

# Little association between birth weight and health of preweaned dairy calves

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## Introduction

Preweaned dairy calf morbidity and mortality remains high. A UK study found 3.6 per cent mortality between 24 hours and 28 days, and 3.6 per cent between one and six months old.<sup>1</sup> Preweaning mortality ranged from 7.8 to 10.8 per cent in the USA.<sup>2</sup> Neonatal calf diarrhoea (NCD) and bovine respiratory disease (BRD) are predominant diseases<sup>3</sup> and, excepting stillbirth, the most common cause of mortality.<sup>4</sup> Heifer rearing is a significant investment and disease reduces efficiency. The cost of rearing each heifer to calving has been found to be €1567<sup>5</sup> and £1819.<sup>6</sup> For a 100 cowherd, the annual rearing cost was US\$32,344.<sup>7</sup> Understanding factors which contribute to calthood disease is desirable for welfare and economic reasons as well as environmentally sustainable and efficient food production. Birth weight (BW) is directed by genotype, but modified by gestation length (GL)<sup>8-9</sup> and uterine environment (UE).<sup>10-12</sup> Intrauterine growth retardation (IUGR), where foetal development is modified by a suboptimal UE, is common among livestock<sup>10</sup> and causes much variation in BW.<sup>10-13</sup> IUGR is mediated by nutrient limitation or alteration of placental size or function.<sup>10-12-14</sup> Causes include dam undernutrition,<sup>10-12-14-15</sup> overnutrition<sup>14-16</sup> and nutrient partitioning from gestation towards lactation in high-yielding cows or growth in immature heifers.<sup>10-12-17</sup> Negative energy balance and body condition score of the dam are associated with IUGR,<sup>11-12</sup> as are disease and thermal stress.<sup>10-15</sup> Resource sharing between fetuses in multiple pregnancies results in IUGR.<sup>10</sup>

IUGR affects organogenesis and immunity as well as overall fetal growth.<sup>18-21</sup> Consequences are dependent on retardation severity and on the stage of gestation at which it occurs.<sup>15</sup> Growth patterns of IUGR fetuses are therefore variable and dependent on the nature and timing of insults to which they are subjected.

Neonates which have been subjected to IUGR are at risk of various pathologies both in the short term and long term. Documented consequences during the early postnatal period in livestock and humans include dysfunction of nervous, cardiovascular, digestive and endocrine organs; metabolic and hormonal abnormalities; immunodeficiency; and increased morbidity and mortality.<sup>10-15-22</sup>

The conceptus may also adapt to a suboptimal UE through epigenetic modifications known as 'foetal programming', leading to permanent physiological changes with long-term consequences.<sup>10</sup>

Few studies have examined IUGR and 'foetal programming' in dairy cattle.<sup>12-14</sup> In light of the potential effects of IUGR on BW and health, this study aimed to investigate if there is an association between BW of dairy calves, and preweaning morbidity and mortality.

## Materials and methods

### Data collection

A convenience sample of Holstein and Holstein-Friesian calves on three farms in South-West England was recruited. Farms were chosen because of their locality to the veterinary practice and their willingness to participate in the study. [Table 1](#) shows details of herds and husbandry.

Calves were eligible for recruitment if they were sired by a Holstein bull and were from singleton pregnancies. Calves were weighed by farm staff within 24 hours of birth using a calf weigh crate (Farms A and C; to the nearest kilogram) or by placement of the calf in a bucket suspended from digital weigh scales (Farm B; to the nearest 100 g). Farmers recorded BW, sex and birth date. Farms were visited weekly by the first author

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	Farm A	Farm B	Farm C
Herd size	490 cows	150 cows	285 cows
Breed	Holstein	Holstein-Friesian	Holstein-Swedish Red
Calving pattern	All year	Predominantly summer and autumn	Predominantly autumn
Colostrum provision	All calves receive 4 litres via oesophageal tube.	Natural suckling, supplemented with oesophageal tube as deemed necessary	All calves receive 4 litres via oesophageal tube.
Calving accommodation	Individual calving pens	Group calving straw yard	Individual calving pens
Calf accommodation	Housed and kept in groups of five animals from one day of age until weaning. Female and male calves kept in different sheds.	Housed in group pens of five animals until 10–14 days old, then housed in large group straw yards of 15–20 animals until weaning.	Individual calf hutches outside until three weeks of age. Group hutches outside thereafter until weaning.
Feeding	Twice daily 15% milk replacer fed up to a maximum of 6 litres of liquid per day. Ad libitum concentrate.	Twice daily whole milk up to 4 l/day until 10–14 days old; thereafter 15% milk replacer fed by automatic feeder up to a maximum of 6 litres of liquid per day. Ad libitum concentrate containing 100 mg/kg decoquinat.	Twice daily 15% milk replacer fed up to a maximum of 6 litres of liquid per day. Ad libitum concentrate containing 100 mg/kg decoquinat.
Preventive treatments or vaccination	Heifer calves: halofuginone lactate (Halocur, MSD Animal Health, UK) and Intranasal PI3 and RSV vaccine (Risposal RS+PI3 Intranasal, Zoetis, UK)	Vaccination of all late-gestation cows with combined rotavirus, coronavirus and <i>Escherichia coli</i> K99 vaccine (Rotavec Corona, MSD Animal Health)	All calves: halofuginone lactate (Halocur, MSD Animal Health)
Period of calf recruitment	June 6, 2014 to May 3, 2015	July 6, 2014 to January 31, 2015	September 17, 2014 to May 1, 2015

or, rarely, another veterinarian. At each visit, calves born since the previous visit were blood sampled into anticoagulant-free blood tubes. Samples clotted at ambient temperature, and serum was decanted and centrifuged at 890 g for 10 minutes. Serum total protein (STP) was estimated with a temperature-compensating optical refractometer, in line with normal practice protocols for managing herd health. Blood sampling was performed with approval from the Royal College of Veterinary Surgeons Ethics Committee.

At each visit all preweaned calves were assessed (table 2) for BRD using the California Calf Health Score (CalCHS)<sup>23</sup> and the Wisconsin Calf Health Score (WisCHS),<sup>4</sup> and for NCD using a Faeces Score (FS).<sup>4</sup> Farmers kept written records of treatments for BRD or NCD. The visiting veterinarian notified farmers of any calves showing overt signs of BRD (specifically calves with two or more of the following: fever, dyspnoea or spontaneous coughing) or calves with an FS of at least 2. These overt clinical signs were chosen in order to emulate diagnosis based on diagnostic criteria commonly used by farm personnel, so as not to bias treatment data. Repeat diagnoses by health scoring or repeat treatments for the same disease were counted as a new incident if they were at least seven days after the previous diagnosis or treatment. Dam parity was obtained from milk records and GL was calculated using farm records of service dates.

### Data exploration

Data consisted of independent baseline variables and longitudinal, dependent health-outcome variables. Continuous baseline variables were BW, GL and STP. Categorical baseline variables were SEX, SEASON (of birth) and FARM. Few older cows were present in the data set, so PARITY (of the dam) was treated as an ordinal variable (1, 2, 3 or 4+). Longitudinal dependent variables were organised by week of life (WOL), with the aim of allocating one health score to each calf for

each WOL. If a calf had greater than one health score for any WOL, the earlier of the two scores was deleted from the data set. Therefore, for each WOL, each calf had data consisting of a positive or negative status for the following health outcomes: WisCHS, CalCHS, FS, farmer diagnosis of BRD (fBRD) and farmer diagnosis of NCD (fNCD).

Missing data within variables were quantified and explained in terms of their relationship with other variables. Data were considered missing at random (MAR) if missingness was associated with observed variables; missing completely at random (MCAR) if missingness was not associated with any variables; missing not at random if missingness was associated with unobserved (missing) variables.<sup>24</sup> Intermittent missingness within longitudinal data were instances where a health outcome was missing for a particular WOL and a health outcome was present in the data set in a subsequent WOL for that calf. Monotone missingness (due to dropout) was missing health outcome data where all health outcome data were missing in subsequent WOLs for that calf.

### Statistical analysis

Multiple imputation<sup>25</sup> followed by generalised estimating equations (MI-GEE analysis)<sup>26</sup> was used for analysis. Data were stored and processed in Access and Excel. Statistical analysis was performed in R V.3.4.1.<sup>27</sup>

Sample size calculations were performed retrospectively using G\*Power,<sup>28</sup> based on the ability to detect a difference in probability of a positive diagnosis of disease of 0.1 (from 0.3 to 0.4) at 1 sd from the mean BW.

### Multiple imputation

Baseline and longitudinal variables were imputed using the R package Amelia II.<sup>29</sup> Longitudinal (health outcome) data were imputed for all calves up to and including WOL 10. Prevalence of disease was expected

**Table 2** Description of calf health scoring systems: Wisconsin Calf Health Score,<sup>4</sup> California Calf Health Score<sup>23</sup> and Faeces Score<sup>4</sup>

Wisconsin Calf Health Score (WisCHS) and California Calf Health Score (CalCHS)			
Category	Observation	Score assigned	
		Wisconsin Calf Health Score*	California Calf Health Score†
Nasal discharge	Normal serous discharge	0	0
	Small amount of unilateral cloudy discharge	1	4
	Bilateral, cloudy or excessive mucus discharge	2	4
	Copious bilateral mucopurulent discharge	3	4
Ocular discharge	Normal	0	0
	Small amount of ocular discharge	1	2
	Moderate amount of bilateral discharge	2	2
	Heavy ocular discharge	3	2
Rectal temperature °F (°C)	<100.9 (<38.3)	0	0
	101.0–101.9 (38.3–38.8)	1	0
	102.0–102.4 (38.9–39.1)	2	0
	102.5–102.9 (39.2–39.4)	2	2
	≥103.0 (≥39.5)	3	2
Ears and head	Normal	0	0
	Ear flick or head shake	1	0
	Slight unilateral droop	2	5
	Head tilt or bilateral droop	3	5
Cough‡	None	0	0
	Single induced	1	0
	Repeated induced	2	0
	Occasional spontaneous	2	2
	Repeated spontaneous	3	2
Respiration§	Normal		0
	Abnormal		2
Faeces Score			
Category	Observation	Score assigned	
Faeces¶	Normal	0	
	Semiformed, pasty	1	
	Loose, but stays on top of bedding	2	
	Watery, sifts through bedding	3	

\*The Wisconsin Calf Health Score is the sum of the scores for rectal temperature, cough and nasal discharge, plus the score for ocular discharge or ears and head, whichever is greater. A positive score (ie, a diagnosis of bovine respiratory disease (BRD)) is a score greater or equal to 5 when at least two individual categories have a score of at least 2. [http://www.vetmed.wisc.edu/dms/fapm/fapmtools/8calf/calf\\_health\\_scoring\\_chart.pdf](http://www.vetmed.wisc.edu/dms/fapm/fapmtools/8calf/calf_health_scoring_chart.pdf).

†The California Calf Health Score is the sum of the scores for each category. A positive score (ie, a diagnosis of BRD) is a score greater or equal to 5.<sup>23</sup>

‡For the Wisconsin and California Calf Health Scores, coughing is induced by gently pinching the trachea.

§The Wisconsin Calf Health Score does not include assessment of respiration.

¶A Faeces Score of greater or equal to 2 is considered abnormal.

to vary with WOL. For example, NCD incidence was likely higher during the first two weeks of life than during subsequent WOLs. Incorporation of the second-order polynomial of time into the imputation process allowed disease prevalence to vary with calf age, and also allowed the pattern of change of disease prevalence over time to vary between farms. Thirty data sets were imputed.

Validity of MI was assessed by visual comparison of the distribution of observed and imputed data.

### Generalised estimating equations

Correlation was expected between health outcomes during different WOLs for any given calf. GEEs with a logit link were constructed using the R package Zelig,<sup>30</sup> using Rubin's rule for combination of multiply imputed data sets. Calf identification indicated clusters. Models were constructed for each dependent variable: WisCHS, CalCHS, FS, fBRD and fNCD. Covariance structure

was chosen by comparing the quasilielihood under the independence model criterion (QIC) for initial models created using differing covariance structures. Exchangeable covariance structures were used for the WisCHS, CalCHS and fNCD models, while autoregressive covariance structures were used for the FS and fBRD models. Initial models were created using all independent variables including WOL, plus quadratic and cubic transformations of BW, to allow for non-linear associations between BW and dependent variables. Backwards model selection was performed according to the change in QIC, until the most parsimonious model was found. Variables were investigated for confounding and retained if their removal resulted in greater than 30 per cent change in coefficients of variables with  $P < 0.05$ . Plausible two-way interactions between each permutation of covariate pairs were tested by introducing them to the models, and interactions were retained if  $P < 0.05$ .

### Analysis of calf mortality

A second, non-imputed data set was constructed including only calves that were not sold. The same predictor variables were used, and the binary dependent variable MORTALITY was defined as death or euthanasia prior to weaning. One multivariable logistic regression model for MORTALITY was constructed using the second data set. Significance was assessed using the Z-value. Variables with  $P < 0.25$  in univariable analysis were included in initial models.<sup>31</sup> FARM and BIRTH WEIGHT were forced into models, to examine the association of BIRTH WEIGHT with the dependent variable and to account for clustering within farms. Covariates were eliminated in a backwards stepwise fashion until only terms with  $P < 0.05$ , plus BIRTH WEIGHT and FARM, remained. As above, variables were investigated for confounding and retained if their removal resulted in greater than 30 per cent change in coefficients of variables with  $P < 0.05$ . Quadratic and cubic transformations of BIRTH WEIGHT were offered to the model to allow for non-linear associations.

All two-way interactions were added in turn to the model and were retained if biologically plausible and if  $P < 0.05$ . Goodness of fit was assessed using the Hosmer-Lemeshow goodness of fit test, following comparison of number of covariate patterns with number of subjects. Predictive ability of the model was assessed with receiver operating characteristic analysis. Plots of delta deviance, delta Pearson chi-square and delta-beta were examined. The model was rebuilt following

removal of influential data points and the new model was accepted if outliers were considered to be unduly influencing the conclusions drawn.

## Results

### Descriptive statistics

A total of 476 calves were recruited during the study period. The median interval between consecutive health scores for any calf was seven days and the percentage of intervals that were less than or equal to nine days was 93. The median number of health scores per calf was 4 for males and 10 for females, due to a greater number of male calves dying, being sold or euthanased. Age at weaning was variable (median 76.0 days, minimum 33.0 days, maximum 110.0 days). **Table 3** describes the distribution of variables prior to MI.

**Table 4** describes disease incidence on the three farms during the study period.

A total sample size of 290 was required to detect a difference in probability of a positive diagnosis of BRD of 0.1 at 1 sd from the mean BW.

### Missing data

The proportion of missing data for each variable prior to MI is described in **figure 1**. Missingness within the longitudinal health outcome variables increased as WOL increased due to monotone dropout. For the baseline variables, missingness was greatest within the GL variable, at 29.2 per cent. Data were subject to missingness within all but the following variables:

	Farm A	Farm B	Farm C	Total
Number of calves	341	55	80	476
Sex				
Male	175	20	39	234
Female	166	35	41	242
Birth weight (kg)				
Median	42.0	42.1	39.0	42.0
IQR	38.0–46.0	38.0–44.5	37.0–42.0	38.0–45.0
Minimum	26.0	32.3	29.0	26.0
Maximum	62.0	49.7	51.0	62.0
Serum total protein (g/dl)				
Median	5.2	5.8	5.6	5.4
IQR	4.8–5.6	5.2–6.7	5.2–6.2	4.9–5.8
Minimum	3.1	4.0	3.7	3.1
Season of birth (number of calves)				
Maximum	7.2	8.4	7.8	8.4
Spring	72	0	20	92
Summer	69	7	1	77
Autumn	105	34	30	169
Winter	95	14	29	138
Parity of dam (number of calves)				
1	115	7	27	149
2	86	27	12	125
3	63	8	15	86
≥4	65	13	24	102
Percentage of calves with FPT*	49	26	23	42

\*FPT, failure of passive transfer, defined by serum total protein less than 5.2 g/dl.

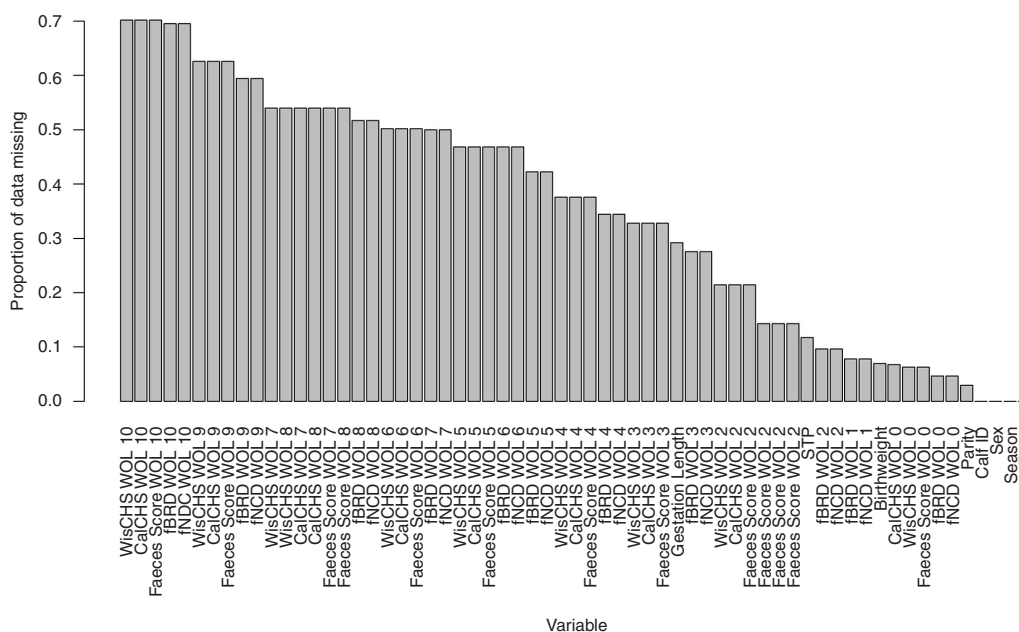
**Table 4** Percentage of calves with at least one disease incident, overall disease incidence and fate of calves along with detailed information on each of the three farms

	Farm A	Farm B	Farm C	Total
Number of Calf Health Scores*	2032	357	438	2827
Percentage of calves receiving at least one positive Wisconsin Calf Health Score†	74.9	64.9	33.9	67.4
Percentage of calves receiving at least one positive California Calf Health Score†	69.1	51.4	37.1	62.3
Percentage of calves receiving at least one positive Faeces Score†	53.6	51.4	46.8	52.3
Percentage of calves receiving at least one treatment for bovine respiratory disease (BRD)‡	58.8	40.5	9.7	49.2
Percentage of calves receiving at least one treatment for neonatal calf diarrhoea (NCD)‡	12.4	21.6	1.6	11.5
Disease incidence (cases/calf/week)§				
Positive Wisconsin Score	0.3	0.1	0.07	0.2
Positive California Score	0.2	0.1	0.1	0.2
Positive Faecal Score	0.1	0.07	0.06	0.09
BRD treatment	0.1	0.05	0.01	0.09
NCD treatment	0.02	0.02	0.00	0.02
Mortality (%)	14.4	5.4	1.6	11.5
Euthanased (%)	3.0	3.0	0.0	3.0
Sold prior to weaning (%)	37.0	0.0	44.0	35.0
Weaned (%)	45.6	91.6	54.4	50.5

\*Number of health scores in the data set for each farm and overall.  
 †Percentage of calves (on each farm and overall) receiving at least one positive Wisconsin Calf Health Score, California Calf Health Score or Faeces Score prior to exit from the study through sale, death, euthanasia or weaning. A positive Wisconsin Calf Health Score or positive California Calf Health Score represents a diagnosis of bovine respiratory disease (BRD). A positive Faeces Score represents a diagnosis of neonatal calf diarrhoea (NCD).  
 ‡Percentage of calves (on each farm and overall), which received at least one treatment for BRD or NCD.  
 §Incidence of disease according to Calf Health Scores and farm records of disease treatment. Incidence was calculated by dividing the total number of disease or treatment incidents by the number of calf-weeks. Positive Calf Health Scores or disease treatments were counted as disease incidents if there had been no previous diagnosis of the same disease in the same calf within seven days.

SEX, FARM and SEASON. Reasons for missingness were errors in collecting or recording data (intermittent missingness) and dropout of calves prior to weaning due to death, euthanasia or sale (monotone missingness). Intermittent missingness was mainly considered to be MCAR as failure to collect or record data was due to human error and was not conceivably influenced by any of the observed data. However, in the case of the GL variable, missingness was observed predominantly in calves from primiparous dams on Farm A. This was due to the use of natural service in heifers, which precluded the recording of service dates and thus calculation of GL. Thus missing GL data were considered to be MAR.

BW was missing for several calves born during winter months, and this was due to a reluctance by farmers to weigh calves over the Christmas period. Missingness in the BW variable was therefore considered to be MAR. Most missingness within the STP variable was in calves born during autumn. This was due to some blood samples being lost during a short period in Autumn 2014. STP missingness was therefore MAR. Monotone missingness of the health outcome data due to dropout was MAR as missingness may have been dependent on observed data (eg, mortality of calves associated with low STP), but was not conceivably dependent on missing data. Among calves with missing health outcome data,



**Figure 1** Proportion of subjects in the data set for which data were missing in each variable. CalCHS, California Calf Health Score; fBRD, farmer diagnosis of BRD; fNCD, farmer diagnosis of NCD; STP, serum total protein; WisCHS, Wisconsin Calf Health Score; WOL, week of life (WOL 0=0–7 days of age, WOL 1=8–14 days of age, etc).

males were over-represented, especially on Farm A, reflecting the sale of male calves prior to weaning. Table 5 describes the distribution of variables for calves with complete data and calves with data missing within individual variables.

### Multiple imputation

Uneventful convergence of imputation algorithms was confirmed by the Amelia II package. Visual examination of plots of non-imputed and imputed data confirmed that distributions of imputed data were within the lower and upper limits of values for non-imputed data. Time-series cross-sectional plots confirmed that prevalence of disease varied with WOL in imputed data.

### Generalised estimating equations

A significant association between BW and the dependent variable was found in only the FS model. In this model, there was a significant interaction between BW and Farm such that increasing BW was associated with an increase in the odds of a positive FS on Farm A only (OR 1.03, 95% CI 1.0005 to 1.05,  $P=0.046$ ). BW was not associated with any other health outcomes. Increasing STP was associated with lower odds of a positive CalCHS (OR 0.82, 95% CI 0.72 to 0.93,  $P=0.002$ ) and there was a trend towards an association between STP and odds of a positive WisCHS (OR 0.87, 95% CI 0.76 to 1.00,  $P=0.05$ ). STP was not associated with odds of any other outcomes. Calves born during spring had higher odds of fBRD (OR 1.51, 95% CI 1.07 to 2.14,  $P=0.02$ ) compared with calves born during other seasons. There was also a trend towards an association between Season of birth and odds of a positive WisCHS, with calves at higher risk during winter and spring (OR 1.25, 95% CI 0.98 to 1.58,  $P=0.07$ ). GL and parity were not associated with any of the outcomes. Calves on Farm A had higher odds of disease than calves on Farms B and C in all three BRD models (WisCHS, CalCHS and fBRD). Sex was associated with the outcome in several models. For two of the BRD models, male calves had significantly higher odds of disease on all farms (WisCHS OR 1.46, 95% CI 1.21 to 1.75,  $P=0.00007$ ; fBRD OR 1.35, 95% CI 1.06 to 1.72,  $P=0.02$ ). A significant interaction emerged between Sex and Farm in the CalCHS, FS and fNCD models such that male calves had higher odds of these disease outcomes on Farm A only. WOL was often associated with odds of disease outcomes (data not shown). For example, odds of a positive WisCHS or CalCHS showed a quadratic association with WOL, with highest odds in WOL 3 for WisCHS and fBRD, and in WOL 5 for CalCHS. For FS and fNCD, odds of a positive diagnosis were highest in WOL 1, thereafter declining in subsequent weeks. Prevalence of disease in different WOLs is shown in figure 2. No significant interactions were found between WOL and any other variable.

### Analysis of mortality

In order to preserve sample size, calves with missing GL were retained in the data set and the GL variable was not included in any models. Following deletion from the data set of calves with missing data in the remaining baseline variables, 390 calves remained. Following deletion of calves that were sold, 244 remained. Of all covariates in the model, STP alone was associated with odds of mortality (OR 0.39, 95% CI 0.158 to 0.940,  $P=0.036$ ). No significant interactions between covariates were found.

### Discussion

In this study, BW was rarely associated with any health outcomes. In the GEE models, BW was associated only with odds of a positive FS on one farm. Type 1 error may explain this single association. However, lack of association in GEE models between BW and FS on the other two farms or between BW and health outcomes in all other models is surprising in light of evidence that IUGR may result in organ dysfunction.<sup>10</sup> It is possible that IUGR is associated with increased risk of disease in later life, as in humans.<sup>32</sup> Calves in this study were only observed until weaning. Dystocical calves are more likely to suffer morbidity<sup>33 34</sup> and mortality<sup>33-35</sup> subsequent to the perinatal period. Perhaps prevalence of dystocia was highest on Farm A due to greater BW or to some other unmeasured factor. This could explain the association of higher BW with increased odds of positive FS on this farm. However, the linear association in this model suggests medium BW calves on Farm A had higher odds of diarrhoea than low BW calves. This is unlikely to be due to dystocia as predominantly calves with high BWs would be expected to have experienced calving difficulty. Calves on all three farms were not fed according to size, as all calves in any age group were fed the same, so smaller calves were possibly on a comparatively high plane of nutrition, resulting in increased resilience to disease. Farmers were not blinded to BW so husbandry of smaller calves may have been improved consciously or subconsciously on Farm A only.

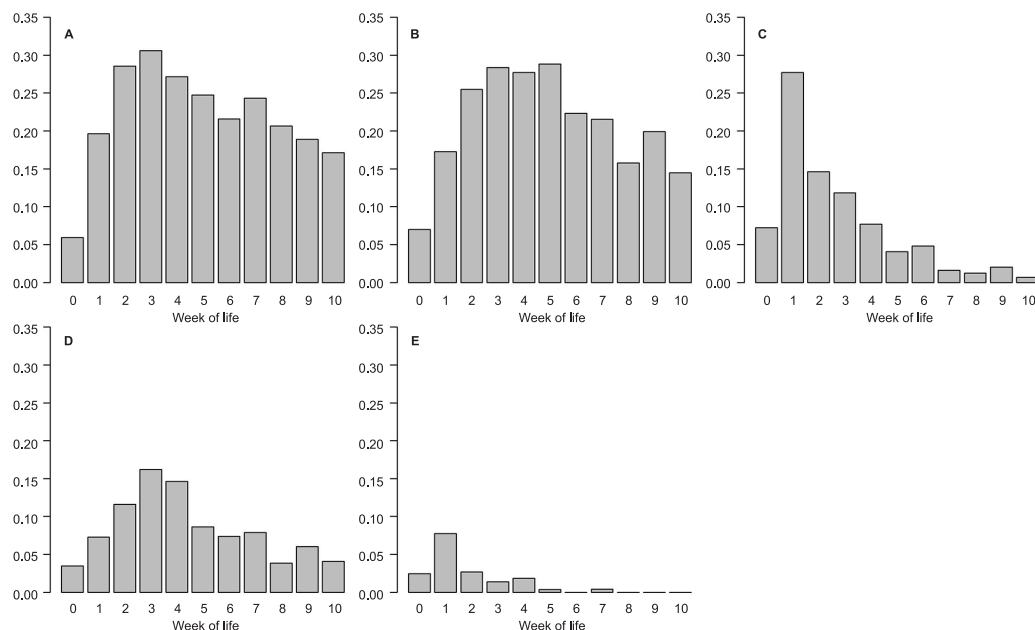
The findings of this study contrast with previous work which has found associations between low BW and disease or mortality. Windeyer and others<sup>36</sup> found low BW heifer calves have higher odds of NCD. Although least squares mean (LSM) BW (38 kg) was slightly lower than mean female BW in the current study, BW distribution was not described. A study by Corah and others<sup>37</sup> found low BW beef calves from nutrient-restricted dams had higher NCD incidence. Again, BW distribution was not described, but LSM BW of the lightest category was 26.7 kg, only slightly greater than the lowest BW in the current study. It is difficult to draw BW comparisons due to the differing genetics of calves across studies, but perhaps those two studies<sup>36 37</sup>

**Table 5** Distribution of variables for calves with no missing data or missing data in each of the covariates

Variable with missingness										
	None (complete data)	BW	STP	Gestation length	Parity category	WisCHS	CalCHS	Faeces Score	IBRD	INCD
Median BW (IQR)	42.4 (39.0–46.0)		42.0 (38.1–44.9)	38 (36–43)	44.0 (43.0–48.0)	42.0 (38.0–45.1)	42 (38.0–45.1)	42 (38–45.1)	42 (38–46)	42 (38–46)
Median STP (IQR)	5.3 (4.9–5.8)	5.4 (5.1–5.8)		5.1 (4.7–5.6)	NA	5.2 (4.9–5.8)	5.2 (4.9–5.8)	5.2 (4.9–5.8)	5.2 (4.8–5.7)	5.2 (4.8–5.7)
SEX (number of calves)										
Male	139	17	29	68	9	227	227	227	217	217
Female	144	16	27	71	5	169	169	169	116	116
SEASON (number of calves)										
Spring	55	2	2	36	1	80	80	80	72	72
Summer	64	2	0	11	0	63	63	63	57	57
Autumn	98	3	41	42	8	144	144	144	115	115
Winter	66	26	13	50	5	109	109	109	89	89
Median GL (IQR)	280 (277–283)	283 (276.5–285.5)	278 (275.8–282.0)		NA	280 (277–283)	280 (277–283)	280 (277–283)	280 (277–283)	280 (277–283)
Parity category (number of calves)										
1	25	1	13	116		123	123	123	106	106
2	98	6	16	5		103	103	103	84	84
3	74	3	7	2		75	75	75	63	63
4+	86	9	6	2		81	81	81	66	66
Farm										
A	181	26	29	136	12	281	281	281	249	249
B	39	0	16	0	0	46	46	46	23	23
C	63	7	11	3	2	69	69	69	61	61

NA: missingness affecting two variables simultaneously (eg, all calves with missing parity category data also had missing gestation length data).

BW, birth weight; CalCHS, California, Calf Health Score; IBRD, farmer diagnosis of IBRD; INCD, farmer diagnosis of INCD; GL, gestation length; NA, missingness affecting two variables simultaneously (eg, all calves with missing parity category data also had missing gestation length data); STP, serum total protein; WisCHS, Wisconsin Calf Health Score.



**Figure 2** Proportion of preweaned calves diagnosed by different methods with disease in each week of life. (A) Wisconsin Calf Health Score, (B) California Calf Health Score, (C) Faeces Score, (D) farmer-recorded bovine respiratory disease (BRD), (E) farmer-recorded neonatal calf diarrhoea (NCD).

included calves of lower BW and more subjected to IUGR than those in the current study.

Other researchers<sup>38</sup> found both low and high BW Holstein calves on two Californian farms succumbed to NCD sooner than medium BW calves during winter. BW ranged from 29 to 68 kg (mean 41.5 kg), similar to the current study, but with greater range of BW. The authors speculated that small calves experienced thermal stress during winter, and large calves suffered dystocia, causing earlier NCD onset. Minimum Californian winter temperatures were unlikely to be substantially lower than South-West England, and the smallest calves in the study were larger than the smallest calves in the current study. Calves in the present study were born during all seasons, and no significant interactions between season and BW were found. Perhaps if time to onset of NCD had been measured in the current study an association would have been found with low BW.

Varying associations have been found between BW and mortality of calves over 48 hours old. McCorquodale and others<sup>39</sup> found low BW Holstein heifer calves (under 39 kg) were more likely to die before 90–120 days of age. Another large-scale study by Moore and others<sup>40</sup> of Holstein bull calves found that low BW (under 48 kg) was associated with increased mortality prior to three weeks old.<sup>40</sup> Henderson and others<sup>41</sup> found that both low (under 37 kg) and high (over 42 kg) BW female Holstein calves were more likely to die prior to first calving.

Henderson and others included calves with lower BW (minimum 22 kg) than the current study. If the present study had included calves with such low BW, an association between BW and mortality may have been evident. However, the definitions of low BW made by McCorquodale and others and Moore and others were high compared with the current study, and yet in those studies lower BW was associated with mortality. Calves

in the present study were only observed until weaning, while Henderson and others studied animals until first calving (and most mortalities occurred after weaning) and McCorquodale and others followed animals until 90–120 days old. It would appear that on the whole previous studies have found an association between low BW and poor outcomes for calves, in contrast to the present study. Again, perhaps BW is associated less with disease incidence in the preweaned period than in later life.

GL is an important confounder in that it is associated with BW and may be associated with increased risk of neonatal disease, for example, through reduced intestinal absorption of immunoglobulins immediately following birth.<sup>42</sup> It is conceivable that some IUGR calves in this study had BWs closer to the mean due to GLs that were greater than average. As GL was not included as a predictor in the mortality model, a tendency to find no association between BW and mortality may have resulted. However, the study by Corah and others<sup>37</sup> found that induction of IUGR through feed restriction of late-gestation cows led to reduced calf BW and reduced GL, which does not support such speculation. In the studies<sup>36 38–41</sup> discussed above which found an association between BW and disease or mortality, GL of dams was not described, so it may be that the data sets included premature calves which were of low BW and more susceptible to disease. Future studies on the subject of IUGR would benefit from the measurement of GL.

The aim of this study was to investigate the association of BW, and indirectly of IUGR, with disease incidence. One factor, not measured in this study, which influences BW through mechanisms other than IUGR is genetics.<sup>13 43</sup> The inclusion of some measure of genetic effect on BW in the regression models, for example, sire identity or percentage



Holstein genotype of the dam, may have improved the statistical modelling.

## Conclusions

This paper suggests that low BW, and thus IUGR, is not associated with susceptibility to respiratory or enteric infections in dairy calves during the preweaning period.

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