

Embryo-fetal development study in rabbits under AAALAC-compliant cage environment -historical control data comparison-

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Objective

Rabbits are typically used in non-rodent embryo-fetal development studies. As the AAALAC-compliant cages used in this study have a floor area approximately twice that of conventional cages (W650 mm × D570 mm), we investigated the effects of cage size on maternal and fetal parameters.

Materials and Methods

Strain: Kbl: NZW
Mated animals: 20 animals (Test 1)
22 animals (Test 2)
Pregnant animals: 17 animals (Test 1)
21 animals (Test 2)
Mating method: natural mating
(mating confirmed = GD 0)
Administration period: GD 6 to 19 (once daily for 14 days)
Administration route: oral gavage
(test article: drinking water)
Caesarean section day: GD 28
Examination items: clinical signs, body weight, food consumption, cesarean section, sex ratio, external examinations, weight of fetuses, visceral examinations, skeletal examinations (Includes degree of ossification)

Result and Conclusion

Result:

Food consumption in the dams was comparable to the historical control data. Because the dams had lower body weights on gestation day (GD) 0, their weights remained near the lower limit of the historical control range throughout the gestation period. Fetal body weights were also slightly lower, corresponding to maternal weight. However, other parameters, including fetal visceral and skeletal examinations, were comparable to the historical control data.

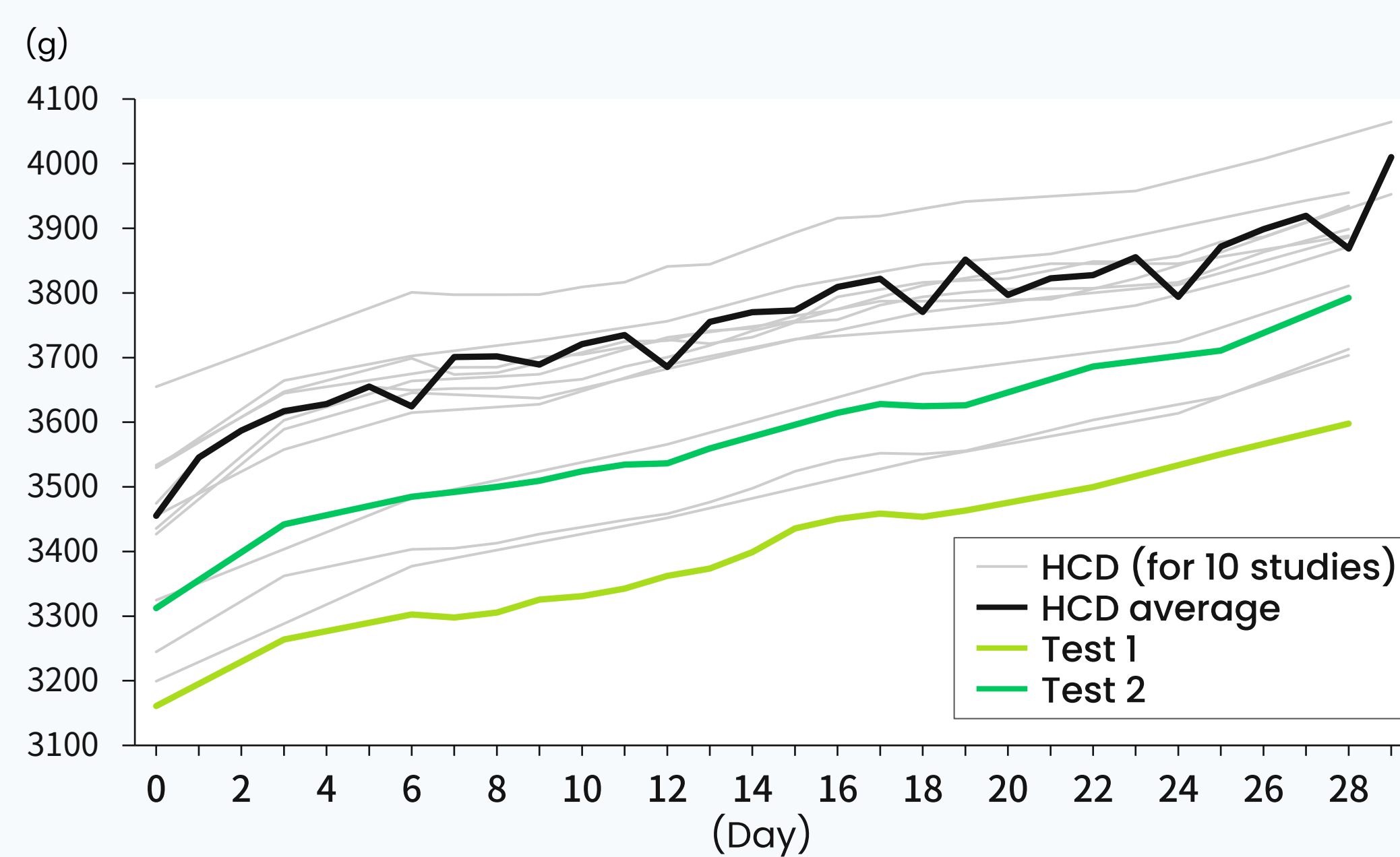
Conclusion:

Differences in cage size had no effect on maternal food consumption, weight gain, or key parameters of embryo-fetal development. Therefore, the larger cage size did not significantly affect the study outcomes.

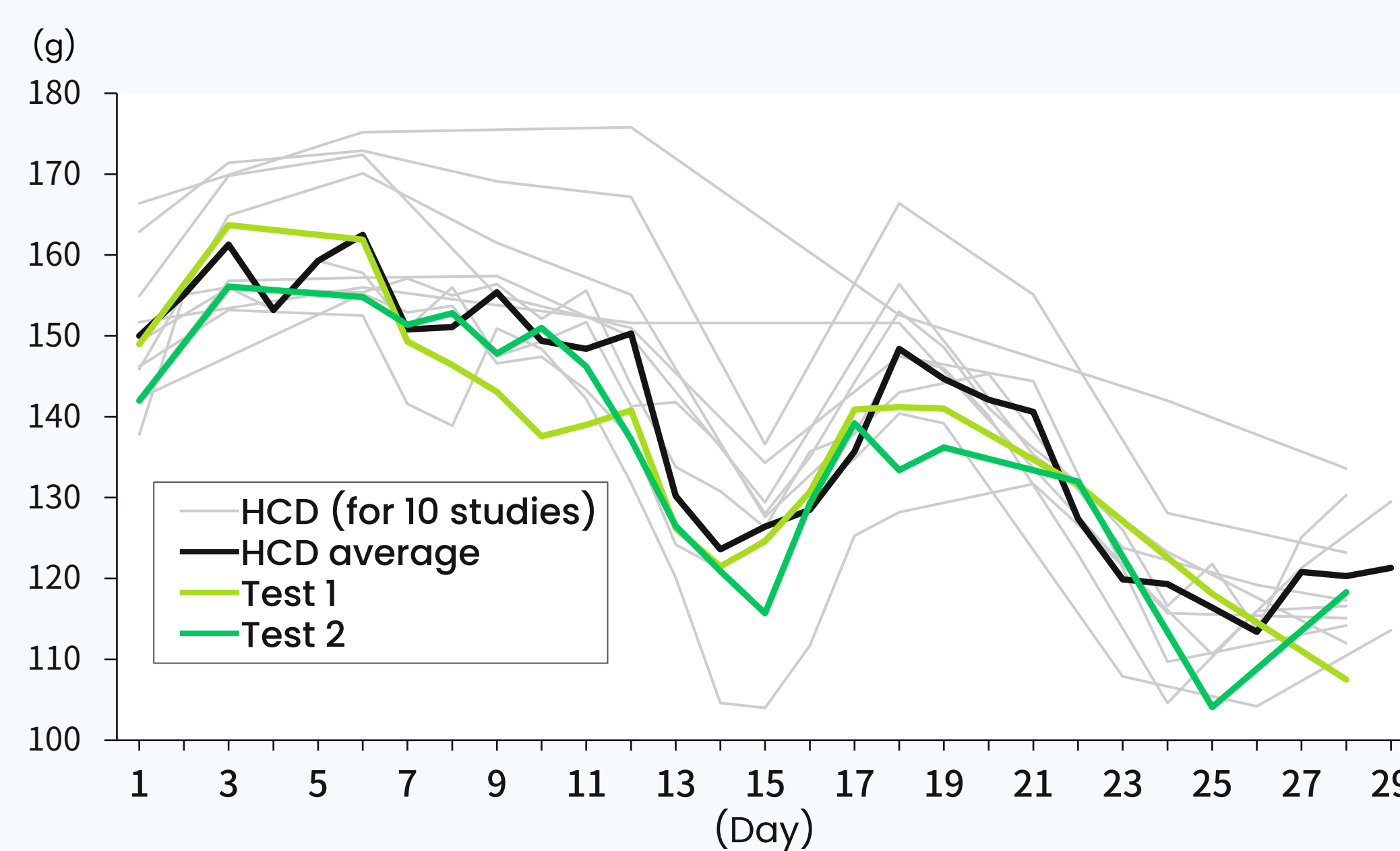
These findings support the continued use of previously established historical control data, even after changes in cage size.

Results

Body Weight



Food Consumption



Cesarean Section Examinations

	Test 1	Test 2	HCD 1	HCD 2	HCD 3	HCD 4	HCD 5	HCD 6	HCD 7	HCD 8	HCD 9	HCD 10
No. of dams	17	19	19	19	20	21	22	16	18	19	18	16
No. of corpora lutea	158 (9.3±1.6)	167 (8.8±1.5)	157 (8.26±1.48)	187 (9.84±1.54)	189 (9.45±1.23)	198 (9.43±2.46)	196 (8.91±1.57)	148 (9.25±1.73)	147 (7.68±1.53)	146 (7.72±1.71)	139 (7.72±1.71)	144 (9.00±2.00)
No. of implantations	146 (8.6±1.9)	137 (7.2±2.5)	150 (7.89±1.79)	176 (9.30±1.73)	184 (9.20±1.24)	182 (8.67±2.78)	178 (8.09±2.02)	136 (8.50±2.37)	137 (7.61±2.40)	124 (6.53±2.74)	124 (6.89±1.84)	136.0 (8.50±2.19)
No. of pre-implantation loss	12 (7.2±9.9)	30 (18.8±24.9)	7 (4.46)	6 (6.06±8.49)	5 (2.65)	16 (9.61)	18 (9.46)	12 (8.94)	10 (8.33±11.88)	22 (18.30)	15 (10.74)	8 (5.81)
No. of total dead fetuses	9 (5.6±12.5)	7 (5.1±9.3)	6 (4.00)	12 (6.57±7.63)	12 (7.07)	14 (10.63)	9 (5.21)	4 (2.50)	15 (10.48±14.73)	22 (16.09)	19 (9.09)	19 (9.09)
Early resorptions	8 (5.1±2.5)	3 (2.4±5.9)	3 (2.00)	5 (2.59±4.52)	5 (2.72)	10 (8.81)	2 (1.25)	2 (1.25)	3 (5.11±11.56)	18 (13.22)	11 (7.27)	11 (7.27)
Late resorptions	1 (0.5±2.2)	4 (2.7±6.5)	3 (2.00)	3 (3.46±6.27)	4 (4.35)	4 (1.82)	3 (1.37)	2 (1.25)	9 (5.37±11.38)	5 (3.43)	4 (2.88)	2 (1.52)
Dead fetuses	0	0	1 (0.53±2.29)	0	0	0	0	0	0	0	0	0
No. of live fetuses	137 (8.1±2.0)	130 (6.8±2.6)	144 (7.56±1.80)	164 (8.83±1.61)	171 (8.55±1.47)	168 (8.03±2.66)	169 (7.68±1.94)	132 (8.25±2.29)	122 (6.78±2.32)	116 (6.11±2.94)	102 (5.67±2.35)	123 (7.69±2.55)
Sex ratio of live fetuses	48.7±21.5 (67/70)	52.7±24.4 (61/69)	0.95 (70/74)	1.00 (82/82)	1.14 (91/80)	1.20 (92/76)	1.50 (84/55)	1.10 (57/75)	1.45 (64/58)	1.03 (58/58)	0.7 (58/44)	0.7 (50/73)
Body weight of fetuses	♂ ^a 33.15±2.50 (32.50±3.24)	34.60±5.19 (31.96±4.80)	35.61±4.16 (34.47±4.39)	39.61±3.63 (39.25±3.04)	34.17±2.55 (32.08±3.42)	33.251±4.671 (32.521±3.433)	35.369±4.332 (34.059±4.234)	35.466±3.988 (33.398±5.219)	41.731±4.776 (40.820±5.310)	36.163±4.210 (35.366±4.062)	35.602±3.535 (35.137±3.100)	33.930±4.434 (33.207±3.116)
Placental weight of fetuses	♀ ^a 3.16±0.43 (3.07±0.47)	3.33±0.69 (2.92±0.67)	3.35±0.94 (3.10±0.80)	3.10±0.44 (2.83±0.61)	3.10±0.44 (2.83±0.61)	3.286±0.627 (3.141±0.613)	-	-	3.697±0.642 (3.236±0.583)	3.663±0.688 (3.585±0.747)	-	-

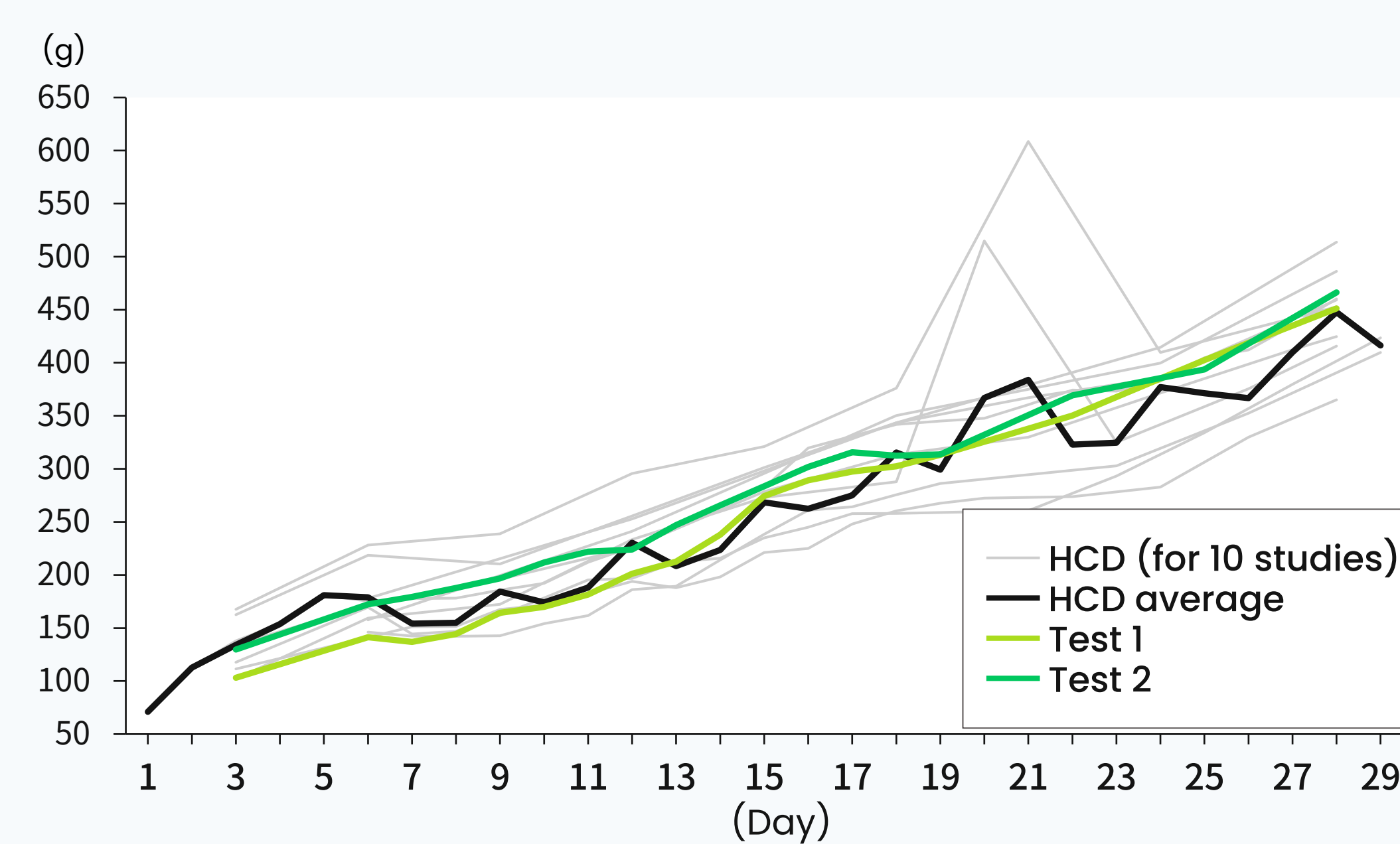
Fetal Skeletal Examinations (Malformation)

	Test 1	Test 2	HCD 1	HCD 2	HCD 3	HCD 4	HCD 5	HCD 6	HCD 7	HCD 8	HCD 9	HCD 10
No. of dams	17	19	19	19	20	21	22	16	18	19	18	16
No. of fetuses examined	137	130	144	164	171	168	169	132	122	116	102	123
No. of fetuses with skeletal malformation	4 (2.7)	1 (0.5)	4 (2.78)	12 (7.19)	8 (4.68)	6 (3.07)	4 (2.08)	4 (3.13)	0 (6.90)	2 (2.04)	1 (1.18)	3 (4.79)
Bifurcation of the rib	0	0	0 (0.69)	0	0	0	0	0	0	0	0	0
Fusion of the rib	0	0	0	0	0	0	0	0	0	0	0	0
Fusion of the sternbra	3 (1.8)	0	1 (0.69)	10 (6.13)	0	0	3 (1.58)	0	0	0	0	0
Supernumerary thoracic arch	0	0	1 (0.69)	0	0	0	0	0	0	0	0	0
Fused rib	0	0	0	0	0	1 (0.45)	0	0	2 (1.25)	1 (1.11)	0	0
Fused sternbra	0	0	0	0	4 (2.34)	2 (1.01)	0	0	4 (3.01)	0	1 (1.18)	2 (2.71)
Fused thoracic centrum	0	0	0	0	0	0	0	0	2 (1.25)	1 (1.11)	0	0
Absent thoracic arch	0	0	0	0	0	0	0	0	1 (0.56)	0	0	0
Rib, Knobby	0	0	2 (1.39)	2 (1.06±3.20)	4 (2.34)	4 (2.06)	0	2 (1.56)	0	0	0	0
Caudal centrum, Fused	0	0	0	0	0	0	0	0	1 (0.69)	0	0	0
Caudal centrum, Misaligned	0	0	0	0	0	0	0	0	1 (0.69)	0	0	0
Lumbar arch, Absent	0	0	0	0	0	0	0	0	0	0	0	0
Lumbar arch, Supernumerary	0	0	0	0	0	0	1 (0.51)	0	0	0	0	0
Lumbar centrum, Fused	0	0	0	0	0	0	0	0	1 (0.56)	0	0	0
Misshapen hyoid	1 (0.8)	1 (0.5)	0	0	0	0	0	0	0	0	0	0

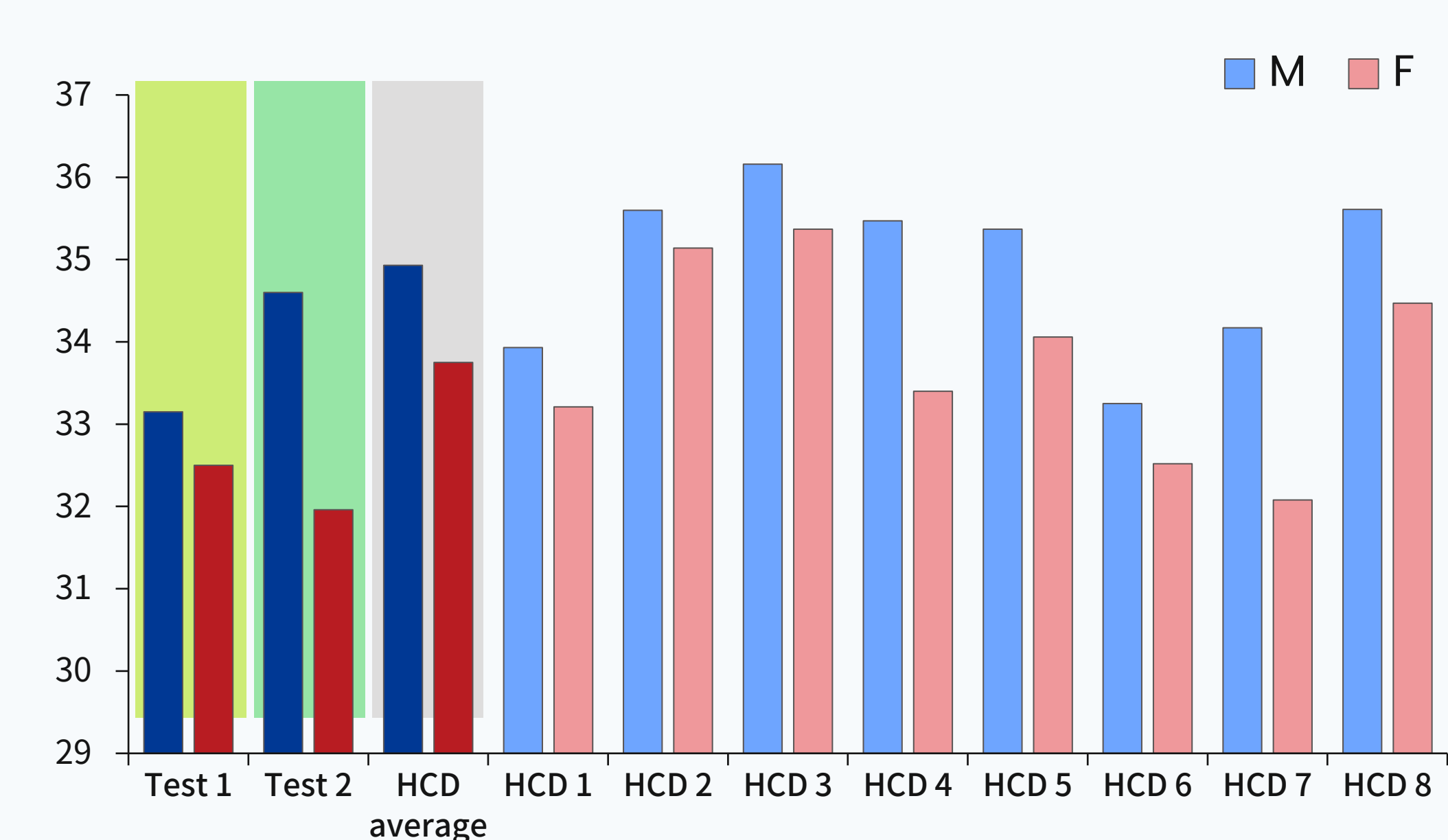
Fetal Skeletal Examinations (Malformation)

	Test 1	Test 2	HCD 1	HCD 2	HCD 3	HCD 4	HCD 5	HCD 6	HCD 7	HCD 8
No. of dams	17	19	19	21	22	16	18	19	18	16
No. of fetuses examined	137	130	164	168	169	132	122	116	102	123
Sacrocaudal body	19.4±0.4	19.4±0.5	19.52±0.48	19.639±0.305	19.545±0.505	19.522±0.317	19.945±0.566	19.420±0.439	19.594±0.440	19.273±0.582
Sterebrae	5.7±0.2	5.9±0.2	5.77±0.35	5.635±0.362	5.857±0.182	5.502±0.367	5.905±0.129	5.547±0.489	5.609±0.413	5.691±0.349

Body Weight Gain (form GD 0)



Body Weight of Fetuses (GD 20)



Fetal Visceral Examinations (Malformation • Variation)

	Test 1	Test 2	HCD 1	HCD 2	HCD 3	HCD 4	HCD 5	HCD 6	HCD 7	HCD 8	HCD 9	HCD 10
No. of dams	17	19	19	19	20	21	22	16	18	19	18	16
No. of fetuses examined	137	130	144	164	171	168	169	132	122	116	102	123
No. of fetuses with visceral malformation	0	0	0	0	0	0	0	0	0	0	0	0
No. of fetuses with visceral variation	0	0	0	5 (2.87±6.17)	3 (1.75)	5 (2.68)	3 (1.55)	0	0	0	0	0
Thymic remnant in the neck	0	0	0	5 (2.87±6.17)	2 (1.17)	3 (1.67)	1 (0.57)	0	0	1 (2.78)	0	0
Dilatation of the renal pelvis	0	0	0	0	0	1 (0.38)	0	0	0	0	0	0

Fetal Skeletal Examinations (Variation)

	Test 1	Test 2	HCD 1	HCD 2	HCD 3	HCD 4	HCD 5	HCD 6	HCD 7	HCD 8	HCD 9	HCD 10
No. of dams	17	19	19	19	20	21	22	16	18	19	18	16
No. of fetuses examined	137	130	144	164	171	168	169	132	122	116	102	123
No. of fetuses with skeletal variations	87 (64.0)	79 (57.3)	105 (72.92)	104 (63.62±28.87)	107 (62.57)	117 (69.87)	132 (79.40)	76 (58.28)	83 (68.97)	56 (47.82)	73 (70.97)	89 (70.90)
Cervical ribs	0	0	2 (1.39)	2 (2.94±8.86)	0	0	0	0	0	1 (0.69)	0	0
Short supernumerary rib	15 (11.9)	13 (12.9)	0	2 (1.24±3.73)	0	4 (2.77)	0	3 (3.13)	34 (24.93)	0	1 (1.18)	1 (0.63)
Full supernumerary rib	72 (53.3)	70 (50.8)	103 (71.53)	99 (60.71±27.37)	107 (62.57)	115 (68.53)	129 (77.82)	74 (56.25)	63 (54.28)	56 (47.03)	70 (67.44)	88 (68.96)
13 rib	0	0	1 (0.69)	0	0	0	0	0	0	0	0	0
Splitting of the sternbra	0	0	1 (0.69)	2 (1.32±5.74)	0	0	0	0	0	0	0	0
Asymmetry of the sternbra	3 (2.0)	2 (1.3)	0	1 (0.48±2.09)	0	0	0	0	0	0	0	0
6 lumbar vertebrae	0	0	0	0	0	0	0	0	0	0	2 (2.35)	1 (2.08)
8 lumbar vertebrae	0	0	0	0	0	0	0	0	0	0	0	0
Sterebra, Bipartite ossification	3 (2.8)	5 (3.7)	0	0	0	5 (1.88)	3 (3.31)	3 (2.39)	2 (1.25)	0	1 (1.96)	2 (1.32)
Thoracic centrum, Bipartite ossification	0	0	0	0	0	0	0	0	0	2 (1.25)	0	0

Abbreviations

Test 1 and Test 2: Background data from two independent repetitions of the same experiment conducted under identical conditions.

HCD1 to HCD10: Historical control data obtained from ten previously conducted studies.

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