G-TWYST
GM PLANTS TWO YEAR SAFETY TESTING

G-TwYST Study A

Combined chronic toxicity and carcinogenicity study in rats fed GM maize NK603

Statistical report, 12 months data

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Abstract

The purpose of oral toxicity study A in the EU project G-TwYST was to assess the chronic and carcinogenic effects of genetically modified (GM) maize NK 603, grown both with and without the use of RoundUp, when fed to rats for a period of two years at incorporation rates of 11% and 33% in the feed. The effects were assessed relative to the responses for rats fed the near-isogenic non-GM maize, and the differences were compared.

The results of G-TwYST study A, except for the histopathological results which are reported separately, are given in five reports: four specific reports about the statistical analysis for data measured after 3, 6, 12 and 24 months, and a main report summarising all study results (Goedhart & van der Voet 2018). This report is about the results after 12 months.

The differences between feeding groups were compared, using a recently developed method for equivalence testing, to differences between non-GM feeds obtained in previous studies performed in the EU project GRACE. No historical data for 12 months old rats were available. Therefore it was only possible to perform equivalence tests using the 3 months data from the GRACE study as reference data. However, variation within the dose groups was much larger after 12 months than after 3 months for many endpoints, which obstructed the use of equivalence tests with historical references. It is concluded that reference data for 12 months would need to be collected for this type of equivalence testing in chronic animal studies.

This report also contains results for equivalence testing using external target effect sizes for a limited set of variables, results for classical statistical analysis of differences, graphs of standardised effect sizes such as performed in the GRACE study and results of a factorial analysis.

1 Introduction

The purpose of oral toxicity study A in the EU project G-TwYST was to assess the effects of genetically modified (GM) maize NK 603, grown both with and without the use of RoundUp, when fed to rats for a period of one year (chronic toxicity study) and two years (carcinogenicity study), at incorporation rates of 11% and 33% in the feed. The effects of the GM maize were assessed relative to the responses for rats fed the near-isogenic non-GM maize. The chronic toxicity and carcinogenicity study ran in parallel. At 12 months part of the rats were euthanized and their organs were obtained, weighted and examined by the G-TwYST histopathological expert. The remaining rats were kept until 24 months, or until premature death, and were then assessed in the same way.

Rat weights and feed intake were measured weekly or bi-weekly. Haematology, clinical biochemistry in blood and urine, differential white blood cell counts, and urine volume and colour were obtained for a subset of animals after 3, 6, 12 and 24 months. This report describes in detail the results of the statistical analyses for the following data obtained after 12 months:

- Body weight at 6 months, growth rate months 6-12, mean feed intake (35 cages/group);
- Haematology (20 cages/group);
- Clinical biochemistry in blood (20 cages/group);
- Clinical biochemistry in urine (15 cages/group);
- Urine volume and colour (15 cages/group);
- Organ weights as percentage of body weight (10 cages/group).

This report is organised as follows. Section 2 describes the data obtained after 12 months, initial data pre-processing, graphical summaries of growth and feed intake over time, outlier identification and checking of assumptions which are made in the statistical analysis. Section 3 presents detailed results of the statistical analyses. More details are provided in several appendices to this report. For a description of the statistical methods, and for a summary and discussion of results for all months, the reader is referred to the main study A report (Goedhart & van der Voet 2018).

2 Data

2.1 Data obtained after 12 months in G-TwYST study A

The available files for the data obtained after 12 months in G-TwYST study A are given in Table 1. Note that the animal weights and intakes for months 7-9 and for months 10-12 were given in separate files. There were also "*Tab_10*" and "*Tab_12*" files with relative organ weights; and it was checked that these indeed contain absolute organ weights divided by the last observed weight. GenStat programs "*12-Males.gen*" and "*12-Females.gen*" were used to combine all the data into single Excel files, separately for males and females. All animals survived the first 12 months, except for 7 male and 9 female rats (Table 2). It is assumed that these premature deaths are not connected to the experiment.

Some CHOL and cHGB were given as bounds; the number of such values are given in Table 3. The original Excel files with the haematology data (*Tab_5* and *Tab_6*) contain remarks given in Table 4. Values with such remarks were set to missing, see for Table 6 for details. For most Urine variables

only a limited number of values have been observed, see Table 5. It is evident that a statistical analysis of uColour, uBil, uNit, uProtein, uGlu, uHemogl and uUrobili is not very useful. Therefore, only the Urine variables uVol, uVolW, uLeu, uOsmoll, uKeton and upH were statistically analysed.

Table 1 Data files for G-TwYST study A after 9/12 months.

Data files after 9 months	**Date**	**Time**	**Size (b)**
Tab_1_G_TwYST_2yr st_A_9_mon_Body weight_Mal.xlsx	09-01-2017	15:44	185,641
Tab_2_G_TwYST_2yr st_A_9_mon_Body weight_Fem.xlsx	09-01-2017	15:45	184,803
Correct data_rev_1_Feed consumption_12_mon_G_TwYST_A_Females.xlsx	20-10-2017	07:08	164,942
Correkt data_rev_1_Feed consumption_12_mon_G_TwYST_A_Males.xlsx	20-09-2017	12:00	168,346
Data files after 12 months	**Date**	**Time**	**Size (b)**
Tab_1_G_TwYST_2yr st_A_12_mon_Body weight_Mal.xlsx	20-01-2017	09:59	122,835
Tab_2_G_TwYST_2yr st_A_12_mon_Body weight_Fem.xlsx	10-01-2017	10:26	127,372
Correct data_rev_1_Feed consumption_12_mon_G_TwYST_A_Females.xlsx	20-10-2017	07:08	164,942
Correkt data_rev_1_Feed consumption_12_mon_G_TwYST_A_Males.xlsx	20-09-2017	12:00	168,346
Tab_5_G_TwYST_2yr st_12 mon_Haemat_Mal.xlsx	04-01-2017	14:08	83,193
Tab_6_G_TwYST_2yr st_12 mon_Haemat_Fem.xlsx	04-01-2017	15:14	86,254
Tab_7a_G_TwYST_2yr st_A_12 mon_Clin_Chem_bl_Mal.xlsx	04-01-2017	14:07	101,064
Tab_7b_G_TwYST_2yr st_A_12 mon_Clin_Chem_ur_Mal.xlsx	04-01-2017	14:06	87,697
Tab_8a_G_TwYST_2yr st_A_12 mon_Clin_Chem_bl_Fem.xlsx	04-01-2017	15:34	102,362
Tab_8b_G_TwYST_2yr st_A_12 mon_Clin_Chem_ur_Fem.xlsx	04-01-2017	15:38	88,887
Bl_ur_12 mon_G_TwYST_2yr st_A_Fem_time course.xlsx	11-01-2017	15:18	116,198
Bl_ur_12 mon_G_TwYST_2yr st_A_Mal_time course.xlsx	11-01-2017	15:21	113,188
Tab_9_G_TwYST_2yr st_A_Abs_organ weights_Mal.xlsx	10-01-2017	10:52	48,673
Tab_11_G_TwYST_2yr st_A_Abs_weight organs_Fem.xlsx	10-01-2017	10:50	40,189

Table 2 Animals that died before the end of month 12.

Sex	Rat	Cage	Feed	Day of Death
Female	610	555	NK11-	86
Female	785	643	Control	98
Male	199	100	NK11+	182
Female	667	584	NK11+	202
Male	148	74	NK11+	231
Female	632	566	NK11-	238
Male	101	51	NK11-	245
Female	848	674	Control	245
Female	745	623	NK33-	299
Female	613	557	NK11-	323
Female	804	652	Control	332
Male	2	1	NK33+	347
Male	85	43	NK11-	351
Male	33	17	NK33+	352
Male	228	114	NK33-	363
Female	770	635	NK33-	363

Table 3 Number of animals for which bounded values were provided.

Variable	Males					Females				
	Con	NK11-	NK33-	NK11+	NK33+	Con	NK11-	NK33-	NK11+	NK33+
CHOL < 1.16	-	-	-	-	-	-	-	-	-	-
cHGB < 27.5	-	1	2	2	-	6	11	7	4	9
cHGB > 522.5	-	-	-	-	-	-	-	-	-	-
ALP < 0.17	-	-	-	-	-	1	-	-	-	1

Table 4 Remarks by SZU in original Excel data files; the accompanying values have been set to missing.

Variable	Remark
WBC	High count WBC
WBC	High count of WBC and PLT, no calculated lymphocytes
WBC	Low WBC and platelet count, probably due to microclots
HGB	No calculated HGB (low blood)
PLT	Low platelet count, probably due to microclots
PLT	High count PLT
PLT	High count of WBC and PLT, no calculated lymphocytes
PLT	Low WBC and platelet count, probably due to microclots

Table 5 Urine variables with only a limited set of observed values which are given in the heading of each sub-tables The table entries give the number of times each value occurs for male and female rats. Only uLeu and uKeton were statistically analysed.

uColour	Missing	1	2	3		
Male	204	-	145	1		
Female	199	2	147	2		
uBil	**Missing**	**0**				
Male	203	147				
Female	199	151				
uLeu	**Missing**	**0**	**25**	**100**	**500**	
Male	203	5	28	66	48	
Female	199	43	51	42	15	
uNit	**Missing**	**0**				
Male	203	147				
Female	199	151				
uProtein	**Missing**	**0.00**	**0.25**	**0.75**	**1.50**	**5.00**
Male	203	99	22	6	14	6
Female	199	128	14	8	1	-
uGlu	**Missing**	**1**				
203	203	147	5	8	28	203
199	199	151	3	2	7	199
uHemogl	**Missing**	**0**	**10**	**25**	**50**	**250**
Male	203	98	8	5	8	28
Female	199	132	7	3	2	7
uKeton	**Missing**	**0.0**	**0.5**	**1.5**		
Male	203	66	37	44		
Female	199	110	32	9		

uUrobili	Missing	1				
Male	203	147				
Female	199	151				

2.2 Growth curves and feed intake

For each individual rat a simple linear regression, $Weight = \alpha + \beta\ Week$, was fitted to the observed weights between weeks 27 and 52, and the growthRate was defined as $\gamma = \log(\beta)$. In Appendix 1 the observed weights are graphically displayed along with the fitted line and, in the bottom right corner, the resulting estimate of the growth rate γ. Initially, absolute standardized residuals, resulting from the fitted curve, which were larger than 3, were marked and these were checked for errors by SZU. This led to some corrections. The corrections are listed in Table 6. The linear regression line generally fits very well, especially for male rats. Only for male rats 74, 301 and 341 one or more observed weights differ more than 5% from the fitted values, as is depicted by the larger plotting symbols in Appendix 1. However, such discrepancies were observed for 88 female rats. For female rats 841 and 843 the estimate of β was negative; this estimate was replaced by 0.217 which is half the minimum of all other estimates. For these two female rats these values are marked as outliers. The final weight Weight_52 and the growthRate parameter γ were statistically analysed. The mean weight for each feeding group is given in Figure 1, while the mean weight gain per day per animal in each week is given in Figure 2. Feed consumption for each cage in units g/animal/day is depicted in Appendix 2. The mean feed consumption for each feeding group is given in Figure 3.

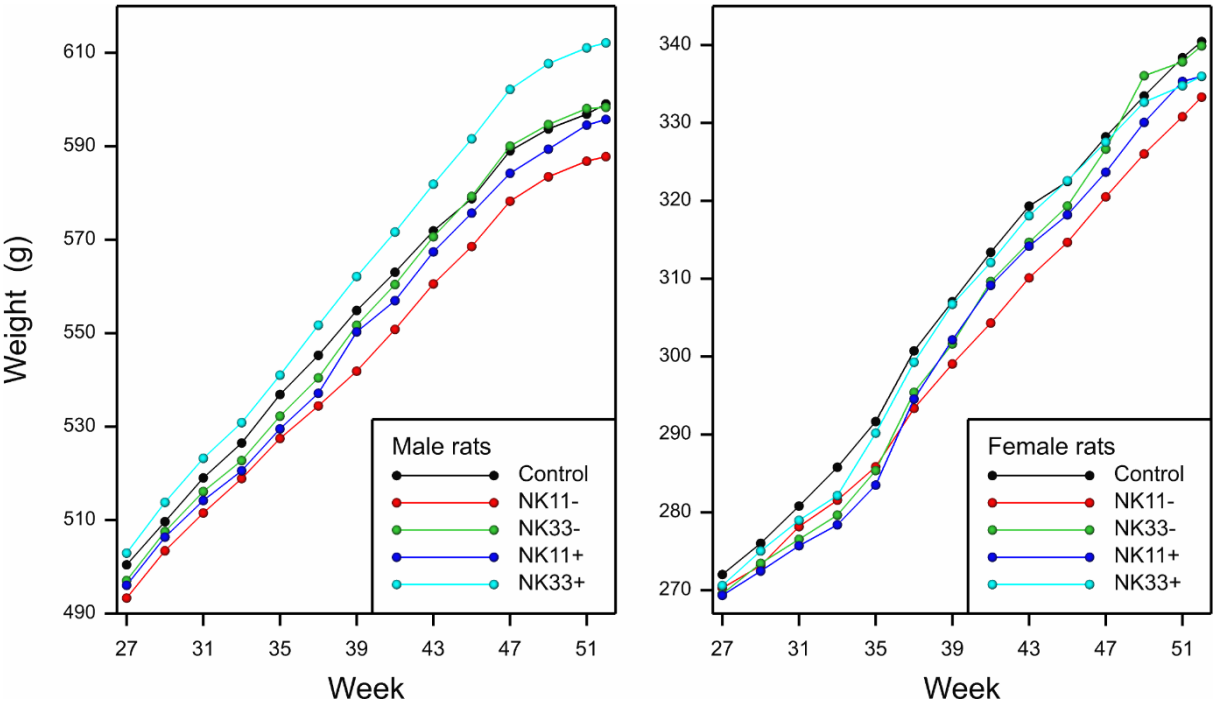

Figure 1 Mean body weights versus week for each feeding group for male rats (left) and for female rats (right).

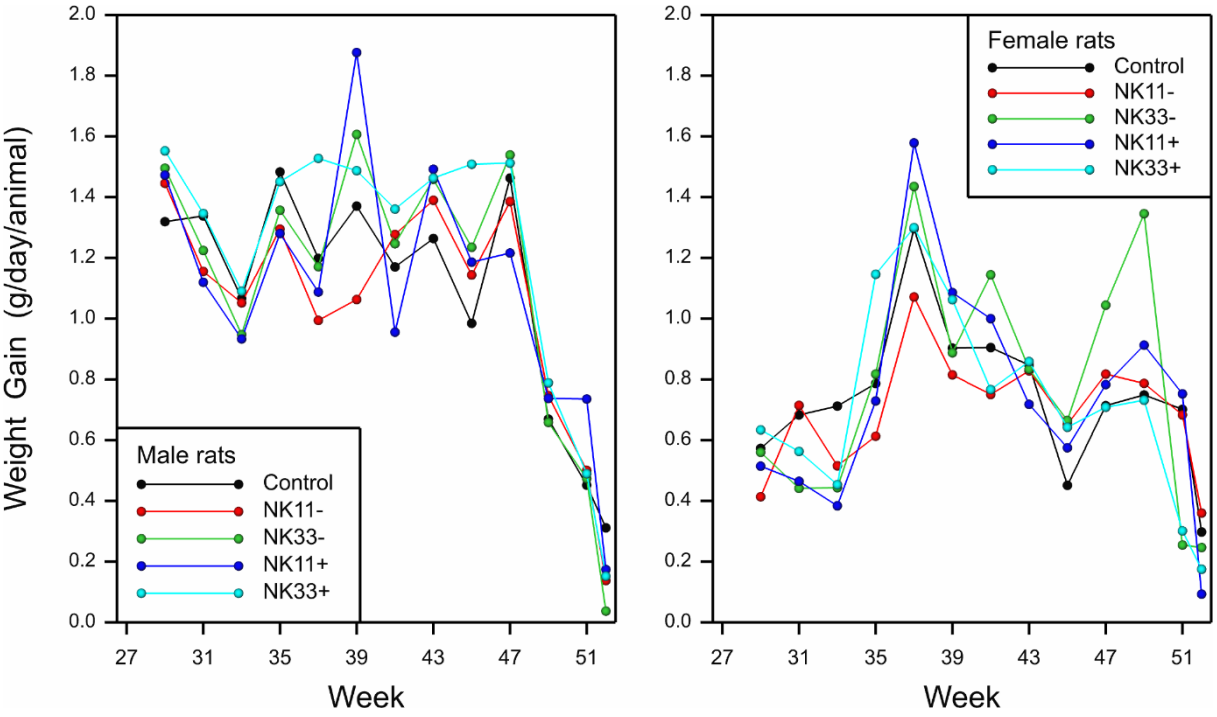

Figure 2 **Mean body weights gain (g/day/animal) versus week for each feeding group for male rats (left) and for female rats (right).**

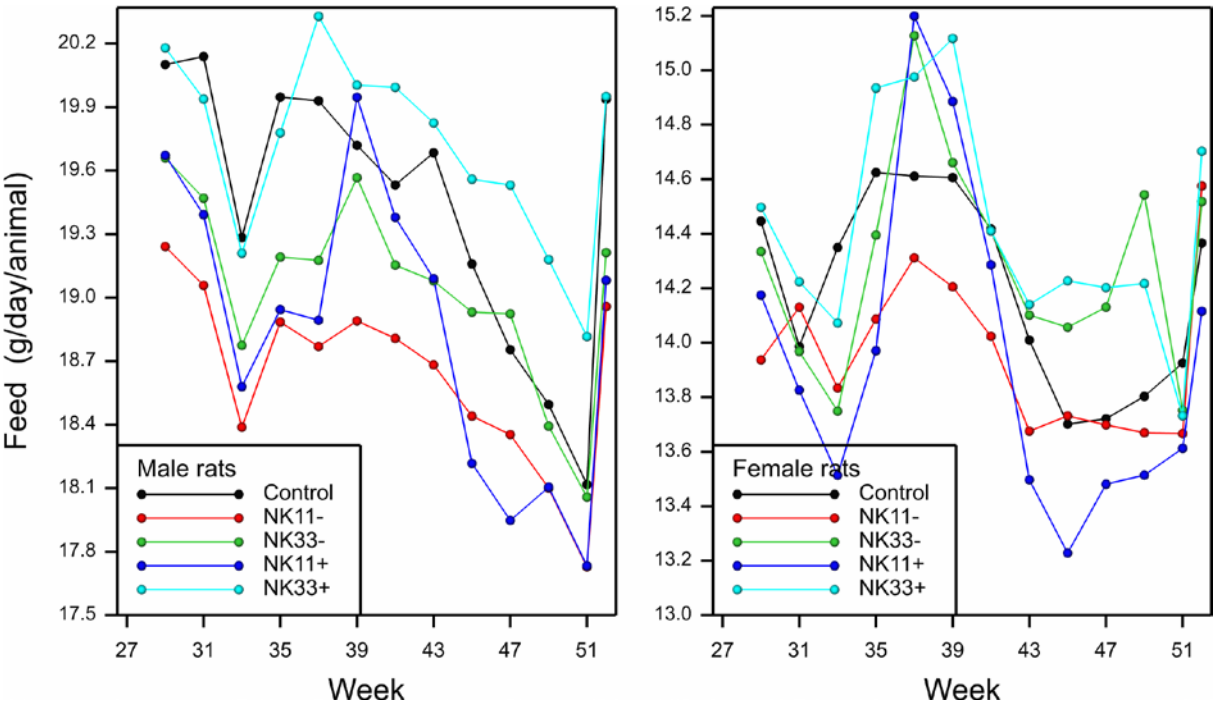

Figure 3 **Mean feed consumption (g/day/animal) versus week for each feeding group for male rats (left) and for female rats (right).**

2.3 Outliers and checking of ANOVA assumptions

These analyses and changes to the data were made before the feeding group codes were unblinded. The cage means, after a log transformation, for each observed variable were statistically analysed by means of an analysis of variance using the model "Block + Group" according to the randomized block design. Grubbs' outlier test at the 1% level was sequentially applied to the residuals to detect outliers. This resulted in a number of outliers which were first presented to the study director and then to the G-TwYST coordinator. Outliers were classified as either (1) typos or physiologically improbable values or (2) values that might be realistic. For the first category the values were set to missing, effectively removing the outlier completely. For the second category a statistical analysis without and with these outlier was performed. The analyses presented in this report are without the outliers. Analyses including outliers are presented in Appendix 11. Table 6 lists all the initially modified values and outliers. Residual plots which include the outliers (i.e. including the yellow values in Table 6) are given in Figure 4. From this it is clear that these are indeed outliers; note that the outliers for growthRate in females are due to negative regression coefficients in the linear regression of weights.

Table 6 Values that have been modified, deleted, or were considered as possible outliers, before unblinding of the feeding groups. Values which are not coloured were modified or deleted following comments of SZU. The red and yellow values were presented to the G-TwYST coordinator. He decided which values should be deleted (red) and which values should be considered as possible outliers (yellow). Comments by the authors of this report are given in black, while comments of the G-TwYST coordinator are given in red.

Sex	Variable	Animal	Cage	oldValue	newValue	Comment
Males	WBC	35	18	2.9	delete	Comment in datafile: microclots
Males	WBC	59	30	14.6	delete	Comment in datafile: highCount
Males	WBC	81	41	15.6	delete	Comment in datafile: highCount
Males	WBC	89	45	14.6	delete	Comment in datafile: highCount
Males	PLT	35	18	177	delete	Comment in datafile: microclots
Males	PLT	59	30	1576	delete	Comment in datafile: highCount
Males	PLT	89	45	1524	delete	Comment in datafile: highCount
Males	Weight_35	101	51	415.23	delete	Rat died between week 35 and 37
Males	Feed_35	101	51	13.64	delete	Rat died between week 35 and 37
Males	Weight_33	148	74	383.61	delete	Rat died between week 33 and 35
Males	Feed_33	148	74	11.07	delete	Rat died between week 33 and 35
Males	Weight_45	2	1	602.09	delete	Rat died between week 49 and 51
Males	Weight_47	2	1	534.66	delete	Rat died between week 49 and 51
Males	Weight_49	2	1	493.23	delete	Rat died between week 49 and 51
Males	Feed_45	2	1	19.49	delete	Rat died between week 49 and 51
Males	Feed_47	2	1	15.08	delete	Rat died between week 49 and 51
Males	Feed_49	2	1	16.56	delete	Rat died between week 49 and 51
Males	Feed_51	33	17	22.18	delete	Rat died between week 49 and 51
Males	Weight_51	228	114	537.05	delete	Rat died between week 51 and 54
Males	Feed_51	228	114	15.21	delete	Rat died between week 51 and 52
Males	Feed_52	228	114	22.77	delete	Rat died between week 51 and 52
Males	Weight_29	222	111	598.55	559.55	Mistake in copying from primary
Males	growthRate	86	43	1.823	outlier	Grubbs' test significant (p=0.001)

Males	RBC	35	18	5.06	outlier	Same animal 35; smallest value; the value is still realistic
Males	HGB	35	18	11.2	outlier	Same animal 35; smallest value; the value is still realistic
Males	HCT	35	18	32.2	outlier	Same animal 35; smallest value; the value is still realistic
Males	Crea	156	78	74.9	outlier	Largest value; if Urea is also high, could indicate renal insufficiency
Males	Testis_R	160	80	0.5066	outlier	Extremely small value; the value is still realistic
Males	Testis_L	160	80	0.4908	outlier	Extremely small value; the value is still realistic
Males	Testis	160	80	0.4987	outlier	Extremely small value; the value is still realistic
Males	Kidney_L	224	112	3.1137	1.55685	Weight of BOTH kidneys; corrected such that the sum equals 3.1137
Sex	**Variable**	**Animal**	**Cage**	**oldValue**	**newValue**	**Comment**
Females	WBC	506	503	*	delete	Comment in datafile: noBlood
Females	WBC	680	590	41.7	delete	Comment in datafile: highCount
Females	WBC	726	613	*	delete	Comment in datafile: clottedBlood
Females	WBC	846	673	1.6	delete	Comment in datafile: microclots
Females	WBC	799	650	24.1	delete	Comment in datafile: highCount
Females	HGB	654	577	1	delete	Comment in datafile: lowBlood
Females	PLT	680	590	1959	delete	Comment in datafile: highCount
Females	PLT	799	650	1872	delete	Comment in datafile: highCount
Females	PLT	846	673	61	delete	Comment in datafile: microclots
Females	Weight_33	632	566	260.8	delete	Rat died between week 33 and 35
Females	Feed_35	632	566	17.51	delete	Rat died between week 33 and 35
Females	Feed_29	667	584	24.76	delete	Rat died between week 27 and 29
Females	Feed_35	847	674	25.79	delete	Rat died between week 33 and 35
Females	Feed_45	613	557	11.48	delete	Rat died between week 45 and 47
Females	Feed_52	770	635	26.49	delete	Rat died between week 45 and 48
Females	Weight_47	804	652	264.77	delete	Rat died between week 47 and 49
Females	Feed_47	803	652	11.79	delete	Rat died between week 47 and 49
Females	Feed_49	803	652	25.11	delete	Rat died between week 47 and 49
Females	Weight_39	786	643	248.57	298.57	Mistake in copying from primary
Females	growthRate	841	671	-1.528	outlier	Estimate β is negative
Females	growthRate	843	672	-1.528	outlier	Estimate β is negative
Females	MCV	718	609	67.7	outlier	Animal 718 has consistent large values in all three months; outlier
Females	RBC	588	544	4.75	delete	Same animal 588; smallest value in this month; very low value
Females	HGB	588	544	5.9	delete	Same animal 588; two smallest values in this month are considered
Females	HCT	588	544	26.6	delete	Same animal 588; smallest value in this month; un-physiologically low
Females	MCH	588	544	12.4	delete	Same animal 588; three smallest values in this month are considered outliers (see animals 588, 654 & 762); because extremely low HGB

Females	MCHC	588	544	22.2	delete	Same animal 588; three smallest values in this month are considered outliers (see animals 588, 654 & 762); because extremely low HGB
Females	MCH	654	577	1.3	delete	Same animal 654; three smallest values in this month are considered outliers (see animals 588, 654 & 762); un-physiologically low value
Females	MCHC	654	577	2.3	delete	Same animal 654; three smallest values in this month are considered outliers (see animals 588, 654 & 762); un-physiologically low value
Females	HGB	762	631	8.4	delete	Same animal 762; two smallest values in this month are considered outliers (see animals 588 & 762); extremely low HGB
Females	MCH	762	631	11	delete	Same animal 762; three smallest values in this month are considered outliers (see animals 588, 654 & 762); because of very low HGB
Females	MCHC	762	631	18.7	delete	Same animal 762; three smallest values in this month are considered outliers (see animals 588, 654 & 762); because of extremely low HGB
Females	LYMR	585	543	41.1	outlier	Only a single value in this cage; There is a smaller value; outlier
Females	LYMA	846	673	1.2	outlier	Smallest value in this month; outlier

Without these outliers cage means on the original scale are given in Appendix 3, while cage means after a log transformation of the individual data are given in Appendix 4. Normal probability plots of the ANOVA residuals, of an analysis on cage means after log transformation, are given in Appendix 5. To aid interpretation a 99% envelope is added to the probability plots, such that only values outside the envelop might be suspicious. Appendix 6 gives plots of residuals versus fitted values after the same analysis of variance. These residual plots are generally satisfactory implying that the ANOVA assumptions, homogeneity of variance and, less importantly, normality, are generally fulfilled.

2.4 Summary tables

Summary tables, on the original non-transformed scale, of number of observations, means, standard deviations and coefficients of variation (%), classified by the feeding groups, are given in Table 7 for males and in Table 8 for females. These tables were obtained by first calculating cage means and then calculating the summary statistics. The number of cages per feeding group is 35 for weights, 20 for haematology, differential WBC and clinical biochemistry, and 10 for Urine data.

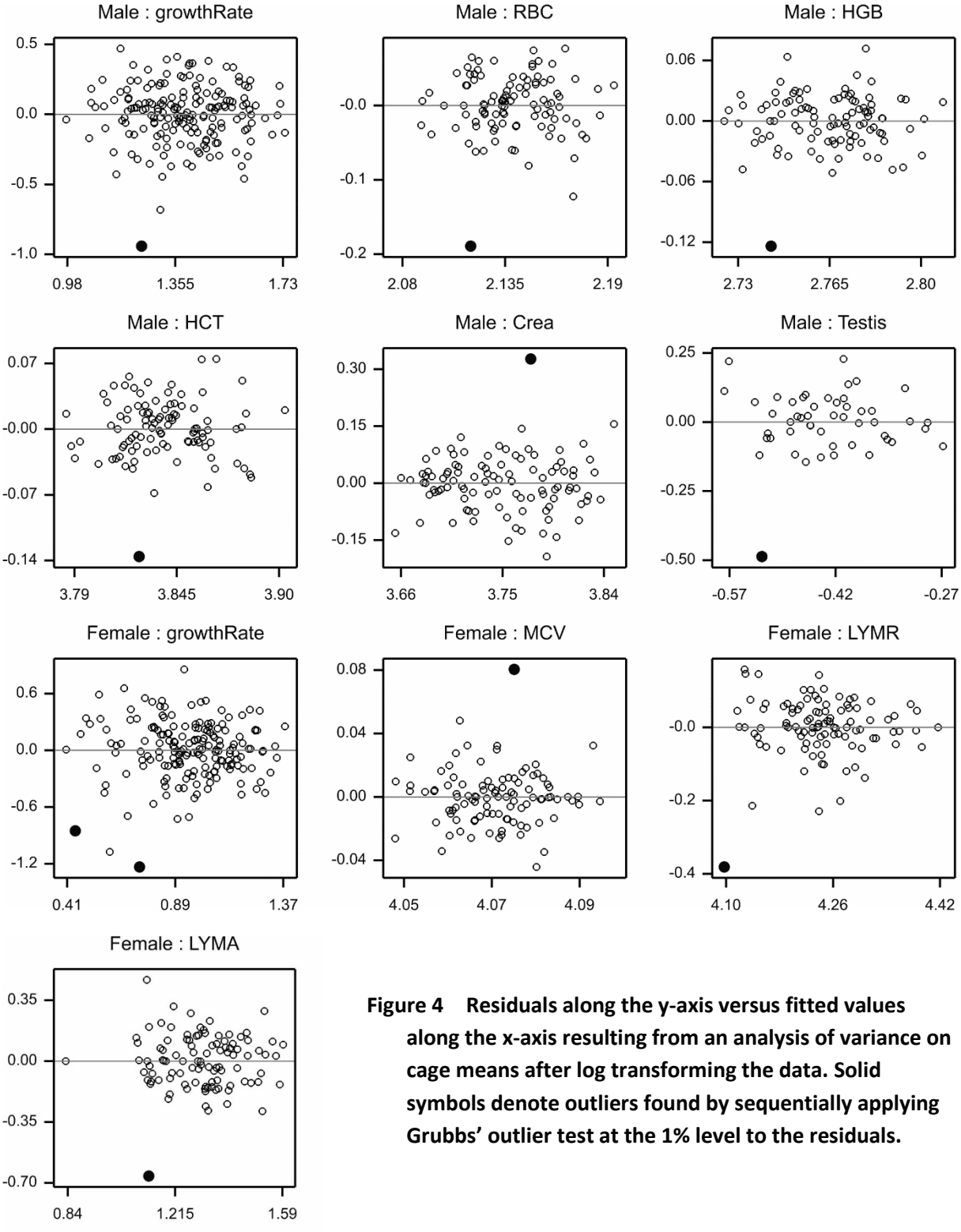

Figure 4 Residuals along the y-axis versus fitted values along the x-axis resulting from an analysis of variance on cage means after log transforming the data. Solid symbols denote outliers found by sequentially applying Grubbs' outlier test at the 1% level to the residuals.

Table 7 Summary statistics for male rats classified by the feeding groups: number of cages (N), means (Mean), standard deviations (Sd) and coefficients of variation (CV). The summary statistics are obtained from cage means.

Weights	Control				NK11-				NK33-				NK11+				NK33+			
Male	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
Weight_52	35	599	41.6	6.9	35	586	60.3	10.3	35	598	56.2	9.4	35	597	54.2	9.1	35	614	60.0	9.8
growthRate	35	1.37	0.21	15.5	34	1.32	0.27	20.1	35	1.39	0.23	16.6	35	1.38	0.24	17.2	35	1.50	0.26	17.6
FeedMean	35	19.4	0.89	4.6	35	18.6	1.33	7.2	34	19.0	1.46	7.7	35	18.8	1.38	7.3	35	19.7	1.47	7.4
Haematology	**Control**				**NK11-**				**NK33-**				**NK11+**				**NK33+**			
Male	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
WBC	20	7.66	1.59	20.8	20	7.20	1.50	20.9	20	8.57	1.59	18.6	20	7.81	1.18	15.1	20	8.15	1.08	13.2
RBC	20	8.48	0.27	3.2	20	8.50	0.35	4.1	20	8.45	0.38	4.5	20	8.65	0.35	4.0	20	8.58	0.44	5.2
HGB	20	15.8	0.26	1.7	20	15.9	0.50	3.1	20	15.9	0.49	3.1	20	16.0	0.45	2.8	20	16.0	0.61	3.8
HCT	20	46.1	1.29	2.8	20	46.3	1.53	3.3	20	46.5	2.07	4.5	20	47.2	1.35	2.9	20	46.8	2.15	4.6
MCV	20	54.4	1.55	2.9	20	54.6	1.56	2.9	20	55.0	1.56	2.8	20	54.6	1.52	2.8	20	54.8	1.20	2.2
MCH	20	18.7	0.63	3.4	20	18.8	0.73	3.9	20	18.8	0.74	3.9	20	18.5	0.76	4.1	20	18.7	0.65	3.5
MCHC	20	34.3	0.57	1.7	20	34.3	0.76	2.2	20	34.2	0.90	2.6	20	33.9	0.64	1.9	20	34.2	0.72	2.1
PLT	20	814	66.5	8.2	20	807	60.7	7.5	20	879	84.5	9.6	20	834	80.8	9.7	20	883	83.6	9.5
LYMR	20	66.9	8.77	13.1	20	66.8	5.02	7.5	20	69.5	8.88	12.8	20	67.5	8.09	12.0	20	65.5	7.83	12.0
LYMA	20	5.13	1.25	24.4	20	4.98	1.18	23.8	20	5.90	1.23	20.9	20	5.25	0.85	16.2	20	5.31	1.10	20.7
ClinChem	**Control**				**NK11-**				**NK33-**				**NK11+**				**NK33+**			
Male	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
ALP	20	1.23	0.22	17.7	20	1.33	0.26	19.5	20	1.26	0.21	16.3	20	1.31	0.21	16.1	20	1.26	0.22	17.7
ALT	20	0.66	0.11	17.2	20	0.68	0.19	28.6	20	0.64	0.11	16.9	20	0.72	0.18	24.6	20	0.69	0.14	19.8
AST	20	2.30	0.38	16.6	20	2.39	0.52	21.8	20	2.29	0.33	14.6	20	2.28	0.54	23.8	20	2.32	0.58	25.0
BIL	20	7.10	1.62	22.8	20	6.82	1.02	15.0	20	6.94	1.03	14.8	20	6.71	1.15	17.1	20	7.20	1.14	15.8
ALB	20	37.7	1.22	3.2	20	37.4	1.05	2.8	20	38.0	1.02	2.7	20	37.5	1.10	2.9	20	37.5	1.37	3.6
TP	20	69.0	1.80	2.6	20	68.4	1.79	2.6	20	69.3	1.51	2.2	20	68.8	2.05	3.0	20	68.8	1.80	2.6
Glu	20	5.35	0.59	11.1	20	5.43	0.82	15.1	20	5.26	0.47	8.9	20	5.69	1.16	20.4	20	5.40	0.60	11.2
CHOL	20	2.74	0.35	12.8	20	2.82	0.38	13.6	20	2.85	0.50	17.4	20	2.64	0.45	17.1	20	2.88	0.65	22.6
TAG	20	1.78	0.59	33.0	20	1.82	0.45	24.6	20	2.01	0.58	28.6	20	2.05	0.67	32.5	20	2.01	0.56	28.0
Crea	20	43.7	4.80	11.0	20	42.1	3.30	7.8	20	43.1	2.49	5.8	20	42.1	3.35	7.9	20	42.3	3.66	8.6
Urea	20	4.37	0.39	9.0	20	4.32	0.49	11.4	20	4.38	0.46	10.6	20	4.58	0.58	12.6	20	4.28	0.54	12.7
cHGB	20	65.0	33.7	51.8	20	57.3	16.3	28.4	20	66.6	20.6	31.0	20	67.6	33.3	49.3	20	65.9	22.8	34.7

Ca	20	2.54	0.034	1.3	20	2.55	0.051	2.0	20	2.55	0.045	1.8	20	2.54	0.062	2.4	20	2.54	0.043	1.7
Cl	20	104	1.31	1.3	20	103	1.54	1.5	20	102	1.33	1.3	20	103	1.80	1.8	20	103	1.65	1.6
K	20	4.80	0.34	7.1	20	4.77	0.23	4.8	20	4.88	0.30	6.1	20	4.81	0.26	5.4	20	4.80	0.27	5.7
Na	20	143	2.07	1.4	20	144	1.84	1.3	20	143	1.55	1.1	20	144	2.28	1.6	20	143	2.74	1.9
P	20	1.77	0.17	9.5	20	1.67	0.19	11.2	20	1.81	0.28	15.2	20	1.71	0.17	9.8	20	1.69	0.16	9.3
Urine	**Control**				**NK11-**				**NK33-**				**NK11+**				**NK33+**			
Male	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
uVol	15	15.6	3.48	22.4	15	15.2	2.70	17.8	15	12.9	3.28	25.4	16	13.1	4.12	31.4	15	14.8	3.05	20.6
uVolW	15	2.67	0.69	25.7	15	2.63	0.57	21.6	15	2.19	0.57	26.1	16	2.21	0.74	33.2	15	2.48	0.62	24.9
uLeu	15	276	153	55.5	15	174	141	80.9	15	285	141	49.4	16	157	138	87.8	15	168	146	86.6
uOsmoll	15	561	107	19.0	15	558	114	20.4	15	646	94	14.5	16	650	172	26.5	15	595	85	14.4
uKeton	15	0.52	0.39	76.4	15	0.55	0.48	87.9	15	0.92	0.28	30.3	16	0.36	0.36	101.5	15	0.55	0.46	82.8
upH	15	6.77	0.29	4.3	15	6.63	0.34	5.1	15	6.82	0.36	5.3	16	6.88	0.38	5.5	15	6.62	0.43	6.5
Organs	**Control**				**NK11-**				**NK33-**				**NK11+**				**NK33+**			
Male	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
Kidney	10	0.45	0.042	9.5	10	0.47	0.037	7.7	10	0.48	0.082	17.1	10	0.45	0.050	11.1	10	0.45	0.044	9.8
Spleen	10	0.17	0.018	10.6	10	0.17	0.013	7.7	10	0.18	0.017	9.6	10	0.17	0.031	18.6	10	0.17	0.017	10.1
Liver	10	2.10	0.19	9.2	10	2.08	0.21	10.2	10	2.11	0.14	6.5	10	2.09	0.12	5.8	10	2.01	0.20	10.0
AdrenGl	10	0.0088	0.0008	8.8	10	0.0094	0.0008	8.4	10	0.0095	0.0013	13.4	10	0.0083	0.0008	9.9	10	0.0091	0.0010	10.5
Heart	10	0.20	0.011	5.4	10	0.21	0.020	9.2	10	0.22	0.024	10.9	10	0.20	0.008	4.1	10	0.20	0.012	6.2
Testis	10	0.64	0.045	7.1	10	0.69	0.082	11.9	10	0.65	0.077	11.8	10	0.65	0.059	9.2	10	0.68	0.078	11.5
Epididymis	10	0.22	0.024	11.1	10	0.24	0.028	11.5	10	0.22	0.030	13.3	10	0.21	0.027	13.1	10	0.23	0.030	13.2
Brain	10	0.38	0.028	7.4	10	0.40	0.045	11.2	10	0.39	0.038	9.8	10	0.37	0.041	11.2	10	0.39	0.039	10.1

Table 8 Summary statistics for female rats classified by the feeding groups: number of cages (N), means (Mean), standard deviations (Sd) and coefficients of variation (CV). The summary statistics are obtained from cage means.

Weights	Control				NK11-				NK33-				NK11+				NK33+			
Female	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
Weight_52	35	340	37.0	10.9	35	333	31.8	9.5	35	339	32.2	9.5	35	336	35.6	10.6	35	336	31.1	9.3
growthRate	35	0.98	0.32	33.0	35	0.88	0.35	39.3	35	1.03	0.34	32.7	35	0.97	0.37	37.8	35	0.95	0.31	33.1
FeedMean	35	14.2	0.94	6.6	35	13.9	1.17	8.4	34	14.3	0.95	6.7	35	13.9	1.02	7.3	35	14.4	0.92	6.4
Haematology	**Control**				**NK11-**				**NK33-**				**NK11+**				**NK33+**			
Female	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
WBC	20	5.57	1.34	24.0	20	5.94	1.53	25.8	20	5.13	0.96	18.7	20	5.45	1.19	21.8	20	5.88	1.28	21.8
RBC	20	7.37	0.36	4.9	20	7.37	0.31	4.2	20	7.44	0.35	4.8	20	7.55	0.29	3.9	20	7.54	0.25	3.3
HGB	20	15.4	0.53	3.4	20	15.4	0.52	3.4	20	15.5	0.51	3.3	20	15.6	0.48	3.1	20	15.5	0.54	3.5
HCT	20	43.2	2.00	4.6	20	43.4	1.90	4.4	20	43.8	1.63	3.7	20	44.1	1.56	3.5	20	43.9	1.38	3.1
MCV	20	58.7	0.86	1.5	20	58.9	1.16	2.0	20	58.7	1.25	2.1	20	58.4	0.98	1.7	20	58.2	1.19	2.0
MCH	20	21.0	0.55	2.6	20	21.0	0.60	2.9	20	20.8	0.75	3.6	20	20.6	0.42	2.0	20	20.6	0.50	2.4
MCHC	20	35.8	0.72	2.0	20	35.6	0.86	2.4	20	35.3	0.73	2.1	20	35.2	0.63	1.8	20	35.4	0.82	2.3
PLT	20	755	75	10.0	20	792	103	13.0	20	751	74	9.9	20	764	79	10.3	20	784	97	12.4
LYMR	20	69.9	7.41	10.6	19	70.0	5.44	7.8	20	71.4	7.50	10.5	20	70.0	6.10	8.7	20	70.6	3.68	5.2
LYMA	20	3.86	0.97	25.0	20	3.92	0.63	16.1	20	3.57	0.60	16.9	20	3.78	0.67	17.7	20	4.04	0.80	19.8
ClinChem	**Control**				**NK11-**				**NK33-**				**NK11+**				**NK33+**			
Female	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
ALP	20	0.59	0.13	22.7	20	0.55	0.08	14.8	20	0.60	0.16	27.2	20	0.59	0.13	21.4	20	0.54	0.12	21.7
ALT	20	0.74	0.18	24.2	20	0.70	0.18	26.0	20	0.71	0.15	21.3	20	0.65	0.27	40.9	20	0.72	0.13	17.7
AST	20	2.59	0.62	23.8	20	2.52	0.49	19.6	20	2.69	0.50	18.8	20	2.55	0.81	31.7	20	2.73	0.73	26.6
BIL	20	8.33	2.33	27.9	20	7.68	1.57	20.4	20	7.76	1.35	17.4	20	7.92	1.46	18.4	20	8.03	2.72	33.9
ALB	20	42.4	1.91	4.5	20	42.5	2.12	5.0	20	43.0	2.14	5.0	20	43.3	3.00	6.9	20	42.4	2.16	5.1
TP	20	71.9	2.11	2.9	20	71.8	2.30	3.2	20	72.1	2.23	3.1	20	71.9	2.63	3.7	20	71.7	2.72	3.8
Glu	20	5.03	0.87	17.4	20	5.04	0.60	11.9	20	4.75	0.71	15.0	20	5.10	0.70	13.7	20	5.18	0.84	16.3
CHOL	20	2.64	0.50	19.0	20	2.61	0.50	19.1	20	2.57	0.47	18.3	20	2.47	0.45	18.3	20	2.49	0.36	14.6
TAG	20	0.96	0.22	22.7	20	0.90	0.23	25.8	20	1.01	0.31	30.2	20	1.21	1.08	89.1	20	0.98	0.25	25.2
Crea	20	43.2	4.47	10.3	20	45.4	3.66	8.1	20	45.2	3.86	8.5	20	46.1	4.99	10.8	20	44.3	3.46	7.8
Urea	20	4.63	0.44	9.5	20	4.99	0.48	9.5	20	5.17	0.57	10.9	20	5.05	0.68	13.5	20	4.98	0.54	10.9
cHGB	20	54.0	35.1	65.1	20	43.1	13.5	31.3	20	47.3	18.1	38.3	20	50.8	29.2	57.5	20	52.4	37.8	72.2

Ca	20	2.57	0.042	1.7	20	2.58	0.049	1.9	20	2.58	0.054	2.1	20	2.59	0.058	2.2	20	2.56	0.032	1.2
Cl	20	101	1.52	1.5	20	101	1.24	1.2	20	100	1.43	1.4	20	100	1.50	1.5	20	101	1.66	1.7
K	20	4.36	0.28	6.5	20	4.38	0.40	9.1	20	4.36	0.29	6.7	20	4.37	0.39	8.9	20	4.42	0.52	11.7
Na	20	141	1.92	1.4	20	142	2.28	1.6	20	142	1.80	1.3	20	142	2.17	1.5	20	142	2.30	1.6
P	20	1.45	0.23	16.1	20	1.46	0.22	15.4	20	1.56	0.24	15.4	20	1.57	0.37	23.3	20	1.42	0.25	17.6
Urine	**Control**				**NK11-**				**NK33-**				**NK11+**				**NK33+**			
Female	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
uVol	15	13.6	2.52	18.5	16	14.0	5.66	40.4	16	13.1	3.71	28.4	15	14.1	4.89	34.7	15	12.7	3.36	26.4
uVolW	15	4.00	0.72	17.9	16	4.28	1.63	38.1	16	3.91	1.26	32.1	15	4.27	1.83	43.0	15	3.87	1.01	26.1
uLeu	15	66	88	133.0	16	84	92	110.4	16	134	148	110.2	15	79	100	126.3	15	73	96	131.4
uOsmoll	15	491	77	15.7	16	498	120	24.1	16	534	185	34.7	15	482	109	22.7	15	531	115	21.7
uKeton	15	0.15	0.21	138.0	16	0.27	0.38	143.6	16	0.28	0.33	116.5	15	0.05	0.10	207.0	15	0.20	0.24	117.6
upH	15	6.53	0.28	4.3	16	6.44	0.40	6.3	16	6.42	0.35	5.5	15	6.70	0.33	4.9	15	6.42	0.29	4.6
Organs	**Control**				**NK11-**				**NK33-**				**NK11+**				**NK33+**			
Female	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV	N	Mean	Sd	CV
Kidney	10	0.48	0.051	10.7	10	0.51	0.038	7.4	10	0.50	0.045	9.0	10	0.52	0.050	9.7	10	0.52	0.037	7.1
Spleen	10	0.20	0.027	13.5	10	0.21	0.019	9.2	10	0.19	0.027	14.2	10	0.20	0.027	13.2	10	0.22	0.048	21.9
Liver	10	2.01	0.19	9.5	10	2.05	0.18	8.8	10	2.02	0.15	7.3	10	2.06	0.11	5.3	10	2.06	0.15	7.3
AdrenGl	10	0.019	0.0030	15.7	10	0.019	0.0016	8.3	10	0.019	0.0029	15.0	10	0.020	0.0034	17.4	10	0.020	0.0034	17.0
Heart	10	0.25	0.022	8.8	10	0.26	0.018	6.7	10	0.27	0.032	11.9	10	0.26	0.017	6.7	10	0.26	0.016	5.9
Uterus	10	0.26	0.062	23.9	10	0.28	0.071	25.8	10	0.24	0.056	23.7	10	0.25	0.052	20.4	10	0.25	0.048	19.1
Ovary	10	0.018	0.0060	33.5	10	0.019	0.0033	17.4	10	0.021	0.0038	18.4	10	0.021	0.0066	31.5	10	0.021	0.0056	26.1
Brain	10	0.59	0.061	10.2	10	0.65	0.069	10.6	10	0.64	0.067	10.5	10	0.64	0.060	9.3	10	0.65	0.038	5.8

3 Statistical analysis

The statistical methods are described in the main study A report (Goedhart & van der Voet 2018).

3.1 Equivalence testing using historical data

Equivalence testing was only performed for those variables that were also observed in the GRACE study. Note that this is a comparison between data obtained after 12 months for the current study, and data obtained after 3 months for the historical GRACE study. It should be noted that the residual variances between cages may be much larger after 12 months than after 3 months (Figure 17). This in indicated by a yellow background colour of the endpoint labels in Figure 5 to Figure 8, and it shows that the model for equivalence testing which compares the current 12 months data to reference data obtained after 3 months data is not useful. The results reported in this section are only meant to illustrate this fact and are given for completeness only.

The sample size in the current study, i.e. the number of cages per feeding group, equals 35 for the weight variables, 20 for haematology and clinical biochemistry, and 10 for relative organ weights. These sample sizes were used as the regulatory replication n_0 in the equivalence analysis. Moreover regulatory values $\alpha = 0.05$ and $\beta = 0.05$ were employed. Equivalence testing was only performed for those variables that were also observed in the GRACE study. Note that this is a comparison between data obtained after 12 months for the current study, and data obtained after 3 months for the historical GRACE study.

Each GMO feed was tested for equivalence with respect to the control feed. The DWE intervals showing the main results of the equivalence tests for 34 variables are given in Figure 5 to Figure 8. The hypothesis of no difference is rejected in case the interval does not contain zero, which is denoted by fuchsia coloured estimates. The non-equivalence hypothesis is rejected when the interval fully lies inside the interval (-1,1). For further interpretation the 95% confidence intervals for the ratios are given in Table 9 and Table 10. These confidence intervals at the ratio scale are also given in Figure 9 to Figure 16, with inclusion of the estimated equivalence limits (red bars) and their uncertainty (blue bars). Note that the latter graphs cannot be used directly for performing the equivalence test. However, they show the effects and equivalence limits at a more familiar scale.

Among 8×34 = 272 equivalence tests, there were 65 failures (24%) to prove equivalence (i.e. reject the hypothesis of non-equivalence). This high rate is mostly due to the fact that the residual variances after 12 months in the current study were often much larger than the residual variance after 3 months in the historical studies. The ratio of these residual variances (variance ratio or VR) was larger than 150% in 33 of the 68 cases (49%), in particular for the relative organ weights (Figure 17). These endpoints with much more variation explain 63 of the 65 failures to prove equivalence, including 2 endpoints where the median estimate was outside the equivalence limits (Ovary, females NK33- and NK33+). For the other 63 cases of non-proven equivalence, the median estimate is within the equivalence limits, and thus, according to the terminology of EFSA (2011a), equivalence is still more likely than lack of equivalence. Only for 2 cases with a residual variance ratio smaller than 150%, a failure to prove equivalence occurs (FeedMean, male NK11-, and Brain, female NK11-)

Although not the primary result of the equivalence analysis, it can also be observed from the fuchsia symbols in Figure 5 to Figure 8 and from Table 9 and Table 10 that, for those variables for which the equivalence test is performed, the number of significant differences, employing classical two-sided t-tests at the 5% level, equals 31 (11% of 272 difference tests, 13 for males and 18 for females). For the following cases both a significant difference and a failure to show equivalence occurred: FeedMean (NK11-) and Epididymus (NK11-) in males, and in females for MCHC (NK33-, NK11+), Kidney (NK11+, NK33+), Heart (NK33-) and Brain (NK11-, NK33+).

For all difference tests, i.e. including those for which the equivalence test was not performed, 38 out of 352 t-tests were significant which is 11% of the tests.

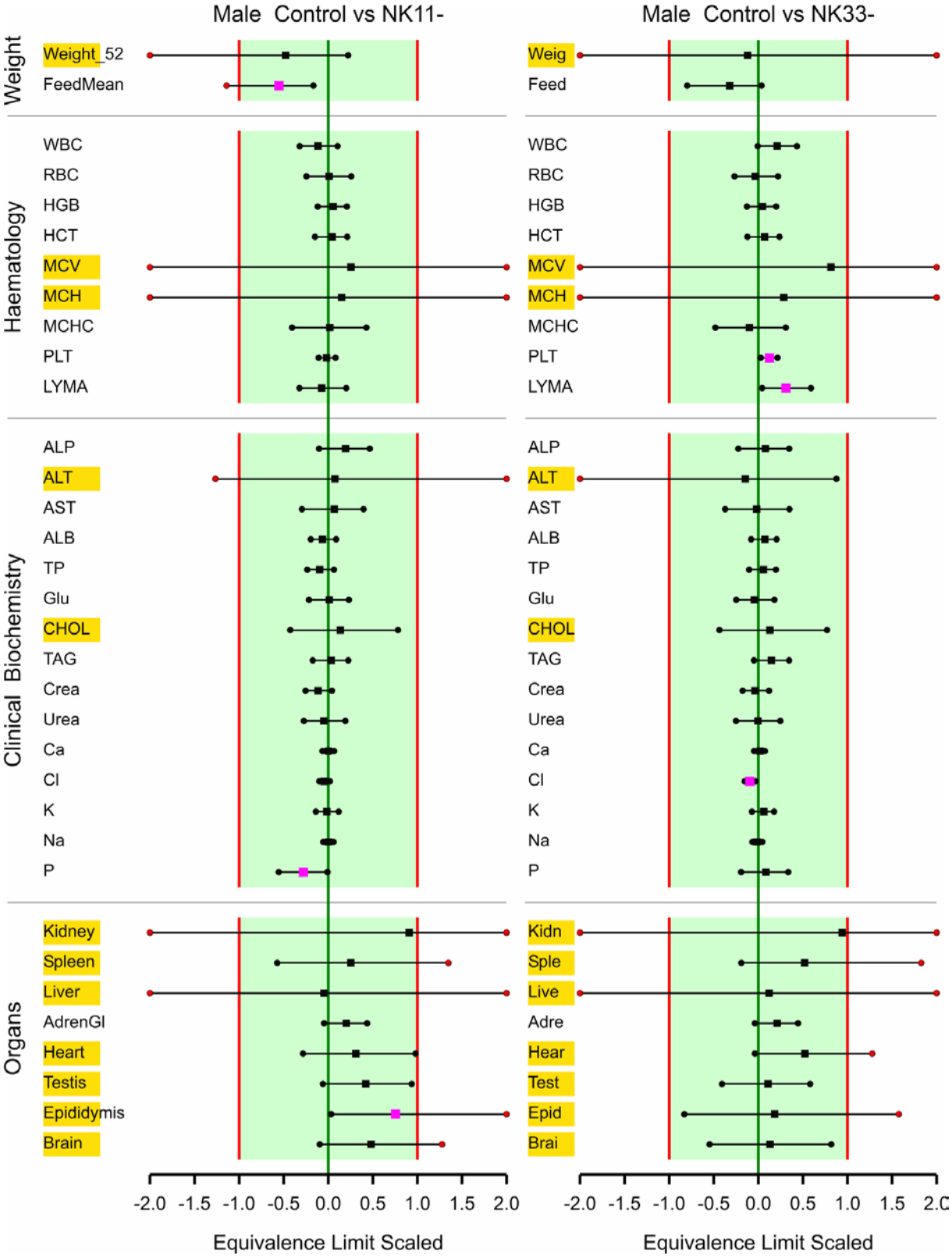

Figure 5 **Equivalence testing of NK11- and NK33- versus the control feed for males. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed. See Table 9, Figure 9 and Figure 10 for further interpretation. Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%). Fuchsia coloured symbols denote a significant difference.**

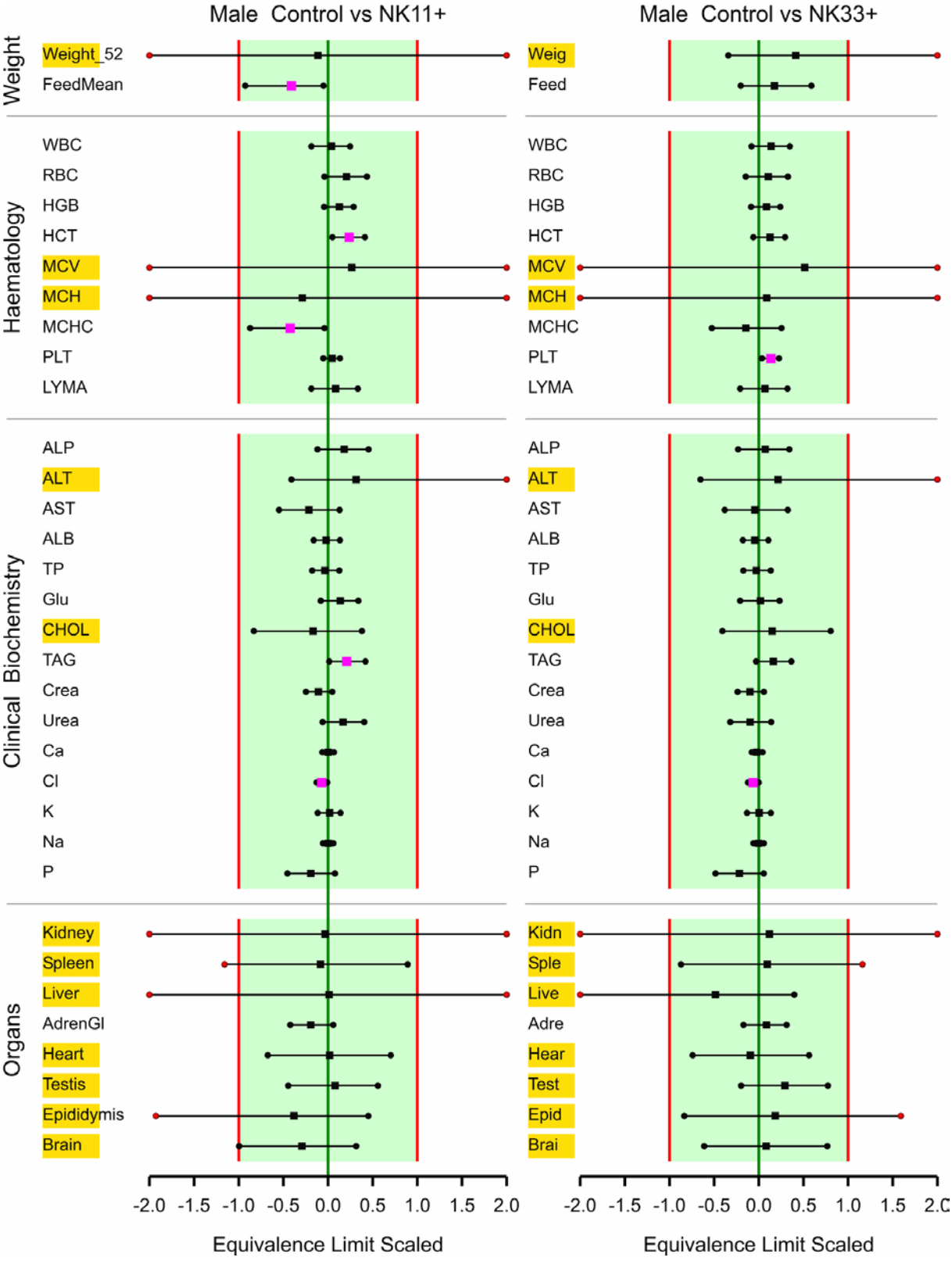

Figure 6 **Equivalence testing of NK11+ and NK33+ versus the control feed for males. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed. See Table 9, Figure 11 and Figure 12 for further interpretation. Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%). Fuchsia coloured symbols denote a significant difference.**

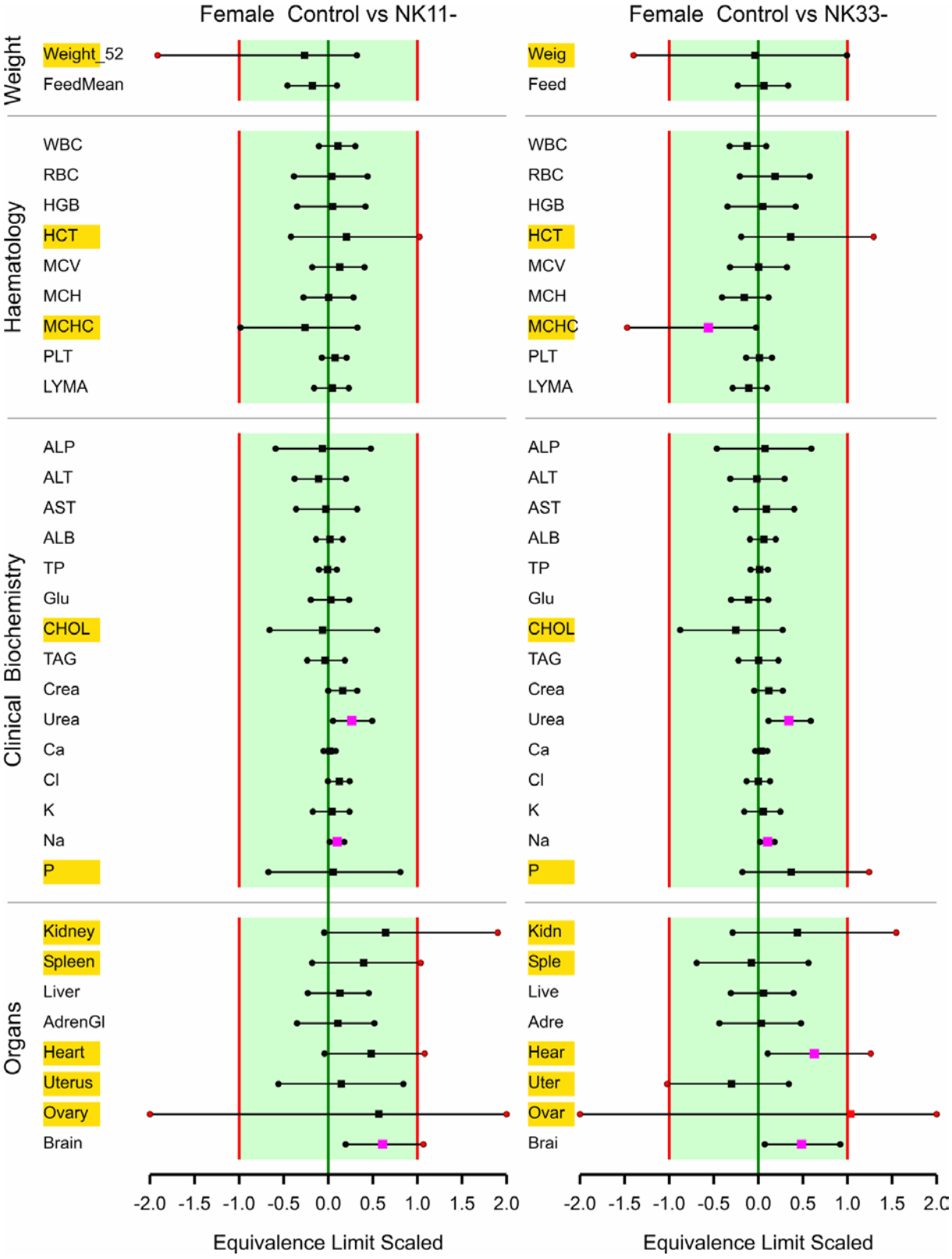

Figure 7 **Equivalence testing of NK11- and NK33- versus the control feed for females. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed. See Table 10, Figure 13 and Figure 14 for further interpretation. Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%). Fuchsia coloured symbols denote a significant difference.**

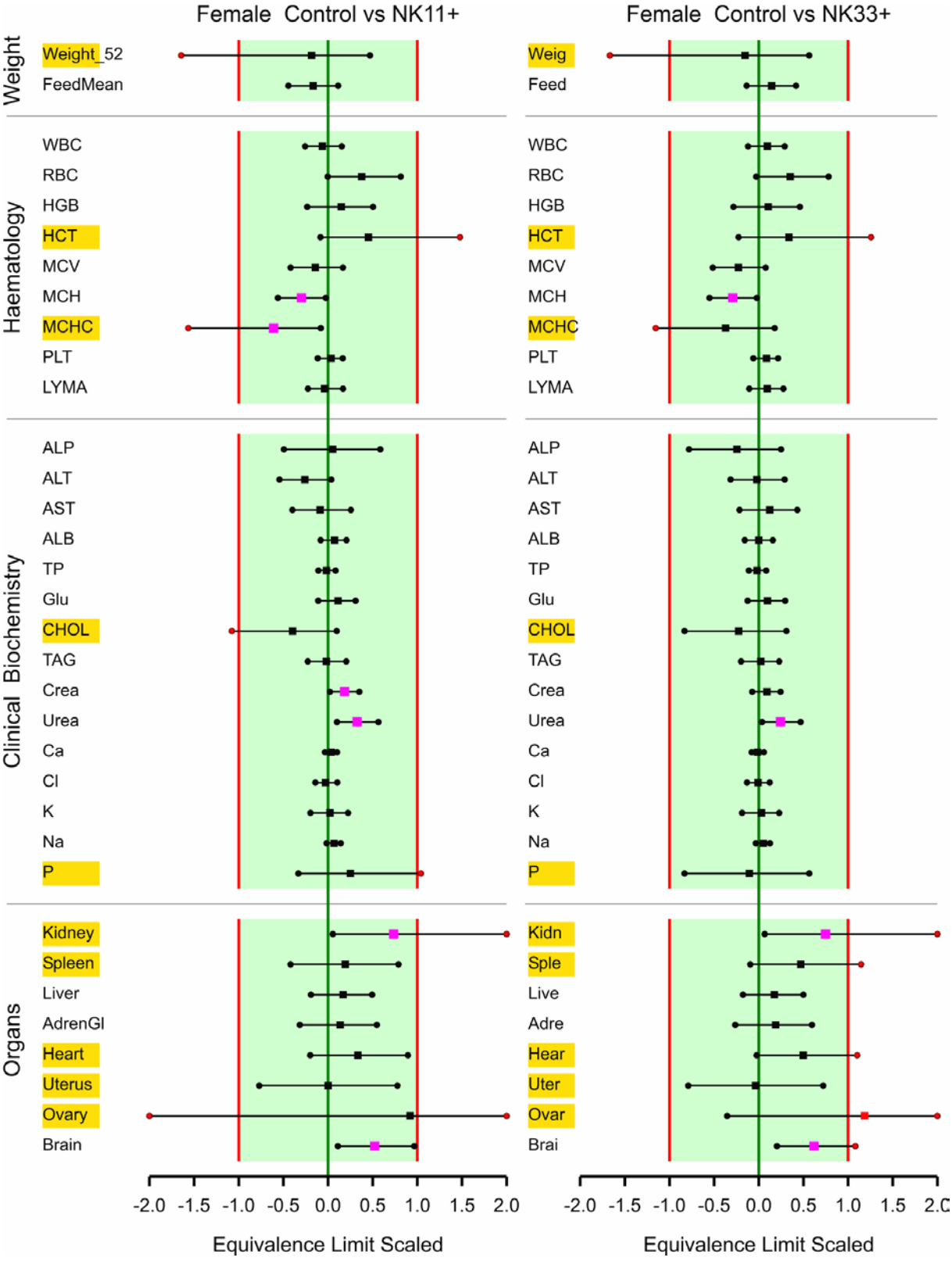

Figure 8 **Equivalence testing of NK11+ and NK33+ versus the control feed for females. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed. See Table 10, Figure 15 and Figure 16 for further interpretation. Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%). Fuchsia coloured symbols denote a significant difference.**

Table 9 95% Confidence interval plus estimate for the ratio Δ of the GMO feeds versus the Control feed for males. Intervals are based on an ANOVA with 5 feeding groups. Ratios with corresponding Intervals that do not encompass the value 1 are coloured red; this is equivalent to a significant difference according to a t-test with significance level 5%.

Weights	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Males	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
Weight_52	0.943	0.975	1.008	0.961	0.994	1.028	0.961	0.994	1.028	0.988	1.022	1.057
growthRate	0.861	0.956	1.060	0.922	1.022	1.132	0.909	1.007	1.117	1.020	1.131	1.254
FeedMean	0.931	0.958	0.985	0.948	0.975	1.003	0.941	0.968	0.996	0.986	1.014	1.043
Haematology	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Males	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
WBC	0.840	0.941	1.054	0.997	1.116	1.250	0.910	1.021	1.146	0.960	1.075	1.204
RBC	0.976	1.001	1.027	0.971	0.996	1.022	0.996	1.022	1.049	0.985	1.011	1.037
HGB	0.989	1.005	1.022	0.988	1.005	1.021	0.996	1.013	1.030	0.992	1.008	1.025
HCT	0.985	1.005	1.025	0.987	1.007	1.028	1.005	1.026	1.047	0.993	1.014	1.034
MCV	0.986	1.004	1.021	0.994	1.011	1.029	0.986	1.004	1.022	0.990	1.007	1.025
MCH	0.981	1.005	1.029	0.985	1.009	1.033	0.967	0.991	1.016	0.979	1.003	1.027
MCHC	0.989	1.001	1.012	0.985	0.997	1.009	0.975	0.987	0.999	0.984	0.996	1.007
PLT	0.933	0.989	1.048	1.015	1.076	1.141	0.969	1.028	1.090	1.021	1.082	1.147
LYMR	0.938	1.003	1.073	0.972	1.040	1.112	0.953	1.020	1.092	0.918	0.981	1.049
LYMA	0.850	0.965	1.095	1.021	1.159	1.316	0.916	1.042	1.185	0.911	1.034	1.174
ClinChem	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Males	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
ALP	0.965	1.070	1.186	0.928	1.028	1.139	0.960	1.065	1.182	0.926	1.026	1.137
ALT	0.915	1.012	1.119	0.883	0.977	1.080	0.950	1.052	1.166	0.937	1.036	1.146
AST	0.922	1.020	1.128	0.899	0.994	1.100	0.847	0.939	1.040	0.892	0.987	1.092
BIL	0.900	0.974	1.055	0.914	0.989	1.071	0.871	0.944	1.023	0.946	1.024	1.109
ALB	0.974	0.992	1.011	0.991	1.009	1.027	0.979	0.997	1.016	0.977	0.995	1.013
TP	0.977	0.991	1.006	0.991	1.005	1.020	0.983	0.997	1.011	0.983	0.997	1.012
Glu	0.934	1.004	1.080	0.916	0.985	1.059	0.973	1.047	1.127	0.936	1.006	1.082
CHOL	0.933	1.030	1.138	0.931	1.029	1.137	0.872	0.964	1.067	0.935	1.033	1.141
TAG	0.880	1.027	1.199	0.963	1.124	1.312	1.009	1.181	1.382	0.976	1.139	1.329
Crea	0.918	0.964	1.013	0.941	0.988	1.038	0.920	0.966	1.016	0.923	0.969	1.018
Urea	0.930	0.987	1.047	0.942	0.999	1.060	0.984	1.045	1.110	0.919	0.975	1.034

cHGB	0.769	0.927	1.118	0.877	1.057	1.275	0.851	1.029	1.245	0.869	1.047	1.262
Ca	0.990	1.000	1.010	0.993	1.003	1.012	0.990	1.000	1.010	0.987	0.997	1.006
Cl	0.987	0.995	1.002	0.981	0.989	0.996	0.984	0.992	0.999	0.985	0.992	1.000
K	0.964	0.996	1.029	0.983	1.015	1.049	0.972	1.005	1.039	0.969	1.001	1.034
Na	0.993	1.000	1.008	0.991	0.998	1.006	0.993	1.000	1.008	0.992	1.000	1.007
P	0.887	0.941	0.998	0.960	1.019	1.080	0.903	0.959	1.018	0.899	0.954	1.012
Urine	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Males	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
uVol	0.860	1.003	1.170	0.716	0.835	0.974	0.734	0.856	0.998	0.823	0.960	1.120
uVolW	0.860	1.007	1.181	0.710	0.832	0.975	0.712	0.834	0.977	0.801	0.939	1.100
uLeu	0.350	0.606	1.051	0.585	1.014	1.757	0.345	0.598	1.036	0.337	0.585	1.013
uOsmoll	0.882	1.012	1.161	1.031	1.182	1.357	0.998	1.145	1.314	0.942	1.081	1.240
uKeton	0.715	1.029	1.480	1.168	1.680	2.417	0.552	0.794	1.142	0.748	1.076	1.548
upH	0.666	0.875	1.151	0.800	1.051	1.382	0.841	1.105	1.453	0.655	0.861	1.132
Organs	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Males	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
Kidney	0.963	1.060	1.167	0.964	1.062	1.169	0.906	0.997	1.098	0.915	1.008	1.110
Spleen	0.932	1.043	1.168	0.974	1.090	1.221	0.880	0.986	1.104	0.907	1.016	1.138
Liver	0.927	0.996	1.070	0.941	1.011	1.086	0.932	1.001	1.076	0.890	0.957	1.028
AdrenGl	0.984	1.067	1.157	0.987	1.070	1.161	0.867	0.940	1.019	0.949	1.028	1.115
Heart	0.972	1.037	1.107	0.996	1.063	1.135	0.939	1.003	1.070	0.926	0.989	1.055
Testis	0.990	1.075	1.167	0.938	1.019	1.106	0.934	1.013	1.100	0.969	1.052	1.142
Epididymis	1.004	1.116	1.240	0.924	1.027	1.141	0.851	0.946	1.052	0.925	1.028	1.142
Brain	0.990	1.057	1.128	0.951	1.016	1.084	0.905	0.967	1.032	0.946	1.010	1.078

Table 10 95% Confidence interval plus estimate for the ratio Δ of the GMO feeds versus the Control feed for females. Intervals are based on an ANOVA with 5 feeding groups. Ratios with corresponding Intervals that do not encompass the value 1 are coloured red; this is equivalent to a significant difference according to a t-test with significance level 5%.

Weights	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Females	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
Weight_52	0.944	0.980	1.018	0.960	0.997	1.036	0.950	0.986	1.024	0.952	0.989	1.027
growthRate	0.776	0.903	1.051	0.904	1.052	1.224	0.848	0.986	1.148	0.828	0.963	1.121
FeedMean	0.952	0.981	1.010	0.977	1.007	1.037	0.953	0.982	1.012	0.986	1.016	1.046
Haematology	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Females	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
WBC	0.940	1.062	1.200	0.825	0.932	1.053	0.856	0.965	1.089	0.938	1.055	1.187
RBC	0.976	1.003	1.030	0.986	1.013	1.041	0.999	1.026	1.053	0.998	1.024	1.051
HGB	0.981	1.003	1.025	0.981	1.003	1.025	0.987	1.009	1.031	0.985	1.006	1.028
HCT	0.985	1.009	1.034	0.992	1.016	1.041	0.996	1.020	1.045	0.991	1.015	1.039
MCV	0.993	1.005	1.017	0.988	1.000	1.012	0.983	0.994	1.006	0.980	0.991	1.003
MCH	0.983	1.000	1.018	0.973	0.990	1.008	0.965	0.982	0.999	0.966	0.982	0.999
MCHC	0.981	0.994	1.007	0.974	0.987	1.000	0.973	0.985	0.998	0.979	0.991	1.004
PLT	0.970	1.030	1.093	0.947	1.005	1.067	0.956	1.013	1.075	0.977	1.034	1.096
LYMR	0.954	1.006	1.061	0.958	1.009	1.063	0.958	1.008	1.061	0.967	1.017	1.069
LYMA	0.917	1.026	1.148	0.844	0.944	1.056	0.877	0.979	1.093	0.945	1.053	1.173
ClinChem	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Females	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
ALP	0.869	0.983	1.113	0.901	1.020	1.154	0.898	1.014	1.145	0.834	0.940	1.059
ALT	0.809	0.946	1.107	0.848	0.992	1.160	0.750	0.875	1.021	0.851	0.989	1.151
AST	0.867	0.990	1.129	0.907	1.036	1.182	0.849	0.966	1.100	0.923	1.049	1.191
BIL	0.840	0.924	1.017	0.874	0.962	1.058	0.879	0.965	1.060	0.870	0.954	1.046
ALB	0.972	1.004	1.037	0.980	1.013	1.046	0.983	1.015	1.048	0.969	1.000	1.032
TP	0.979	0.999	1.018	0.984	1.003	1.023	0.978	0.997	1.016	0.978	0.996	1.015
Glu	0.938	1.010	1.087	0.897	0.965	1.039	0.965	1.037	1.115	0.962	1.032	1.108
CHOL	0.889	0.987	1.096	0.854	0.949	1.054	0.831	0.921	1.021	0.863	0.955	1.056
TAG	0.826	0.974	1.148	0.851	1.002	1.181	0.839	0.986	1.159	0.868	1.017	1.192
Crea	0.998	1.052	1.110	0.984	1.038	1.095	1.006	1.060	1.118	0.978	1.029	1.084
Urea	1.015	1.081	1.151	1.038	1.106	1.177	1.034	1.100	1.170	1.012	1.075	1.142

cHGB	0.731	0.884	1.068	0.811	0.981	1.185	0.800	0.964	1.161	0.807	0.969	1.162
Ca	0.991	1.003	1.015	0.994	1.006	1.018	0.994	1.006	1.017	0.986	0.998	1.009
Cl	0.999	1.008	1.017	0.991	1.000	1.009	0.990	0.998	1.007	0.991	0.999	1.008
K	0.959	1.010	1.065	0.962	1.014	1.068	0.955	1.005	1.058	0.958	1.007	1.059
Na	1.001	1.007	1.012	1.001	1.007	1.013	0.999	1.004	1.010	0.998	1.003	1.009
P	0.906	1.011	1.129	0.965	1.078	1.204	0.944	1.053	1.173	0.880	0.979	1.089
Urine	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Females	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
uVol	0.738	0.898	1.092	0.824	0.998	1.208	0.833	1.008	1.221	0.771	0.934	1.131
uVolW	0.775	0.948	1.160	0.830	1.011	1.232	0.842	1.025	1.249	0.795	0.969	1.180
uLeu	0.555	1.036	1.935	0.816	1.504	2.770	0.493	0.909	1.674	0.606	1.116	2.056
uOsmoll	0.875	1.037	1.230	0.846	0.999	1.180	0.817	0.964	1.139	0.903	1.067	1.259
uKeton	0.886	1.169	1.541	0.876	1.148	1.505	0.641	0.840	1.100	0.852	1.116	1.463
upH	0.715	0.895	1.121	0.738	0.920	1.147	0.948	1.181	1.472	0.714	0.890	1.109
Organs	**NK11- vs Control**			**NK33- vs Control**			**NK11+ vs Control**			**NK33+ vs Control**		
Females	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper	Lower	Ratio	Upper
Kidney	0.996	1.071	1.152	0.974	1.048	1.127	1.006	1.081	1.163	1.007	1.083	1.165
Spleen	0.965	1.087	1.224	0.874	0.984	1.108	0.925	1.042	1.173	0.981	1.105	1.245
Liver	0.960	1.025	1.094	0.947	1.011	1.080	0.967	1.032	1.102	0.968	1.034	1.104
AdrenGl	0.911	1.031	1.167	0.892	1.010	1.143	0.919	1.040	1.178	0.932	1.055	1.195
Heart	0.995	1.063	1.136	1.014	1.083	1.157	0.977	1.043	1.115	0.997	1.065	1.138
Uterus	0.851	1.053	1.304	0.726	0.899	1.113	0.808	1.000	1.239	0.797	0.987	1.223
Ovary	0.867	1.110	1.420	0.940	1.202	1.539	0.922	1.180	1.509	0.963	1.233	1.577
Brain	1.032	1.100	1.173	1.012	1.079	1.151	1.018	1.085	1.157	1.033	1.102	1.175

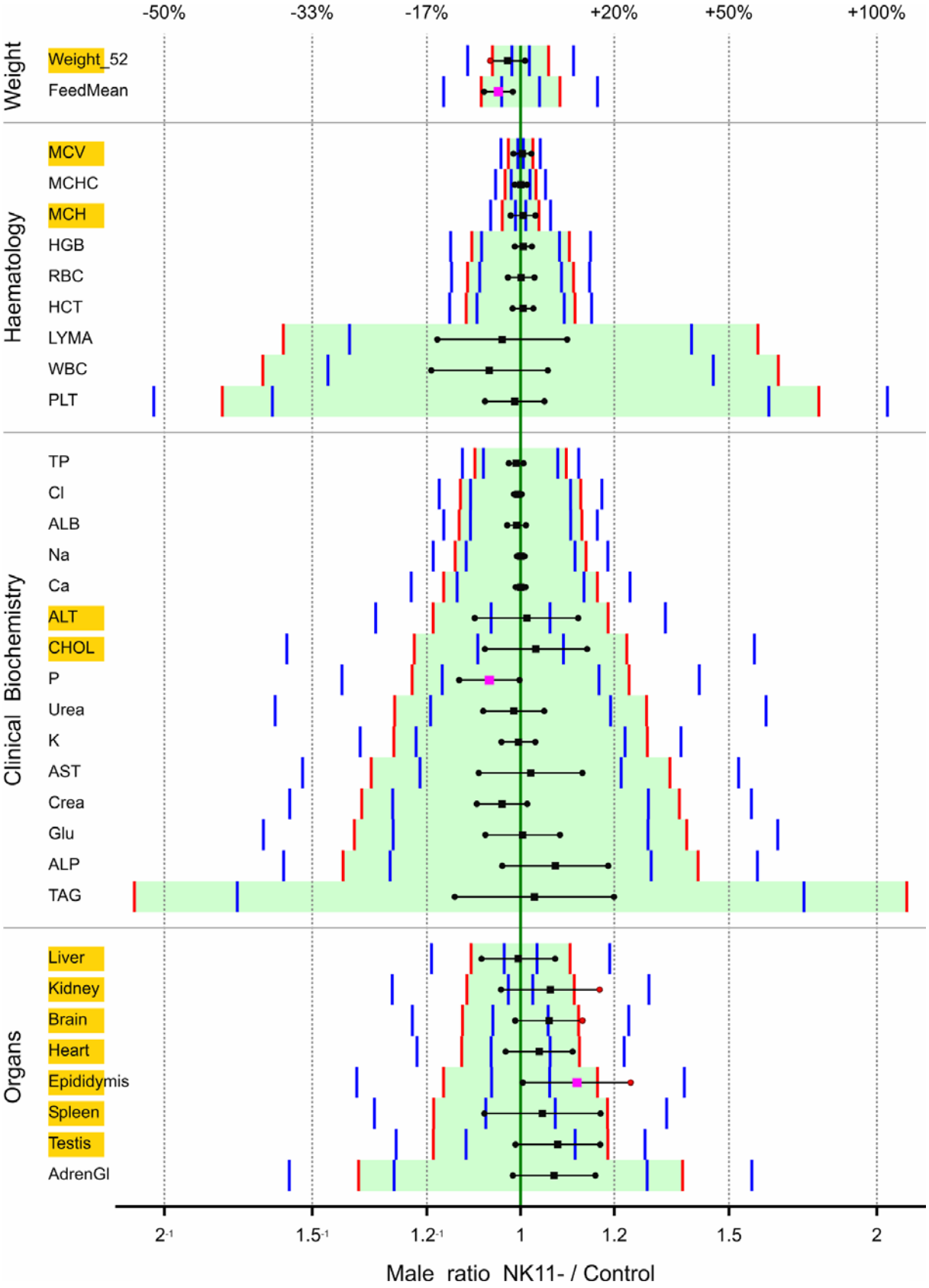

Figure 9 **95% confidence intervals for the ratio of NK11- and the Control feed for males with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).**

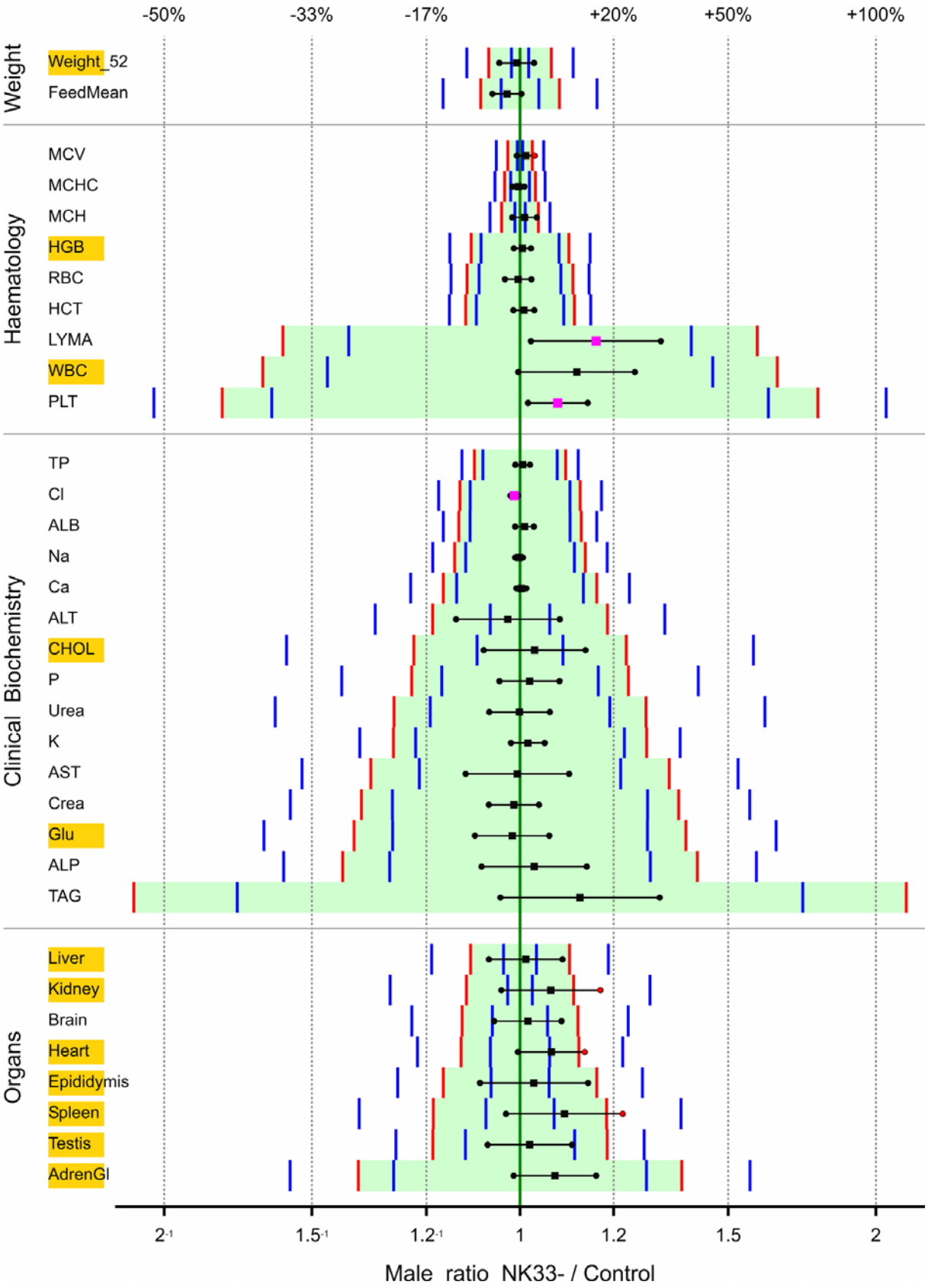

Figure 10 95% confidence intervals for the ratio of NK33- and the Control feed for males with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

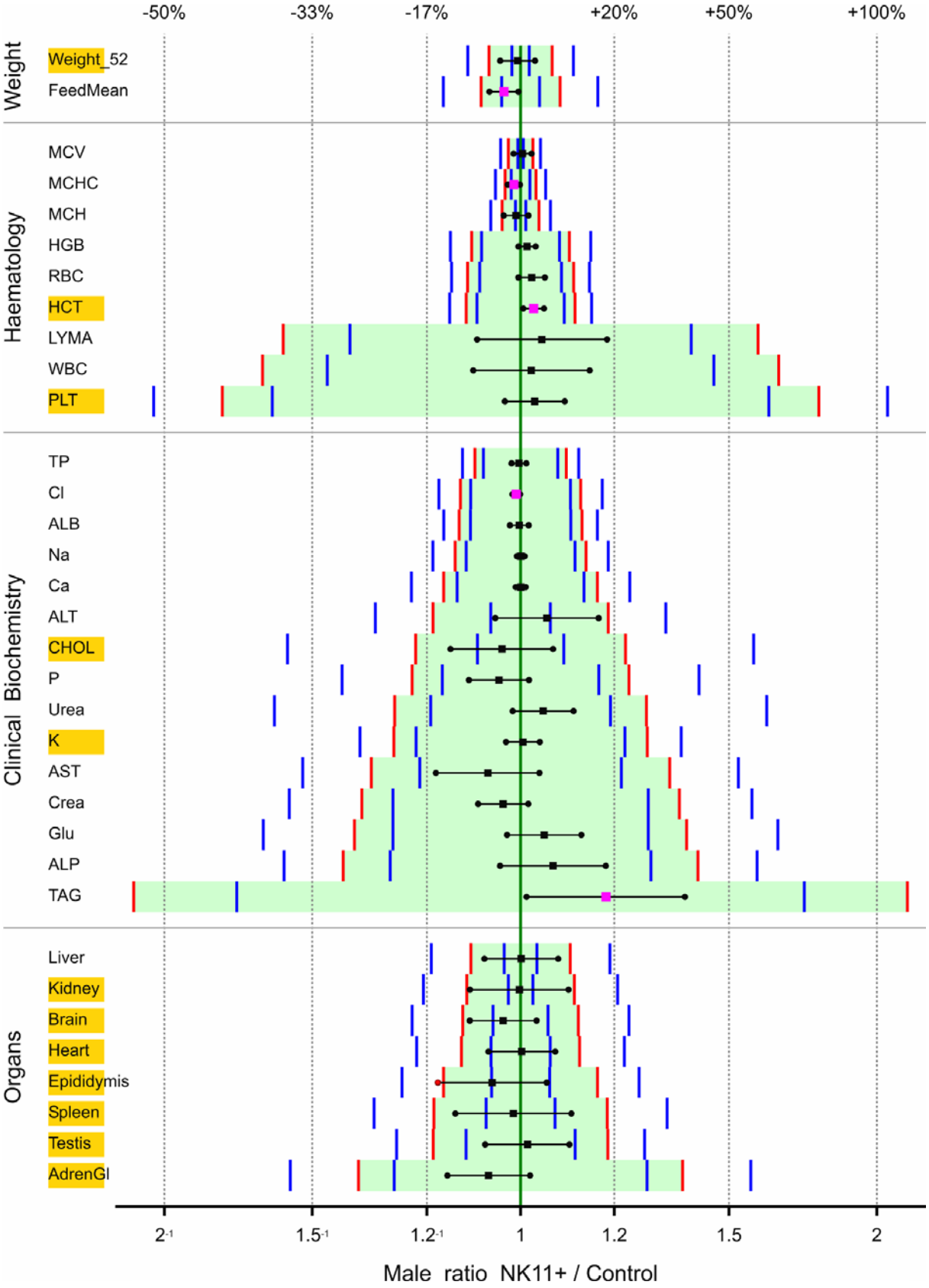

Figure 11 95% confidence intervals for the ratio of NK11+ and the Control feed for males with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

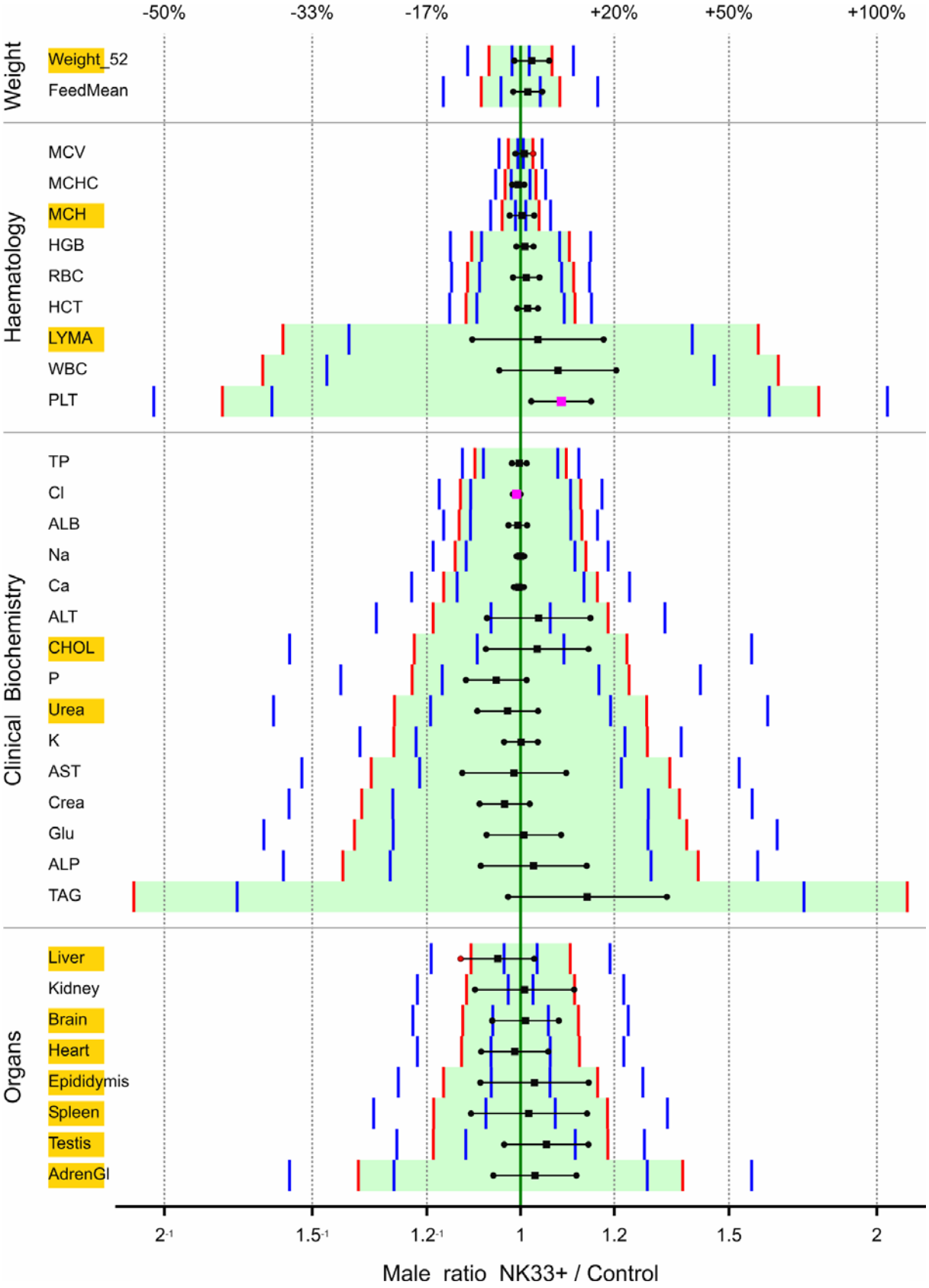

Figure 12 95% confidence intervals for the ratio of NK33+ and the Control feed for males with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

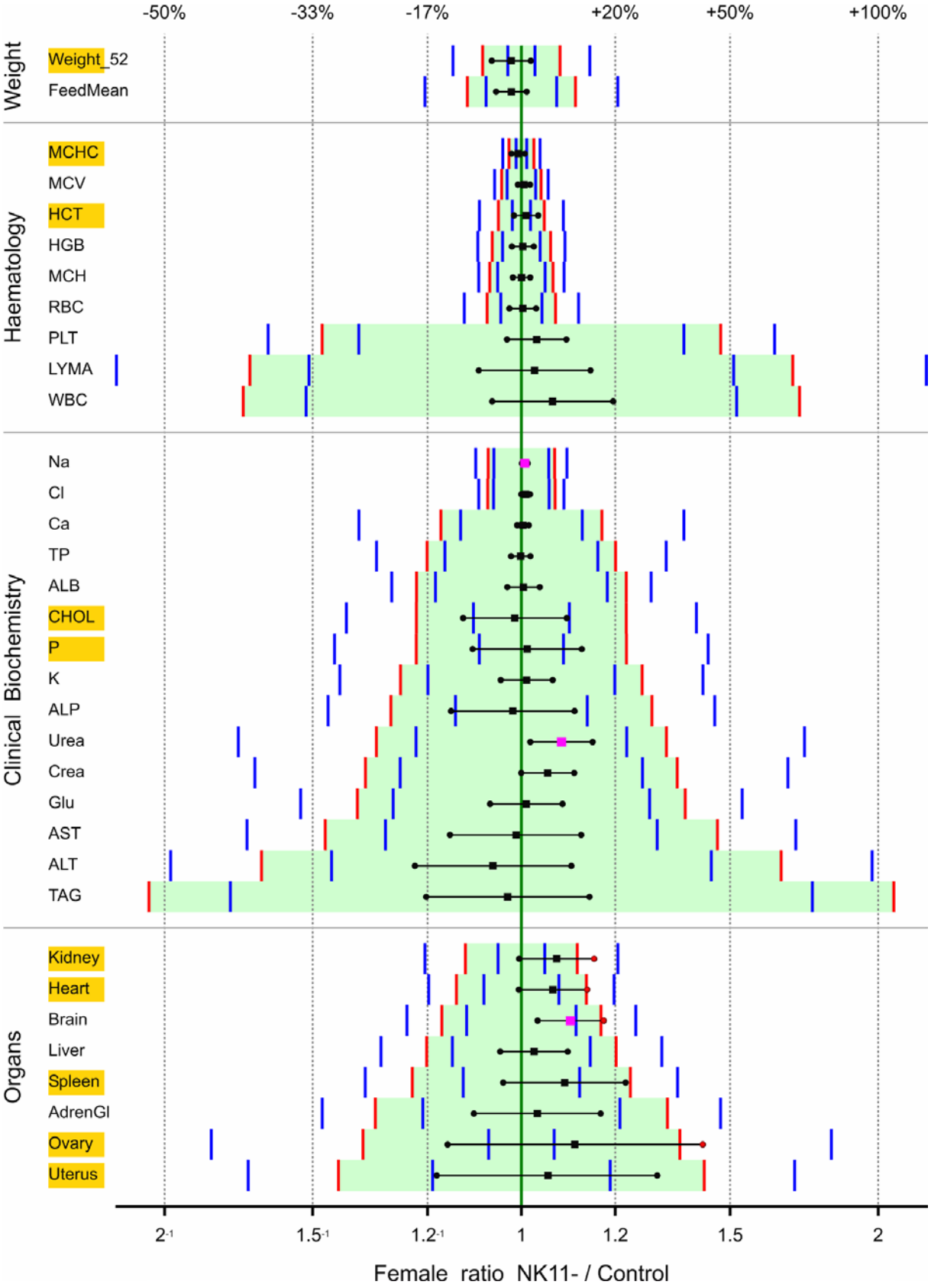

Figure 13 95% confidence intervals for the ratio of NK11- and the Control feed for females with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

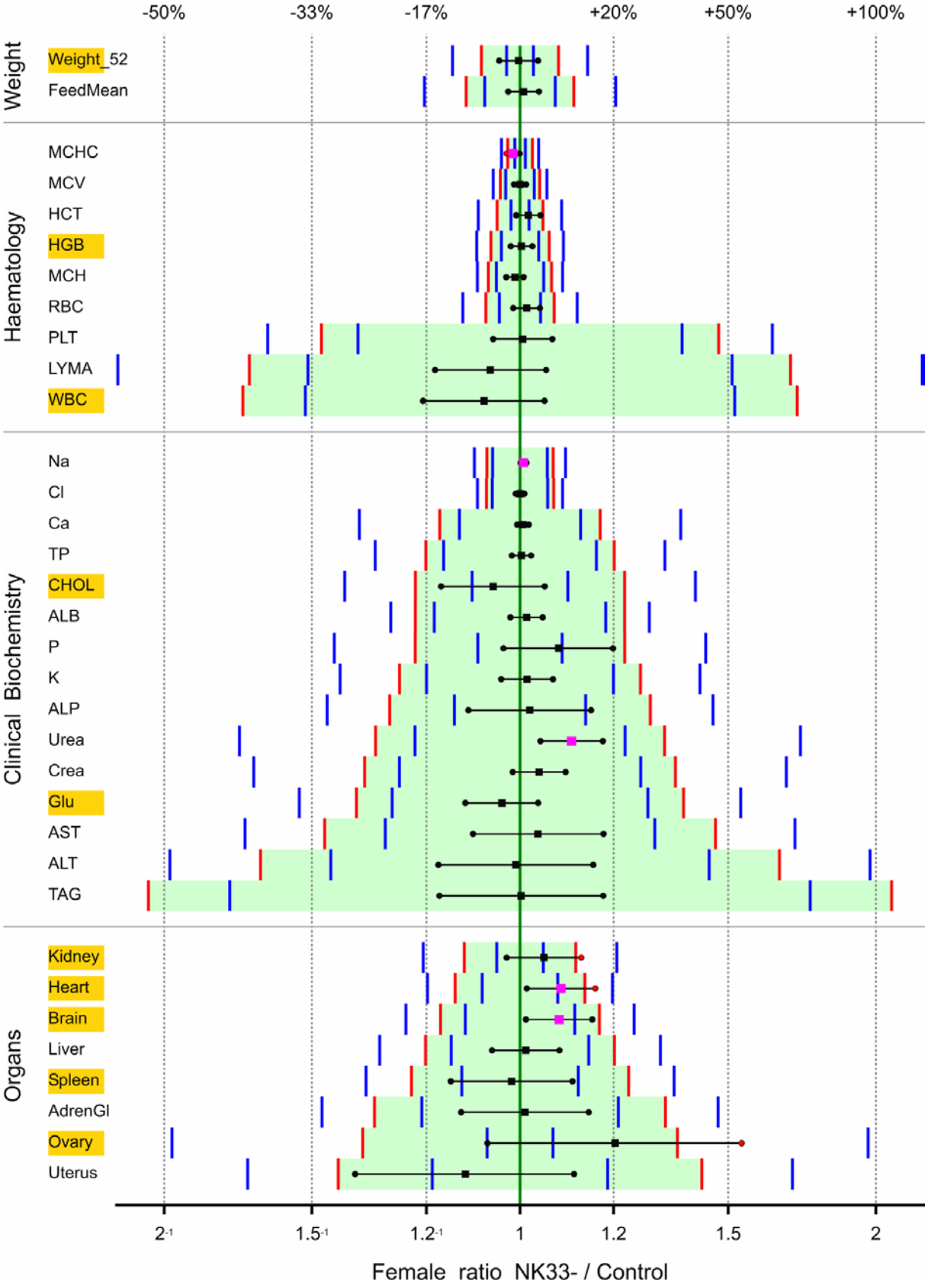

Figure 14 95% confidence intervals for the ratio of NK33- and the Control feed for females with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

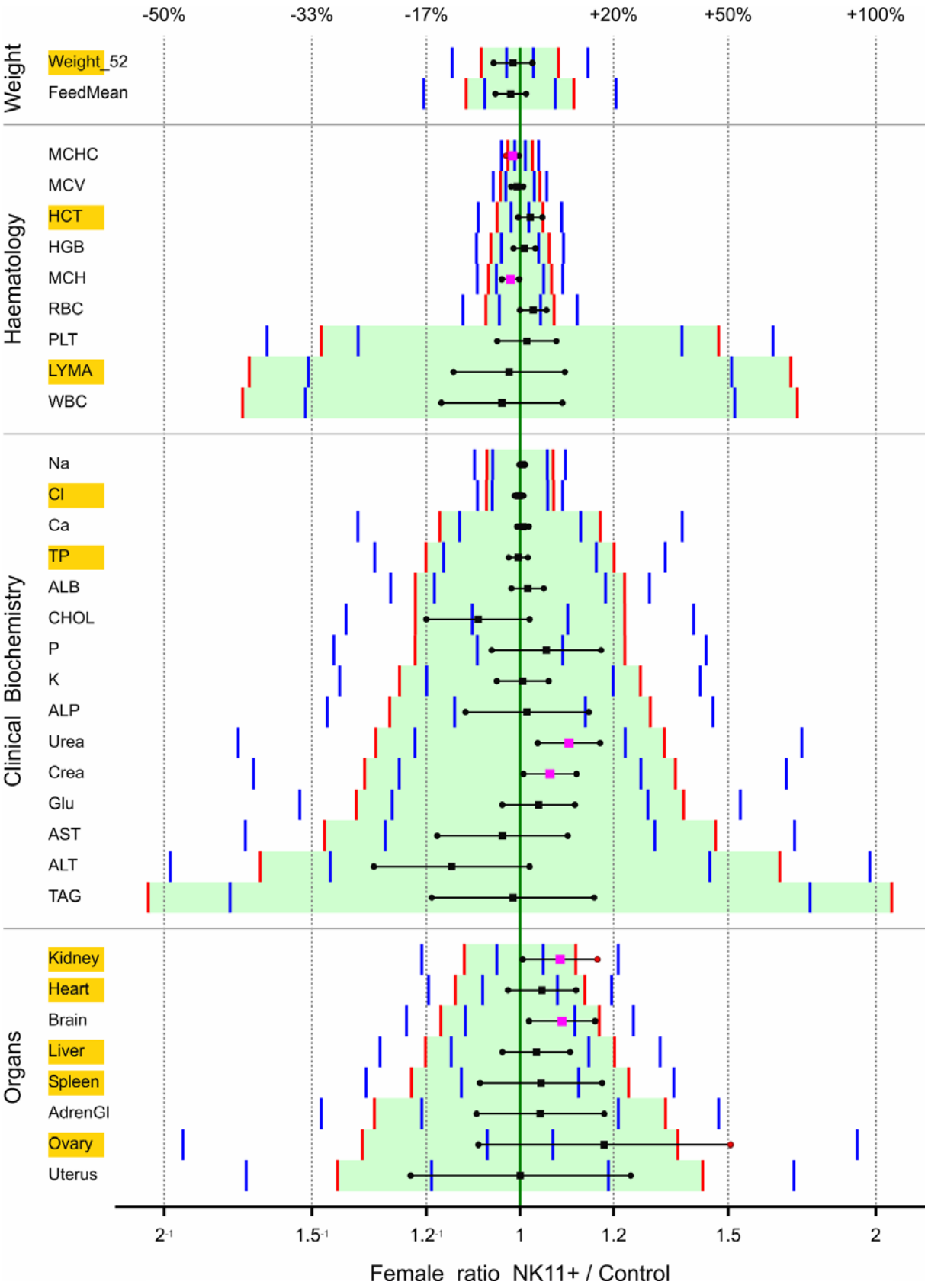

Figure 15 95% confidence intervals for the ratio of NK11+ and the Control feed for females with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

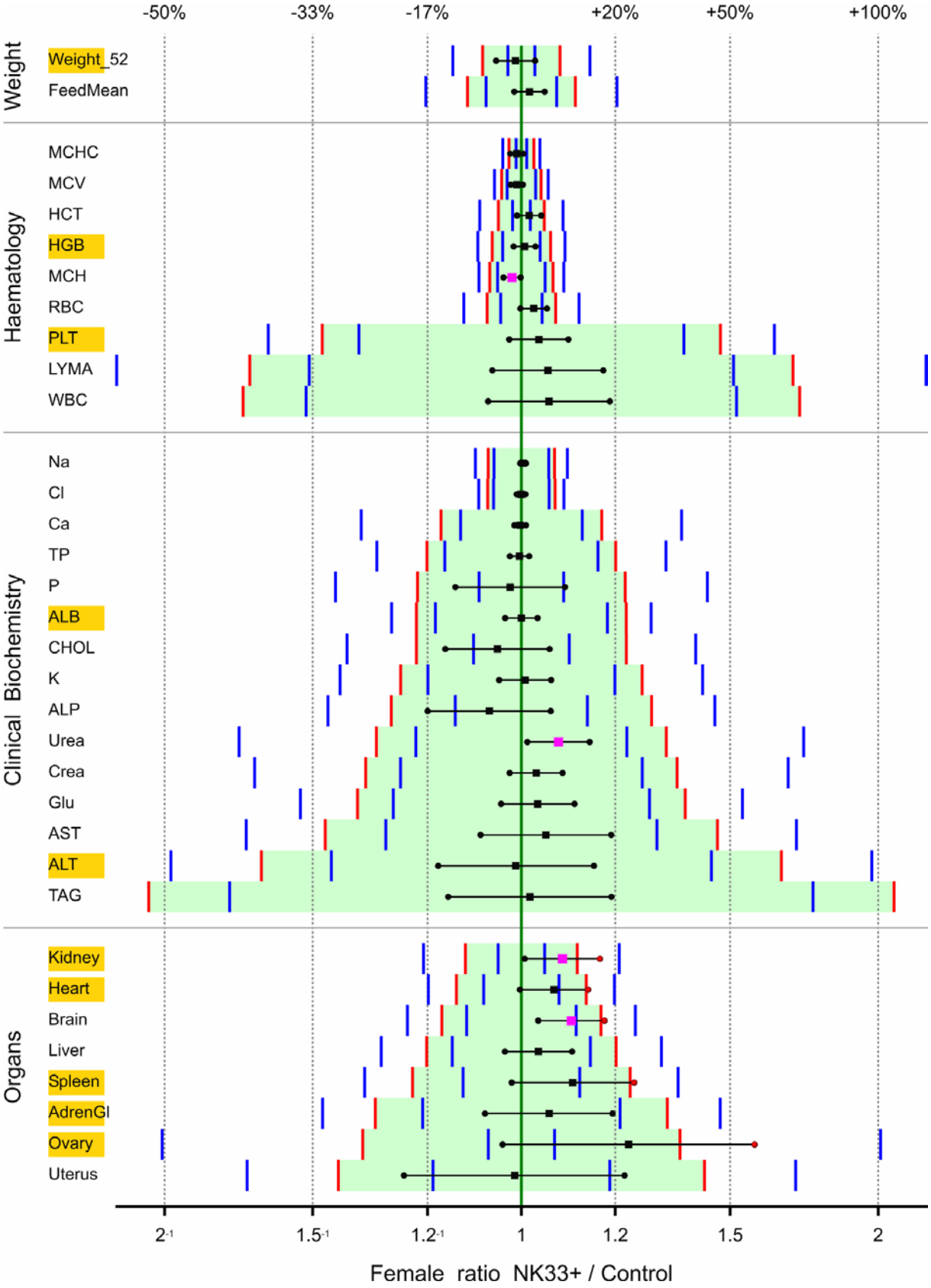

Figure 16 95% confidence intervals for the ratio of NK33+ and the Control feed for females with added intervals for the equivalence limits (blue and red bars, see text).

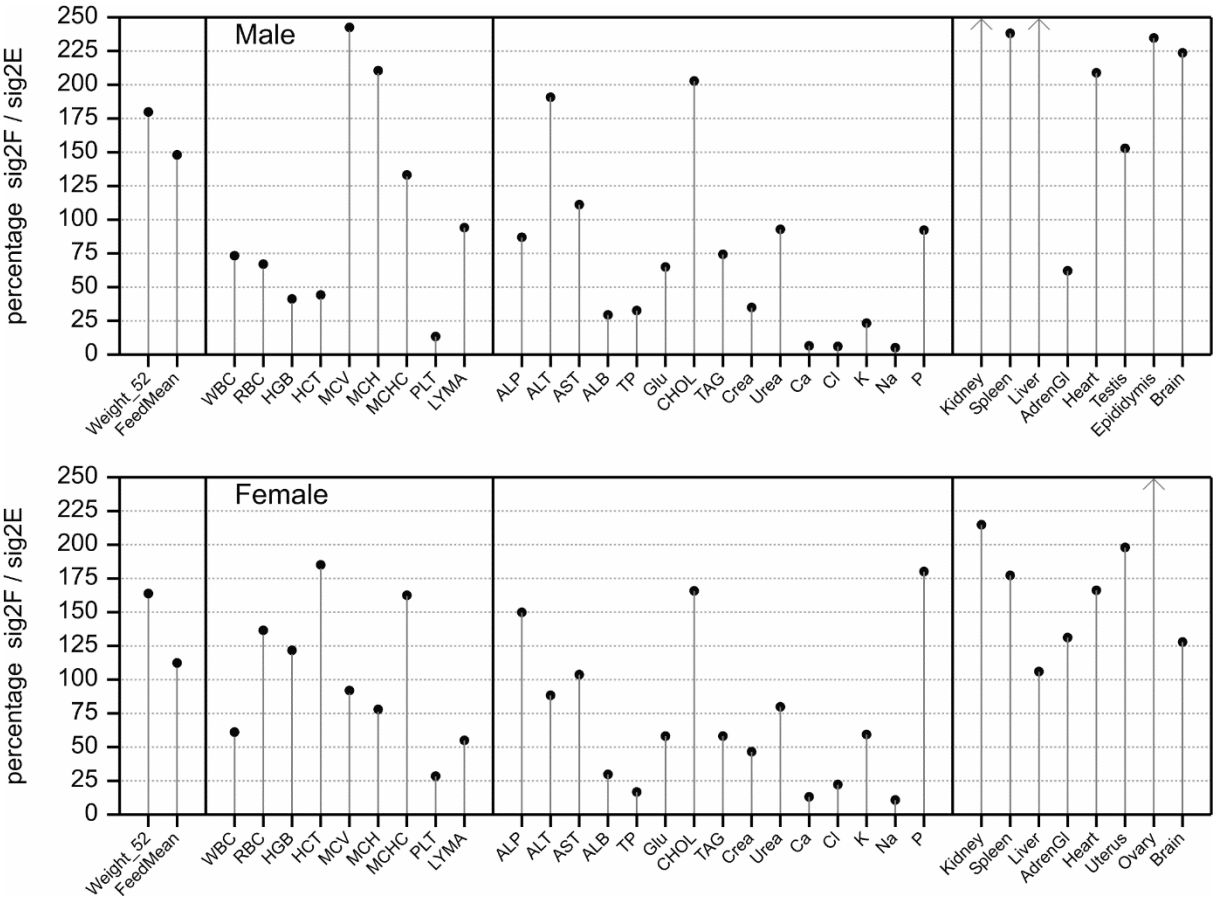

Figure 17 Residual variance (sig2F or σ_F^2) in the current G-TwYST A study as a percentage of the residual variance (sig2E or σ_E^2) in the historical GRACE studies for males (top panel) and females (bottom panel).

3.2 Equivalence testing using target effect sizes

90% confidence intervals for 9 variables, with equivalence limits according to the targeted effect sizes in Hong *et al.* (2017), are given in Figure 18 for males and in Figure 19 for females. Note that these are 90% intervals, rather than the 95% intervals in Figure 9 to Figure 16. In all cases the null hypothesis of non-equivalence is rejected with most p-values smaller than 0.001 (Table 11).

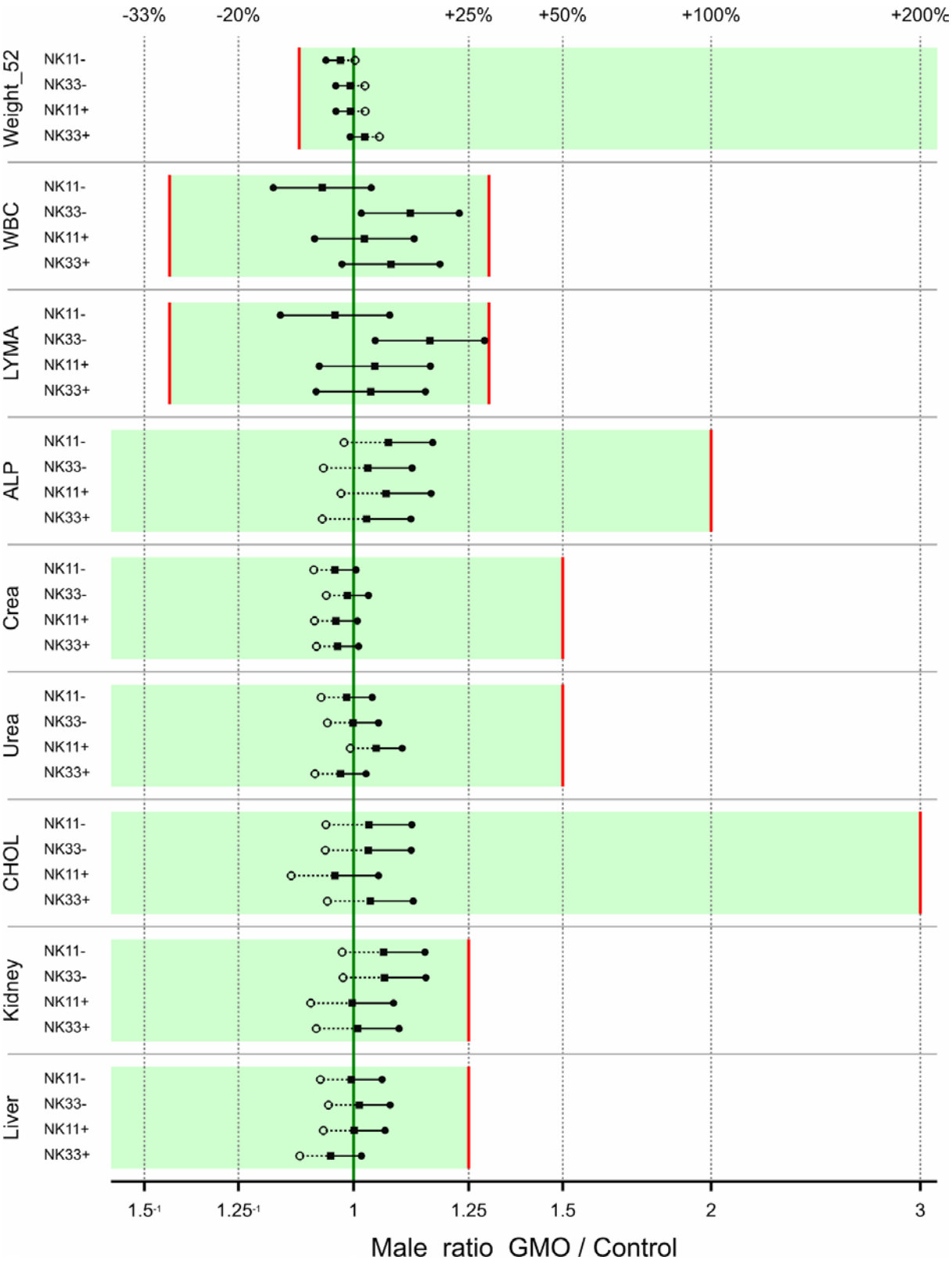

Figure 18 90% confidence intervals for the ratio of the mean of the GMO feed and the control feed for selected variables for males along with equivalence intervals defined by targeted effect sizes of Hong *et al.* (2017).

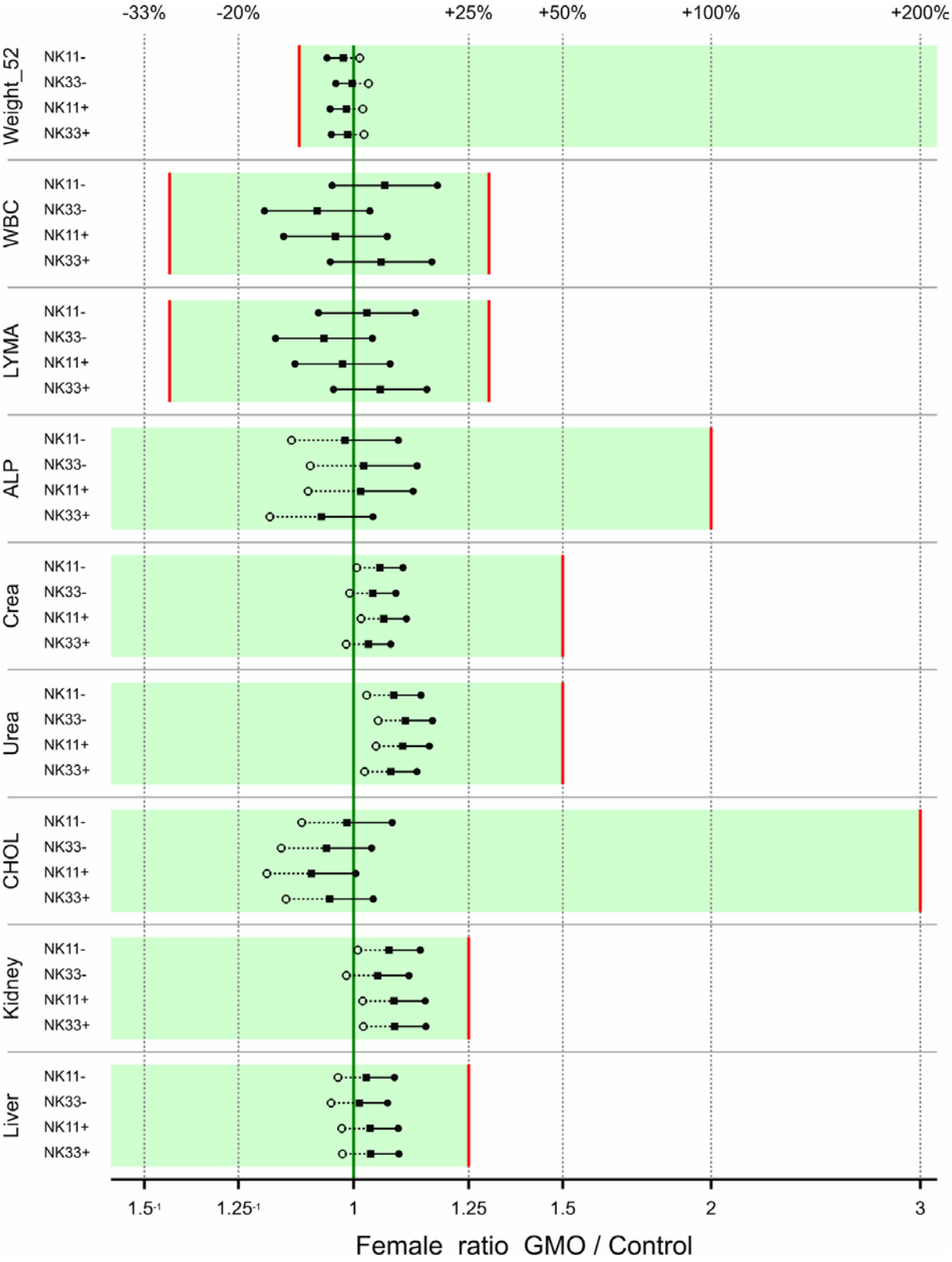

Figure 19 90% confidence intervals for the ratio of the mean of the GMO feed and the control feed for selected variables for females along with equivalence intervals defined by targeted effect sizes of Hong *et al.* (2017).

Table 11 P-values of equivalence tests for the ratio of the mean of the GMO feed versus the mean of the control feed using targeted effect sizes of Hong *et al.* (2017) as equivalence limits. P-values smaller than 0.01/0.05 have a gold/yellow background.

Variable	Males				Females			
	NK11-	NK33-	NK11+	NK33+	NK11-	NK33-	NK11+	NK33+
Weight_52	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
WBC	0.000	0.005	0.000	0.001	0.001	0.000	0.000	0.000
LYMA	0.000	0.038	0.001	0.000	0.000	0.000	0.000	0.000
ALP	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Crea	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Urea	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
CHOL	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Kidney	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000
Liver	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

3.3 Classical statistical analysis

A classical analysis of variance was performed on the cage means after log transforming the data. Note that the ANOVA residuals were already assessed by means of a normal probability plot (Appendix 5) and a plot of residuals versus fitted values (Appendix 6). Table 12 (males) and Table 13 (females) present the results of the t-tests, of Dunnett's tests and of Wilcoxon tests for the 44 variables divided in five groups. For ease of interpretation results are expressed as means and coefficients of variation on the original scale, rather than as means and standard deviations on the log scale. Note however that 95% confidence intervals on the ratio scale are given in Table 9 (males) and Table 10 (females).

Results of the t-test and Dunnett's test for the difference are summarized by letters which indicate significance at 5% and at 1%. Results for the non-parametric Wilcoxon test, where each test only uses data for the specific GM feed and the non-GM Control feed, are summarized in the same way. Exact p-values for these tests are given in Appendix 9.

It can be seen (Table 12 and Table 13) that the relative precision of variables ranges from high to low precision. CVs smaller than 10% are observed for many variables, while CVs larger than 50% are observed for cHGB, uLeu and uKeton. For cHGB, growthRate, uLeu and uKeton there is a large difference in precision for males and females.

In 46 cases (13% of the 352 comparisons) a difference was significant in at least one of the tests at the 5% level. On their own, Dunnett's test resulted in 10 significant differences (2.8%), the t-test resulted in 38 significant differences (11%), and Wilcoxon's test resulted in 32 significant differences (9%). Note that cells coloured red in Table 9 and Table 10, with 95% confidence intervals for ratios, correspond to cells coloured red in Table 12 and Table 13 with letters "t", "T", "d" or "D".

Results of the Shapiro-Wilks test for normality and Bartlett's and Levene's test for homogeneity of variance are given in Appendix 10. Bartlett's' test is significant at the 5% level for males for 3 variables (FeedMean, HGB, Glu) and for females also for 3 variables (LYMR, TAG, uKeton). Levene's test is significant for uOsmoll in males, and for 5 variables in females (LYMR, TAG, uOsmoll, uKeton, Ovary). This implies that the important assumption of homogeneity of variance is generally fulfilled.

For these significant cases, one might resort to Wilcoxon's test which is, for these cases, only significant for FeedMean in males (NK11-, NK33- and NK11+).

The Shapiro-Wilks test for non-normality for separate feeding groups (Appendix 10) is frequently significant. However the normality assumptions is not very important. Moreover normal probability plots (Appendix 5) and plots of residuals versus fitted values (Appendix 6) were generally satisfactory. Also, graphs of cage means on the log scale in Appendix 4 indicate that significance of non-normality seems mostly due to one outlying observation in a feeding group.

3.4 Standardized effect sizes

SES intervals were calculated for all 44 variables. Results for the four treatment groups, separately for males and females, are given in Figure 20 to Figure 23. The number of intervals that extend outside the -/+ 1 SD limits equals 141 out of 352 (40%).

Table 12 Means and coefficient of variation (CV) for male rats. Means of GM feeds which are significantly different from the non-GM Control feed are marked, with red background colouring, as follows: D: P<0.01 by Dunnett-test, d: P<0.05 by Dunnett-test, T: P<0.01 by t-test but not by Dunnett-test, t: P<0.05 by t-test but not by Dunnett-test, W: P<0.01 by Wilcoxon signed rank test, w: P<0.05 by Wilcoxon signed rank test. Dunnett- and t-tests are based on an ANOVA with 5 treatment groups, while Wilcoxon tests only uses data for the specific GM feed and the control feed.

Weights	Control		NK11-			NK33-			NK11+			NK33+		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
Weight_52	599.1	6.9	586.1	10.3		597.7	9.4		596.8	9.1		614.1	9.8	
growthRate	1.372	15.5	1.322	20.1		1.394	16.6		1.380	17.2		1.495	17.6	tw
FeedMean	19.42	4.6	18.63	7.2	dTW	19.02	7.7	w	18.83	7.3	tW	19.73	7.4	
Haematology	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
WBC	7.657	20.8	7.197	20.9		8.570	18.6		7.807	15.1		8.155	13.2	
RBC	8.482	3.2	8.496	4.1		8.453	4.5		8.647	4.0		8.582	5.2	
HGB	15.82	1.7	15.91	3.1		15.90	3.1		15.99	2.8		15.96	3.8	
HCT	46.12	2.8	46.34	3.3		46.49	4.5		47.19	2.9	tw	46.77	4.6	
MCV	54.41	2.9	54.61	2.9		55.03	2.8		54.63	2.8		54.81	2.2	
MCH	18.68	3.4	18.77	3.9		18.85	3.9		18.53	4.1		18.74	3.5	
MCHC	34.33	1.7	34.35	2.2		34.23	2.6		33.89	1.9	tw	34.18	2.1	
PLT	813.8	8.2	807.0	7.5		878.7	9.6	d	834.4	9.7		882.5	9.5	dTW
LYMR	66.92	13.1	66.78	7.5		69.53	12.8		67.55	12.0		65.49	12.0	
LYMA	5.127	24.4	4.978	23.8		5.900	20.9	t	5.255	16.2		5.315	20.7	
ClinChem	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
ALP	1.231	17.7	1.332	19.5		1.262	16.3		1.312	16.1		1.263	17.7	
ALT	0.659	17.2	0.679	28.6		0.643	16.9		0.720	24.6		0.690	19.8	
AST	2.304	16.6	2.386	21.8		2.291	14.6		2.281	23.8		2.319	25.0	
BIL	7.100	22.8	6.820	15.0		6.942	14.8		6.712	17.1		7.197	15.8	
ALB	37.66	3.2	37.38	2.8		37.99	2.7		37.46	2.9		37.46	3.6	
TP	68.99	2.6	68.40	2.6		69.34	2.2		68.77	3.0		68.81	2.6	
Glu	5.354	11.1	5.426	15.1		5.263	8.9		5.687	20.4		5.396	11.2	
CHOL	2.738	12.8	2.820	13.6		2.854	17.4		2.643	17.1		2.882	22.6	
TAG	1.781	33.0	1.821	24.6		2.011	28.6		2.048	32.5	tw	2.008	28.0	

Crea	43.72	11.0	42.08	7.8		43.05	5.8		42.12	7.9		42.28	8.6	
Urea	4.372	9.0	4.323	11.4		4.376	10.6		4.579	12.6		4.282	12.7	
cHGB	65.01	51.8	57.30	28.4		66.60	31.0		67.57	49.3		65.92	34.7	
Ca	2.545	1.3	2.545	2.0		2.552	1.8		2.542	2.4		2.537	1.7	
Cl	103.6	1.3	103.0	1.5		102.4	1.3	dTW	102.6	1.8	tw	102.8	1.6	t
K	4.805	7.1	4.775	4.8		4.880	6.1		4.815	5.4		4.803	5.7	
Na	143.5	1.4	143.5	1.3		143.2	1.1		143.6	1.6		143.4	1.9	
P	1.775	9.5	1.672	11.2	tW	1.812	15.2		1.713	9.8		1.693	9.3	w
Urine	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
uVol	15.57	22.4	15.23	17.8		12.90	25.4	t	13.09	31.4	t	14.80	20.6	
uVolW	2.672	25.7	2.625	21.6		2.193	26.1	t	2.212	33.2	t	2.475	24.9	
uLeu	275.8	55.5	174.2	80.9		285.0	49.4		157.0	87.8	w	168.3	86.6	
uOsmoll	560.6	19.0	558.0	20.4		645.6	14.5	t	649.6	26.5		594.8	14.4	
uKeton	0.517	76.4	0.550	87.9		0.917	30.3	dTw	0.359	101.5		0.550	82.8	
upH	6.767	4.3	6.633	5.1		6.817	5.3		6.875	5.5		6.617	6.5	
Organs	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
Kidney	0.447	9.5	0.472	7.7	w	0.477	17.1		0.446	11.1		0.449	9.8	
Spleen	0.166	10.6	0.173	7.7		0.181	9.6		0.166	18.6		0.169	10.1	
Liver	2.101	9.2	2.084	10.2		2.113	6.5		2.088	5.8		2.006	10.0	
AdrenGl	0.00883	8.8	0.00942	8.4	w	0.00948	13.4		0.00832	9.9		0.00913	10.5	
Heart	0.204	5.4	0.212	9.2		0.218	10.9		0.205	4.1		0.202	6.2	
Testis	0.640	7.1	0.691	11.9		0.653	11.8		0.649	9.2		0.676	11.5	
Epididymis	0.218	11.1	0.244	11.5	tw	0.224	13.3		0.207	13.1		0.225	13.2	
Brain	0.382	7.4	0.404	11.2		0.389	9.8		0.370	11.2		0.386	10.1	

Table 13 Means and coefficient of variation (CV) for female rats. Means of GMO feeds which are significantly different from the Control feed are marked, with red background colouring, as follows: D: P<0.01 by Dunnett-test, d: P<0.05 by Dunnett-test, T: P<0.01 by t-test but not by Dunnett-test, t: P<0.05 by t-test but not by Dunnett-test, W: P<0.01 by Wilcoxon signed rank test, w: P<0.05 by Wilcoxon signed rank test. Note that Dunnett- and t-tests are based on a ANOVA with 5 treatment groups, while Wilcoxon tests only uses data for the specific GM feed and the control feed.

Weights	Control		NK11-			NK33-			NK11+			NK33+		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
Weight_52	340.3	10.9	332.9	9.5		339.1	9.5		335.7	10.6		336.0	9.3	
growthRate	0.984	33.0	0.882	39.3		1.034	32.7		0.970	37.8		0.946	33.1	
FeedMean	14.18	6.6	13.93	8.4		14.29	6.7		13.94	7.3		14.41	6.4	
Haematology	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
WBC	5.565	24.0	5.935	25.8		5.130	18.7		5.447	21.8		5.877	21.8	
RBC	7.368	4.9	7.368	4.2		7.444	4.8		7.547	3.9	w	7.543	3.3	
HGB	15.45	3.4	15.44	3.4		15.46	3.3		15.57	3.1		15.54	3.5	
HCT	43.23	4.6	43.43	4.4		43.79	3.7	w	44.06	3.5		43.87	3.1	
MCV	58.70	1.5	58.94	2.0		58.71	2.1		58.41	1.7		58.19	2.0	
MCH	20.99	2.6	21.00	2.9		20.81	3.6		20.62	2.0	tW	20.61	2.4	t
MCHC	35.76	2.0	35.58	2.4		35.32	2.1	tw	35.25	1.8	tw	35.45	2.3	
PLT	755.1	10.0	792.4	13.0		751.4	9.9		764.1	10.3		783.7	12.4	
LYMR	69.94	10.6	70.03	7.8		71.43	10.5		70.00	8.7		70.64	5.2	
LYMA	3.863	25.0	3.915	16.1		3.575	16.9		3.778	17.7		4.035	19.8	
ClinChem	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
ALP	0.586	22.7	0.549	14.8		0.602	27.2		0.593	21.4		0.542	21.7	
ALT	0.736	24.2	0.695	26.0		0.709	21.3		0.650	40.9		0.723	17.7	
AST	2.586	23.8	2.515	19.6		2.688	18.8		2.545	31.7		2.730	26.6	
BIL	8.332	27.9	7.678	20.4		7.758	17.4		7.922	18.4		8.027	33.9	
ALB	42.38	4.5	42.51	5.0		43.03	5.0		43.29	6.9		42.38	5.1	
TP	71.89	2.9	71.81	3.2		72.14	3.1		71.93	3.7		71.66	3.8	
Glu	5.028	17.4	5.043	11.9		4.745	15.0		5.103	13.7		5.175	16.3	
CHOL	2.638	19.0	2.607	19.1		2.574	18.3		2.474	18.3		2.487	14.6	
TAG	0.956	22.7	0.901	25.8		1.011	30.2		1.211	89.1		0.976	25.2	

Crea	43.19	10.3	45.45	8.1		45.17	8.5		46.10	10.8	t	44.27	7.8	
Urea	4.634	9.5	4.986	9.5	tW	5.169	10.9	Dw	5.052	13.5	dTw	4.981	10.9	tw
cHGB	54.00	65.1	43.06	31.3		47.27	38.3		50.78	57.5		52.42	72.2	
Ca	2.570	1.7	2.575	1.9		2.583	2.1		2.586	2.2		2.563	1.2	
Cl	100.6	1.5	101.3	1.2		100.5	1.4		100.2	1.5		100.5	1.7	
K	4.362	6.5	4.380	9.1		4.363	6.7		4.365	8.9		4.422	11.7	
Na	141.2	1.4	142.0	1.6	t	142.3	1.3	t	141.9	1.5		141.7	1.6	
P	1.450	16.1	1.456	15.4		1.562	15.4		1.573	23.3		1.424	17.6	
Urine	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
uVol	13.60	18.5	14.00	40.4		13.06	28.4		14.10	34.7		12.73	26.4	
uVolW	4.003	17.9	4.280	38.1		3.914	32.1		4.271	43.0		3.874	26.1	
uLeu	65.8	133.0	83.6	110.4		134.4	110.2		79.2	126.3		73.3	131.4	
uOsmoll	490.6	15.7	497.8	24.1		533.7	34.7		482.0	22.7		531.1	21.7	
uKeton	0.150	138.0	0.266	143.6		0.281	116.5		0.050	207.0		0.200	117.6	
upH	6.533	4.3	6.438	6.3		6.422	5.5		6.700	4.9		6.417	4.6	
Organs	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
Kidney	0.480	10.7	0.512	7.4		0.502	9.0		0.517	9.7	tw	0.518	7.1	tw
Spleen	0.197	13.5	0.211	9.2		0.192	14.2		0.203	13.2		0.220	21.9	
Liver	2.005	9.5	2.051	8.8		2.017	7.3		2.063	5.3		2.064	7.3	
AdrenGl	0.0189	15.7	0.0192	8.3		0.0190	15.0		0.0196	17.4		0.0199	17.0	
Heart	0.248	8.8	0.263	6.7	w	0.271	11.9	t	0.258	6.7		0.264	5.9	
Uterus	0.261	23.9	0.277	25.8		0.237	23.7		0.253	20.4		0.254	19.1	
Ovary	0.0179	33.5	0.0192	17.4		0.0207	18.4		0.0209	31.5		0.0214	26.1	
Brain	0.592	10.2	0.651	10.6	dTW	0.640	10.5	t	0.643	9.3	dw	0.651	5.8	dTW

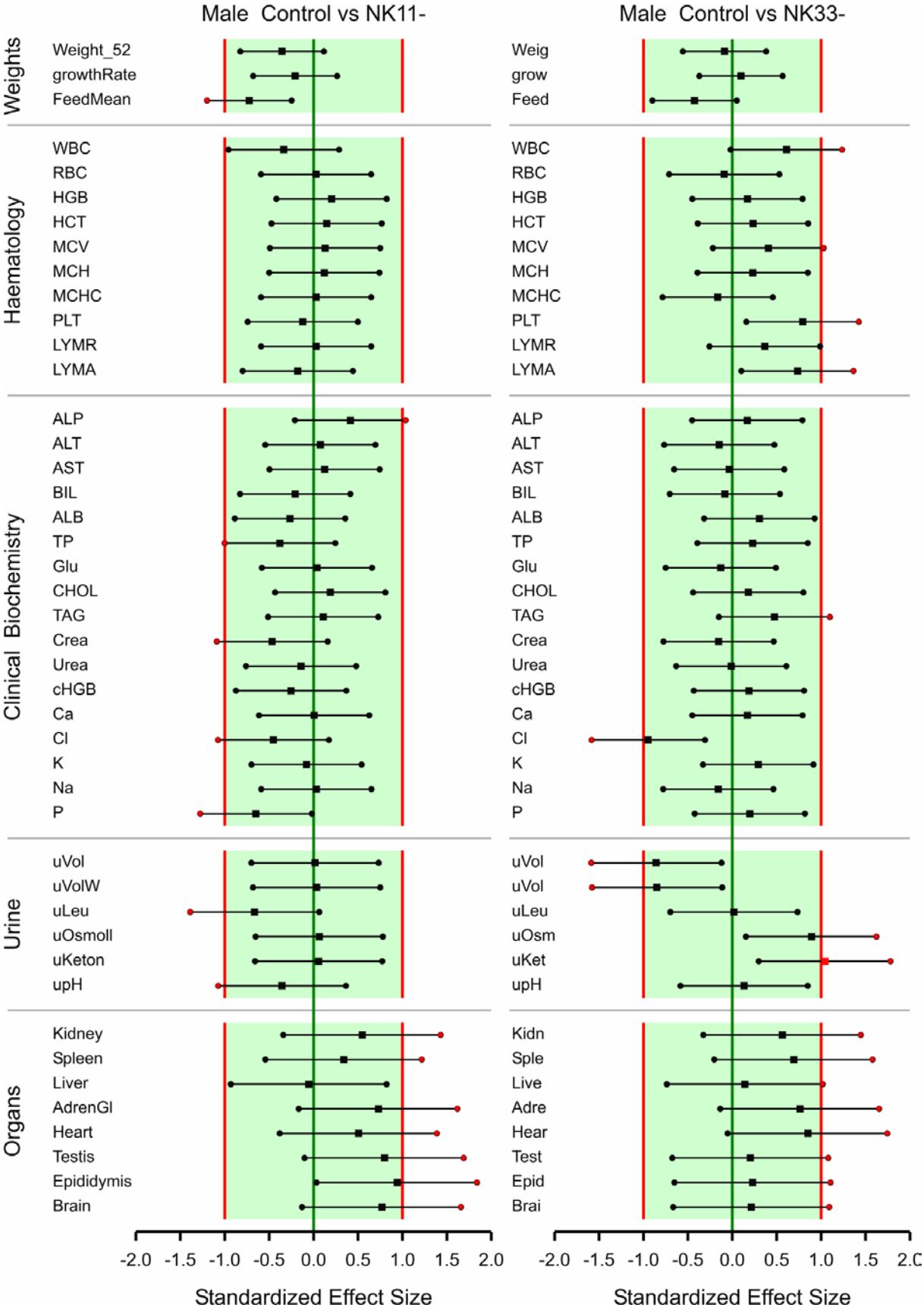

Figure 20 Confidence intervals for Standardized Effect Sized (SES) for male rats for GMO feeds NK11- and NK33- versus the control feed.

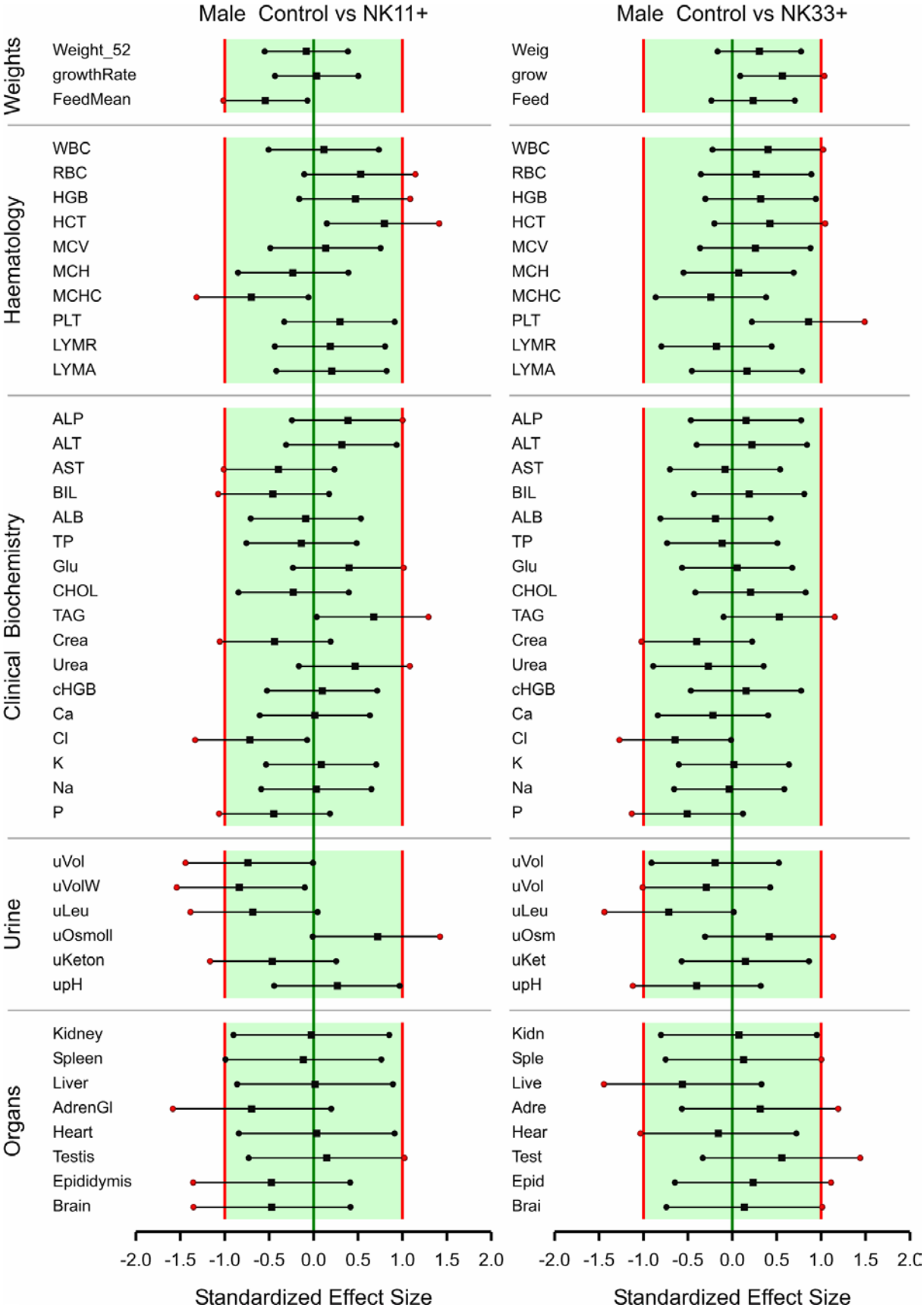

Figure 21 Confidence intervals for Standardized Effect Sized (SES) for male rats for GMO feeds NK11+ and NK33+ versus the control feed.

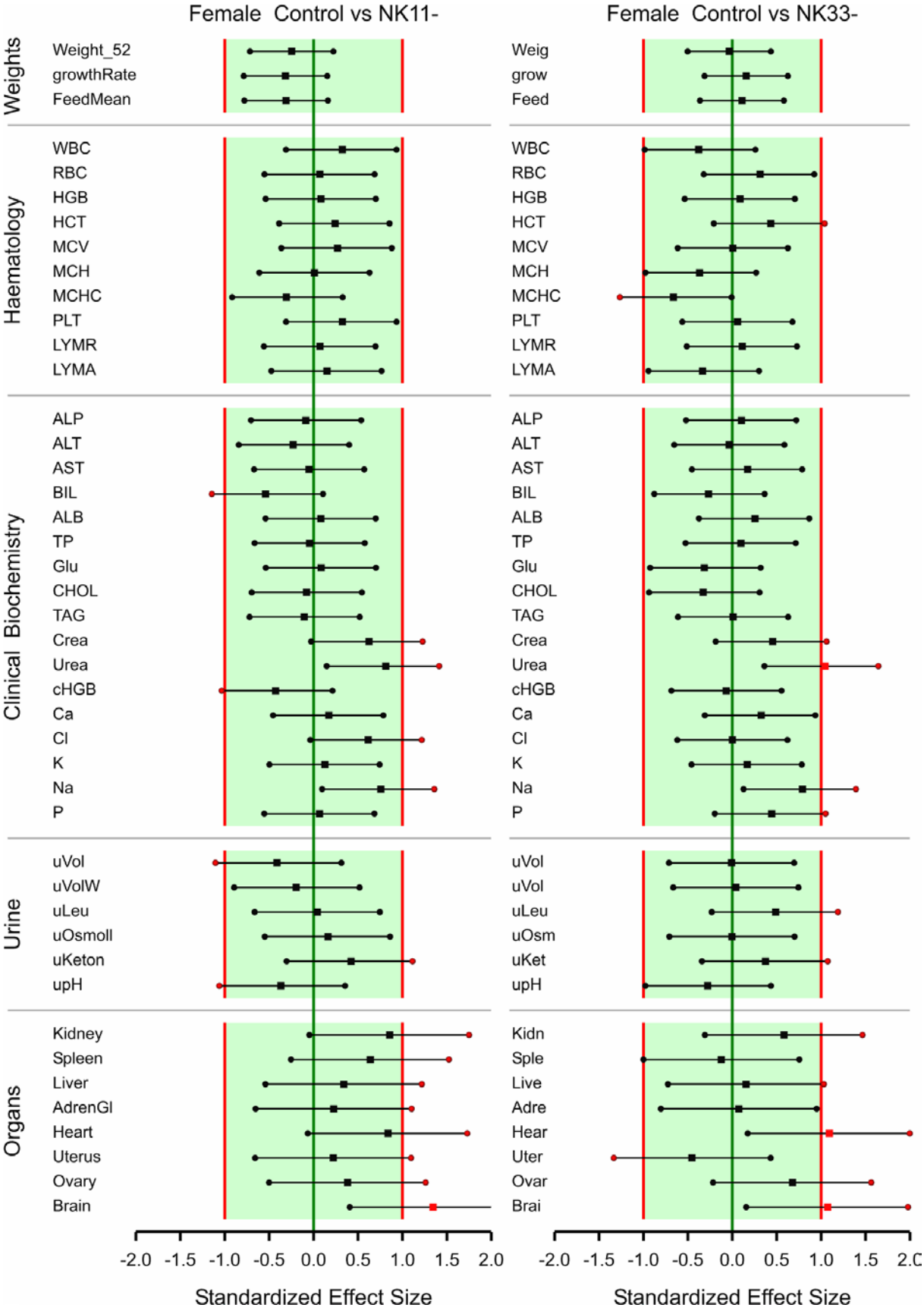

Figure 22 Confidence intervals for Standardized Effect Sized (SES) for female rats for GMO feeds NK11- and NK33- versus the control feed.

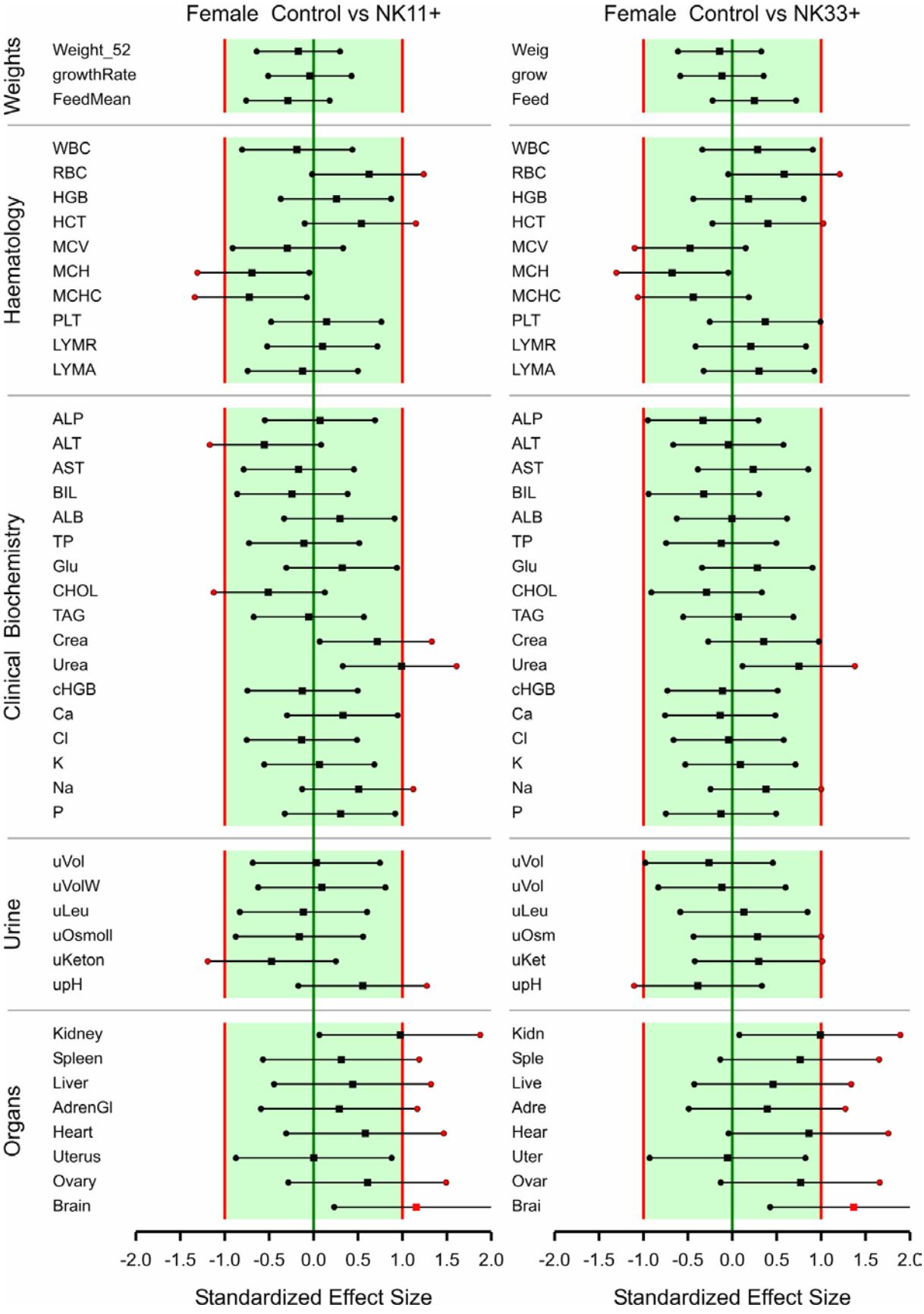

Figure 23 Confidence intervals for Standardized Effect Sized (SES) for female rats for GMO feeds NK11+ and NK33+ versus the control feed.

3.5 Factorial analysis

The significance results from fitting the factorial model to the 44 variables are given in Table 14. The ratios for the significant cases are shown in Table 15 and

Table 16. As an example, consider the results for WBC which has a significant GM inclusion rate effect for males and a significant interaction for females. The effect of a higher GM inclusion rate is positive for males with a mean WBC value which is 12% higher at a GM inclusion rate of 33% as compared to a rate of 11% (Table 15). For females the effect of GM inclusion rate is negative for GM feeds without Roundup (1.00 to 0.88, i.e. -12%,

Table 16), while the effect is positive for GM feeds with Roundup (0.91 to 0.99, i.e. +9%,

Table 16). The only main significant GM inclusion rate effects larger than 10% were observed for WBC and uKeton in males. A significant Roundup main effects larger than 10% was observed for uKeton both in males and females.

The p-values in Table 14 can be summarized as follows. In 8 out of 88 cases (9%) there was a significant difference at the 5% level between the mean of the GM feeds and the non-GM control feed. In 11 cases (12.5%) there was a significant interaction term at the 5% level. In these latter cases the main effects should not be used for assessing effects of GM inclusion rate or Roundup. Among the remaining 77 cases, i.e. where the interaction is not significant, there were 6 cases (7.8%) with a significant differences between GM inclusion rates, and 11 cases (14.3%) with a significant difference between the GM feeds with and without roundup.

Table 14 P values for significance of effects obtained with the factorial model. P-values smaller than 0.01/0.05 have a gold/yellow background.

Response	Males				Females			
Weights	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
Weight_52	0.771	0.055	0.051	0.723	0.432	0.474	0.922	0.588
growthRate	0.520	0.015	0.038	0.510	0.674	0.238	0.995	0.107
FeedMean	0.056	0.002	0.014	0.158	0.750	0.005	0.637	0.724
Haematology	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
WBC	0.419	0.006	0.574	0.133	0.964	0.571	0.700	0.004
RBC	0.454	0.390	0.052	0.748	0.080	0.613	0.043	0.480
HGB	0.237	0.679	0.344	0.786	0.499	0.867	0.499	0.844
HCT	0.106	0.517	0.059	0.298	0.075	0.890	0.510	0.416
MCV	0.342	0.363	0.752	0.725	0.580	0.274	0.011	0.842
MCH	0.846	0.346	0.244	0.656	0.057	0.371	0.014	0.329
MCHC	0.273	0.546	0.069	0.140	0.020	0.860	0.632	0.114
PLT	0.066	0.001	0.273	0.421	0.316	0.917	0.743	0.223
LYMR	0.681	0.953	0.378	0.112	0.583	0.704	0.757	0.872
LYMA	0.346	0.048	0.669	0.032	0.991	0.883	0.367	0.026
ClinChem	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
ALP	0.252	0.277	0.928	0.977	0.790	0.602	0.502	0.140
ALT	0.631	0.463	0.165	0.778	0.336	0.081	0.409	0.434
AST	0.693	0.725	0.199	0.283	0.838	0.118	0.892	0.657
BIL	0.569	0.081	0.954	0.234	0.130	0.631	0.548	0.385
ALB	0.806	0.280	0.466	0.129	0.482	0.752	0.910	0.237
TP	0.680	0.149	0.813	0.186	0.842	0.753	0.480	0.688

Glu	0.713	0.246	0.216	0.691	0.676	0.272	0.041	0.366
CHOL	0.726	0.328	0.370	0.312	0.182	0.947	0.329	0.248
TAG	0.071	0.613	0.159	0.243	0.926	0.552	0.782	0.983
Crea	0.138	0.419	0.614	0.536	0.019	0.189	0.980	0.630
Urea	0.964	0.170	0.426	0.051	0.000	0.991	0.772	0.240
cHGB	0.850	0.254	0.470	0.383	0.416	0.352	0.520	0.394
Ca	0.977	0.881	0.384	0.368	0.441	0.436	0.454	0.124
Cl	0.006	0.339	0.929	0.196	0.626	0.199	0.051	0.081
K	0.747	0.485	0.802	0.317	0.616	0.872	0.733	0.975
Na	0.893	0.565	0.781	0.776	0.008	0.814	0.105	0.683
P	0.154	0.075	0.255	0.041	0.444	0.890	0.406	0.047
Urine	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
uVol	0.118	0.517	0.855	0.006	0.539	0.818	0.689	0.147
uVolW	0.087	0.503	0.531	0.006	0.865	0.958	0.782	0.350
uLeu	0.072	0.195	0.138	0.160	0.603	0.147	0.277	0.673
uOsmoll	0.066	0.301	0.717	0.027	0.791	0.553	0.943	0.203
uKeton	0.486	0.002	0.006	0.455	0.559	0.130	0.044	0.089
upH	0.752	0.720	0.857	0.024	0.651	0.076	0.091	0.033
Organs	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
Kidney	0.417	0.855	0.102	0.895	0.021	0.685	0.409	0.650
Spleen	0.465	0.353	0.115	0.862	0.268	0.628	0.381	0.063
Liver	0.747	0.550	0.325	0.228	0.331	0.792	0.526	0.750
AdrenGl	0.437	0.107	0.005	0.130	0.491	0.940	0.548	0.686
Heart	0.388	0.810	0.025	0.400	0.022	0.402	0.448	0.968
Testis	0.235	0.772	0.641	0.121	0.841	0.256	0.776	0.335
Epididymis	0.515	0.996	0.032	0.031	0.093	0.474	0.619	0.834
Brain	0.649	0.933	0.044	0.074	0.001	0.926	0.873	0.452

Table 15 Ratios for significant variables at the 5% level in the factorial analysis for males. Main effects are "GM vs Contrl" (ratio of the mean of the four GM feeds vs the control feed), "33 vs 11" (ratio of the two GM feeds with 33% GM inclusion rate vs the two feeds with 11% GM inclusion rate) and "+RU vs -RU" (ratio of the two GM feeds with roundup vs the two feeds without roundup). The interaction ratios are scaled such that NK11- equals 1. The InclRate and RndUp main effects are only given when the interaction is not significant.

Males Group	Variable	GM vs Contrl	33 vs 11	+RU vs -RU	Interaction			
					NK11-	NK33-	NK11+	NK33+
Weights	growthRate	-	1.10	1.08	-	-	-	-
Weights	FeedMean	-	1.03	1.03	-	-	-	-
Haematology	WBC	-	1.12	-	-	-	-	-
Haematology	PLT	-	1.07	-	-	-	-	-
Haematology	LYMA	-	-	-	1.00	1.20	1.08	1.07
ClinChem	Cl	0.99	-	-	-	-	-	-
ClinChem	P	-	-	-	1.00	1.08	1.02	1.01
Urine	uVol	-	-	-	1.00	0.83	0.85	0.96
Urine	uVolW	-	-	-	1.00	0.83	0.83	0.93
Urine	uOsmoll	-	-	-	1.00	1.17	1.13	1.07
Urine	uKeton	-	1.49	0.70	-	-	-	-
Urine	upH	-	-	-	1.00	1.20	1.26	0.98

Organs	AdrenGl	-	-	0.92	-	-	-	-
Organs	Heart	-	-	0.95	-	-	-	-
Organs	Epididymis	-	-	-	1.00	0.92	0.85	0.92
Organs	Brain	-	-	0.95	-	-	-	-

Table 16 Ratios for significant variables at the 5% level in the factorial analysis for females. Main effects are "GM vs Contrl" (ratio of the mean of the four GM feeds vs the control feed), "33 vs 11" (ratio of the two GM feeds with 33% GM inclusion rate vs the two feeds with 11% GM inclusion rate) and "+RU vs -RU" (ratio of the two GM feeds with roundup vs the two feeds without roundup). The interaction ratios are scaled such that NK11- equals 1. The InclRate and RndUp main effects are only given when the interaction is not significant.

Females Group	Variable	GM vs Contrl	33 vs 11	+RU vs -RU	Interaction			
					NK11-	NK33-	NK11+	NK33+
Weights	FeedMean	-	1.03	-	-	-	-	-
Haematology	WBC	-	-	-	1.00	0.88	0.91	0.99
Haematology	RBC	-	-	1.02	-	-	-	-
Haematology	MCV	-	-	0.99	-	-	-	-
Haematology	MCH	-	-	0.99	-	-	-	-
Haematology	MCHC	0.99	-	-	-	-	-	-
Haematology	LYMA	-	-	-	1.00	0.92	0.95	1.03
ClinChem	Glu	-	-	1.05	-	-	-	-
ClinChem	Crea	1.04	-	-	-	-	-	-
ClinChem	Urea	1.09	-	-	-	-	-	-
ClinChem	Na	1.01	-	-	-	-	-	-
ClinChem	P	-	-	-	1.00	1.07	1.04	0.97
Urine	uKeton	-	-	0.84	-	-	-	-
Urine	upH	-	-	-	1.00	1.03	1.32	0.99
Organs	Kidney	1.07	-	-	-	-	-	-
Organs	Heart	1.06	-	-	-	-	-	-
Organs	Brain	1.09	-	-	-	-	-	-

3.6 Correlation analysis

The correlation plots for three liver-related and three kidney-related variables in males and females are shown in Figure 24 - Figure 27. For males there were significant positive correlations between Urea and Crea for all comparisons (Figure 25), without accompanying correlations with the relative Kidney weights. Further significant (positive) correlations were found between ALP and CHOL in males, and between Kidney and Urea in females. Simultaneous exceedance of the threshold for two variables was only observed for Kidney and Urea for a single cage in females; the accompanying Crea value was close to the threshold for this cage.

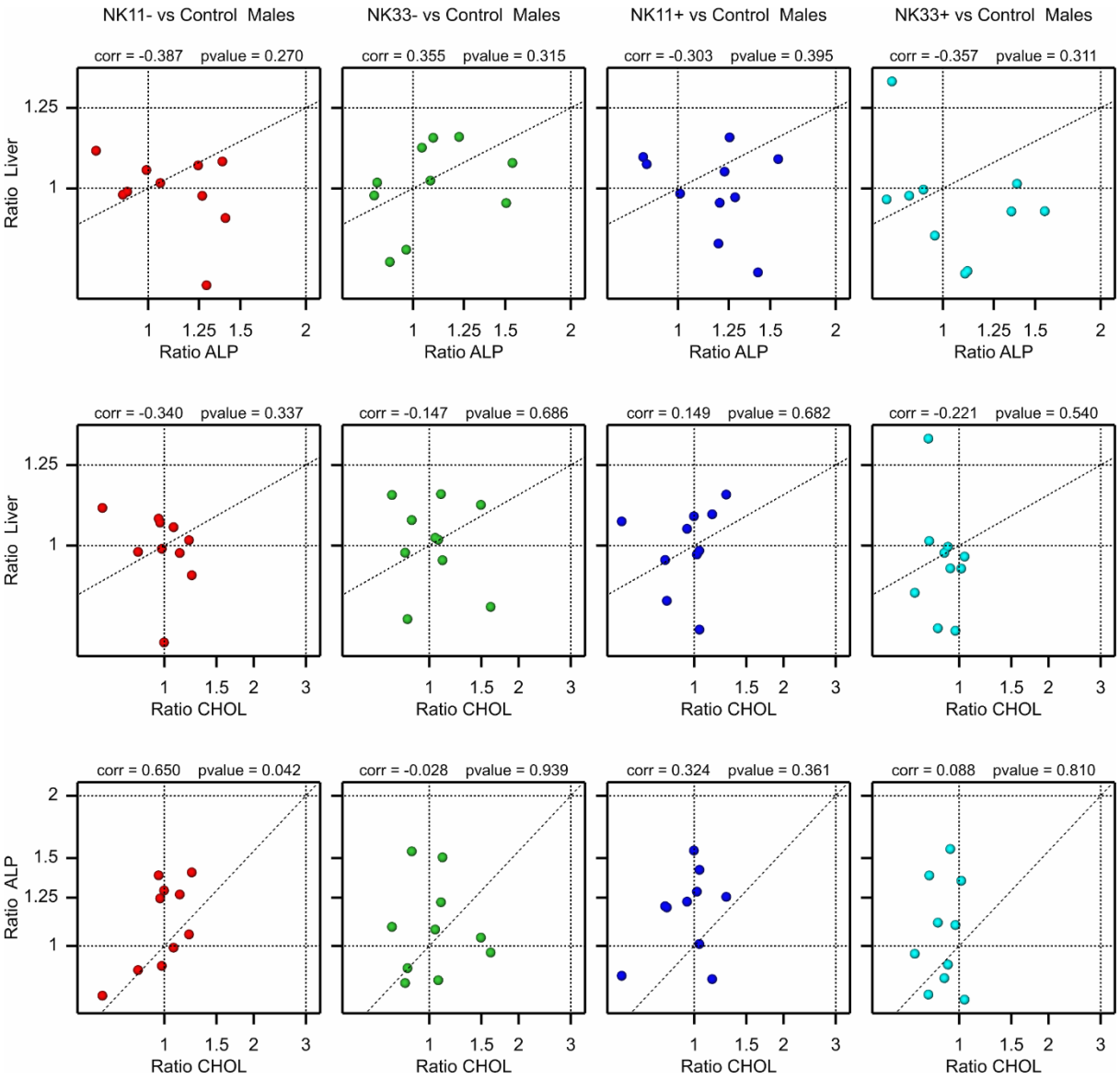

Figure 24 Pairwise results for variables with set target effect sizes related to liver damage in Males. In each row there are four graphs corresponding to the four GM feed groups. Points represent the ratio of the cage mean for the GM group vs. the cage mean for the control feed in ten blocks. Horizontal and vertical lines represent a ratio of 1 and the target effect sizes from Hong et al. (2017).

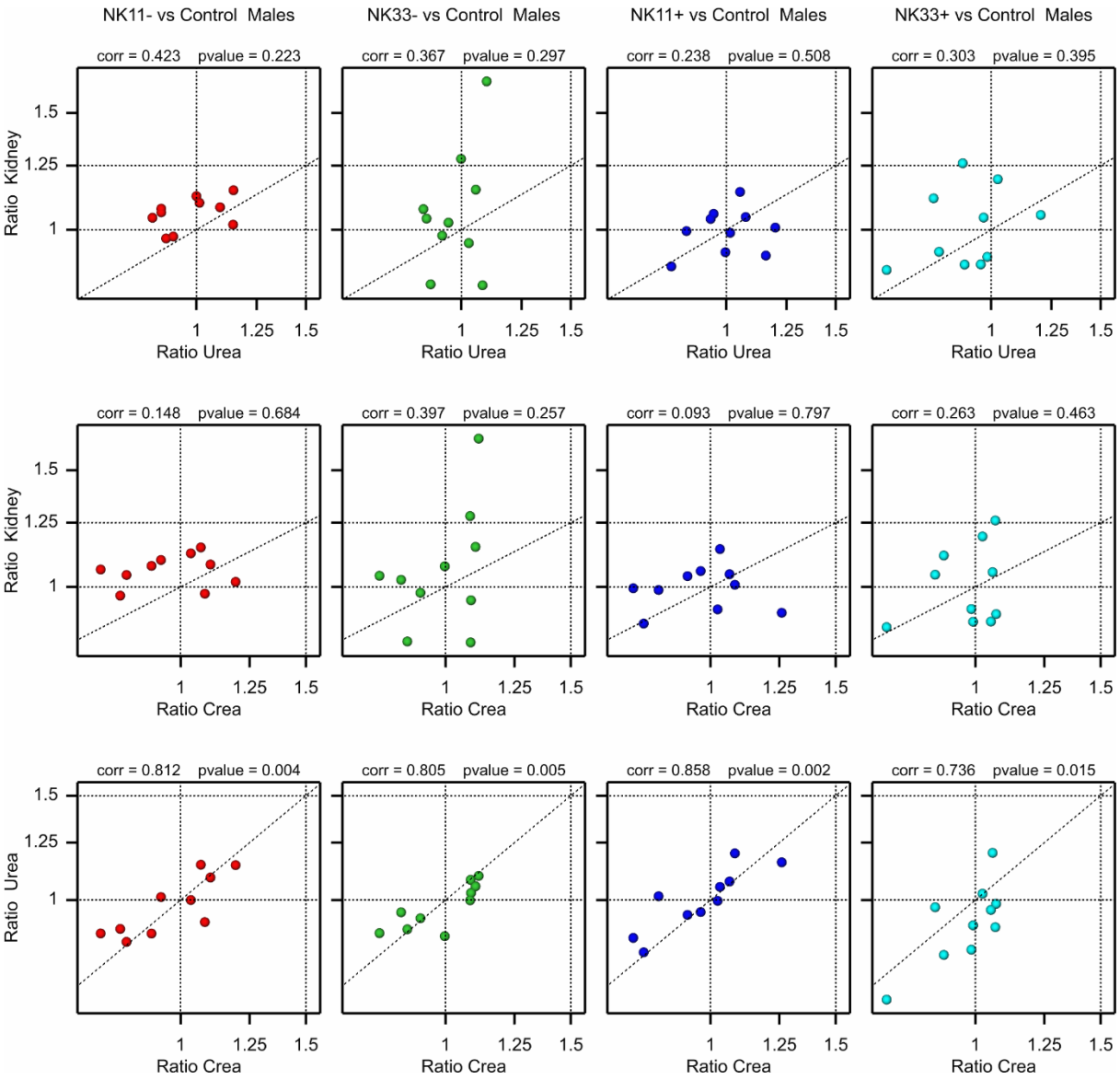

Figure 25 Pairwise results for variables with set target effect sizes related to kidney damage in Males. In each row there are four graphs corresponding to the four GM feed groups. Points represent the ratio of the cage mean for the GM group vs. the cage mean for the control feed in ten blocks. Horizontal and vertical lines represent a ratio of 1 and the target effect sizes from Hong et al. (2017).

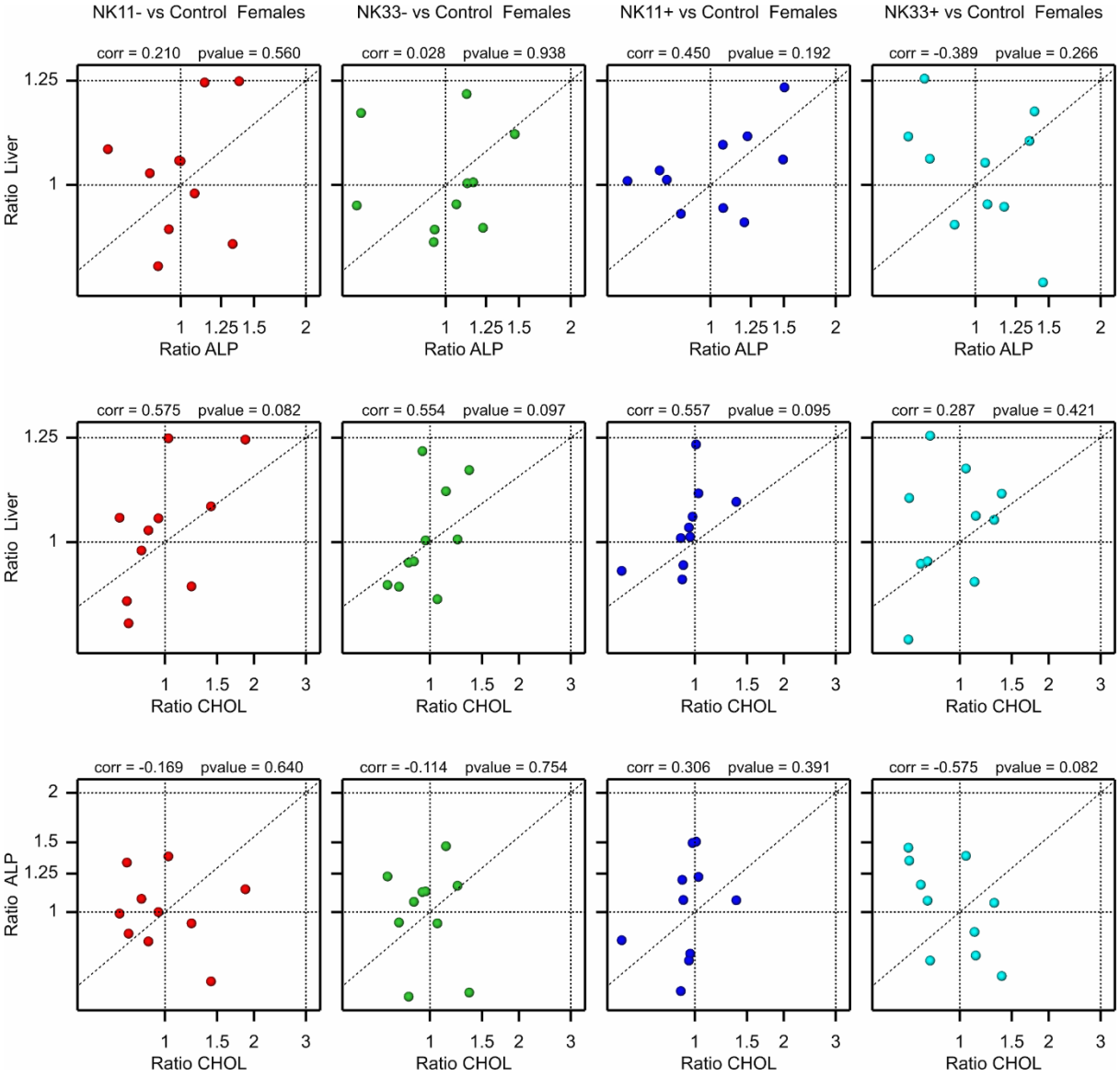

Figure 26 Pairwise results for variables with set target effect sizes related to liver damage in Females. In each row there are four graphs corresponding to the four GM feed groups. Points represent the ratio of the cage mean for the GM group vs. the cage mean for the control feed in ten blocks. Horizontal and vertical lines represent a ratio of 1 and the target effect sizes from Hong et al. (2017).

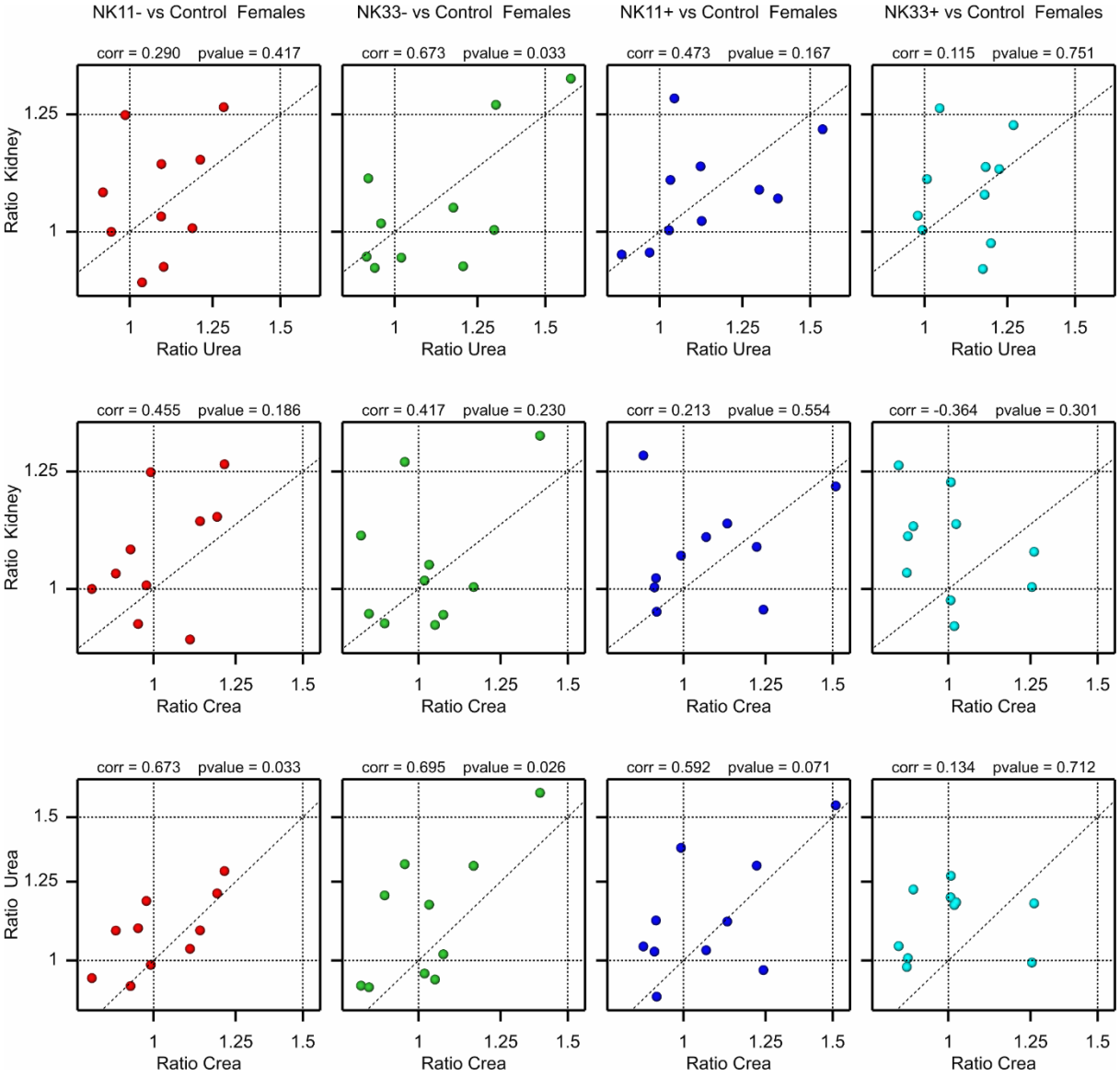

Figure 27 Pairwise results for variables with set target effect sizes related to kidney damage in Females. In each row there are four graphs corresponding to the four GM feed groups. Points represent the ratio of the cage mean for the GM group vs. the cage mean for the control feed in ten blocks. Horizontal and vertical lines represent a ratio of 1 and the target effect sizes from Hong et al. (2017).

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Goedhart, P.W. & van der Voet, H. (2017). G TwYST Study B. A 90-day toxicity study in rats fed GM maize NK603. Statistical report. Report 31.10.17, Biometris, Wageningen, The Netherlands.

Goedhart, P.W. & van der Voet, H. (2018). G TwYST Study A. Combined chronic toxicity and carcinogenicity study in rats fed GM maize NK603. Main statistical report. Report 32.02.18, Biometris, Wageningen, The Netherlands.

EFSA (2011a). Scientific Opinion on Guidance for risk assessment of food and feed from genetically modified plants. EFSA Journal 2011;9(5): 2150. [37 pp.] http://dx.doi.org/10.2903/j.efsa.2011.2150.

Hong B, Du Y, Mukerji P, Roper JM, Appenzeller LM (2017). Safety assessment of food and feed from GM crops in Europe: Evaluating EFSA's alternative framework for the rat 90-day feeding study. Journal of Agricultural and Food Chemistry, 65(27): 5545-5560. http://dx.doi.org/10.1021/acs.jafc.7b01492.

List of Tables

Table 13 Means and coefficient of variation (CV) for female rats. Means of GMO feeds which are significantly different from the Control feed are marked, with red background colouring, as follows: D: P<0.01 by Dunnett-test, d: P<0.05 by Dunnett-test, T: P<0.01 by t-test but not by Dunnett-test, t: P<0.05 by t-test but not by Dunnett-test, W: P<0.01 by Wilcoxon signed rank test, w: P<0.05 by Wilcoxon signed rank test. Note that Dunnett- and t-tests are based on a ANOVA with 5 treatment groups, while Wilcoxon tests only uses data for the specific GM feed and the control feed.

Table 14 P values for significance of effects obtained with the factorial model. P-values smaller than 0.01/0.05 have a gold/yellow background.

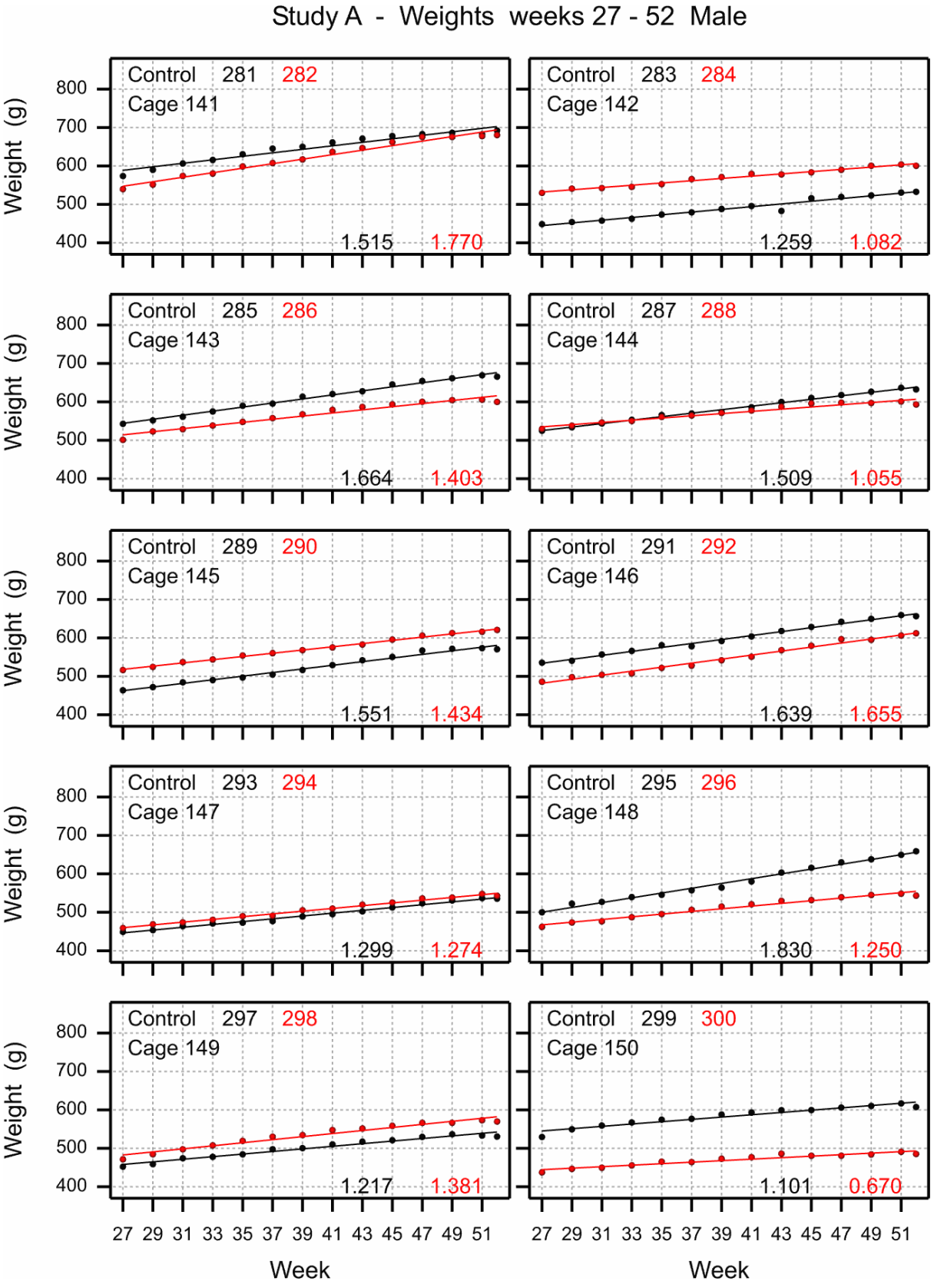
Table 15 Ratios for significant variables at the 5% level in the factorial analysis for males. Main effects are “GM vs Contrl” (ratio of the mean of the four GM feeds vs the control feed), “33 vs 11” (ratio of the two GM feeds with 33% GM inclusion rate vs the two feeds with 11% GM inclusion rate) and “+RU vs -RU“ (ratio of the two GM feeds with roundup vs the two feeds without roundup). The interaction ratios are scaled such that NK11- equals 1. The InclRate and RndUp main effects are only given when the interaction is not significant.

Table 16 Ratios for significant variables at the 5% level in the factorial analysis for females. Main effects are “GM vs Contrl” (ratio of the mean of the four GM feeds vs the control feed), “33 vs 11” (ratio of the two GM feeds with 33% GM inclusion rate vs the two feeds with 11% GM inclusion rate) and “+RU vs -RU“ (ratio of the two GM feeds with roundup vs the two feeds without roundup). The interaction ratios are scaled such that NK11- equals 1. The InclRate and RndUp main effects are only given when the interaction is not significant.

List of Figures

Appendix 1. Growth curves per animal pair

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



Appendix 1. Growth curves per animal pair (continued)

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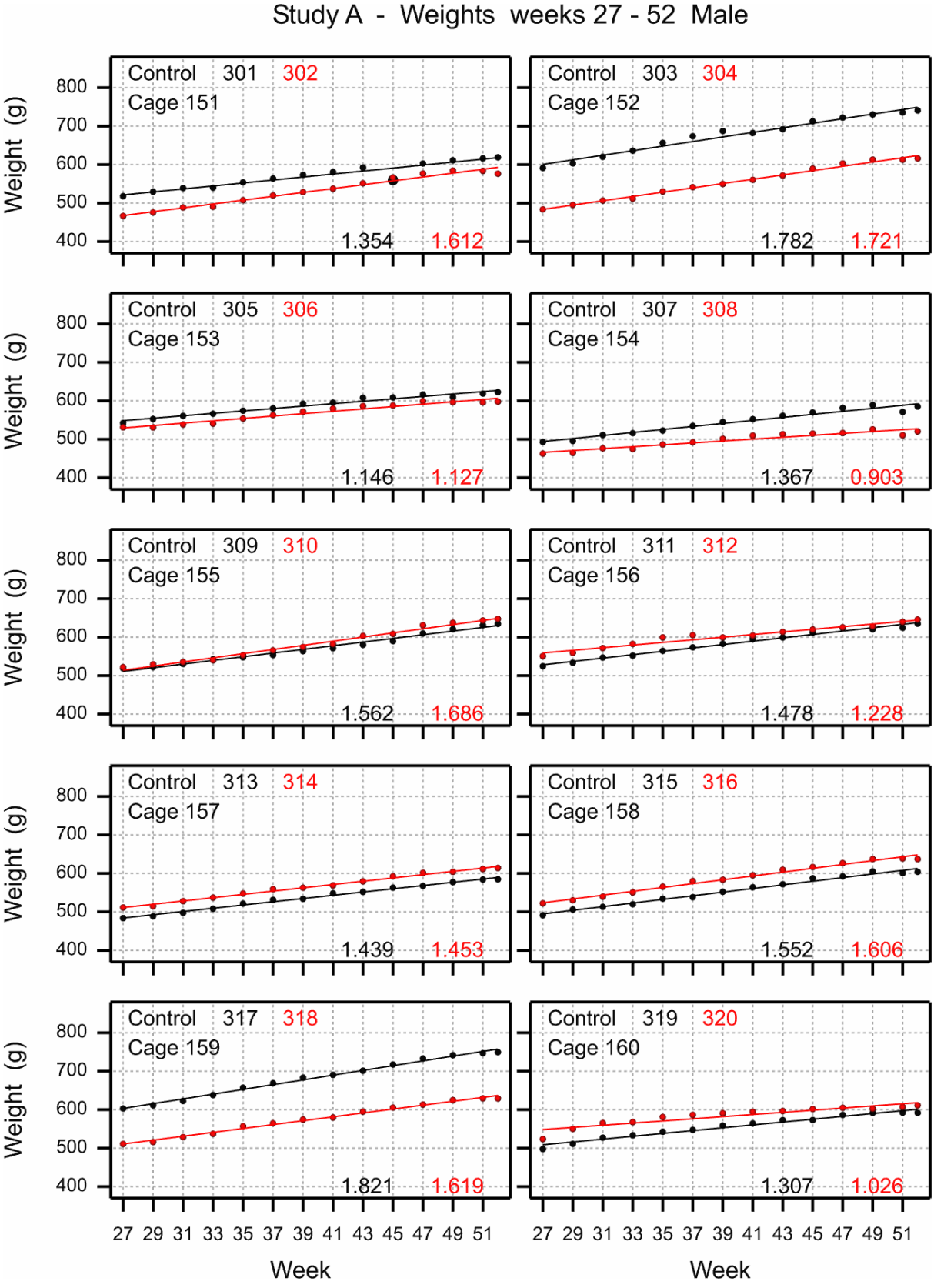

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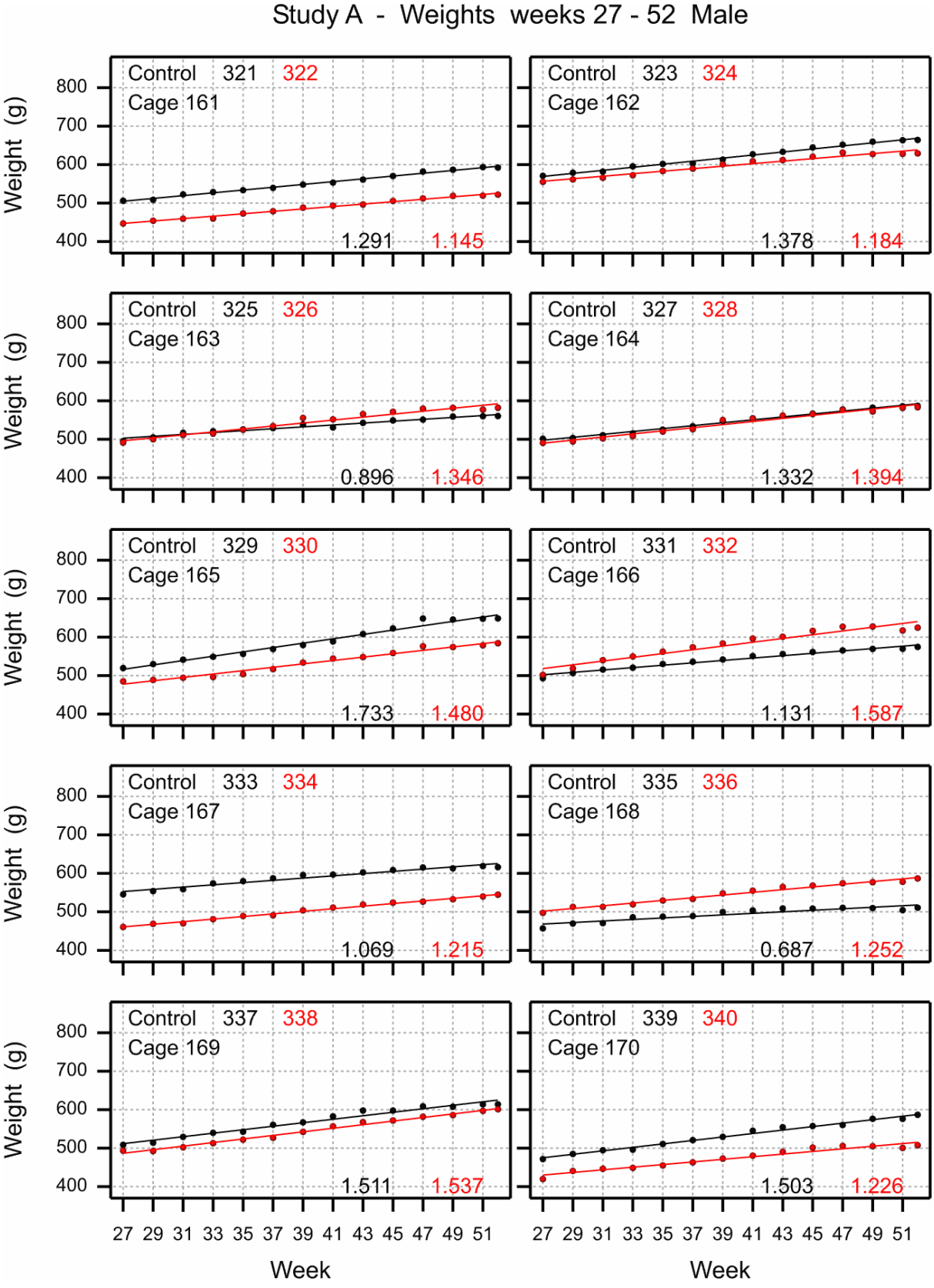

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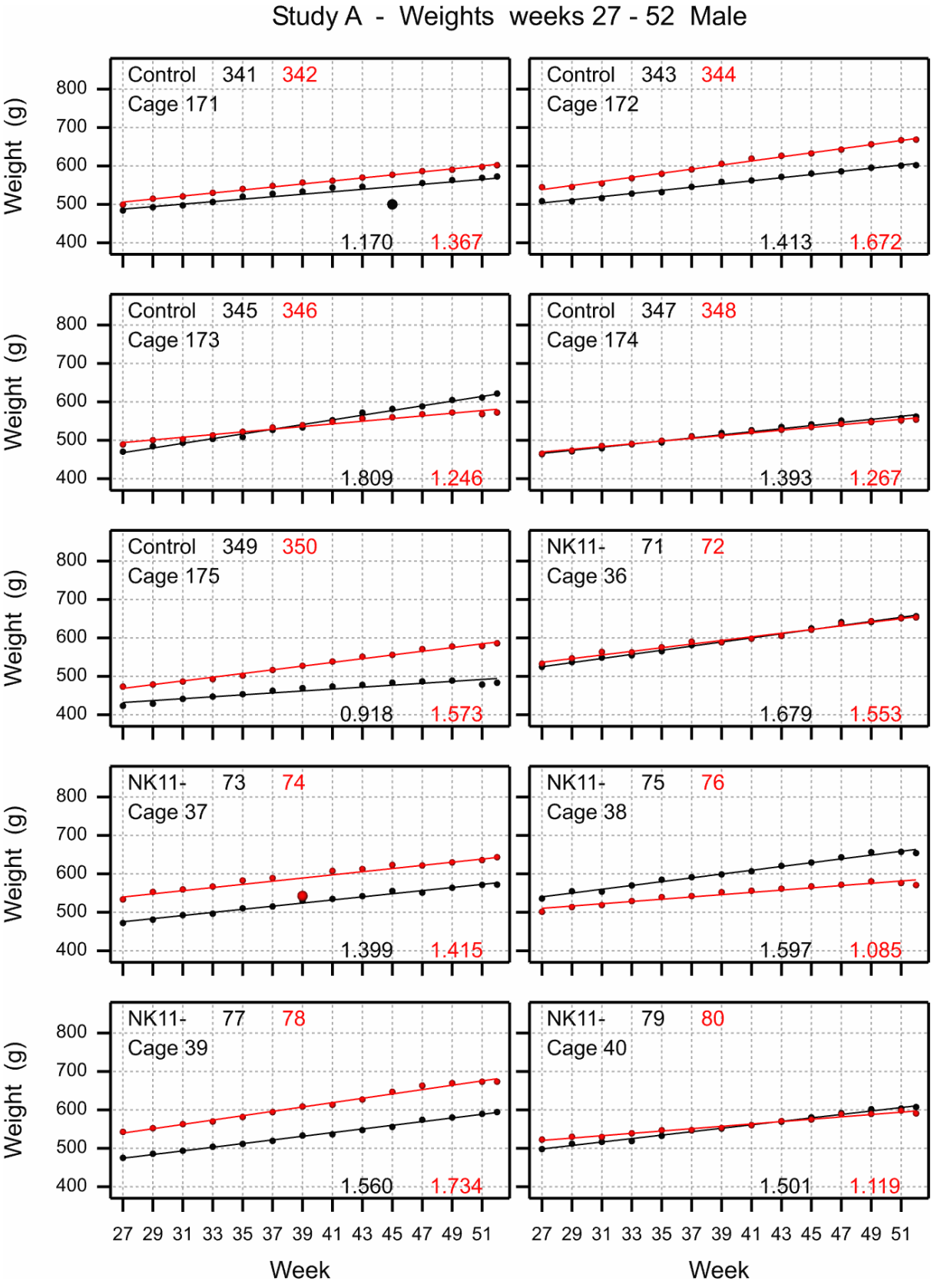

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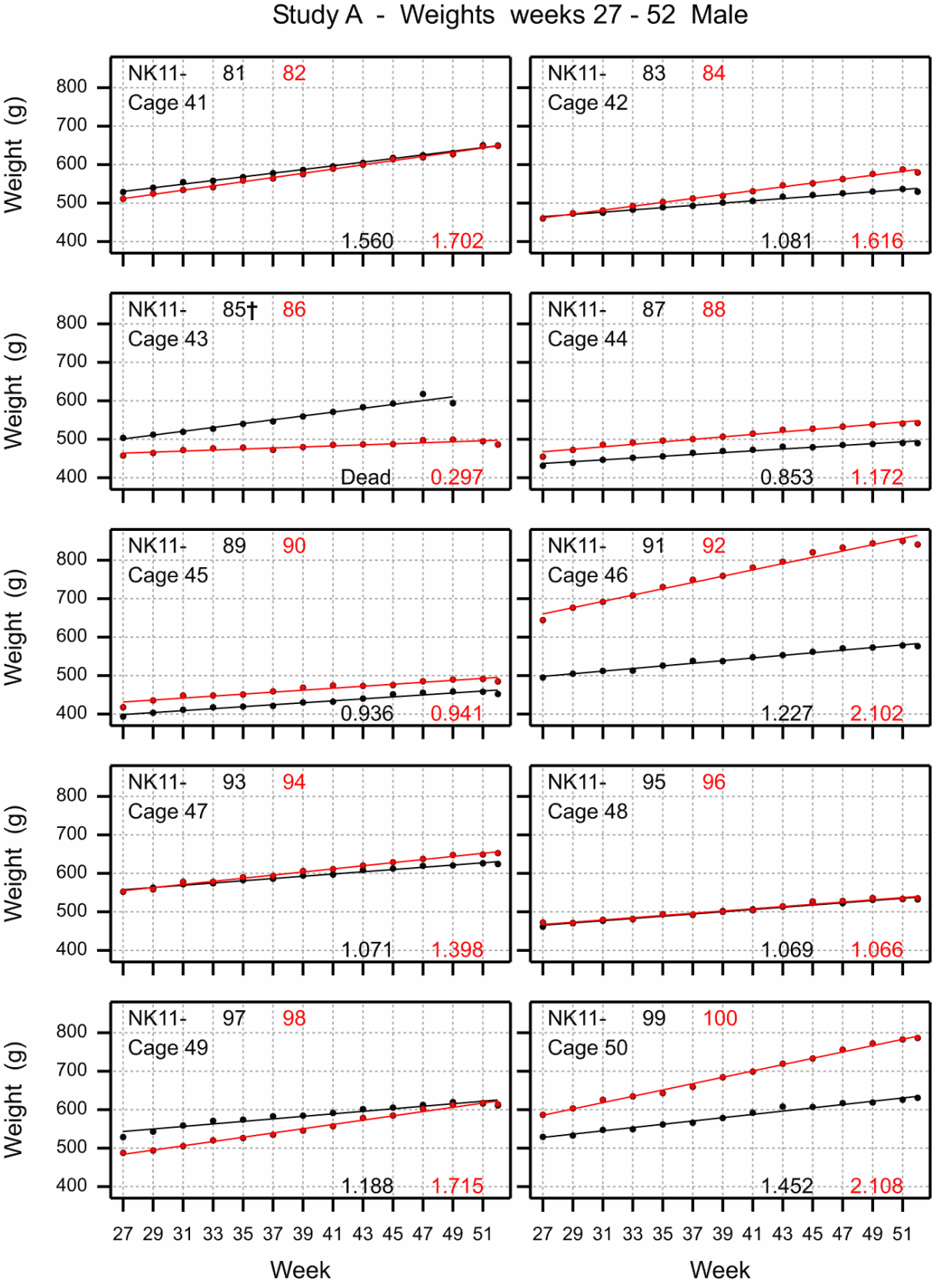

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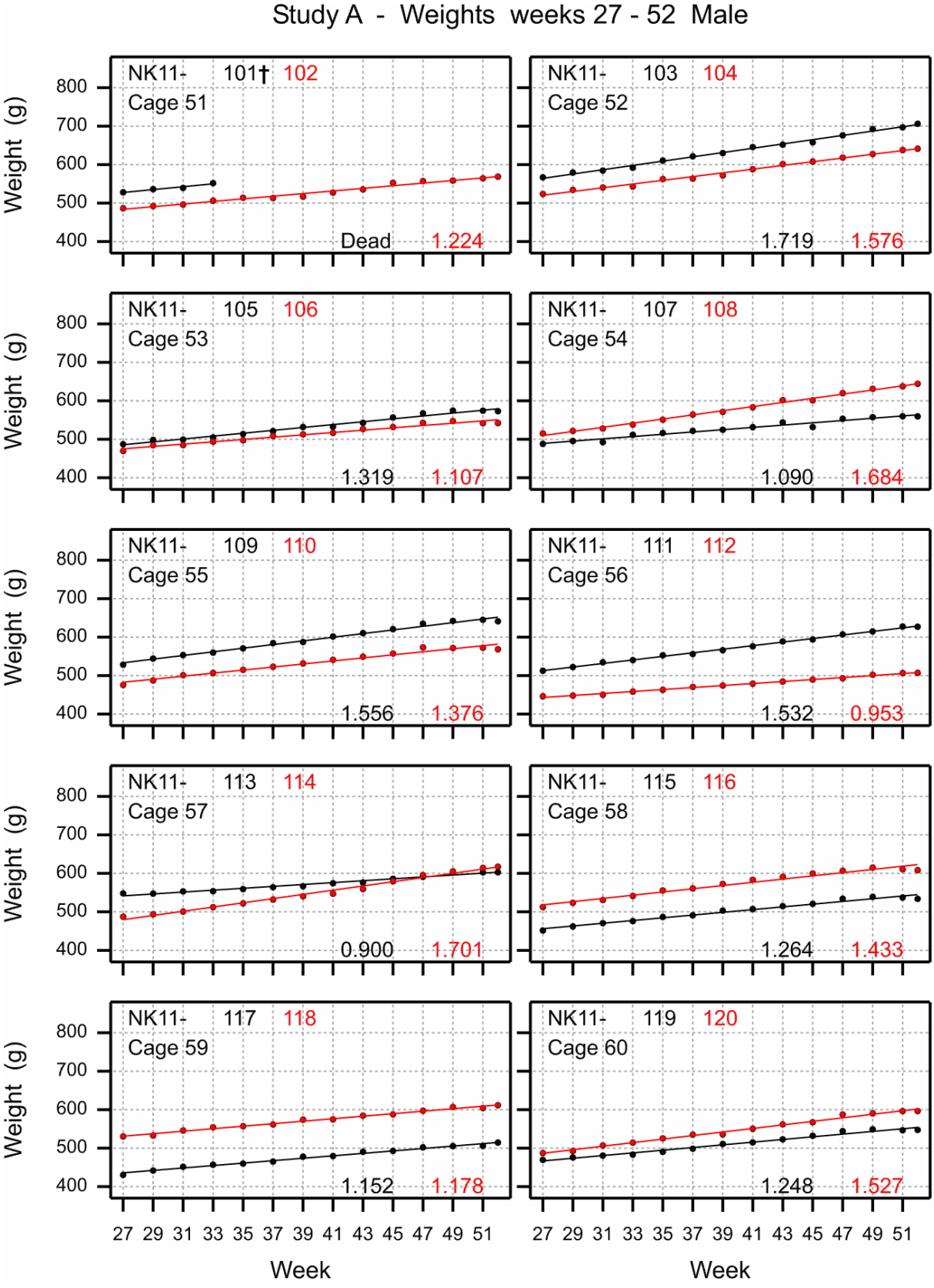

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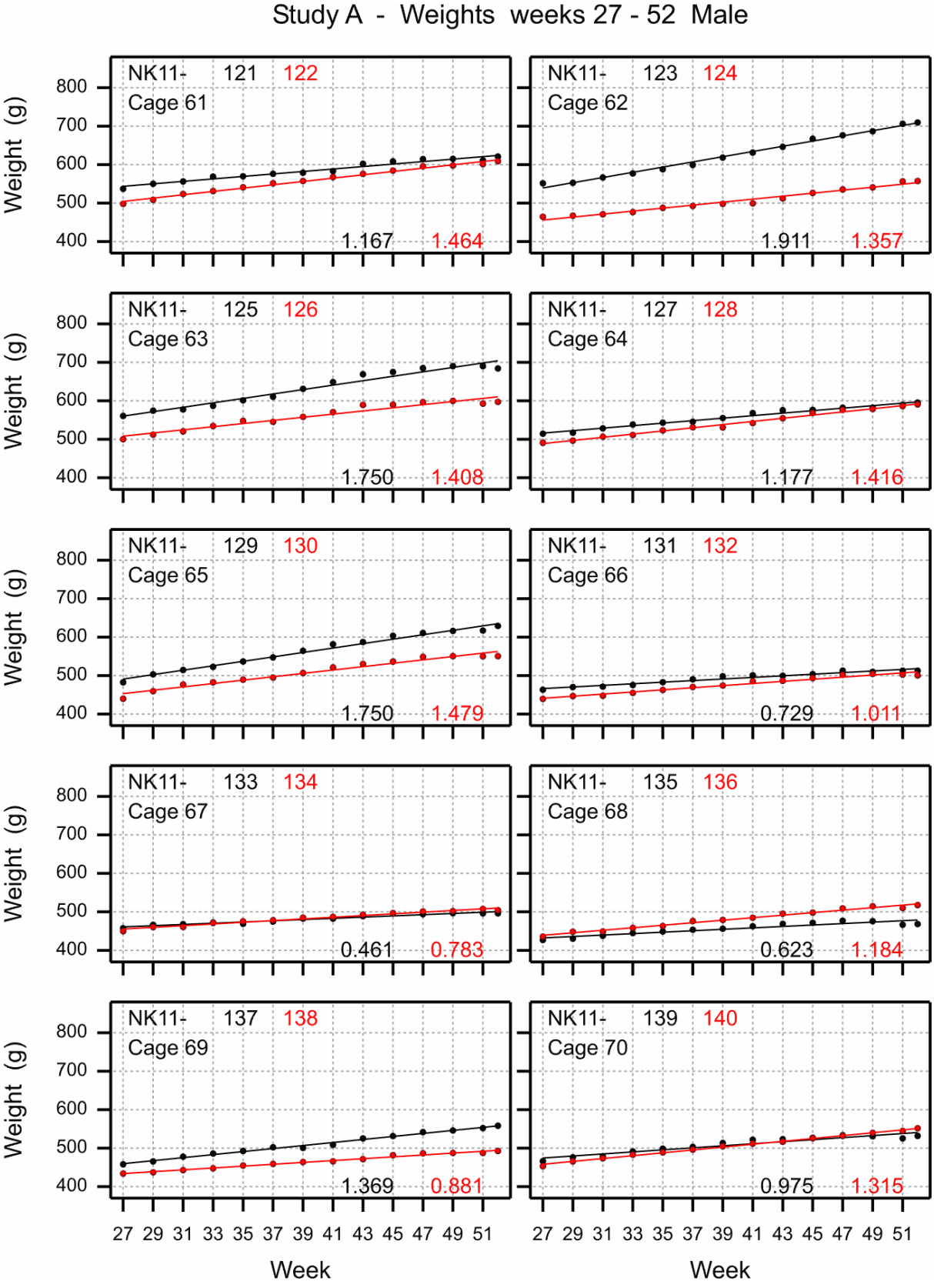

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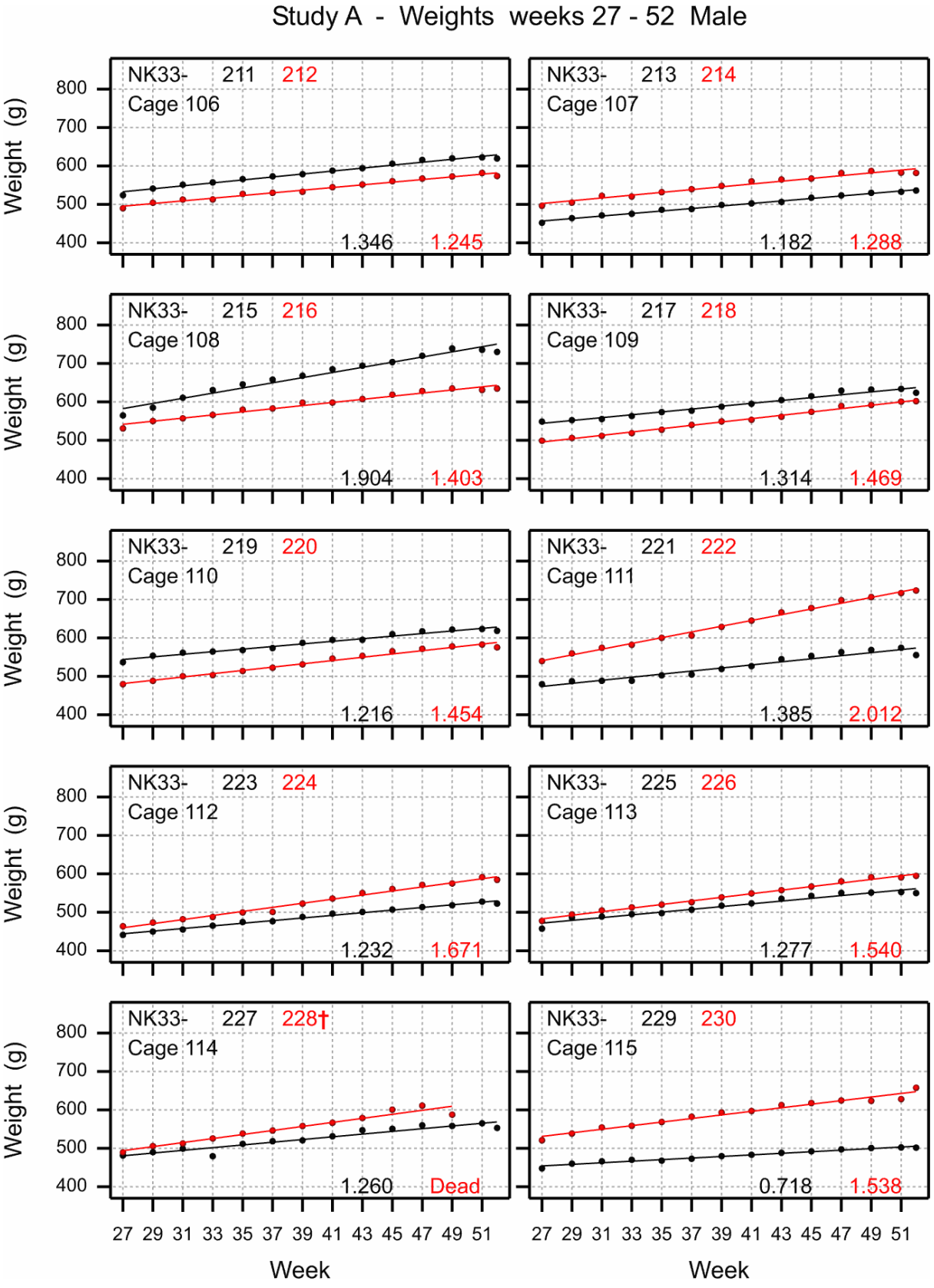

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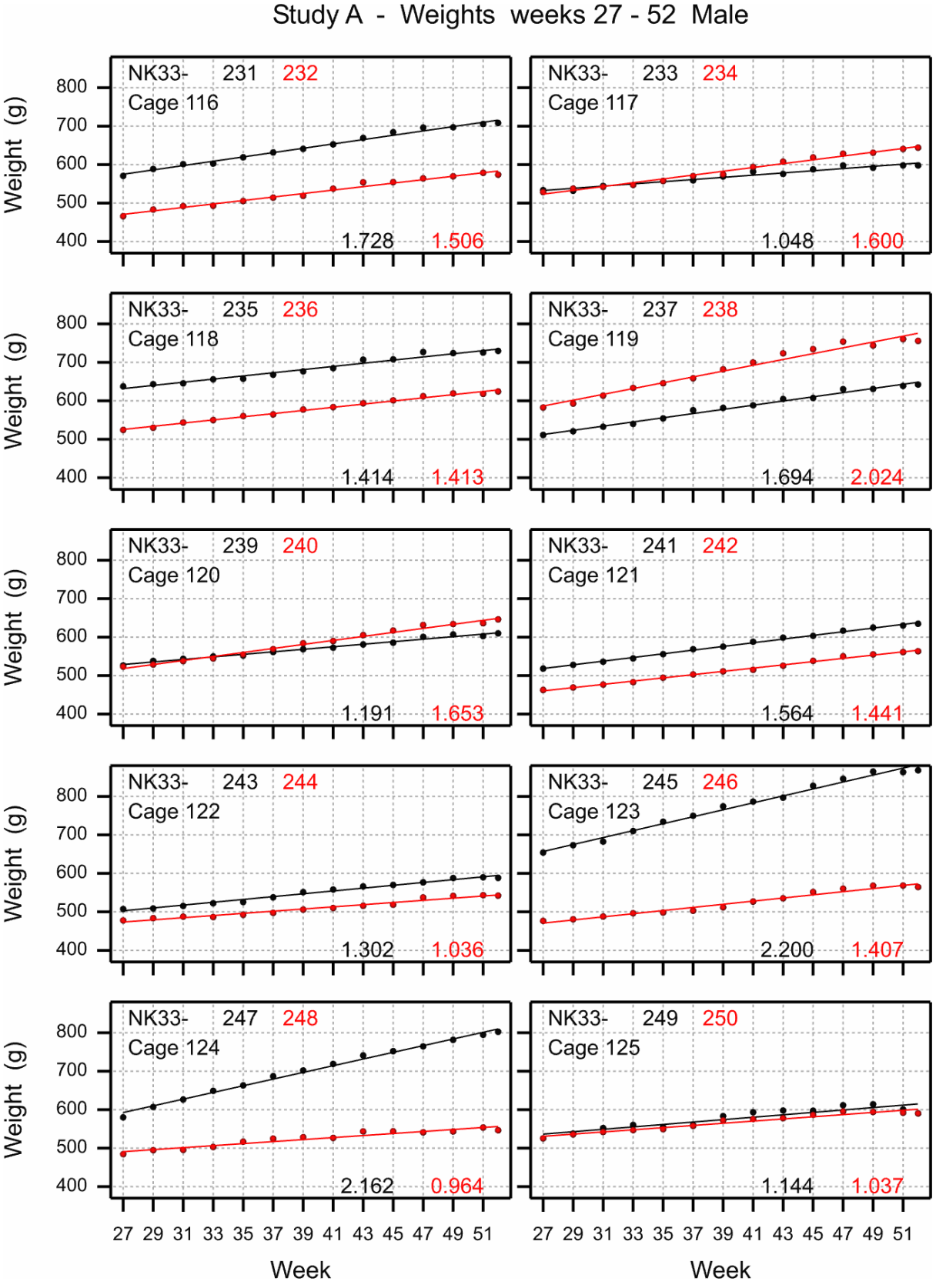

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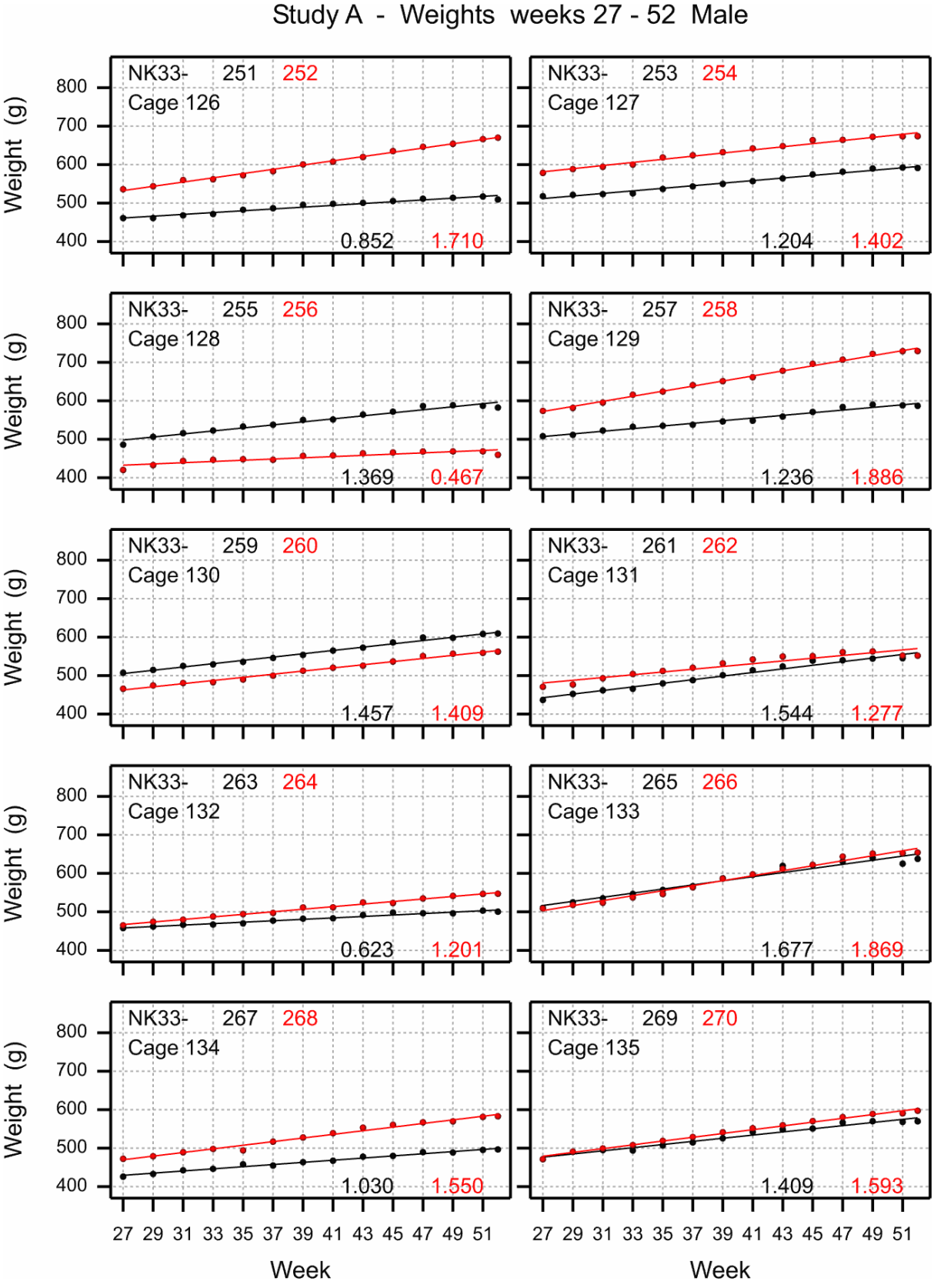

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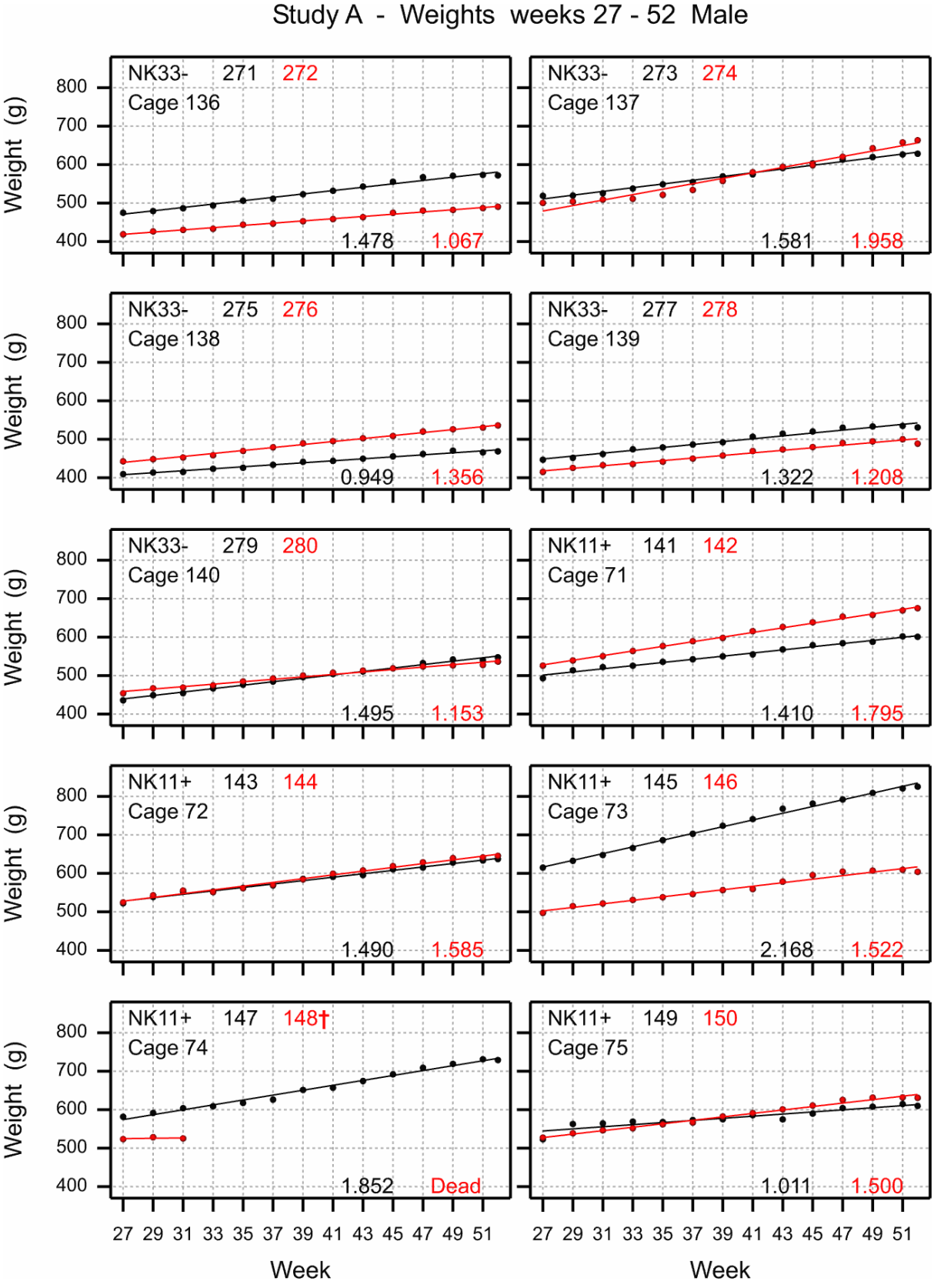

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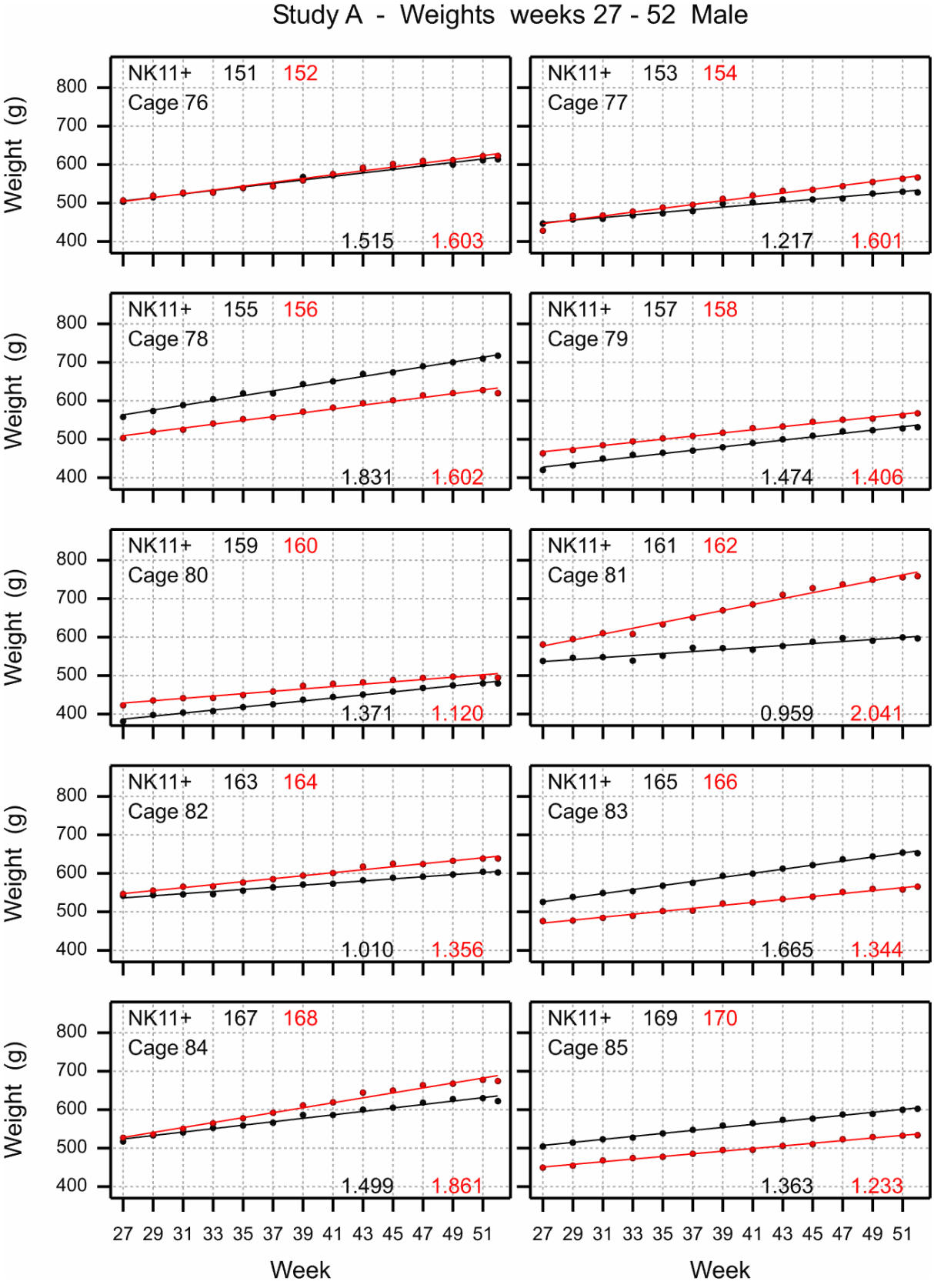

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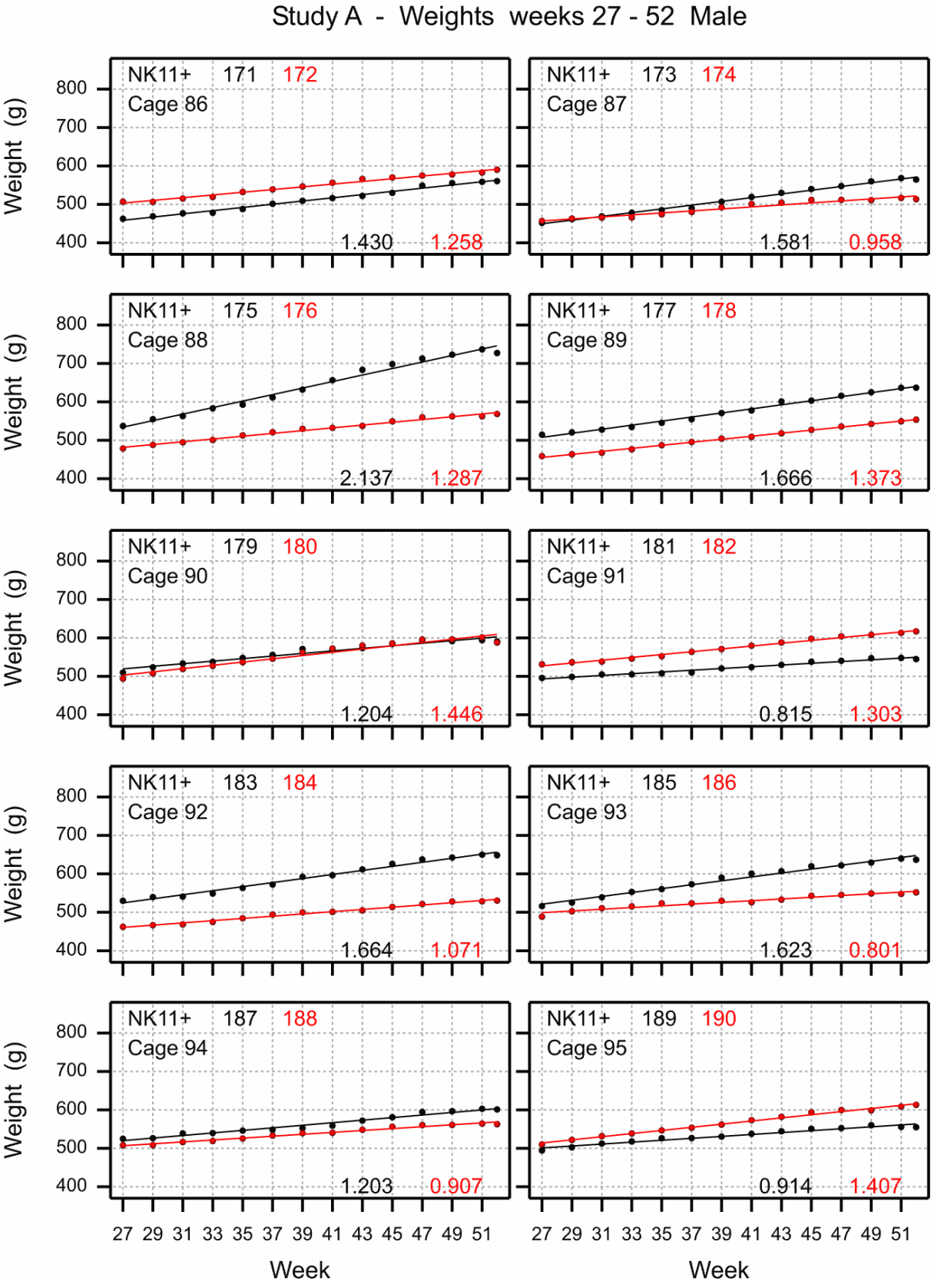

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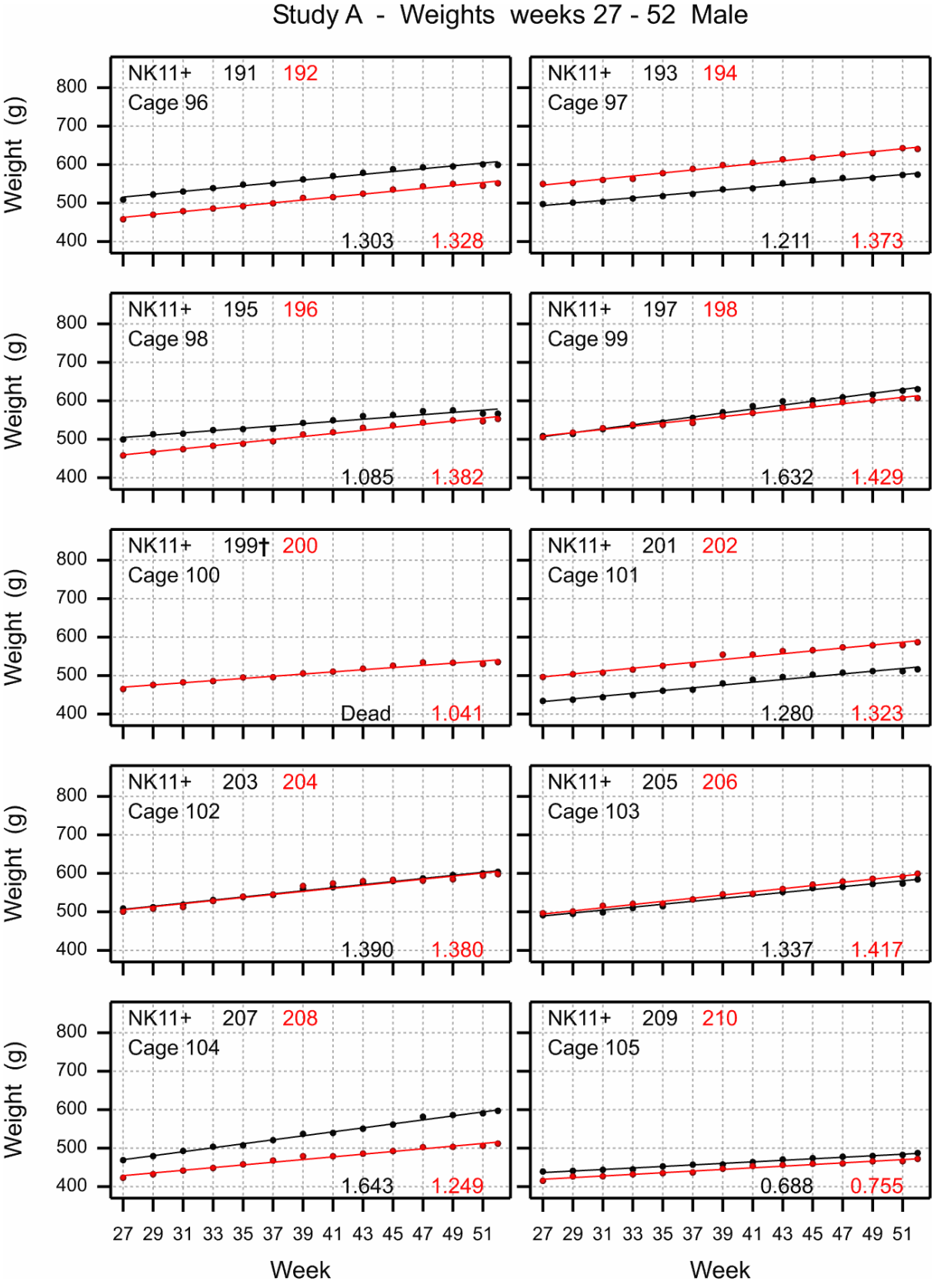

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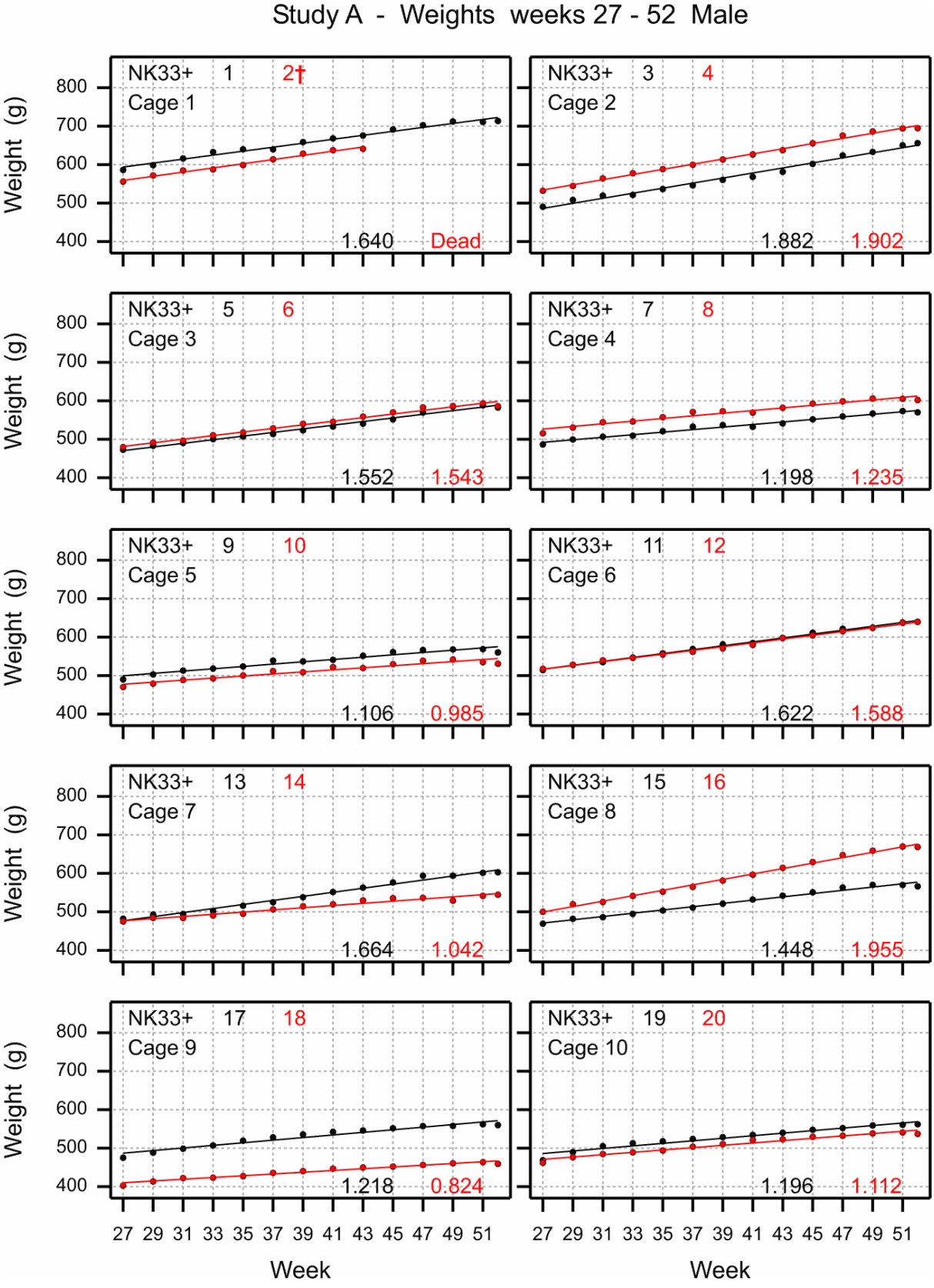

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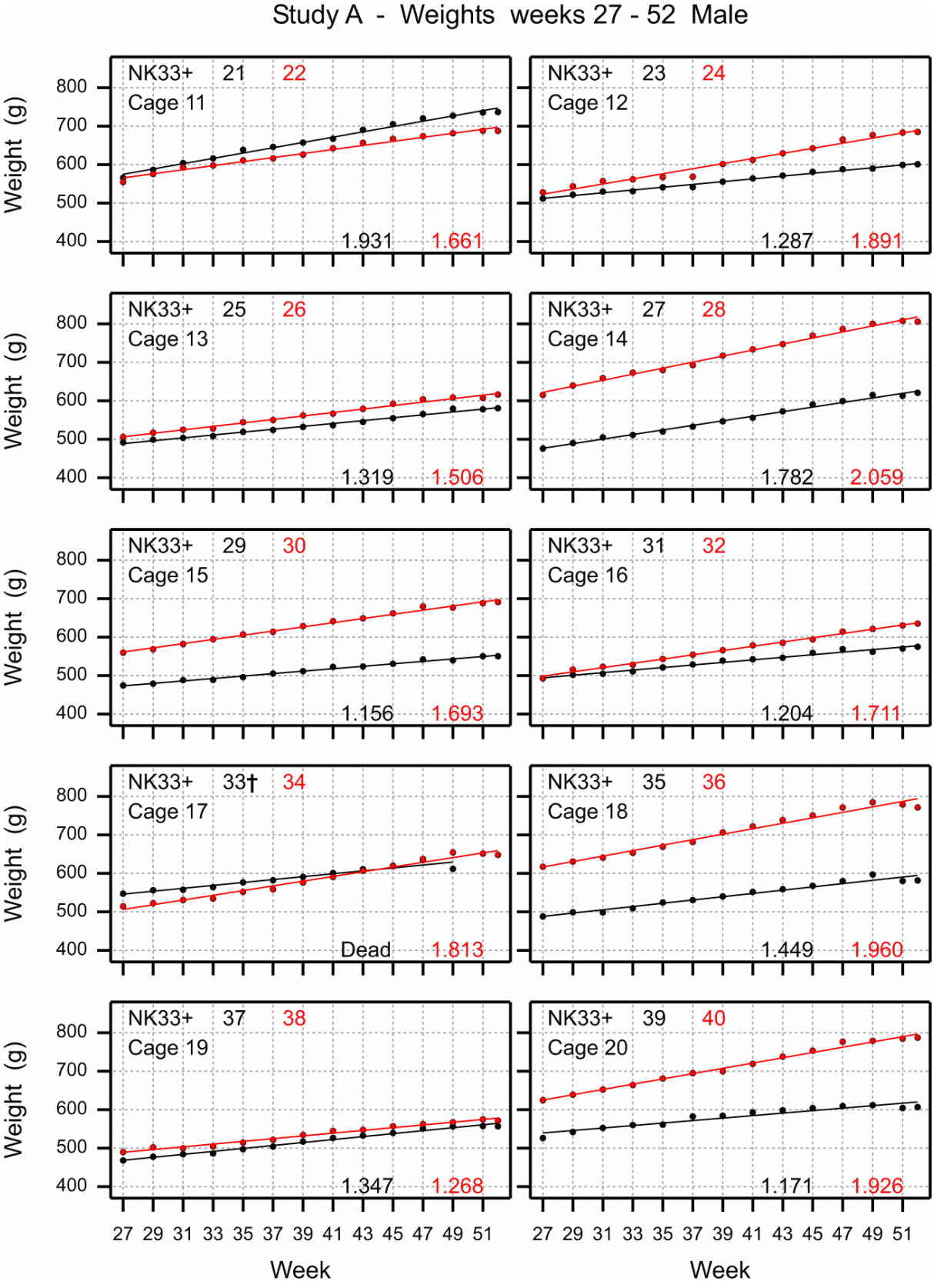

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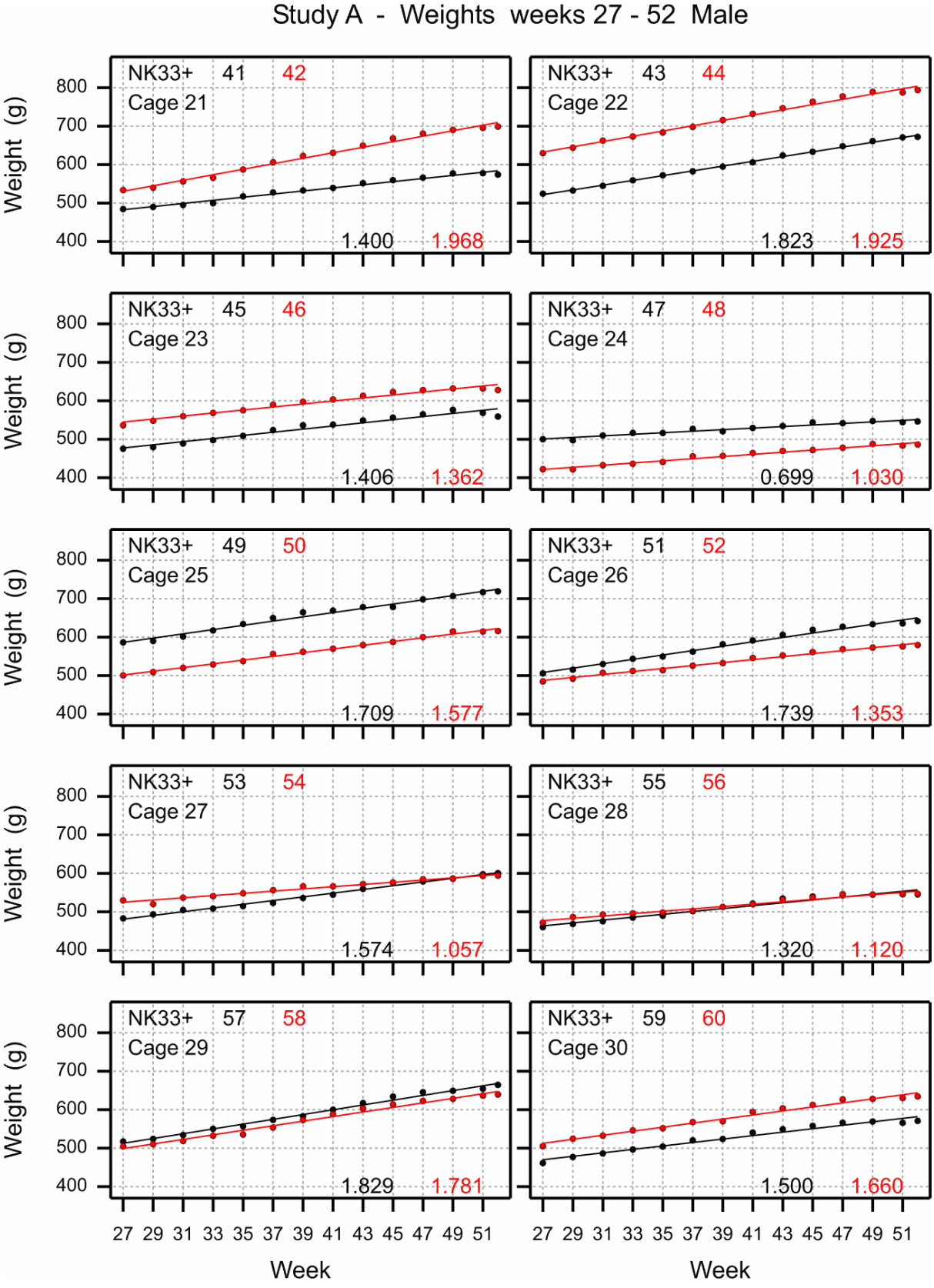

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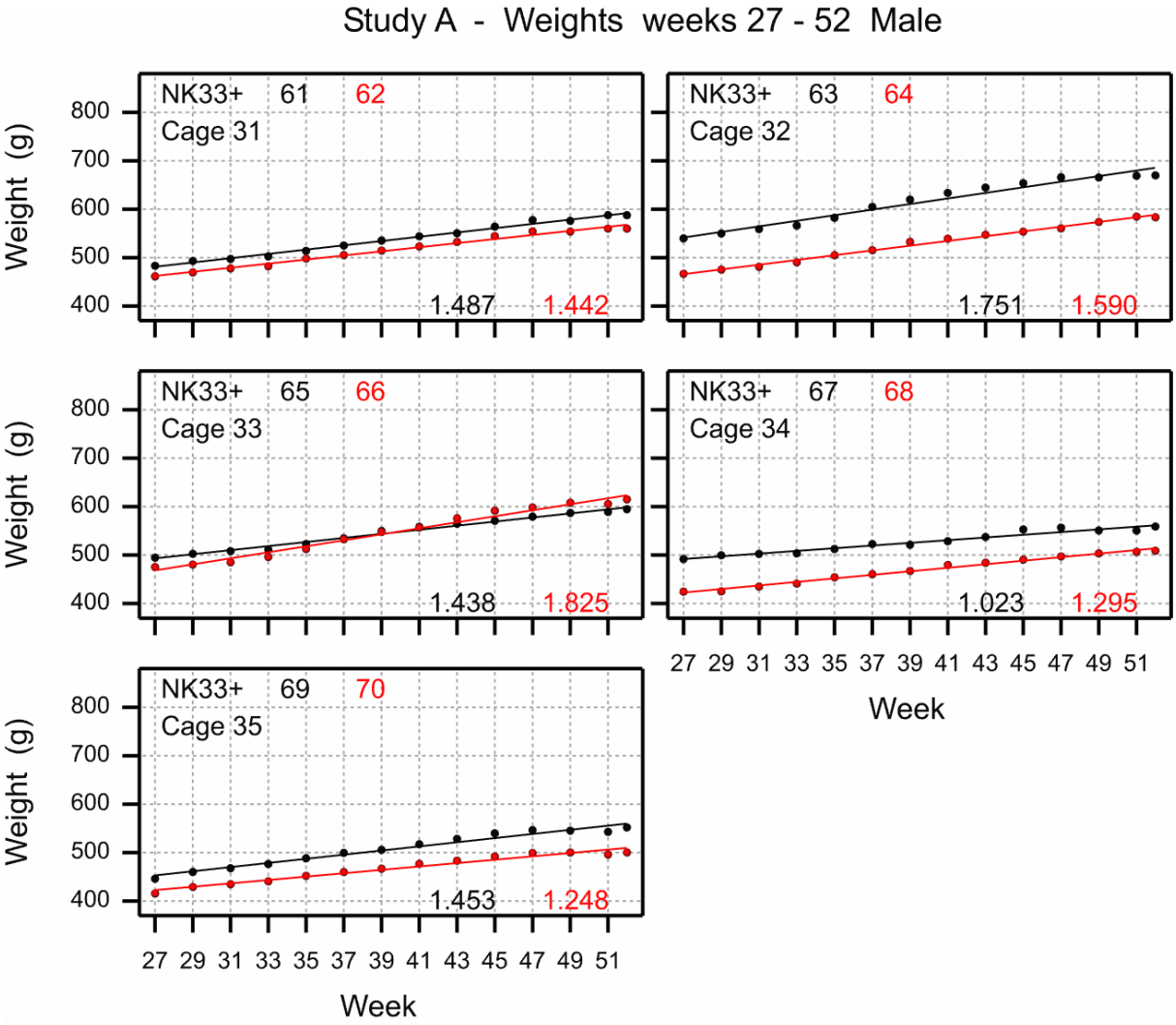

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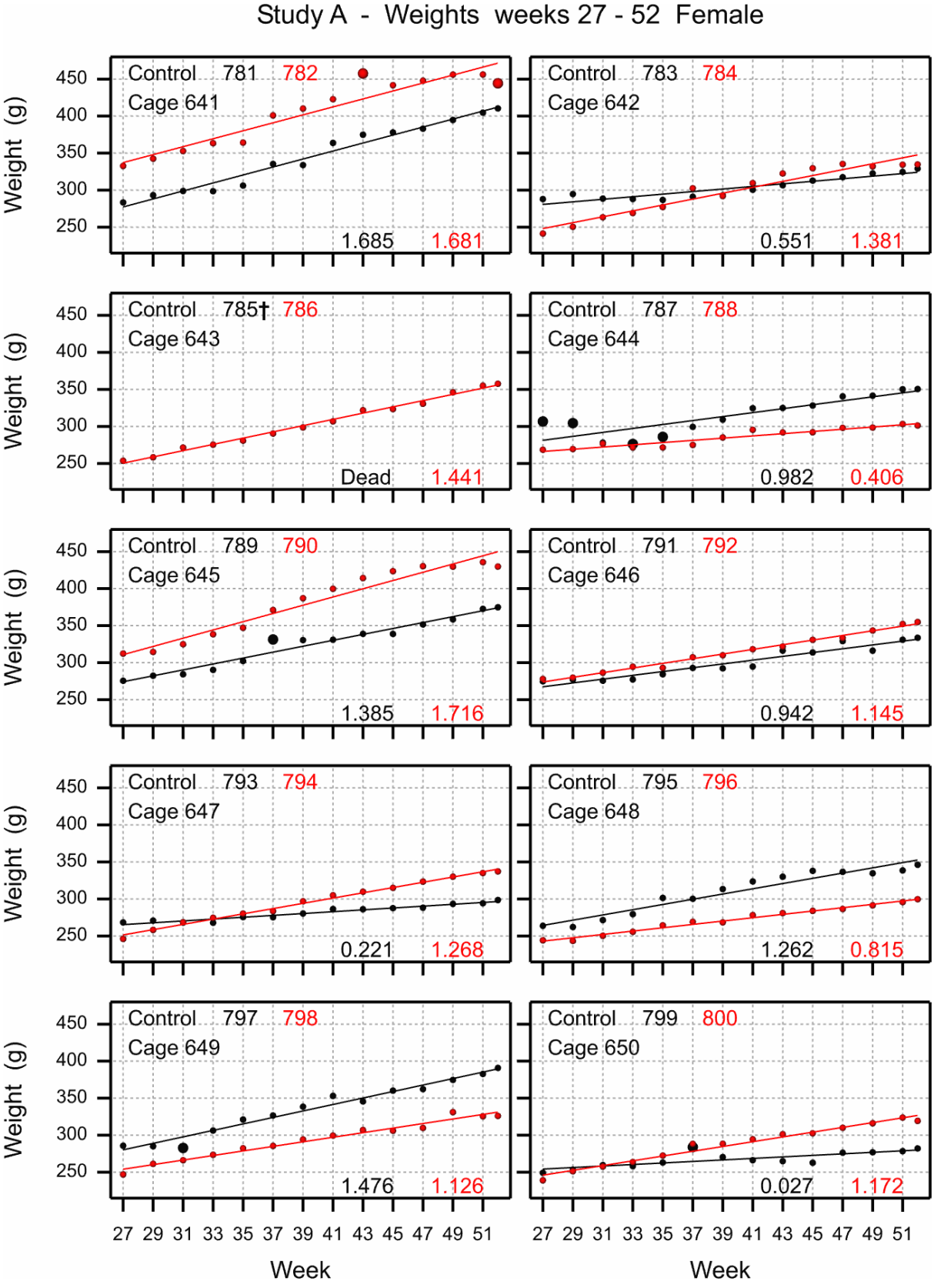

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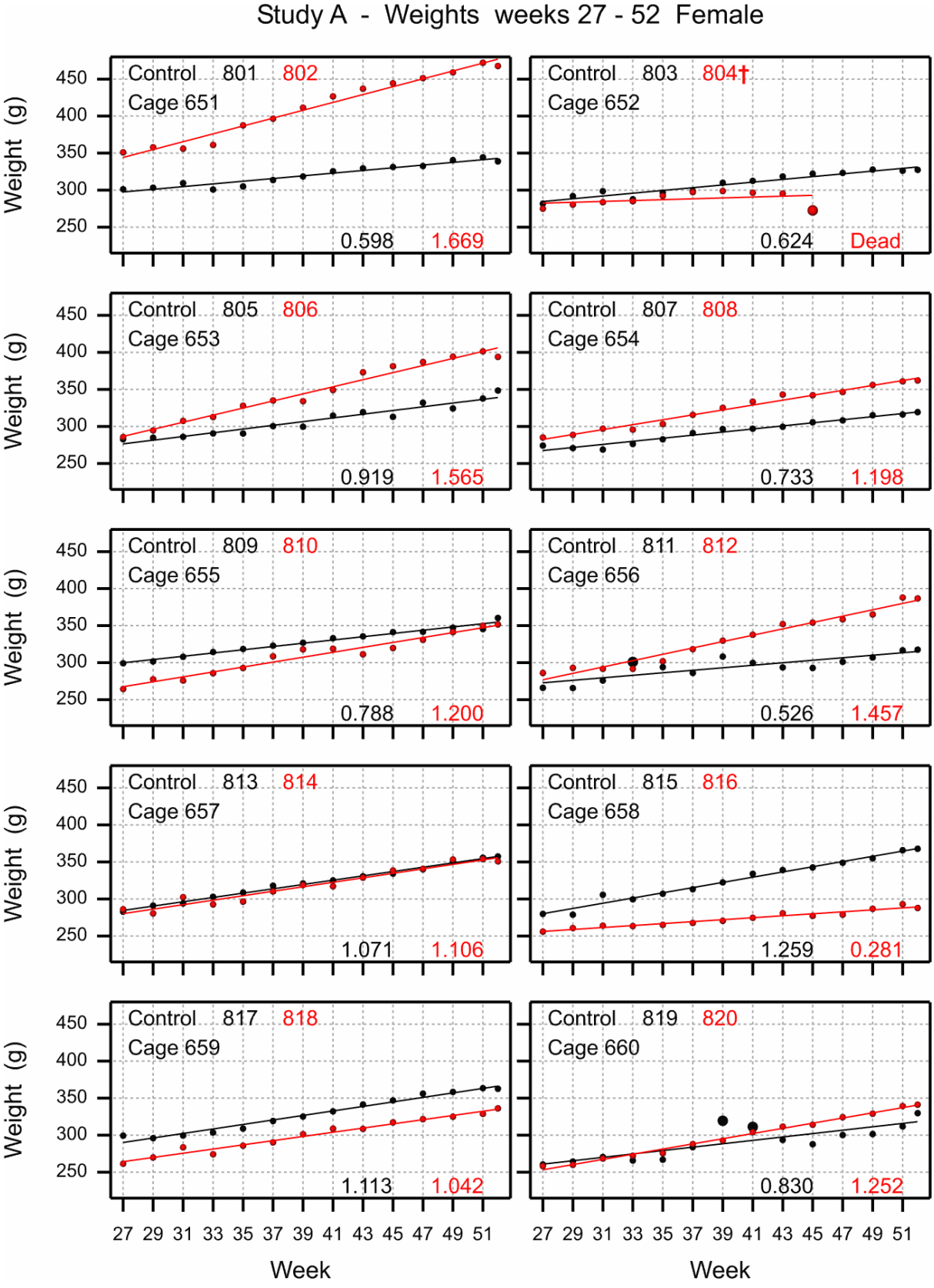

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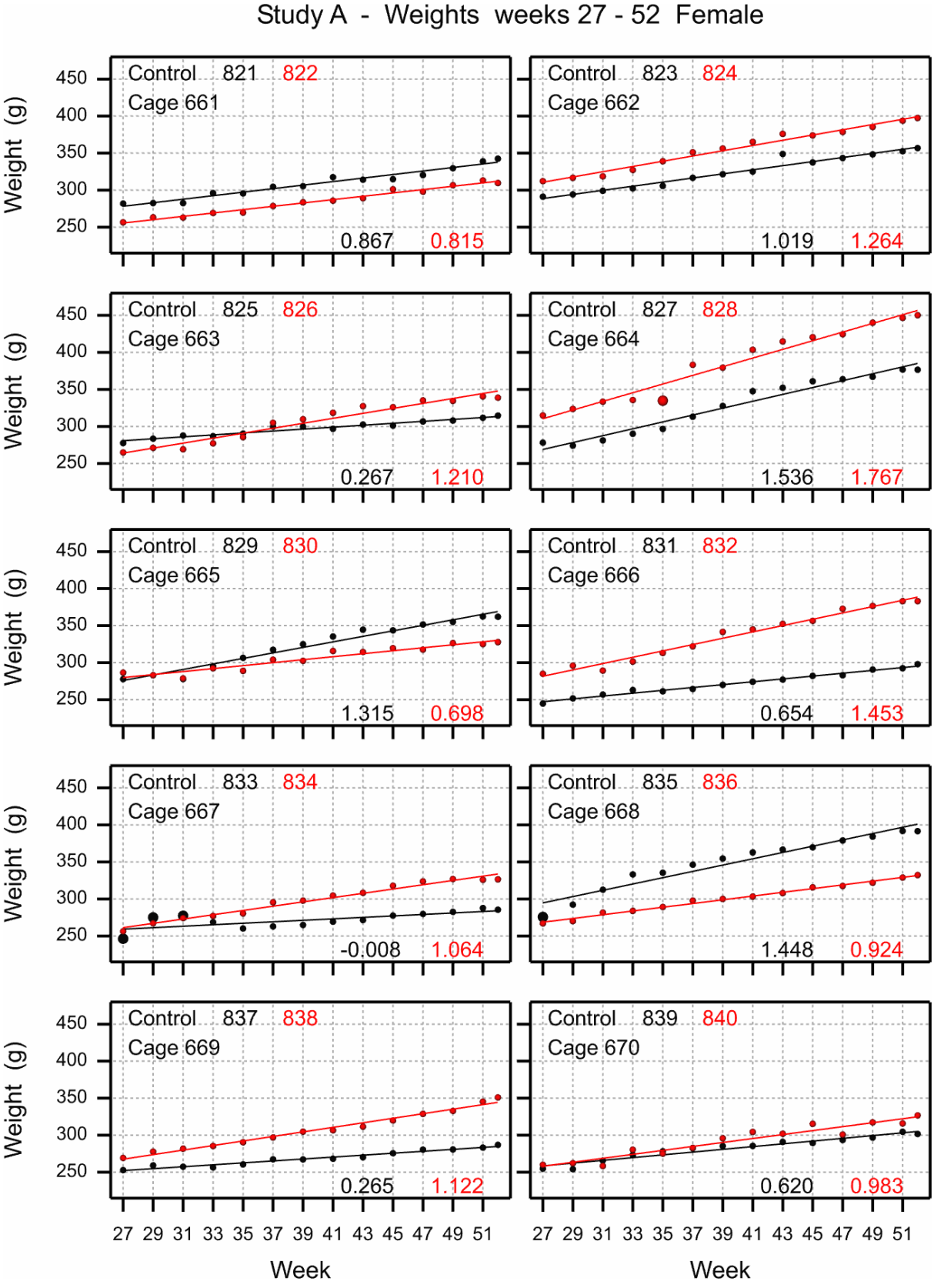
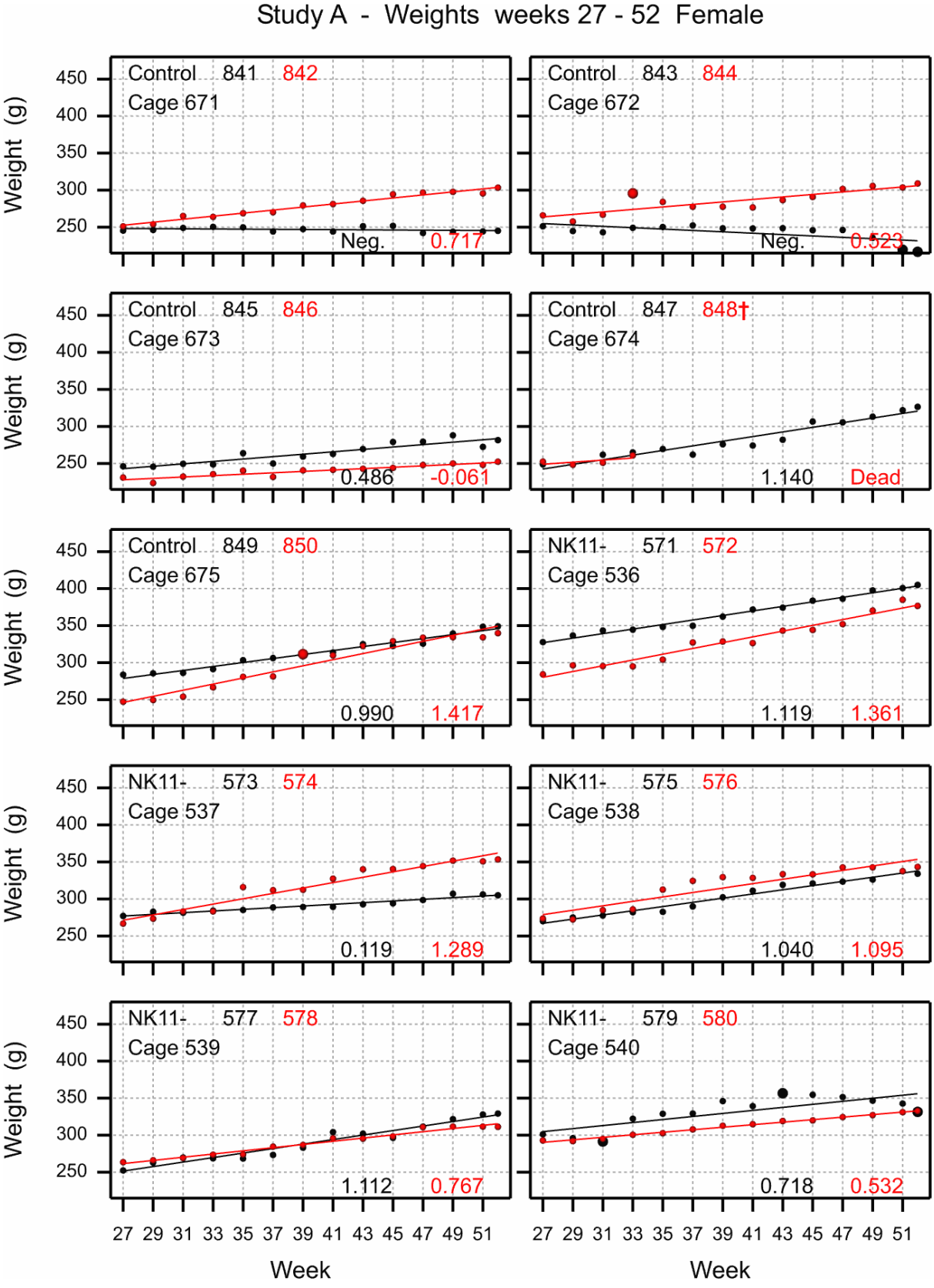


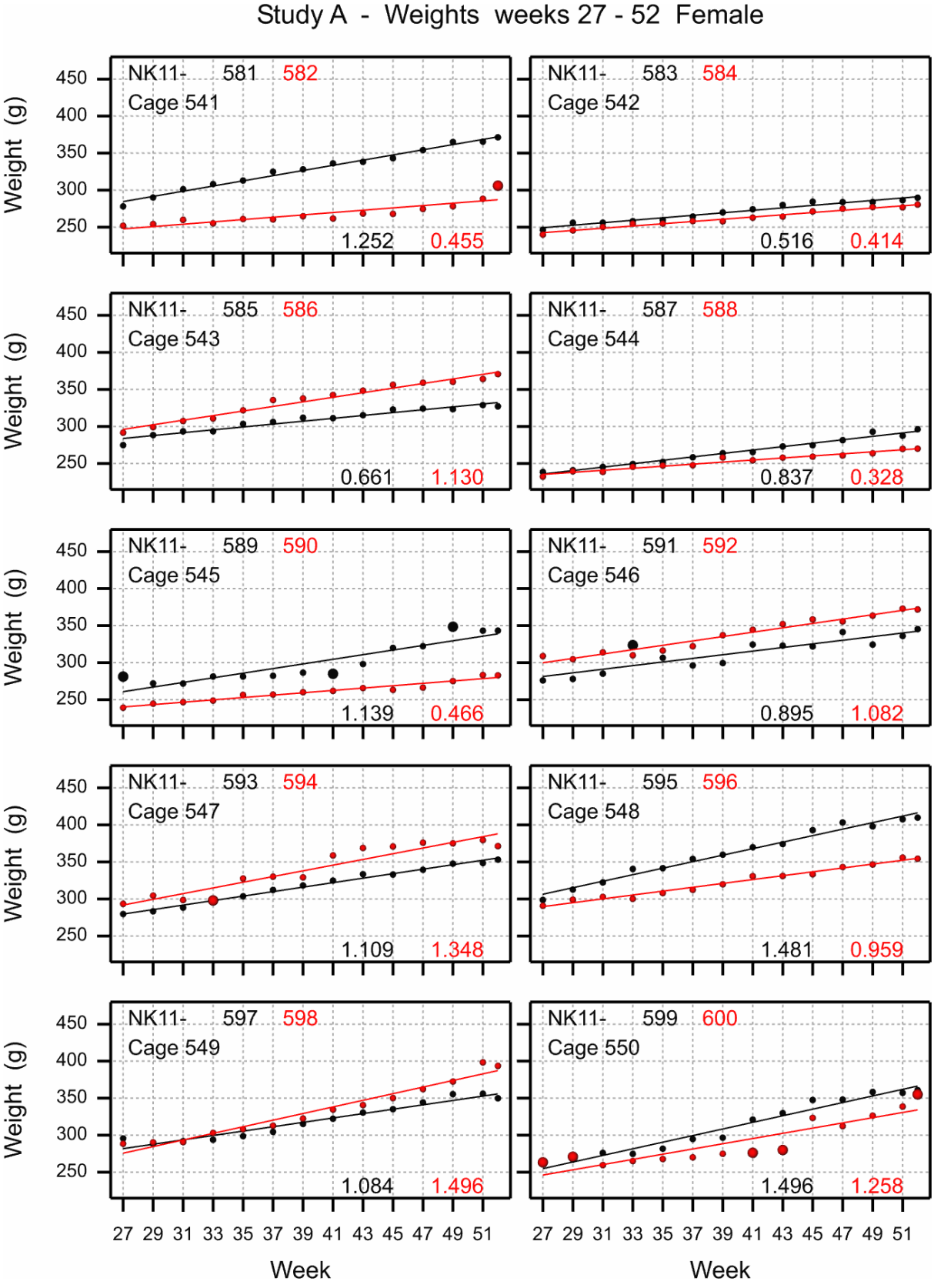
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



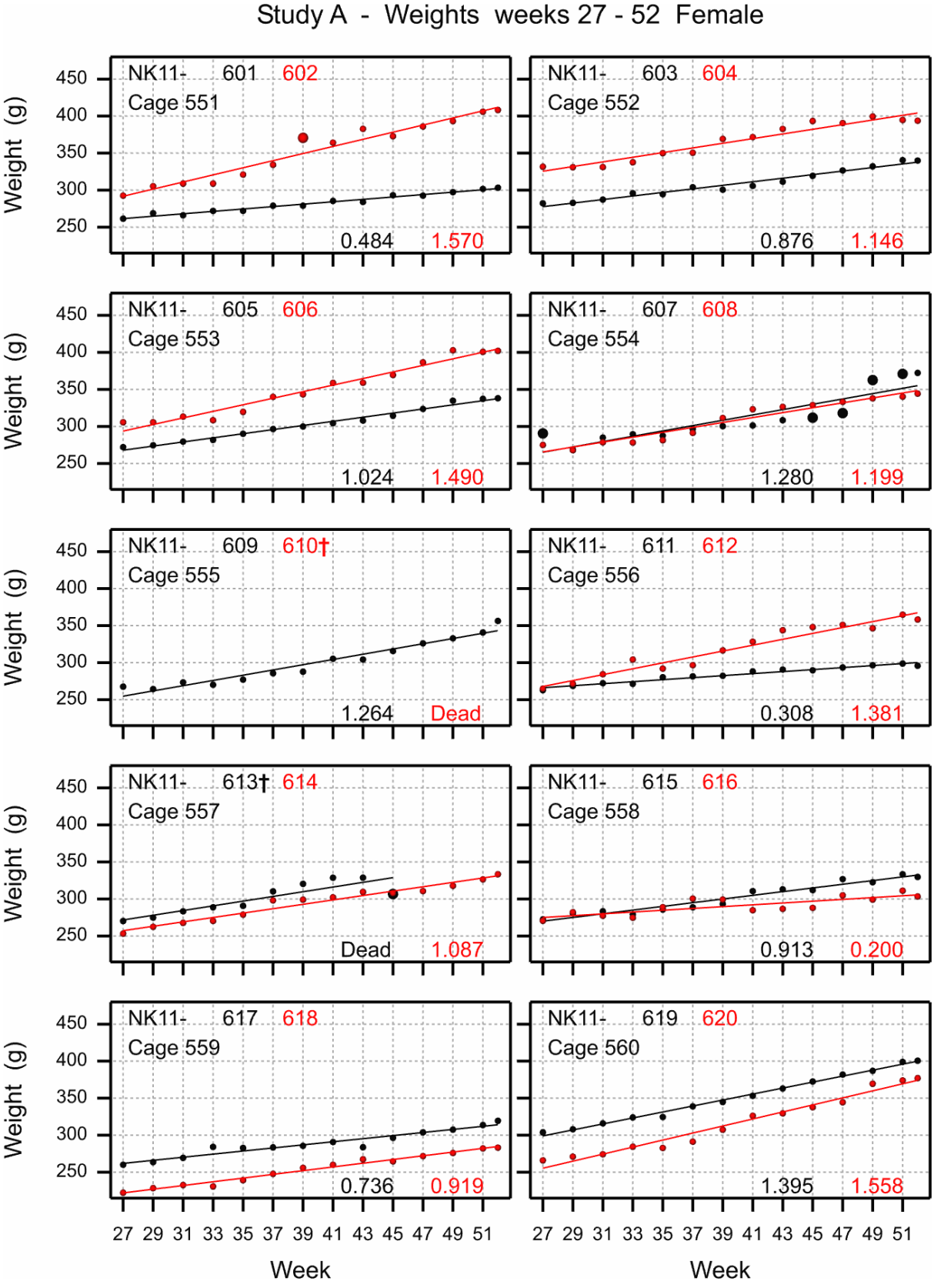
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



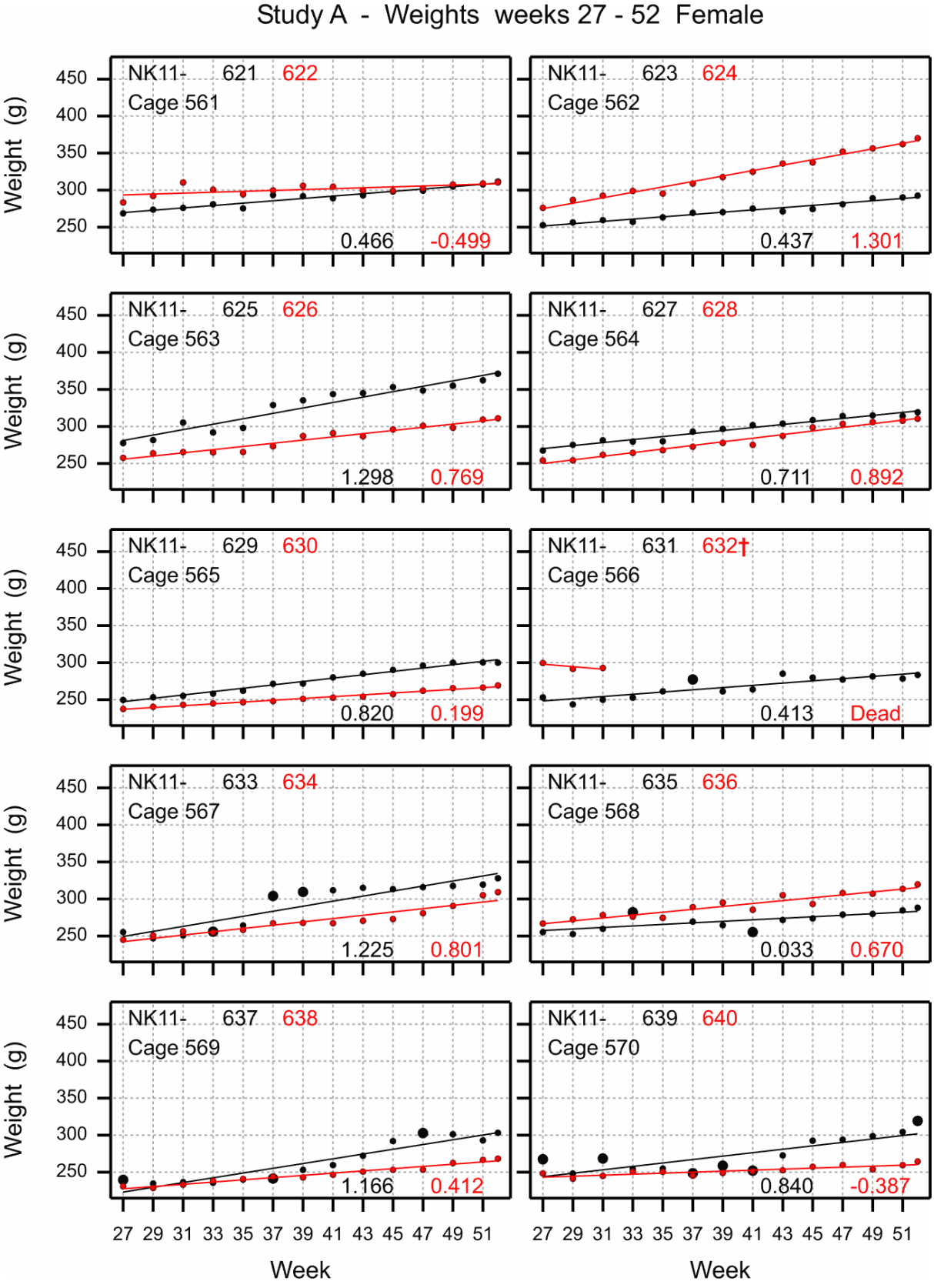
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



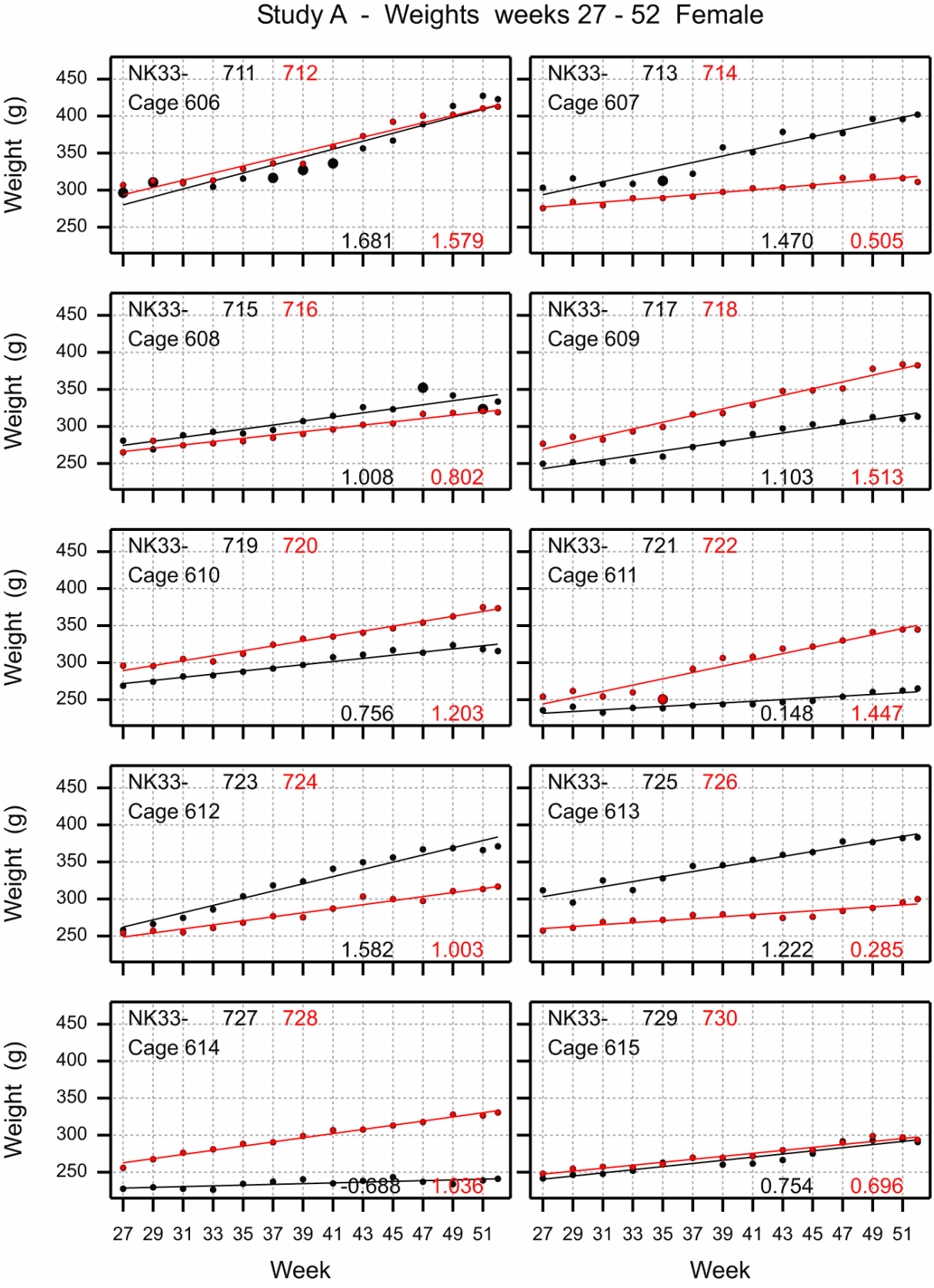
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



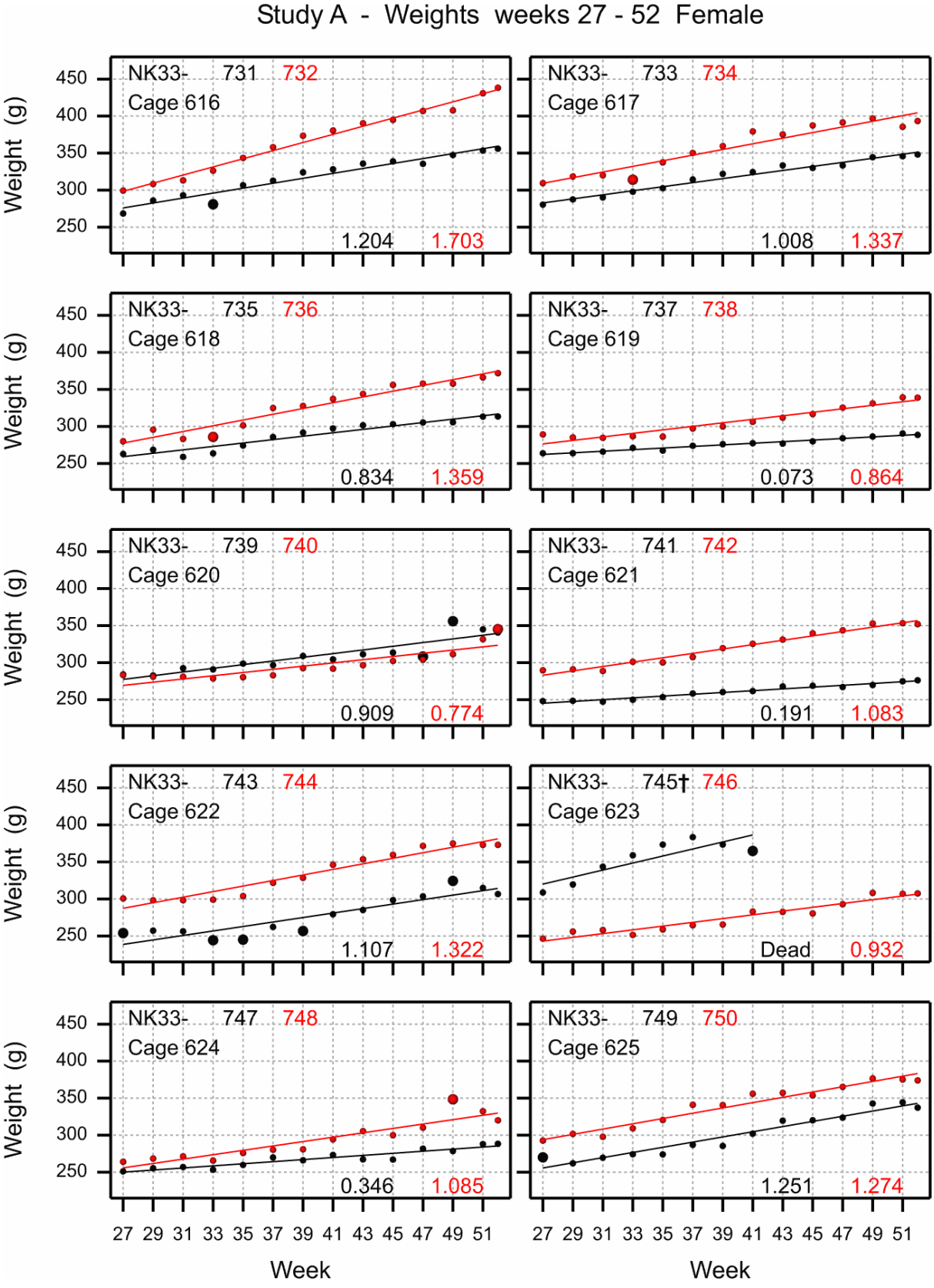
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



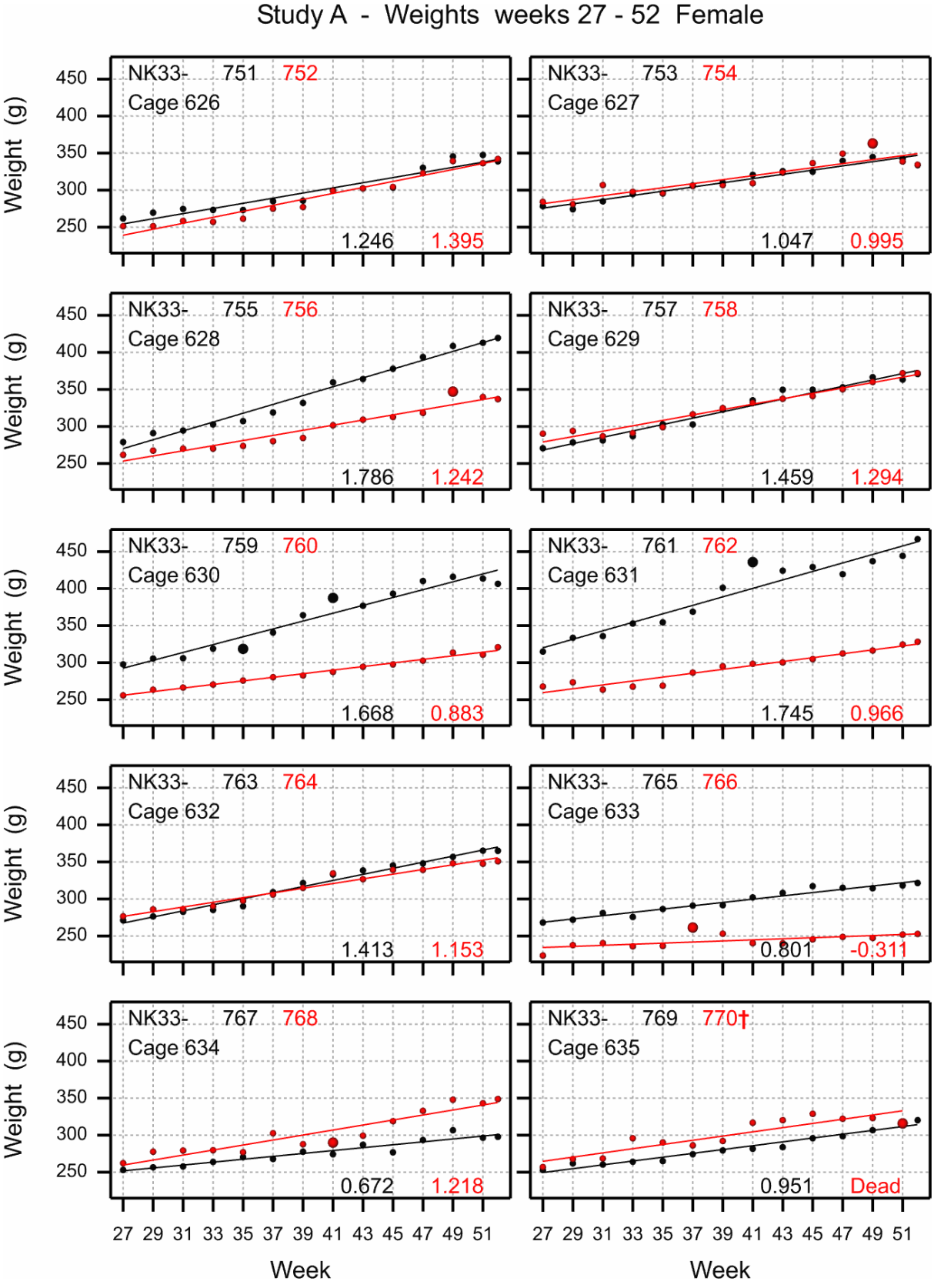
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



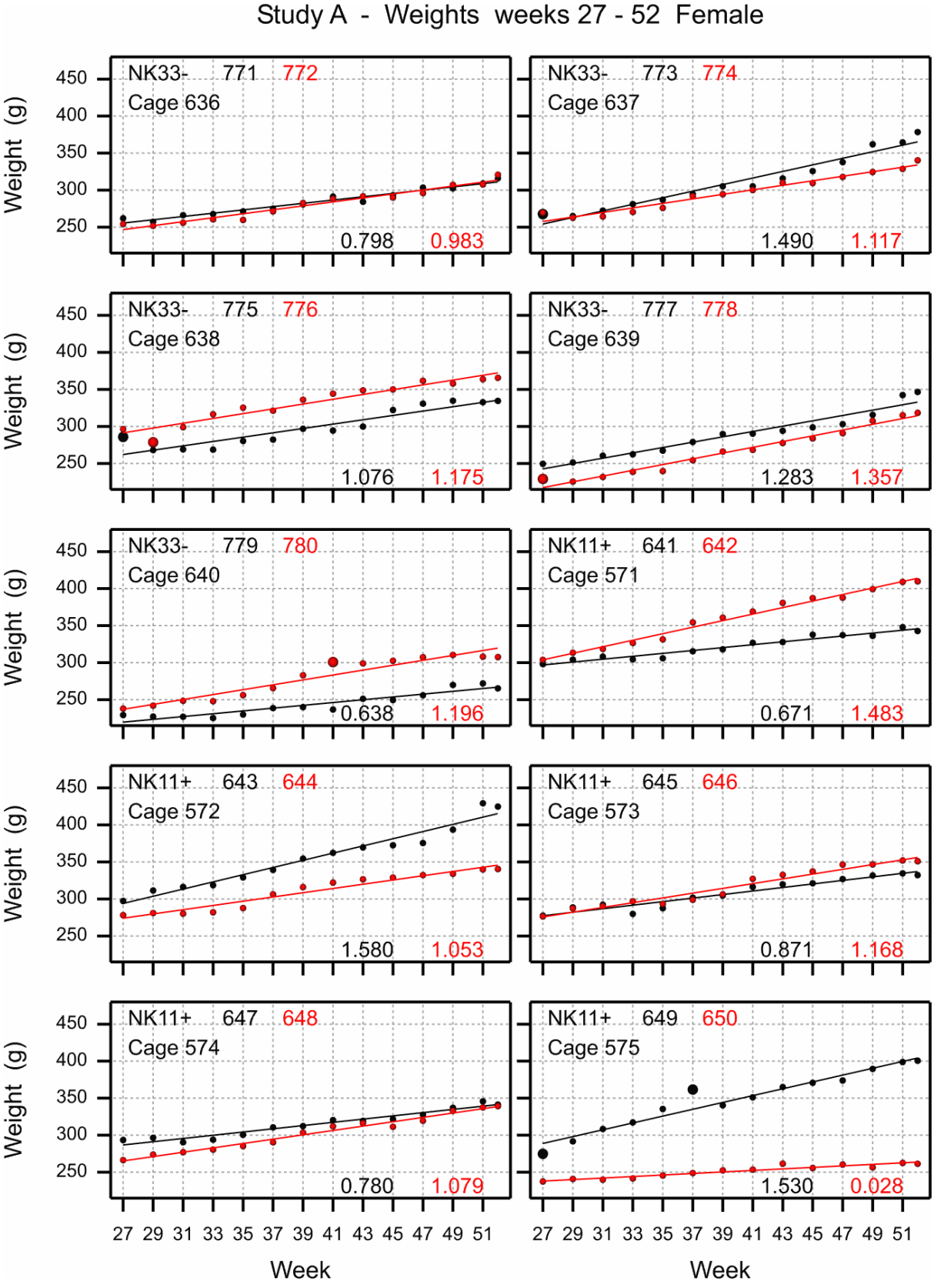
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



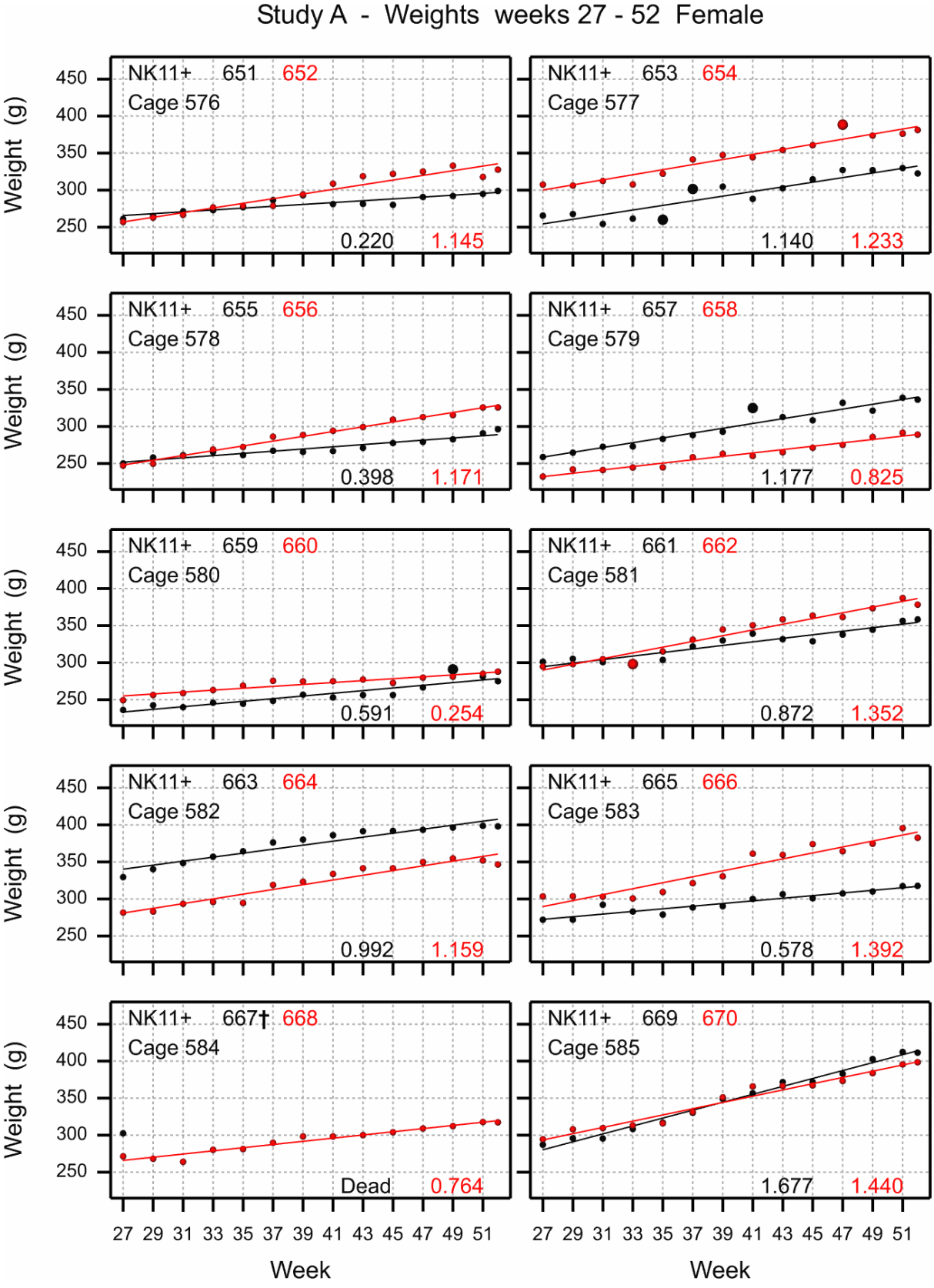
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



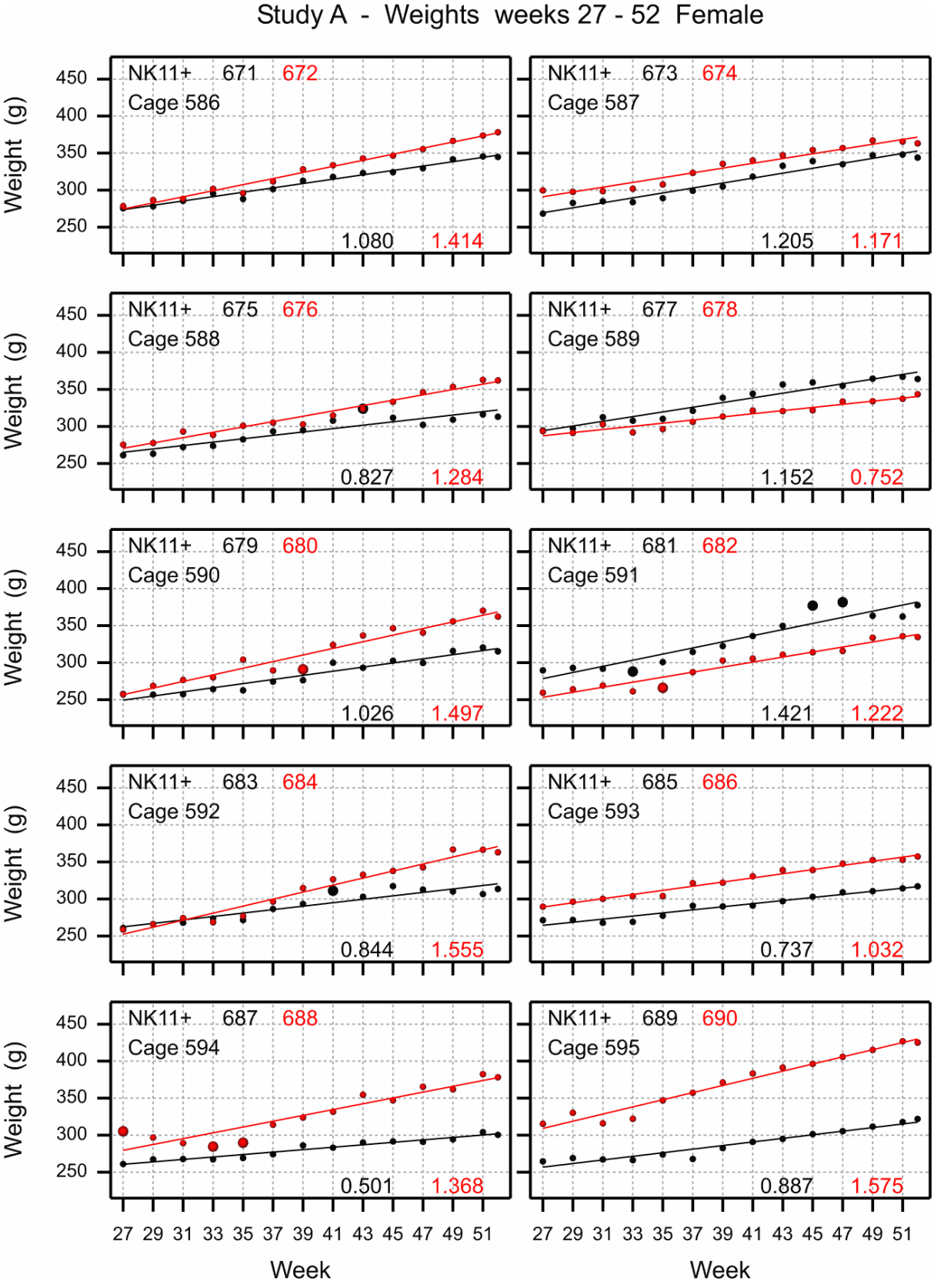
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



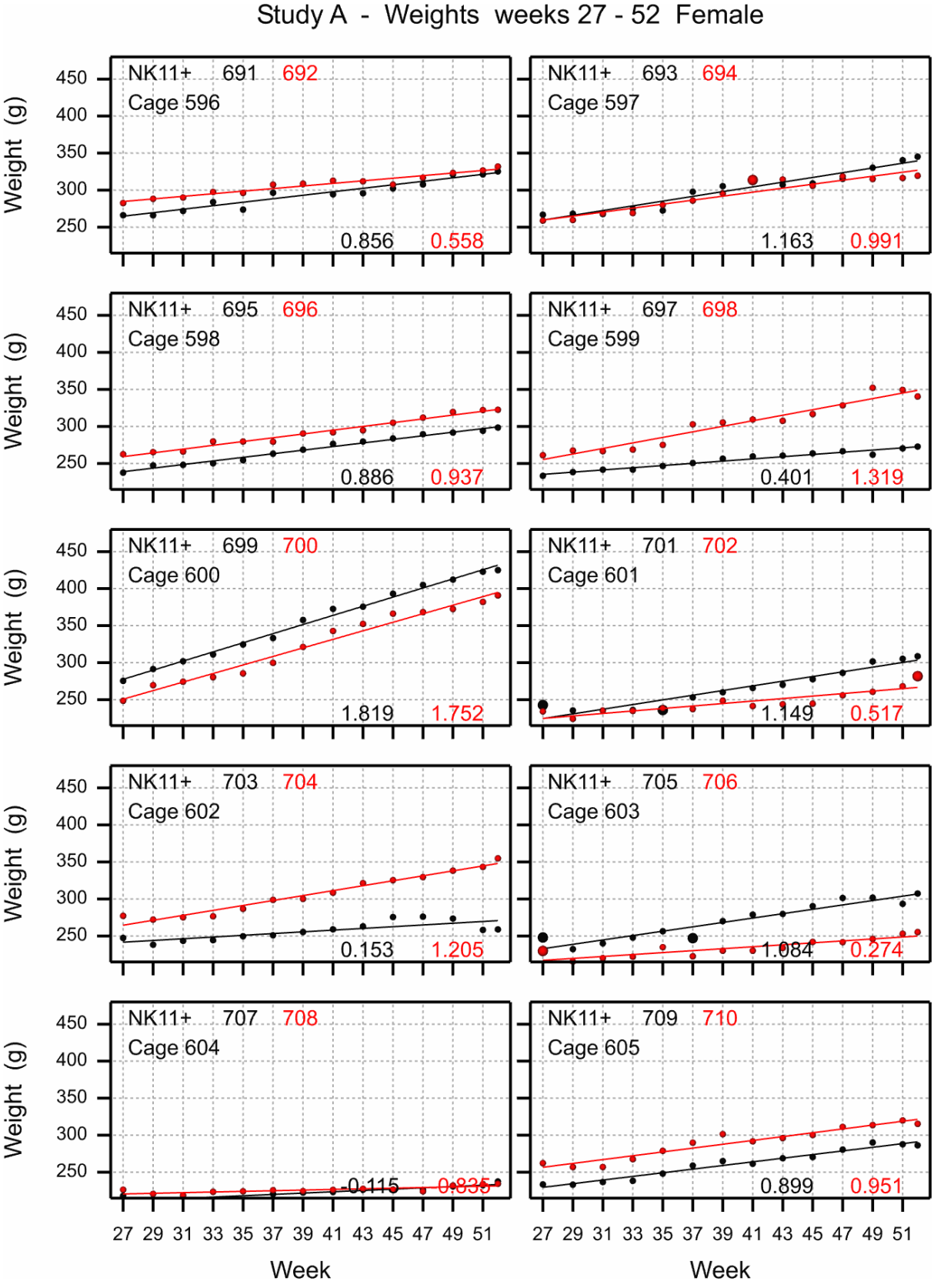
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



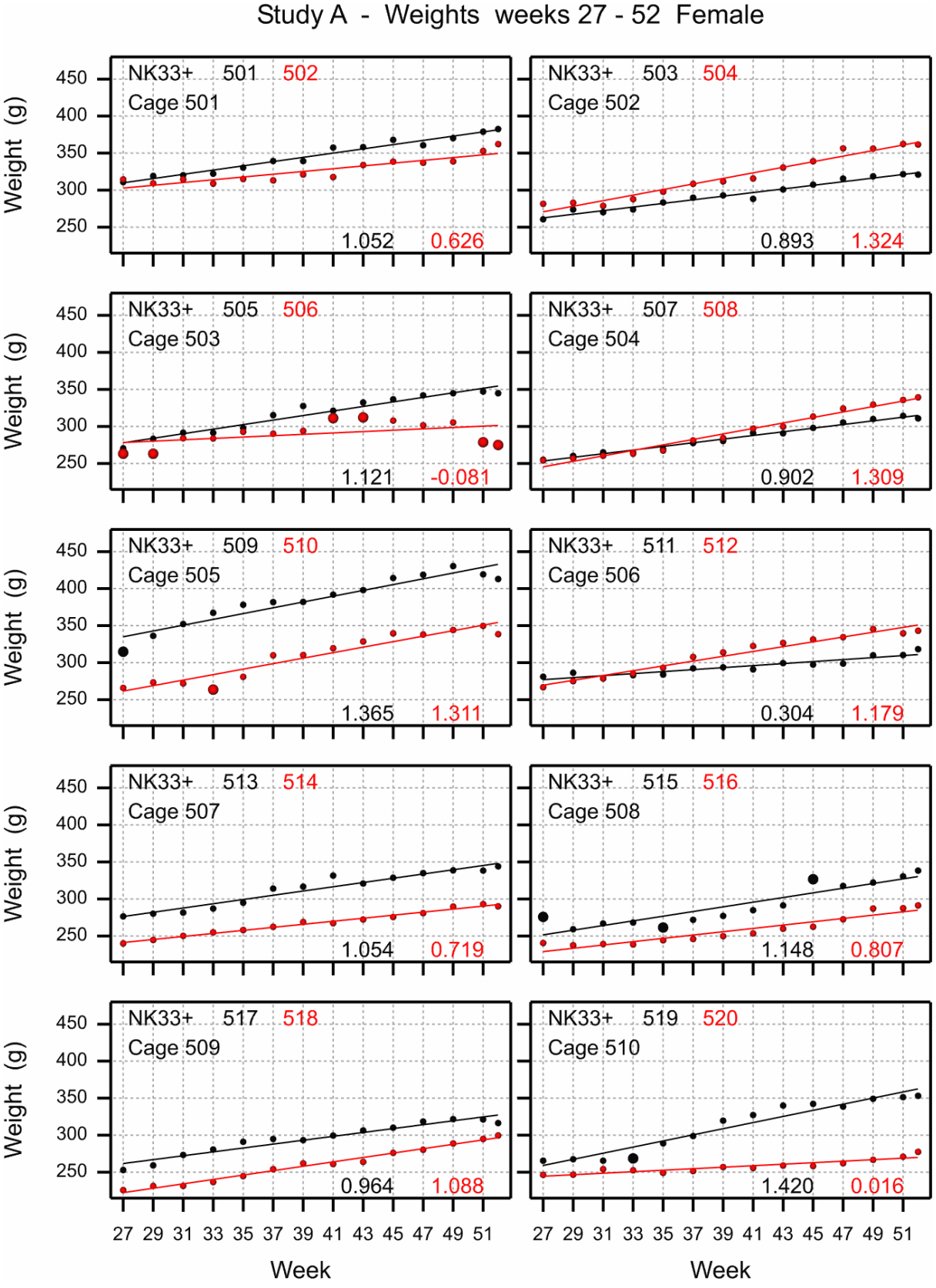
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



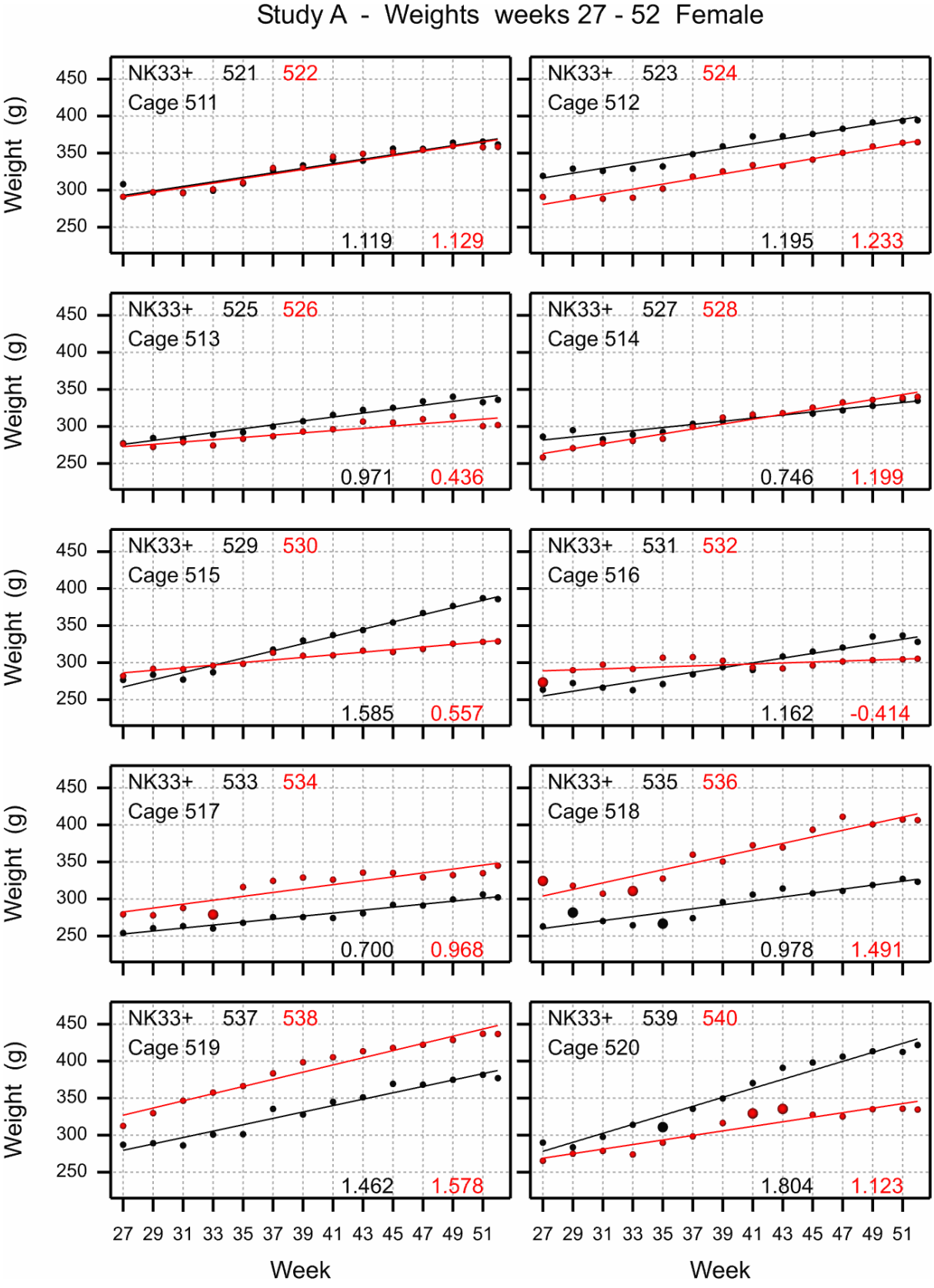
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



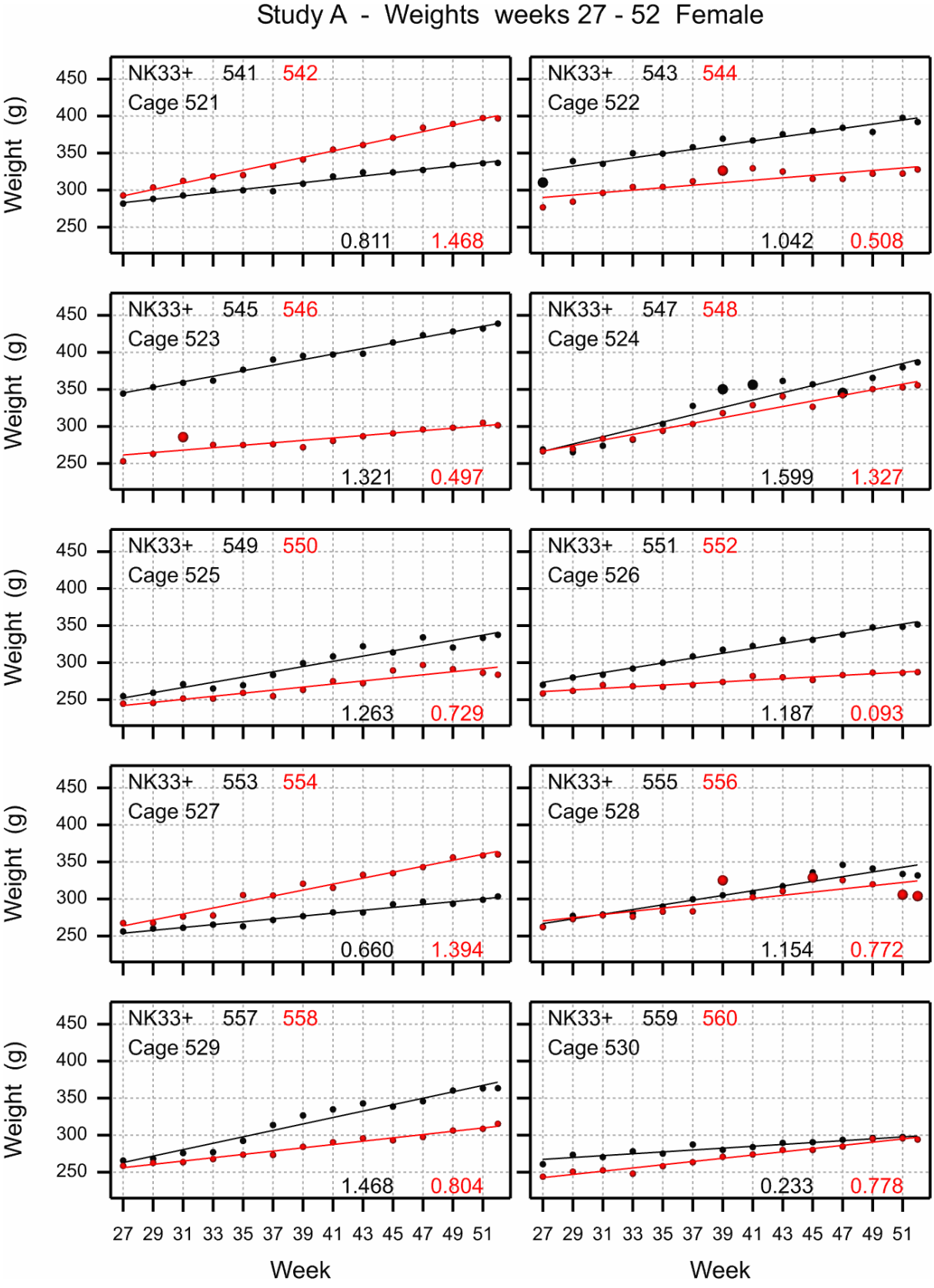
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



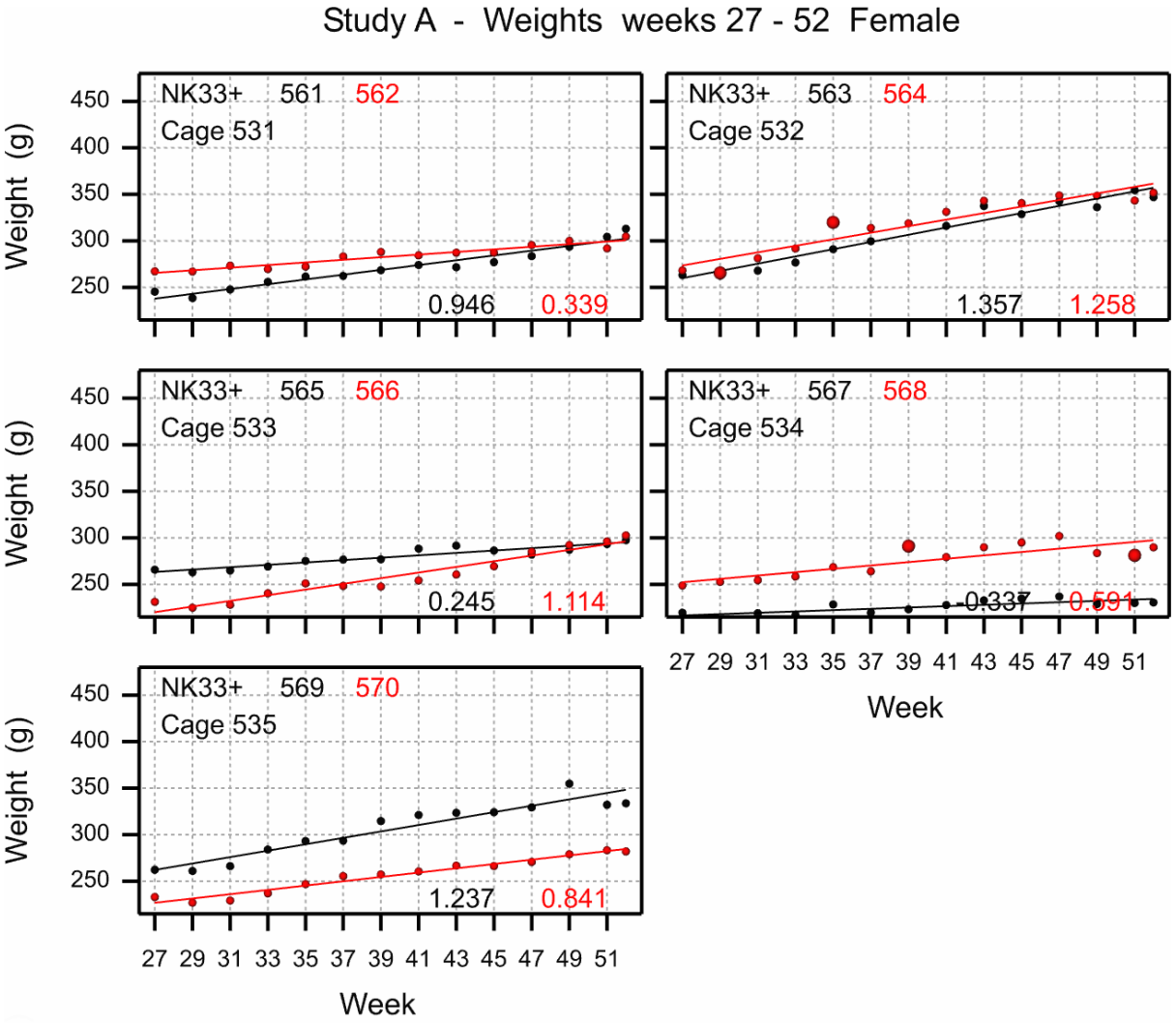
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



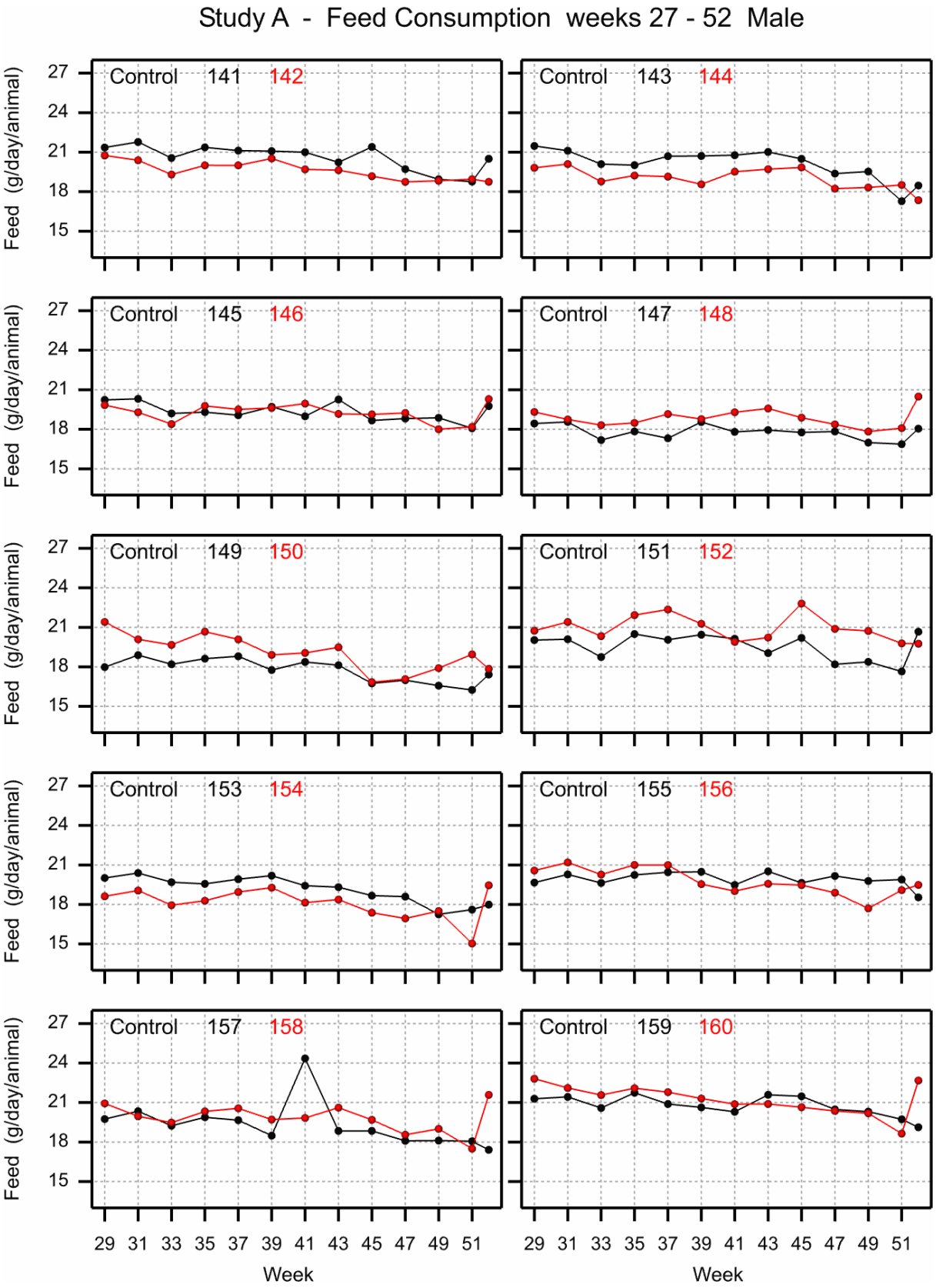
Appendix 1. Growth curves per animal pair (continued)

The feed group and animal numbers are given in the left top corner of the graph, while the estimated growth rate, i.e. $\gamma = \log(\beta)$, is given in the right-bottom corner.



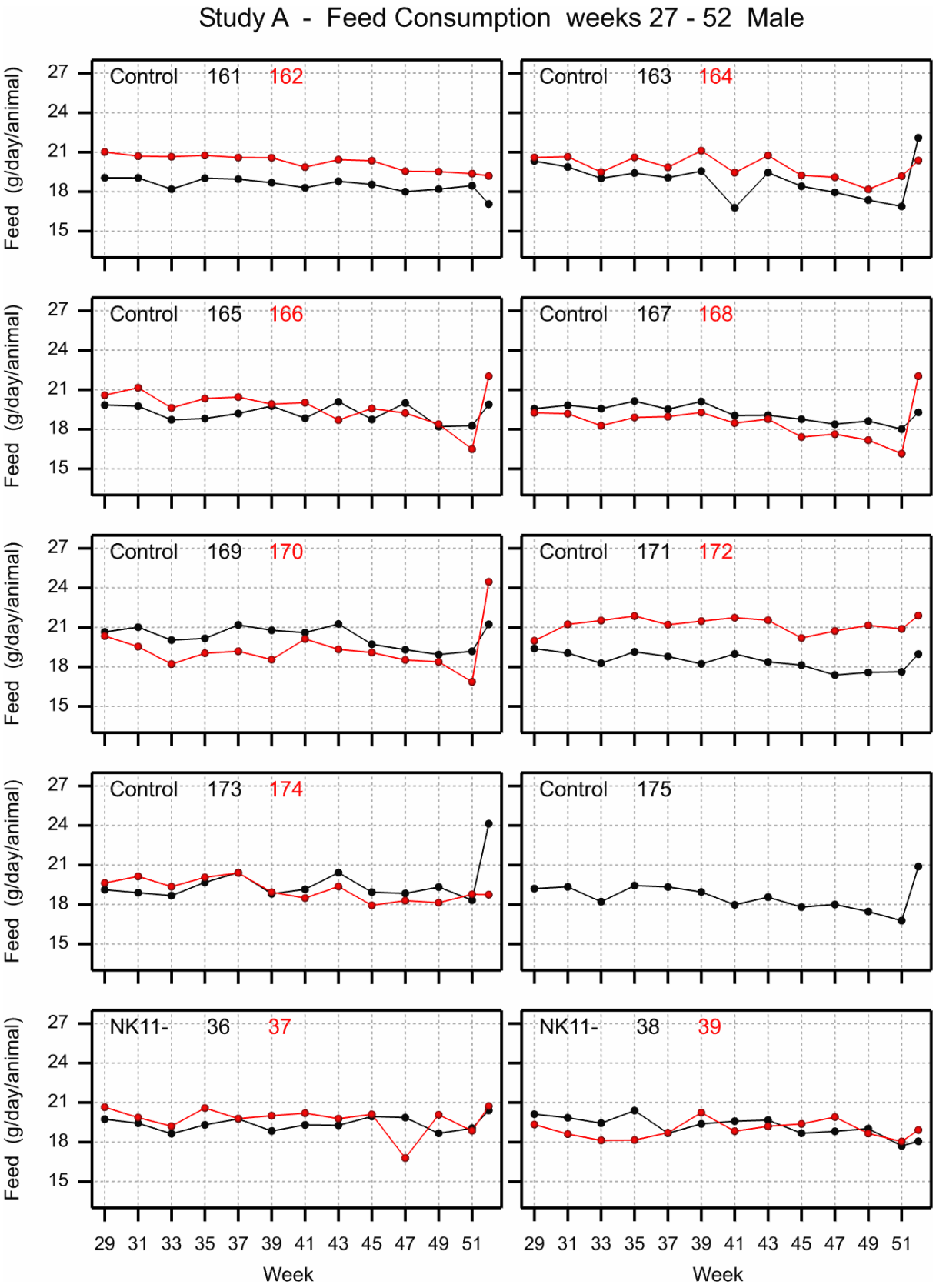
Appendix 2. Feed consumption per cage

The feed group and cage numbers are given in the left top corner of the graph.



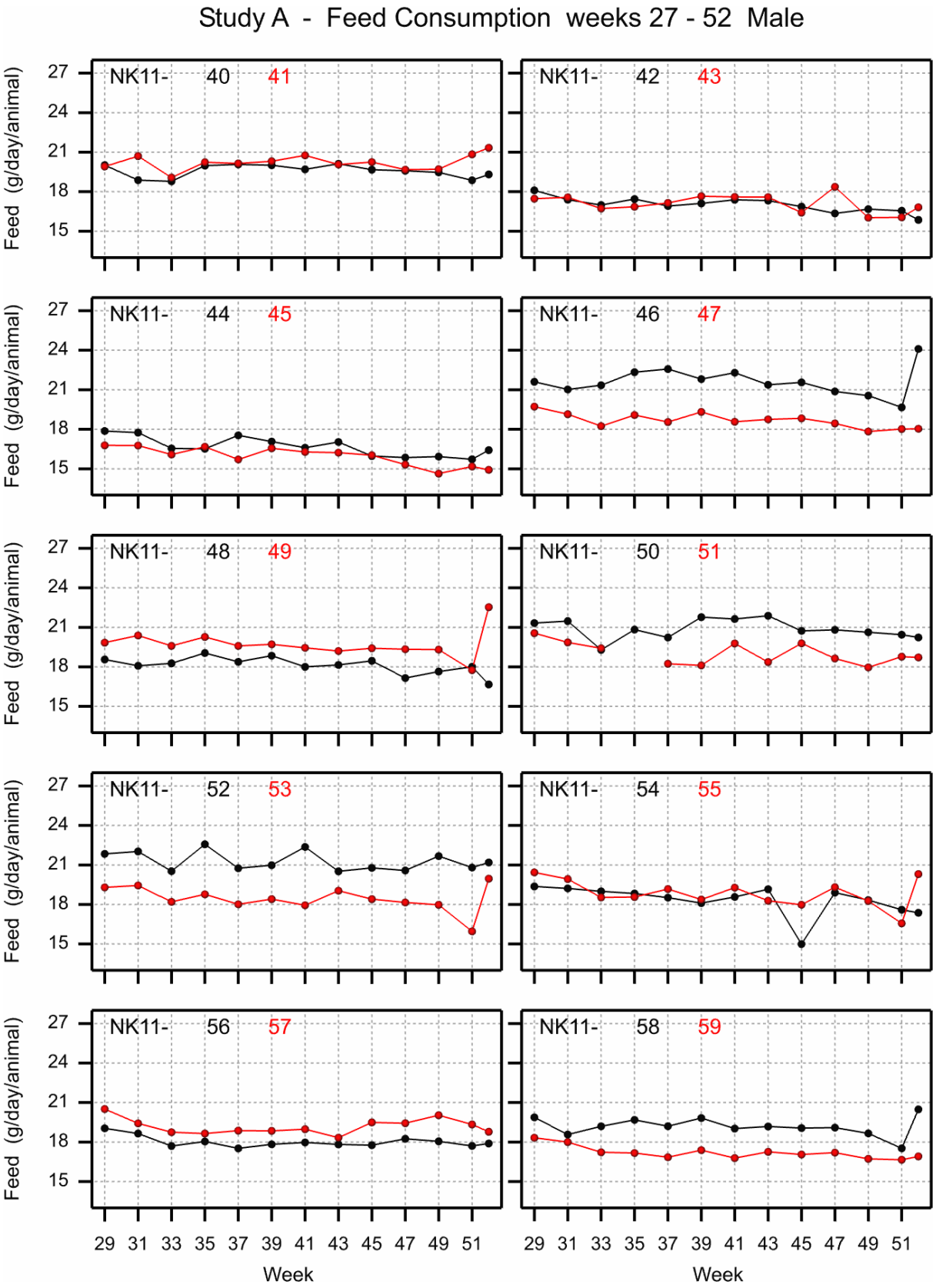
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



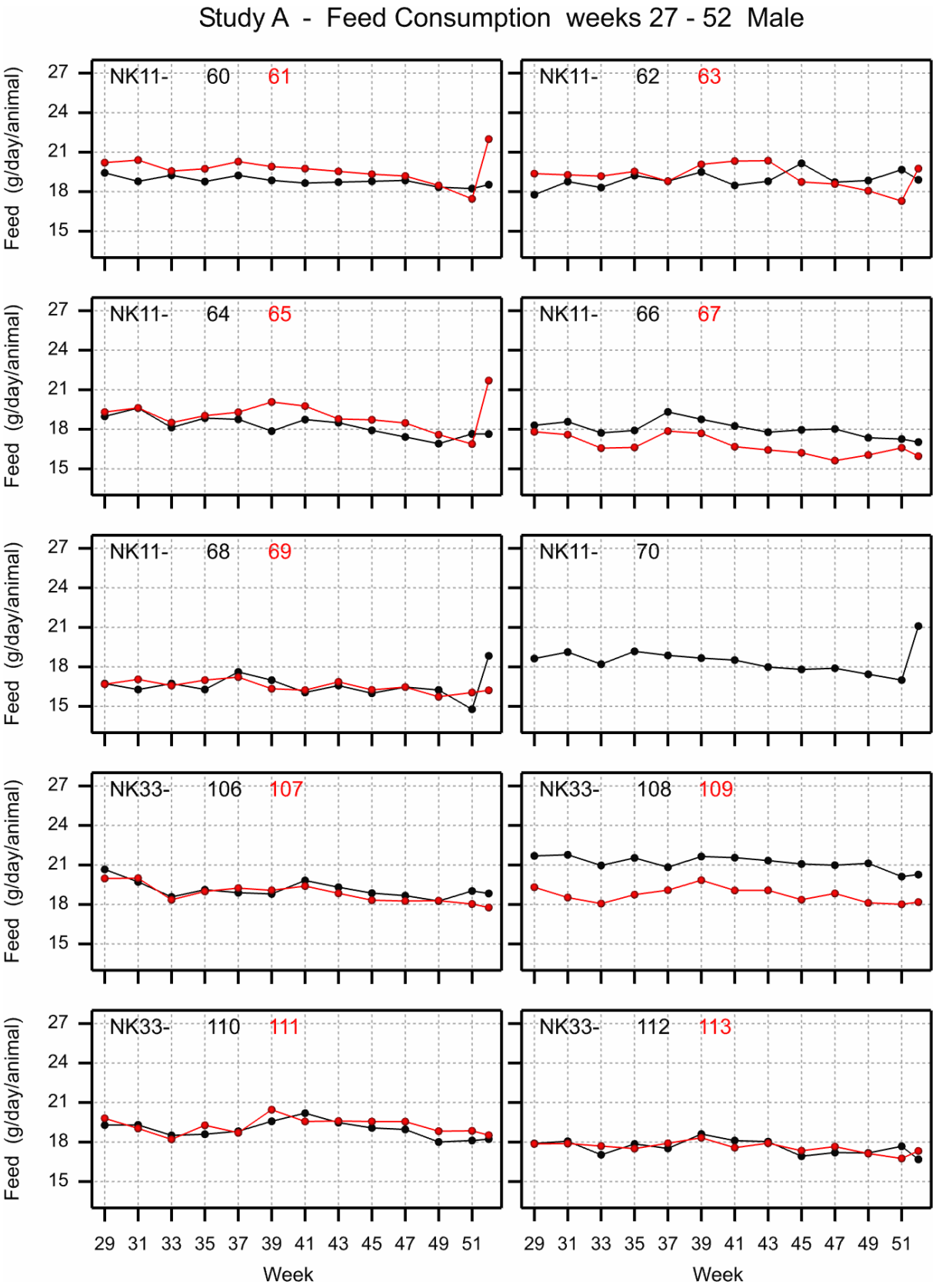
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



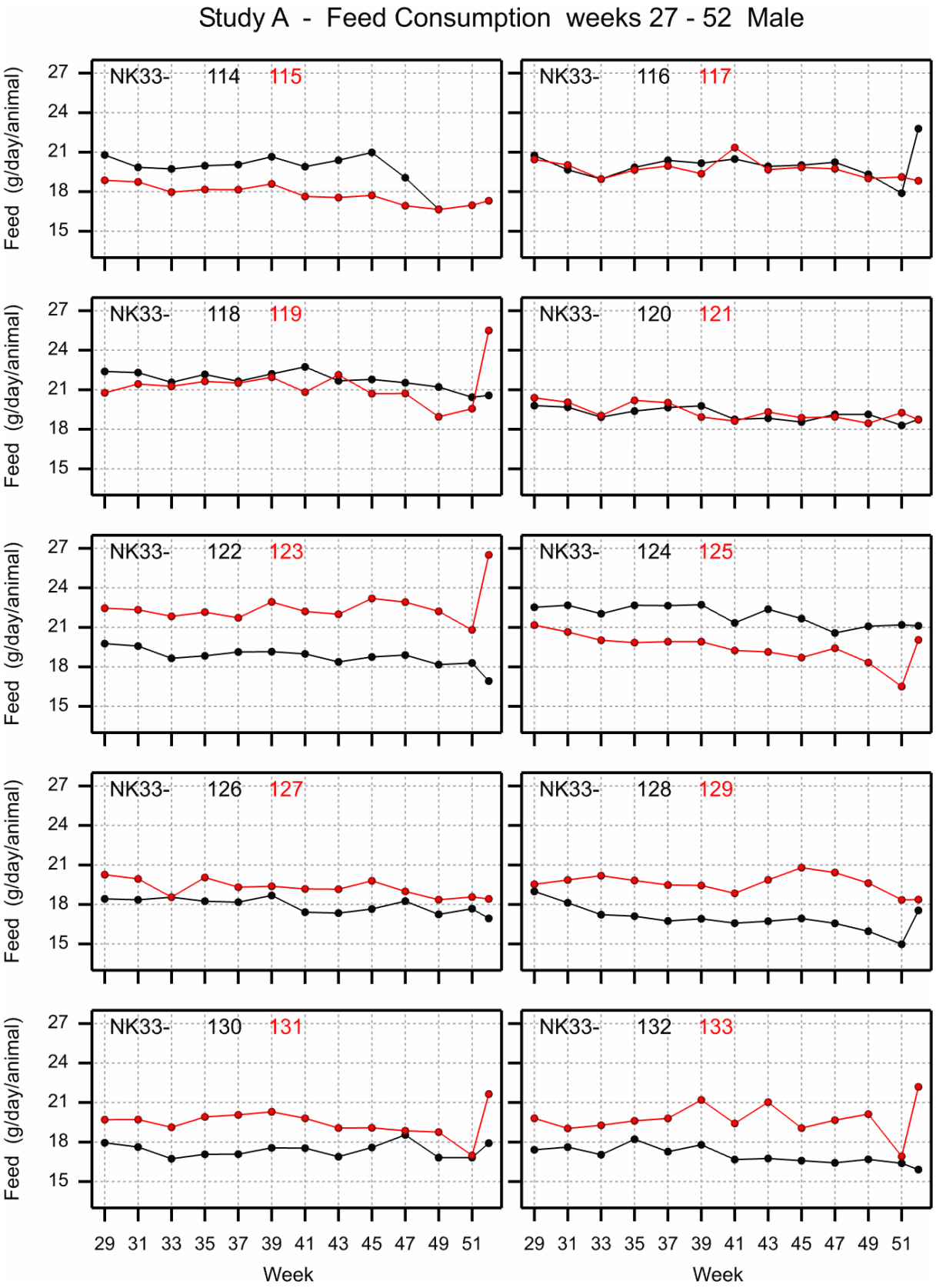
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



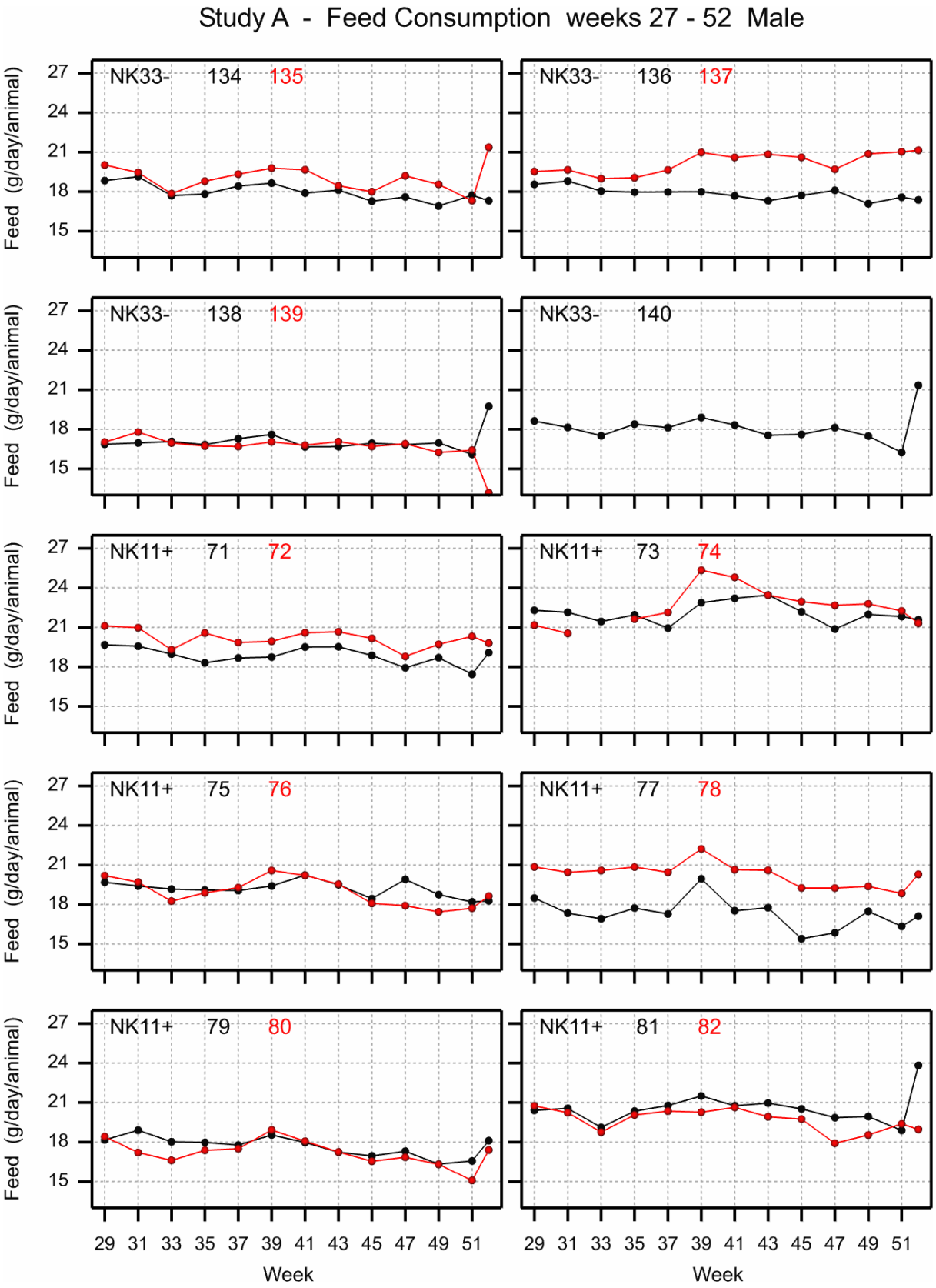
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



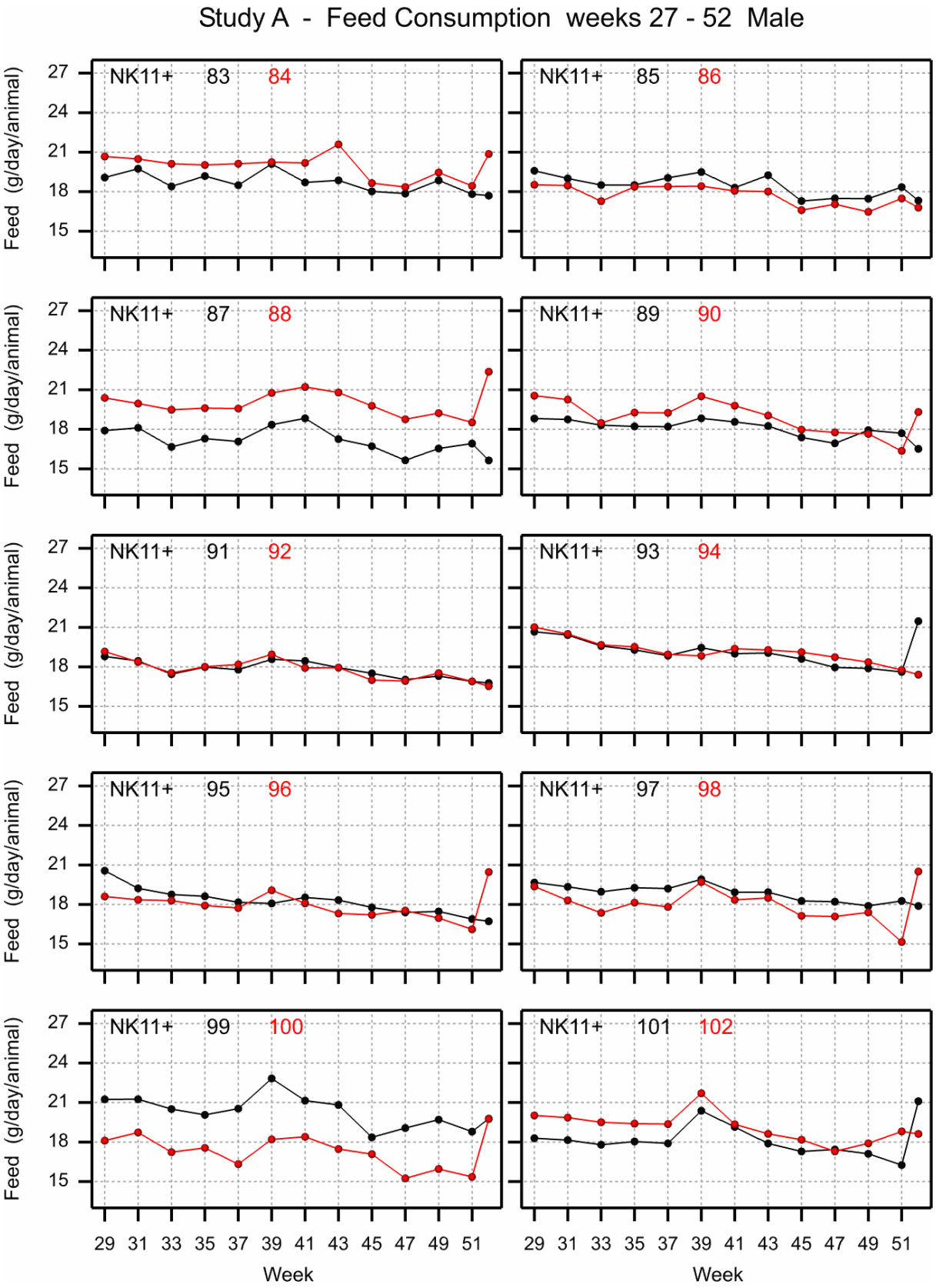
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



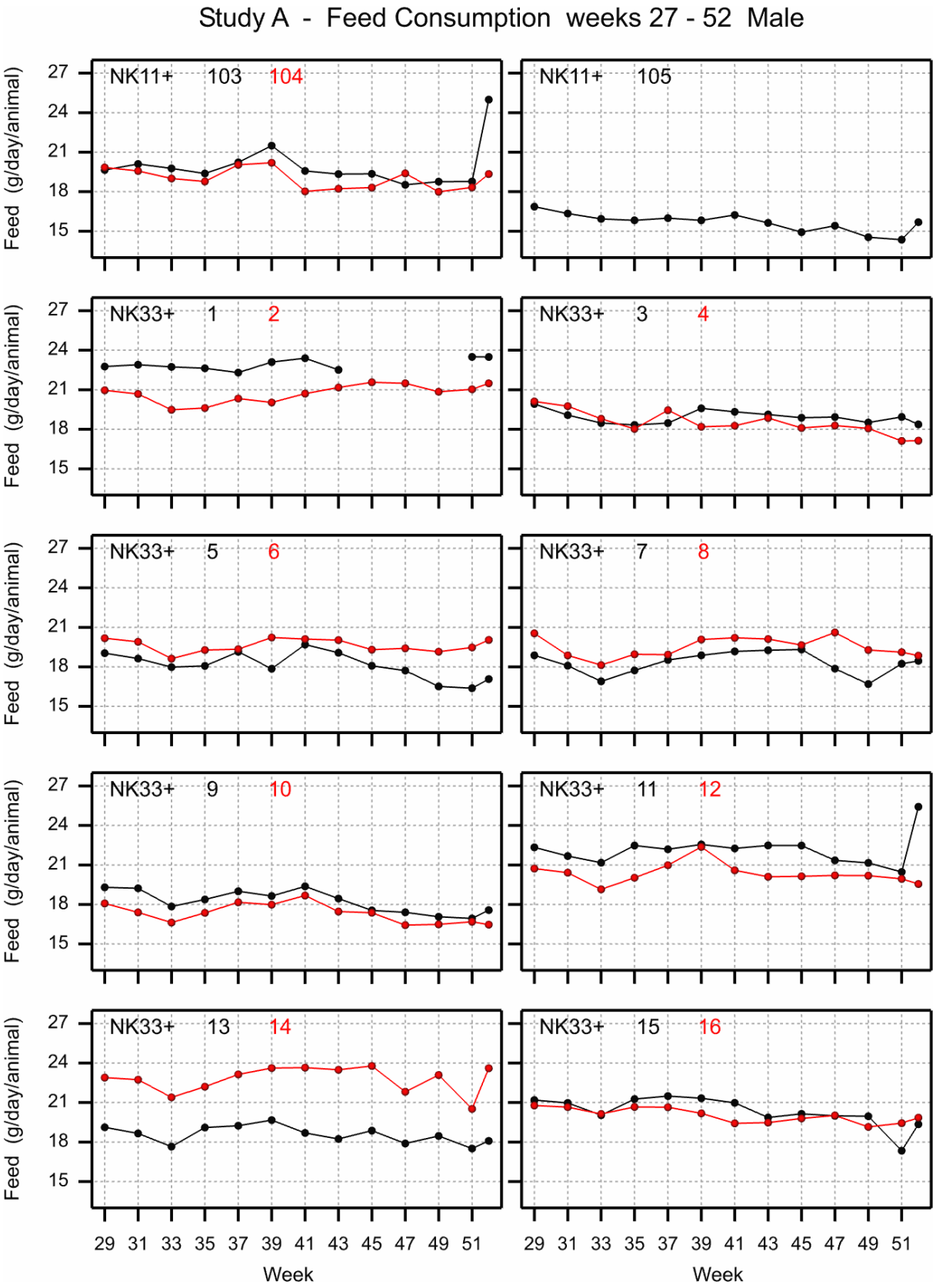
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



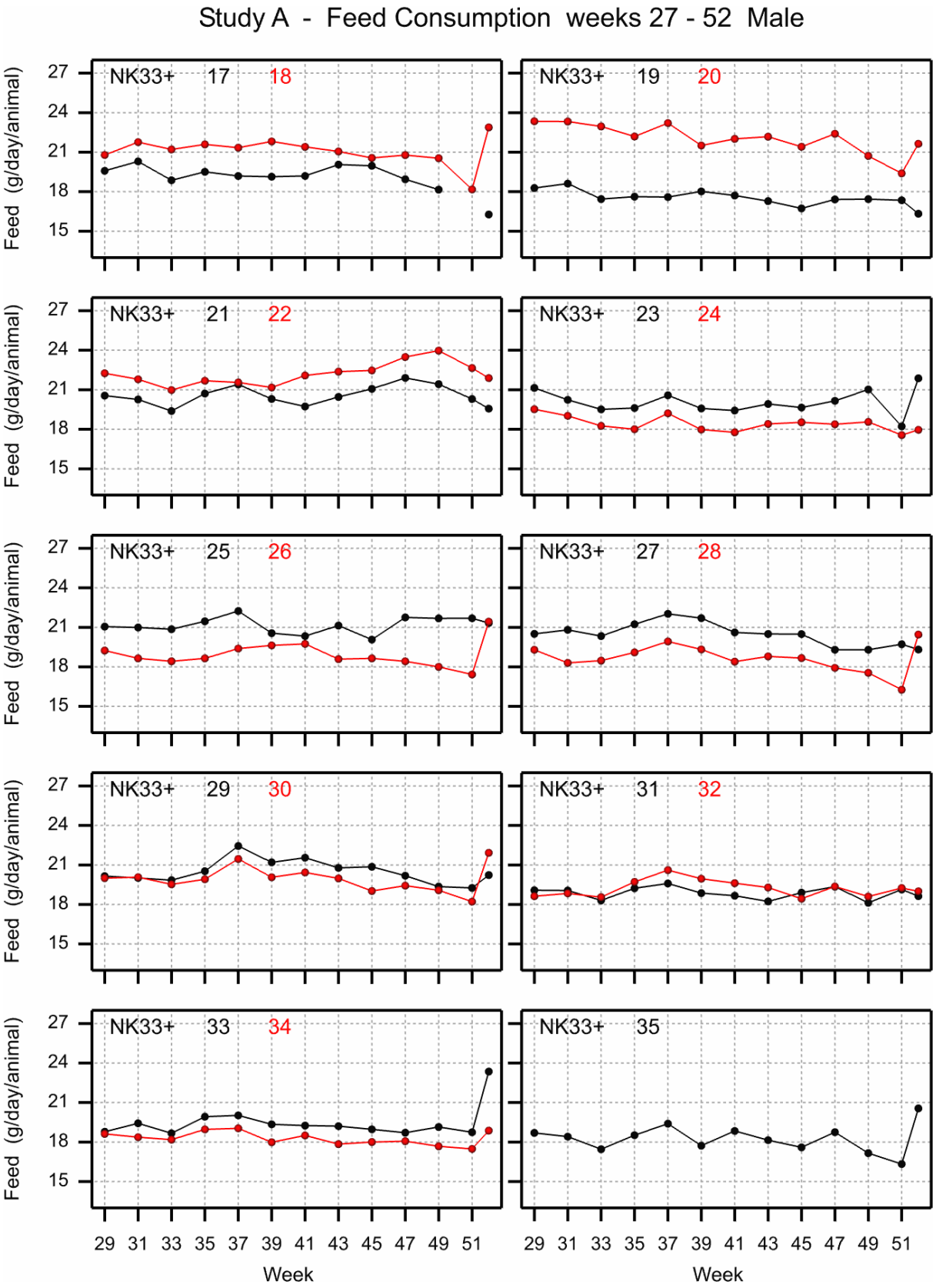
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



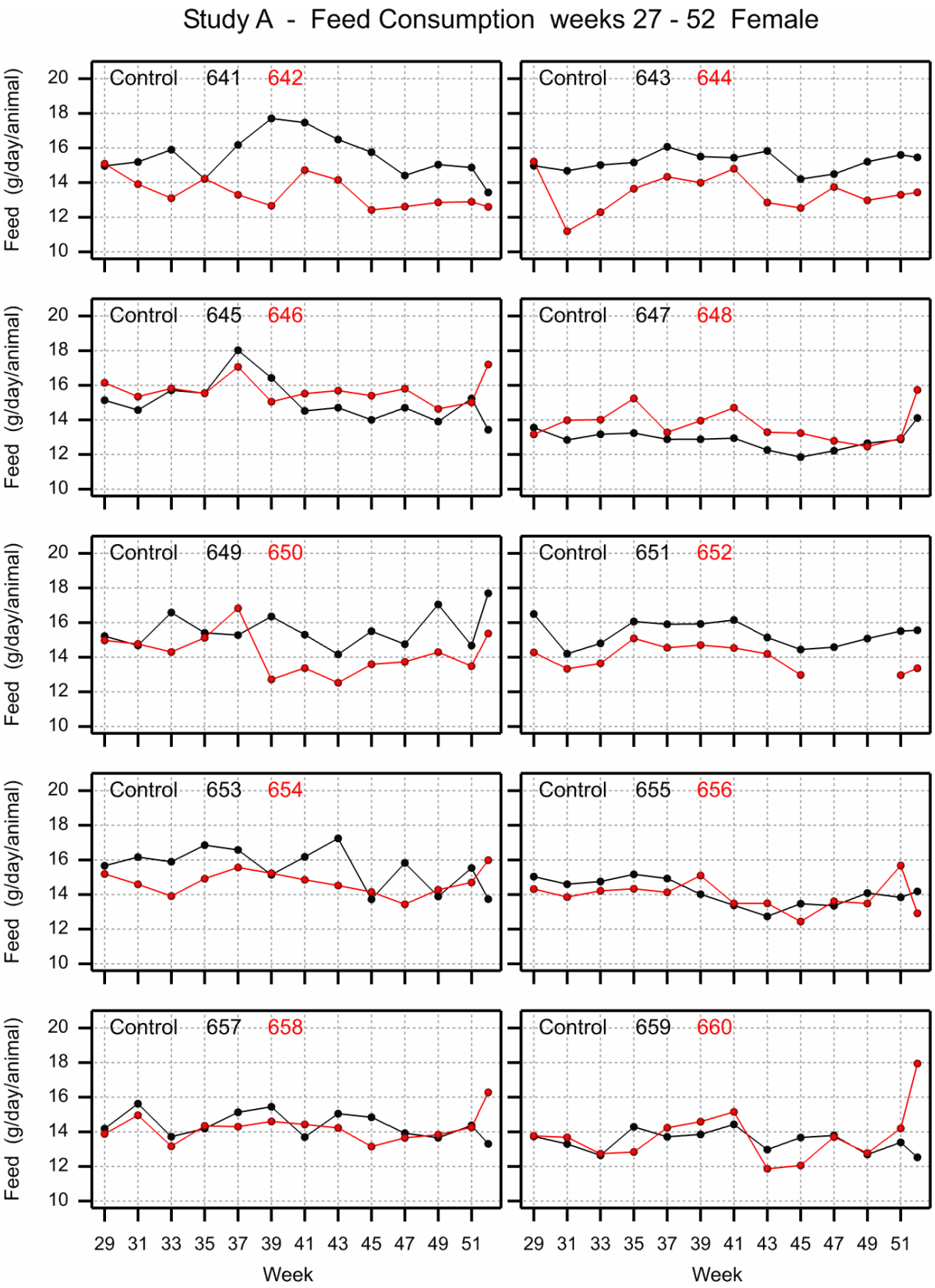
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



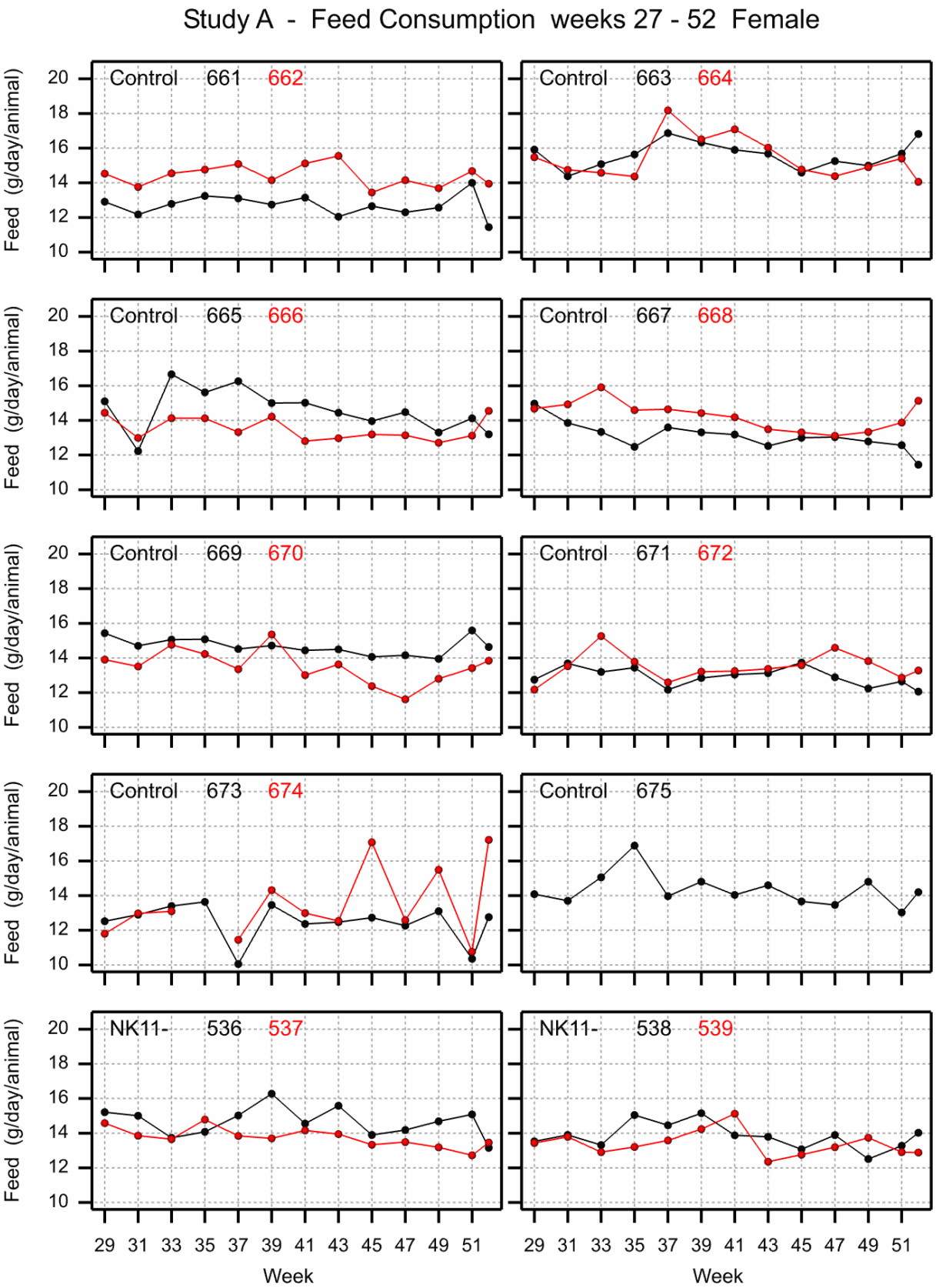
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



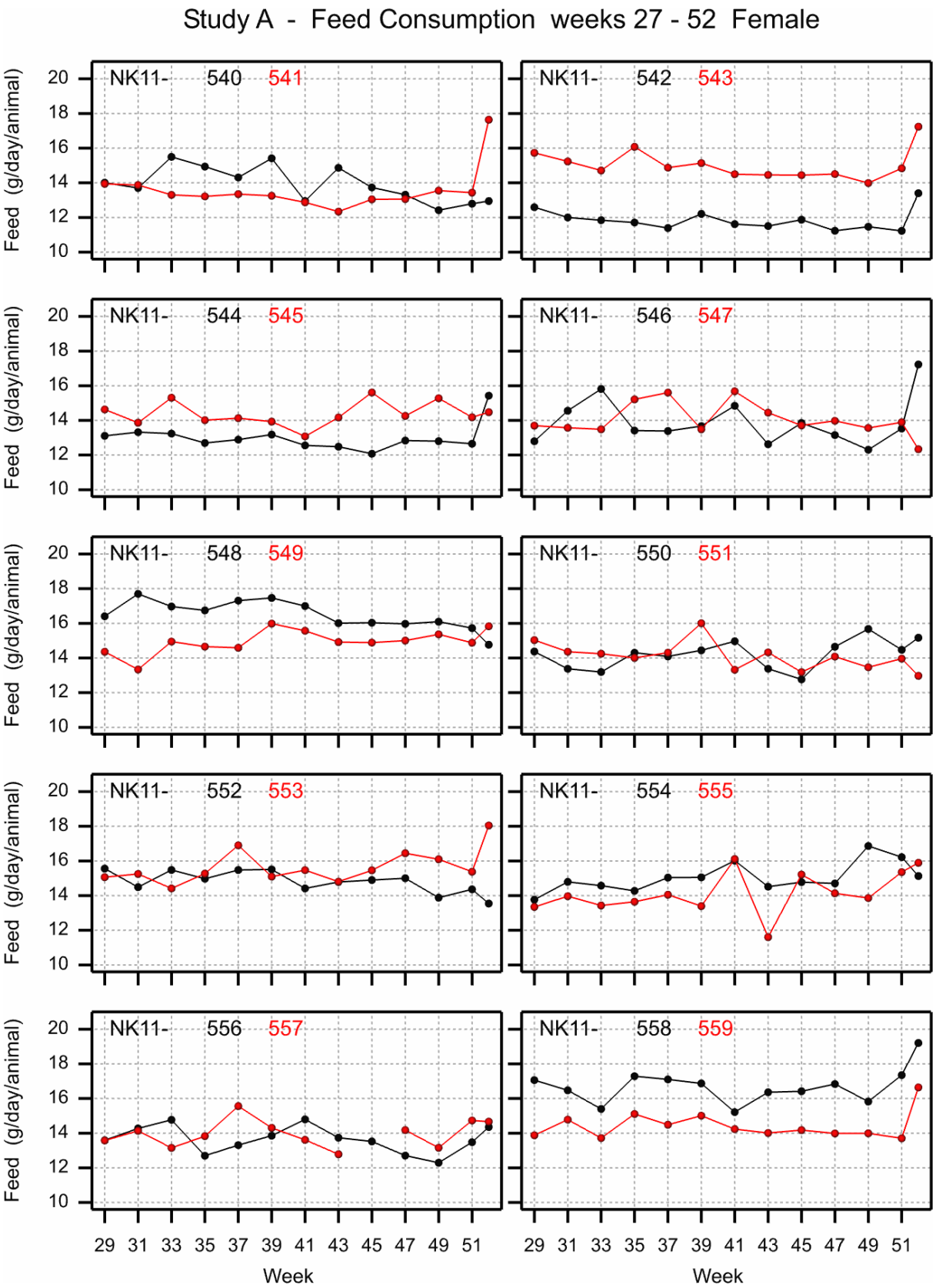
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



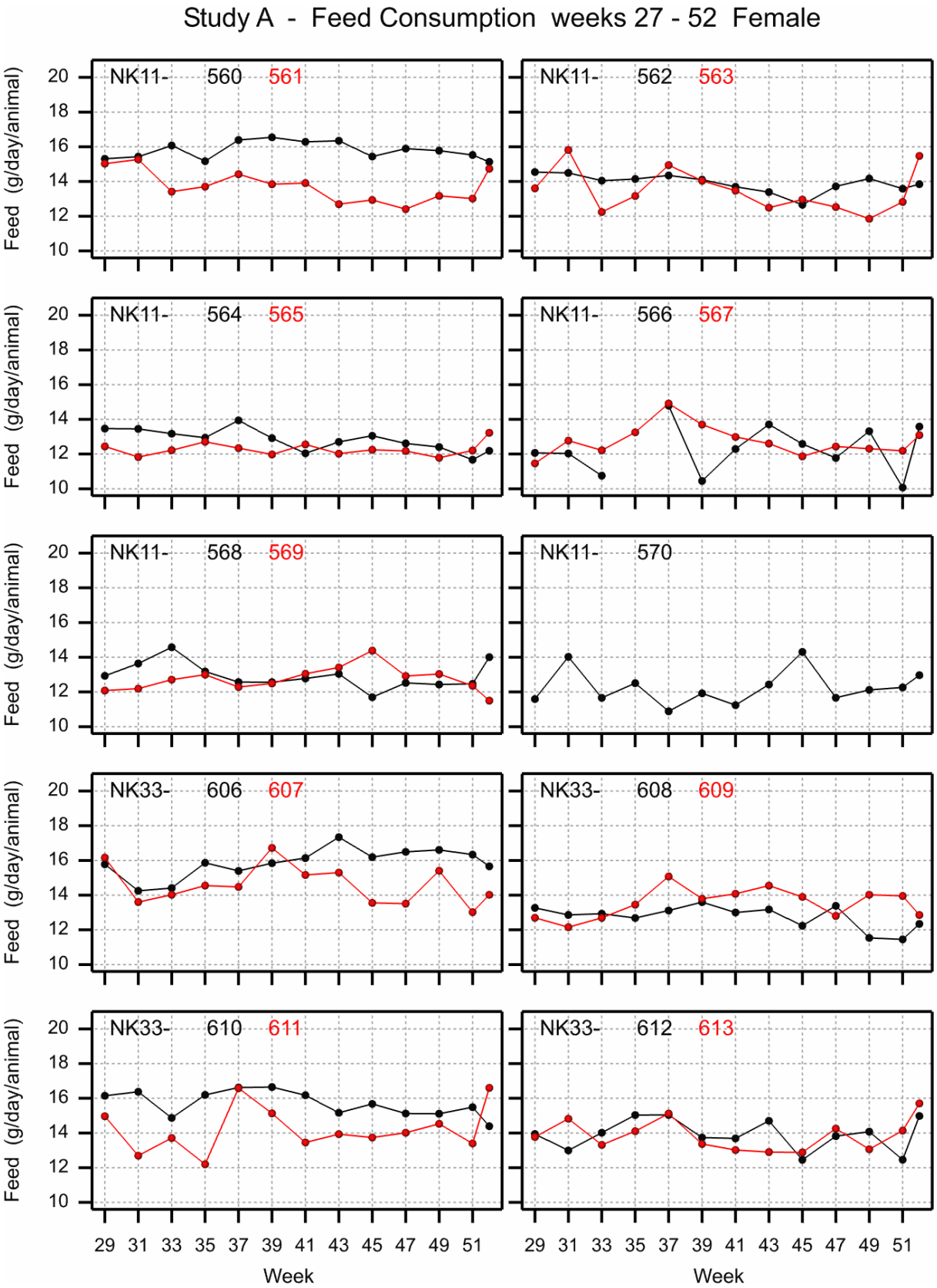
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



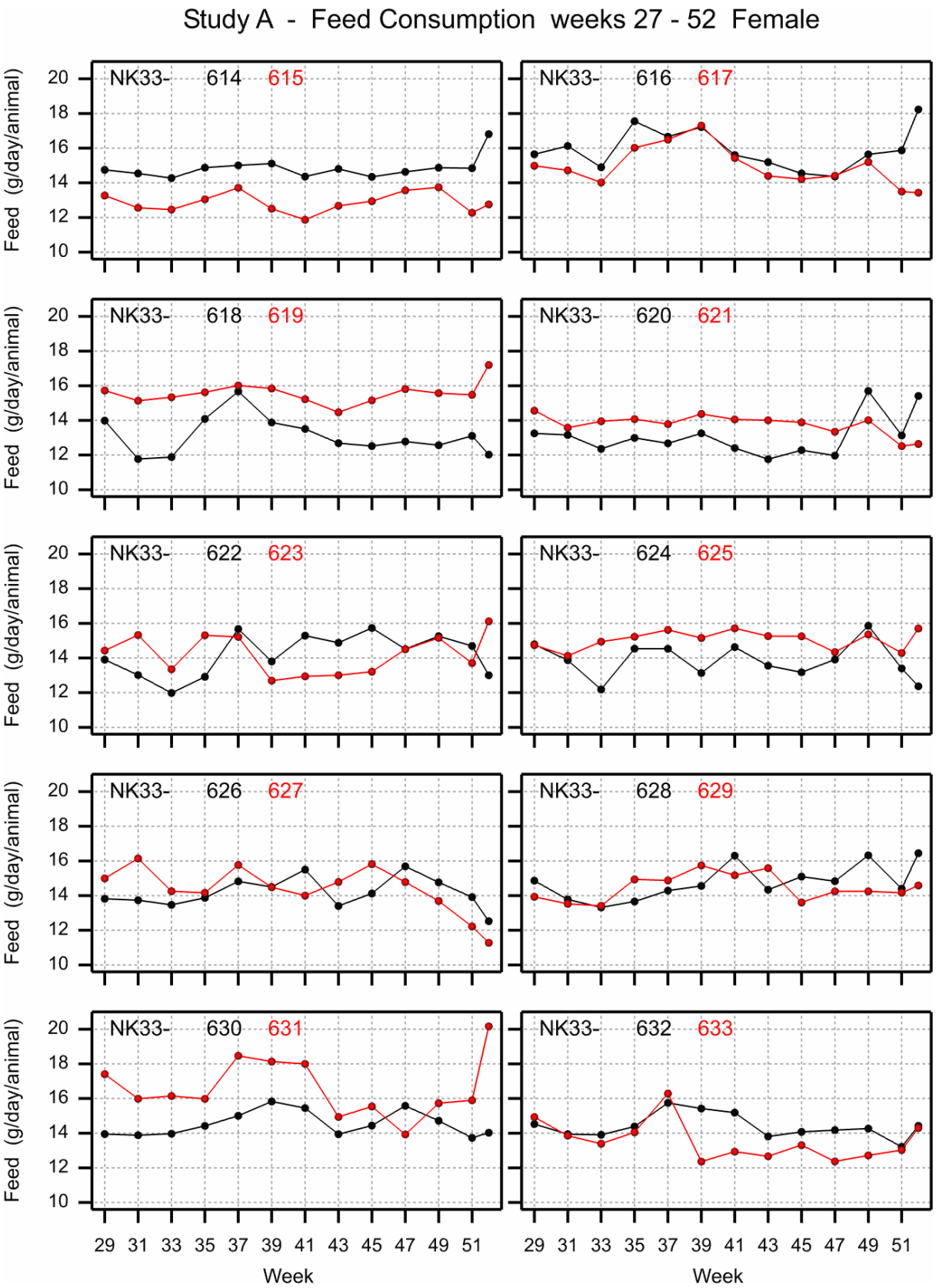
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



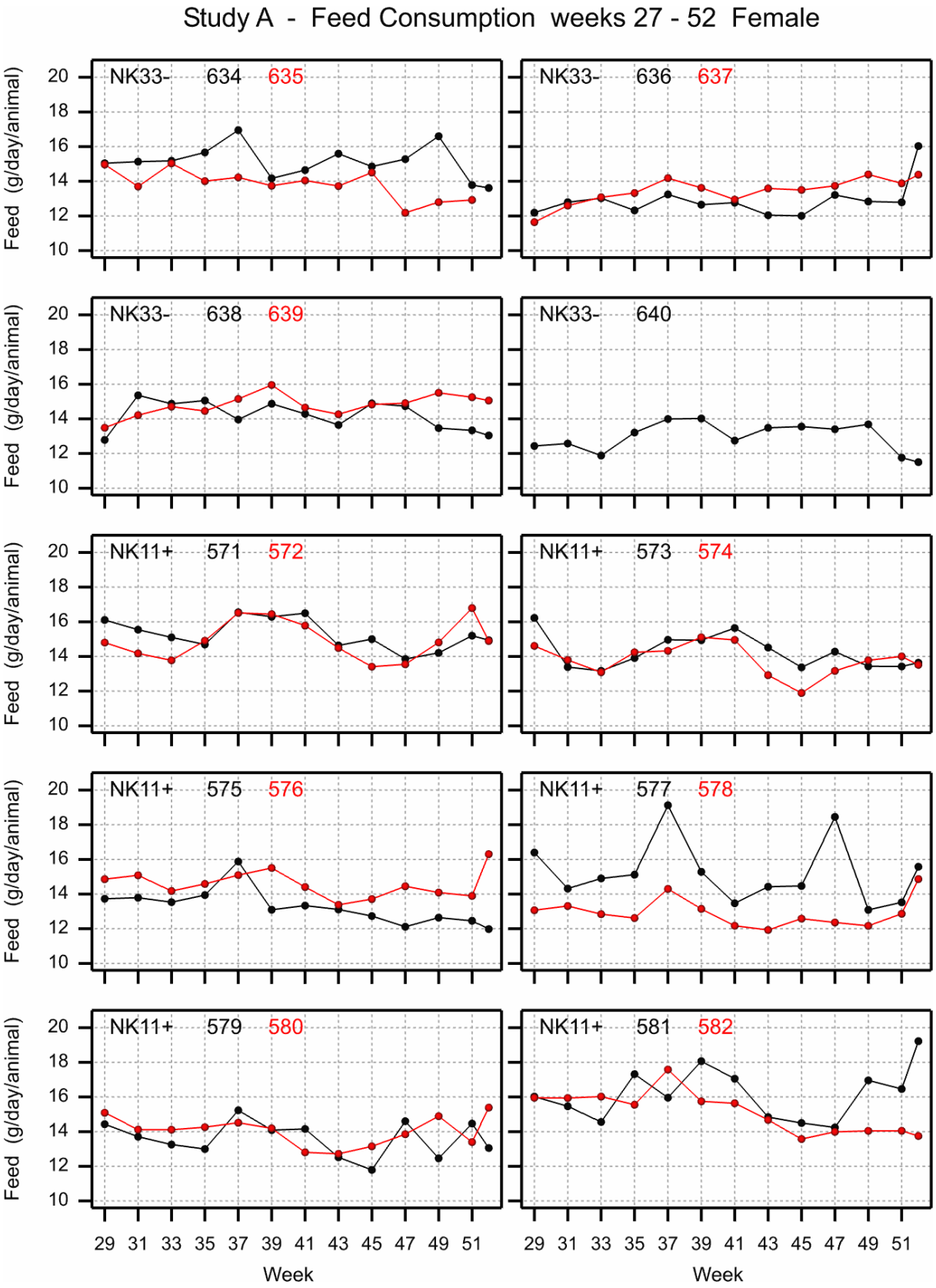
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



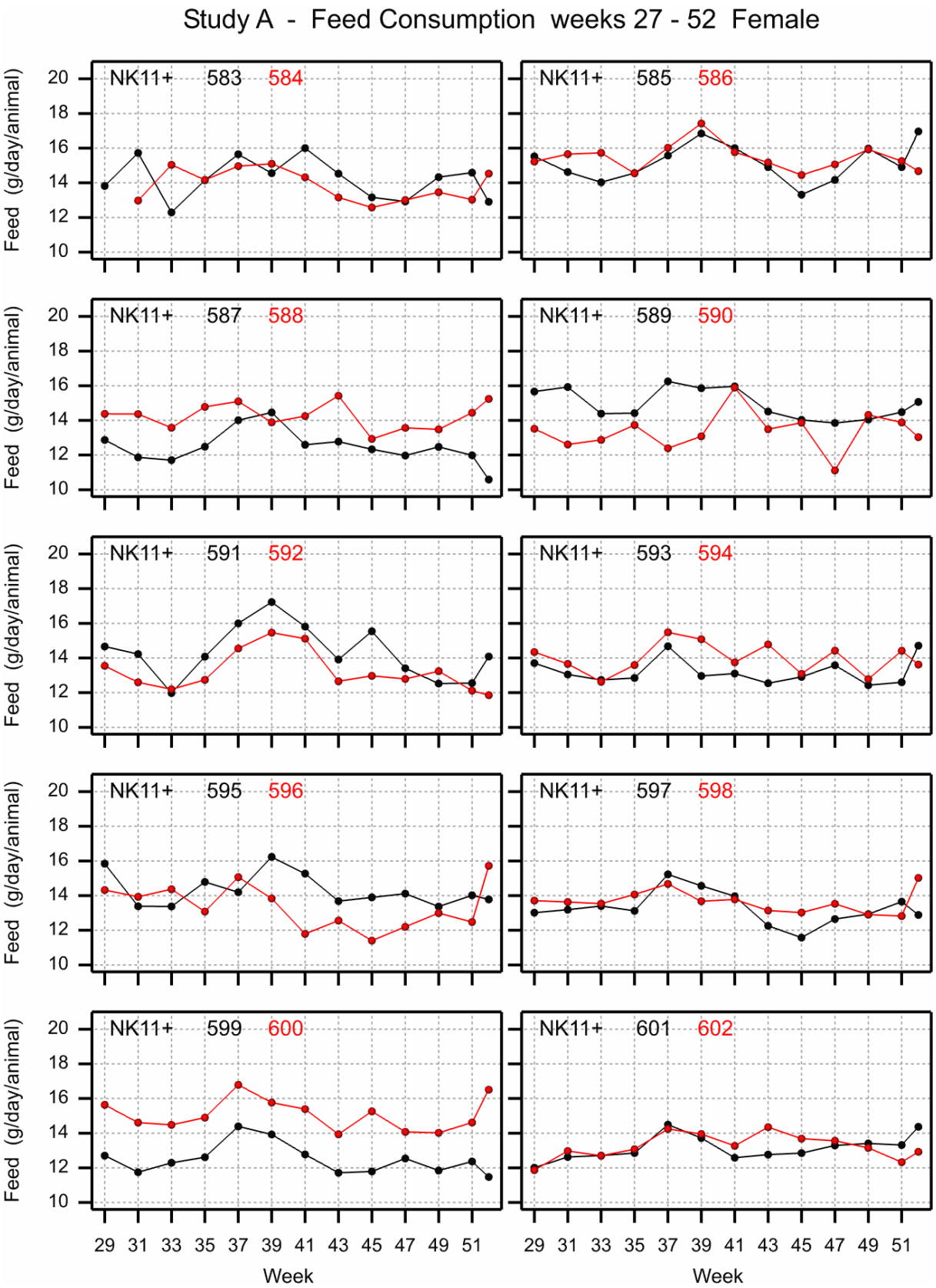
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



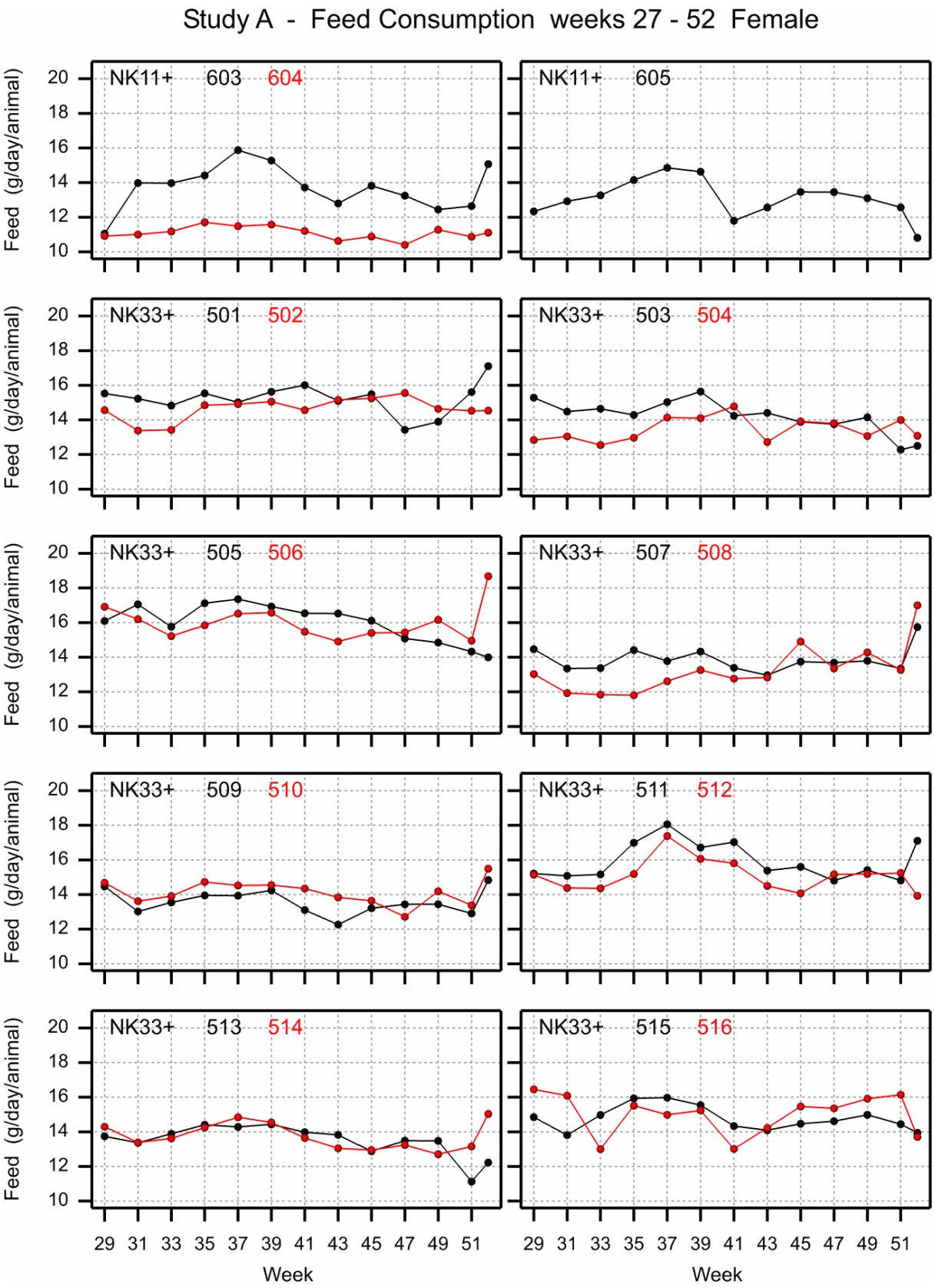
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



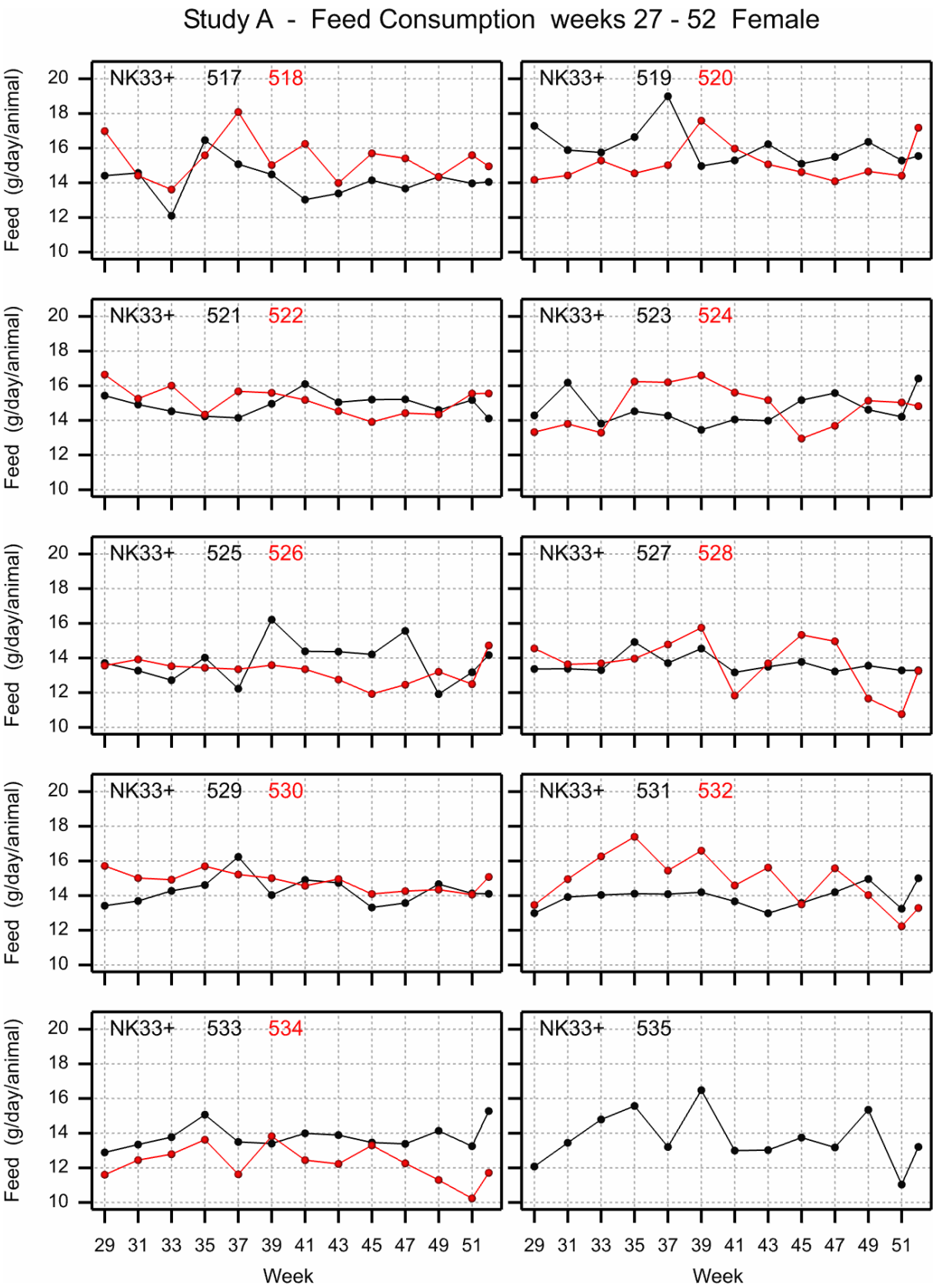
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



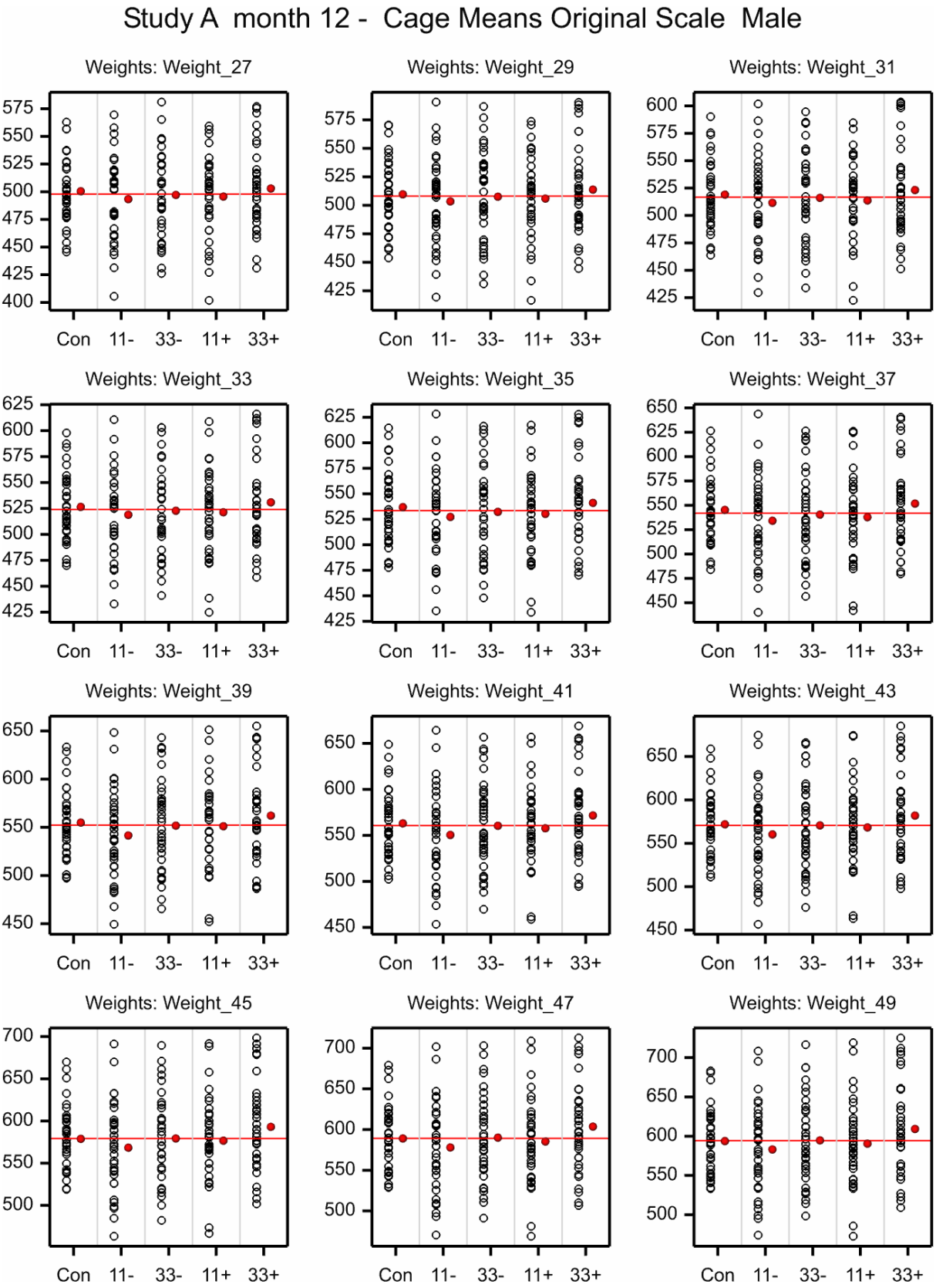
Appendix 2. Feed consumption per cage (continued)

The feed group and cage numbers are given in the left top corner of the graph.



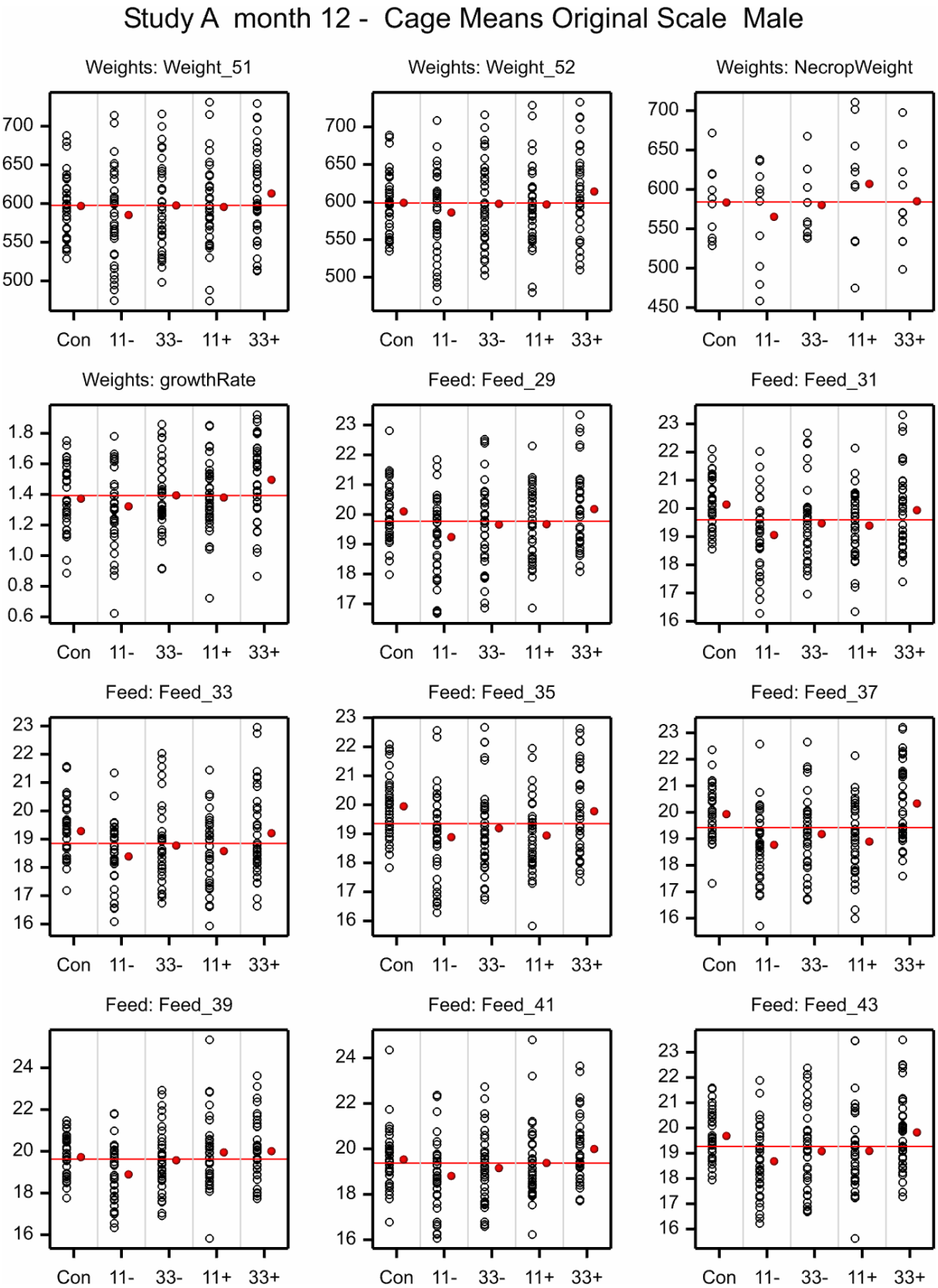
Appendix 3. Graphs of cage means on the original scale

Red symbols denote means for feeding groups while the red line denotes the overall mean.



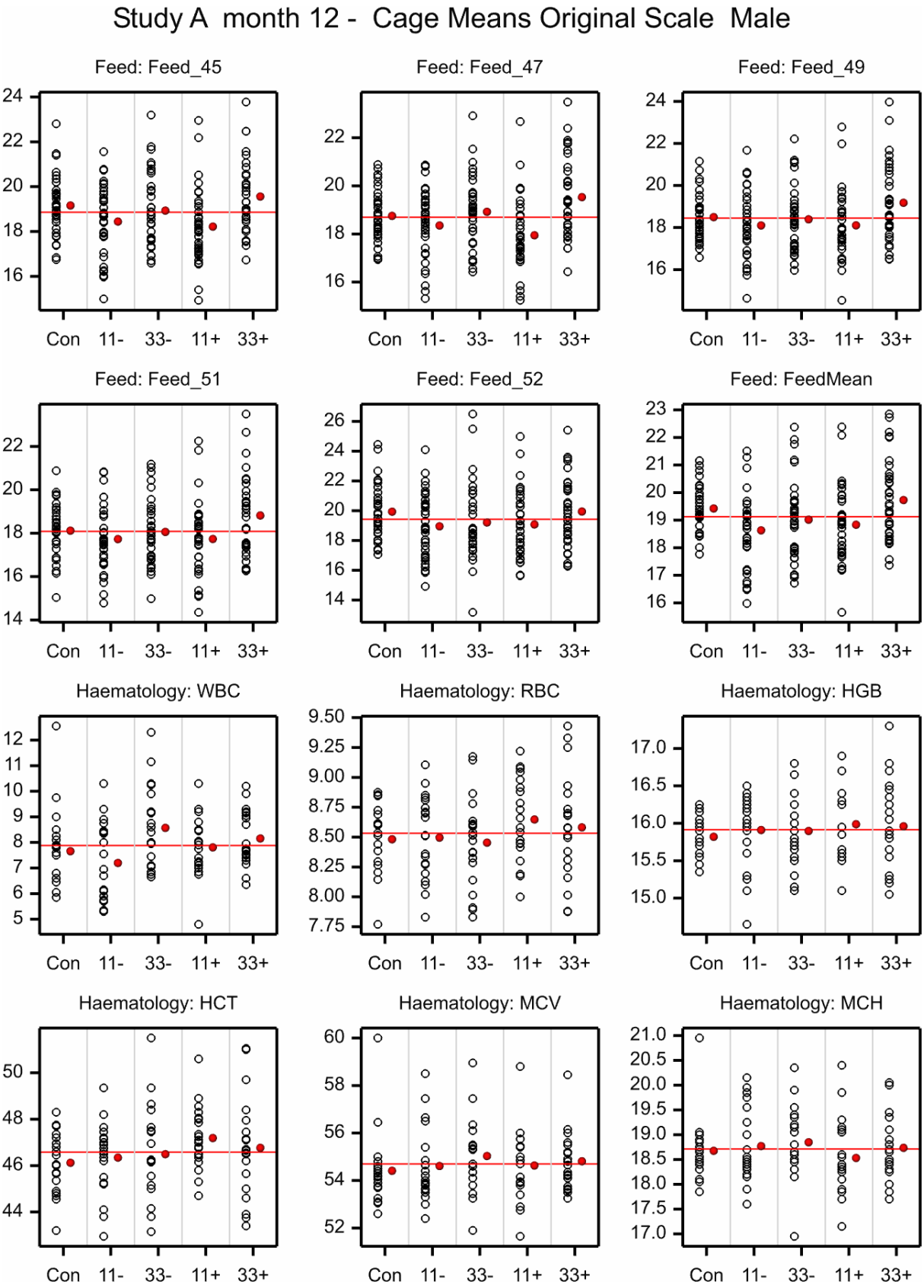
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



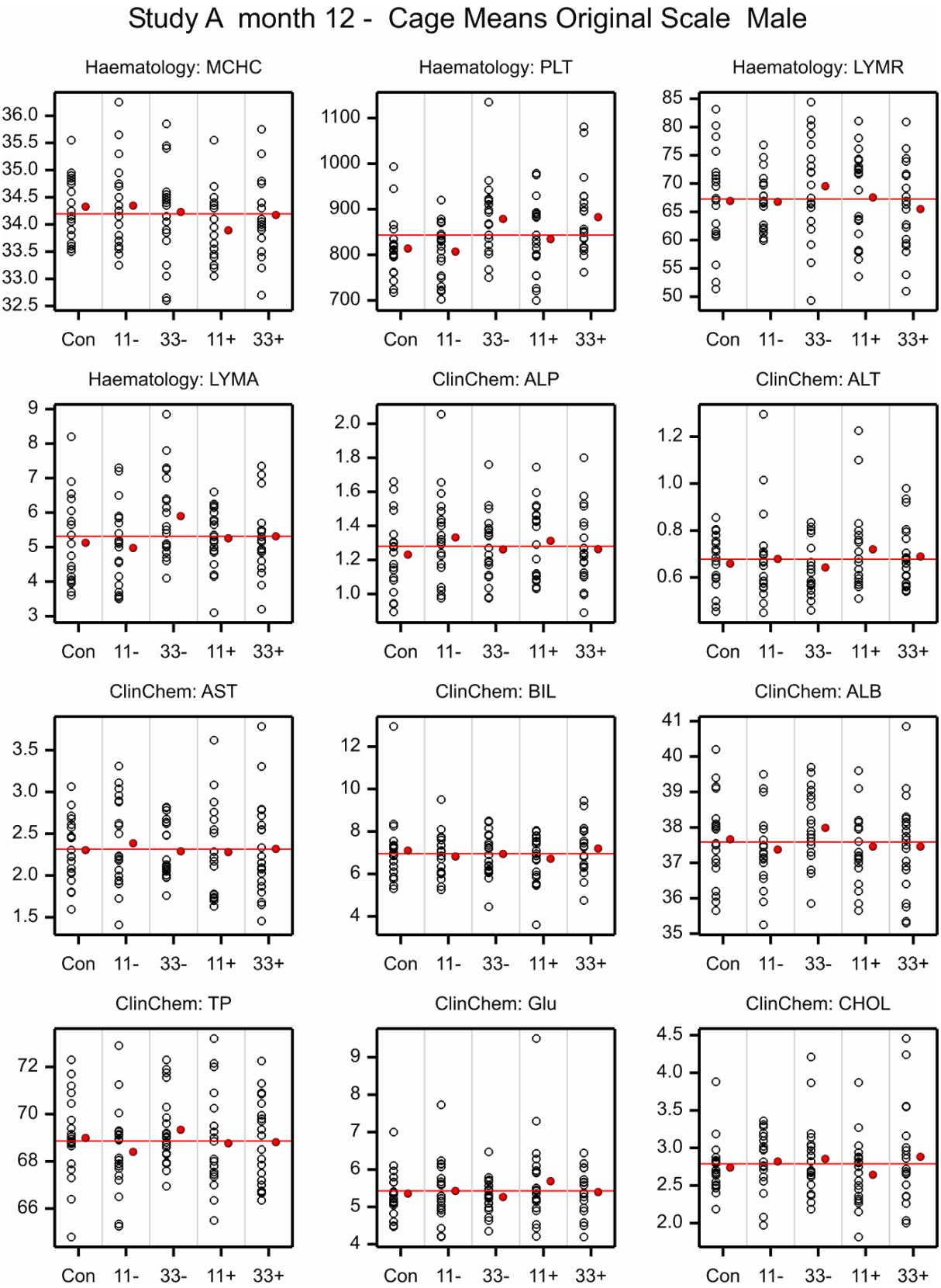
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



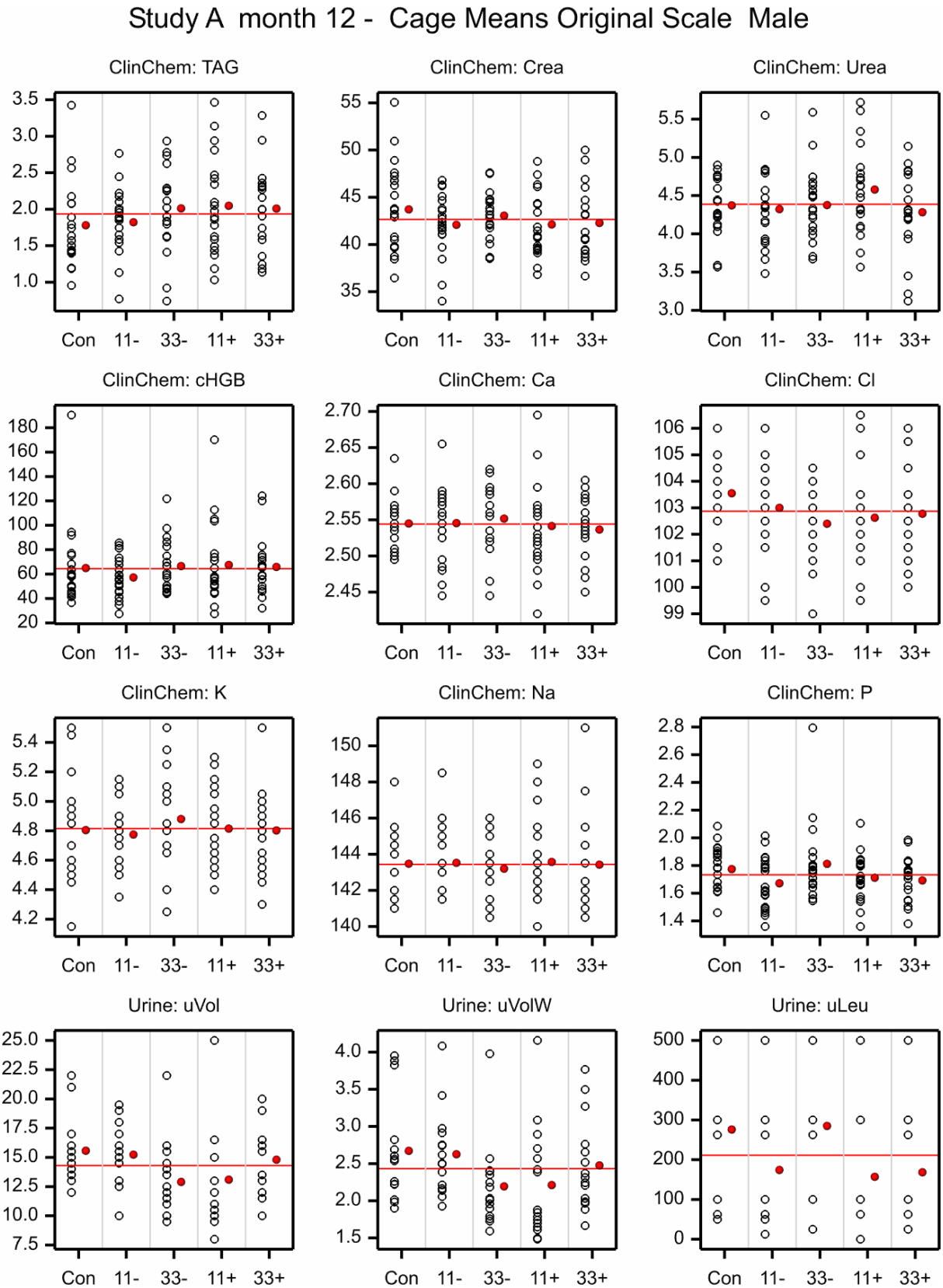
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



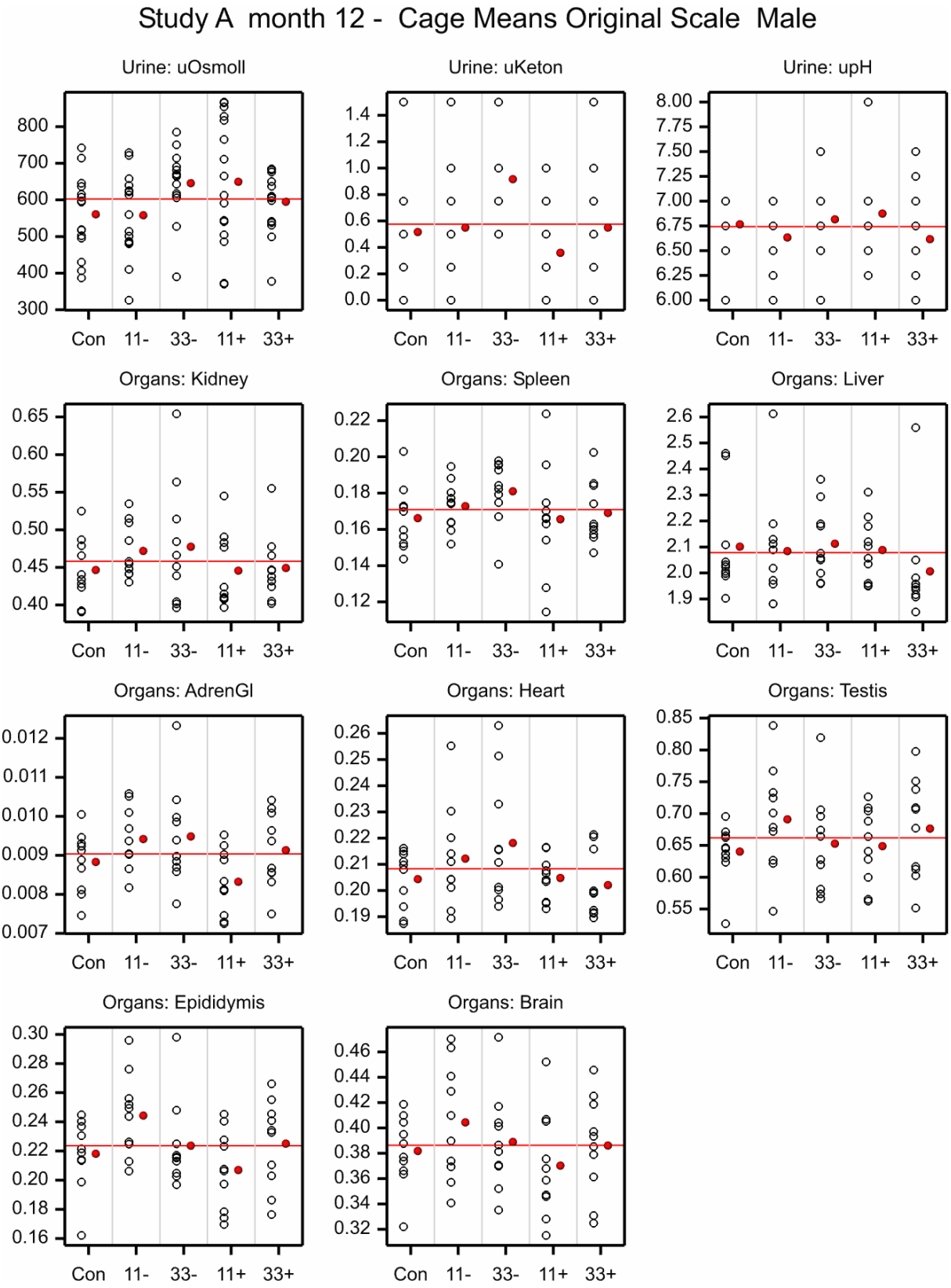
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



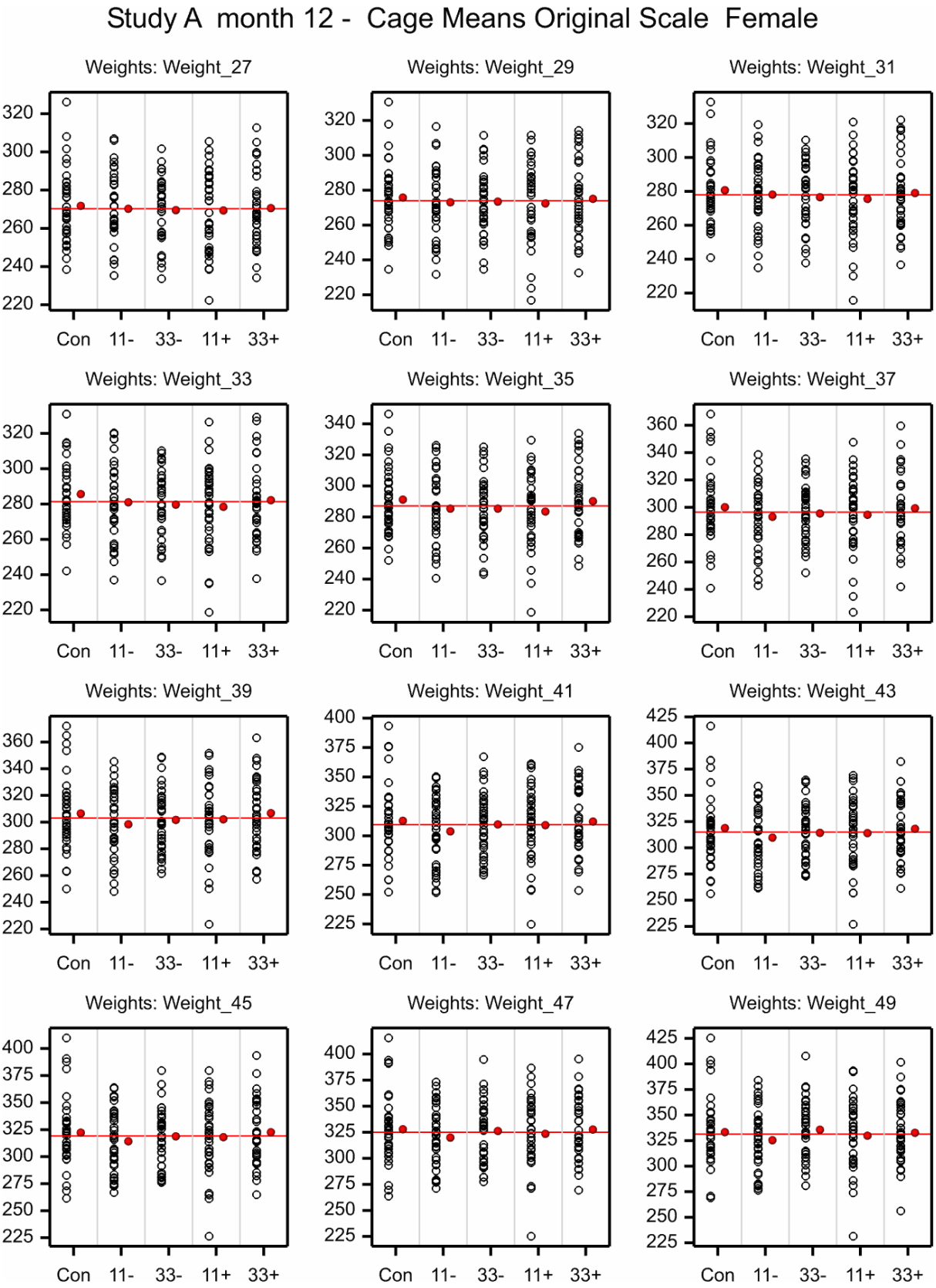
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



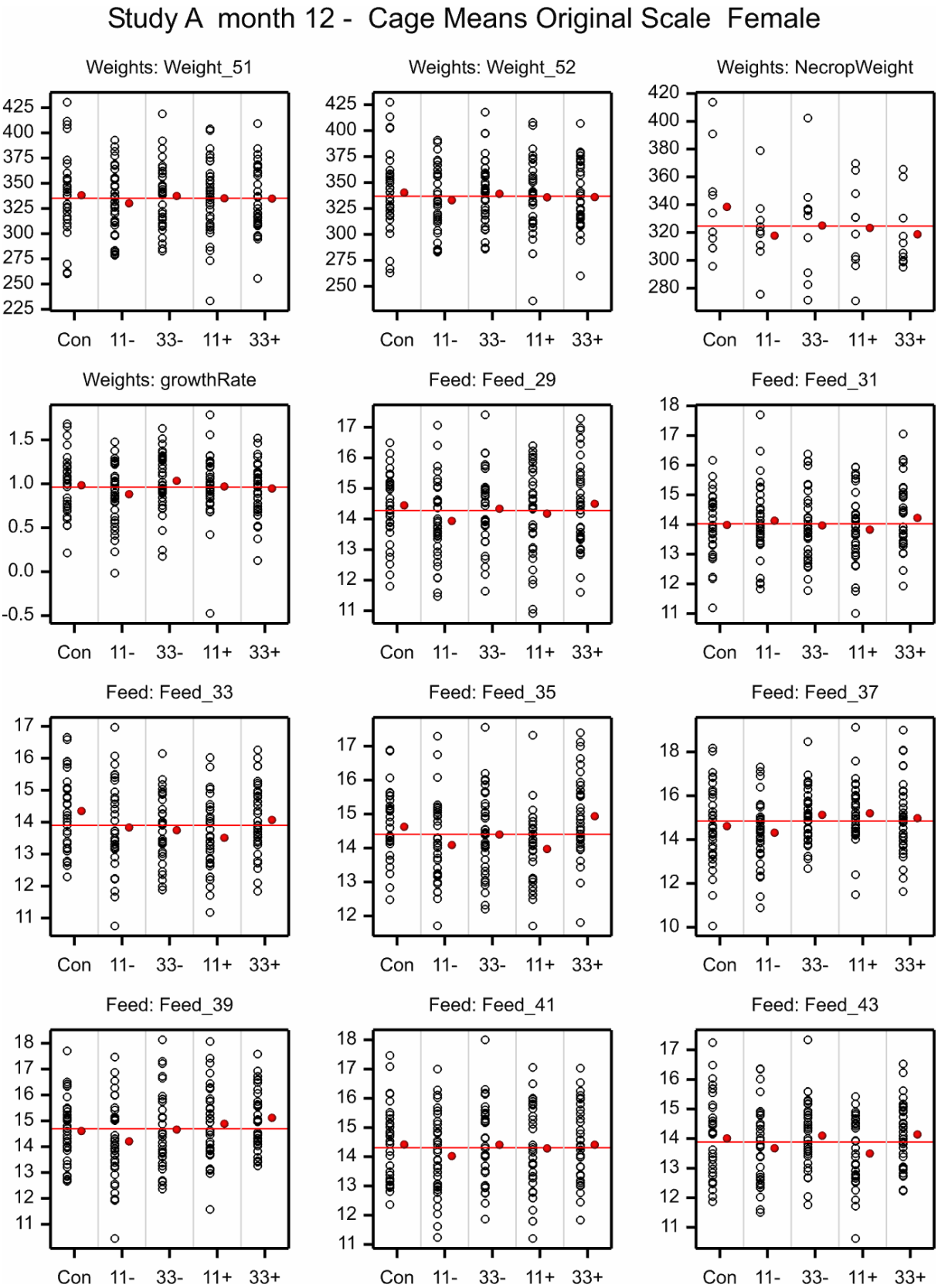
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



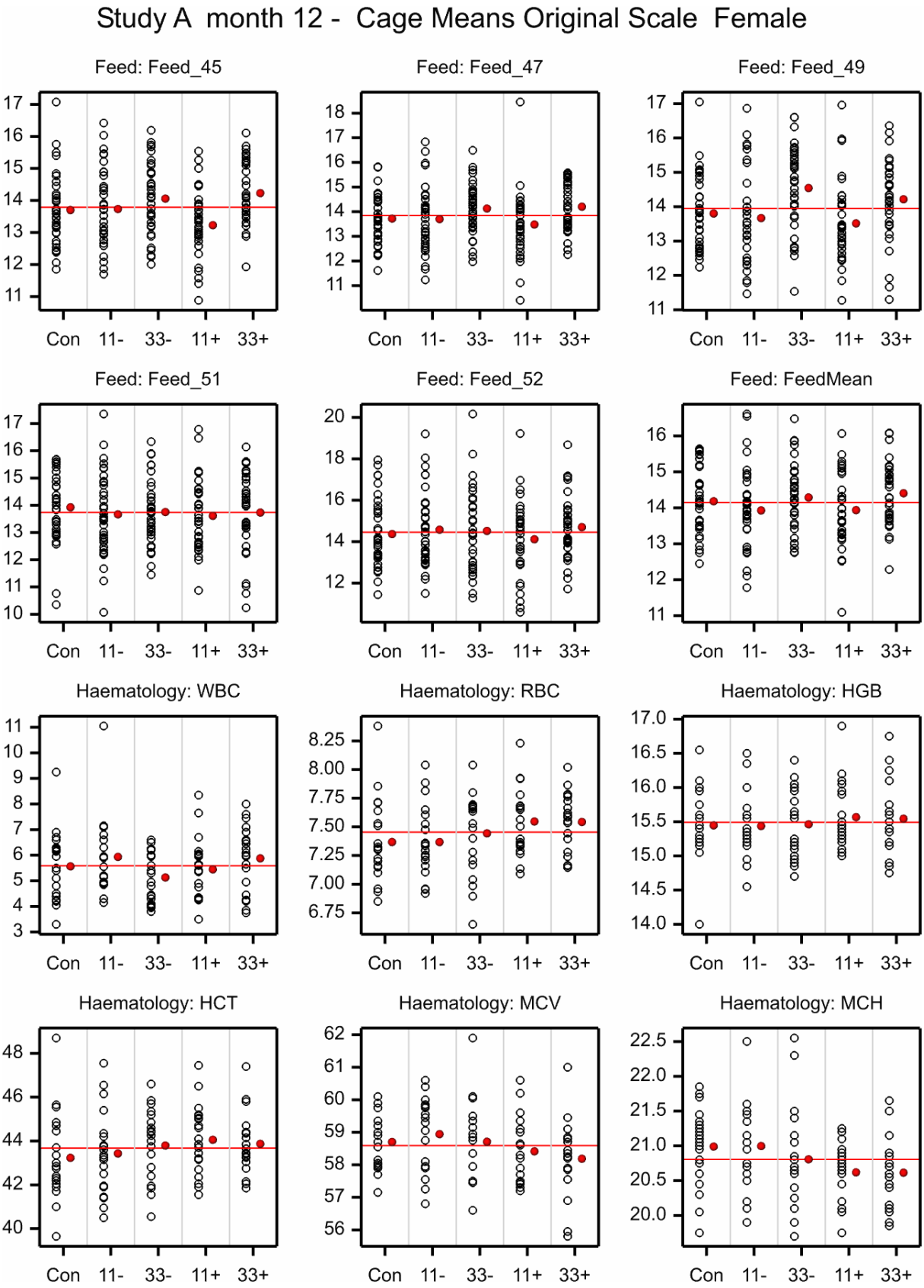
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



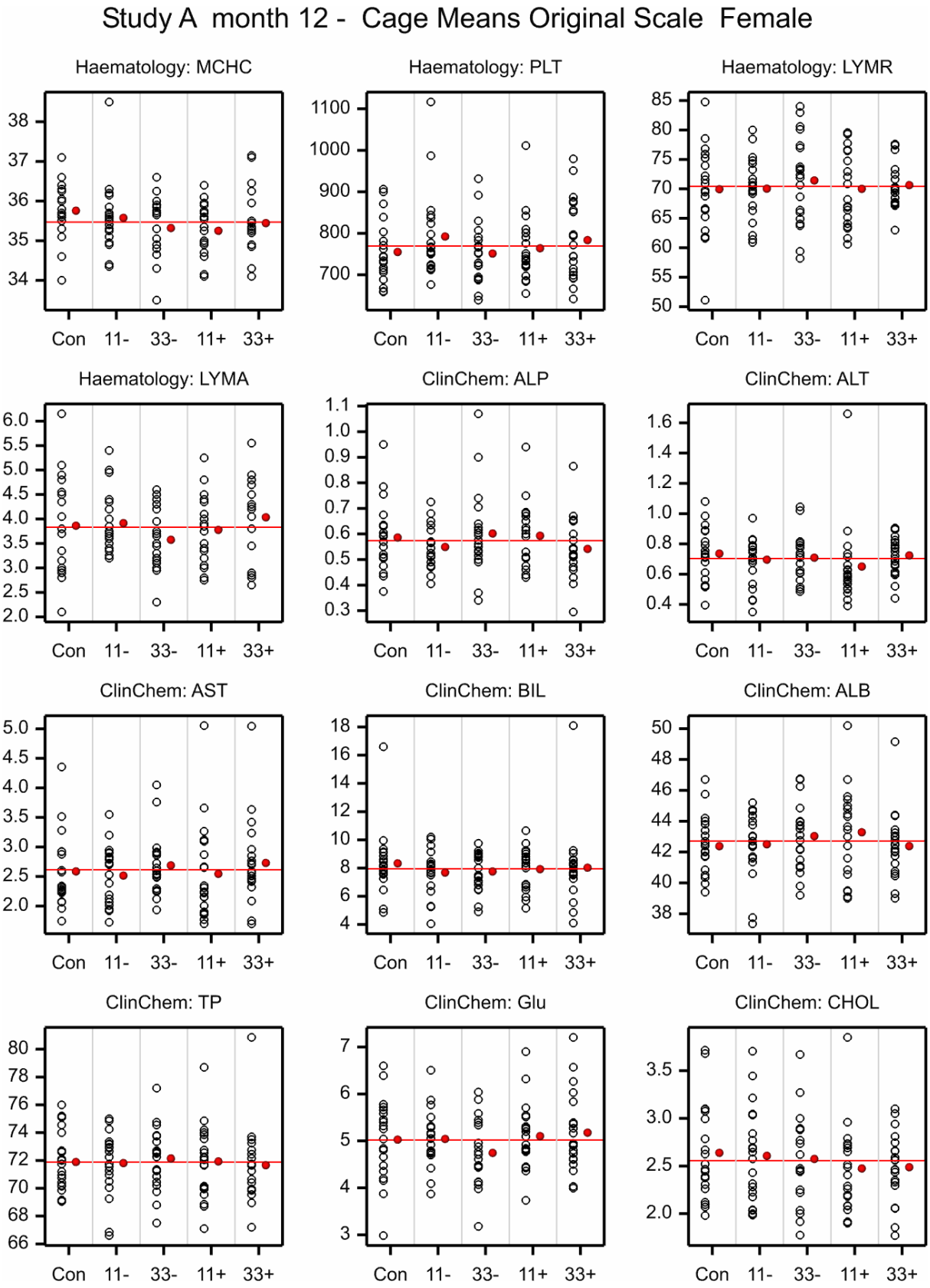
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



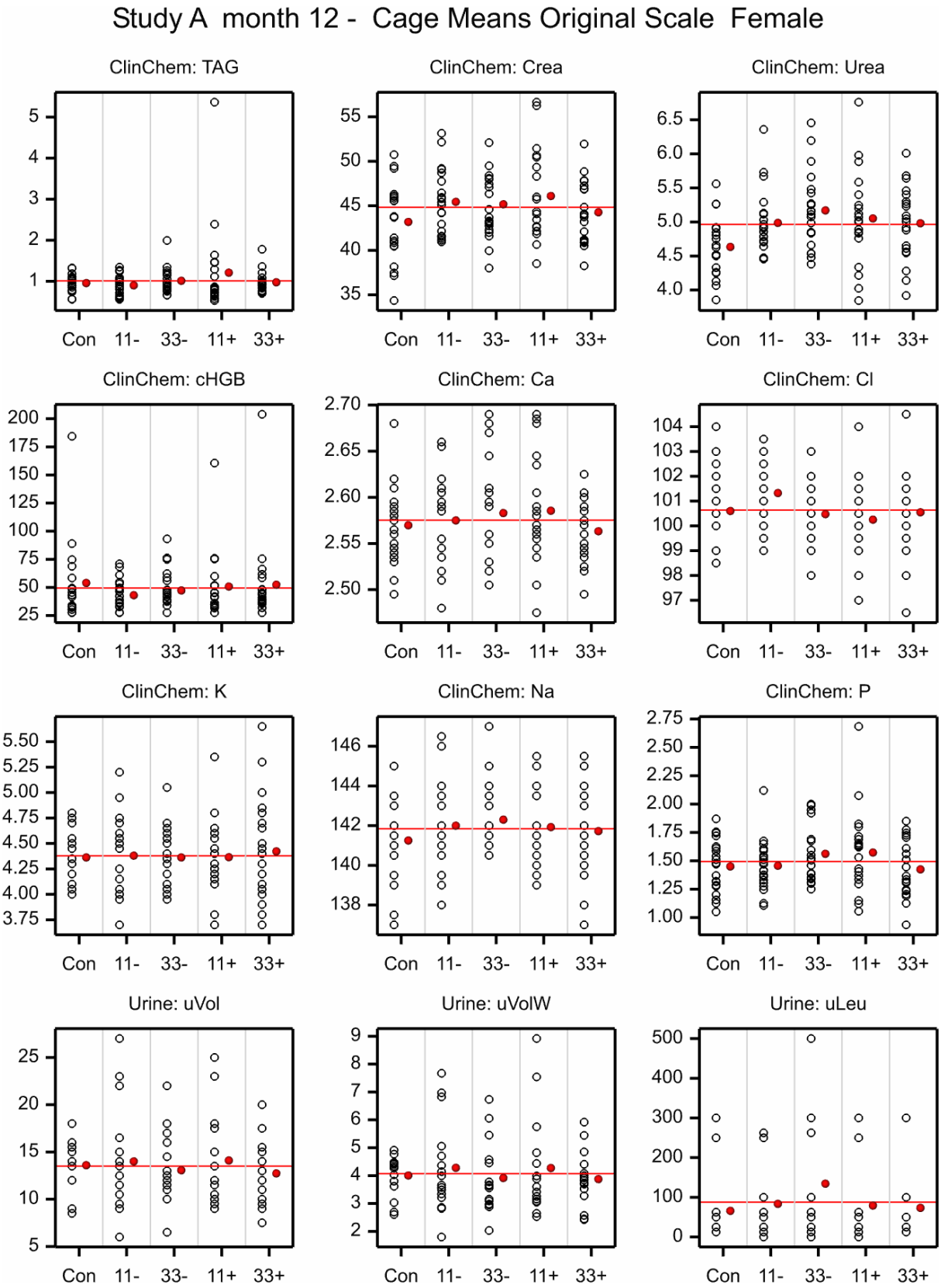
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



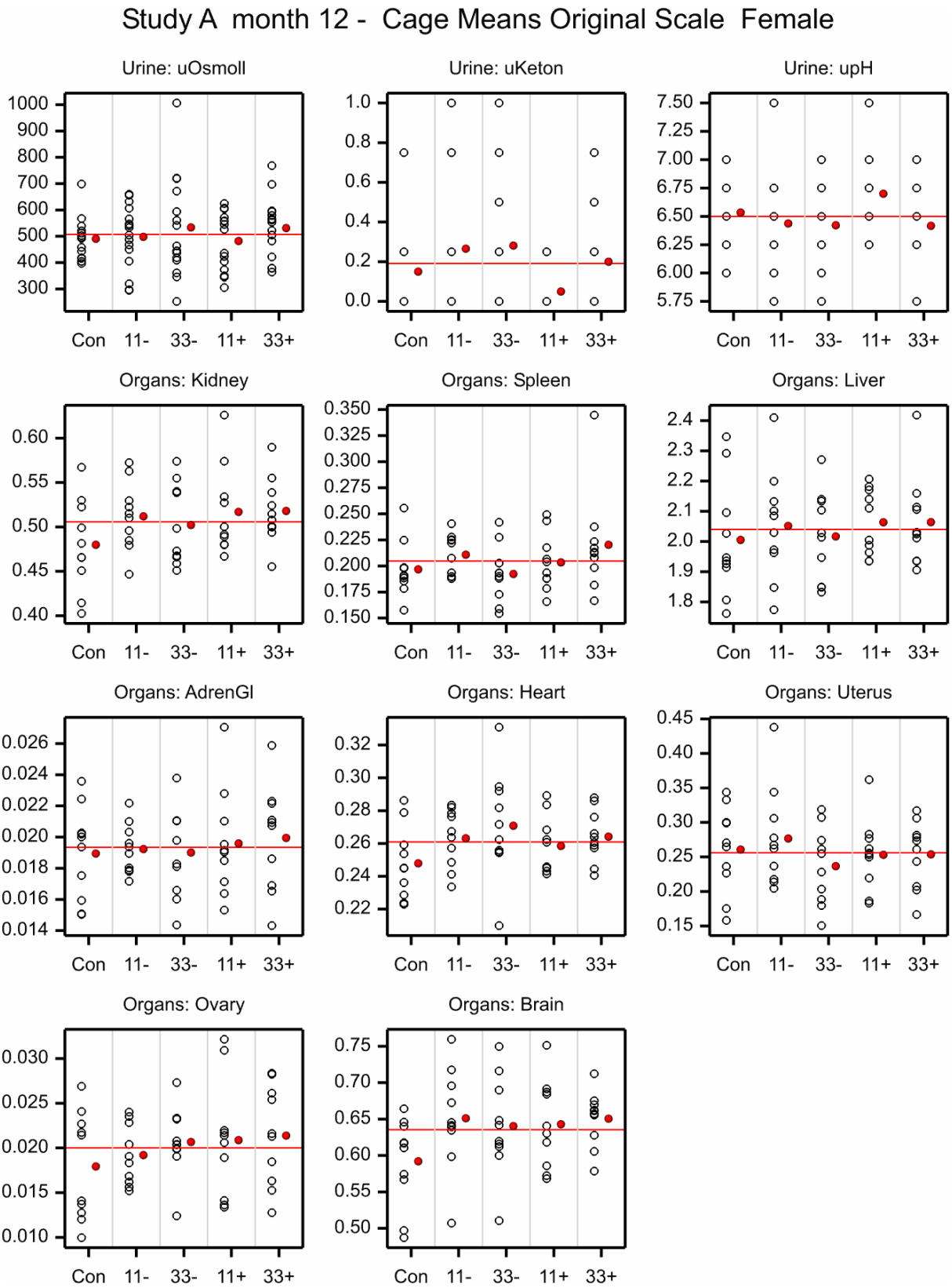
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



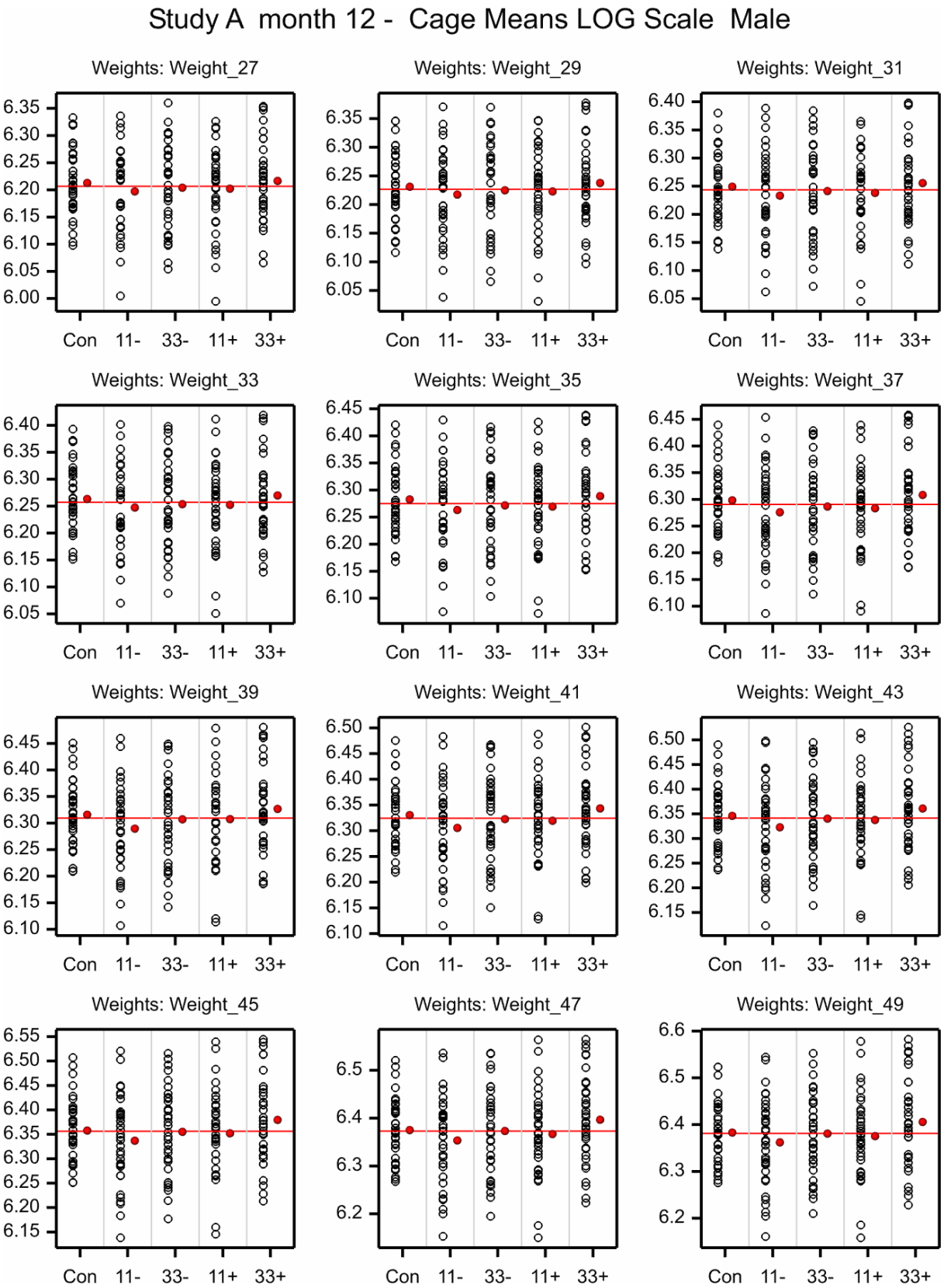
Appendix 3. Graphs of cage means on the original scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



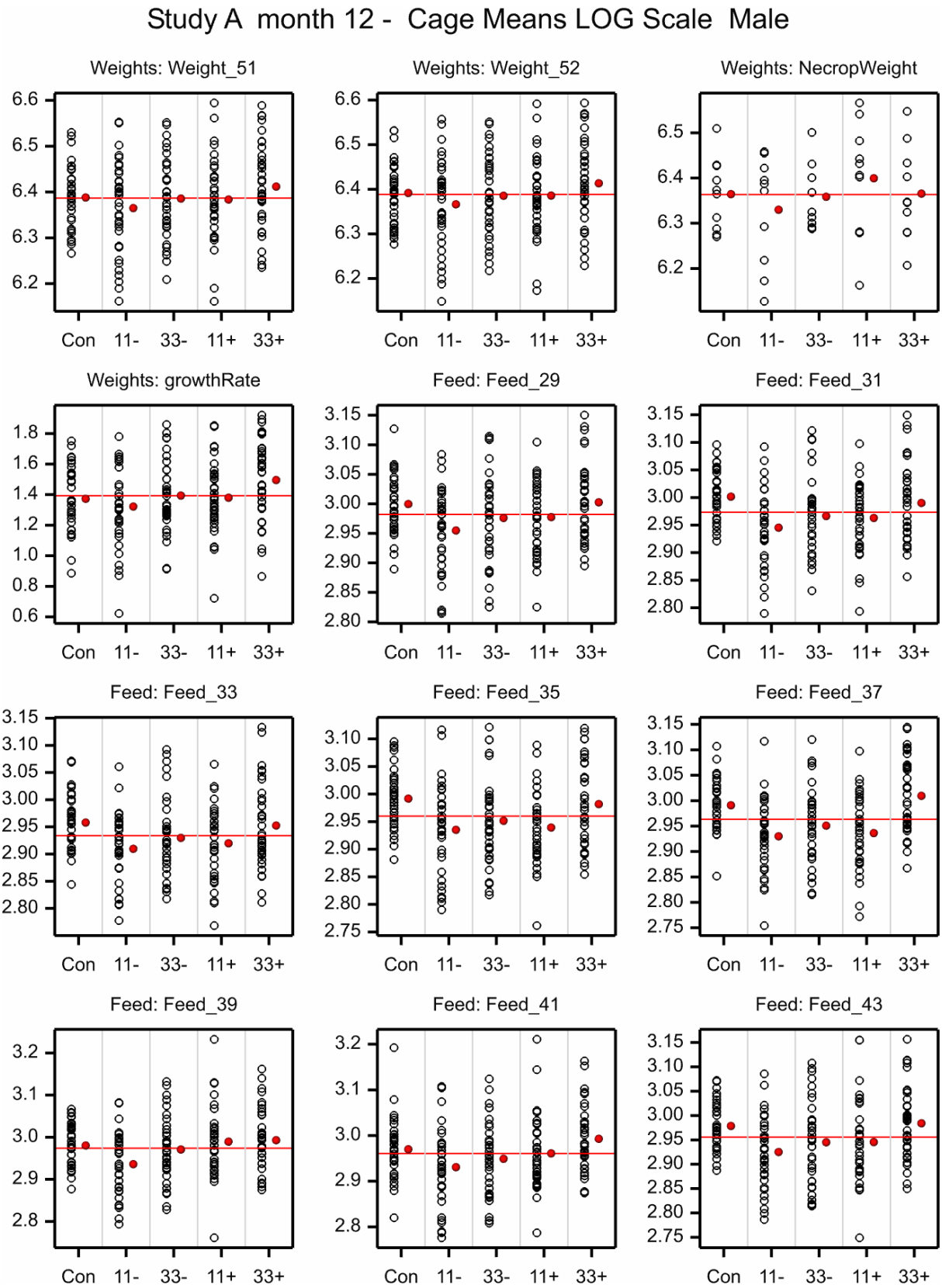
Appendix 4. Graphs of cage means on the log scale

Red symbols denote means for feeding groups while the red line denotes the overall mean.



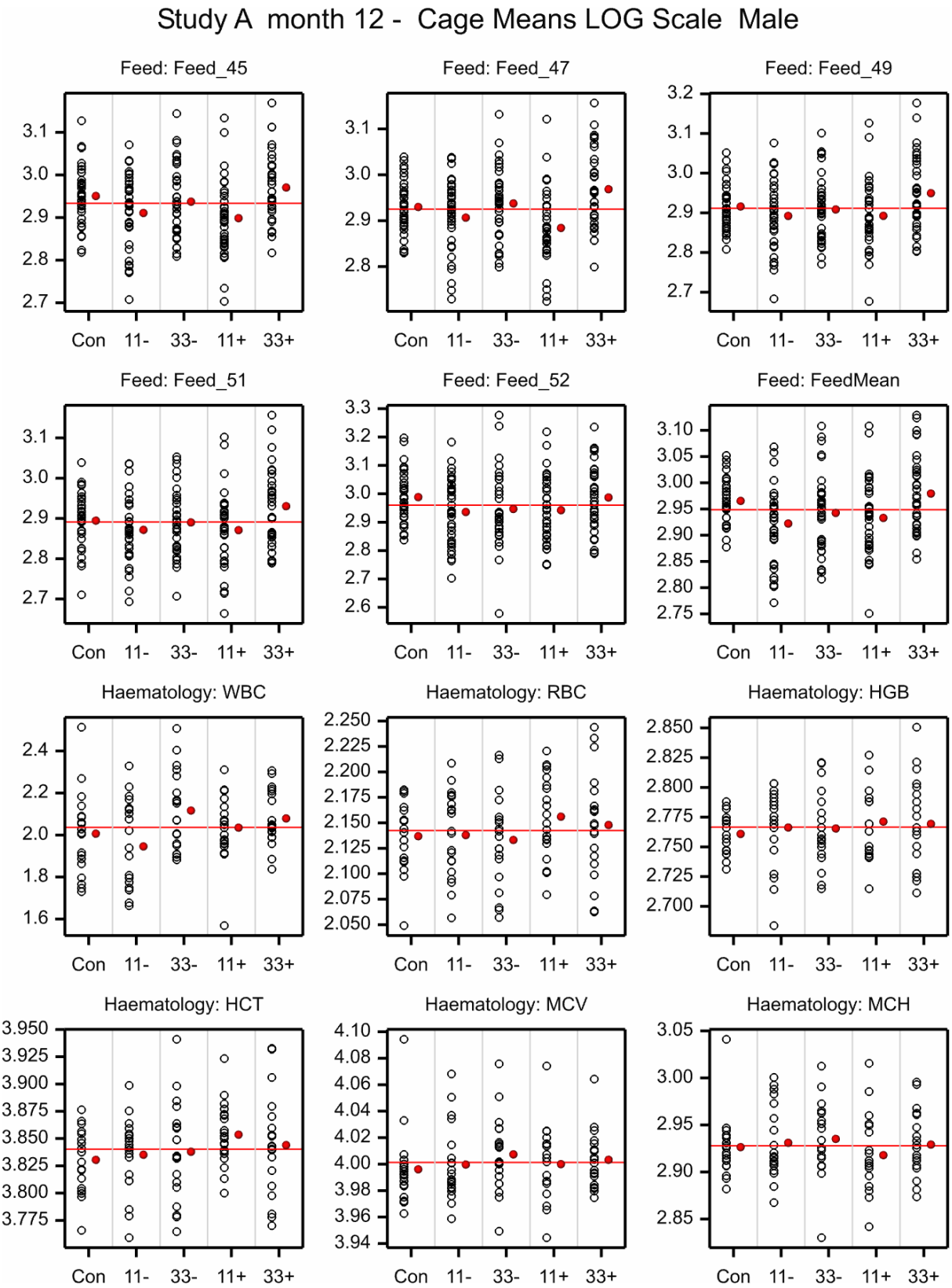
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



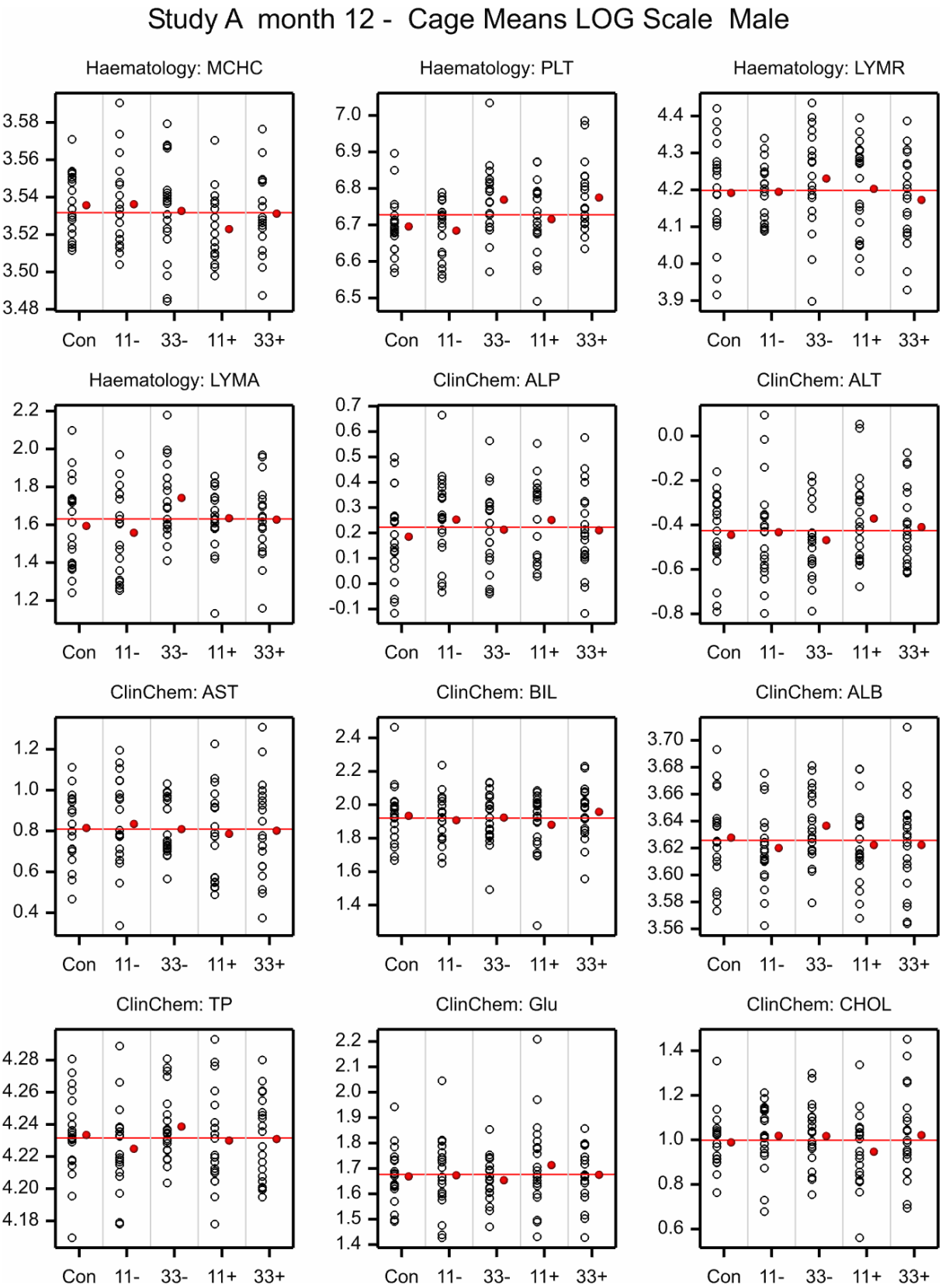
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



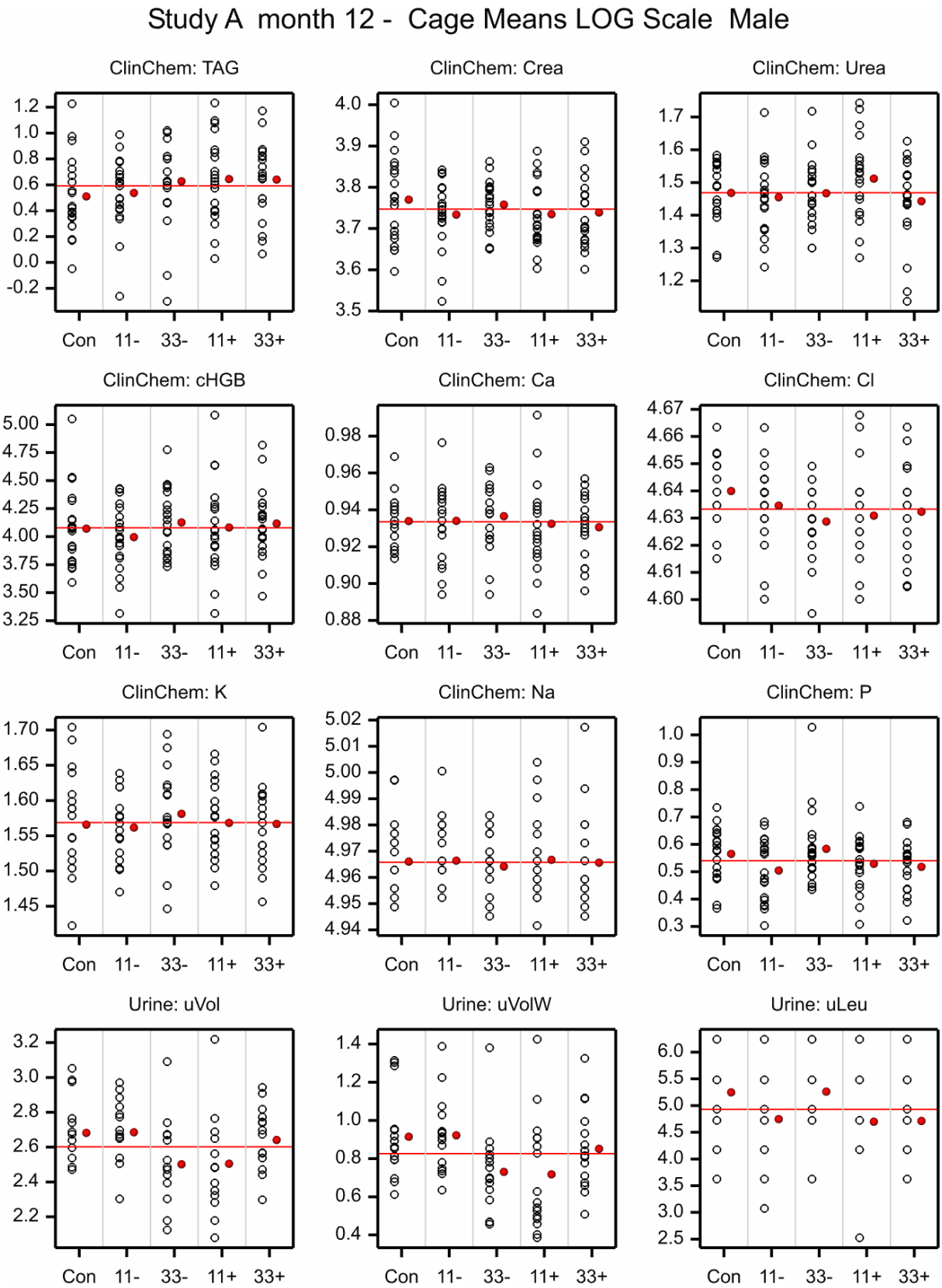
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



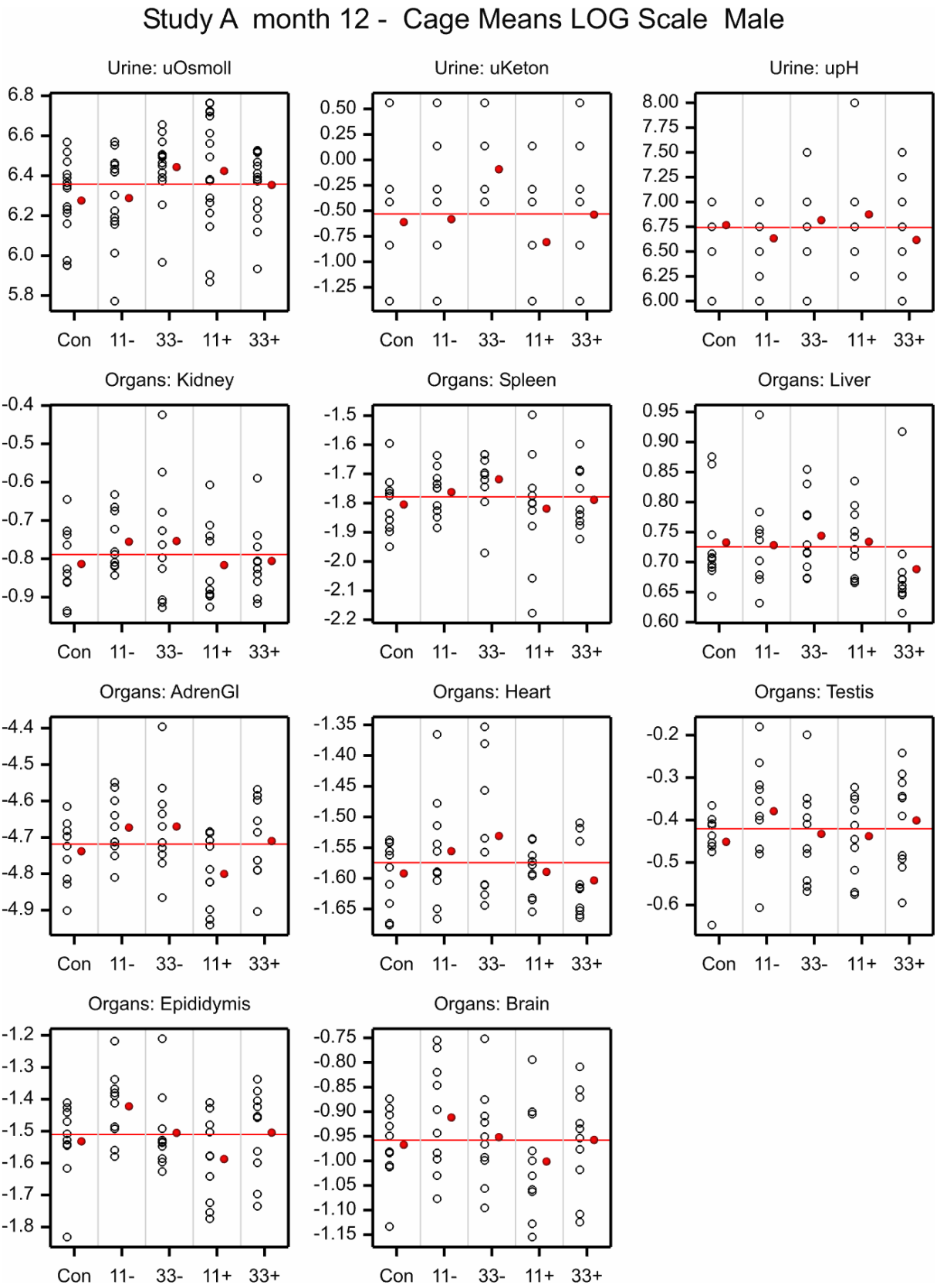
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



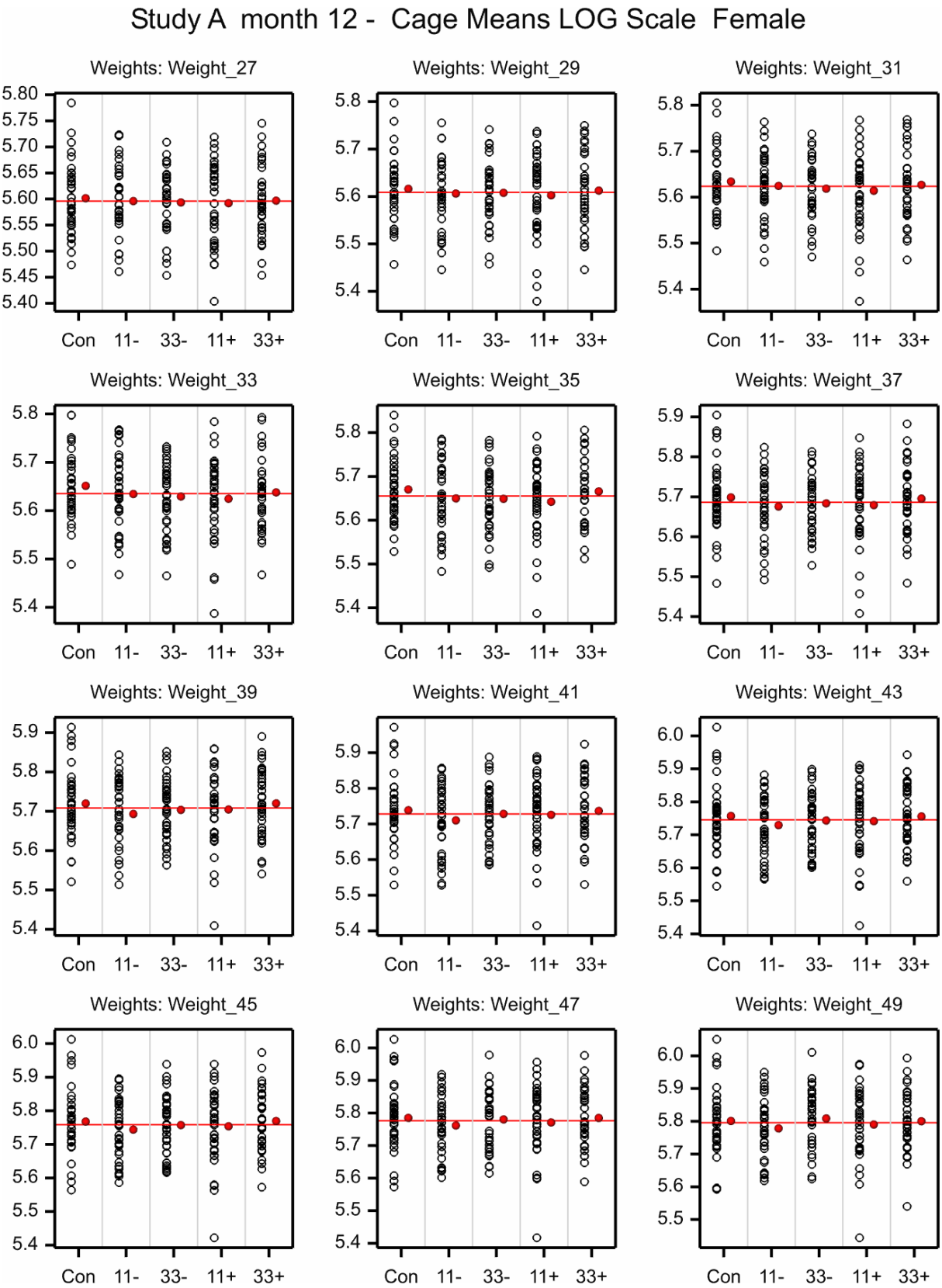
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



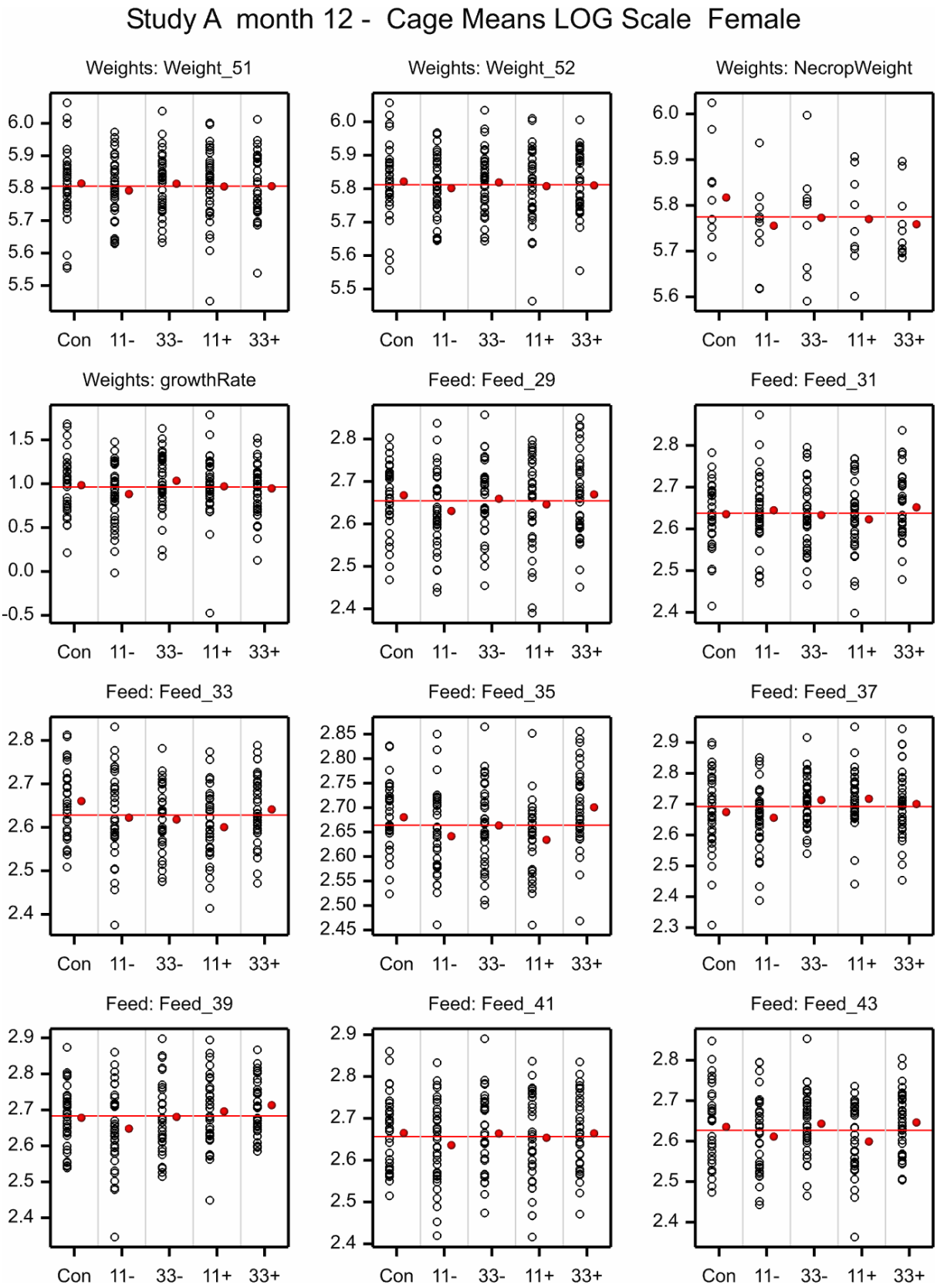
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



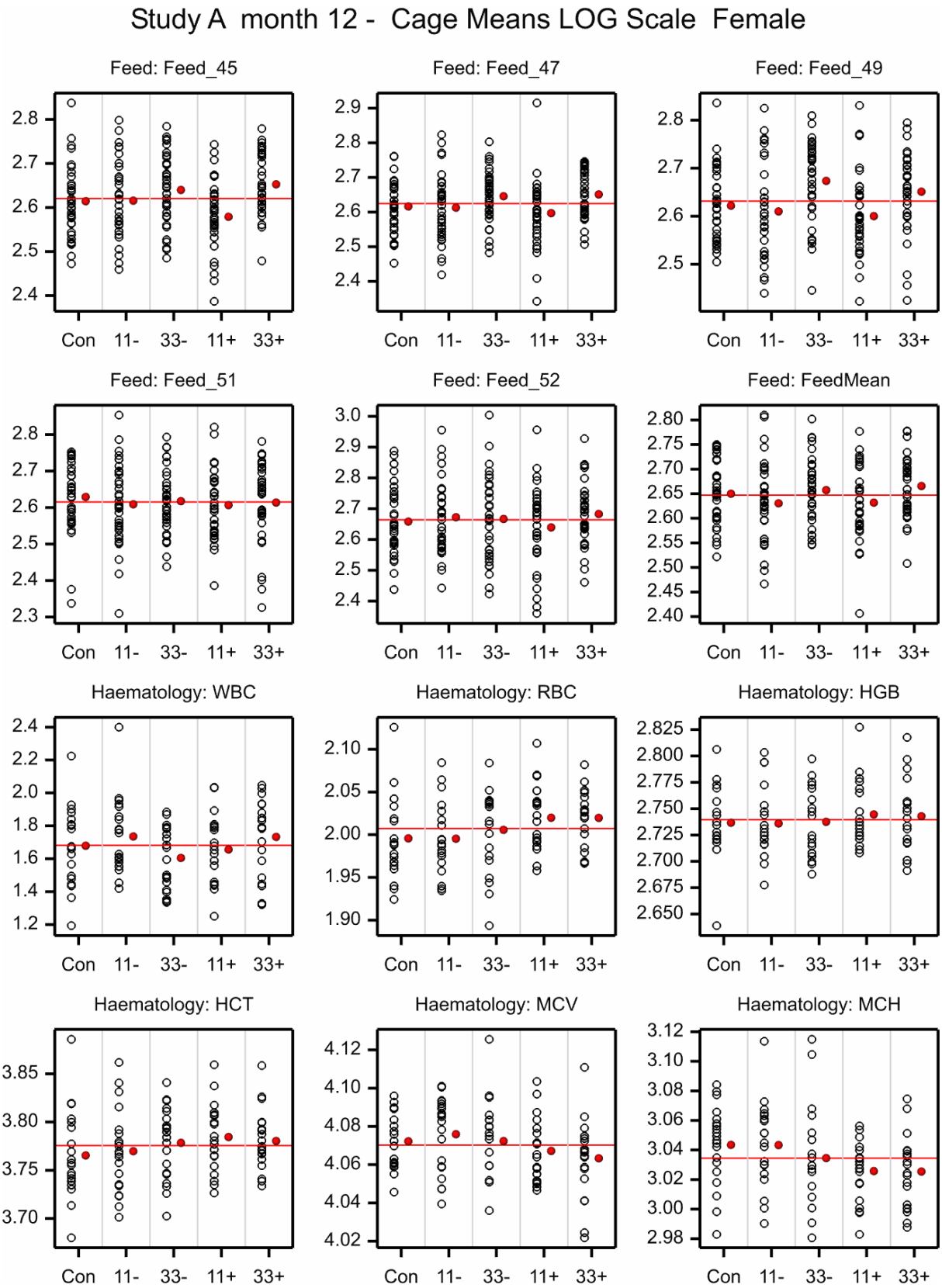
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



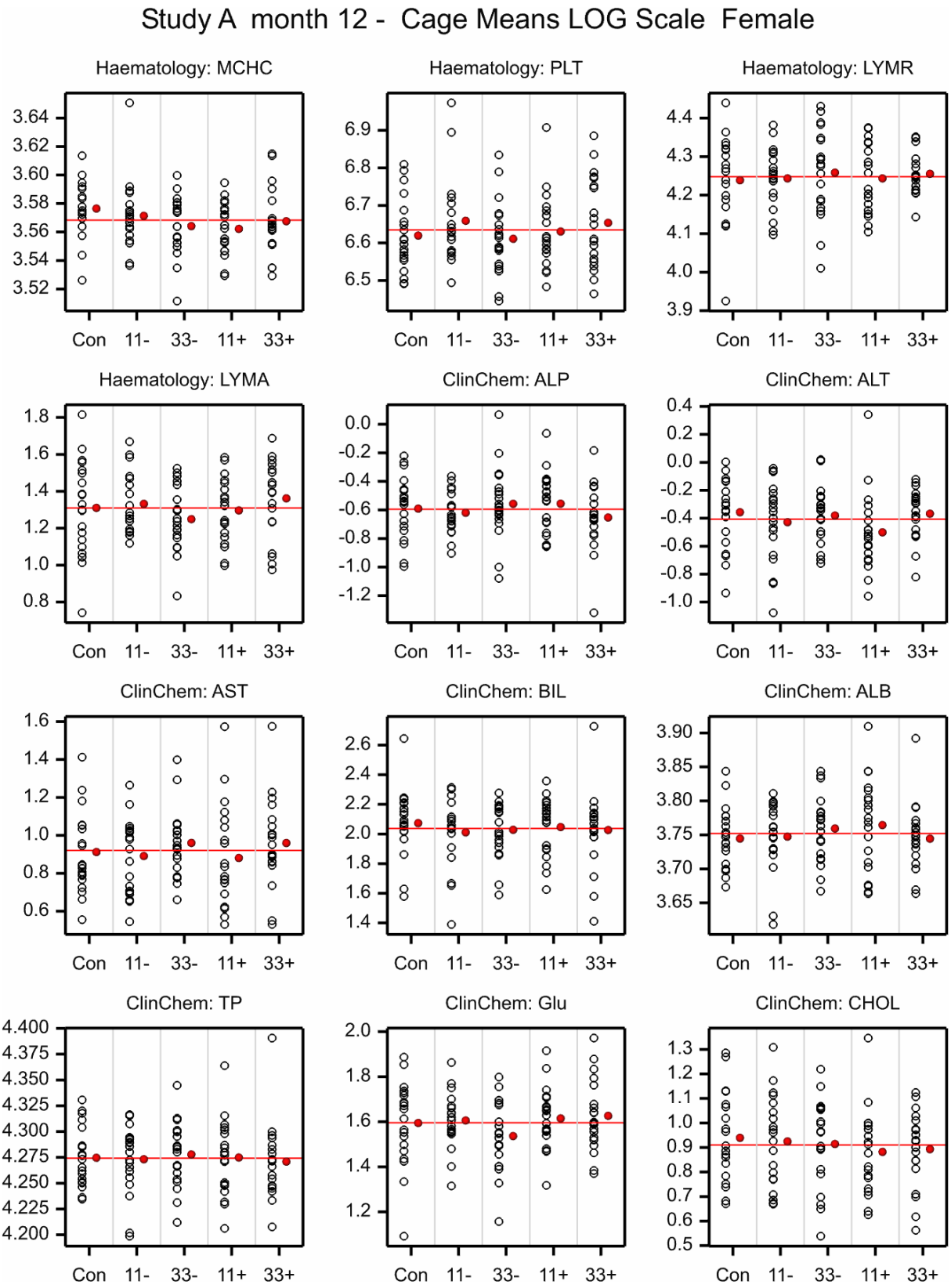
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



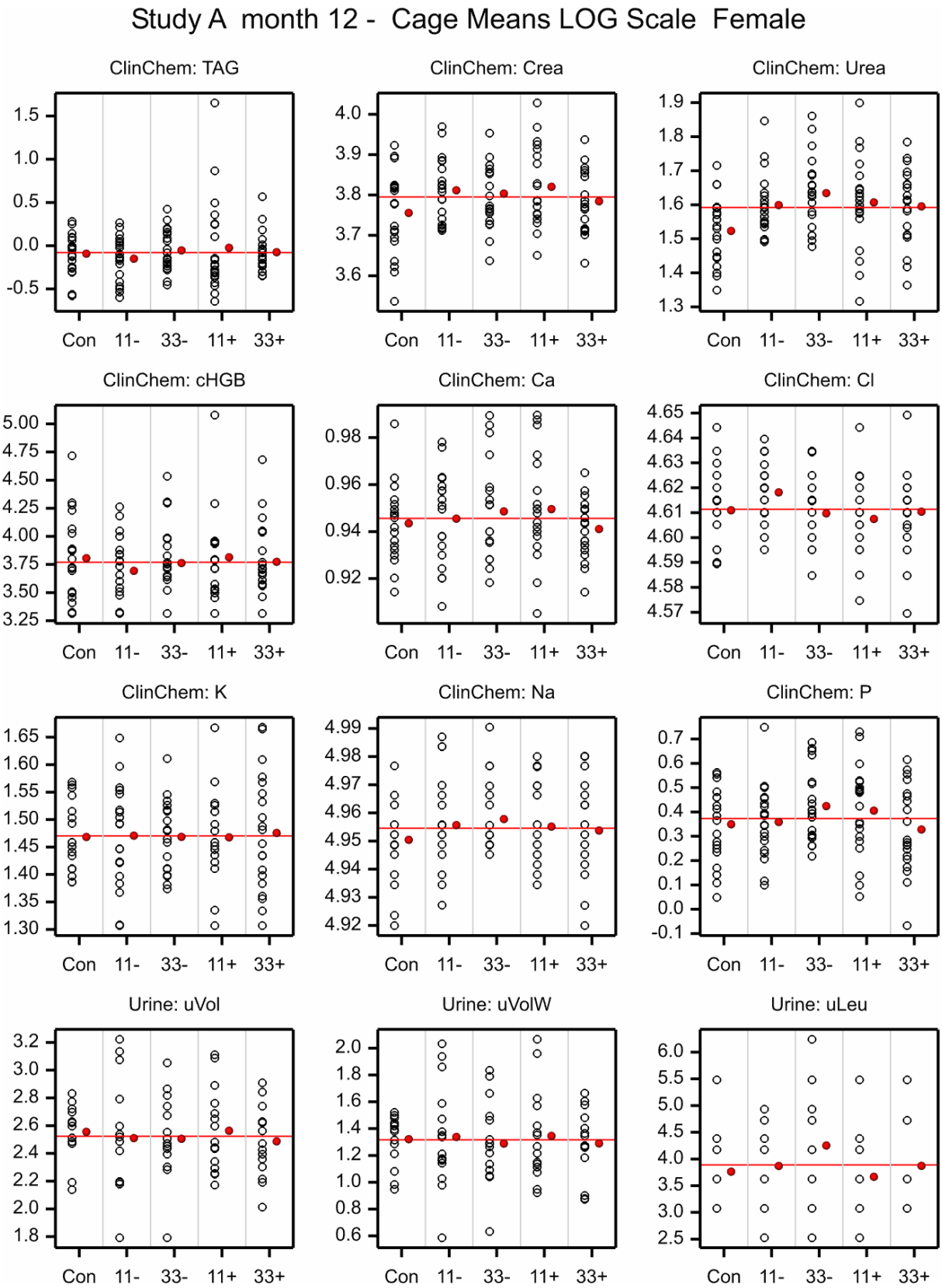
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



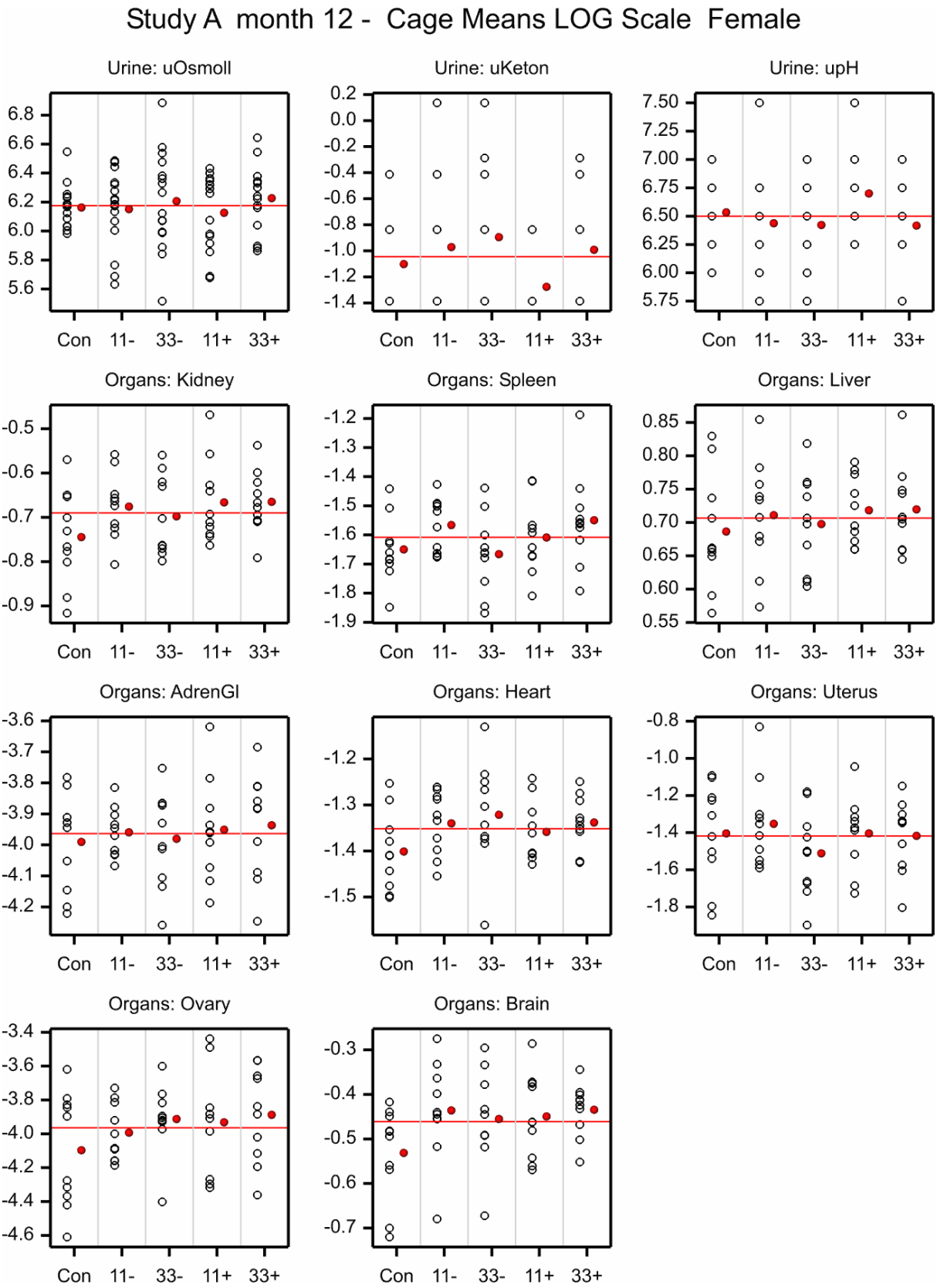
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



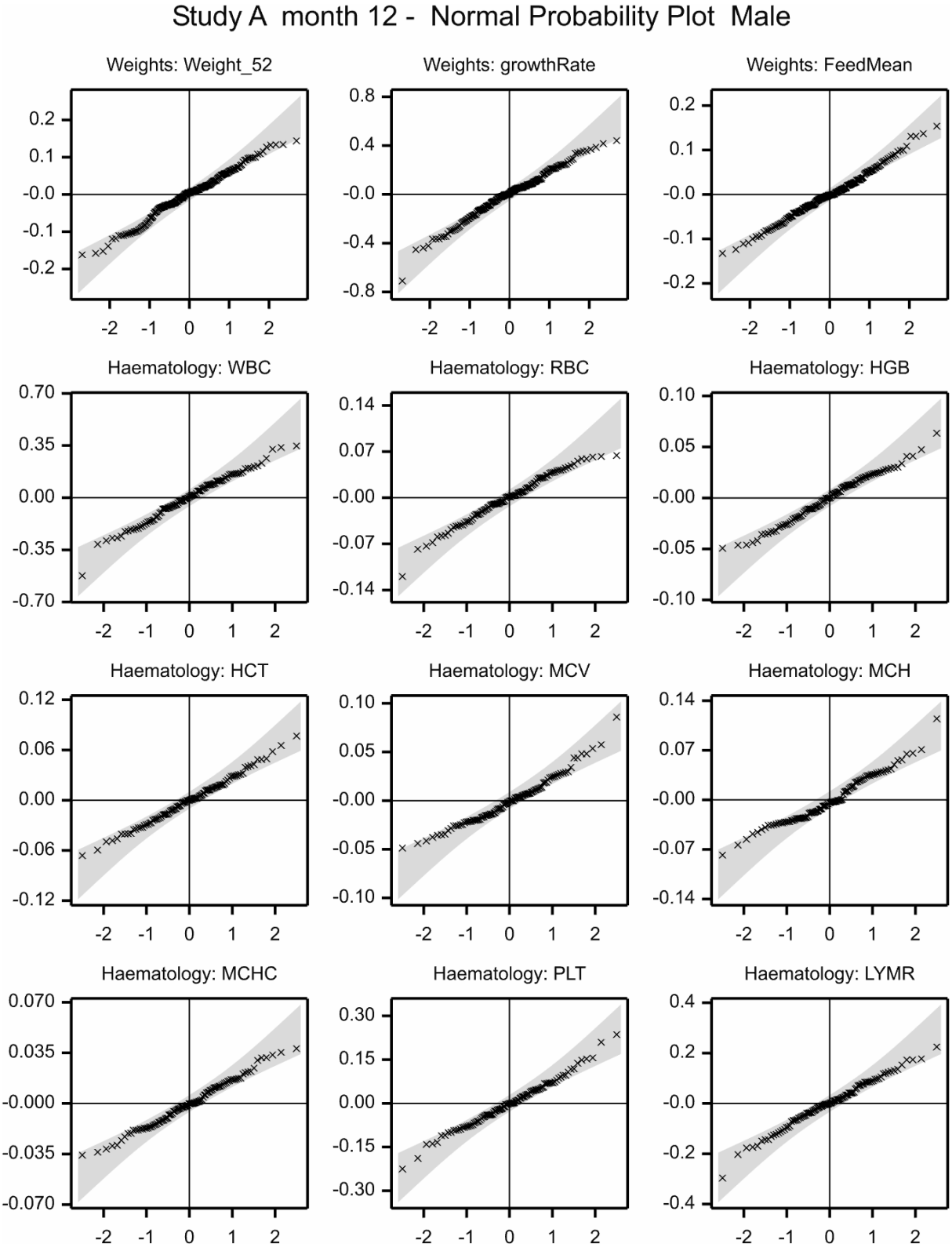
Appendix 4. Graphs of cage means on the log scale (continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean.



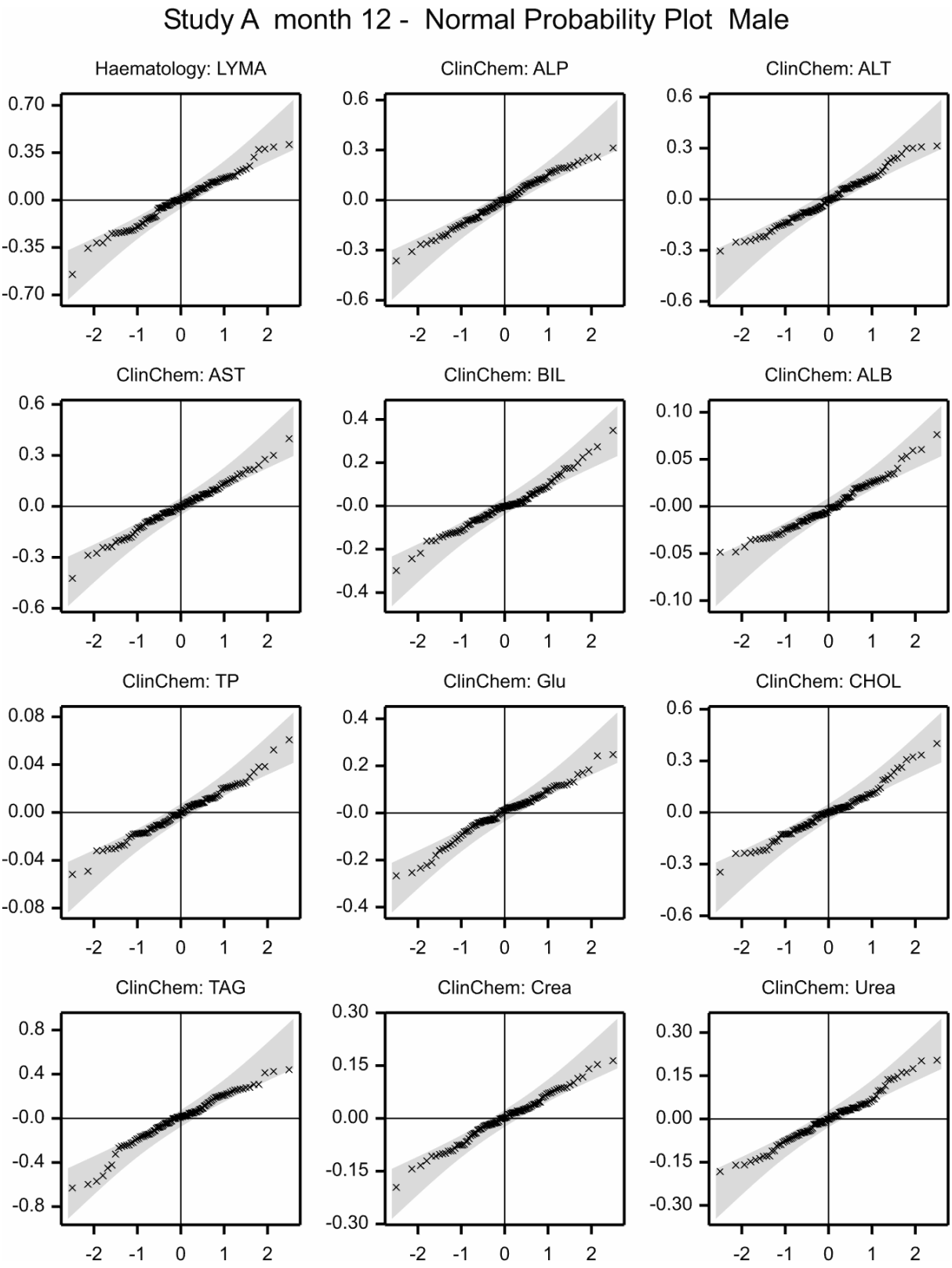
Appendix 5. Normal probability plots of residuals after ANOVA

Residuals are obtained from ANOVA of cage means (log scale). A 99% confidence envelop is added.



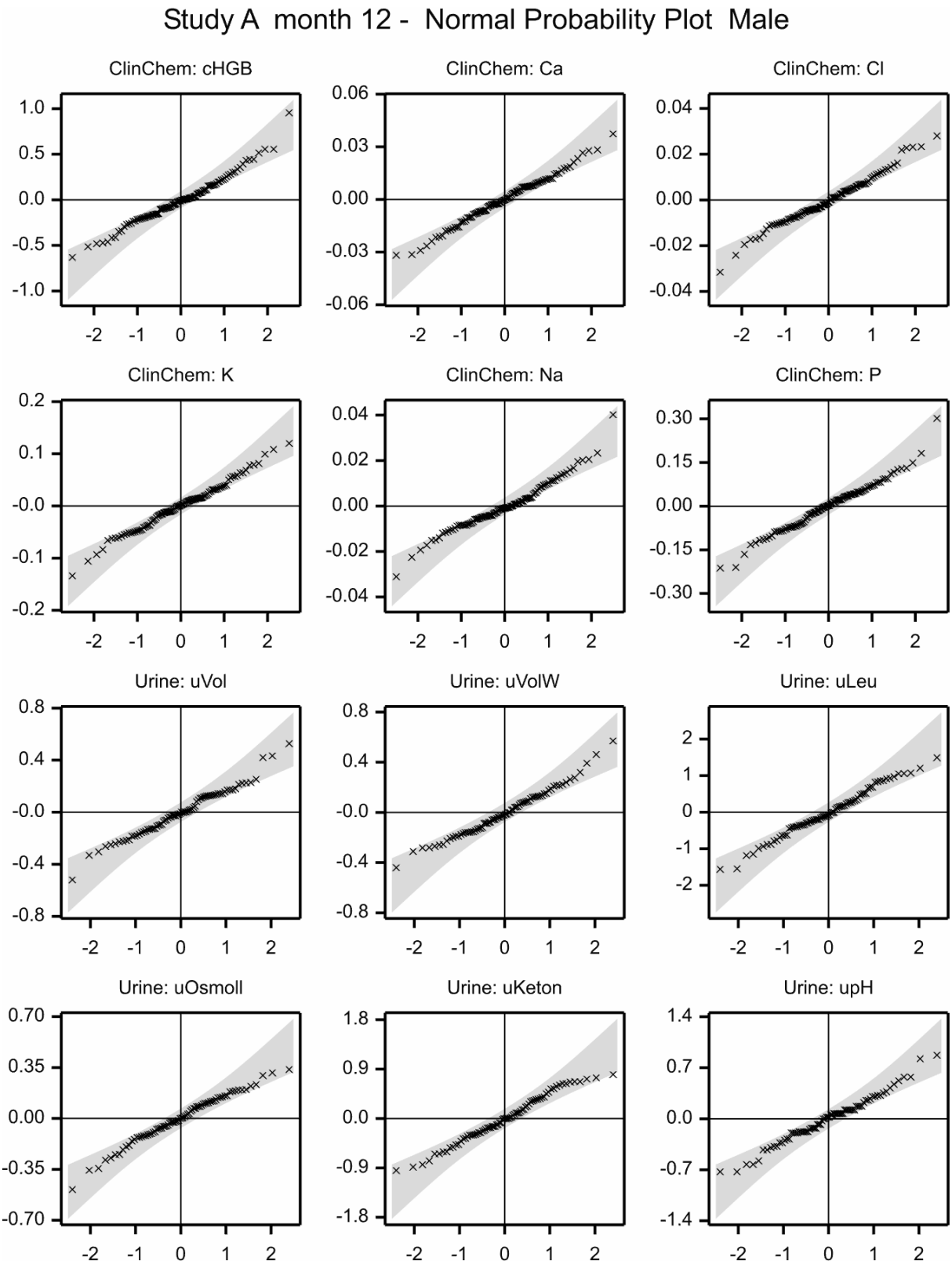
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

Residuals are obtained from ANOVA of cage means (log scale). A 99% confidence envelop is added.



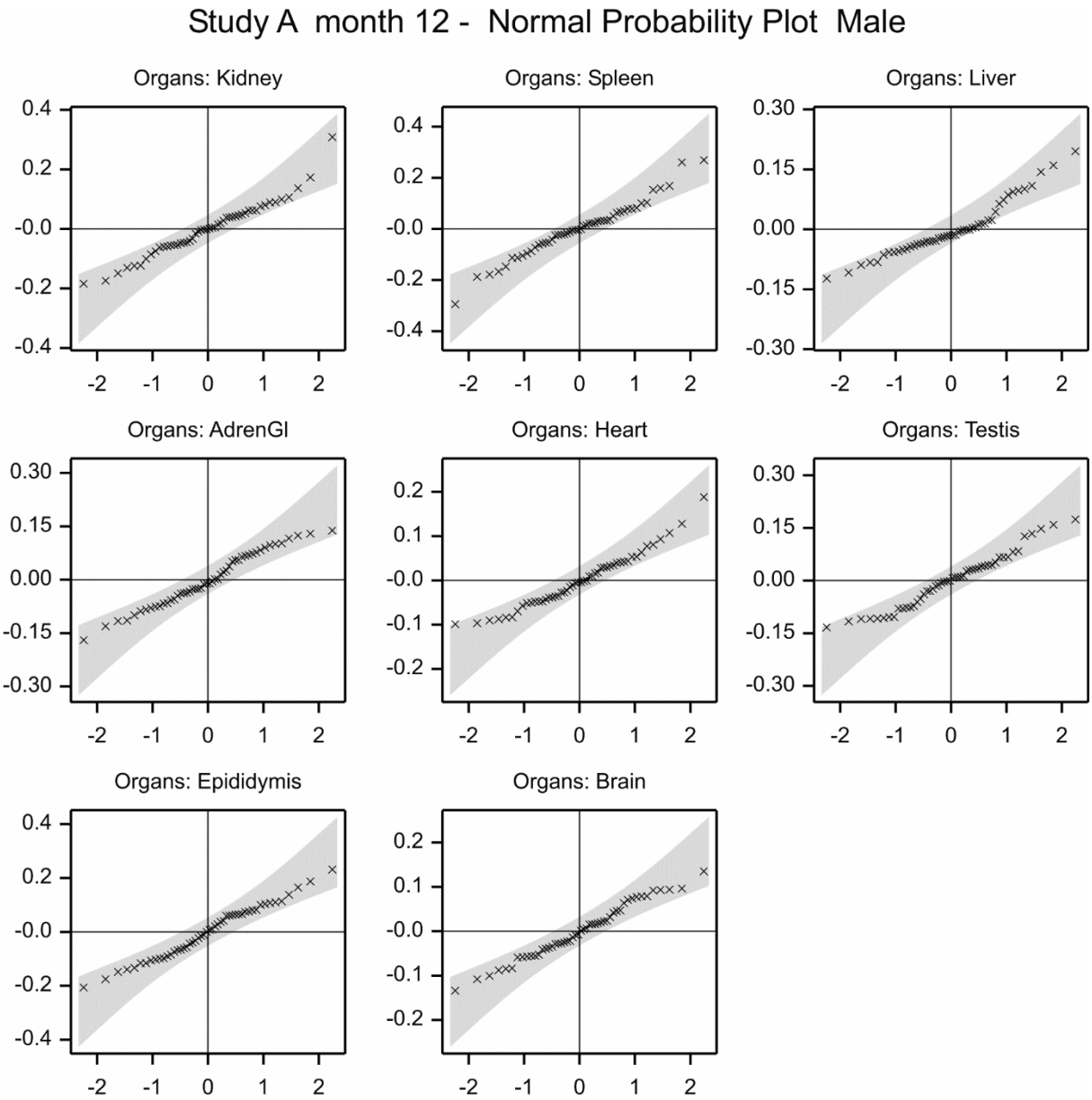
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

Residuals are obtained from ANOVA of cage means (log scale). A 99% confidence envelop is added.



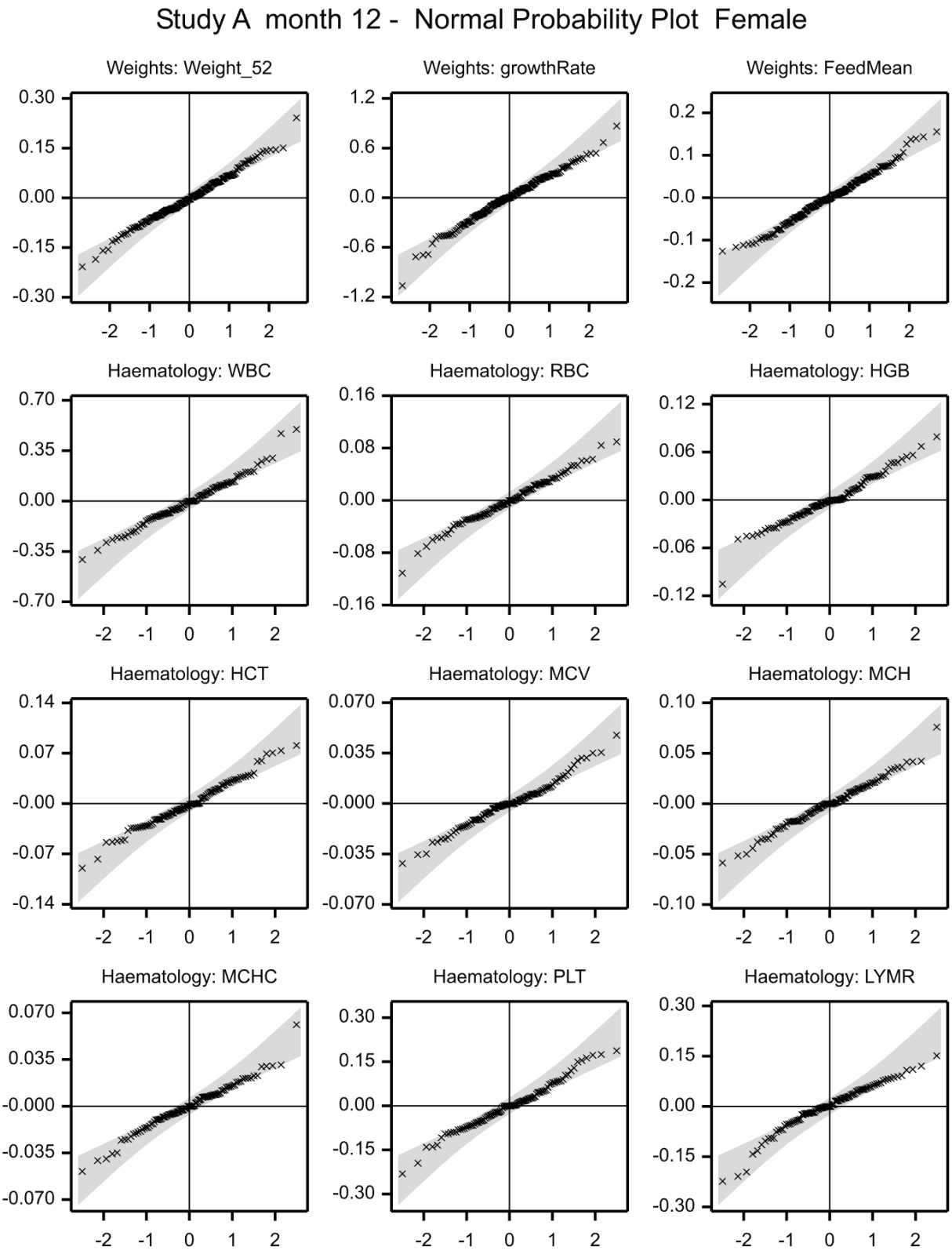
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

Residuals are obtained from ANOVA of cage means (log scale). A 99% confidence envelop is added.



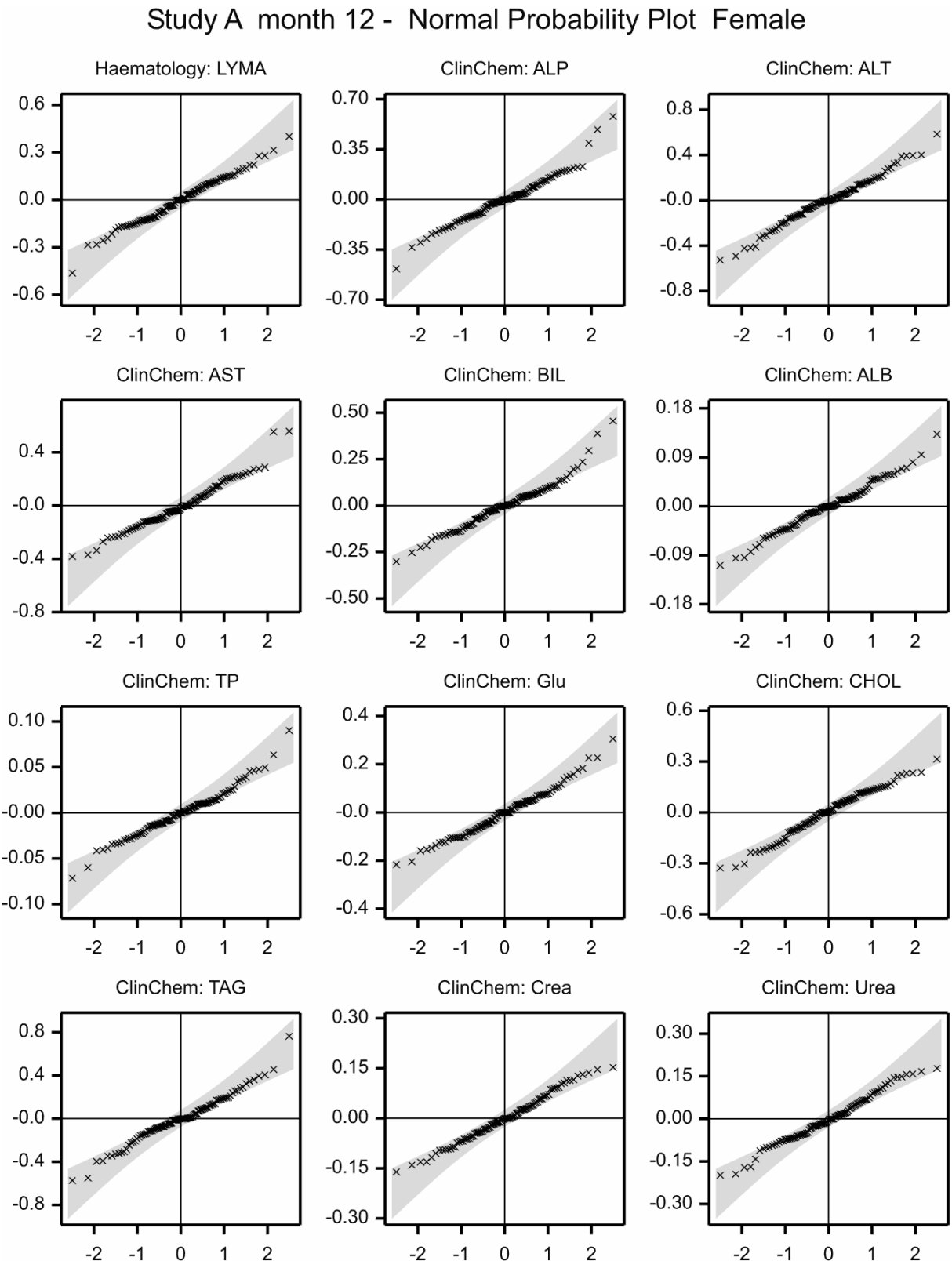
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

Residuals are obtained from ANOVA of cage means (log scale). A 99% confidence envelop is added.



Appendix 5. Normal probability plots of residuals after ANOVA (continued)

Residuals are obtained from ANOVA of cage means (log scale). A 99% confidence envelop is added.



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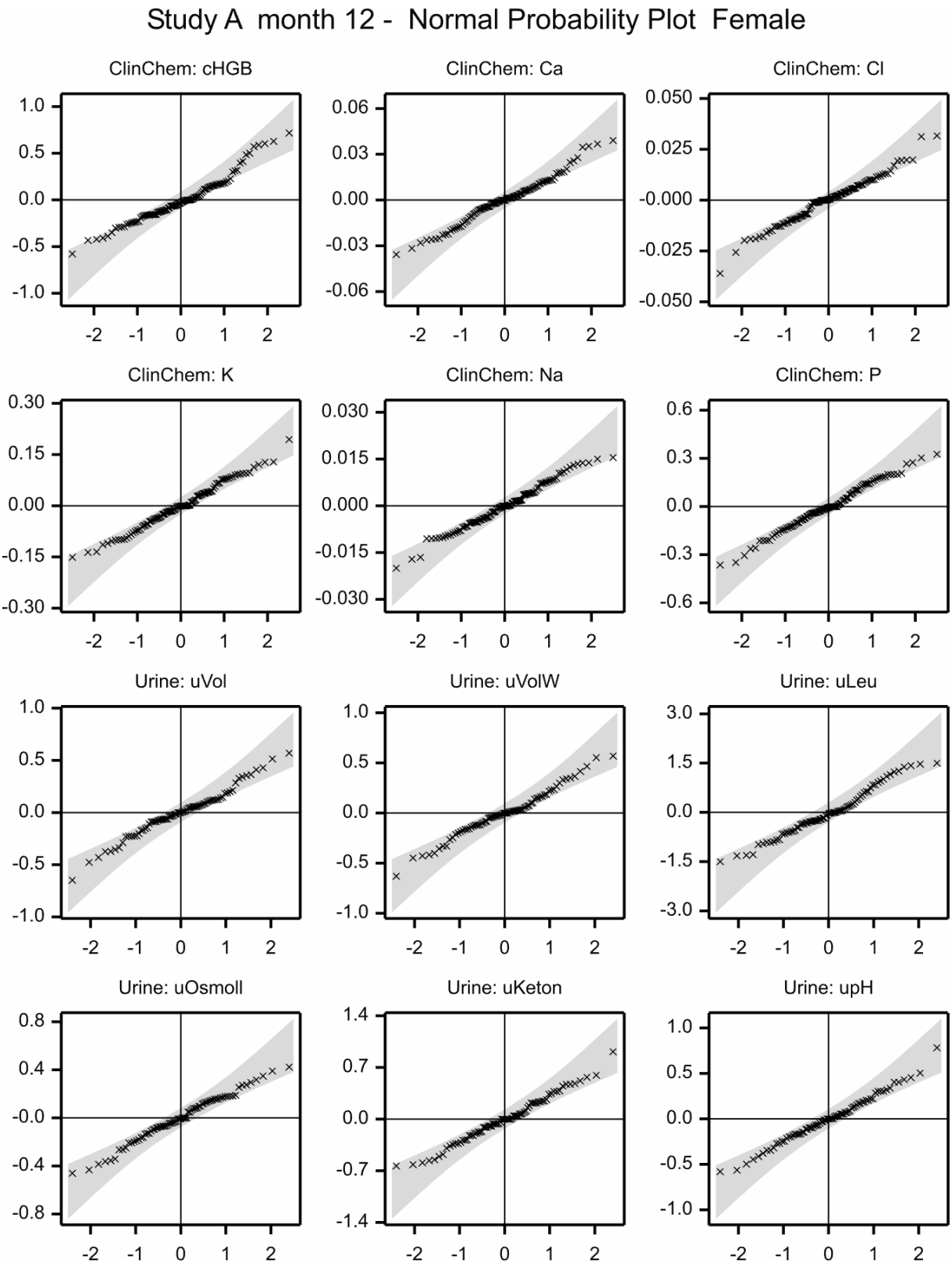
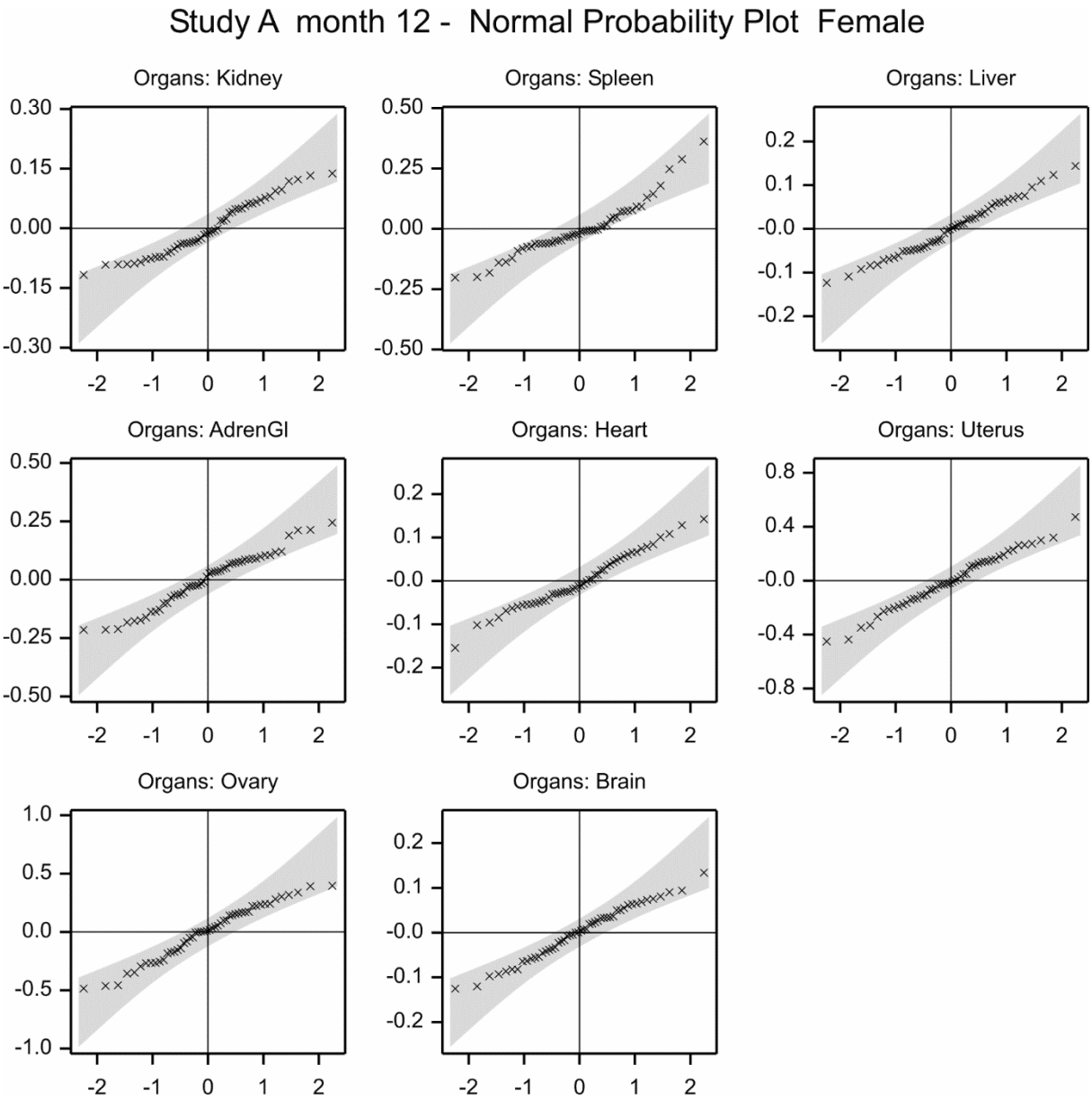
Residuals are obtained from ANOVA of cage means (log scale). A 99% confidence envelop is added.



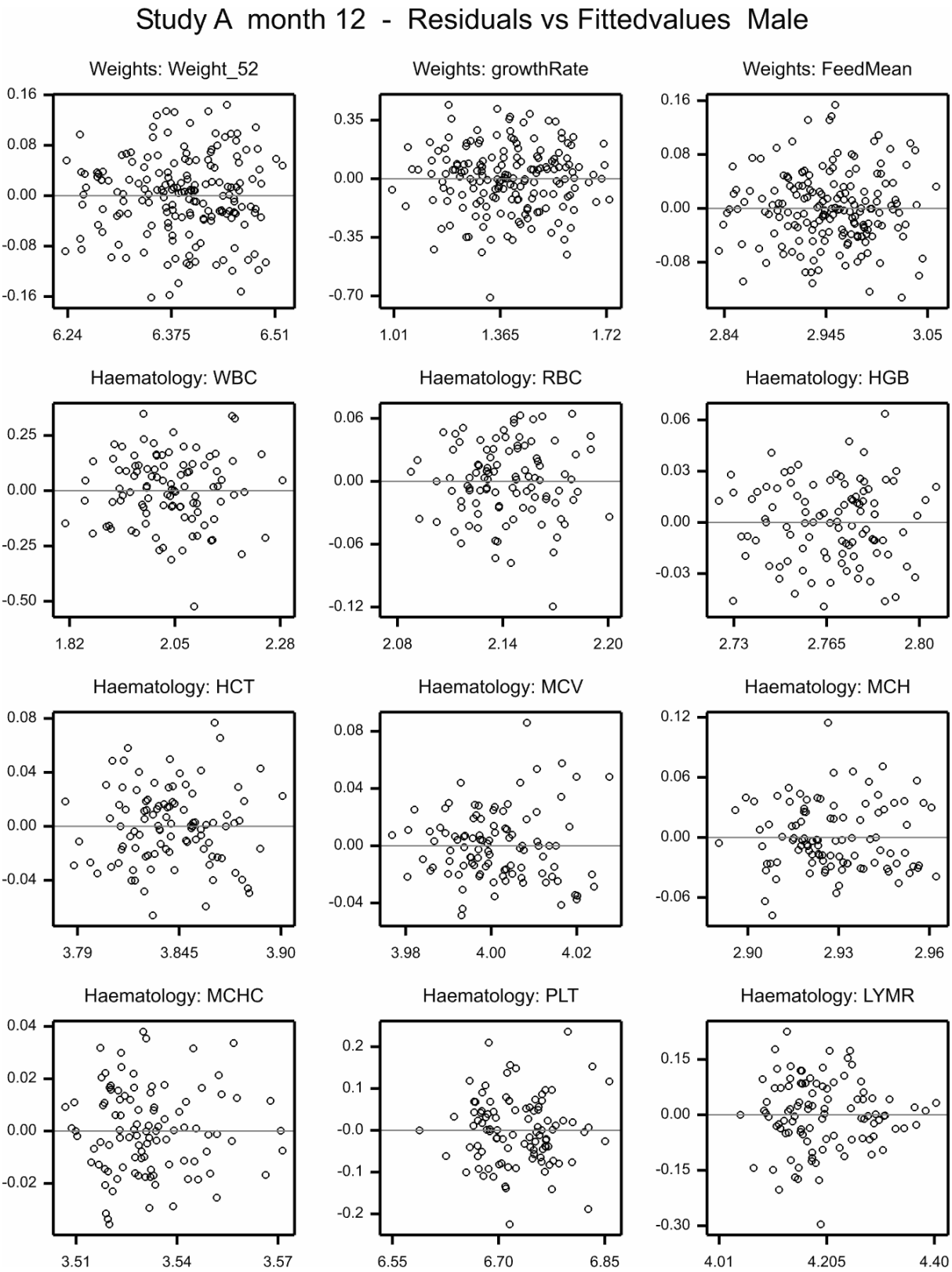
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

Residuals are obtained from ANOVA of cage means (log scale). A 99% confidence envelop is added.



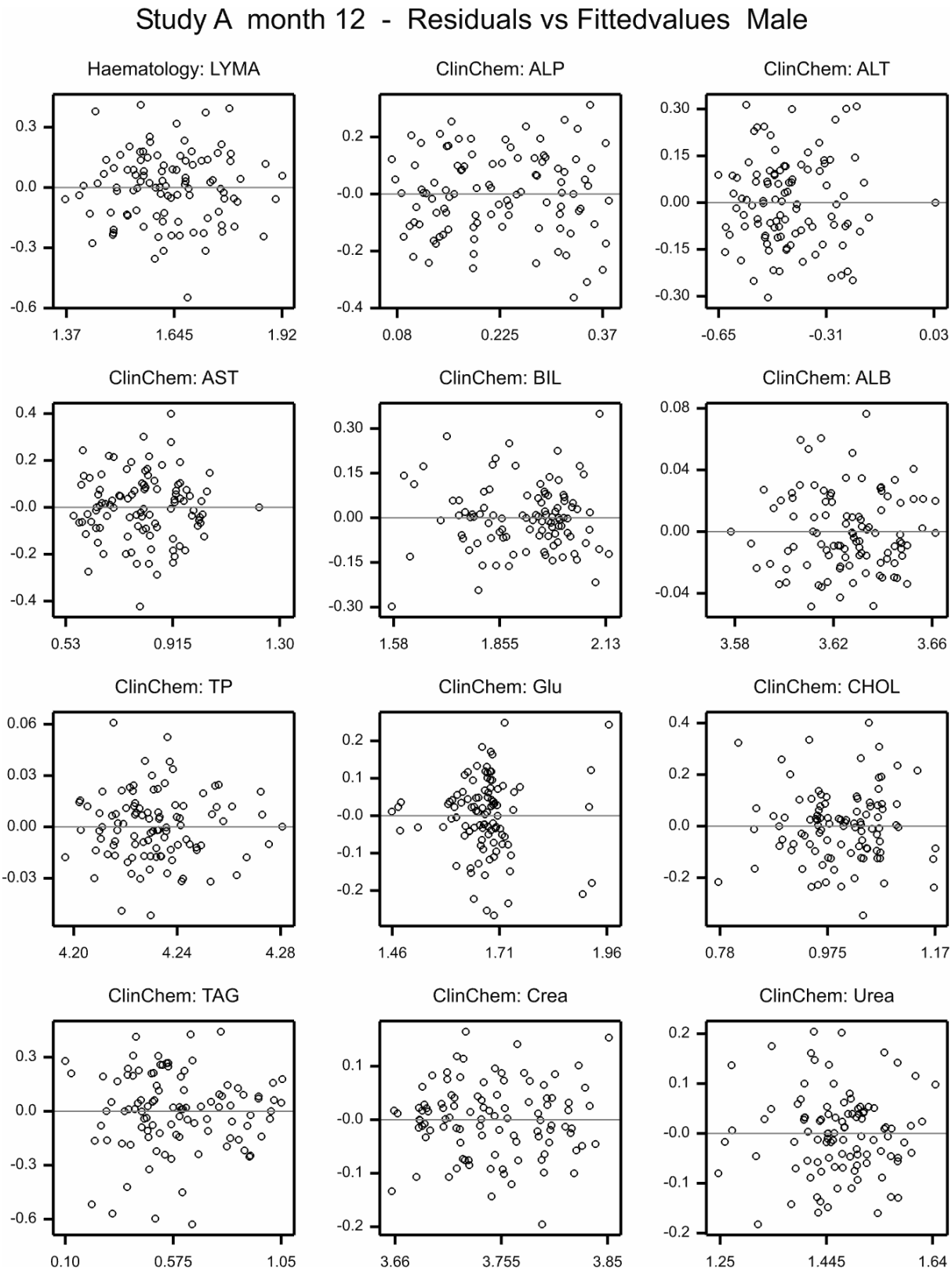
Appendix 6. Graphs of residuals versus fitted values after ANOVA

Residuals and fitted values are obtained from ANOVA of cage means (after a log transformation).



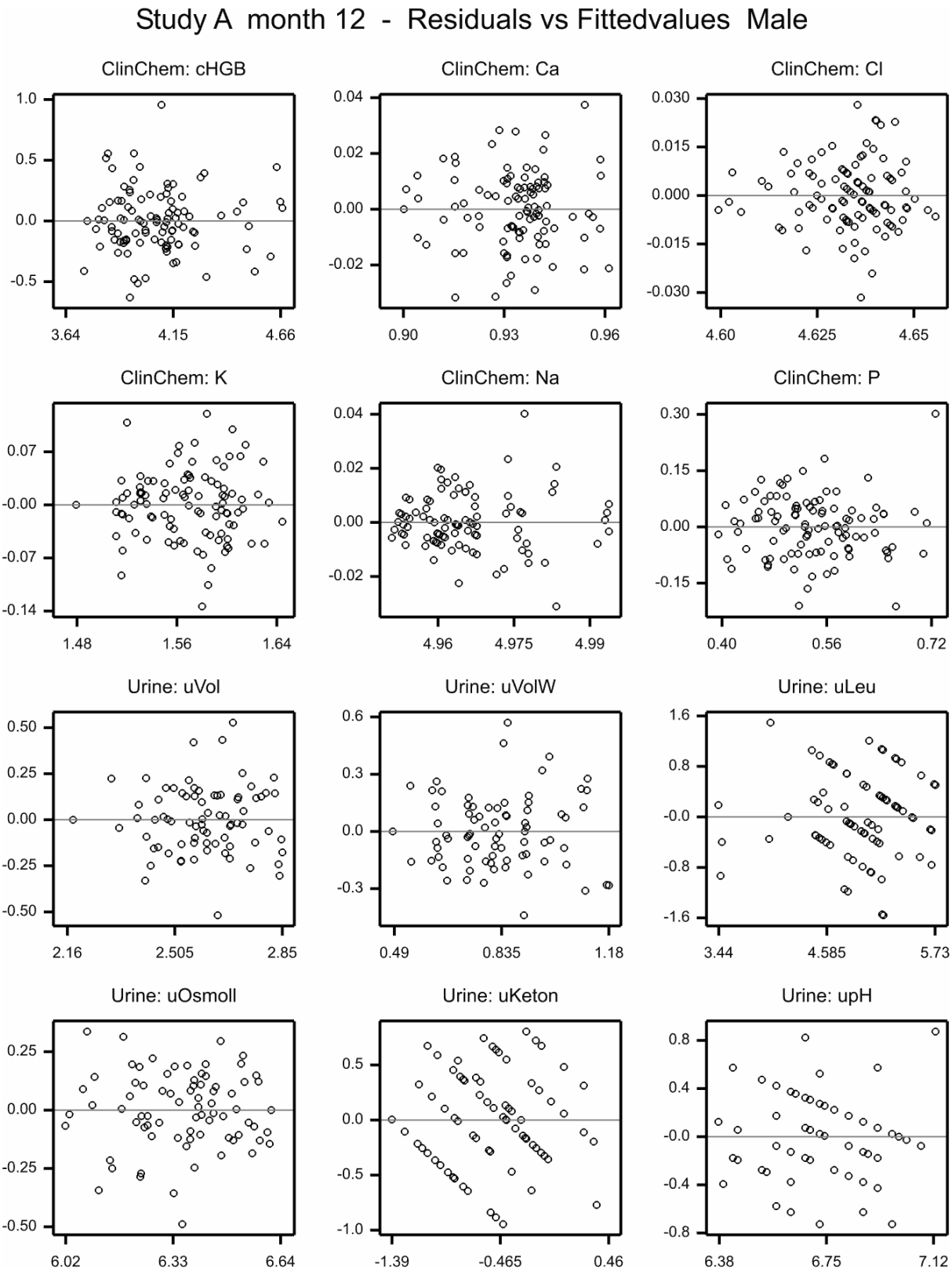
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

Residuals and fitted values are obtained from ANOVA of cage means (after a log transformation).



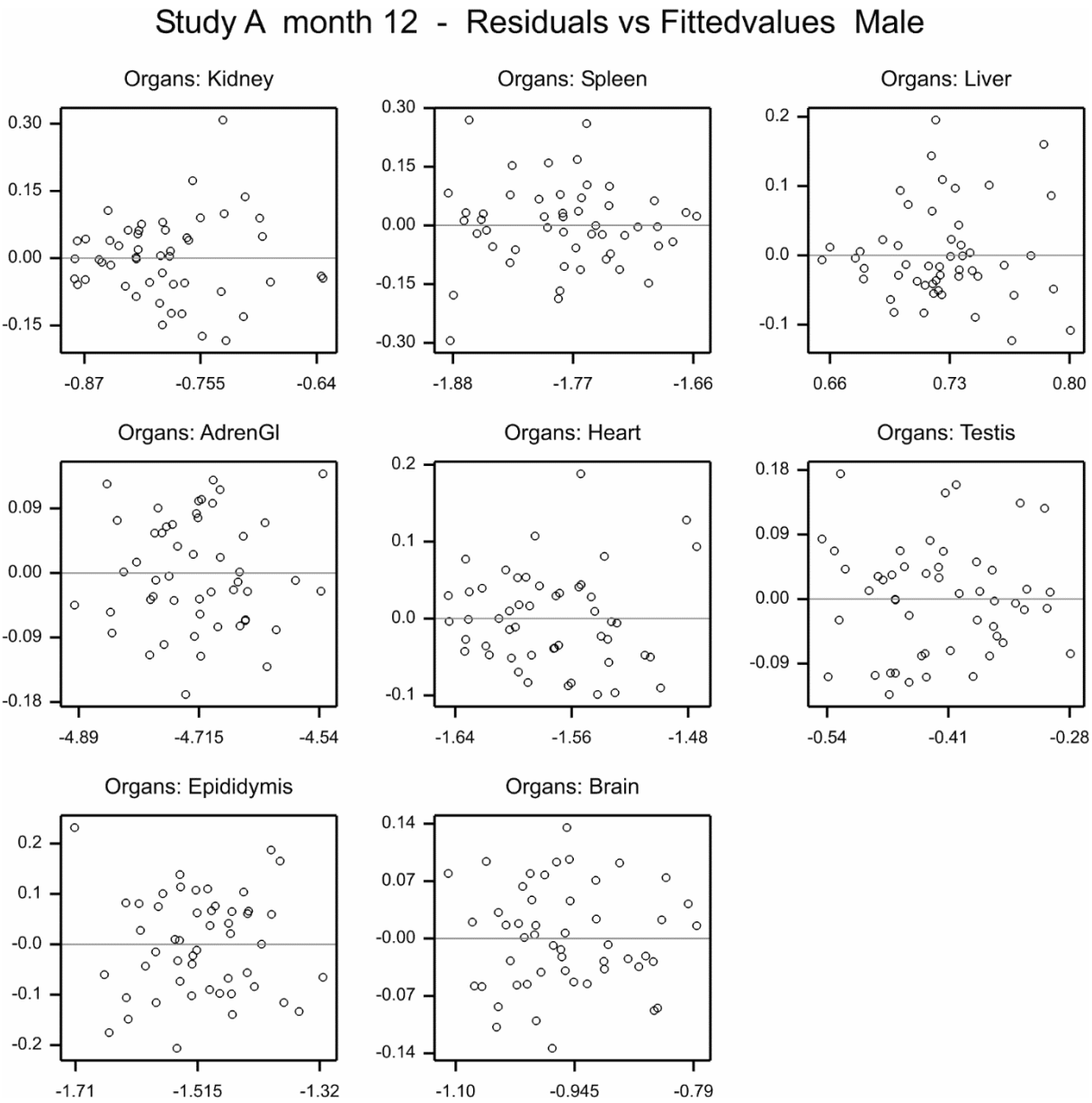
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

Residuals and fitted values are obtained from ANOVA of cage means (after a log transformation).



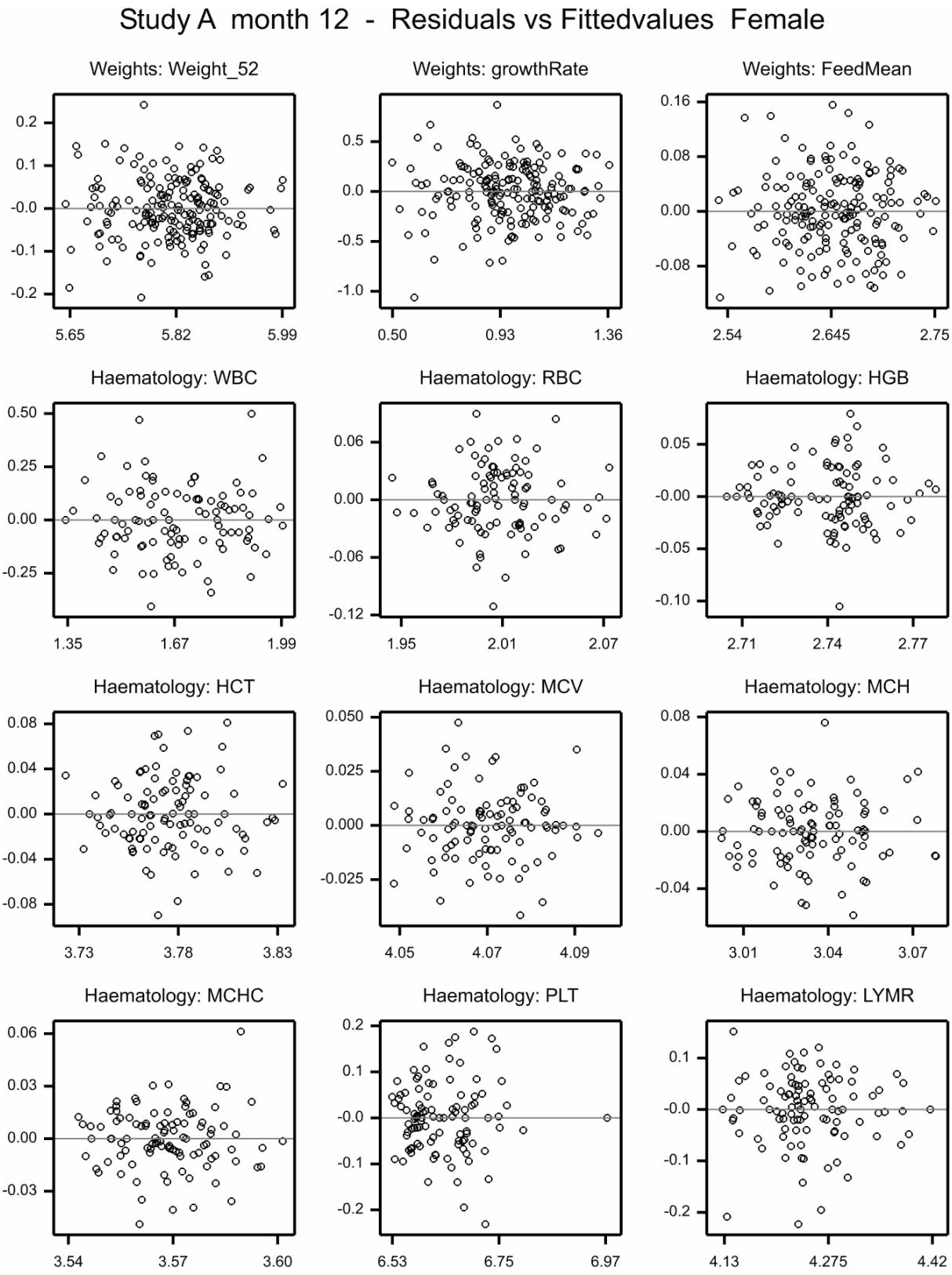
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

Residuals and fitted values are obtained from ANOVA of cage means (after a log transformation).



Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

Residuals and fitted values are obtained from ANOVA of cage means (after a log transformation).



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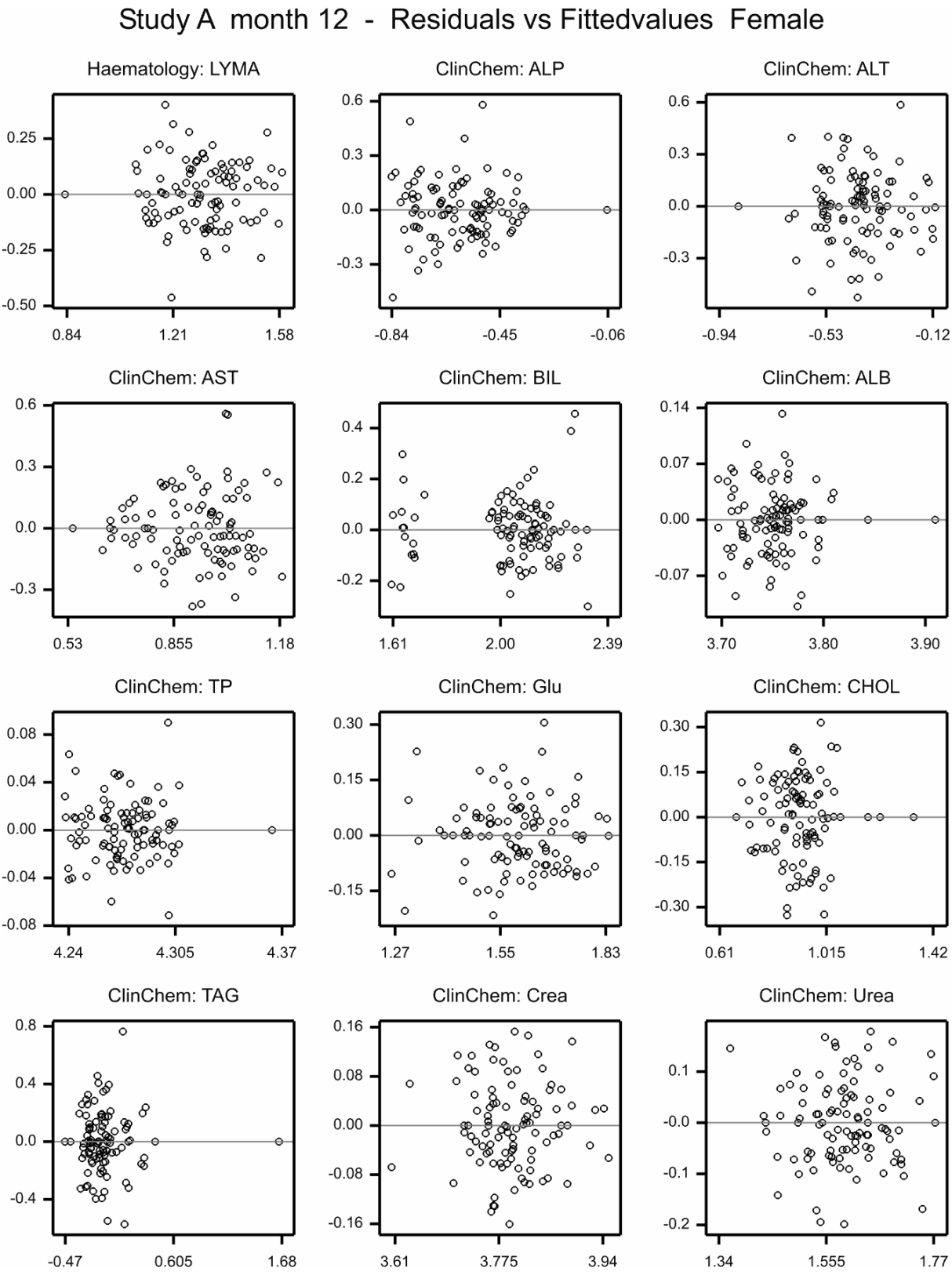

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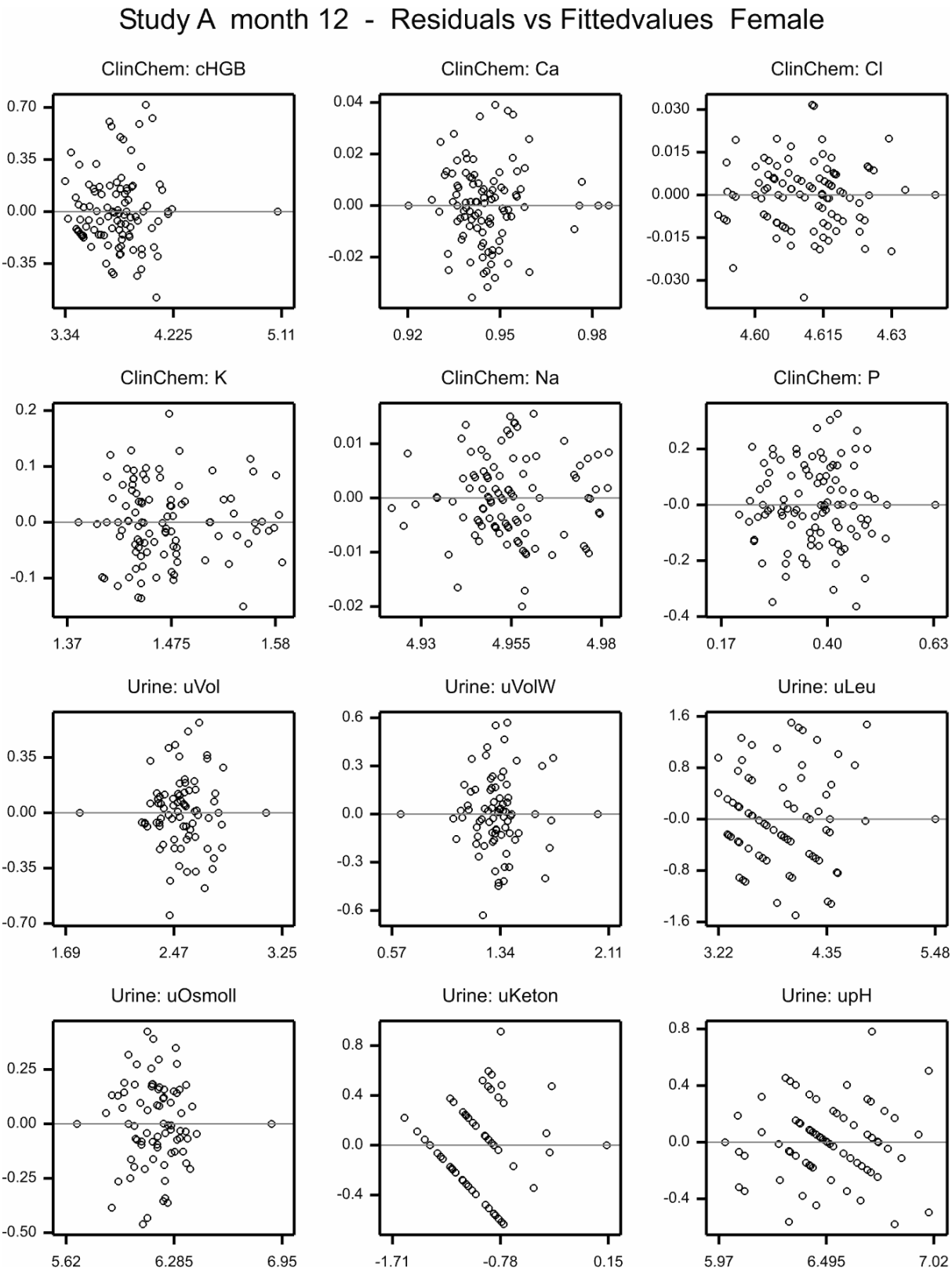
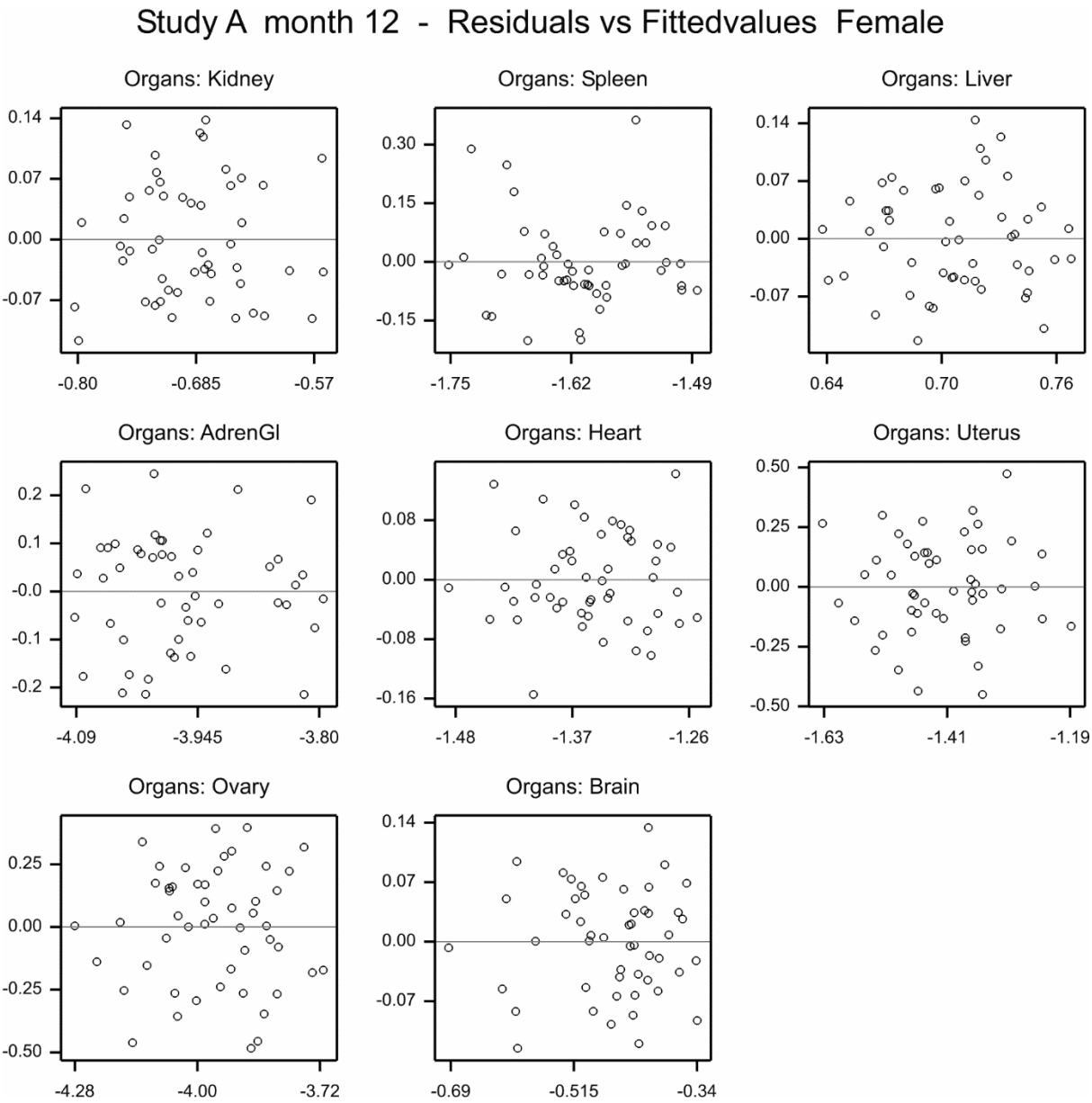


Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

Residuals and fitted values are obtained from ANOVA of cage means (after a log transformation).



Appendix 7. Estimated differences between GMO feeds and the control feed

The differences are given along with the residual sums of squares SS_F based on ANOVA on cage means after a log-transform. The degrees of freedom for the residual sums of squares equals 136 for Weight_13, growthRate and FeedMean, 76 for the other Male variables, and 75 for the other Female variables. Degrees of freedom are sometimes one less due to an occasional missing cage mean.

Variable	Male rats					Female rats				
	NK11-	NK33-	NK11+	NK33+	SS_F	NK11-	NK33-	NK11+	NK33+	SS_F
Weight_52	-0.0254	-0.0063	-0.0059	0.0218	0.8692	-0.0198	-0.0027	-0.0138	-0.0114	0.8692
FeedMean	-0.0432	-0.0253	-0.0324	0.0140	0.5322	-0.0195	0.0069	-0.0182	0.0156	0.5322
WBC	-0.0607	0.1100	0.0209	0.0725	2.4769	0.0605	-0.0705	-0.0352	0.0533	2.4769
RBC	0.0011	-0.0037	0.0216	0.0110	0.1197	0.0029	0.0129	0.0257	0.0240	0.1197
HGB	0.0054	0.0045	0.0125	0.0084	0.0802	0.0028	0.0030	0.0086	0.0062	0.0802
HCT	0.0047	0.0075	0.0255	0.0136	0.0992	0.0091	0.0162	0.0201	0.0150	0.0992
MCV	0.0036	0.0113	0.0038	0.0072	0.0246	0.0050	0.0001	-0.0055	-0.0089	0.0246
MCH	0.0046	0.0088	-0.0089	0.0027	0.0505	0.0002	-0.0098	-0.0185	-0.0181	0.0505
MCHC	0.0005	-0.0031	-0.0130	-0.0045	0.0291	-0.0062	-0.0134	-0.0146	-0.0089	0.0291
PLT	-0.0113	0.0733	0.0274	0.0793	0.5907	0.0296	0.0055	0.0133	0.0338	0.5907
LYMA	-0.0359	0.1479	0.0412	0.0334	2.0886	0.0258	-0.0574	-0.0214	0.0516	2.0886
ALP	0.0675	0.0276	0.0631	0.0253	2.5449	-0.0167	0.0196	0.0138	-0.0623	2.5449
ALT	0.0121	-0.0235	0.0509	0.0353	4.0788	-0.0552	-0.0084	-0.1330	-0.0106	4.0788
AST	0.0199	-0.0056	-0.0634	-0.0130	2.8953	-0.0105	0.0350	-0.0344	0.0474	2.8953
BIL	-0.0263	-0.0106	-0.0578	0.0241	1.5103	-0.0789	-0.0390	-0.0356	-0.0469	1.5103
ALB	-0.0077	0.0088	-0.0026	-0.0055	0.1771	0.0041	0.0128	0.0148	-0.0002	0.1771
TP	-0.0086	0.0052	-0.0031	-0.0026	0.0624	-0.0014	0.0029	-0.0032	-0.0037	0.0624
Glu	0.0044	-0.0150	0.0460	0.0064	0.8968	0.0096	-0.0354	0.0362	0.0317	0.8968
CHOL	0.0297	0.0285	-0.0362	0.0325	1.8216	-0.0127	-0.0525	-0.0818	-0.0464	1.8216
TAG	0.0265	0.1168	0.1663	0.1300	4.4734	-0.0265	0.0023	-0.0139	0.0171	4.4734
Crea	-0.0362	-0.0120	-0.0342	-0.0310	0.4750	0.0510	0.0372	0.0585	0.0289	0.4750
Urea	-0.0133	-0.0011	0.0439	-0.0253	0.6561	0.0780	0.1003	0.0952	0.0721	0.6561
cHGB	-0.0754	0.0558	0.0289	0.0460	5.9418	-0.1237	-0.0197	-0.0369	-0.0319	5.9418
Ca	0.0001	0.0026	0.0002	-0.0034	0.0225	0.0030	0.0058	0.0059	-0.0024	0.0225
Cl	-0.0054	-0.0112	-0.0085	-0.0076	0.0128	0.0083	0.0000	-0.0018	-0.0006	0.0128
K	-0.0042	0.0153	0.0045	0.0010	0.4542	0.0102	0.0135	0.0052	0.0073	0.4542
Na	0.0004	-0.0019	0.0004	-0.0004	0.0054	0.0066	0.0069	0.0044	0.0033	0.0054
P	-0.0608	0.0184	-0.0419	-0.0473	2.0237	0.0113	0.0750	0.0513	-0.0215	2.0237
Kidney	0.0582	0.0599	-0.0027	0.0079	0.2316	0.0687	0.0467	0.0783	0.0796	0.2316
Spleen	0.0423	0.0864	-0.0144	0.0159	0.6181	0.0837	-0.0162	0.0408	0.1002	0.6181
Liver	-0.0044	0.0112	0.0013	-0.0444	0.1887	0.0246	0.0112	0.0319	0.0332	0.1887
AdrenGl	0.0651	0.0681	-0.0622	0.0281	0.6723	0.0309	0.0100	0.0395	0.0539	0.6723
Heart	0.0363	0.0611	0.0025	-0.0113	0.1926	0.0612	0.0799	0.0426	0.0631	0.1926
Testis Uterus	0.0722	0.0184	0.0133	0.0504	1.9999	0.0520	-0.1070	0.0005	-0.0127	1.9999
Epididymis Ovary	0.1096	0.0266	-0.0553	0.0273	2.6593	0.1040	0.1843	0.1652	0.2092	2.6593
Brain	0.0555	0.0155	-0.0340	0.0099	0.1810	0.0953	0.0762	0.0819	0.0969	0.1810

Appendix 8. Intervals for equivalence tests

95% Confidence interval plus estimate for the ratio Δ of a GMO feed versus the control feed, 95% Confidence interval plus median for (upper) equivalence limits, and the confidence interval plus median for Δ on the ELSD scale. Red background colouring indicates significant differences, green background colouring indicates significant equivalences (in all remaining cases equivalence is still more likely than not).

Males NK11- versus Control									
Weights	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
Weight_52	0.943	0.975	1.008	1.017	1.056	1.109	-2.000	-0.478	0.222
FeedMean	0.931	0.958	0.985	1.037	1.080	1.161	-1.141	-0.554	-0.166
Haematology	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.840	0.941	1.054	1.455	1.651	2.407	-0.321	-0.115	0.105
RBC	0.976	1.001	1.027	1.083	1.109	1.144	-0.245	0.010	0.258
HGB	0.989	1.005	1.022	1.079	1.100	1.146	-0.118	0.055	0.208
HCT	0.985	1.005	1.025	1.089	1.112	1.148	-0.149	0.044	0.212
MCV	0.986	1.004	1.021	1.005	1.024	1.039	-2.000	0.255	2.000
MCH	0.981	1.005	1.029	1.010	1.036	1.060	-2.000	0.150	2.000
MCHC	0.989	1.001	1.012	1.019	1.031	1.050	-0.406	0.017	0.428
PLT	0.933	0.989	1.048	1.621	1.787	2.042	-0.108	-0.019	0.081
LYMA	0.850	0.965	1.095	1.395	1.587	2.213	-0.323	-0.074	0.201
ClinChem	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
ALP	0.965	1.070	1.186	1.289	1.413	1.586	-0.103	0.194	0.466
ALT	0.915	1.012	1.119	1.059	1.186	1.326	-1.266	0.075	2.000
AST	0.922	1.020	1.128	1.216	1.337	1.528	-0.295	0.067	0.396
ALB	0.974	0.992	1.011	1.102	1.127	1.161	-0.196	-0.065	0.088
TP	0.977	0.991	1.006	1.075	1.093	1.120	-0.236	-0.096	0.064
Glu	0.934	1.004	1.080	1.281	1.382	1.649	-0.217	0.012	0.231
CHOL	0.933	1.030	1.138	1.087	1.230	1.576	-0.426	0.136	0.782
TAG	0.880	1.027	1.199	1.736	2.120	4.335	-0.174	0.033	0.224
Crea	0.918	0.964	1.013	1.282	1.362	1.567	-0.255	-0.114	0.041
Urea	0.930	0.987	1.047	1.191	1.278	1.612	-0.274	-0.050	0.191
Ca	0.990	1.000	1.010	1.131	1.161	1.237	-0.064	0.001	0.065
Cl	0.987	0.995	1.002	1.102	1.124	1.171	-0.101	-0.045	0.018
K	0.964	0.996	1.029	1.225	1.280	1.366	-0.139	-0.017	0.117
Na	0.993	1.000	1.008	1.112	1.136	1.185	-0.056	0.003	0.060
P	0.887	0.941	0.998	1.165	1.235	1.416	-0.555	-0.279	-0.009
Organs	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
Kidney	0.963	1.060	1.167	1.024	1.110	1.284	-2.000	0.907	2.000
Spleen	0.932	1.043	1.168	1.070	1.184	1.329	-0.573	0.253	1.348
Liver	0.927	0.996	1.070	1.032	1.101	1.189	-2.000	-0.048	2.000
AdrenGl	0.984	1.067	1.157	1.279	1.371	1.568	-0.047	0.202	0.436
Heart	0.972	1.037	1.107	1.059	1.121	1.223	-0.283	0.309	0.978
Testis	0.990	1.075	1.167	1.112	1.185	1.274	-0.060	0.420	0.936
Epididymis	1.004	1.116	1.240	1.058	1.162	1.375	0.033	0.754	2.000
Brain	0.990	1.057	1.128	1.055	1.120	1.234	-0.095	0.481	1.276

Appendix 8. Intervals for equivalence tests (continued)

Males NK33- versus Control									
Weights	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
Weight_52	0.961	0.994	1.028	1.017	1.063	1.109	-2.000	-0.121	2.000
FeedMean	0.948	0.975	1.003	1.037	1.080	1.162	-0.798	-0.321	0.036
Haematology	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.997	1.116	1.250	1.455	1.650	2.389	-0.007	0.211	0.433
RBC	0.971	0.996	1.022	1.083	1.109	1.144	-0.267	-0.035	0.221
HGB	0.988	1.005	1.021	1.079	1.100	1.146	-0.127	0.047	0.200
HCT	0.987	1.007	1.028	1.089	1.112	1.148	-0.122	0.070	0.237
MCV	0.994	1.011	1.029	1.005	1.024	1.047	-2.000	0.815	2.000
MCH	0.985	1.009	1.033	1.010	1.037	1.060	-2.000	0.285	2.000
MCHC	0.985	0.997	1.009	1.018	1.030	1.050	-0.482	-0.100	0.308
PLT	1.015	1.076	1.141	1.622	1.786	2.041	0.026	0.126	0.216
LYMA	1.021	1.159	1.316	1.396	1.587	2.217	0.043	0.310	0.591
ClinChem	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
ALP	0.928	1.028	1.139	1.289	1.413	1.585	-0.224	0.079	0.347
ALT	0.883	0.977	1.080	1.060	1.186	1.326	-2.000	-0.145	0.876
AST	0.899	0.994	1.100	1.217	1.337	1.529	-0.372	-0.019	0.349
ALB	0.991	1.009	1.027	1.102	1.127	1.161	-0.080	0.073	0.204
TP	0.991	1.005	1.020	1.075	1.093	1.120	-0.103	0.058	0.198
Glu	0.916	0.985	1.059	1.282	1.381	1.647	-0.248	-0.045	0.180
CHOL	0.931	1.029	1.137	1.087	1.230	1.576	-0.436	0.130	0.771
TAG	0.963	1.124	1.312	1.735	2.122	4.306	-0.049	0.146	0.345
Crea	0.941	0.988	1.038	1.282	1.362	1.564	-0.176	-0.038	0.120
Urea	0.942	0.999	1.060	1.191	1.278	1.611	-0.251	-0.004	0.246
Ca	0.993	1.003	1.012	1.131	1.161	1.237	-0.047	0.017	0.074
Cl	0.981	0.989	0.996	1.102	1.124	1.172	-0.153	-0.094	-0.031
K	0.983	1.015	1.049	1.225	1.280	1.366	-0.072	0.061	0.176
Na	0.991	0.998	1.006	1.112	1.136	1.185	-0.066	-0.015	0.044
P	0.960	1.019	1.080	1.165	1.235	1.415	-0.193	0.085	0.336
Organs	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
Kidney	0.964	1.062	1.169	1.024	1.110	1.288	-2.000	0.940	2.000
Spleen	0.974	1.090	1.221	1.069	1.184	1.368	-0.191	0.519	1.827
Liver	0.941	1.011	1.086	1.033	1.101	1.188	-2.000	0.122	2.000
AdrenGl	0.987	1.070	1.161	1.279	1.370	1.565	-0.038	0.211	0.445
Heart	0.996	1.063	1.135	1.059	1.122	1.221	-0.039	0.523	1.278
Testis	0.938	1.019	1.106	1.112	1.185	1.273	-0.407	0.109	0.581
Epididymis	0.924	1.027	1.141	1.058	1.161	1.269	-0.830	0.183	1.576
Brain	0.951	1.016	1.084	1.055	1.119	1.235	-0.547	0.131	0.818

Appendix 8. Intervals for equivalence tests (continued)

Males NK11+ versus Control									
Weights	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
Weight_52	0.961	0.994	1.028	1.017	1.063	1.108	-2.000	-0.113	2.000
FeedMean	0.941	0.968	0.996	1.038	1.080	1.162	-0.927	-0.410	-0.051
Haematology	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.910	1.021	1.146	1.457	1.652	2.408	-0.186	0.039	0.246
RBC	0.996	1.022	1.049	1.083	1.109	1.144	-0.040	0.207	0.436
HGB	0.996	1.013	1.030	1.079	1.100	1.146	-0.044	0.127	0.287
HCT	1.005	1.026	1.047	1.089	1.112	1.148	0.049	0.237	0.413
MCV	0.986	1.004	1.022	1.005	1.024	1.040	-2.000	0.265	2.000
MCH	0.967	0.991	1.016	1.010	1.037	1.060	-2.000	-0.288	2.000
MCHC	0.975	0.987	0.999	1.018	1.031	1.050	-0.872	-0.424	-0.041
PLT	0.969	1.028	1.090	1.621	1.787	2.042	-0.053	0.047	0.133
LYMA	0.916	1.042	1.185	1.394	1.587	2.224	-0.187	0.085	0.334
ClinChem	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
ALP	0.960	1.065	1.182	1.289	1.412	1.584	-0.118	0.181	0.454
ALT	0.950	1.052	1.166	1.060	1.186	1.327	-0.410	0.314	2.000
AST	0.847	0.939	1.040	1.217	1.337	1.528	-0.549	-0.214	0.129
ALB	0.979	0.997	1.016	1.103	1.127	1.161	-0.161	-0.021	0.133
TP	0.983	0.997	1.011	1.075	1.093	1.120	-0.178	-0.035	0.126
Glu	0.973	1.047	1.127	1.282	1.381	1.650	-0.081	0.138	0.339
CHOL	0.872	0.964	1.067	1.088	1.227	1.574	-0.831	-0.168	0.380
TAG	1.009	1.181	1.382	1.737	2.123	4.346	0.014	0.209	0.419
Crea	0.920	0.966	1.016	1.282	1.362	1.569	-0.247	-0.107	0.048
Urea	0.984	1.045	1.110	1.191	1.278	1.614	-0.060	0.169	0.405
Ca	0.990	1.000	1.010	1.131	1.161	1.237	-0.064	0.002	0.065
Cl	0.984	0.992	0.999	1.102	1.124	1.172	-0.128	-0.071	-0.009
K	0.972	1.005	1.039	1.225	1.280	1.367	-0.116	0.018	0.139
Na	0.993	1.000	1.008	1.112	1.136	1.186	-0.056	0.003	0.060
P	0.903	0.959	1.018	1.164	1.235	1.415	-0.455	-0.193	0.078
Organs	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
Kidney	0.906	0.997	1.098	1.024	1.110	1.208	-2.000	-0.033	2.000
Spleen	0.880	0.986	1.104	1.069	1.184	1.330	-1.159	-0.085	0.892
Liver	0.932	1.001	1.076	1.032	1.101	1.190	-2.000	0.013	2.000
AdrenGl	0.867	0.940	1.019	1.279	1.371	1.565	-0.423	-0.193	0.058
Heart	0.939	1.003	1.070	1.059	1.122	1.224	-0.675	0.018	0.702
Testis	0.934	1.013	1.100	1.112	1.185	1.273	-0.446	0.079	0.558
Epididymis	0.851	0.946	1.052	1.058	1.162	1.259	-1.928	-0.381	0.451
Brain	0.905	0.967	1.032	1.055	1.119	1.235	-0.995	-0.292	0.315

Appendix 8. Intervals for equivalence tests (continued)

Males NK33+ versus Control									
Weights	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
Weight_52	0.988	1.022	1.057	1.017	1.063	1.108	-0.341	0.414	2.000
FeedMean	0.986	1.014	1.043	1.039	1.080	1.162	-0.202	0.176	0.589
Haematology	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.960	1.075	1.204	1.458	1.651	2.377	-0.081	0.138	0.347
RBC	0.985	1.011	1.037	1.083	1.109	1.144	-0.146	0.106	0.326
HGB	0.992	1.008	1.025	1.079	1.100	1.146	-0.086	0.086	0.240
HCT	0.993	1.014	1.034	1.089	1.112	1.148	-0.061	0.127	0.294
MCV	0.990	1.007	1.025	1.005	1.024	1.043	-2.000	0.514	2.000
MCH	0.979	1.003	1.027	1.010	1.037	1.060	-2.000	0.089	2.000
MCHC	0.984	0.996	1.007	1.019	1.031	1.050	-0.526	-0.144	0.254
PLT	1.021	1.082	1.147	1.622	1.786	2.042	0.035	0.136	0.226
LYMA	0.911	1.034	1.174	1.397	1.588	2.221	-0.208	0.069	0.321
ClinChem	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
ALP	0.926	1.026	1.137	1.289	1.413	1.586	-0.231	0.072	0.342
ALT	0.937	1.036	1.146	1.059	1.186	1.324	-0.653	0.216	2.000
AST	0.892	0.987	1.092	1.217	1.337	1.530	-0.382	-0.044	0.325
ALB	0.977	0.995	1.013	1.102	1.127	1.161	-0.178	-0.045	0.107
TP	0.983	0.997	1.012	1.075	1.093	1.120	-0.173	-0.028	0.134
Glu	0.936	1.006	1.082	1.281	1.382	1.648	-0.208	0.019	0.233
CHOL	0.935	1.033	1.141	1.088	1.230	1.567	-0.407	0.149	0.805
TAG	0.976	1.139	1.329	1.736	2.122	4.344	-0.030	0.162	0.365
Crea	0.923	0.969	1.018	1.282	1.362	1.569	-0.237	-0.098	0.057
Urea	0.919	0.975	1.034	1.191	1.278	1.617	-0.319	-0.097	0.139
Ca	0.987	0.997	1.006	1.131	1.161	1.236	-0.078	-0.022	0.042
Cl	0.985	0.992	1.000	1.102	1.124	1.172	-0.120	-0.064	-0.002
K	0.969	1.001	1.034	1.225	1.280	1.367	-0.132	0.004	0.135
Na	0.992	1.000	1.007	1.112	1.136	1.186	-0.060	-0.003	0.056
P	0.899	0.954	1.012	1.165	1.235	1.419	-0.485	-0.217	0.055
Organs	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
Kidney	0.915	1.008	1.110	1.024	1.111	1.222	-2.000	0.119	2.000
Spleen	0.907	1.016	1.138	1.070	1.184	1.331	-0.871	0.095	1.161
Liver	0.890	0.957	1.028	1.033	1.101	1.190	-2.000	-0.486	0.397
AdrenGl	0.949	1.028	1.115	1.279	1.371	1.568	-0.171	0.086	0.312
Heart	0.926	0.989	1.055	1.059	1.122	1.222	-0.741	-0.095	0.563
Testis	0.969	1.052	1.142	1.112	1.185	1.272	-0.198	0.293	0.774
Epididymis	0.925	1.028	1.142	1.059	1.162	1.269	-0.834	0.185	1.591
Brain	0.946	1.010	1.078	1.055	1.119	1.233	-0.611	0.083	0.767

Appendix 8. Intervals for equivalence tests (continued)

Females NK11- versus Control									
Weights	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
Weight_52	0.944	0.980	1.018	1.027	1.078	1.142	-1.914	-0.266	0.321
FeedMean	0.952	0.981	1.010	1.071	1.111	1.206	-0.457	-0.178	0.097
Haematology	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.940	1.062	1.200	1.519	1.717	2.264	-0.105	0.108	0.303
RBC	0.976	1.003	1.030	1.041	1.069	1.117	-0.384	0.041	0.441
HGB	0.981	1.003	1.025	1.037	1.058	1.088	-0.349	0.048	0.417
HCT	0.985	1.009	1.034	1.018	1.046	1.085	-0.418	0.204	1.024
MCV	0.993	1.005	1.017	1.028	1.039	1.053	-0.180	0.129	0.406
MCH	0.983	1.000	1.018	1.047	1.063	1.086	-0.278	0.004	0.283
MCHC	0.981	0.994	1.007	1.010	1.024	1.037	-0.984	-0.261	0.327
PLT	0.970	1.030	1.093	1.371	1.473	1.635	-0.072	0.076	0.205
LYMA	0.917	1.026	1.148	1.511	1.694	2.196	-0.159	0.047	0.230
ClinChem	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
ALP	0.869	0.983	1.113	1.136	1.289	1.456	-0.590	-0.066	0.477
ALT	0.809	0.946	1.107	1.446	1.657	1.977	-0.378	-0.108	0.199
AST	0.867	0.990	1.129	1.302	1.464	1.704	-0.360	-0.026	0.324
ALB	0.972	1.004	1.037	1.182	1.226	1.287	-0.136	0.020	0.162
TP	0.979	0.999	1.018	1.160	1.201	1.325	-0.105	-0.007	0.096
Glu	0.938	1.010	1.087	1.283	1.375	1.536	-0.196	0.030	0.234
CHOL	0.889	0.987	1.096	1.098	1.226	1.405	-0.658	-0.063	0.547
TAG	0.826	0.974	1.148	1.760	2.062	2.751	-0.236	-0.036	0.187
Crea	0.998	1.052	1.110	1.265	1.354	1.678	-0.001	0.162	0.325
Urea	1.015	1.081	1.151	1.227	1.325	1.733	0.053	0.264	0.493
Ca	0.991	1.003	1.015	1.125	1.169	1.371	-0.052	0.018	0.082
Cl	0.999	1.008	1.017	1.055	1.068	1.086	-0.004	0.125	0.240
K	0.959	1.010	1.065	1.199	1.264	1.423	-0.173	0.042	0.238
Na	1.001	1.007	1.012	1.055	1.067	1.093	0.016	0.100	0.179
P	0.906	1.011	1.129	1.085	1.227	1.437	-0.671	0.055	0.808
Organs	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
Kidney	0.996	1.071	1.152	1.046	1.115	1.206	-0.045	0.643	1.901
Spleen	0.965	1.087	1.224	1.120	1.236	1.355	-0.181	0.397	1.037
Liver	0.960	1.025	1.094	1.143	1.202	1.314	-0.229	0.131	0.454
AdrenGl	0.911	1.031	1.167	1.211	1.328	1.472	-0.350	0.108	0.517
Heart	0.995	1.063	1.136	1.076	1.134	1.197	-0.042	0.481	1.081
Uterus	0.851	1.053	1.304	1.188	1.427	1.700	-0.559	0.146	0.842
Ovary	0.867	1.110	1.420	1.066	1.360	1.826	-2.000	0.567	2.000
Brain	1.032	1.100	1.173	1.112	1.167	1.249	0.195	0.609	1.067

Appendix 8. Intervals for equivalence tests (continued)

Females NK33- versus Control									
Weights	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
Weight_52	0.960	0.997	1.036	1.027	1.078	1.141	-1.399	-0.037	0.994
FeedMean	0.977	1.007	1.037	1.071	1.111	1.205	-0.230	0.063	0.334
Females NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.825	0.932	1.053	1.519	1.716	2.261	-0.321	-0.126	0.088
RBC	0.986	1.013	1.041	1.041	1.069	1.118	-0.207	0.188	0.576
HGB	0.981	1.003	1.025	1.037	1.058	1.088	-0.345	0.050	0.419
HCT	0.992	1.016	1.041	1.018	1.046	1.085	-0.191	0.363	1.293
MCV	0.988	1.000	1.012	1.028	1.039	1.054	-0.317	0.004	0.320
MCH	0.973	0.990	1.008	1.047	1.063	1.086	-0.407	-0.158	0.114
MCHC	0.974	0.987	1.000	1.010	1.024	1.037	-1.471	-0.560	-0.026
PLT	0.947	1.005	1.067	1.371	1.472	1.635	-0.137	0.013	0.153
LYMA	0.844	0.944	1.056	1.511	1.694	2.189	-0.287	-0.107	0.096
ClinChem	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
ALP	0.901	1.020	1.154	1.136	1.289	1.456	-0.465	0.075	0.594
ALT	0.848	0.992	1.160	1.446	1.658	1.978	-0.314	-0.016	0.294
AST	0.907	1.036	1.182	1.300	1.463	1.708	-0.252	0.090	0.402
ALB	0.980	1.013	1.046	1.182	1.226	1.286	-0.093	0.062	0.195
TP	0.984	1.003	1.023	1.160	1.201	1.326	-0.087	0.015	0.107
Glu	0.897	0.965	1.039	1.283	1.375	1.537	-0.305	-0.109	0.111
CHOL	0.854	0.949	1.054	1.098	1.226	1.407	-0.876	-0.252	0.273
TAG	0.851	1.002	1.181	1.760	2.062	2.759	-0.222	0.003	0.225
Crea	0.984	1.038	1.095	1.265	1.354	1.680	-0.046	0.118	0.275
Urea	1.038	1.106	1.177	1.227	1.325	1.727	0.115	0.343	0.588
Ca	0.994	1.006	1.018	1.125	1.169	1.368	-0.034	0.034	0.100
Cl	0.991	1.000	1.009	1.055	1.068	1.086	-0.131	0.000	0.131
K	0.962	1.014	1.068	1.200	1.264	1.420	-0.157	0.056	0.247
Na	1.001	1.007	1.013	1.055	1.067	1.093	0.021	0.105	0.182
P	0.965	1.078	1.204	1.086	1.226	1.436	-0.178	0.369	1.243
Organs	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
Kidney	0.974	1.048	1.127	1.046	1.115	1.207	-0.288	0.438	1.547
Spleen	0.874	0.984	1.108	1.120	1.236	1.350	-0.691	-0.077	0.562
Liver	0.947	1.011	1.080	1.143	1.202	1.314	-0.308	0.059	0.394
AdrenGl	0.892	1.010	1.143	1.211	1.328	1.471	-0.436	0.034	0.478
Heart	1.014	1.083	1.157	1.076	1.135	1.197	0.106	0.629	1.261
Uterus	0.726	0.899	1.113	1.186	1.425	1.700	-1.023	-0.300	0.342
Ovary	0.940	1.202	1.539	1.066	1.359	1.970	-2.000	1.038	2.000
Brain	1.012	1.079	1.151	1.113	1.167	1.249	0.072	0.485	0.919

Appendix 8. Intervals for equivalence tests (continued)

Females NK11+ versus Control									
Weights	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
Weight_52	0.950	0.986	1.024	1.026	1.078	1.141	-1.644	-0.184	0.470
FeedMean	0.953	0.982	1.012	1.071	1.111	1.206	-0.444	-0.167	0.113
Haematology	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.856	0.965	1.089	1.519	1.717	2.261	-0.257	-0.063	0.154
RBC	0.999	1.026	1.053	1.041	1.069	1.118	-0.003	0.377	0.814
HGB	0.987	1.009	1.031	1.037	1.058	1.088	-0.233	0.148	0.504
HCT	0.996	1.020	1.045	1.018	1.046	1.085	-0.085	0.453	1.478
MCV	0.983	0.994	1.006	1.028	1.039	1.054	-0.420	-0.142	0.167
MCH	0.965	0.982	0.999	1.047	1.063	1.087	-0.561	-0.297	-0.025
MCHC	0.973	0.985	0.998	1.010	1.024	1.037	-1.564	-0.610	-0.081
PLT	0.956	1.013	1.075	1.371	1.473	1.637	-0.115	0.034	0.165
LYMA	0.877	0.979	1.093	1.510	1.695	2.202	-0.225	-0.039	0.168
ClinChem	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
ALP	0.898	1.014	1.145	1.136	1.289	1.456	-0.494	0.053	0.586
ALT	0.750	0.875	1.021	1.447	1.659	1.977	-0.544	-0.260	0.036
AST	0.849	0.966	1.100	1.300	1.464	1.707	-0.399	-0.089	0.256
ALB	0.983	1.015	1.048	1.181	1.226	1.287	-0.083	0.072	0.206
TP	0.978	0.997	1.016	1.160	1.201	1.327	-0.108	-0.017	0.084
Glu	0.965	1.037	1.115	1.283	1.375	1.536	-0.110	0.112	0.309
CHOL	0.831	0.921	1.021	1.097	1.226	1.403	-1.077	-0.396	0.097
TAG	0.839	0.986	1.159	1.759	2.063	2.757	-0.227	-0.018	0.204
Crea	1.006	1.060	1.118	1.265	1.354	1.680	0.021	0.185	0.350
Urea	1.034	1.100	1.170	1.227	1.325	1.731	0.100	0.325	0.564
Ca	0.994	1.006	1.017	1.125	1.169	1.371	-0.034	0.035	0.101
Cl	0.990	0.998	1.007	1.055	1.068	1.086	-0.142	-0.028	0.104
K	0.955	1.005	1.058	1.199	1.264	1.421	-0.197	0.022	0.225
Na	0.999	1.004	1.010	1.055	1.067	1.093	-0.016	0.067	0.142
P	0.944	1.053	1.173	1.087	1.227	1.437	-0.332	0.251	1.040
Organs	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
Kidney	1.006	1.081	1.163	1.046	1.115	1.211	0.054	0.734	2.000
Spleen	0.925	1.042	1.173	1.121	1.236	1.349	-0.420	0.193	0.789
Liver	0.967	1.032	1.102	1.143	1.202	1.314	-0.191	0.170	0.494
AdrenGl	0.919	1.040	1.178	1.211	1.328	1.473	-0.316	0.137	0.547
Heart	0.977	1.043	1.115	1.075	1.134	1.195	-0.199	0.335	0.894
Uterus	0.808	1.000	1.239	1.188	1.427	1.705	-0.770	0.001	0.777
Ovary	0.922	1.180	1.509	1.066	1.359	1.928	-2.000	0.919	2.000
Brain	1.018	1.085	1.157	1.112	1.167	1.247	0.110	0.522	0.966

Appendix 8. Intervals for equivalence tests (continued)

Females NK33+ versus Control									
Weights	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
Weight_52	0.952	0.989	1.027	1.026	1.078	1.142	-1.668	-0.154	0.564
FeedMean	0.986	1.016	1.046	1.071	1.111	1.204	-0.136	0.144	0.417
Haematology	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.938	1.055	1.187	1.519	1.717	2.261	-0.120	0.096	0.290
RBC	0.998	1.024	1.051	1.041	1.069	1.118	-0.028	0.351	0.782
HGB	0.985	1.006	1.028	1.037	1.058	1.088	-0.283	0.106	0.460
HCT	0.991	1.015	1.039	1.017	1.046	1.084	-0.226	0.339	1.256
MCV	0.980	0.991	1.003	1.028	1.039	1.054	-0.515	-0.228	0.077
MCH	0.966	0.982	0.999	1.047	1.063	1.086	-0.552	-0.291	-0.022
MCHC	0.979	0.991	1.004	1.010	1.024	1.037	-1.154	-0.372	0.178
PLT	0.977	1.034	1.096	1.371	1.472	1.635	-0.061	0.087	0.216
LYMA	0.945	1.053	1.173	1.510	1.695	2.195	-0.107	0.095	0.276
ClinChem	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
ALP	0.834	0.940	1.059	1.137	1.288	1.456	-0.781	-0.245	0.249
ALT	0.851	0.989	1.151	1.447	1.657	1.975	-0.316	-0.021	0.290
AST	0.923	1.049	1.191	1.301	1.464	1.707	-0.216	0.123	0.431
ALB	0.969	1.000	1.032	1.182	1.226	1.287	-0.157	0.000	0.157
TP	0.978	0.996	1.015	1.160	1.201	1.324	-0.111	-0.019	0.083
Glu	0.962	1.032	1.108	1.283	1.375	1.536	-0.125	0.097	0.295
CHOL	0.863	0.955	1.056	1.097	1.226	1.403	-0.832	-0.225	0.309
TAG	0.868	1.017	1.192	1.762	2.063	2.740	-0.198	0.023	0.228
Crea	0.978	1.029	1.084	1.265	1.353	1.679	-0.073	0.091	0.244
Urea	1.012	1.075	1.142	1.228	1.325	1.730	0.036	0.243	0.468
Ca	0.986	0.998	1.009	1.125	1.169	1.365	-0.079	-0.014	0.056
Cl	0.991	0.999	1.008	1.055	1.068	1.086	-0.132	-0.008	0.122
K	0.958	1.007	1.059	1.199	1.264	1.422	-0.187	0.030	0.228
Na	0.998	1.003	1.009	1.055	1.067	1.093	-0.033	0.050	0.124
P	0.880	0.979	1.089	1.086	1.224	1.435	-0.832	-0.106	0.565
Organs	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
Kidney	1.007	1.083	1.165	1.046	1.115	1.209	0.066	0.747	2.000
Spleen	0.981	1.105	1.245	1.120	1.235	1.356	-0.096	0.470	1.145
Liver	0.968	1.034	1.104	1.144	1.202	1.313	-0.177	0.175	0.499
AdrenGl	0.932	1.055	1.195	1.211	1.328	1.471	-0.264	0.188	0.595
Heart	0.997	1.065	1.138	1.076	1.134	1.198	-0.024	0.498	1.102
Uterus	0.797	0.987	1.223	1.187	1.427	1.704	-0.790	-0.036	0.721
Ovary	0.963	1.233	1.577	1.066	1.361	2.009	-0.354	1.185	2.000
Brain	1.033	1.102	1.175	1.112	1.167	1.248	0.204	0.618	1.081

Appendix 9. P-values for difference tests between GMO feeds and the control feed

Difference tests are based on log transformed cage means. P-values are given for Dunnett tests (Dunnet), for t-tests and for Wilcoxon signed rank tests (Wilcox). P-values smaller than 0.01/0.05 have a gold/yellow background.

Weights	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Weight_52	0.380	0.140	0.225	0.988	0.714	0.512	0.991	0.731	0.610	0.516	0.204	0.252
growthRate	0.802	0.389	0.499	0.983	0.682	0.968	1.000	0.887	0.903	0.066	0.020	0.017
FeedMean	0.010	0.003	0.003	0.236	0.080	0.021	0.081	0.025	0.008	0.723	0.327	0.280
Haematology	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
WBC	0.668	0.290	0.294	0.175	0.057	0.202	0.989	0.719	0.465	0.522	0.207	0.475
RBC	1.000	0.931	0.674	0.995	0.775	0.648	0.295	0.103	0.123	0.810	0.397	0.756
HGB	0.919	0.524	0.571	0.953	0.589	0.433	0.396	0.147	0.112	0.705	0.315	0.457
HCT	0.973	0.644	0.784	0.874	0.463	0.498	0.052	0.015	0.020	0.476	0.184	0.261
MCV	0.983	0.683	0.648	0.513	0.202	0.143	0.981	0.673	0.798	0.827	0.413	0.123
MCH	0.987	0.703	0.674	0.879	0.468	0.277	0.879	0.469	0.441	0.998	0.821	0.648
MCHC	1.000	0.929	0.841	0.959	0.604	0.475	0.104	0.032	0.023	0.860	0.447	0.701
PLT	0.986	0.700	0.898	0.048	0.014	0.064	0.765	0.359	0.145	0.029	0.008	0.006
LYMR	1.000	0.928	0.898	0.601	0.250	0.349	0.940	0.562	0.515	0.947	0.575	0.701
LYMA	0.947	0.574	0.312	0.075	0.023	0.083	0.920	0.526	0.395	0.958	0.601	1.000
ClinChem	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
ALP	0.496	0.194	0.143	0.955	0.594	0.784	0.570	0.233	0.258	0.967	0.625	0.648
ALT	0.998	0.811	0.898	0.973	0.644	0.475	0.719	0.325	0.332	0.893	0.487	0.622
AST	0.985	0.696	0.498	1.000	0.913	0.898	0.549	0.222	0.293	0.997	0.797	0.898
BIL	0.911	0.512	0.927	0.997	0.792	0.898	0.420	0.158	0.113	0.933	0.548	0.522
ALB	0.816	0.402	0.268	0.735	0.337	0.261	0.996	0.781	1.000	0.935	0.552	0.452
TP	0.572	0.234	0.368	0.881	0.471	0.729	0.979	0.667	0.651	0.989	0.720	0.522
Glu	1.000	0.905	0.985	0.983	0.682	0.294	0.544	0.219	0.541	0.999	0.862	0.985
CHOL	0.936	0.554	0.245	0.944	0.570	0.674	0.887	0.478	0.798	0.915	0.517	0.841

TAG	0.991	0.734	0.622	0.374	0.137	0.133	0.122	0.038	0.029	0.282	0.098	0.058
Crea	0.389	0.144	0.261	0.968	0.627	0.648	0.455	0.174	0.145	0.526	0.209	0.475
Urea	0.976	0.656	0.475	1.000	0.971	0.841	0.403	0.150	0.196	0.810	0.397	0.475
cHGB	0.838	0.424	0.841	0.936	0.554	0.154	0.994	0.763	0.465	0.967	0.625	0.522
Ca	1.000	0.985	0.898	0.954	0.590	0.452	1.000	0.965	0.922	0.898	0.493	0.622
Cl	0.416	0.156	0.105	0.013	0.004	0.004	0.093	0.029	0.024	0.141	0.045	0.126
K	0.997	0.801	1.000	0.762	0.357	0.430	0.996	0.788	0.925	1.000	0.954	0.952
Na	1.000	0.923	0.481	0.965	0.620	0.816	1.000	0.924	0.794	1.000	0.913	0.365
P	0.135	0.043	0.006	0.925	0.534	0.927	0.440	0.167	0.134	0.318	0.113	0.036
Urine	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
uVol	1.000	0.966	1.000	0.073	0.022	0.079	0.147	0.048	0.078	0.957	0.599	0.890
uVolW	1.000	0.926	0.934	0.077	0.024	0.107	0.083	0.026	0.055	0.840	0.427	0.599
uLeu	0.218	0.074	0.064	1.000	0.960	0.937	0.198	0.066	0.012	0.169	0.055	0.166
uOsmoll	0.999	0.862	0.599	0.059	0.018	0.064	0.163	0.053	0.151	0.615	0.260	0.421
uKeton	1.000	0.877	0.783	0.021	0.006	0.018	0.522	0.208	0.227	0.983	0.688	0.494
upH	0.729	0.333	0.319	0.988	0.716	0.842	0.876	0.467	0.557	0.644	0.277	0.259
Organs	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Kidney	0.557	0.228	0.014	0.533	0.215	0.492	1.000	0.955	1.000	0.999	0.868	1.000
Spleen	0.862	0.453	0.232	0.354	0.130	0.105	0.997	0.798	1.000	0.995	0.778	1.000
Liver	1.000	0.902	0.922	0.993	0.754	0.770	1.000	0.971	0.770	0.536	0.217	0.131
AdrenGl	0.310	0.111	0.027	0.274	0.096	0.160	0.349	0.128	0.193	0.889	0.486	0.625
Heart	0.622	0.265	0.625	0.193	0.065	0.232	1.000	0.938	1.000	0.990	0.727	0.770
Testis	0.239	0.082	0.064	0.974	0.652	0.770	0.992	0.744	1.000	0.542	0.220	0.160
Epididymis	0.131	0.042	0.027	0.961	0.612	1.000	0.670	0.295	0.375	0.957	0.603	0.492
Brain	0.268	0.094	0.160	0.969	0.634	0.922	0.676	0.299	0.322	0.994	0.762	0.432

Appendix 9. P-values for difference tests between GMO feeds and the control feed (continued)

Difference tests are based on log transformed cage means. P-values are given for Dunnett tests (Dunnet), for t-tests and for Wilcoxon signed rank tests (Wilcox). P-values smaller than 0.01/0.05 have a gold/yellow background.

Weights	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Weight_52	0.688	0.303	0.451	1.000	0.887	0.802	0.883	0.473	0.599	0.936	0.552	0.501
growthRate	0.481	0.187	0.334	0.912	0.513	0.491	0.999	0.860	0.929	0.968	0.628	0.765
FeedMean	0.503	0.197	0.245	0.975	0.651	0.601	0.562	0.228	0.265	0.683	0.300	0.184
Haematology	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
WBC	0.726	0.327	0.671	0.611	0.253	0.054	0.941	0.561	0.441	0.781	0.369	0.349
RBC	0.999	0.833	0.734	0.747	0.343	0.081	0.174	0.056	0.045	0.208	0.069	0.090
HGB	0.997	0.801	0.899	0.997	0.790	0.442	0.844	0.428	0.374	0.943	0.564	0.784
HCT	0.876	0.462	0.702	0.493	0.191	0.016	0.288	0.100	0.096	0.527	0.208	0.294
MCV	0.831	0.415	0.347	1.000	0.985	0.899	0.771	0.361	0.332	0.377	0.137	0.070
MCH	1.000	0.977	0.932	0.630	0.265	0.304	0.112	0.035	0.008	0.115	0.036	0.064
MCHC	0.760	0.353	0.347	0.148	0.047	0.030	0.091	0.028	0.016	0.447	0.169	0.189
PLT	0.725	0.326	0.369	0.999	0.856	0.702	0.976	0.653	0.768	0.595	0.245	0.701
LYMR	0.999	0.831	0.854	0.991	0.733	0.734	0.994	0.756	0.984	0.913	0.511	0.546
LYMA	0.975	0.648	0.899	0.703	0.311	0.167	0.986	0.700	0.568	0.750	0.345	0.452
ClinChem	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
ALP	0.997	0.789	0.671	0.994	0.753	1.000	0.998	0.822	0.595	0.689	0.302	0.498
ALT	0.894	0.485	0.393	1.000	0.915	0.495	0.262	0.090	0.156	1.000	0.889	0.409
AST	1.000	0.874	0.899	0.958	0.599	0.442	0.958	0.599	0.651	0.874	0.460	0.498
BIL	0.298	0.104	0.181	0.834	0.417	0.799	0.867	0.452	0.984	0.706	0.313	0.133
ALB	0.997	0.804	0.523	0.855	0.438	0.246	0.771	0.362	0.332	1.000	0.990	0.784
TP	1.000	0.888	0.966	0.995	0.767	0.640	0.992	0.737	0.953	0.985	0.695	0.571
Glu	0.997	0.796	0.799	0.744	0.340	0.766	0.717	0.321	0.241	0.788	0.375	0.812
CHOL	0.998	0.809	0.551	0.717	0.321	0.393	0.332	0.118	0.060	0.773	0.363	0.409

TAG	0.993	0.748	0.523	1.000	0.978	0.932	0.999	0.864	0.860	0.999	0.830	0.546
Crea	0.187	0.061	0.130	0.449	0.170	0.393	0.096	0.030	0.123	0.634	0.267	0.409
Urea	0.053	0.016	0.001	0.008	0.002	0.024	0.011	0.003	0.020	0.068	0.020	0.036
cHGB	0.504	0.196	0.196	0.999	0.836	1.000	0.985	0.694	0.984	0.991	0.728	0.588
Ca	0.960	0.604	0.442	0.722	0.324	0.468	0.698	0.308	0.352	0.980	0.668	0.277
Cl	0.199	0.065	0.074	1.000	0.997	0.798	0.982	0.676	0.828	1.000	0.897	1.000
K	0.986	0.698	0.865	0.962	0.609	0.570	0.999	0.839	0.922	0.995	0.773	0.898
Na	0.079	0.024	0.099	0.062	0.019	0.058	0.336	0.120	0.163	0.576	0.234	0.268
P	0.999	0.839	0.899	0.471	0.180	0.196	0.756	0.349	0.541	0.984	0.688	0.729
Urine	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
uVol	0.640	0.273	0.286	1.000	0.982	0.820	1.000	0.933	0.851	0.885	0.476	0.679
uVolW	0.957	0.600	0.808	1.000	0.912	0.934	0.997	0.801	0.890	0.993	0.750	0.639
uLeu	1.000	0.910	0.918	0.480	0.186	0.344	0.993	0.754	0.918	0.989	0.720	0.844
uOsmoll	0.979	0.666	0.542	1.000	0.992	0.934	0.978	0.662	0.934	0.853	0.440	0.454
uKeton	0.623	0.263	0.348	0.698	0.311	0.438	0.509	0.201	0.120	0.833	0.419	0.399
upH	0.722	0.327	0.433	0.864	0.452	0.365	0.369	0.135	0.204	0.671	0.293	0.233
Organs	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Kidney	0.189	0.063	0.105	0.505	0.201	0.557	0.112	0.036	0.037	0.104	0.033	0.037
Spleen	0.425	0.162	0.105	0.996	0.784	0.770	0.893	0.490	0.432	0.273	0.096	0.084
Liver	0.861	0.452	0.557	0.991	0.732	0.846	0.723	0.331	0.375	0.696	0.312	0.322
AdrenGl	0.962	0.616	0.770	0.999	0.870	0.846	0.915	0.522	0.625	0.791	0.384	0.193
Heart	0.205	0.069	0.037	0.064	0.020	0.105	0.506	0.201	0.105	0.184	0.062	0.084
Uterus	0.966	0.625	1.000	0.703	0.317	0.322	1.000	0.996	1.000	1.000	0.905	1.000
Ovary	0.807	0.398	0.375	0.373	0.138	0.131	0.468	0.183	0.275	0.268	0.094	0.322
Brain	0.017	0.005	0.010	0.070	0.022	0.064	0.047	0.014	0.049	0.015	0.004	0.004

Appendix 10. Tests for normality and homogeneity of variance

P-values for the Shapiro-Wilks (SW) normality test are given separately for each feeding group, and also for the ANOVA residuals. In addition P-values for Bartlett and Levene test for homogeneity of variance are given. P-values smaller than 0.01/0.05 have a gold/yellow background.

Male Weights	SW Control	SW NK11-	SW NK33-	SW NK11+	SW NK33+	SW residual	Bartlett	Levene
Weight_52	0.294	0.742	0.642	0.766	0.771	0.150	0.232	0.189
growthRate	0.589	0.338	0.572	0.684	0.496	0.158	0.670	0.713
FeedMean	0.556	0.314	0.251	0.529	0.230	0.595	0.042	0.082
Male Haematology	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
WBC	0.296	0.090	0.263	0.073	0.313	0.444	0.298	0.081
RBC	0.281	0.774	0.605	0.705	0.680	0.174	0.392	0.445
HGB	0.478	0.032	0.495	0.624	0.771	0.574	0.018	0.063
HCT	0.879	0.356	0.893	0.956	0.368	0.985	0.077	0.238
MCV	0.000	0.043	0.837	0.418	0.093	0.030	0.719	0.745
MCH	0.000	0.070	0.406	0.581	0.637	0.019	0.832	0.473
MCHC	0.409	0.334	0.470	0.129	0.908	0.620	0.345	0.644
PLT	0.116	0.093	0.334	0.779	0.132	0.874	0.662	0.635
LYMR	0.871	0.280	0.572	0.165	0.960	0.829	0.159	0.175
LYMA	0.433	0.272	0.767	0.044	0.755	0.433	0.734	0.251
Male ClinChem	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
ALP	0.739	0.441	0.632	0.093	0.978	0.794	0.988	0.999
ALT	0.414	0.315	0.836	0.251	0.084	0.353	0.694	0.882
AST	0.928	0.776	0.034	0.167	0.985	0.979	0.148	0.183
BIL	0.078	0.957	0.145	0.004	0.701	0.205	0.780	0.948
ALB	0.727	0.828	0.908	0.467	0.644	0.064	0.719	0.802
TP	0.749	0.431	0.141	0.433	0.262	0.559	0.766	0.654
Glu	0.477	0.432	0.990	0.228	0.642	0.185	0.024	0.131
CHOL	0.084	0.101	0.916	0.790	0.700	0.168	0.227	0.248
TAG	0.732	0.136	0.008	0.963	0.530	0.014	0.910	0.932
Crea	0.764	0.048	0.890	0.507	0.535	0.843	0.133	0.088

Urea	0.059	0.930	0.758	0.947	0.033	0.300	0.500	0.819
cHGB	0.080	0.708	0.379	0.669	0.790	0.108	0.546	0.806
Ca	0.280	0.249	0.269	0.910	0.486	0.879	0.137	0.238
Cl	0.394	0.459	0.268	0.523	0.636	0.425	0.606	0.737
K	0.835	0.527	0.524	0.641	0.766	0.771	0.625	0.677
Na	0.040	0.033	0.564	0.045	0.007	0.018	0.159	0.255
P	0.617	0.413	0.001	0.709	0.645	0.162	0.484	0.803
Male Urine	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
uVol	0.054	0.832	0.570	0.333	0.895	0.382	0.392	0.610
uVolW	0.037	0.338	0.023	0.071	0.790	0.526	0.628	0.302
uLeu	0.050	0.659	0.098	0.079	0.236	0.749	0.960	0.981
uOsmoll	0.269	0.228	0.011	0.153	0.051	0.539	0.170	0.037
uKeton	0.039	0.040	0.002	0.002	0.274	0.297	0.228	0.060
upH	0.003	0.052	0.023	0.003	0.233	0.503	0.690	0.457
Male Organs	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
Kidney	0.738	0.163	0.333	0.083	0.211	0.201	0.199	0.214
Spleen	0.743	0.921	0.017	0.678	0.432	0.493	0.064	0.325
Liver	0.016	0.097	0.304	0.575	0.000	0.007	0.639	0.932
AdrenGl	0.730	0.776	0.758	0.246	0.500	0.377	0.706	0.762
Heart	0.074	0.484	0.175	0.595	0.056	0.182	0.056	0.112
Testis	0.010	0.988	0.484	0.357	0.663	0.171	0.695	0.379
Epididymis	0.034	0.784	0.018	0.439	0.329	0.706	0.970	0.760
Brain	0.384	0.693	0.855	0.854	0.711	0.698	0.815	0.642

Appendix 10. Tests for normality and homogeneity of variance (continued)

P-values for the Shapiro-Wilks (SW) normality test are given separately for each feeding group, and also for the ANOVA residuals. In addition P-values for Bartlett and Levene test for homogeneity of variance are given. P-values smaller than 0.01/0.05 have a gold/yellow background.

Female Weights	SW Control	SW NK11-	SW NK33-	SW NK11+	SW NK33+	SW residual	Bartlett	Levene
Weight_52	0.233	0.180	0.845	0.248	0.215	0.690	0.751	0.982
growthRate	0.672	0.407	0.156	0.001	0.842	0.262	0.913	0.958
FeedMean	0.131	0.743	0.665	0.246	0.392	0.397	0.507	0.837
Female Haematology	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
WBC	0.898	0.052	0.067	0.848	0.135	0.388	0.850	0.929
RBC	0.245	0.452	0.086	0.667	0.412	0.845	0.480	0.499
HGB	0.083	0.219	0.194	0.040	0.579	0.057	0.981	0.916
HCT	0.342	0.673	0.737	0.877	0.339	0.474	0.479	0.596
MCV	0.256	0.054	0.560	0.159	0.236	0.271	0.480	0.722
MCH	0.594	0.761	0.339	0.481	0.534	0.595	0.165	0.500
MCHC	0.764	0.003	0.585	0.909	0.140	0.132	0.759	0.993
PLT	0.190	0.012	0.639	0.133	0.460	0.301	0.785	0.563
LYMR	0.288	0.667	0.702	0.270	0.353	0.003	0.012	0.028
LYMA	0.994	0.102	0.493	0.817	0.142	0.775	0.240	0.253
Female ClinChem	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
ALP	0.843	0.914	0.245	0.391	0.081	0.017	0.229	0.650
ALT	0.284	0.293	0.461	0.061	0.202	0.605	0.231	0.492
AST	0.562	0.245	0.234	0.172	0.263	0.035	0.366	0.289
BIL	0.032	0.020	0.063	0.253	0.012	0.009	0.593	0.989
ALB	0.737	0.012	0.748	0.517	0.069	0.562	0.384	0.223
TP	0.179	0.052	0.972	0.806	0.007	0.106	0.836	0.979
Glu	0.346	0.729	0.808	0.904	0.720	0.347	0.432	0.426
CHOL	0.566	0.500	0.656	0.241	0.433	0.261	0.944	0.812
TAG	0.458	0.496	0.775	0.003	0.037	0.118	0.000	0.001
Crea	0.555	0.193	0.717	0.502	0.769	0.678	0.605	0.391

Urea	0.928	0.033	0.525	0.688	0.838	0.372	0.423	0.684
cHGB	0.260	0.313	0.150	0.004	0.066	0.004	0.685	0.876
Ca	0.779	0.788	0.166	0.497	0.999	0.252	0.112	0.188
Cl	0.299	0.614	0.412	0.482	0.159	0.341	0.767	0.942
K	0.043	0.910	0.331	0.292	0.658	0.721	0.131	0.137
Na	0.267	0.182	0.001	0.040	0.751	0.476	0.786	0.739
P	0.330	0.540	0.107	0.663	0.654	0.691	0.774	0.555
Female Urine	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
uVol	0.132	0.311	0.485	0.283	0.991	0.330	0.127	0.245
uVolW	0.022	0.488	0.607	0.165	0.194	0.433	0.102	0.295
uLeu	0.016	0.139	0.220	0.317	0.003	0.149	0.535	0.235
uOsmoll	0.122	0.127	0.997	0.057	0.558	0.642	0.071	0.044
uKeton	0.001	0.001	0.010	0.000	0.003	0.664	0.014	0.002
upH	0.276	0.141	0.278	0.129	0.126	0.905	0.668	0.771
Female Organs	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
Kidney	0.964	0.856	0.102	0.138	0.968	0.051	0.727	0.484
Spleen	0.594	0.159	0.756	0.598	0.302	0.005	0.559	0.950
Liver	0.515	0.988	0.518	0.220	0.291	0.810	0.587	0.679
AdrenGl	0.321	0.811	0.812	0.802	0.685	0.233	0.268	0.286
Heart	0.527	0.393	0.693	0.114	0.612	0.753	0.245	0.365
Uterus	0.352	0.132	0.782	0.451	0.550	0.950	0.879	0.774
Ovary	0.297	0.207	0.033	0.216	0.472	0.209	0.266	0.041
Brain	0.088	0.428	0.614	0.509	0.540	0.747	0.434	0.574

Appendix 11. Statistical analysis of data including outliers

For male animals there are outlying values for growthRate (1×), RBC (1×), HGB (1×), HCT (1×), Crea (1×) and Testis (1×), while for females there are outlying values for growthRate (2×), MCV (1×), LYMR (1×) and LYMA (1×); see Table 6 for a list of outliers. Equivalence tests, using the historical GRACE data, were not considered to be useful for the 12 months data and were therefore not repeated. Results of the classical analysis without and with outliers are given in the tables below. Note that the top tables are identical to the values in Table 12 and Table 13.

Conclusion: there are no essential differences between the analysis with and without outliers.

Without Outliers	Control		NK11-			NK33-			NK11+			NK33+		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
growthRate	1.372	15.5	1.322	20.1		1.394	16.6		1.380	17.2		1.495	17.6	tw
RBC	8.482	3.2	8.496	4.1		8.453	4.5		8.647	4.0		8.582	5.2	
HGB	15.82	1.7	15.91	3.1		15.90	3.1		15.99	2.8		15.96	3.8	
HCT	46.12	2.8	46.34	3.3		46.49	4.5		47.19	2.9	tw	46.77	4.6	
Crea	43.72	11.0	42.08	7.8		43.05	5.8		42.12	7.9		42.28	8.6	
Testis	0.640	7.1	0.691	11.9		0.653	11.8		0.649	9.2		0.676	11.5	
With Outliers	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
growthRate	1.372	15.5	1.292	24.3		1.394	16.6		1.380	17.2		1.495	17.6	tw
RBC	8.482	3.2	8.496	4.1		8.453	4.5		8.647	4.0		8.475	6.0	
HGB	15.82	1.7	15.91	3.1		15.90	3.1		15.99	2.8		15.82	4.5	
HCT	46.12	2.8	46.34	3.3		46.49	4.5		47.19	2.9	tw	46.33	5.2	
Crea	43.72	11.0	42.08	7.8		43.05	5.8		42.77	12.6		42.28	8.6	
Testis	0.640	7.1	0.691	11.9		0.653	11.8		0.627	14.8		0.676	11.5	

Without Outliers	Control		NK11-			NK33-			NK11+			NK33+		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
growthRate	0.984	33.0	0.882	39.3		1.034	32.7		0.970	37.8		0.946	33.1	
MCV	58.70	1.5	58.94	2.0		58.71	2.1		58.41	1.7		58.19	2.0	
LYMR	69.94	10.6	70.03	7.8		71.43	10.5		70.00	8.7		70.64	5.2	
LYMA	3.863	25.0	3.915	16.1		3.575	16.9		3.778	17.7		4.035	19.8	
With Outliers	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
growthRate	0.922	50.3	0.882	39.3		1.034	32.7		0.970	37.8		0.946	33.1	
MCV	58.70	1.5	58.94	2.0		58.90	2.9		58.41	1.7		58.19	2.0	
LYMR	69.94	10.6	68.58	12.2		71.43	10.5		70.00	8.7		70.64	5.2	
LYMA	3.840	26.4	3.915	16.1		3.575	16.9		3.778	17.7		4.035	19.8	