to provide a definition for LBW in non-human mammals based on their absolute birth weight.

Methods

Study design

A scoping review was conducted in a systematic and transparent process following five stages detailed in the methodological framework proposed by Arksey and O'Malley (2005): (1)

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formulation of the research question, (2) identification of relevant studies, (3) selection of eligible studies, (4) charting of the data, and (5) collation and synthesis of the results.

Search strategy

Our research question was stated as ‘what are the methods used to define LBW using absolute birth weight in non-human mammals?’. A literature search algorithm was developed to capture relevant studies in three online databases (PubMed, Web of Science, and CAB abstracts). The search terms were identified by the authors (AG, CS, SC and AM) and combined into a Boolean query (defin* OR recogn* OR identif* OR cut-off? OR threshold? OR cutoff?) AND (‘low birth weight’ OR lbw OR iugr OR ‘birth weight’ OR birthweight) AND (pupp* OR piglet OR calf OR calves OR kitten? OR cub? OR foal? OR monkey? OR mice? OR rats OR ‘guinea pig’ OR offspring?) that was searched in the titles and abstracts of the articles. Further details on the formulation of this search equation in each of the databases are available in the Supplementary Appendix. The final literature search was performed on 8 April 2022. No gray literature sources were searched.

Selection of sources of evidence

After duplicate removal, a two-step screening was carried out independently by two reviewers (AM and AG) to select the final list of publications to be included in the review. In the first screening round, titles and abstracts were examined for their effective pertinence. Publications were selected if they were: (1) research articles or conference abstracts; (2) written in English; (3) focused on non-human mammals; and (4) describing a method to characterize LBW. A conservative approach was adopted for this step: all the publications selected by at least one of the reviewers were kept for the second round. During the second step of the screening, based on their full-text content, publications were included if they met the previously described inclusion criteria and if at least one birth weight threshold was provided. Any disagreement between the two reviewers was resolved by consensus. Additionally, snowball sampling was used to identify any article that was not identified by the algorithm but was cited in the references of the selected articles.

Data extraction and analysis

For each paper selected, key features were recorded by the first author using an Excel® (Microsoft Corporation, Redmond, WA) data-charting form developed in English. Key features included publication information (year, authors, journal, country, number of citations estimated through Google Scholar in April 2022, and keywords), population descriptors (species, breed, and size) and components about threshold definition methodology (statistical method and choice of outcome).

Results

Selection of sources of evidence and general characteristics

Searches in the three selected databases with the identified search terms returned 2478 references. After the removal of duplicates, 1729 papers were included in the screening rounds (Fig. 1). After the first screening, 133 articles were retained and their full

texts analyzed in the second screening, from which 15 were identified as relevant. One additional paper was identified by checking the references of the publications included. Finally, a total of 16 papers were included in the scoping review.

General characteristics of the papers included

The 16 articles selected were published between 1983 and 2022 (three of them before 2015) and eight countries were represented (France ($n=4$), Belgium, United Kingdom, Italy and United States ($n=2$, each), Brazil, Iraq, Ireland, and the Netherlands ($n=1$, each)). Only one paper was the result of an international collaboration. The number of contributing authors per paper ranged from 1 to 11 (median = 8). Eleven studies were the result of collaborative research including several teams, 7 of which were based on public/private partnerships. The most cited paper counted 305 citations. The others were cited in 0 to 54 papers (median = 11.5). The 16 studies were published in 11 different journals (Table 1). Their keywords are represented as a word cloud (Fig. 2). Among the 16 publications included, 8 focused on piglets (Baxter *et al.*, 2008; Magnabosco *et al.*, 2016; Calderón Díaz *et al.*, 2017; Feldpausch *et al.*, 2019; Zeng *et al.*, 2019; Gourley *et al.*, 2020; Van Tichelen *et al.*, 2021a, 2021b), 6 on puppies (Mila *et al.*, 2015; Mugnier *et al.*, 2019a, 2019b, 2020a; Fusi *et al.*, 2020; Schrank *et al.*, 2020) and 1 on calves (Dabdoub, 2005), with sample sizes ranging from 135 to 19,168 neonates (median = 1016). The remaining paper (Wootton *et al.*, 1983) was based on 347 litters from 5 different polytocous species (rat, mouse, dog, pig, and rabbit). Most studies were conducted on one or more commercial facilities ($n=14$) and one in an experimental unit. This information was not provided in one study. Analyses were conducted at the species-level ($n=1$; Wootton *et al.*, 1983), by groups of similar adult size ($n=1$; Mila *et al.*, 2015), at breed-level ($n=11$), by gender within one breed ($n=1$; Dabdoub, 2005) or at litter-level ($n=2$).

Low birth weight definitions

The main characteristics of the method used to define birth weight threshold are summarized in Table 2. In 12 of the 16 studies selected, the weight threshold defining LBW was a raw value based on the relationship between birth weight and a statistical increase of the risk of mortality. Mortality was evaluated over different periods: between birth and weaning in 5 papers (Dabdoub, 2005; Baxter *et al.*, 2008; Feldpausch *et al.*, 2019; Zeng *et al.*, 2019; Gourley *et al.*, 2020), between birth and three weeks in four papers (Mila *et al.*, 2015; Mugnier *et al.*, 2019a, 2019b, 2020a), during the first 24 h of life in Fusi *et al.* (2020 in dog), and over the entire production cycle in Calderón Díaz *et al.* (2017 in swine). For the remaining paper (Magnabosco *et al.*, 2016), mortality was evaluated over three different periods: 0–24 h, 0–20 days and 0–70 days. For one paper, LBW was defined as the tail-end of a normal distribution (Wootton *et al.*, 1983). Finally, in the last three papers considered, the threshold was defined on the basis of the deviation from the mean birth weight for the breed (Schrank *et al.*, 2020) or for the litter (Van Tichelen *et al.*, 2021a, 2021b).

Methods based on the relationship between birth weight and mortality can be grouped into two distinct categories: the arbitrary selection of a birth weight threshold at a given percentile value and the calculation of a raw value without preconceived idea using classification techniques and mortality as outcome.

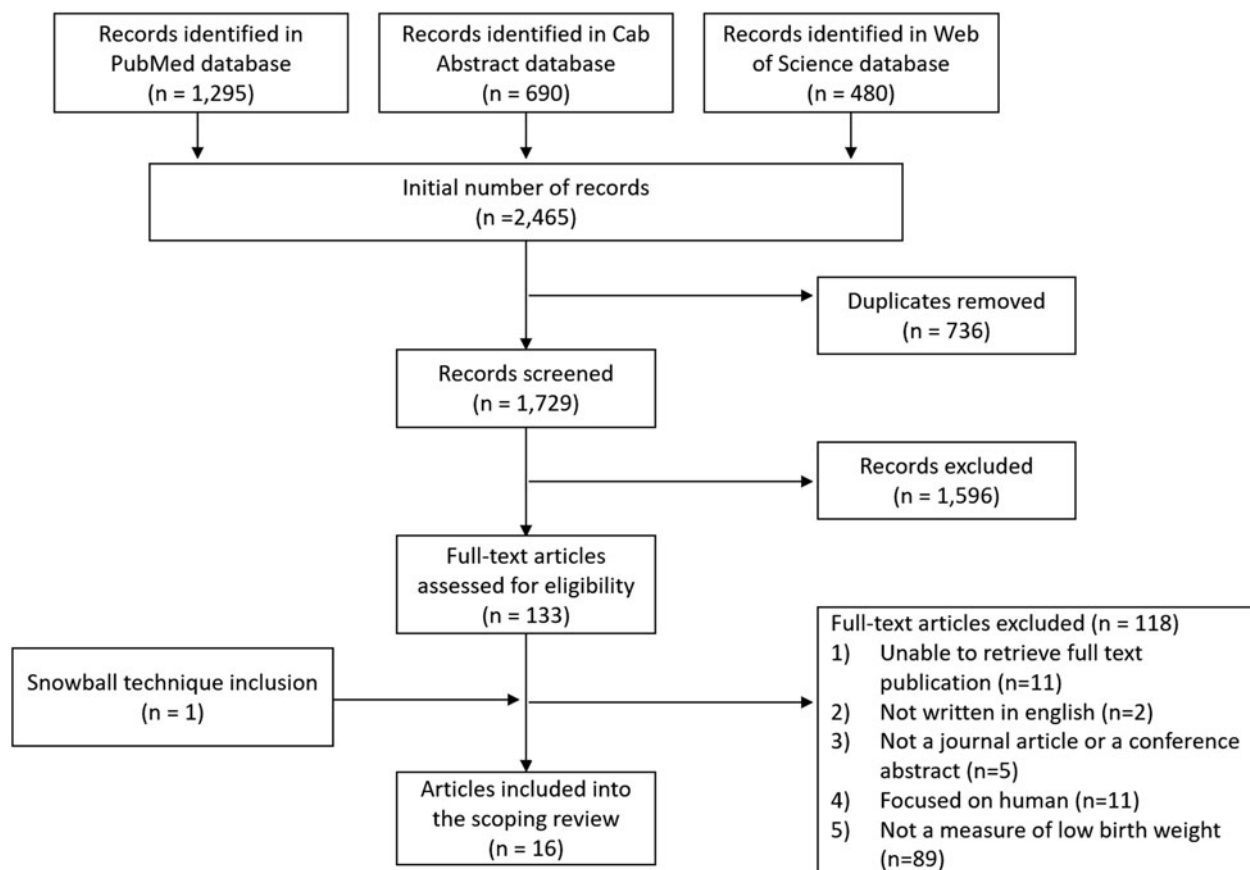


Fig. 1. Flow chart of the selection process.

Three studies used the first quartile value to define LBW (Baxter *et al.*, 2008; Mila *et al.*, 2015; Gourley *et al.*, 2020), with two of them providing an explicit statistical comparison of mortality rates between the quartiles (Mila *et al.*, 2015; Gourley *et al.*, 2020). Three other papers used segmented regression to define the birth weight threshold as a break-point in the relationship between mortality rate and birth weight (Calderón Díaz *et al.*, 2017; Feldpausch *et al.*, 2019; Zeng *et al.*, 2019). The method used by Zeng *et al.* (2019) and Calderón Díaz *et al.* (2017) was based on the maximum likelihood test giving a *P*-value evaluating the significance of the difference between the slopes of the two regression lines. Among different models defined by a breakpoint at each possible birth weight value, Feldpausch *et al.* (2019) chose the best model through the minimization of the Akaike information criterion. Finally, four studies used the birth weight as an indicator to discriminate between dying and surviving newborns using mortality rate as the reference (Dabdoub, 2005; Magnabosco *et al.*, 2016; Mugnier *et al.*, 2019a, 2019b, 2020a; Fusi *et al.*, 2020). Cut-off values were selected based on the maximization of the kappa statistic in Fusi *et al.* (2020), on the maximization of Youden's *J* statistic ($J = Se + Sp - 1$) alone in Magnabosco *et al.* (2016) or with a condition on specificity in Mugnier *et al.* (2019a), on the maximization of efficiency (number of correctly classified/all neonates evaluated) in Dabdoub (2005). For three of these studies, the authors reported the performance of the selected threshold through sensitivity and specificity (ranging from 0.75 to 1 and 0.04 to 0.68, respectively) using mortality status as outcome.

Apart from the 3 papers having chosen the first quartile value as a threshold, the proportion of newborns ultimately categorized as LBW was reported in 7 of the 13 remaining papers (Wootton *et al.*, 1983; Magnabosco *et al.*, 2016; Feldpausch *et al.*, 2019; Mugnier *et al.*, 2019a, 2019b, 2020a; Schrank *et al.*, 2020) and varied from 5% in puppies (Mugnier *et al.*, 2019a) to 24% for mice (Wootton *et al.*, 1983). In the 12 studies based on the relationship with the risk of mortality to define the birth weight cut-off, mortality rates among LBW neonates were explicitly compared with those of higher birth weight in 8 papers, with a 2–9-fold increase in risk (Table 2).

Discussion

As LBW has short- and long-term consequences on health, early identification of affected newborns is recommended for appropriate management. Except for large mammals, birth weight assessment is an easy-to-implement parameter in the field, requiring a simple and inexpensive instrument (a scale). The results are immediately available and do not require invasive manipulation. It is crucial to define the thresholds for comparison to birth weights. The objective of this scoping review was to explore LBW definitions available for non-human mammals in the scientific literature. Apart from LBW, small newborns are identified through a variety of terms, such as small for gestational age or intra-uterine growth restricted (IUGR). These three locutions cover three overlapping but separate concepts without any international consensus about their precise definition (Wilcox, 2001; Ego, 2013; Cutland *et al.*, 2017). The present scoping review

Table 1. Publication information and population description for the eleven selected papers

Reference	Year	Journal ^{1a}	Country	Collab ^{2b}	No of citations ^{3c}	No of authors	Species	Sample size	Origin of the data	Level of analysis
Baxter <i>et al.</i> (2008)	2008	Theriogenology	United Kingdom	Y	305	9	Swine	135	Experimental unit	Breed
Calderón Díaz <i>et al.</i> (2017)	2017	Prev. Vet. Med.	Ireland	Y (PP)	43	9	Swine	1016	Commercial farm	Breed
Dabdoub (2005)	2005	Iraqi J. Vet. Sci.	Iraq	N	1	1	Calf	540	Commercial farm	Gender
Feldpausch <i>et al.</i> (2019)	2019	Transl. Anim. Sci.	United States	Y (PP)	49	11	Swine	4068	Commercial farm	Breed
Fusi <i>et al.</i> (2020)	2020	Acta Vet. Scand.	Italy	N	2	4	Dog	176	Commercial farm	Breed
Gourley <i>et al.</i> (2020)	2020	J. Anim. Sci.	United States	N	8	7	Swine	19,168	Commercial farm	Breed
Magnabosco <i>et al.</i> (2016)	2015	Acta Sci. Vet.	Brazil	Y	25	5	Swine	1495	Commercial farm	Breed
Mila <i>et al.</i> (2015)	2015	J. Anim. Sci.	France	Y (PP)	54	4	Dog	532	Commercial farm	Group of similar adult size
Mugnier <i>et al.</i> (2019b)	2019	Prev. Vet. Med.	France	Y (PP)	15	11	Dog	6694	Commercial farm	Breed
Mugnier <i>et al.</i> (2019a)	2019	SVEPM Proceedings	France	Y (PP)	0	11	Dog	6694	Commercial farm	Breed
Mugnier <i>et al.</i> (2020a)	2020	BMC Vet. Res.	France	Y (PP)	0	9	Dog	4971	Commercial farm	Breed
Schrank <i>et al.</i> (2020)	2019	Animals	Italy	N	6	4	Dog	213	Commercial farm	Breed
Van Tichelen <i>et al.</i> (2021a)	2021	Animals	Belgium	Y	1	9	Swine	76	Commercial farm	Litter
Van Tichelen <i>et al.</i> (2021b)	2022	Animals	Belgium	Y	0	9	Swine	188	Commercial farm	Litter
Wootton <i>et al.</i> (1983)	1983	J. Reprod. Fert.	United Kingdom	N	47	4	Multispecies	347 litters	-	Species
Zeng <i>et al.</i> (2019)	2019	J. Anim. Sci.	The Netherlands + United States	Y (PP)	18	7	Swine	7654	Commercial farm	Breed

^aPrev. Vet. Med.: Preventive Veterinary Medicine; Iraqi J. Vet. Sci.: Iraqi Journal of Veterinary Sciences; Transl. Anim. Sci.: Translational Animal Science; Acta Vet. Scand. J. Anim. Sci.: Journal of Animal Science; Acta Sci. Vet.: Acta Scientiae Veterinaria; SVEPM Proceedings: Proceedings of the Annual meeting of the Society for Veterinary Epidemiology and Preventive Medicine; BMC Vet. Res.: BMC Veterinary Research; J. Reprod. Fert.: Journal of Reproduction and Fertility.

^bCollab: collaboration; Y: yes; Y (PP): yes with a private-public collaboration; N: No.

^cNumbers of citations were estimated through Google Scholar in April 2022.

Table 2. Method applied to define low birth weight

Reference	Species	Global method	Outcome	Threshold definition method	Proportion of LBW	Mortality rate in LBW	Mortality rate in non-LBW
Baxter <i>et al.</i> (2008)	Swine	Raw value	Pre-weaning mortality	First quartile	25%	24%	5%
Calderón Díaz <i>et al.</i> (2017)	Swine	Raw value	Mortality over the entire production cycle	Segmented regression	NS	72%	13%
Dabdoub (2005)	Calf	Raw value	Pre-weaning mortality	Discrimination method	NS	NS	NS
Feldpausch <i>et al.</i> (2019)	Swine	Raw value	Pre-weaning mortality	Segmented regression	15%	34%	8%
Fusi <i>et al.</i> (2020)	Dog	Raw value	Mortality 0–24 h	Discrimination method	NS	NS	NS
Gourley <i>et al.</i> (2020)	Swine	Raw value	Pre-weaning mortality	First quartile	25%	38%	21%
Magnabosco <i>et al.</i> (2016)	Swine	Raw value	Mortality 0–24 h, 0–20 days and 0–70 days	Discrimination method	13%	NS	NS
Mila <i>et al.</i> (2015)	Dog	Raw value	Mortality 0–21 days	First quartile	25%	24%	3%
Mugnier <i>et al.</i> (2019a)	Dog	Raw value	Mortality 0–21 days	Discrimination method	5%	61%	7%
Mugnier <i>et al.</i> (2019b)	Dog	Raw value	Mortality 0–21 days	Discrimination method	48%	NS	NS
Mugnier <i>et al.</i> (2020a, 2020b) ^a	Dog	Raw value	Mortality 0–21 days	Discrimination method	48–3%	9–55%	4%
Schrank <i>et al.</i> (2020)	Dog	Deviation from the mean	NR	Mean – 1 SD	14%	NR	NR
Van Tichelen <i>et al.</i> (2021a)	Swine	Deviation from the mean	NR	Mean – 1 SD	NS	NR	NR
Van Tichelen <i>et al.</i> (2021b)	Swine	Deviation from the mean	NR	Mean – 1 SD	NS	NR	NR
Wootton <i>et al.</i> (1983)	Multispecies	Tail-end of a normal distribution	NR	NR	9–24% ^b	NR	NR
Zeng <i>et al.</i> (2019)	Swine	Raw value	Pre-weaning mortality	Segmented regression	NS	44%	NS

LBW, low birth weight; NS, not specified; NR, not relevant; SD, standard deviation.

^aTwo groups of LBW were defined (LBW and VLBW).

^bProportion of newborns classified as LBW: 9, 13, 16, 21 and 24% for rabbits, rats, dogs, pigs and mice, respectively.

(Baxter *et al.*, 2008; Mila *et al.*, 2015; Gourley *et al.*, 2020), or through a calculation based on ROC curves (in 5 articles: Magnabosco *et al.*, 2016; Mugnier *et al.*, 2019a, 2019b, 2020a; Fusi *et al.*, 2020). The ability of birth weight to discriminate newborns at birth according to their outcome (died vs surviving at the end of the neonatal period) was estimated to be correct based on the areas under the ROC curves obtained in these papers (from 0.69 to 0.98). Although ROC curve analysis is a powerful tool commonly used to measure classifier accuracy in binary-class questions (Hajian-Tilaki, 2013), this method is controversial, with unbalanced datasets such as those dealing with neonatal mortality (around 10% dead newborns compared to 90% newborns still alive at the end of the neonatal period; puppies: Chastant-Maillard *et al.*, 2017; piglets: Koketsu *et al.*, 2021; calves: Del Río *et al.*, 2007). In such situations, it is suspected to provide an optimistic view of the discriminating ability of the model by ignoring the minority class and Precision-Recall or cost curves could be more appropriate (Haibo and Garcia, 2009). Another method for the determination of an optimal cut-off for LBW definition among the articles selected was segmented regression (Calderón Díaz *et al.*, 2017; Feldpausch *et al.*, 2019; Zeng *et al.*, 2019). Zeng *et al.* (2019) described the differences between slopes and the associated p-values to validate their threshold. For the two other articles, the significance of the threshold was evaluated through the comparison of mortality (or survival) rates in categories below and above this cut-off. A validated, consensus standardized process to determine thresholds would allow comparison of the different thresholds obtained in the literature for similar populations (within species, breed, etc). Articles should provide not only elements regarding the statistical significance of the model (such as the comparison of slopes) but also information regarding biological significance (such as the statistical comparison of mortality rates between the groups above and below the threshold). Authors should also detail the proportion of the population qualified as LBW. Regarding the latter, the threshold defined must be of high sensitivity, to allow the detection of the larger proportion of the at-risk newborns, and with a high Positive Predictive Value so that newborns detected with LBW benefit from the care provided.

This review focused on the identification of LBW based on individual absolute birth weight. Other approaches could characterize a newborn by its birth weight expressed as a percentage of its mother's weight. In the specific case of a polytocous species, litter size, heterogeneity of the birth weight within the litter, and weight comparison between individuals and their littermates may play a role in defining LBW. Moreover, not only the birth weight, but also other dimensions of newborns can be considered for characterization of fetal growth and identification of intrauterine growth-retarded individuals, analogous to human newborn chest or arm circumference (Goto, 2011) or piglet crown-rump length and head shape (Chevaux *et al.*, 2010; Hales *et al.*, 2013). These methods could provide complementary information to birth weight and help to differentiate between constitutionally small LBW and LBW consequential to intrauterine growth restriction.

Conclusions and recommendations

Despite LBW being recognized as linked with a range of health outcomes, its definition is not standardized and even lacking in many breeds including in some species of domestic mammals. The arbitrary birth weight thresholds described in the literature tend to be replaced by calculated thresholds, but the variability of the outcome considered (e.g. mortality, quality of growth, or

being overweight) and that of the statistical method implemented from one study to another highlights the need to standardize methods for defining LBW. Work is needed to develop an international consensus for each mammal species (e.g. using the Delphi method, promoting the participation of people who are geographically distant). The process should involve all categories of stakeholders in the sector (veterinarians, breeders, researchers, etc.) and should take into account the breeding objectives of the species under consideration.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S146625232200007X>.

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