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, 6 months data

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G-TwYST (EU grant agreement no: 632165) Deliverable 4.3c

Biometris report 34.02.18 February 2018

https://doi.org/10.18174/455207

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February 2018

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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, using a recently developed method for equivalence testing, to differences between non-GM feeds obtained in previous studies performed in the EU project GRACE.

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 6 months.

No historical data for 6 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. Given tentative settings for regulatory parameters, for a set of 240 comparisons involving body weight, feed intake, haematology, differential white blood cell counts and clinical chemistry, equivalence was established in 92% of cases, close to the nominal confidence level of the test which was 95%. Equivalence was found to be more likely than lack of equivalence in all cases, except for Monocytes in females for feeding group NK33+. Note that this is a comparison between data obtained after 6 months for the current study, and data obtained after 3 months for the historical GRACE study.

In addition to this primary analysis, 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 6 months:

- Body weight at 6 months, growth rate months 3-6, mean feed intake (35 cages/group);
- Haematology (20 cages/group);
- Differential white blood cell counts (20 cages/group);
- Clinical biochemistry in blood (20 cages/group);
- Clinical biochemistry in urine (10 cages/group);
- Urine volume and colour (10 cages/group).

This report is organised as follows. Section 2 describes the data obtained after 6 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 6 months in G-TwYST study A

The available files for the data obtained after 6 months in G-TwYST study A are given in Table 1. GenStat programs "*06-Males.gen*" and "*06-Females.gen*" were used to combine all the data into single Excel files, separately for males and females. All animals survived the first 6 months, except for 2 female rats and 1 male rat (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. 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 6 months.

Data files after 6 months	Date	Time		Size (b)
Tab_1_G_TwYST_2yr st_A_6_mon_Body weight_Mal.xlsx	09-01-2017	15:39		175,037
Tab_2_G_TwYST_2yr st_A_6_mon_Body weight_Fem.xlsx	09-01-2017	15:40		175,585
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_A_6 month_Haemat_Mal.xlsx	03-01-2017	11:54		87,376
Tab_6_G_TwYST_2yr st_A_6 month_Haemat_Fem.xlsx	03-01-2017	12:13		86,763
Differential WBC G-TwYST A - after 6M final 12.12.17.xlsx	12-12-2017	13:17		37,026
Tab_7a_G_TwYST_2yr st_A_6 mon_Clin_Chem_bl_Mal.xlsx	03-01-2017	12:18		100,265
Tab_7b_G_TwYST_2yr st_A_6 mon_Clin_Chem_ur_Mal.xlsx	03-01-2017	12:21		84,688
Tab_8a_G_TwYST_2yr st_A_6 mon_Clin_Chem_bl_Fem.xlsx	03-01-2017	12:22		99,943
Tab_8b_G_TwYST_2yr st_A_6 mon_Clin_Chem_ur_Fem.xlsx	12-01-2017	07:45		84,746
Bl_ur_6 month_G_TwYST_2yr st_A_Fem_time image.xlsx	11-01-2017	15:48		98,021
Bl_ur_6 month_G_TwYST_2yr st_A_Mal_time image.xlsx	11-01-2017	15:14		98,290

Table 2 Animals that died before the end of month 6.

Sex	Rat	Cage	Feed	Day of Death
Female	610	555	NK11-	86
Female	785	643	Control	98
Male	199	100	NK11+	182

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	-	-	-	-	-	-	4	1	1	1
cHGB < 27.5	1	1	1	-	2	-	-	-	-	-
cHGB > 522.5	-	1	-	-	-	-	-	1	1	-
ALP < 0.17	-	-	-	-	-	-	-	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**	**2**	**3**		
Male	247	102	1		
Female	251	99	-		
uBil	**Missing**	**0**			
Male	251	99			
Female	251	99			
uLeu	**Missing**	**0**	**25**	**100**	**500**
Male	251	15	56	26	2
Female	251	54	37	8	-
uNit	**Missing**	**0**			
Male	252	98			
Female	251	99			
uProtein	**Missing**	**0.00**	**0.25**	**1.50**	
Male	251	98	-	1	
Female	251	97	2	-	
uGlu	**Missing**	**1**			
Male	251	99			
Female	251	99			
uHemogl	**Missing**	**0**	**10**	**25**	**250**
Male	251	91	4	3	1
Female	251	94	2	1	2
uKeton	**Missing**	**0.0**	**0.5**	**1.5**	**5.0**
Male	251	56	15	27	1
Female	251	78	13	8	-
uUrobili	**Missing**	**1**			
Male	251	99			
Female	251	99			

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 13 and 27, 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. Some weights at week 13 were not equal to the same weights in the data file after 3 months, and these were also corrected. The corrections are listed in Table 6. The linear regression line generally fits very well. Only for the following animals one or more observed weights differ more than 5% from the fitted values: males 17, 18, 29, 149, 293 and females 507, 509, 539, 546, 582, 594, 622, 639, 649, 663, 675, 722, 733, 787. However, again in general, these outlying weights do not seem to have a major impact on the estimated slope β of the regression line. The final weight Weight_27 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.

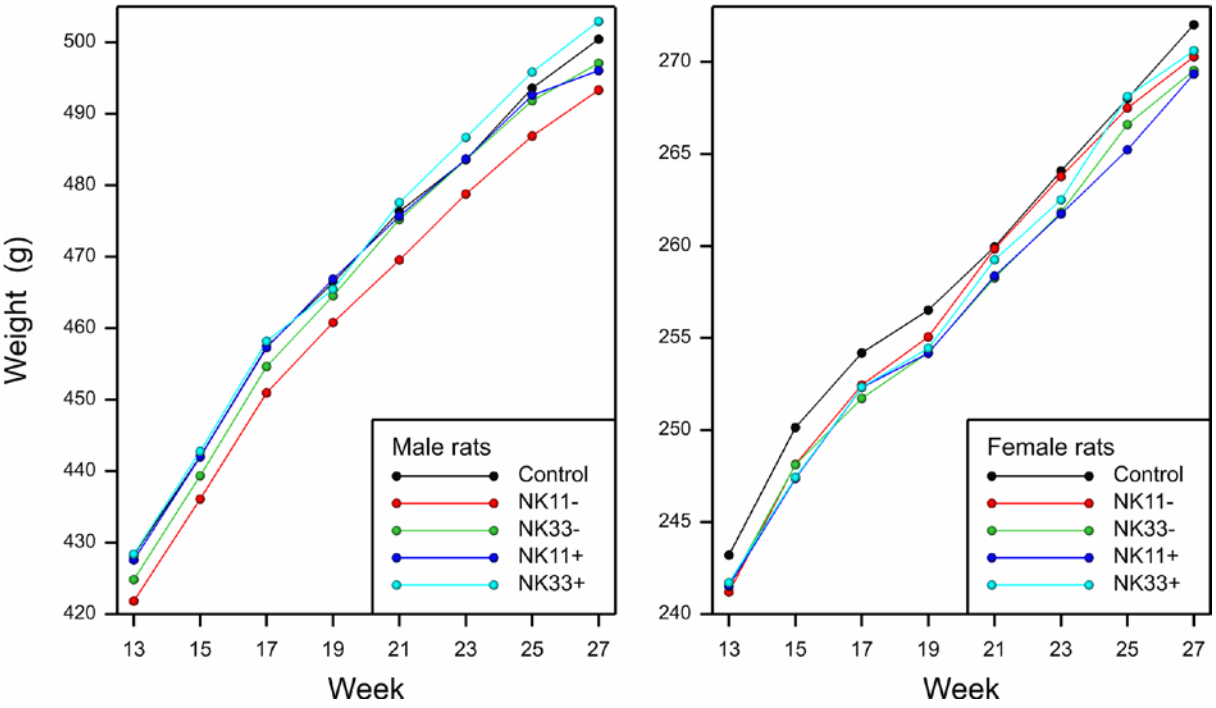

Figure 1 **Mean body weights versus week for each feeding group for male rats (left) and for female rats (right).**

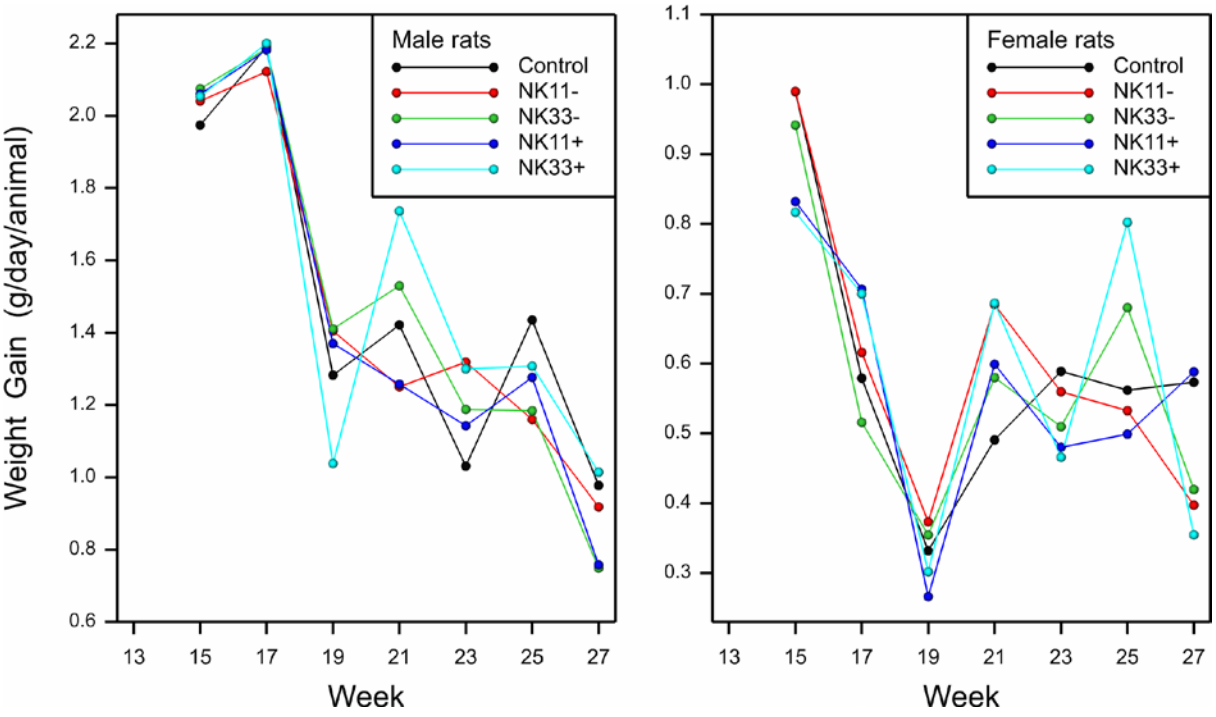

Figure 2 **Mean body weights gain (g/day/animal) versus week for each feeding group for male rats (left) and for female rats (right).**

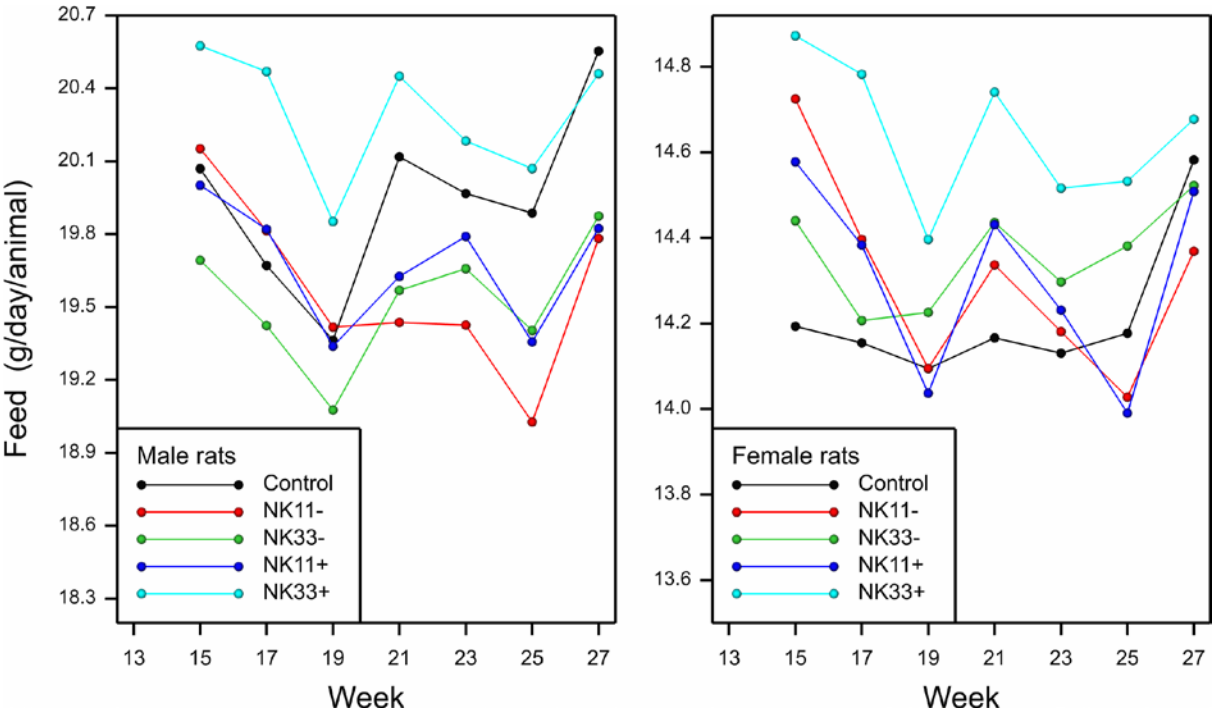

Figure 3 Mean feed consumption (g/day/animal) versus week for each feeding group for male rats (left) and for female rats (right).

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.

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.

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	PLT	69	35	366	delete	Comment in datafile: microclots
Males	PLT	83	42	484	delete	Comment in datafile: microclots
Males	PLT	199	100	420	delete	Comment in datafile: microclots
Males	PLT	227	114	425	delete	Comment in datafile: microclots
Males	PLT	231	116	395	delete	Comment in datafile: microclots
Males	PLT	320	160	153	delete	Comment in datafile: microclots
Males	PLT	345	173	428	delete	Comment in datafile: microclots
Males	PLT	349	175	510	delete	Comment in datafile: microclots
Males	WBC	269	135	17.1	delete	Comment in datafile: highCount
Males	Feed_27	199	100	28.35	delete	Animal 199 died between week 25
Males	Weight_13	53	27	407.62	407.26	Weight at beginning of this period must equal last weight in previous
Males	Weight_27	283	142	488.49	448.49	Weight at end of this period must equal first weight in next period
Males	Weight_23	175	88	467.75	508.62	Change of animals in common cage
Males	Weight_23	176	88	508.62	467.75	Change of animals in common cage
Males	Weight_23	256	128	482.30	428.30	Mistake in copying from primary
Males	MCV	281	141	58.8	outlier	Coincidently two large values in the same cage; possible outlier
Males	MCV	282	141	59.6	outlier	Coincidently two large values in the same cage; possible outlier
Males	ALT	199	100	2.4	outlier	Not extremely large; possible outlier
Males	BIL	130	65	36.4	outlier	Larger values in other months; possibly hemolysis; if so, delete
Sex	**Variable**	**Animal**	**Cage**	**oldValue**	**newValue**	**Comment**
Females	PLT	516	508	361	delete	Comment in datafile: microclots
Females	PLT	522	511	317	delete	Comment in datafile: microclots
Females	PLT	579	540	290	delete	Comment in datafile: microclots
Females	PLT	586	543	304	delete	Comment in datafile: microclots
Females	PLT	588	544	1853	delete	Comment in datafile: highCount
Females	PLT	592	546	315	delete	Comment in datafile: microclots
Females	PLT	680	590	1868	delete	Comment in datafile: highCount
Females	PLT	846	673	98	delete	Comment in datafile: microclots
Females	WBC	680	590	24	delete	Comment in datafile: highCount
Females	Feed_15	785	643	21.95	delete	Animal 785 died between week 13
Females	Weight_13	791	646	239.28	239.38	Weight at beginning of this period
Females	Weight_13	803	652	261.39	261.99	Weight at beginning of this period
Females	Lymphocytes	616	558	24	outlier	Extremely small value
Females	Neutrophils	616	558	69.5	outlier	Extremely large value
Females	MCV	718	609	66	outlier	Animal has consistent large values in months 3, 6, 12; possible outlier

Females	BIL	649	575	47.7	outlier	Two large values for BIL (K also large); possibly hemolysis; if so, delete;
Females	BIL	746	623	45.7	outlier	Two large values for BIL; possibly hemolysis; if so, delete
Females	K	649	575	8.4	delete	There is a larger value (BIL also large); definitely hemolysis; delete
Females	Na	769	635	157	delete	Not extremely large; too high;

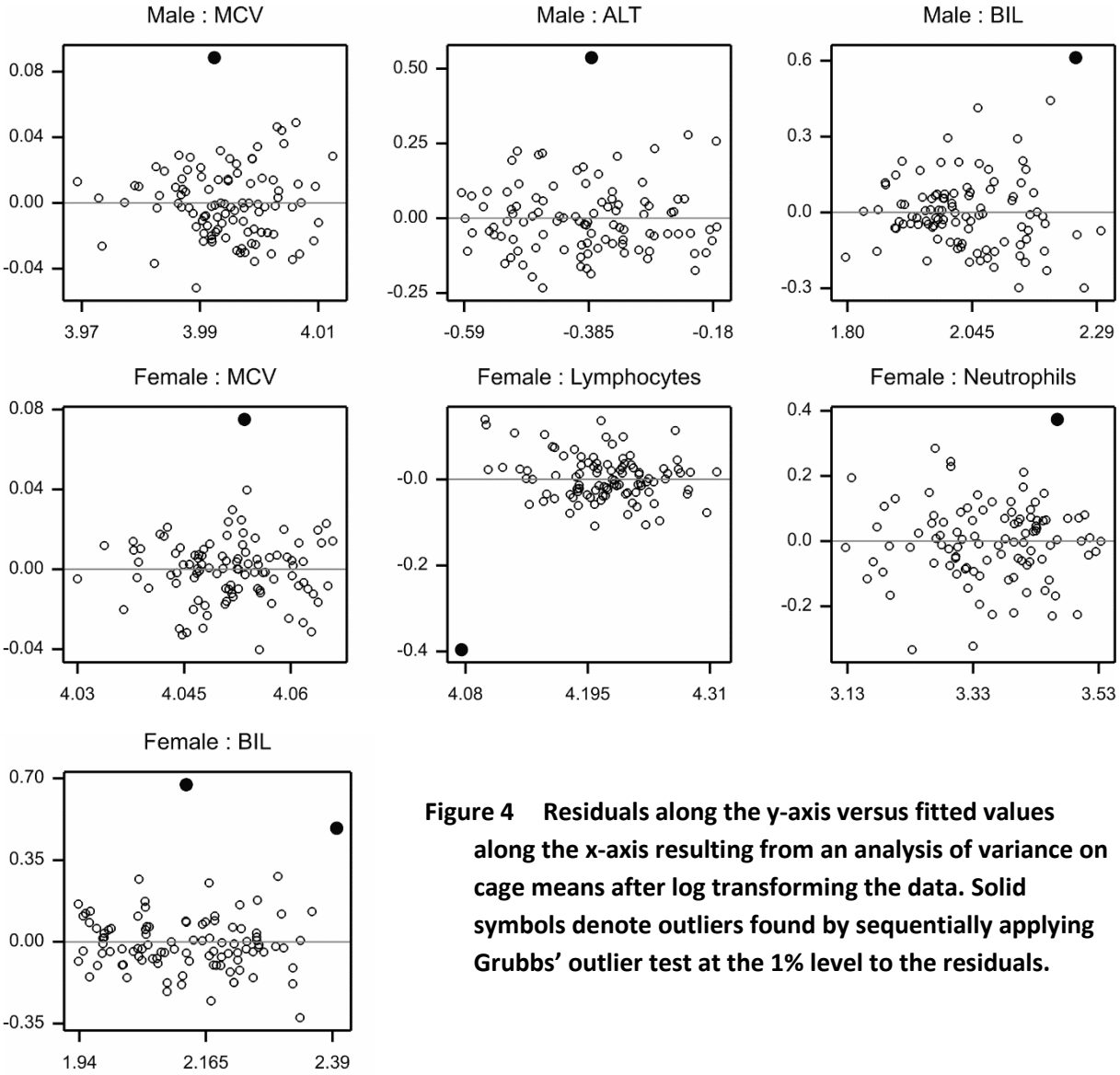

Figure 4 Residuals along the y-axis versus fitted values along the x-axis resulting from an analysis of variance on cage means after log transforming the data. Solid symbols denote outliers found by sequentially applying Grubbs' outlier test at the 1% level to the residuals.

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.

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_27	35	500	30.0	6.0	35	493	37.4	7.6	35	497	39.7	8.0	35	496	36.8	7.4	35	503	37.0	7.4
growthRate	35	1.60	0.15	9.7	35	1.59	0.17	10.8	35	1.60	0.18	11.4	35	1.57	0.18	11.3	35	1.63	0.21	12.7
FeedMean	35	19.9	0.73	3.7	35	19.6	1.27	6.5	35	19.5	1.27	6.5	35	19.7	1.16	5.9	35	20.3	1.32	6.5
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	9.1	1.63	17.8	20	8.9	1.95	21.9	20	10.8	1.88	17.4	20	10.5	1.84	17.6	20	9.6	1.94	20.1
RBC	20	8.46	0.33	4.0	20	8.49	0.31	3.7	20	8.47	0.28	3.3	20	8.45	0.28	3.3	20	8.52	0.26	3.0
HGB	20	15.6	0.51	3.3	20	15.7	0.57	3.6	20	15.8	0.53	3.3	20	15.6	0.48	3.1	20	15.9	0.43	2.7
HCT	20	45.8	1.54	3.4	20	46.0	1.45	3.1	20	46.2	1.67	3.6	20	45.6	1.47	3.2	20	46.4	1.25	2.7
MCV	19	54.0	0.78	1.4	20	54.3	1.47	2.7	20	54.6	1.48	2.7	20	54.0	1.15	2.1	20	54.5	0.98	1.8
MCH	20	18.5	0.61	3.3	20	18.6	0.82	4.4	20	18.7	0.64	3.4	20	18.5	0.55	2.9	20	18.7	0.52	2.8
MCHC	20	34.1	0.62	1.8	20	34.2	0.79	2.3	20	34.3	0.61	1.8	20	34.3	0.71	2.1	20	34.3	0.56	1.6
PLT	20	829	44	5.3	20	812	105	13.0	20	872	88	10.1	20	864	67	7.7	20	865	112	12.9
LYMR	20	71.4	4.48	6.3	20	69.9	4.90	7.0	20	70.5	6.07	8.6	20	71.5	6.06	8.5	20	72.3	3.99	5.5
LYMA	20	6.52	1.17	17.9	20	6.19	1.34	21.6	20	7.53	1.33	17.7	20	7.47	1.37	18.4	20	6.99	1.67	23.9
diffWBC	**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
Lymphocytes	20	69.7	5.24	7.5	20	70.8	4.56	6.4	20	68.7	5.32	7.7	20	70.0	6.50	9.3	20	71.3	4.33	6.1
Neutrophils	20	27.0	4.86	18.0	20	26.1	4.02	15.4	20	27.4	5.30	19.3	20	26.3	5.79	22.0	20	25.1	3.99	15.9
Monocytes	20	1.20	0.49	40.9	20	0.90	0.39	43.7	20	1.10	0.52	46.9	20	0.99	0.50	50.3	20	1.02	0.36	35.3
Eosinophils	20	2.20	1.20	54.5	20	2.16	1.31	60.4	20	2.75	1.25	45.3	20	2.64	1.65	62.6	20	2.53	0.85	33.5
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	1.39	0.30	21.7	20	1.44	0.36	24.8	20	1.34	0.30	22.8	20	1.35	0.24	17.6	20	1.37	0.34	24.5
ALT	20	0.68	0.09	12.7	20	0.70	0.16	23.4	20	0.70	0.15	21.8	20	0.68	0.12	17.8	20	0.69	0.10	14.5
AST	20	2.09	0.41	19.7	20	2.15	0.42	19.4	20	2.25	0.42	18.6	20	2.15	0.32	15.0	20	2.11	0.31	14.8
BIL	20	7.33	1.28	17.5	20	7.54	1.49	19.8	20	8.34	2.15	25.8	20	7.99	1.61	20.2	20	7.83	1.29	16.4
ALB	20	35.0	1.24	3.5	20	35.0	1.32	3.8	20	35.3	1.35	3.8	20	35.2	1.32	3.8	20	35.2	1.35	3.8
TP	20	64.6	1.99	3.1	20	64.3	1.59	2.5	20	64.4	1.72	2.7	20	65.0	1.53	2.3	20	64.4	1.78	2.8

Glu	20	5.94	0.81	13.7	20	5.79	0.78	13.5	20	5.87	0.75	12.7	20	6.04	0.78	12.8	20	6.19	0.57	9.2
CHOL	20	2.20	0.27	12.2	20	2.26	0.23	10.1	20	2.23	0.28	12.7	20	2.21	0.27	12.4	20	2.29	0.30	13.3
TAG	20	1.24	0.50	40.0	20	1.29	0.48	37.4	20	1.33	0.47	35.4	20	1.39	0.53	38.1	20	1.30	0.43	33.5
Crea	20	42.3	3.67	8.7	20	41.0	3.78	9.2	20	41.8	3.95	9.5	20	42.4	3.52	8.3	20	40.8	3.73	9.2
Urea	20	5.16	0.61	11.8	20	5.02	0.75	14.9	20	5.16	0.59	11.5	20	5.19	0.60	11.5	20	5.10	0.51	10.0
cHGB	20	63.6	23.1	36.3	20	82.4	59.3	72.0	20	84.3	49.0	58.1	20	82.6	40.6	49.2	20	72.2	31.5	43.6
Ca	20	2.52	0.044	1.7	20	2.52	0.048	1.9	20	2.54	0.056	2.2	20	2.54	0.056	2.2	20	2.52	0.048	1.9
Cl	20	102	1.36	1.3	20	102	1.38	1.4	20	101	1.44	1.4	20	101	1.25	1.2	20	102	1.18	1.2
K	20	5.06	0.32	6.3	20	5.17	0.59	11.5	20	5.25	0.46	8.7	20	5.32	0.48	9.0	20	5.13	0.37	7.1
Na	20	144	1.80	1.3	20	144	2.23	1.6	20	144	1.78	1.2	20	144	1.69	1.2	20	143	1.39	1.0
P	20	2.04	0.26	12.6	20	1.99	0.27	13.5	20	2.05	0.20	9.6	20	2.09	0.21	10.1	20	2.02	0.18	9.0
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	10	20.5	3.82	18.6	10	21.4	2.85	13.3	10	16.8	5.26	31.4	10	19.0	5.71	30.1	10	21.4	4.65	21.8
uVolW	10	4.16	0.84	20.2	10	4.38	0.61	14.0	10	3.38	0.91	27.0	10	3.95	1.37	34.8	10	4.30	0.89	20.7
uLeu	10	42.5	29.6	69.6	10	32.5	22.2	68.3	10	80.0	81.7	102.1	10	57.5	76.9	133.7	10	38.8	23.2	59.8
uOsmoll	10	420	85	20.1	10	379	58	15.2	10	521	129	24.7	10	466	135	29.0	10	405	84	20.9
uKeton	10	0.72	0.95	131.5	10	0.48	0.48	100.6	10	0.72	0.53	73.5	10	0.47	0.55	114.9	10	0.33	0.47	145.3
upH	10	6.82	0.33	4.9	10	6.72	0.22	3.3	10	6.73	0.18	2.7	10	6.85	0.21	3.1	10	6.67	0.35	5.3

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_27	35	272	19.0	7.0	35	270	18.9	7.0	35	270	17.4	6.4	35	269	20.7	7.7	35	271	19.4	7.2
growthRate	35	0.59	0.25	42.0	35	0.62	0.31	50.5	35	0.55	0.34	61.3	35	0.55	0.32	58.2	35	0.61	0.31	50.8
FeedMean	35	14.2	0.86	6.1	35	14.3	1.19	8.3	35	14.4	1.04	7.3	35	14.3	1.13	7.9	35	14.6	1.18	8.0
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	5.86	1.35	23.1	20	5.97	0.94	15.8	20	6.12	1.71	27.9	20	5.59	1.27	22.6	20	6.05	1.30	21.5
RBC	20	7.66	0.30	3.9	20	7.64	0.25	3.2	20	7.71	0.30	3.9	20	7.68	0.19	2.5	20	7.72	0.27	3.6
HGB	20	15.6	0.44	2.8	20	15.4	0.52	3.4	20	15.5	0.29	1.9	20	15.4	0.29	1.9	20	15.5	0.41	2.6
HCT	20	44.1	1.55	3.5	20	44.0	1.45	3.3	20	44.3	1.03	2.3	20	44.1	0.88	2.0	20	44.2	1.41	3.2
MCV	20	57.7	0.96	1.7	20	57.6	0.90	1.6	20	57.4	1.14	2.0	20	57.4	0.80	1.4	20	57.2	0.99	1.7
MCH	20	20.4	0.52	2.5	20	20.2	0.53	2.6	20	20.1	0.69	3.4	20	20.1	0.49	2.5	20	20.1	0.64	3.2
MCHC	20	35.3	0.76	2.1	20	35.1	0.76	2.2	20	34.9	0.40	1.2	20	34.9	0.59	1.7	20	35.2	0.87	2.5
PLT	20	843	82	9.7	20	794	63	7.9	20	812	69	8.4	20	786	92	11.7	20	819	117	14.3
LYMR	20	72.4	3.94	5.4	20	71.2	4.03	5.7	20	71.6	5.22	7.3	20	72.2	3.88	5.4	20	71.1	5.25	7.4
LYMA	20	4.21	0.85	20.3	20	4.26	0.75	17.6	20	4.35	1.21	27.8	20	4.03	0.94	23.4	20	4.28	1.04	24.2
diffWBC	**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
Lymphocytes	20	67.7	4.28	6.3	20	67.5	4.34	6.4	20	67.4	3.91	5.8	20	67.5	3.49	5.2	20	69.3	4.54	6.5
Neutrophils	20	29.0	4.25	14.7	20	29.5	4.07	13.8	20	29.6	4.13	14.0	20	29.3	3.79	12.9	20	27.9	4.33	15.5
Monocytes	20	1.13	0.60	53.7	20	0.85	0.64	75.4	20	1.01	0.61	60.7	20	0.94	0.36	38.6	20	0.66	0.39	59.1
Eosinophils	20	2.24	0.76	33.9	20	2.21	0.86	38.7	20	1.97	0.98	49.6	20	2.34	0.77	33.0	20	2.12	1.23	58.0
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	0.65	0.13	19.8	20	0.61	0.14	22.7	20	0.63	0.16	26.3	20	0.62	0.13	20.9	20	0.61	0.16	25.4
ALT	20	0.62	0.14	22.4	20	0.61	0.13	20.4	20	0.64	0.12	18.6	20	0.55	0.10	18.1	20	0.61	0.09	15.1
AST	20	1.95	0.36	18.3	20	1.84	0.34	18.5	20	2.11	0.56	26.8	20	1.81	0.30	16.4	20	2.09	0.40	19.1
BIL	20	8.37	1.21	14.4	20	8.34	0.78	9.3	20	8.75	2.02	23.0	20	8.24	1.50	18.2	20	8.36	1.32	15.7
ALB	20	41.5	1.93	4.6	20	41.8	2.27	5.4	20	42.0	2.93	7.0	20	42.4	2.56	6.0	20	41.3	2.70	6.5
TP	20	69.6	2.59	3.7	20	69.7	2.73	3.9	20	70.2	3.54	5.0	20	70.2	2.75	3.9	20	69.1	2.37	3.4

Glu	20	5.55	0.67	12.1	20	5.37	0.76	14.1	20	5.26	0.61	11.5	20	5.45	0.74	13.6	20	5.48	0.74	13.6
CHOL	20	2.23	0.42	19.0	20	2.16	0.41	18.9	20	2.06	0.42	20.2	20	2.01	0.32	15.7	20	2.10	0.35	16.6
TAG	20	0.82	0.24	29.1	20	0.85	0.40	47.6	20	0.74	0.17	23.4	20	0.74	0.20	27.5	20	0.78	0.19	24.0
Crea	20	43.3	7.27	16.8	20	42.5	4.87	11.4	20	41.5	3.88	9.3	20	43.7	6.78	15.5	20	43.5	3.48	8.0
Urea	20	5.52	0.55	10.0	20	5.76	0.54	9.3	20	5.64	0.55	9.8	20	5.50	0.42	7.6	20	5.68	0.49	8.6
cHGB	20	75.2	22.2	29.5	20	77.0	15.9	20.7	20	92.5	56.5	61.1	20	84.8	53.2	62.7	20	71.8	17.6	24.5
Ca	20	2.53	0.045	1.8	20	2.54	0.072	2.8	20	2.56	0.072	2.8	20	2.55	0.067	2.6	20	2.53	0.051	2.0
Cl	20	101	1.58	1.6	20	102	1.45	1.4	20	102	1.67	1.6	20	102	1.48	1.5	20	101	1.85	1.8
K	20	4.17	0.32	7.7	20	4.22	0.29	6.8	20	4.56	0.57	12.6	20	4.32	0.31	7.2	20	4.19	0.35	8.3
Na	20	142	2.28	1.6	20	142	2.04	1.4	20	142	1.97	1.4	20	142	2.06	1.4	20	143	2.19	1.5
P	20	1.34	0.21	16.0	20	1.33	0.23	17.1	20	1.41	0.26	18.2	20	1.35	0.26	19.0	20	1.29	0.16	12.0
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	10	16.8	3.95	23.6	10	16.8	6.01	35.7	10	20.4	5.61	27.4	10	17.8	6.26	35.3	10	13.0	2.97	22.9
uVolW	10	6.34	1.58	25.0	10	6.23	1.99	31.9	10	7.68	2.31	30.0	10	6.59	2.27	34.4	10	4.92	1.11	22.6
uLeu	10	16.2	16.7	102.9	10	26.2	34.1	129.8	10	15.0	19.4	129.1	10	12.5	15.6	124.7	10	16.2	14.5	89.2
uOsmoll	10	381	99	25.9	10	409	131	32.1	10	327	83	25.5	10	404	193	47.7	10	448	108	24.0
uKeton	10	0.20	0.37	184.5	10	0.25	0.46	182.6	10	0.22	0.30	133.0	10	0.12	0.24	194.4	10	0.12	0.24	194.4
upH	10	6.38	0.18	2.8	10	6.25	0.26	4.2	10	6.52	0.22	3.4	10	6.33	0.37	5.9	10	6.30	0.16	2.5

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

The sample size in the current study, i.e. the number of cages per feeding group, equals 35 for the weight variables and 20 for haematology, differential white blood cell counts, and for clinical biochemistry. 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 6 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 30 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.

The DWE equivalence test depends, among other things, on the ratio of the residual variance of the current study and the residual variance of the historical studies. In case this variance ratio (VR) is small the corresponding DWE interval will generally be short, and when VR is large the interval will large. The ratio of the residual variances is given in Figure 17. Large ratios are observed in males for MCV, MCH, MCHC and Lymphocytes, and in females for MCHC, Monocytes and CHOL.

Among 8×30 = 240 equivalence tests, there were 20 failures (8.3%) to prove equivalence (i.e. reject the hypothesis of non-equivalence), which is close to the 5% level of the test. For all these failures the ratio of the residual variances is large (Figure 17). For only 1 of these 20 cases (Monocytes, females NK33+) the median estimate was outside the equivalence limits, therefore for the other 19 cases equivalence is still more likely than lack of equivalence according to the terminology of EFSA (2011a). The 20 cases were observed in males for MCV (2x), MCH (4x) and Lymphocytes (4x), and in females for MCHC (2x), Monocytes (4x) and CHOL (4x).

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 12 (5% of 240 difference tests, 8 for males and 4 for females), which is again close to the 5% level of the test. Only in one of these cases (Monocytes, females NK33+) there was both a significant difference and a failure to show equivalence.

For all difference tests, i.e. including those for which the equivalence test was not performed, 14 out of 320 t-tests were significant which is 4.4% of the tests (Table 9 and Table 10).

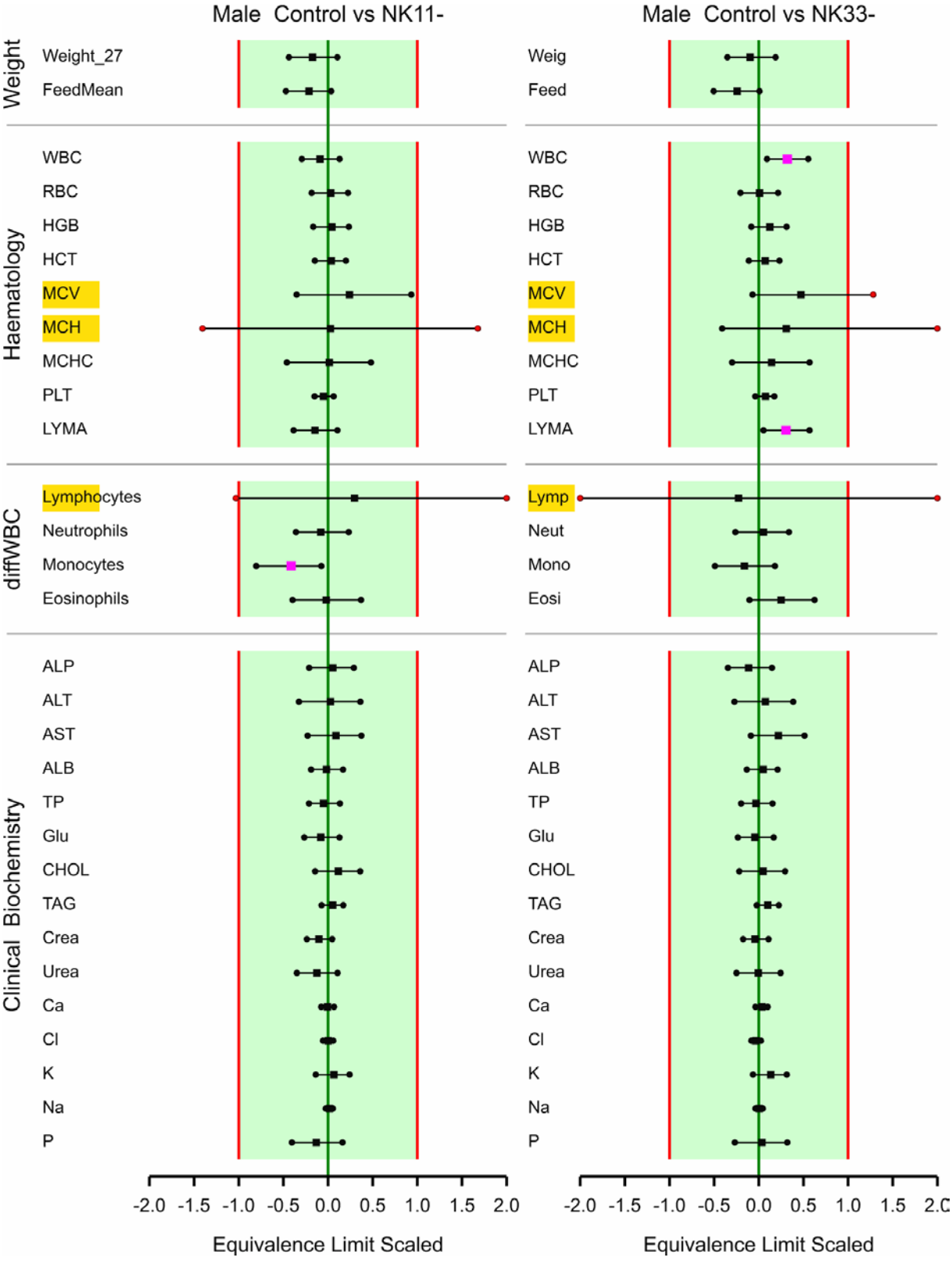

Figure 5 **Equivalence testing of NK11- and NK33- versus the control feed for males. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed. See Table 9, Figure 9 and Figure 10 for further interpretation. Endpoints labelled with a golden background have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

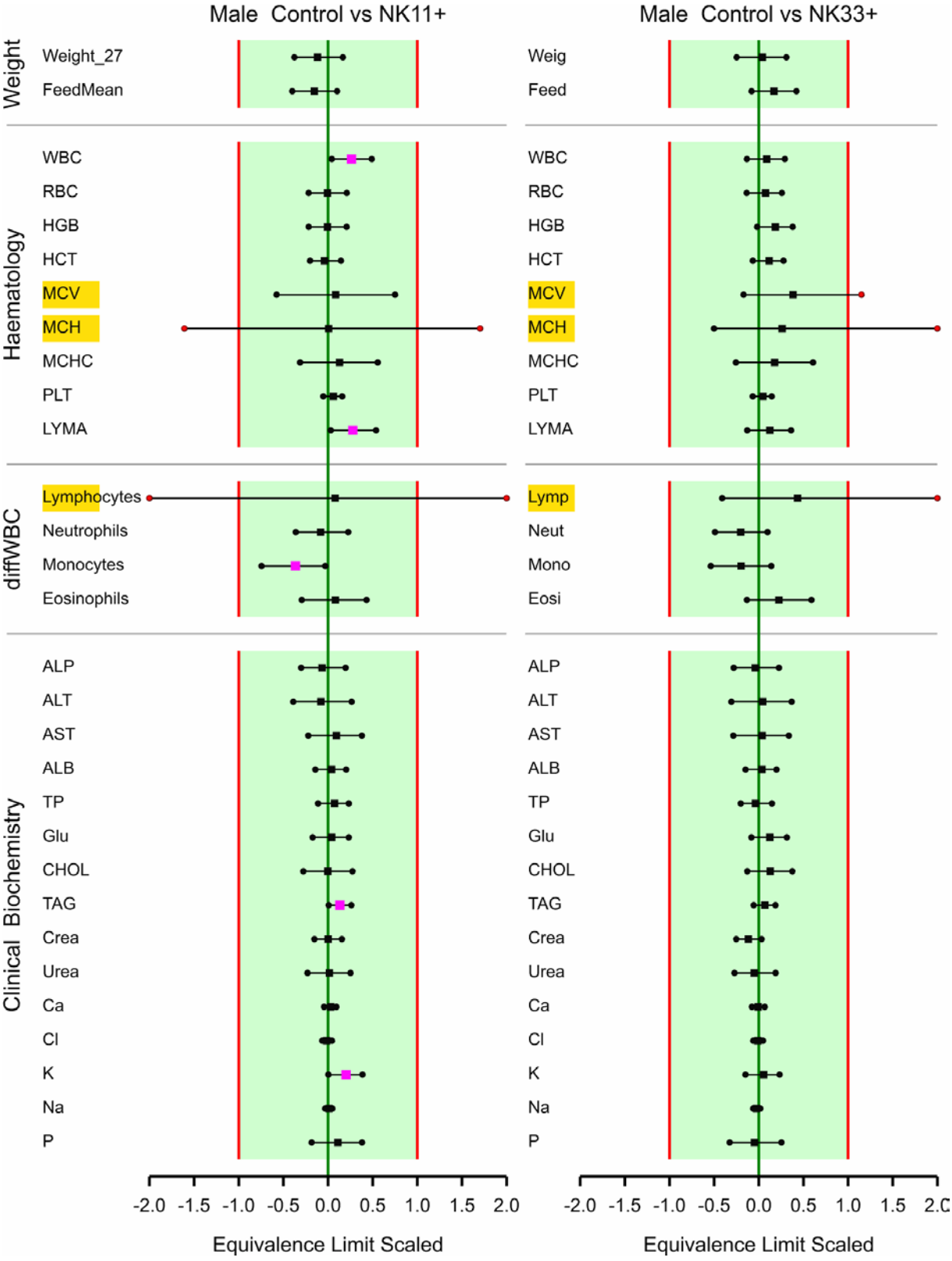

Figure 6 **Equivalence testing of NK11+ and NK33+ versus the control feed for males. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed. See Table 9, Figure 11 and Figure 12 for further interpretation. Endpoints labelled with a golden background have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

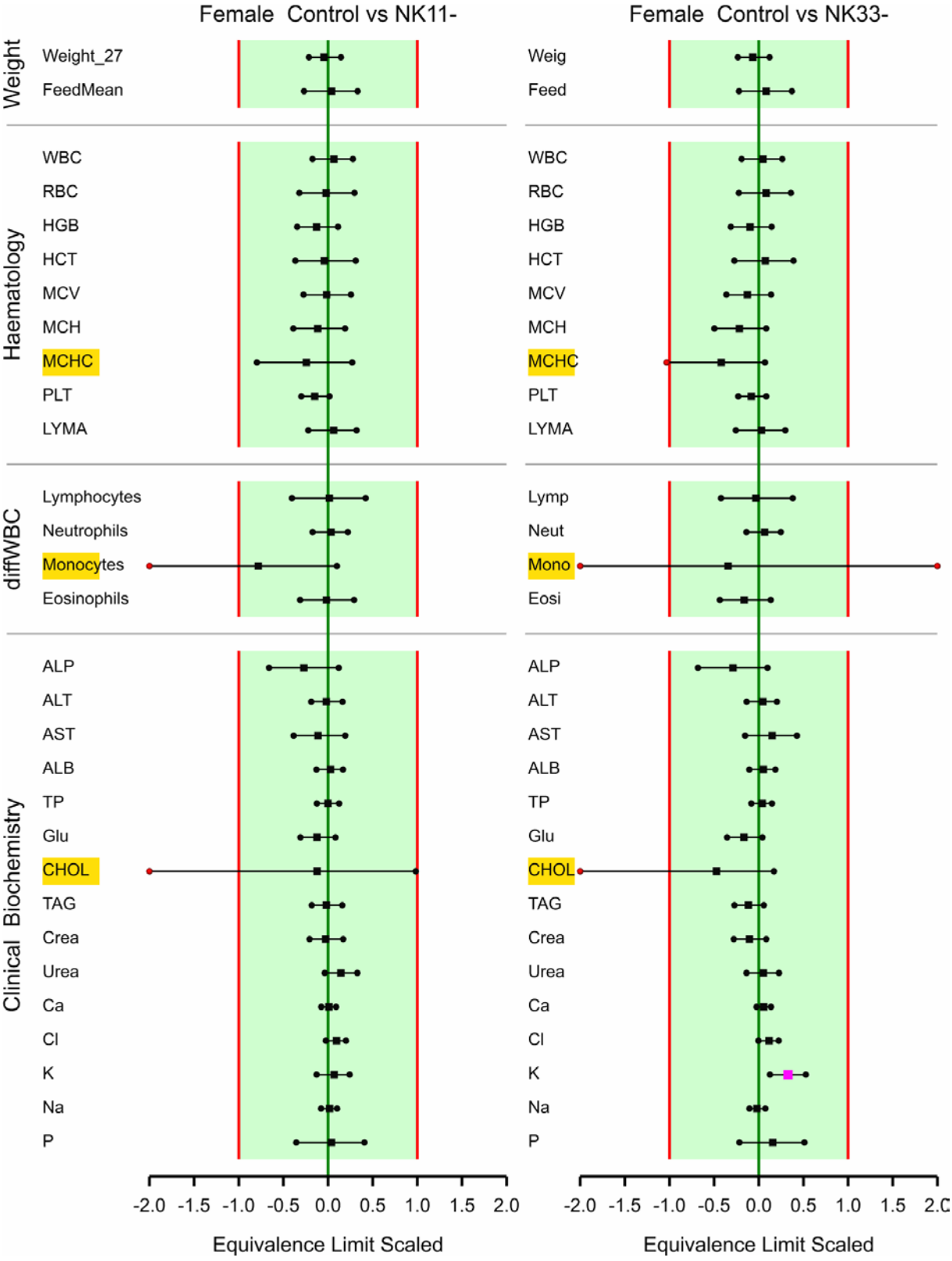

Figure 7 **Equivalence testing of NK11- and NK33- versus the control feed for females. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed. See Table 10, Figure 13 and Figure 14 for further interpretation. Endpoints labelled with a golden background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

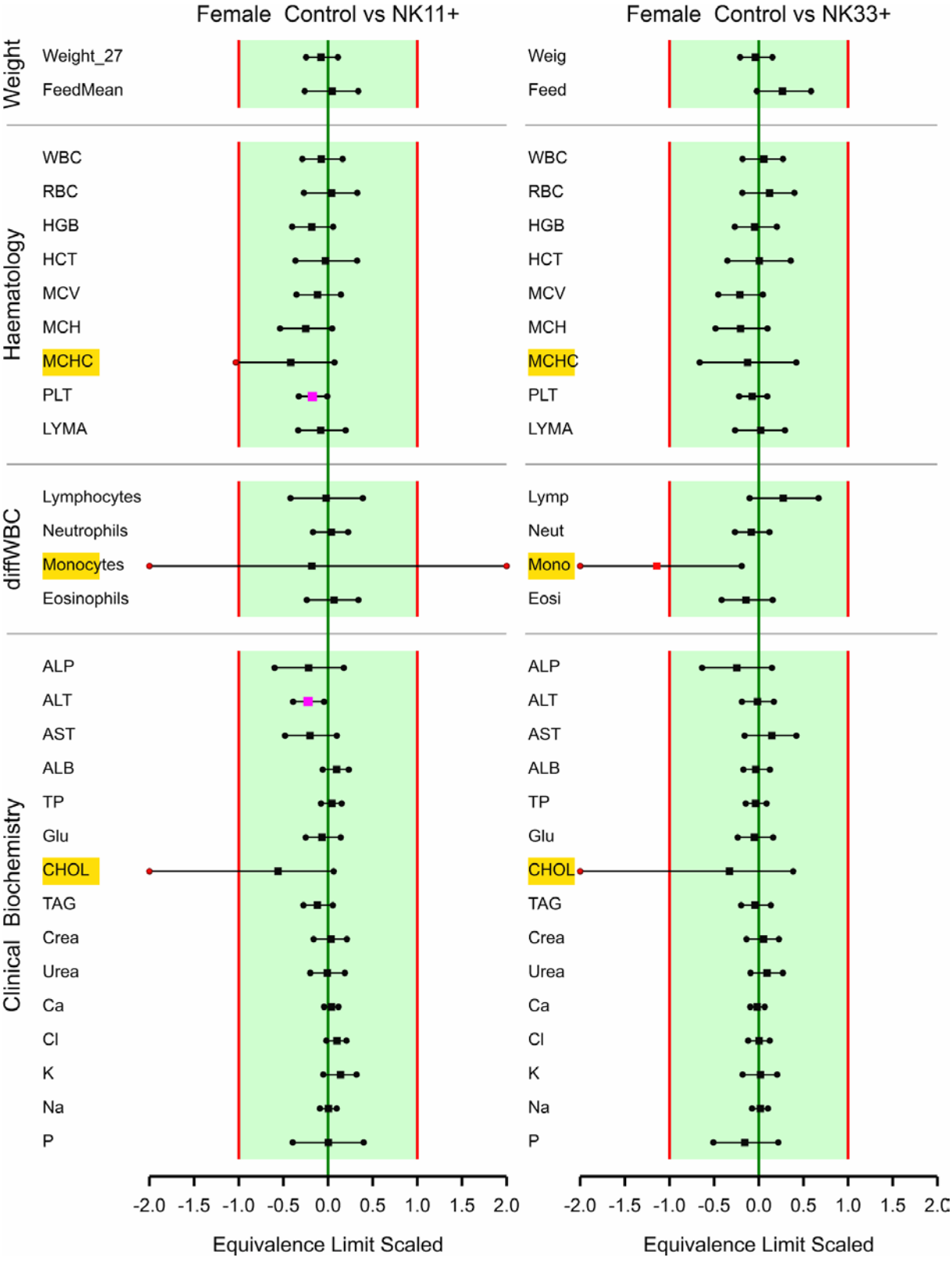

Figure 8 **Equivalence testing of NK11+ and NK33+ versus the control feed for females. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed. See Table 10, Figure 15 and Figure 16 for further interpretation. Endpoints labelled with a golden background 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_27	0.961	0.985	1.009	0.967	0.991	1.016	0.965	0.989	1.014	0.979	1.004	1.029
growthRate	0.923	0.991	1.065	0.931	1.001	1.075	0.902	0.969	1.041	0.956	1.027	1.103
FeedMean	0.958	0.980	1.003	0.955	0.978	1.001	0.963	0.986	1.009	0.993	1.016	1.040
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	0.851	0.953	1.067	1.055	1.181	1.322	1.024	1.146	1.283	0.936	1.048	1.173
RBC	0.981	1.003	1.026	0.979	1.001	1.024	0.977	0.999	1.022	0.986	1.008	1.031
HGB	0.985	1.004	1.024	0.992	1.012	1.032	0.980	0.999	1.019	0.998	1.018	1.038
HCT	0.985	1.004	1.024	0.988	1.008	1.028	0.976	0.996	1.015	0.993	1.012	1.032
MCV	0.992	1.006	1.021	0.998	1.013	1.027	0.988	1.002	1.017	0.996	1.010	1.025
MCH	0.979	1.001	1.024	0.989	1.011	1.034	0.978	1.000	1.023	0.987	1.010	1.033
MCHC	0.988	1.000	1.013	0.992	1.004	1.017	0.992	1.004	1.016	0.993	1.005	1.018
PLT	0.909	0.970	1.036	0.978	1.044	1.115	0.970	1.036	1.106	0.962	1.027	1.097
LYMR	0.936	0.976	1.019	0.945	0.986	1.029	0.958	0.999	1.043	0.971	1.013	1.057
LYMA	0.825	0.931	1.051	1.027	1.159	1.308	1.015	1.145	1.293	0.942	1.063	1.200
diffWBC	**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
Lymphocytes	0.977	1.018	1.060	0.947	0.987	1.028	0.964	1.005	1.047	0.984	1.025	1.068
Neutrophils	0.882	0.973	1.075	0.922	1.018	1.124	0.881	0.973	1.074	0.847	0.935	1.032
Monocytes	0.598	0.752	0.947	0.710	0.894	1.125	0.617	0.777	0.978	0.692	0.871	1.096
Eosinophils	0.698	0.980	1.377	0.908	1.275	1.791	0.772	1.085	1.524	0.886	1.244	1.748
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	0.929	1.020	1.119	0.874	0.959	1.053	0.889	0.976	1.072	0.898	0.986	1.082
ALT	0.934	1.006	1.084	0.944	1.017	1.096	0.911	0.982	1.058	0.937	1.010	1.088
AST	0.935	1.028	1.129	0.974	1.070	1.176	0.937	1.030	1.131	0.921	1.012	1.112
BIL	0.933	1.025	1.127	1.017	1.117	1.228	0.984	1.081	1.188	0.970	1.066	1.171
ALB	0.977	0.998	1.020	0.985	1.006	1.028	0.984	1.005	1.026	0.983	1.004	1.026

TP	0.980	0.995	1.012	0.981	0.997	1.013	0.990	1.006	1.023	0.981	0.997	1.013
Glu	0.908	0.973	1.043	0.919	0.985	1.055	0.946	1.014	1.087	0.973	1.043	1.117
CHOL	0.964	1.032	1.106	0.946	1.013	1.085	0.933	0.999	1.071	0.967	1.036	1.110
TAG	0.943	1.047	1.161	0.981	1.088	1.207	1.007	1.118	1.240	0.954	1.059	1.175
Crea	0.924	0.968	1.015	0.941	0.987	1.034	0.955	1.001	1.049	0.919	0.964	1.010
Urea	0.913	0.968	1.026	0.942	0.999	1.059	0.947	1.004	1.065	0.930	0.987	1.046
cHGB	0.931	1.162	1.451	0.997	1.244	1.553	0.996	1.243	1.552	0.880	1.099	1.371
Ca	0.988	0.999	1.010	0.994	1.005	1.017	0.993	1.005	1.016	0.988	0.999	1.010
Cl	0.993	1.000	1.007	0.989	0.996	1.003	0.992	0.998	1.005	0.992	0.999	1.006
K	0.969	1.016	1.065	0.985	1.032	1.082	1.001	1.049	1.100	0.966	1.013	1.062
Na	0.997	1.002	1.008	0.995	1.001	1.006	0.996	1.001	1.007	0.991	0.997	1.002
P	0.914	0.972	1.033	0.948	1.008	1.071	0.963	1.024	1.089	0.930	0.989	1.052
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	0.870	1.070	1.315	0.654	0.804	0.989	0.737	0.907	1.115	0.843	1.036	1.274
uVolW	0.871	1.081	1.342	0.652	0.809	1.004	0.741	0.920	1.142	0.830	1.031	1.280
uLeu	0.551	0.896	1.458	0.922	1.500	2.441	0.663	1.079	1.755	0.582	0.947	1.540
uOsmoll	0.750	0.918	1.124	0.992	1.215	1.488	0.895	1.096	1.342	0.787	0.964	1.180
uKeton	0.497	0.919	1.700	0.657	1.215	2.247	0.497	0.919	1.700	0.409	0.756	1.399
upH	0.718	0.905	1.141	0.718	0.905	1.141	0.813	1.025	1.293	0.683	0.861	1.085

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_27	0.972	0.994	1.017	0.970	0.992	1.014	0.969	0.991	1.013	0.973	0.995	1.018
growthRate	0.923	0.991	1.065	0.931	1.001	1.075	0.902	0.969	1.041	0.956	1.027	1.103
FeedMean	0.974	1.004	1.035	0.979	1.009	1.040	0.975	1.005	1.036	0.998	1.029	1.060
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	0.912	1.036	1.178	0.904	1.026	1.164	0.846	0.960	1.089	0.910	1.032	1.171
RBC	0.976	0.998	1.021	0.984	1.006	1.029	0.981	1.003	1.026	0.987	1.009	1.032
HGB	0.976	0.991	1.008	0.978	0.994	1.009	0.973	0.988	1.004	0.981	0.997	1.013
HCT	0.979	0.998	1.017	0.986	1.004	1.023	0.980	0.998	1.017	0.982	1.000	1.019
MCV	0.989	0.999	1.010	0.984	0.995	1.005	0.985	0.995	1.006	0.981	0.991	1.002
MCH	0.975	0.993	1.011	0.969	0.987	1.005	0.967	0.985	1.003	0.970	0.988	1.006
MCHC	0.981	0.994	1.006	0.977	0.989	1.002	0.977	0.990	1.002	0.985	0.997	1.009
PLT	0.884	0.944	1.007	0.908	0.968	1.032	0.877	0.935	0.997	0.912	0.972	1.036
LYMR	0.945	0.982	1.021	0.952	0.989	1.027	0.962	0.999	1.037	0.944	0.981	1.019
LYMA	0.898	1.032	1.186	0.886	1.016	1.165	0.836	0.959	1.100	0.881	1.011	1.159
diffWBC	**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
Lymphocytes	0.968	1.001	1.036	0.964	0.997	1.031	0.965	0.998	1.032	0.991	1.025	1.060
Neutrophils	0.933	1.014	1.102	0.947	1.027	1.115	0.936	1.016	1.102	0.890	0.966	1.048
Monocytes	0.561	0.764	1.039	0.653	0.885	1.198	0.691	0.936	1.268	0.498	0.674	0.913
Eosinophils	0.726	0.982	1.329	0.629	0.847	1.141	0.795	1.071	1.442	0.642	0.864	1.164
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	0.831	0.927	1.035	0.828	0.922	1.027	0.845	0.941	1.048	0.838	0.933	1.040
ALT	0.892	0.989	1.097	0.926	1.026	1.136	0.795	0.880	0.975	0.895	0.992	1.098
AST	0.847	0.956	1.079	0.943	1.062	1.196	0.820	0.923	1.039	0.941	1.060	1.194
BIL	0.940	1.014	1.095	0.957	1.032	1.112	0.910	0.981	1.058	0.928	1.000	1.078
ALB	0.974	1.006	1.039	0.979	1.011	1.043	0.988	1.020	1.053	0.962	0.993	1.025

TP	0.977	1.000	1.023	0.985	1.007	1.030	0.986	1.008	1.031	0.971	0.993	1.016
Glu	0.897	0.960	1.028	0.886	0.947	1.013	0.915	0.978	1.046	0.920	0.984	1.052
CHOL	0.875	0.978	1.094	0.824	0.919	1.026	0.811	0.905	1.010	0.845	0.943	1.053
TAG	0.862	0.985	1.127	0.802	0.915	1.044	0.800	0.913	1.041	0.848	0.968	1.104
Crea	0.935	0.992	1.052	0.914	0.968	1.026	0.954	1.011	1.071	0.960	1.017	1.077
Urea	0.988	1.045	1.105	0.962	1.016	1.074	0.944	0.997	1.054	0.974	1.029	1.087
cHGB	0.905	1.055	1.229	0.947	1.101	1.280	0.875	1.018	1.183	0.838	0.974	1.133
Ca	0.988	1.002	1.015	0.996	1.009	1.023	0.993	1.006	1.020	0.984	0.997	1.010
Cl	0.998	1.006	1.014	1.000	1.008	1.016	0.999	1.007	1.015	0.992	1.000	1.008
K	0.969	1.017	1.067	1.033	1.082	1.135	0.987	1.035	1.085	0.959	1.005	1.053
Na	0.995	1.001	1.007	0.993	0.999	1.005	0.994	1.000	1.006	0.995	1.001	1.007
P	0.923	1.010	1.105	0.951	1.039	1.136	0.916	1.001	1.093	0.881	0.962	1.052
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	0.664	0.885	1.182	0.886	1.171	1.547	0.769	1.017	1.344	0.591	0.781	1.033
uVolW	0.665	0.886	1.180	0.876	1.155	1.523	0.763	1.007	1.328	0.588	0.776	1.024
uLeu	0.751	1.227	2.005	0.589	0.947	1.522	0.527	0.848	1.364	0.622	1.000	1.608
uOsmoll	0.840	1.081	1.392	0.659	0.841	1.073	0.785	1.002	1.279	0.943	1.203	1.536
uKeton	0.782	1.134	1.646	0.737	1.056	1.514	0.633	0.907	1.300	0.633	0.907	1.300
upH	0.689	0.882	1.130	0.915	1.162	1.476	0.749	0.951	1.208	0.730	0.928	1.179

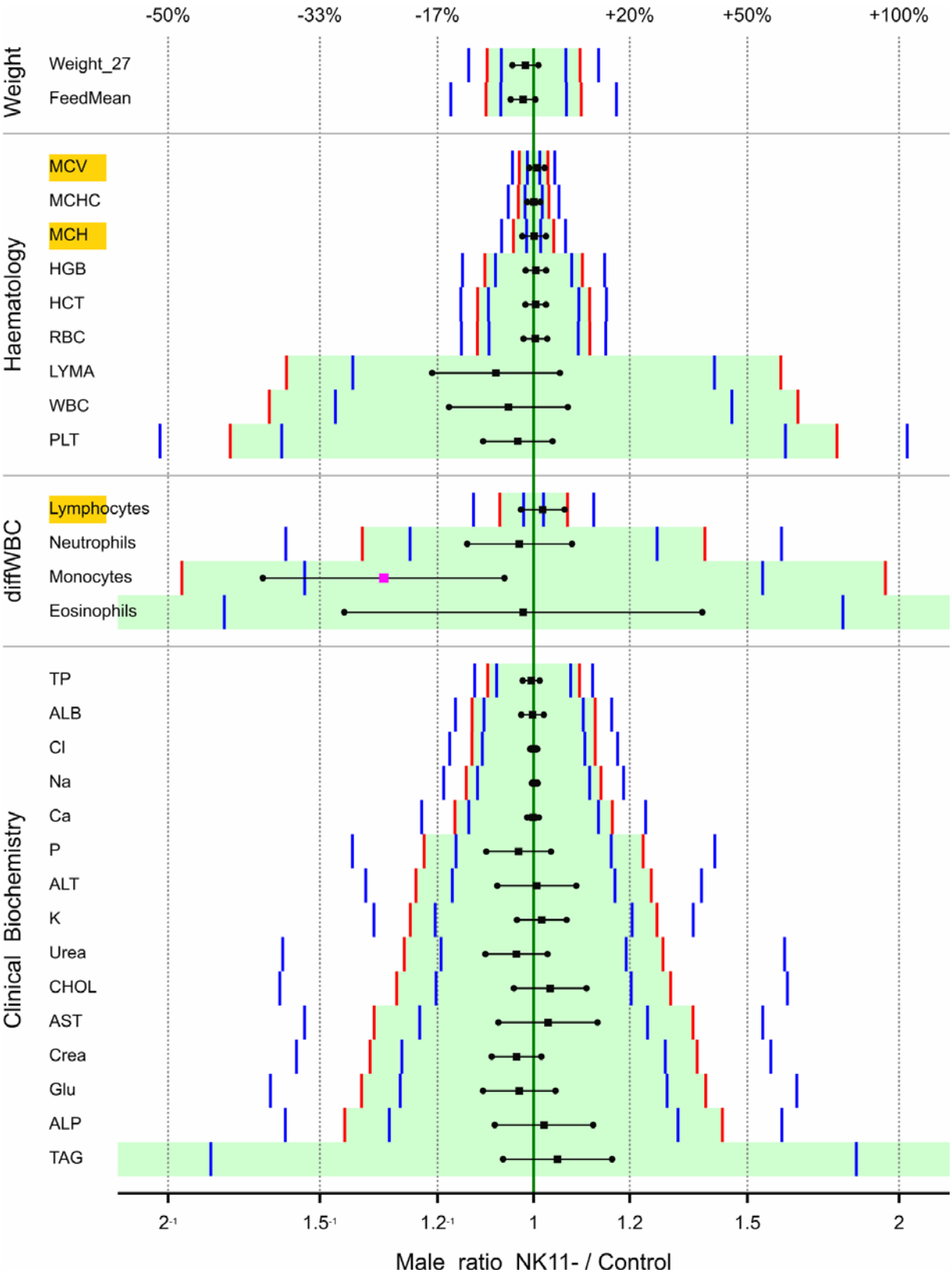

Figure 9 **95% confidence intervals for the ratio of NK11- and the Control feed for males with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).**

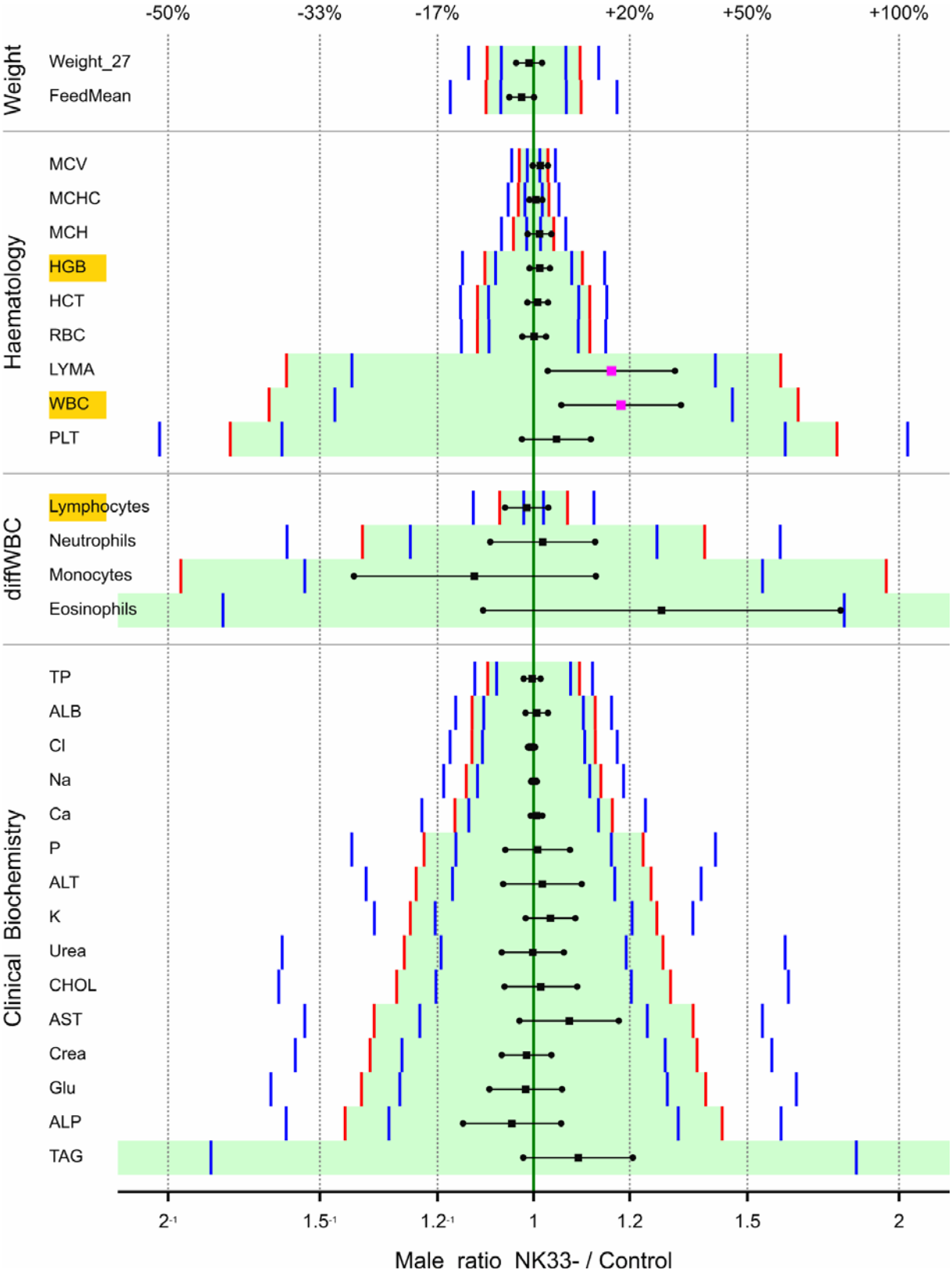

Figure 10 95% confidence intervals for the ratio of NK33- and the Control feed for males with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

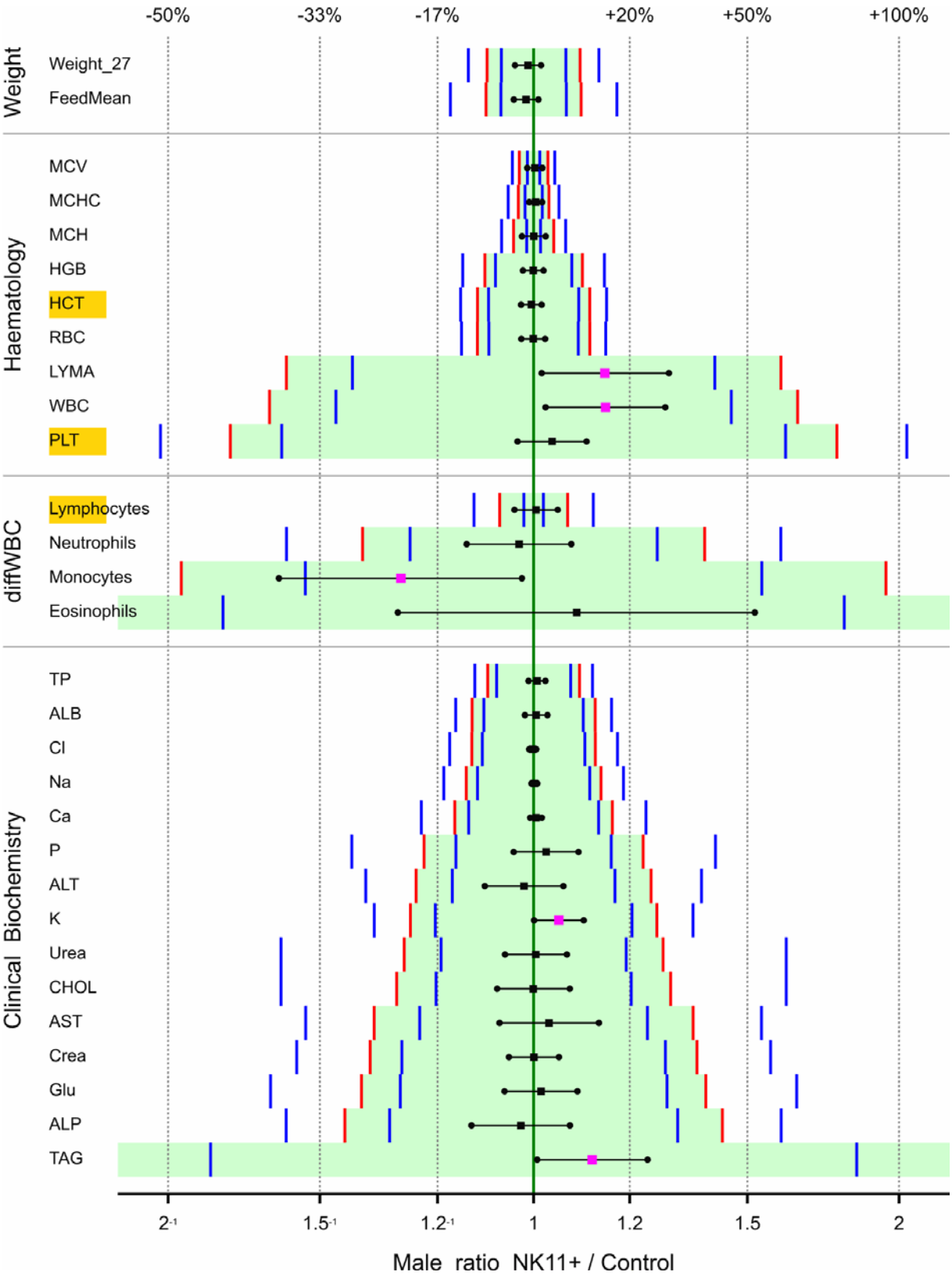

Figure 11 95% confidence intervals for the ratio of NK11+ and the Control feed for males with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

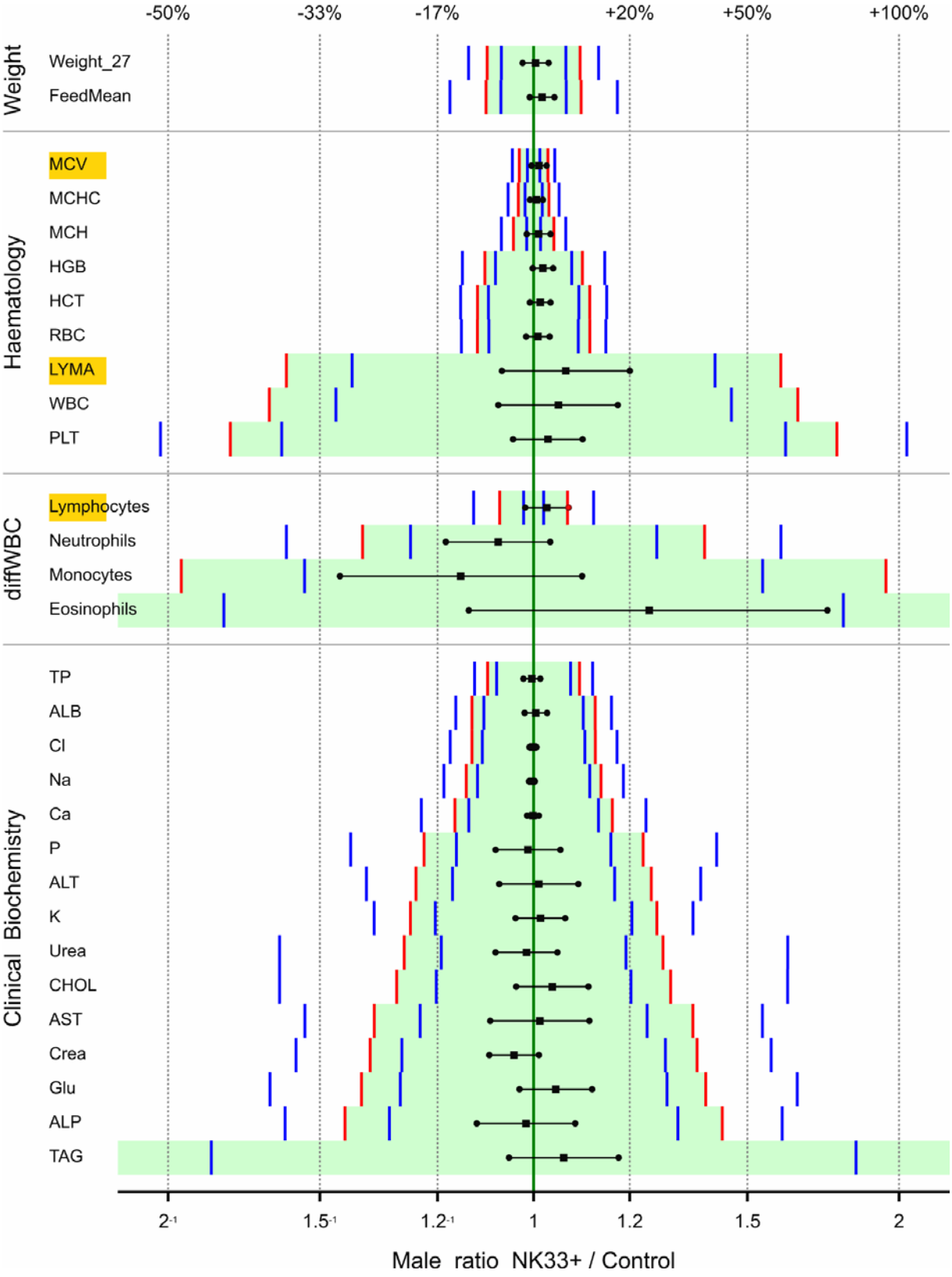

Figure 12 95% confidence intervals for the ratio of NK33+ and the Control feed for males with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

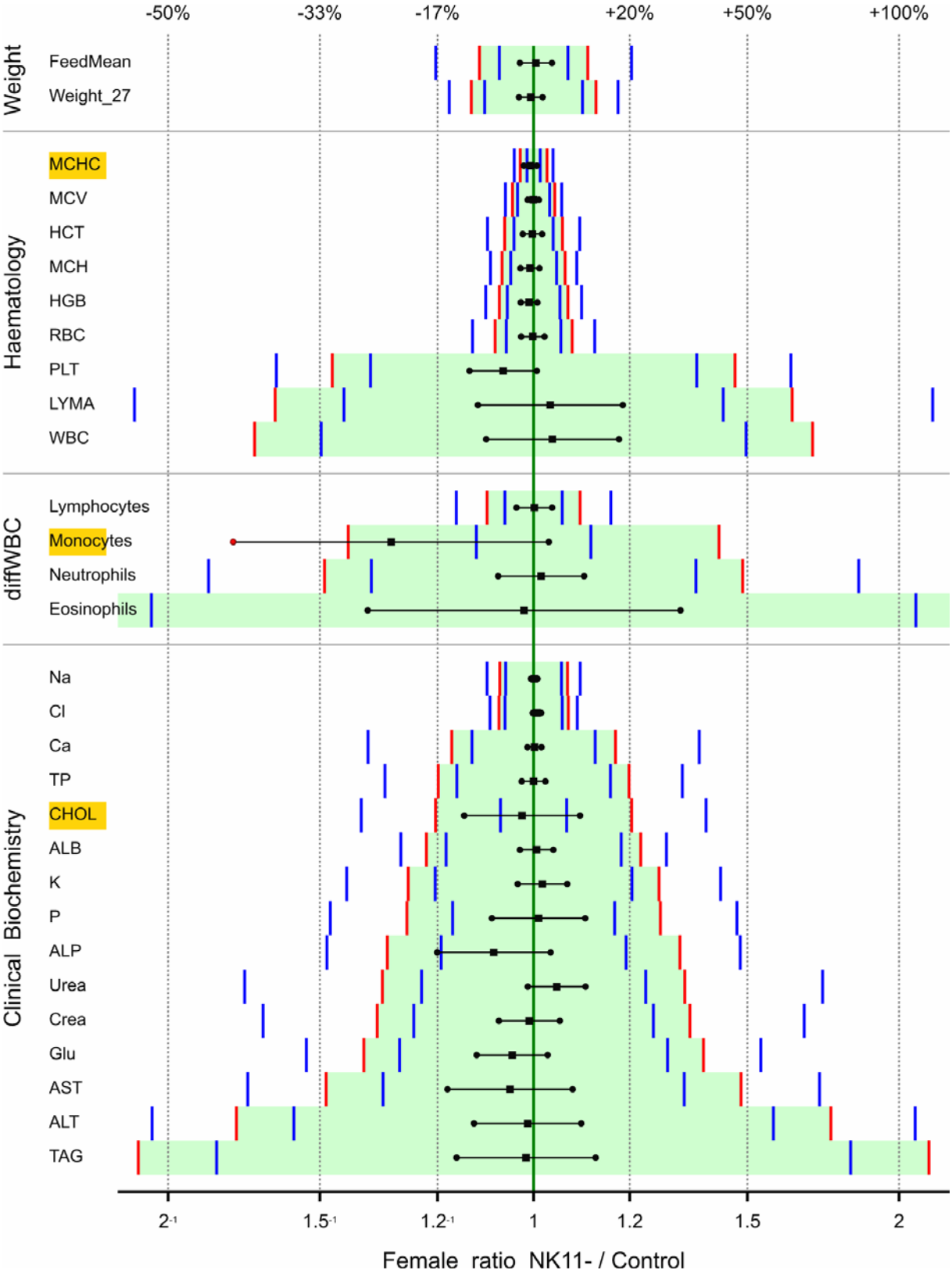

Figure 13 95% confidence intervals for the ratio of NK11- and the Control feed for females with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

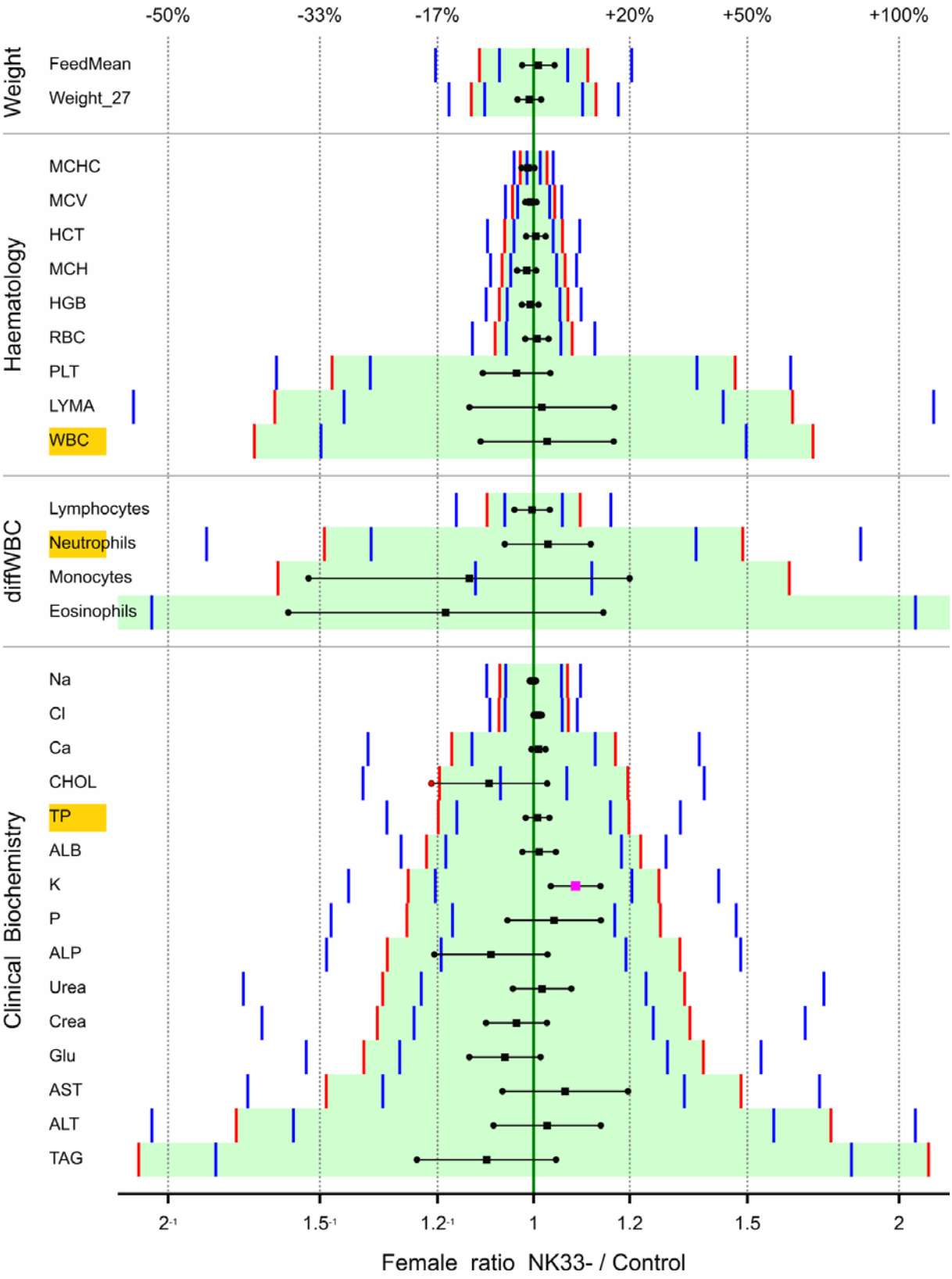

Figure 14 95% confidence intervals for the ratio of NK33- and the Control feed for females with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

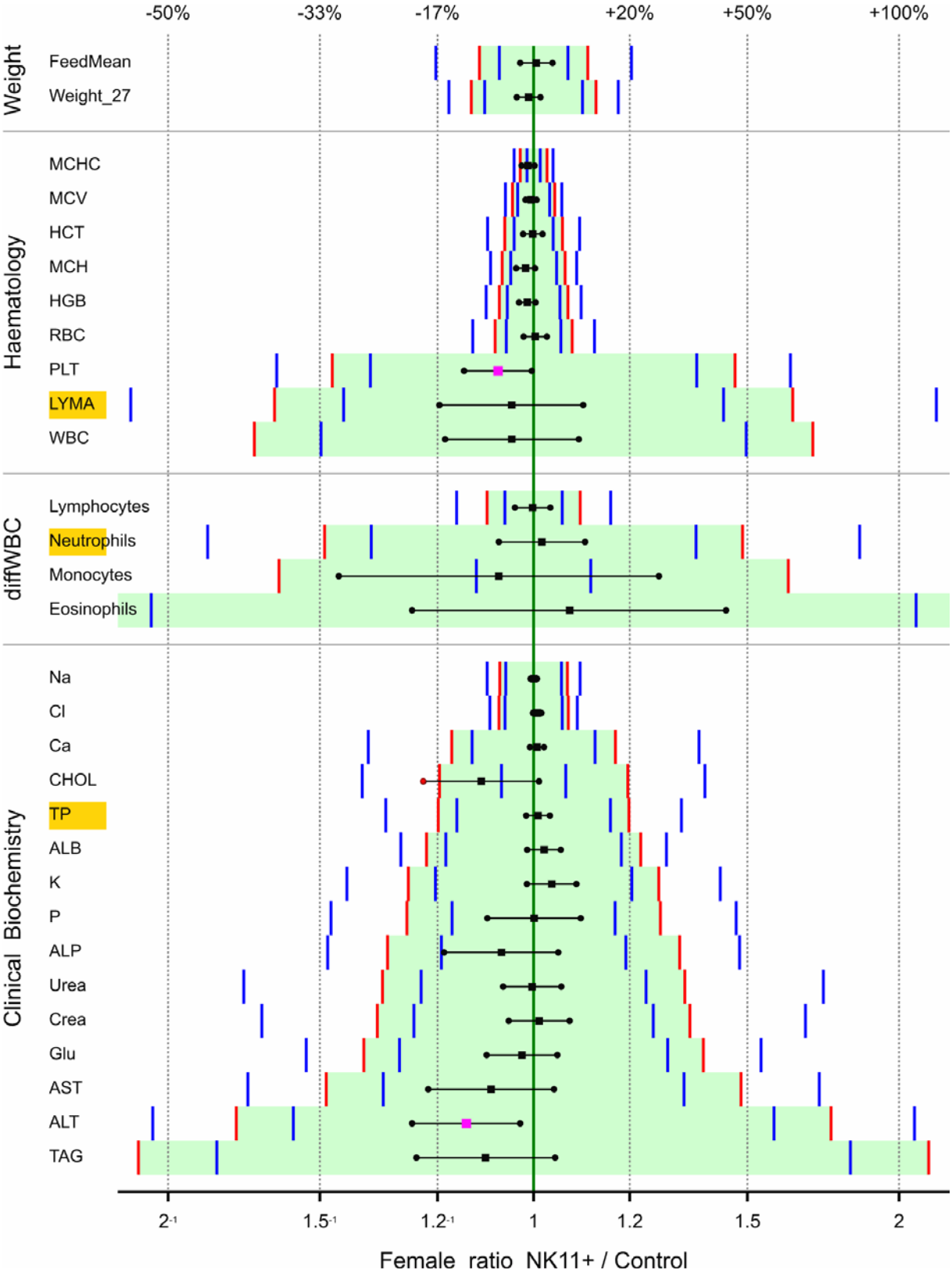

Figure 15 95% confidence intervals for the ratio of NK11+ and the Control feed for females with added intervals for the equivalence limits (blue and red bars, see text). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%).

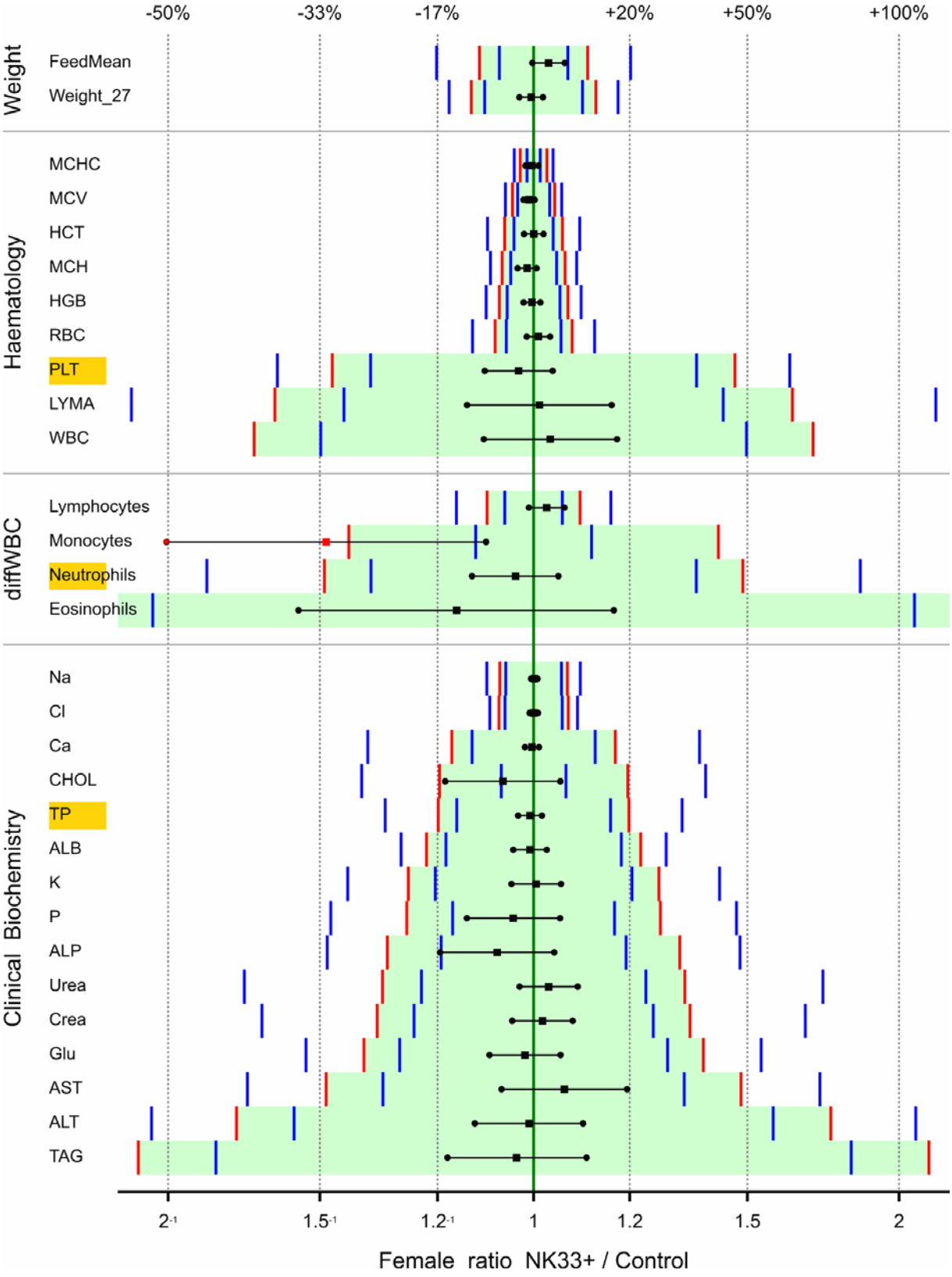

Figure 16 95% confidence intervals for the ratio of NK33+ and the Control feed for females with added intervals for the equivalence limits (blue and red bars, see text).

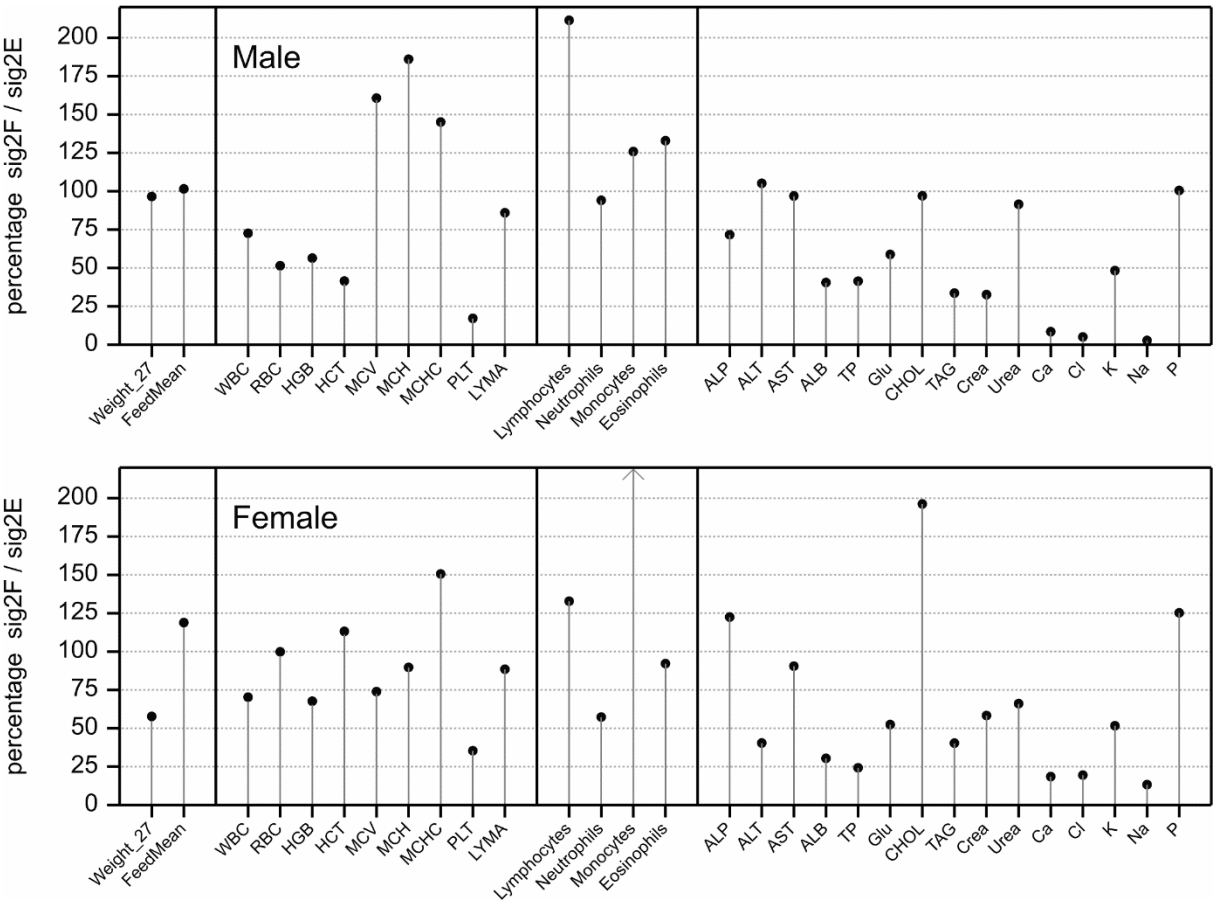

Figure 17 Residual variance (sig2F or σ_F^2) in the current G-TwYST A study as a percentage of the residual variance (sig2E or σ_E^2) in the historical GRACE studies for males (top panel) and females (bottom panel).

3.2 Equivalence testing using target effect sizes

90% confidence intervals for 7 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 a p-value smaller than 0.01 (Table 11).

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_27	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
WBC	0.000	0.047	0.015	0.000	0.000	0.000	0.000	0.000
LYMA	0.000	0.031	0.020	0.001	0.001	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

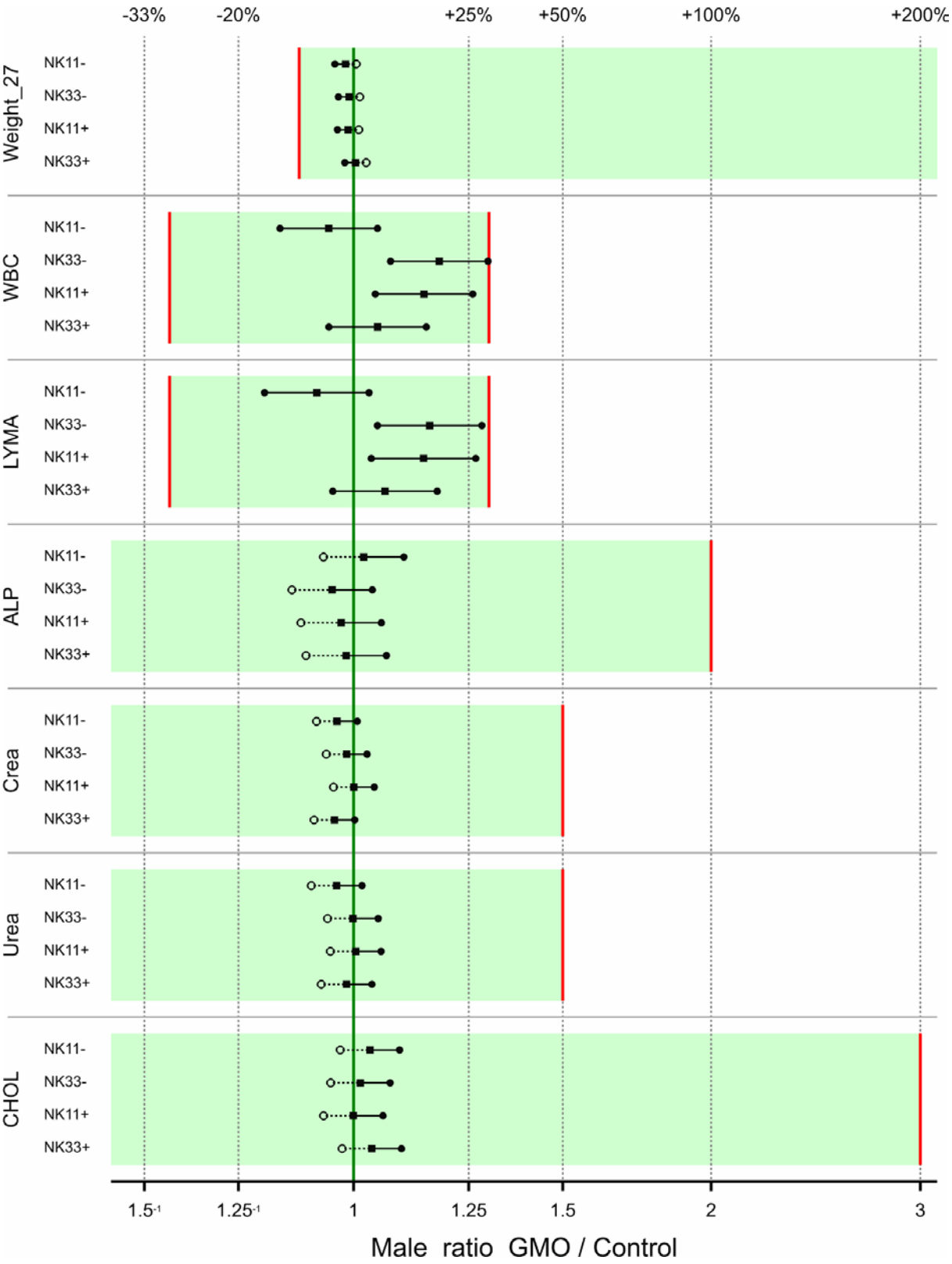

Figure 18 90% confidence intervals for the ratio of the mean of the GMO feed and the control feed for selected variables for males along with equivalence intervals defined by targeted effect sizes of Hong *et al.* (2017).

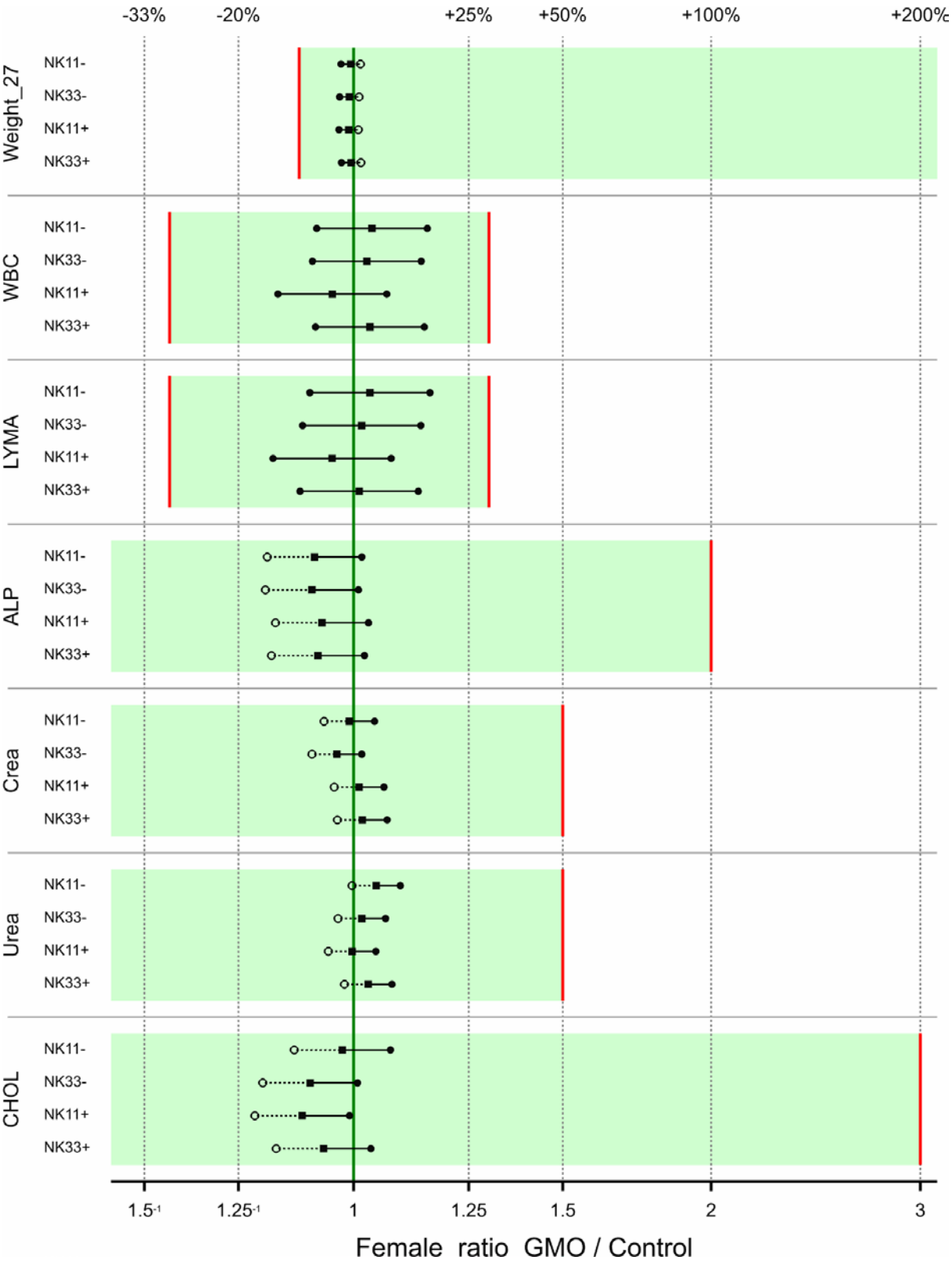

Figure 19 90% confidence intervals for the ratio of the mean of the GMO feed and the control feed for selected variables for females along with equivalence intervals defined by targeted effect sizes of Hong *et al.* (2017).

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 36 variables divided in four 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. For example CVs smaller than 5% are observed for most haematology variables, while CVs larger than 50% are found for Monocytes, Eosinophils, cHGB, uLeu and uKeton. For some variables there is a difference in precision for males and females, e.g. growthRate for males has a CV in the range 10-13%, while for females the range equals 42-61%.

In 20 cases (6.2% of the 320 comparisons) a difference was significant in at least one of the tests at the 5% level. On their own, Dunnett's test resulted in 3 significant differences (0.9%), the t-test resulted in 14 significant differences (4.4%), and Wilcoxon's test resulted in 14 significant differences (4.4%). 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, MCV, PLT) and for females for 5 variables (HGB, MCHC, Eosinophils, BIL and Crea). Levene's test is significant for male variable WBC, and for females for 4 variables (HGB, BIL, Crea, uLeu). 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 significant for FeedMean in males (NK11- and NK33-).

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 40 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 102 out of 320 (32%).

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_27	500.4	6.0	493.3	7.6		497.1	8.0		495.6	7.4		502.9	7.4	
growthRate	1.603	9.7	1.594	10.8		1.604	11.4		1.572	11.3		1.630	12.7	
FeedMean	19.95	3.7	19.58	6.5	w	19.53	6.5	w	19.68	5.9		20.29	6.5	
Haematology	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
WBC	9.12	17.8	8.87	21.9		10.81	17.4	dTw	10.48	17.6	t	9.61	20.1	
RBC	8.459	4.0	8.487	3.7		8.466	3.3		8.451	3.3		8.525	3.0	
HGB	15.65	3.3	15.72	3.6		15.83	3.3		15.63	3.1		15.92	2.7	
HCT	45.84	3.4	46.01	3.1		46.19	3.6		45.63	3.2		46.39	2.7	
MCV	53.96	1.4	54.27	2.7		54.61	2.7		54.03	2.1		54.46	1.8	
MCH	18.52	3.3	18.55	4.4		18.73	3.4		18.52	2.9		18.70	2.8	
MCHC	34.15	1.8	34.16	2.3		34.30	1.8		34.28	2.1		34.33	1.6	
PLT	829.3	5.3	811.8	13.0		871.5	10.1		863.8	7.7		865.3	12.9	
LYMR	71.41	6.3	69.87	7.0		70.55	8.6		71.51	8.5		72.33	5.5	
LYMA	6.518	17.9	6.192	21.6		7.532	17.7	tw	7.467	18.4	t	6.985	23.9	
diffWBC	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
Lymphocytes	69.65	7.5	70.80	6.4		68.72	7.7		70.05	9.3		71.34	6.1	
Neutrophils	26.95	18.0	26.14	15.4		27.43	19.3		26.33	22.0		25.11	15.9	
Monocytes	1.200	40.9	0.899	43.7	tw	1.100	46.9		0.987	50.3	tw	1.025	35.3	
Eosinophils	2.200	54.5	2.161	60.4		2.750	45.3		2.638	62.6		2.525	33.5	
ClinChem	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
ALP	1.386	21.7	1.442	24.8		1.336	22.8		1.352	17.6		1.371	24.5	
ALT	0.679	12.7	0.695	23.4		0.703	21.8		0.675	17.8		0.691	14.5	
AST	2.092	19.7	2.154	19.4		2.253	18.6		2.154	15.0		2.111	14.8	

BIL	7.325	17.5	7.543	19.8		8.338	25.8	t	7.985	20.2		7.830	16.4	w
ALB	35.04	3.5	34.99	3.8		35.26	3.8		35.22	3.8		35.20	3.8	
TP	64.58	3.1	64.28	2.5		64.40	2.7		65.00	2.3		64.37	2.8	
Glu	5.944	13.7	5.785	13.5		5.869	12.7		6.040	12.8		6.192	9.2	
CHOL	2.204	12.2	2.264	10.1		2.235	12.7		2.207	12.4		2.289	13.3	
TAG	1.239	40.0	1.293	37.4		1.334	35.4		1.387	38.1	tw	1.296	33.5	
Crea	42.27	8.7	40.97	9.2		41.83	9.5		42.37	8.3		40.77	9.2	
Urea	5.160	11.8	5.017	14.9		5.161	11.5		5.190	11.5		5.099	10.0	
cHGB	63.62	36.3	82.37	72.0		84.32	58.1		82.55	49.2		72.22	43.6	
Ca	2.524	1.7	2.521	1.9		2.538	2.2		2.535	2.2		2.521	1.9	
Cl	101.7	1.3	101.7	1.4		101.2	1.4		101.5	1.2		101.5	1.2	
K	5.057	6.3	5.167	11.5		5.245	8.7		5.325	9.0	t	5.132	7.1	
Na	143.5	1.3	143.8	1.6		143.6	1.2		143.7	1.2		143.0	1.0	
P	2.042	12.6	1.991	13.5		2.051	9.6		2.088	10.1		2.017	9.0	
Urine	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
uVol	20.50	18.6	21.40	13.3		16.75	31.4	t	18.95	30.1		21.35	21.8	
uVolW	4.162	20.2	4.379	14.0		3.381	27.0		3.951	34.8		4.302	20.7	
uLeu	42.50	69.6	32.50	68.3		80.00	102.1		57.50	133.7		38.75	59.8	
uOsmoll	420.2	20.1	379.1	15.2		520.8	24.7		466.4	29.0		405.0	20.9	
uKeton	0.725	131.5	0.475	100.6		0.725	73.5		0.475	114.9		0.325	145.3	
upH	6.825	4.9	6.725	3.3		6.725	2.7		6.850	3.1		6.675	5.3	

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_27	271.8	7.0	270.2	7.0		269.5	6.4		269.3	7.7		270.6	7.2	
growthRate	0.587	42.0	0.620	50.5		0.553	61.3		0.549	58.2		0.606	50.8	
FeedMean	14.22	6.1	14.30	8.3		14.36	7.3		14.31	7.9		14.65	8.0	
Haematology	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
WBC	5.865	23.1	5.968	15.8		6.120	27.9		5.590	22.6		6.050	21.5	
RBC	7.657	3.9	7.641	3.2		7.707	3.9		7.678	2.5		7.725	3.6	
HGB	15.58	2.8	15.42	3.4		15.48	1.9		15.39	1.9		15.53	2.6	
HCT	44.14	3.5	44.02	3.3		44.31	2.3		44.05	2.0		44.15	3.2	
MCV	57.68	1.7	57.64	1.6		57.39	2.0		57.41	1.4		57.19	1.7	
MCH	20.37	2.5	20.22	2.6		20.11	3.4		20.07	2.5		20.12	3.2	
MCHC	35.31	2.1	35.08	2.2		34.93	1.2		34.94	1.7		35.20	2.5	
PLT	842.8	9.7	793.9	7.9		812.1	8.4		786.2	11.7	t	819.3	14.3	
LYMR	72.35	5.4	71.22	5.7		71.64	7.3		72.19	5.4		71.13	7.4	
LYMA	4.207	20.3	4.262	17.6		4.348	27.8		4.033	23.4		4.282	24.2	
diffWBC	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
Lymphocytes	67.67	6.3	67.46	6.4		67.40	5.8		67.45	5.2		69.30	6.5	
Neutrophils	28.97	14.7	29.54	13.8		29.61	14.0		29.26	12.9		27.91	15.5	
Monocytes	1.125	53.7	0.851	75.4		1.012	60.7		0.938	38.6		0.662	59.1	dW
Eosinophils	2.238	33.9	2.213	38.7		1.975	49.6		2.337	33.0		2.125	58.0	
ClinChem	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
ALP	0.649	19.8	0.609	22.7		0.626	26.3		0.616	20.9		0.613	25.4	
ALT	0.623	22.4	0.615	20.4		0.639	18.6		0.548	18.1	tw	0.610	15.1	
AST	1.954	18.3	1.841	18.5		2.107	26.8		1.814	16.4	w	2.086	19.1	

BIL	8.365	14.4	8.342	9.3		8.755	23.0		8.242	18.2		8.355	15.7	
ALB	41.51	4.6	41.82	5.4		42.03	7.0		42.41	6.0		41.28	6.5	
TP	69.58	3.7	69.67	3.9		70.18	5.0		70.21	3.9		69.10	3.4	
Glu	5.545	12.1	5.370	14.1		5.261	11.5		5.448	13.6		5.485	13.6	
CHOL	2.225	19.0	2.164	18.9		2.063	20.2		2.012	15.7		2.100	16.6	
TAG	0.824	29.1	0.846	47.6		0.744	23.4		0.743	27.5	w	0.781	24.0	
Crea	43.26	16.8	42.52	11.4		41.53	9.3		43.70	15.5		43.51	8.0	
Urea	5.523	10.0	5.765	9.3		5.636	9.8		5.497	7.6		5.679	8.6	
cHGB	75.15	29.5	77.00	20.7		92.51	61.1		84.84	62.7		71.78	24.5	
Ca	2.533	1.8	2.537	2.8		2.557	2.8		2.550	2.6		2.525	2.0	
Cl	101.2	1.6	101.8	1.4		101.9	1.6		101.8	1.5		101.2	1.8	
K	4.175	7.7	4.218	6.8		4.560	12.6	DW	4.318	7.2		4.192	8.3	
Na	142.4	1.6	142.4	1.4		142.2	1.4		142.4	1.4		142.5	1.5	
P	1.344	16.0	1.331	17.1		1.407	18.2		1.350	19.0		1.289	12.0	
Urine	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
uVol	16.75	23.6	16.80	35.7		20.45	27.4		17.75	35.3		13.00	22.9	
uVolW	6.343	25.0	6.233	31.9		7.675	30.0		6.594	34.4		4.922	22.6	w
uLeu	16.25	102.9	26.25	129.8		15.00	129.1		12.50	124.7		16.25	89.2	
uOsmoll	380.6	25.9	409.1	32.1		326.8	25.5		404.4	47.7		448.4	24.0	
uKeton	0.200	184.5	0.250	182.6		0.225	133.0		0.125	194.4		0.125	194.4	
upH	6.375	2.8	6.250	4.2		6.525	3.4		6.325	5.9		6.300	2.5	

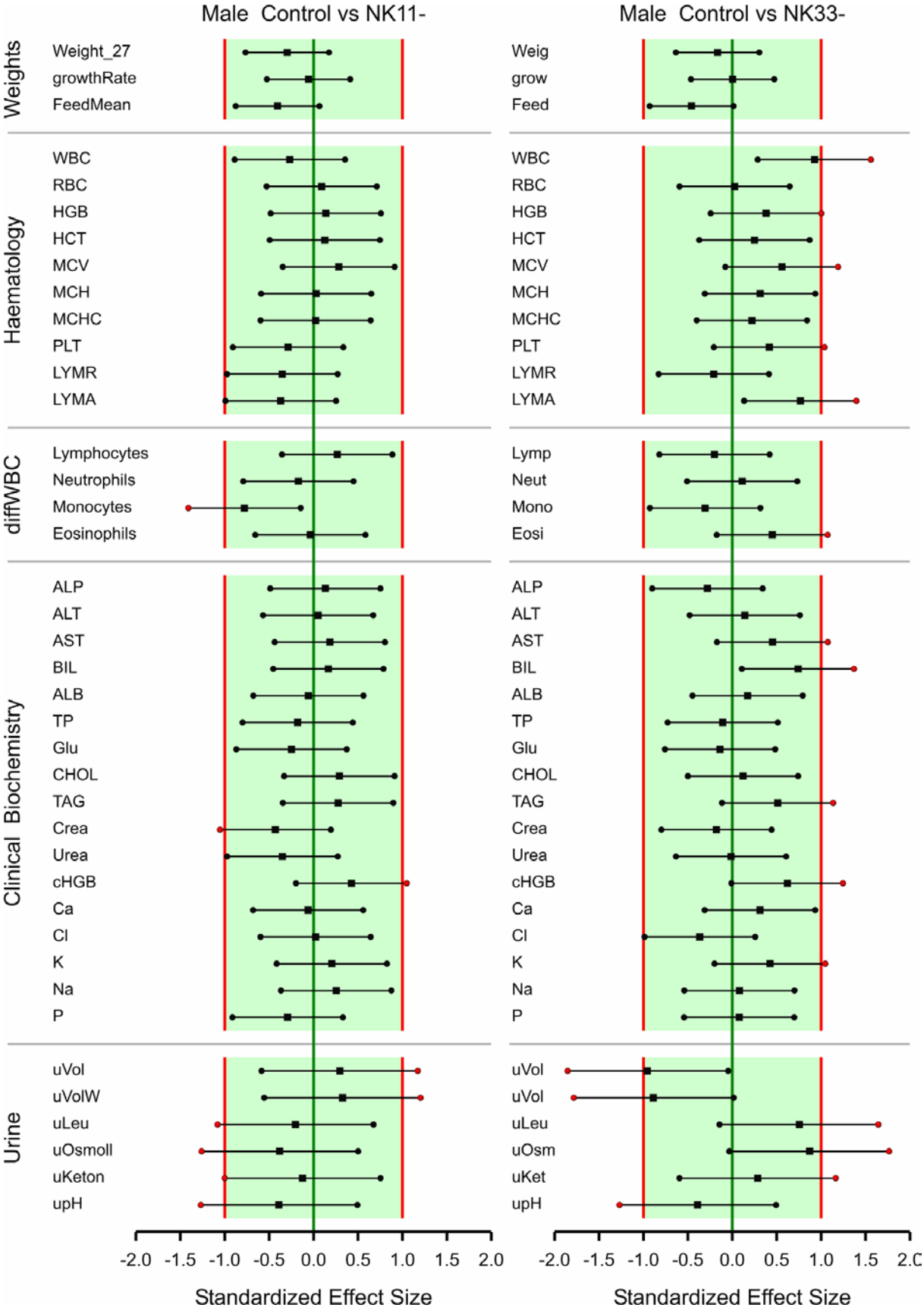

Figure 20 Confidence intervals for Standardized Effect Sized (SES) for male rats for GMO feeds NK11- and NK33- versus the control feed.

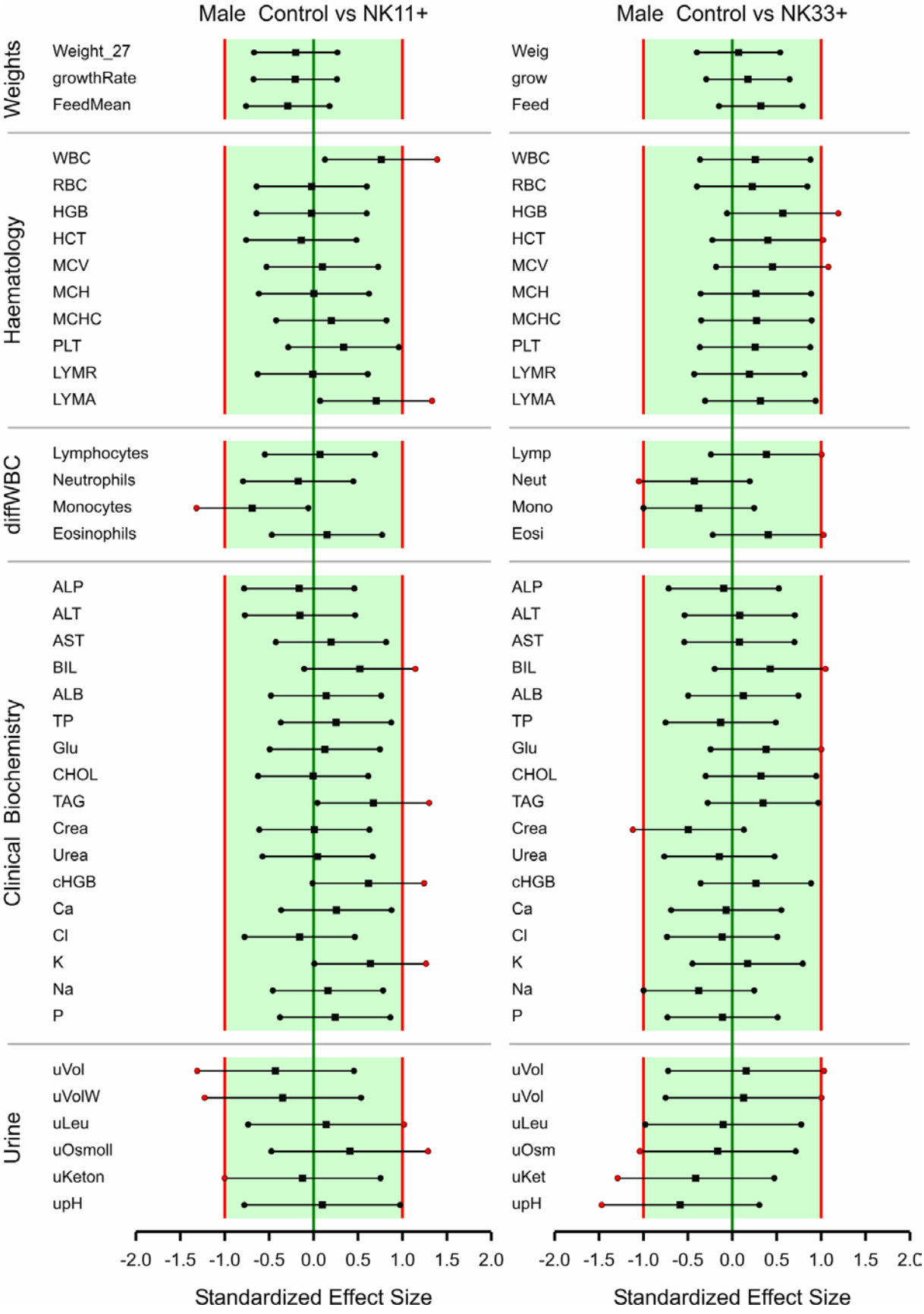

Figure 21 Confidence intervals for Standardized Effect Sized (SES) for male rats for GMO feeds NK11+ and NK33+ versus the control feed.

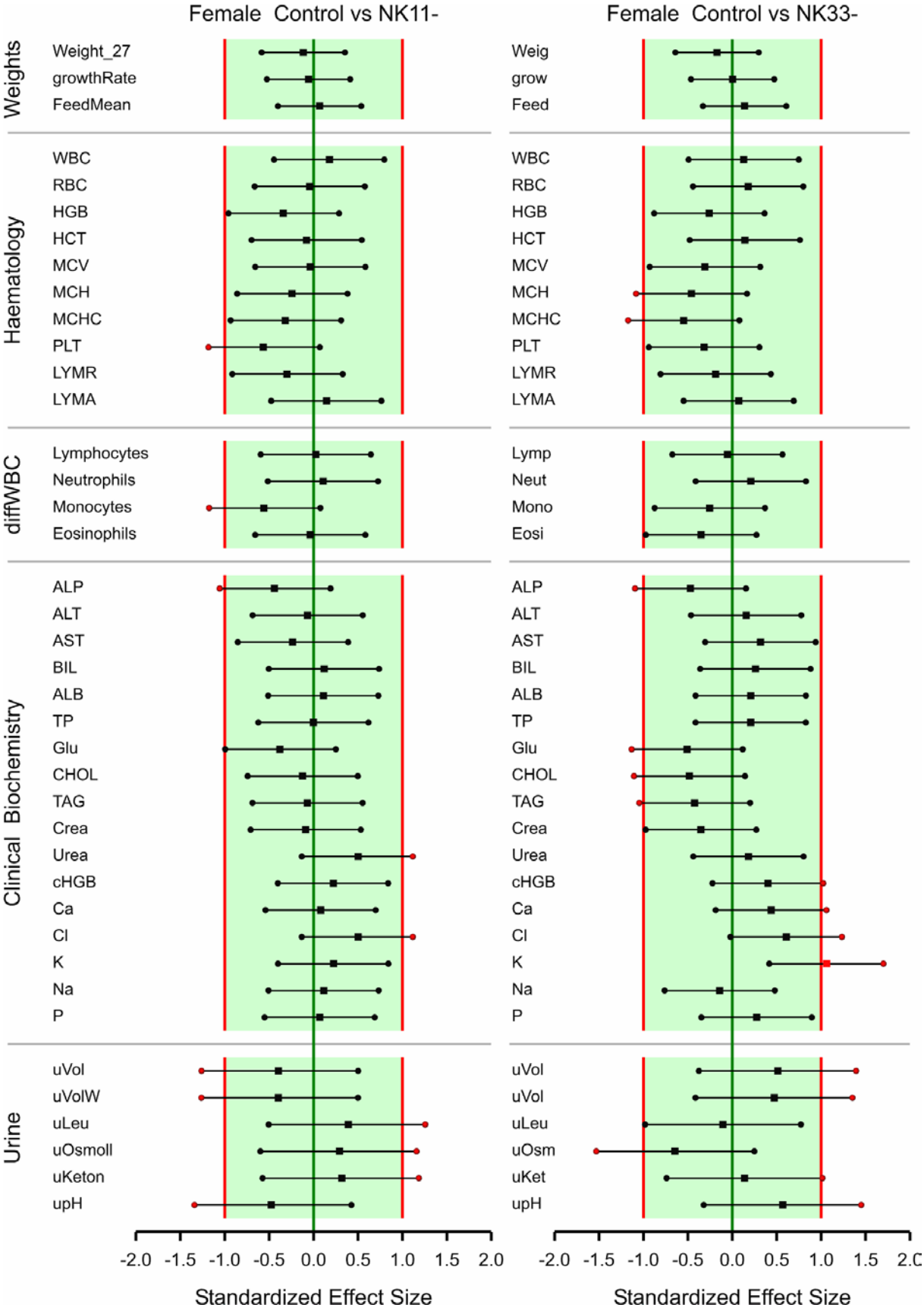

Figure 22 Confidence intervals for Standardized Effect Sized (SES) for female rats for GMO feeds NK11- and NK33- versus the control feed.

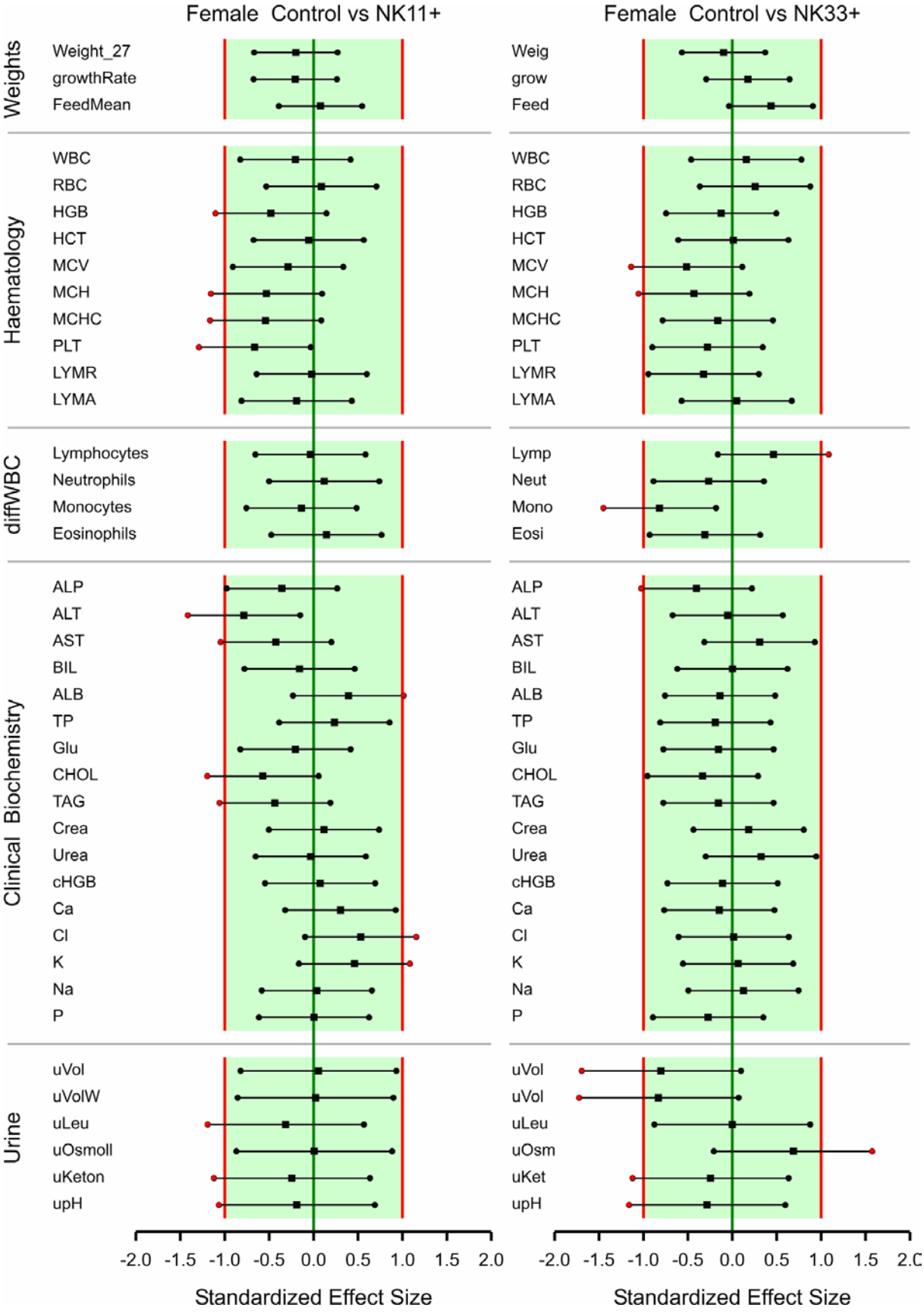

Figure 23 Confidence intervals for Standardized Effect Sized (SES) for female rats for GMO feeds NK11+ and NK33+ versus the control feed.

3.5 Factorial analysis

The significance results from fitting the factorial model to the 40 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 Monocytes. The main GMO effect was significant for males, while the interaction is significant for females. The mean of the four GM feeds had a value which is 82% of the control non-GM feed; note however that in this case there was also a slight indication of a GM inclusion rate effect (p=0.083). For Monocytes in females the effect of GM inclusion rate was positive for GM feeds without Roundup, while it was negative for GM feeds with Roundup. The only main significant GM inclusion rate effect larger than 10% was observed for AST in females. None of the significant Roundup main effects was larger than 10%.

The p-values in Table 14 can be summarized as follows. In 1 out of 80 cases (1.2%) there was a significant difference at the 5% level between the mean of the GM feeds and the non-GM feed. In 10 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 70 cases, i.e. where the interaction is not significant, there were 2 cases (2.9%) with a significant differences between GM inclusion rates, and 3 cases (4.3%) 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_27	0.433	0.234	0.329	0.677	0.440	0.890	0.976	0.642
growthRate	0.912	0.191	0.948	0.342	0.916	0.909	0.833	0.162
FeedMean	0.272	0.100	0.009	0.051	0.342	0.205	0.365	0.397
Haematology	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
WBC	0.097	0.126	0.419	0.000	0.792	0.472	0.421	0.348
RBC	0.750	0.685	0.850	0.489	0.626	0.368	0.629	0.900
HGB	0.290	0.066	0.950	0.438	0.219	0.315	0.993	0.535
HCT	0.525	0.142	0.797	0.355	0.986	0.507	0.812	0.723
MCV	0.167	0.163	0.516	0.862	0.242	0.260	0.301	0.923
MCH	0.542	0.224	0.871	0.961	0.091	0.794	0.556	0.474
MCHC	0.476	0.545	0.611	0.778	0.111	0.732	0.710	0.170
PLT	0.471	0.166	0.300	0.083	0.065	0.149	0.896	0.759
LYMR	0.706	0.439	0.100	0.896	0.397	0.662	0.748	0.347
LYMA	0.160	0.098	0.166	0.001	0.939	0.698	0.415	0.475
diffWBC	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
Lymphocytes	0.605	0.731	0.386	0.085	0.686	0.338	0.296	0.190
Neutrophils	0.510	0.949	0.229	0.233	0.861	0.514	0.291	0.269
Monocytes	0.034	0.083	0.969	0.722	0.074	0.390	0.743	0.027
Eosinophils	0.335	0.102	0.750	0.603	0.571	0.083	0.605	0.747
ClinChem	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
ALP	0.685	0.441	0.805	0.288	0.090	0.866	0.725	0.968
ALT	0.903	0.465	0.560	0.743	0.445	0.031	0.038	0.248
AST	0.364	0.732	0.424	0.391	0.970	0.004	0.656	0.687
BIL	0.067	0.286	0.928	0.139	0.821	0.487	0.224	0.969
ALB	0.706	0.630	0.736	0.580	0.560	0.326	0.885	0.154
TP	0.869	0.487	0.363	0.311	0.801	0.626	0.714	0.148
Glu	0.905	0.416	0.049	0.752	0.204	0.856	0.229	0.684
CHOL	0.468	0.722	0.836	0.269	0.125	0.786	0.500	0.177
TAG	0.075	0.839	0.605	0.213	0.268	0.869	0.825	0.151
Crea	0.276	0.576	0.786	0.095	0.883	0.658	0.091	0.453
Urea	0.643	0.742	0.556	0.242	0.322	0.927	0.374	0.126
cHGB	0.057	0.726	0.719	0.226	0.550	0.996	0.135	0.407
Ca	0.662	0.913	0.890	0.122	0.492	0.837	0.412	0.068
Cl	0.540	0.442	0.872	0.338	0.093	0.352	0.200	0.159
K	0.153	0.584	0.685	0.130	0.067	0.312	0.086	0.006
Na	0.905	0.115	0.222	0.418	0.891	0.707	0.661	0.432
P	0.935	0.969	0.437	0.110	0.940	0.873	0.166	0.271
Urine	GMO	InclRate	Roundup	Interact	GMO	InclRate	Roundup	Interact
uVol	0.513	0.301	0.545	0.006	0.643	0.938	0.159	0.006
uVolW	0.583	0.250	0.592	0.011	0.590	0.982	0.150	0.007
uLeu	0.679	0.265	0.424	0.065	0.981	0.769	0.328	0.189
uOsmoll	0.607	0.290	0.701	0.006	0.803	0.676	0.090	0.011
uKeton	0.793	0.845	0.277	0.277	0.978	0.771	0.126	0.771
upH	0.375	0.287	0.646	0.287	0.780	0.125	0.352	0.067

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	FeedMean	-	-	1.02	-	-	-	-
Haematology	WBC	-	-	-	1.00	1.24	1.20	1.10
Haematology	LYMA	-	-	-	1.00	1.24	1.23	1.14
diffWBC	Monocytes	0.82	-	-	-	-	-	-
ClinChem	Glu	-	-	1.05	-	-	-	-
Urine	uVol	-	-	-	1.00	0.75	0.85	0.97
Urine	uVolW	-	-	-	1.00	0.75	0.85	0.95
Urine	uOsmoll	-	-	-	1.00	1.32	1.19	1.05

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+
diffWBC	Monocytes	-	-	-	1.00	1.16	1.22	0.88
ClinChem	ALT	-	1.08	0.93	-	-	-	-
ClinChem	AST	-	1.13	-	-	-	-	-
ClinChem	K	-	-	-	1.00	1.06	1.02	0.99
Urine	uVol	-	-	-	1.00	1.32	1.15	0.88
Urine	uVolW	-	-	-	1.00	1.30	1.14	0.88
Urine	uOsmoll	-	-	-	1.00	0.78	0.93	1.11

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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.

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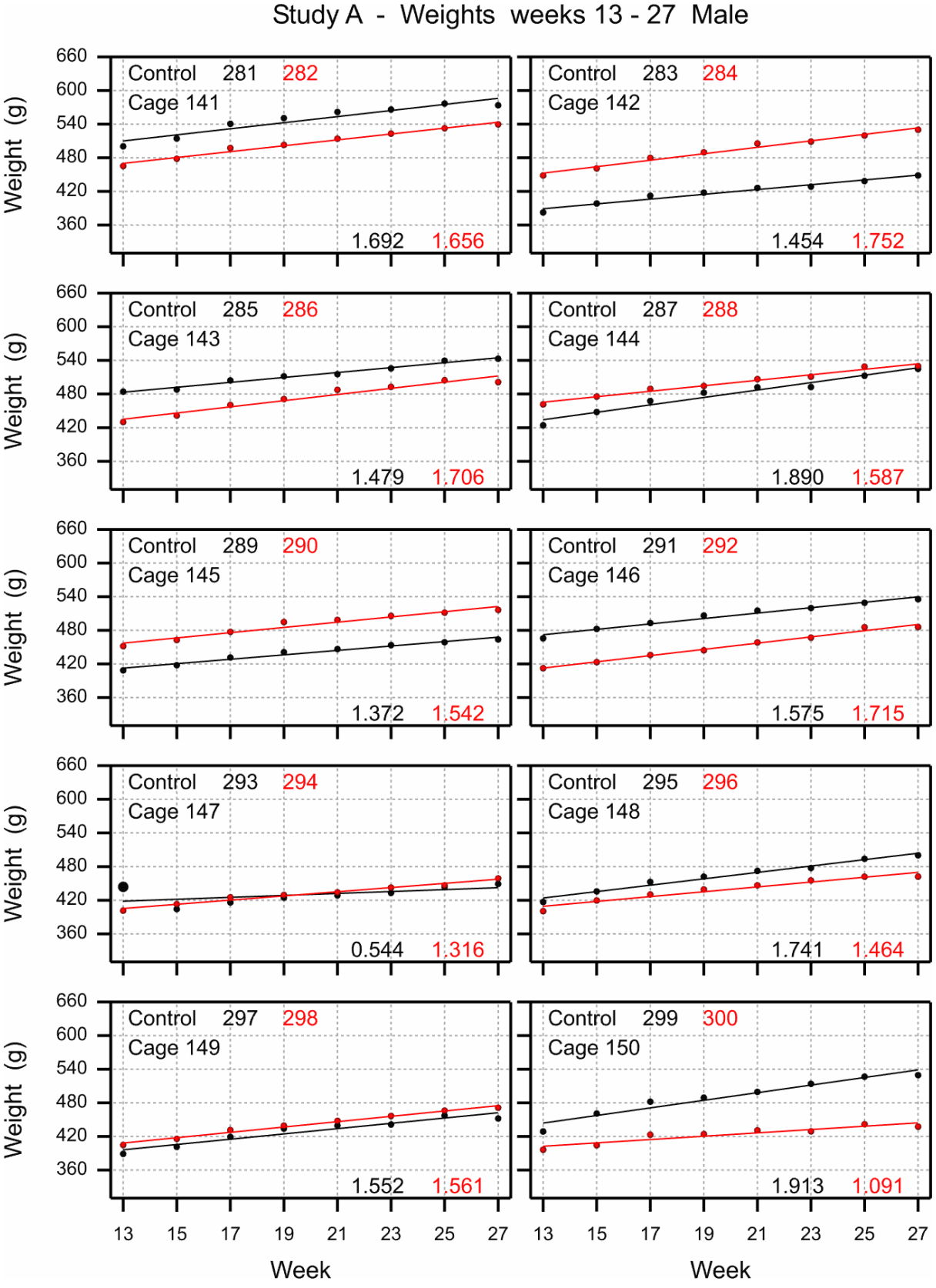
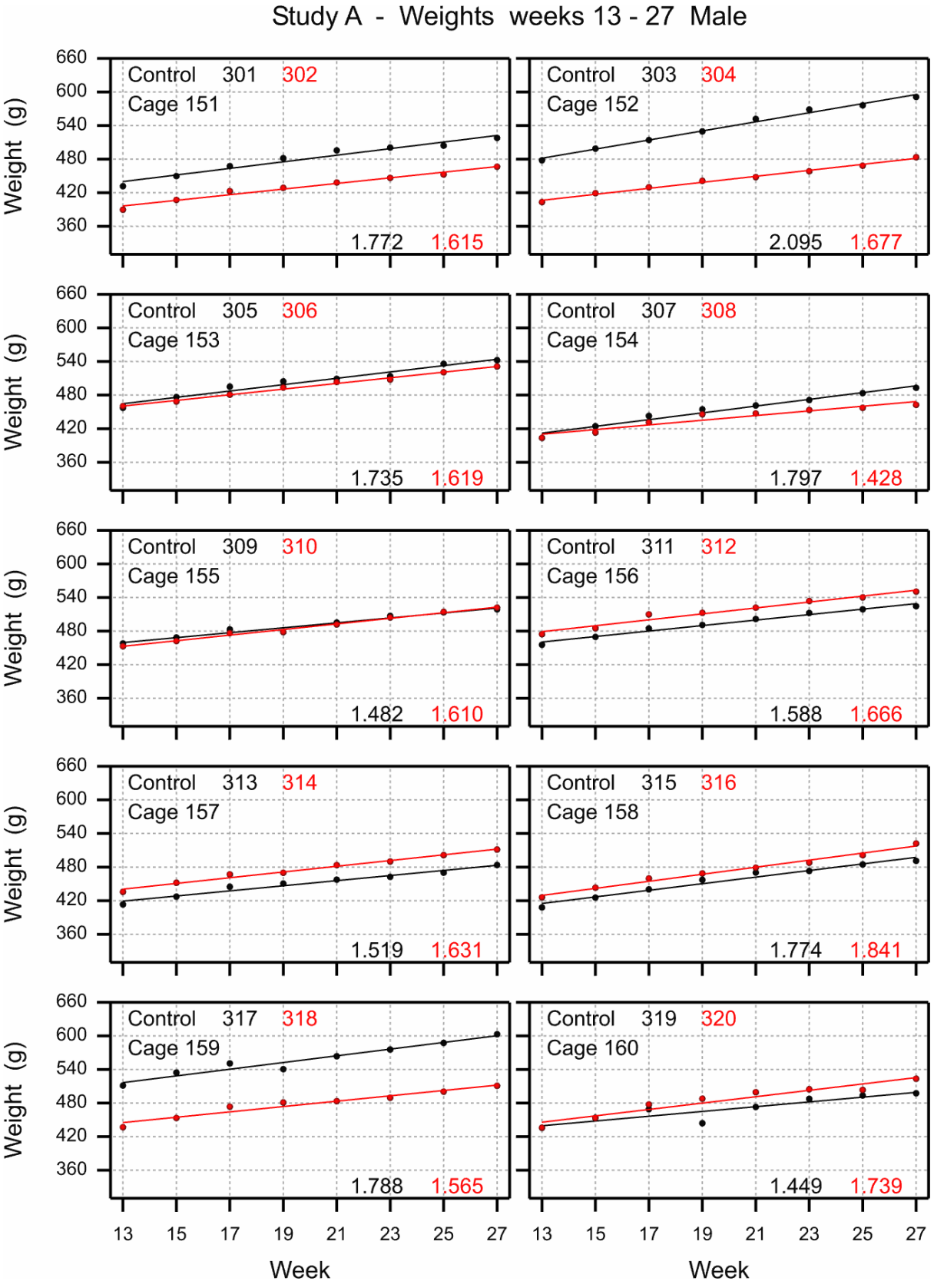
Appendix 1. Growth curves per animal pair

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.



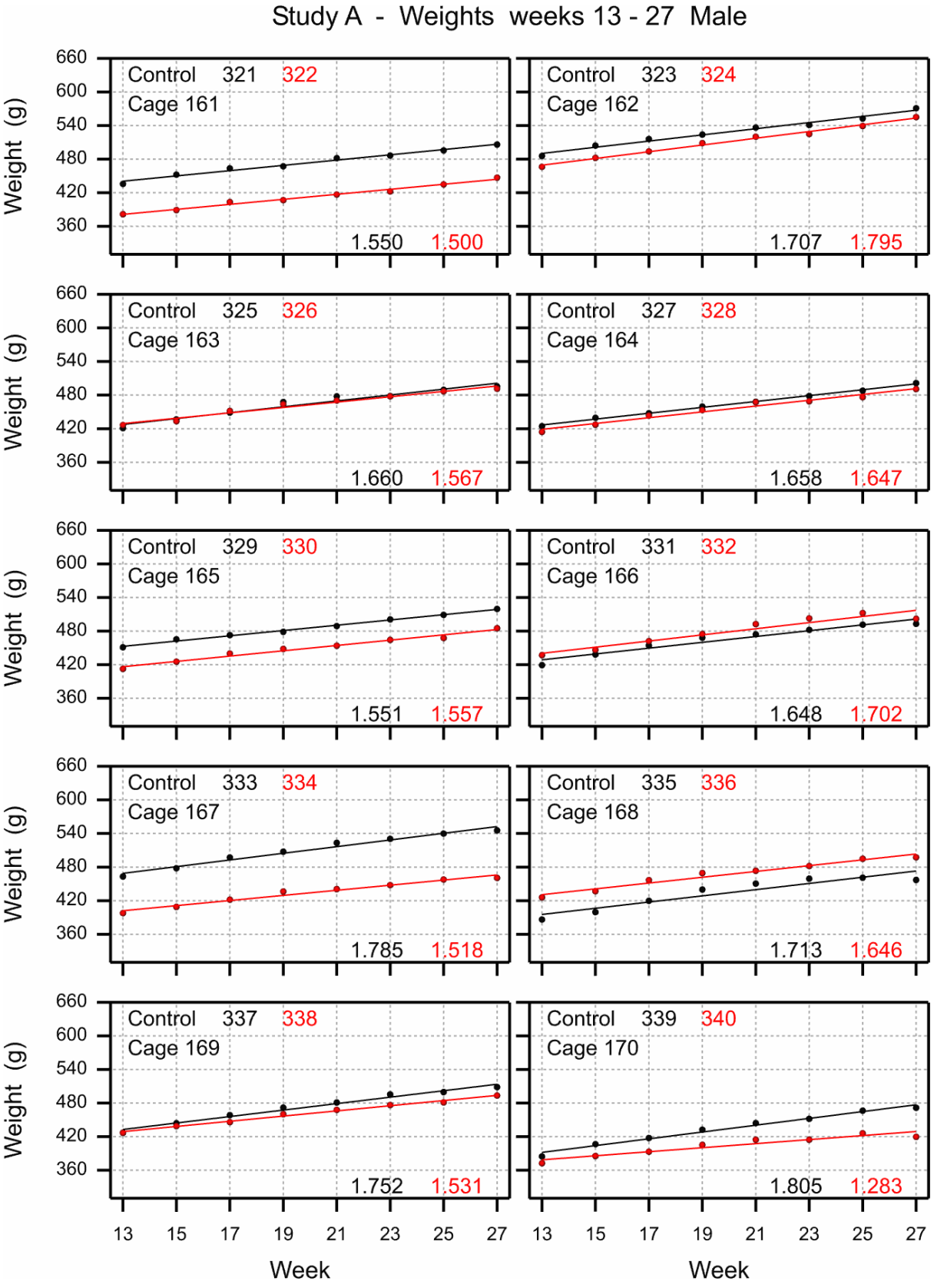
Appendix 1. Growth curves per animal pair (continued)

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.



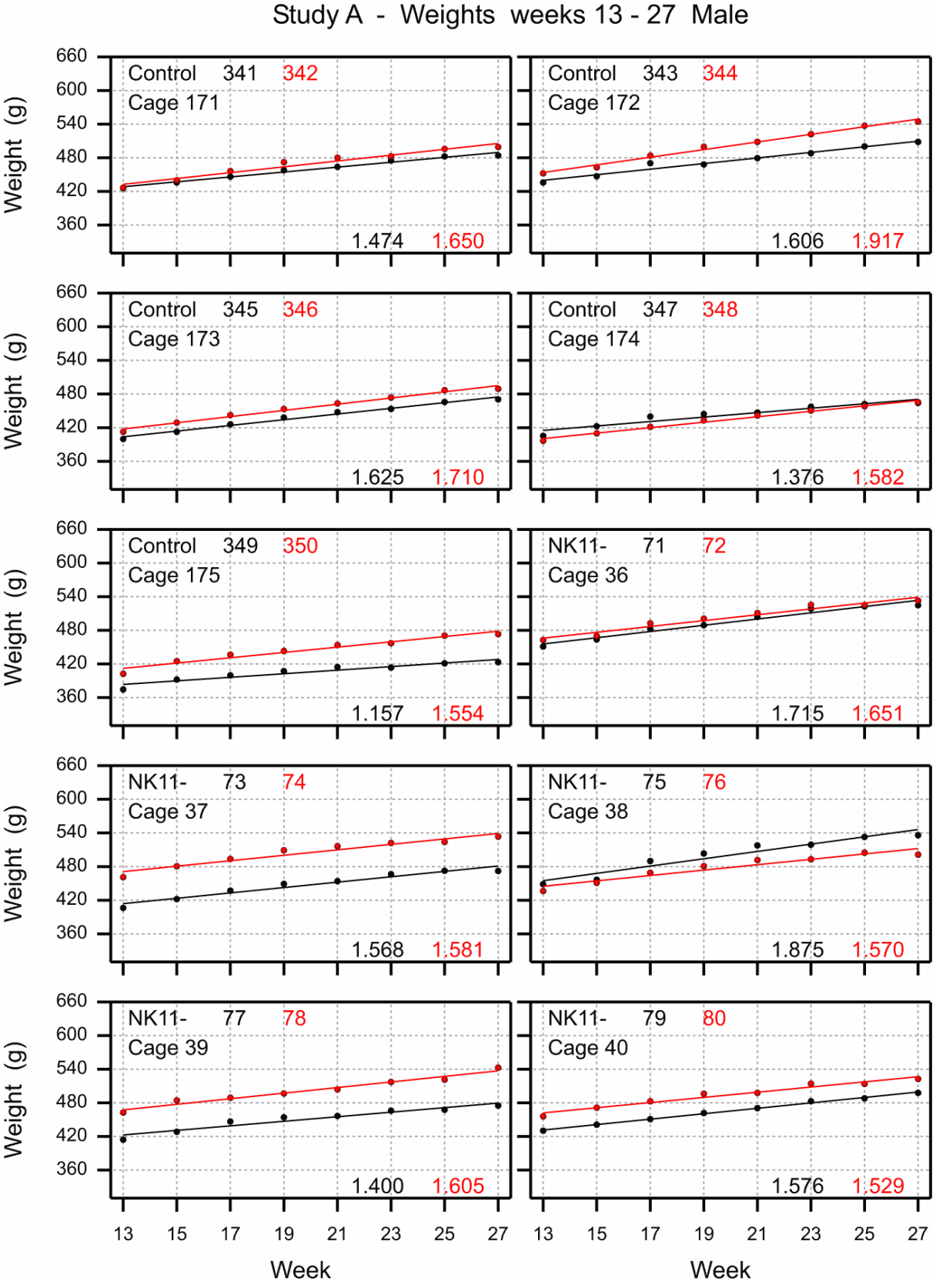
Appendix 1. Growth curves per animal pair (continued)

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.



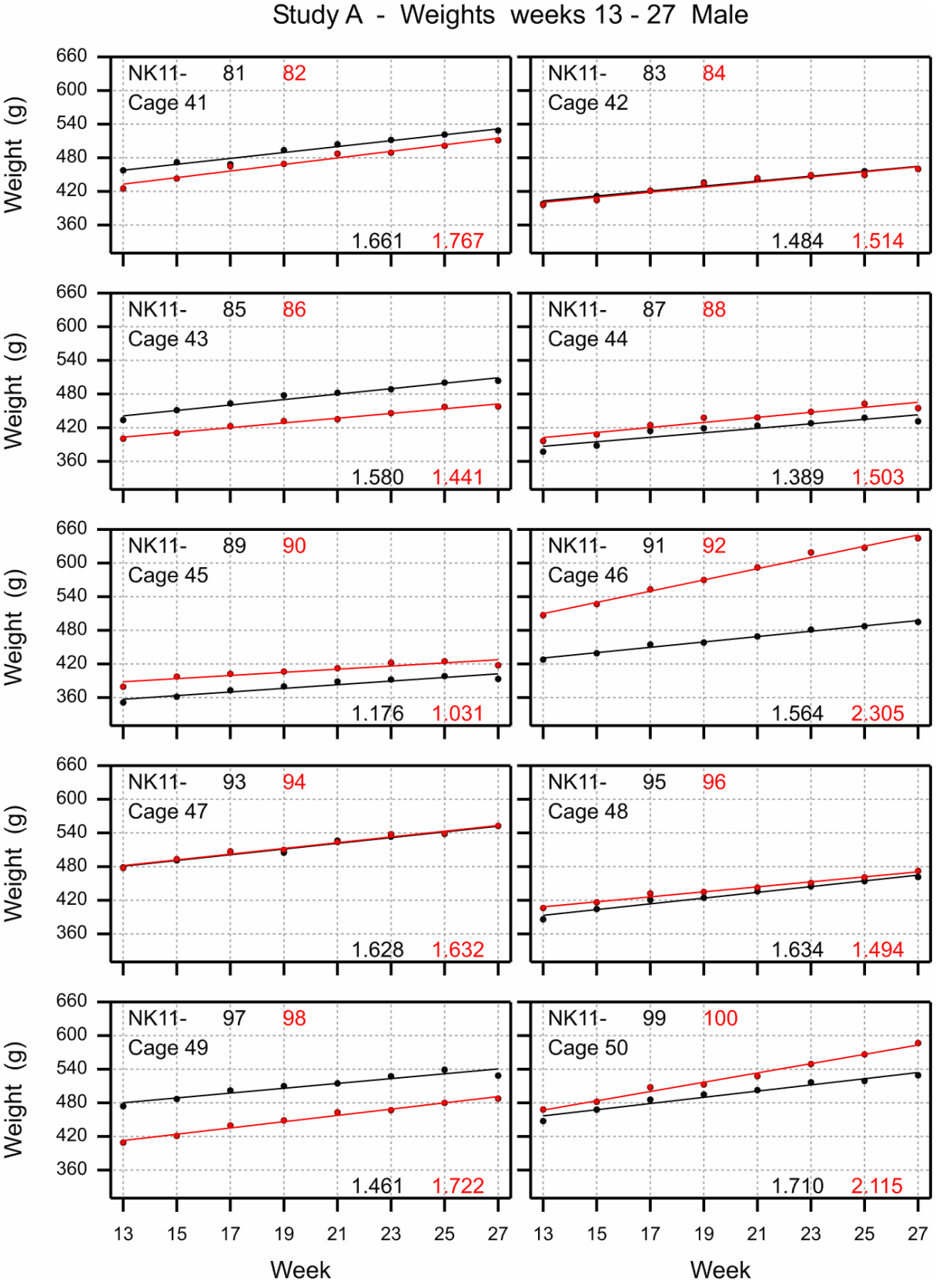
Appendix 1. Growth curves per animal pair (continued)

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.



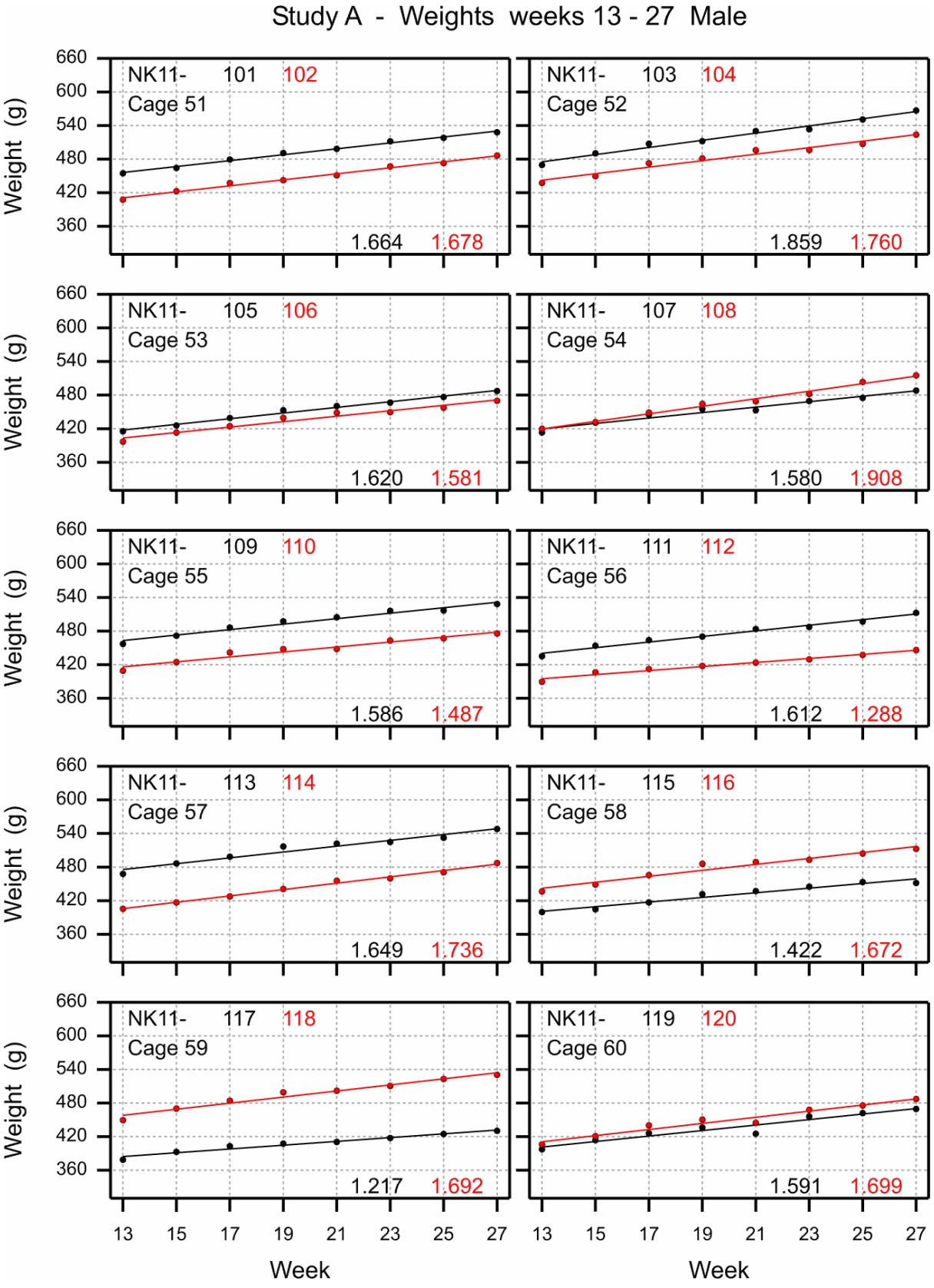
Appendix 1. Growth curves per animal pair (continued)

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.



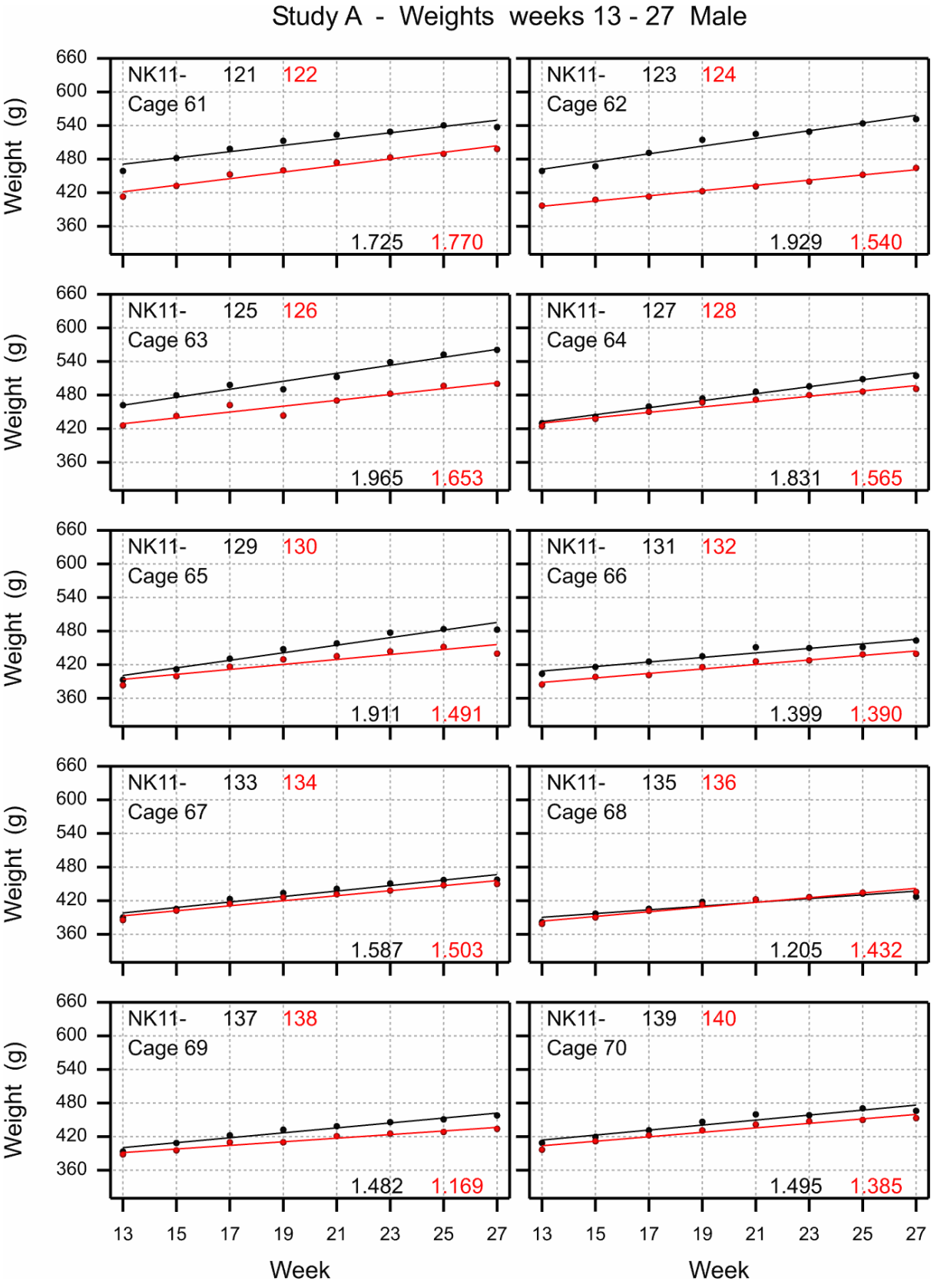
Appendix 1. Growth curves per animal pair (continued)

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.



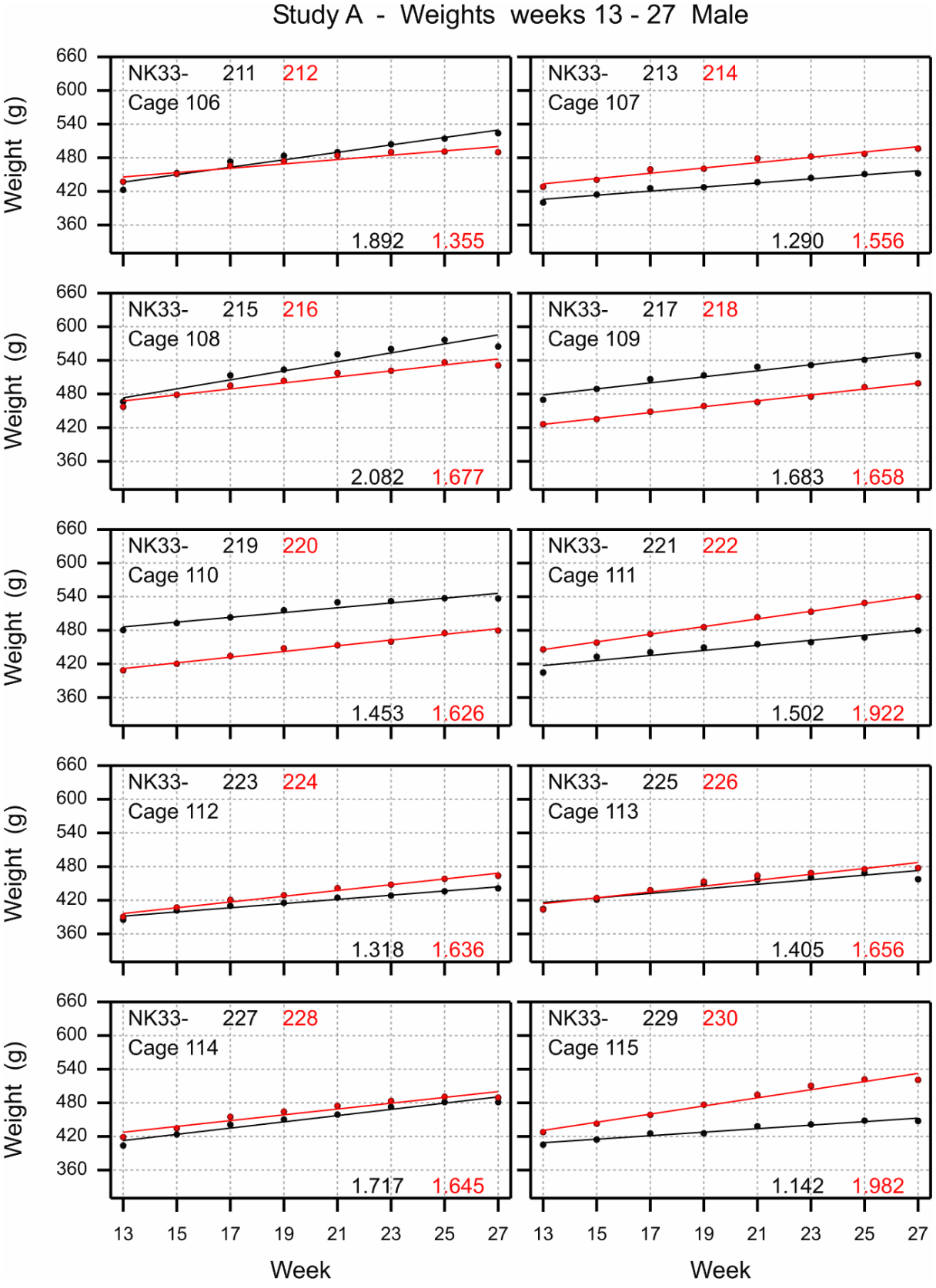
Appendix 1. Growth curves per animal pair (continued)

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.



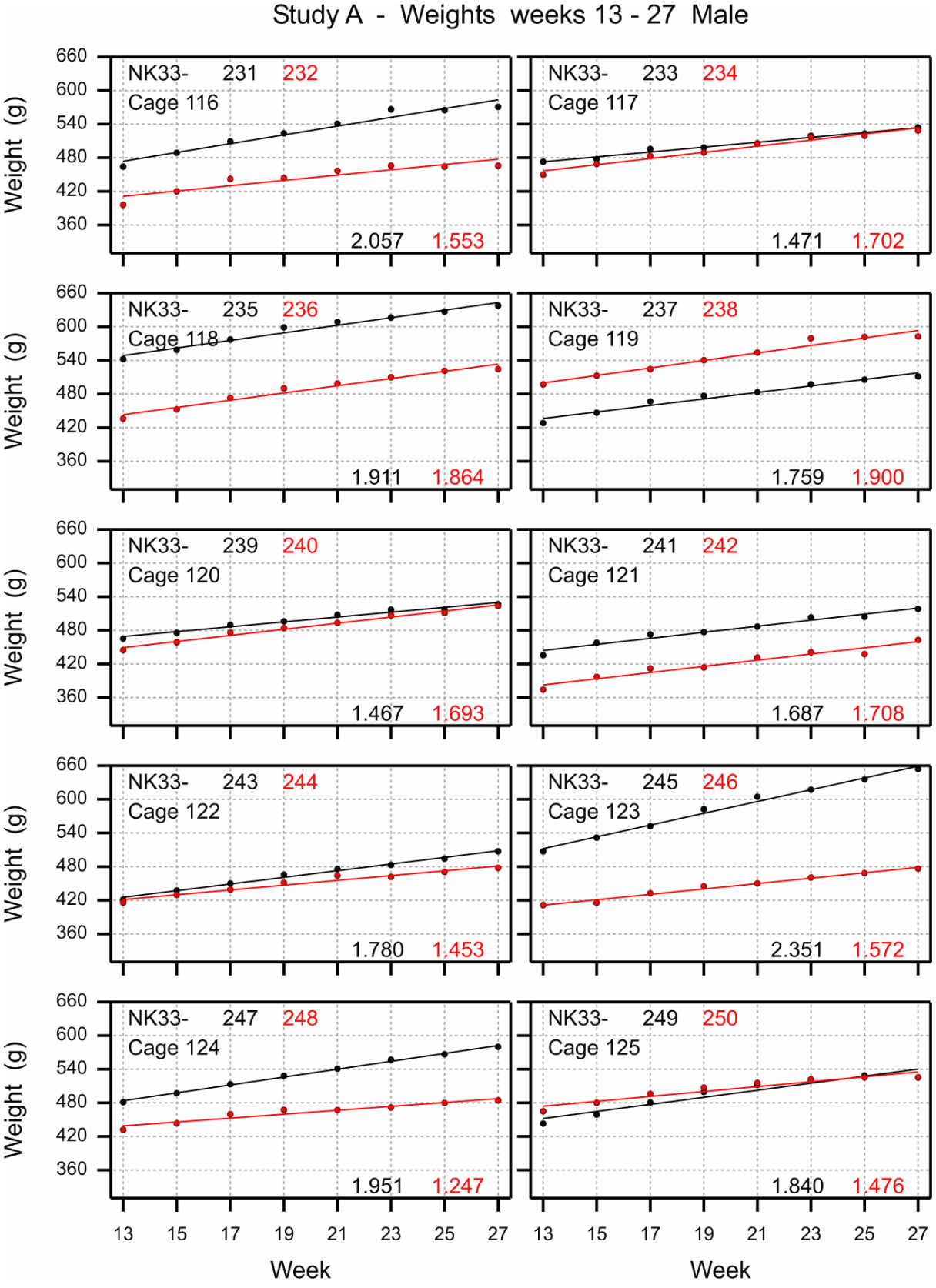
Appendix 1. Growth curves per animal pair (continued)

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.



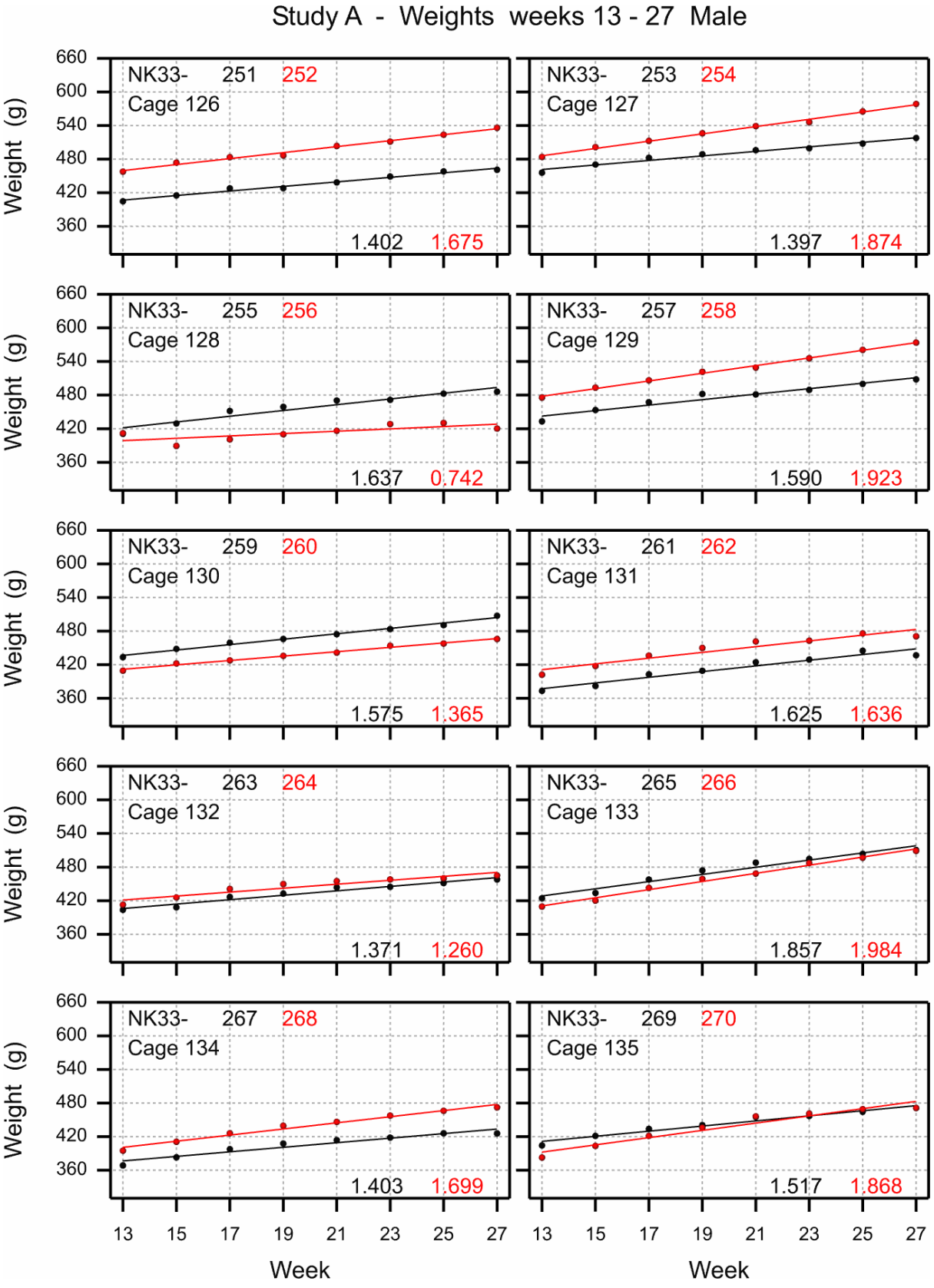
Appendix 1. Growth curves per animal pair (continued)

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.



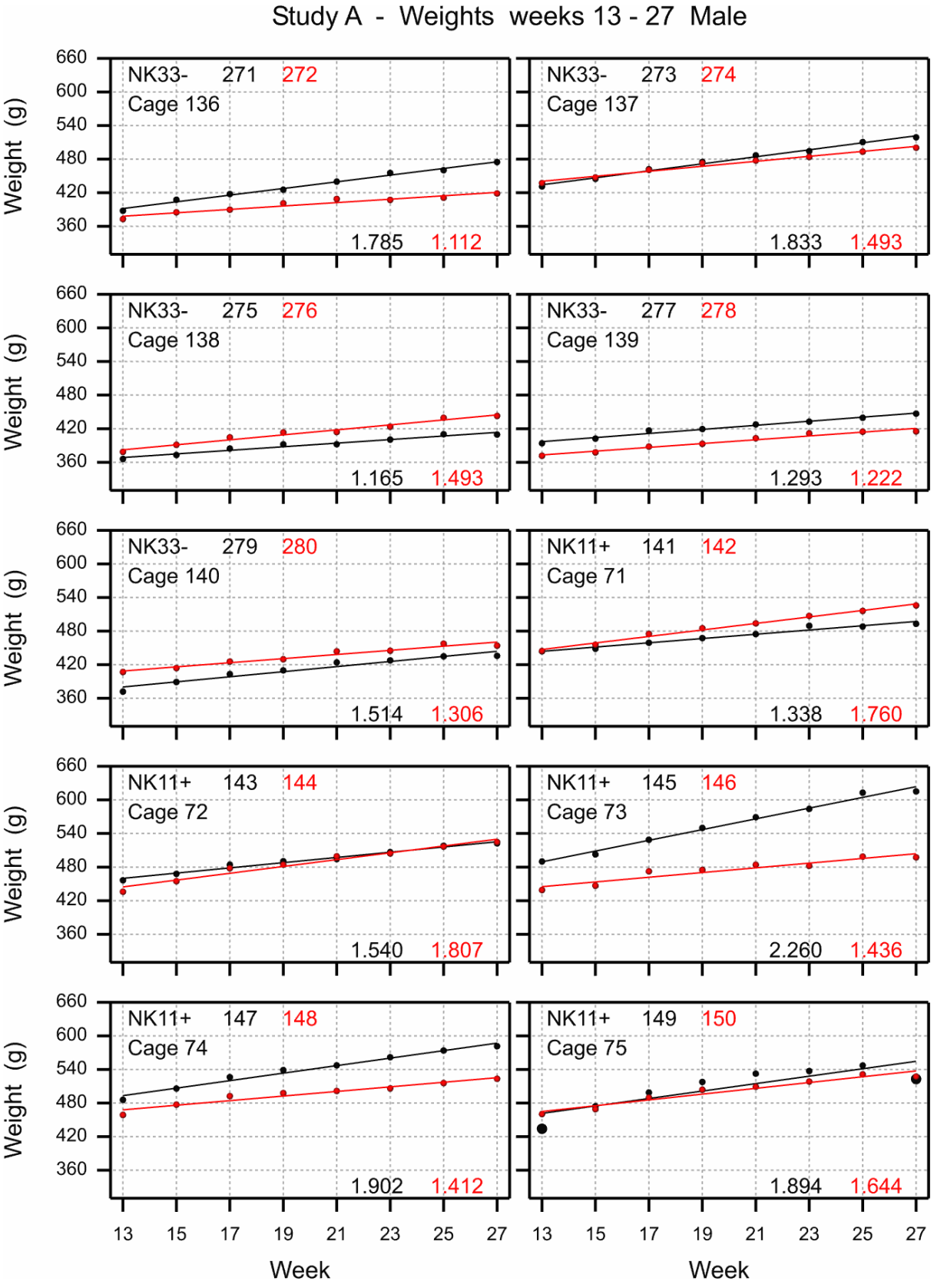
Appendix 1. Growth curves per animal pair (continued)

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.



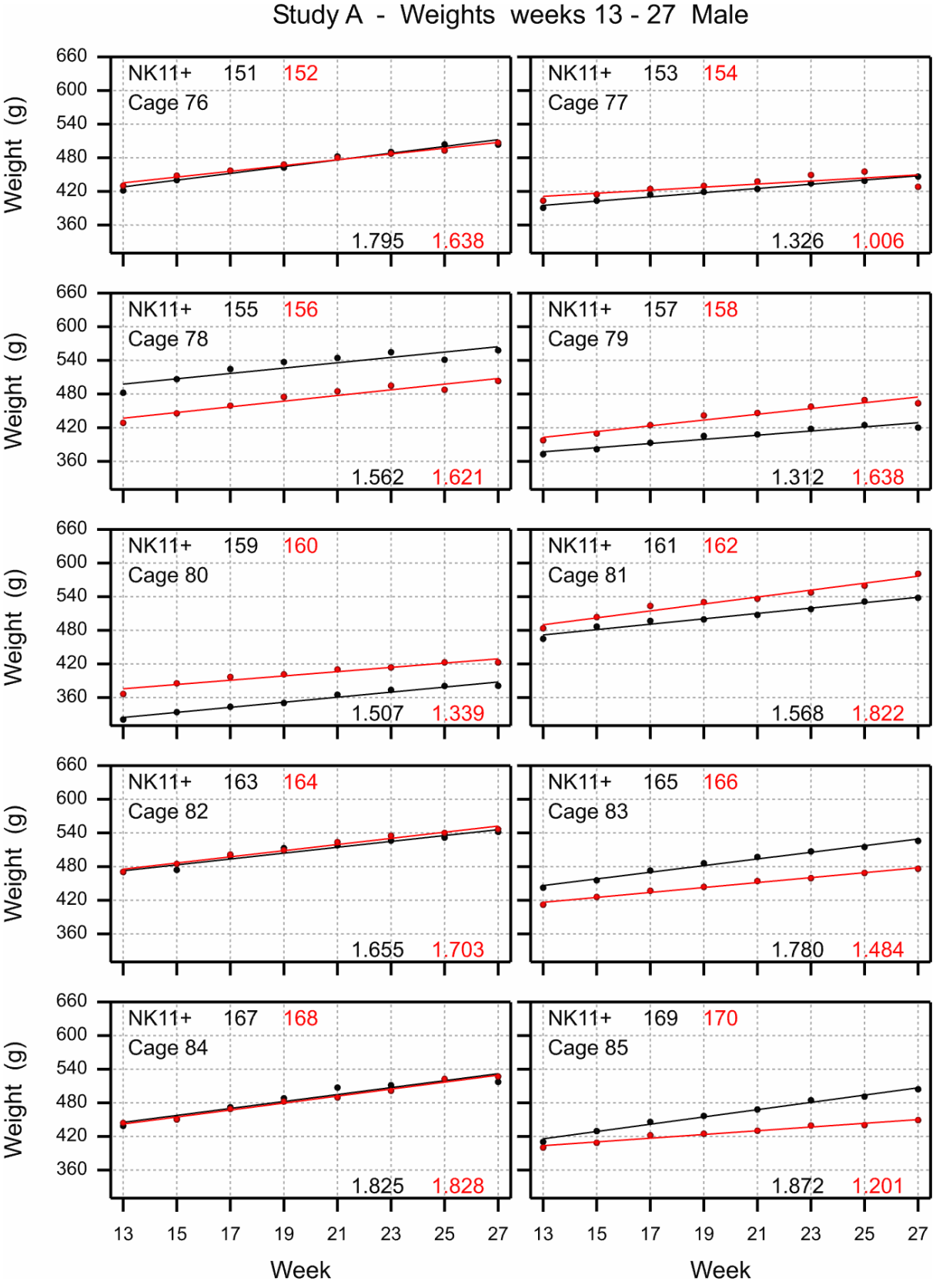
Appendix 1. Growth curves per animal pair (continued)

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.



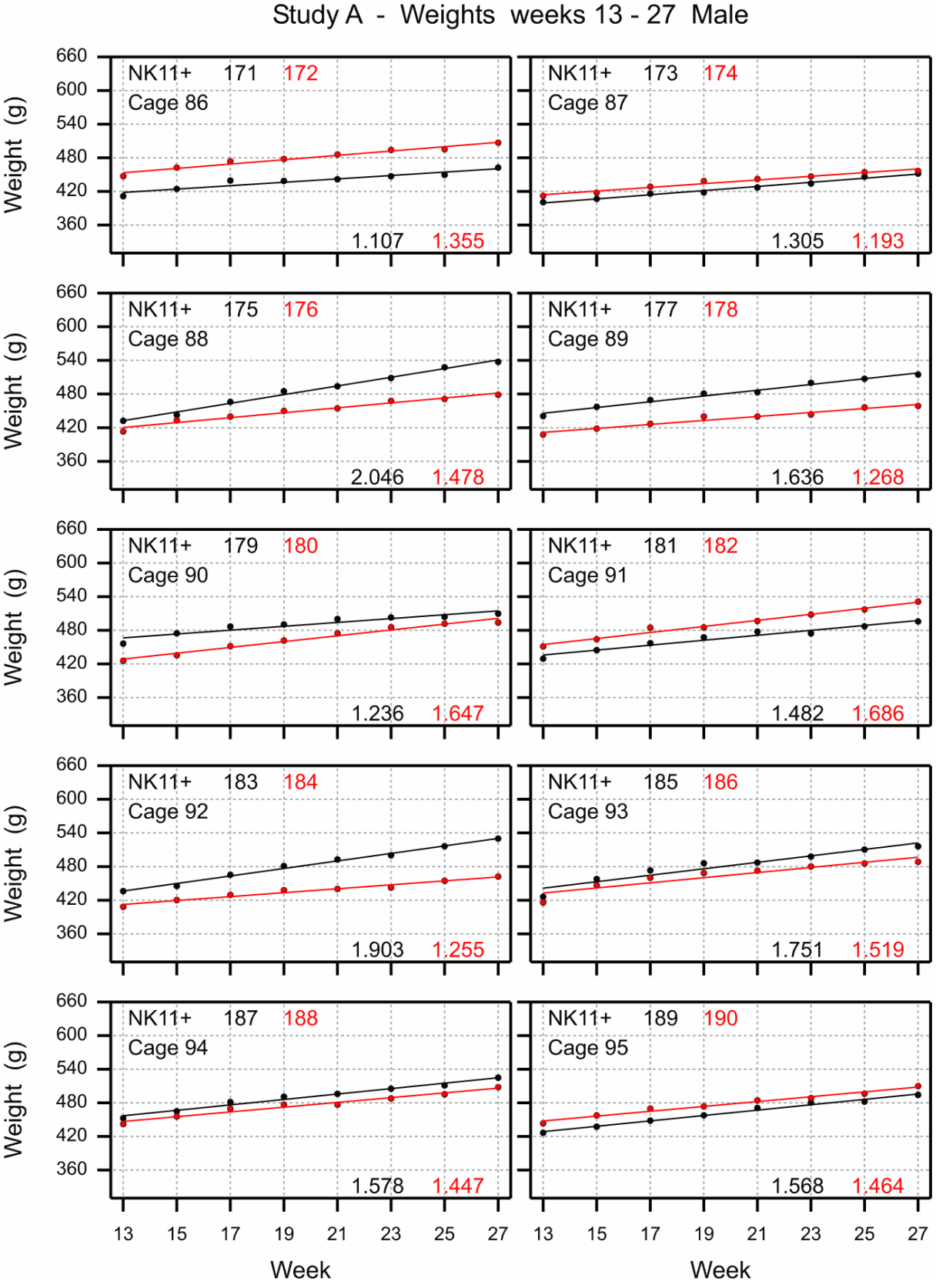
Appendix 1. Growth curves per animal pair (continued)

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.



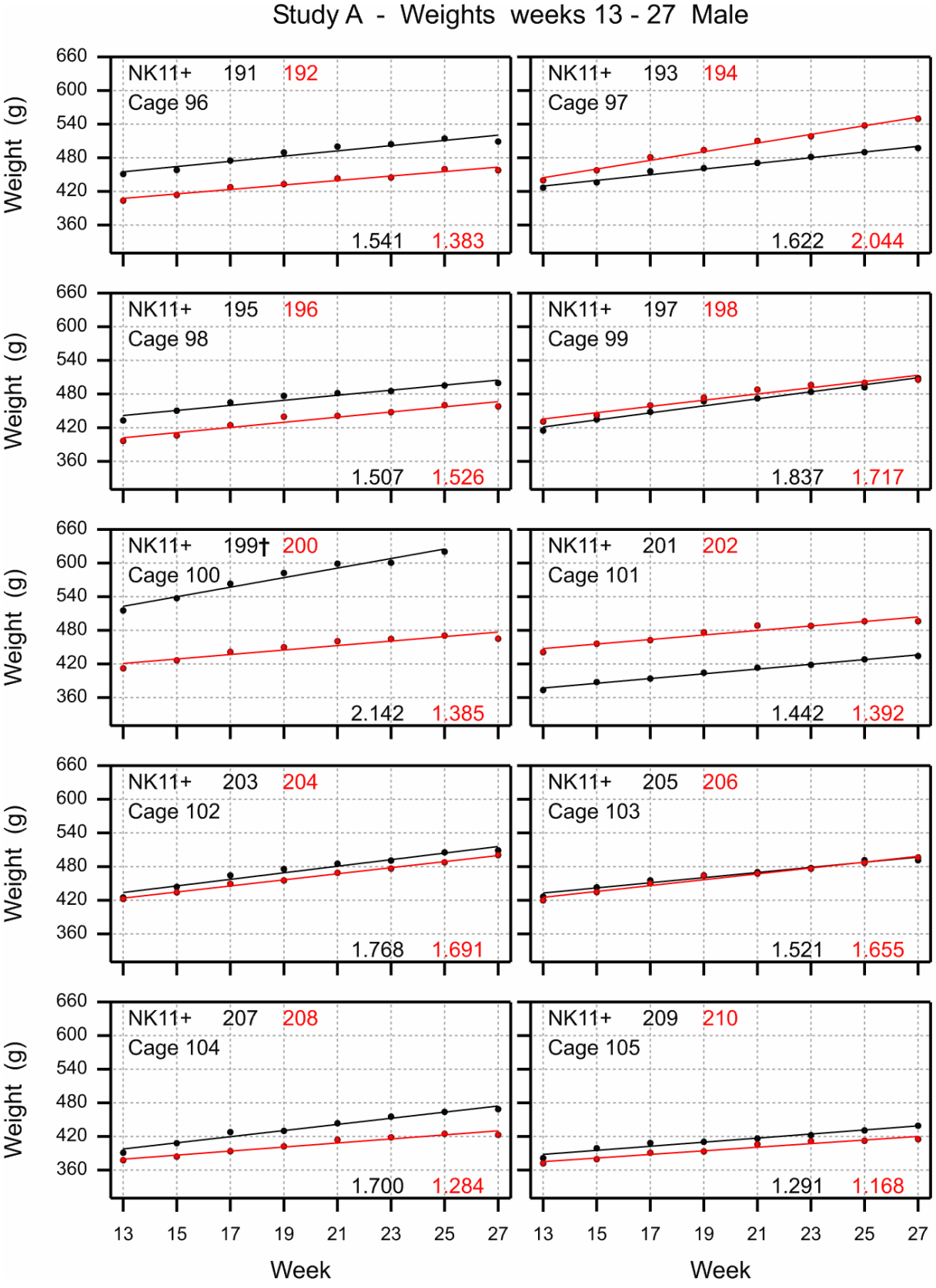
Appendix 1. Growth curves per animal pair (continued)

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.



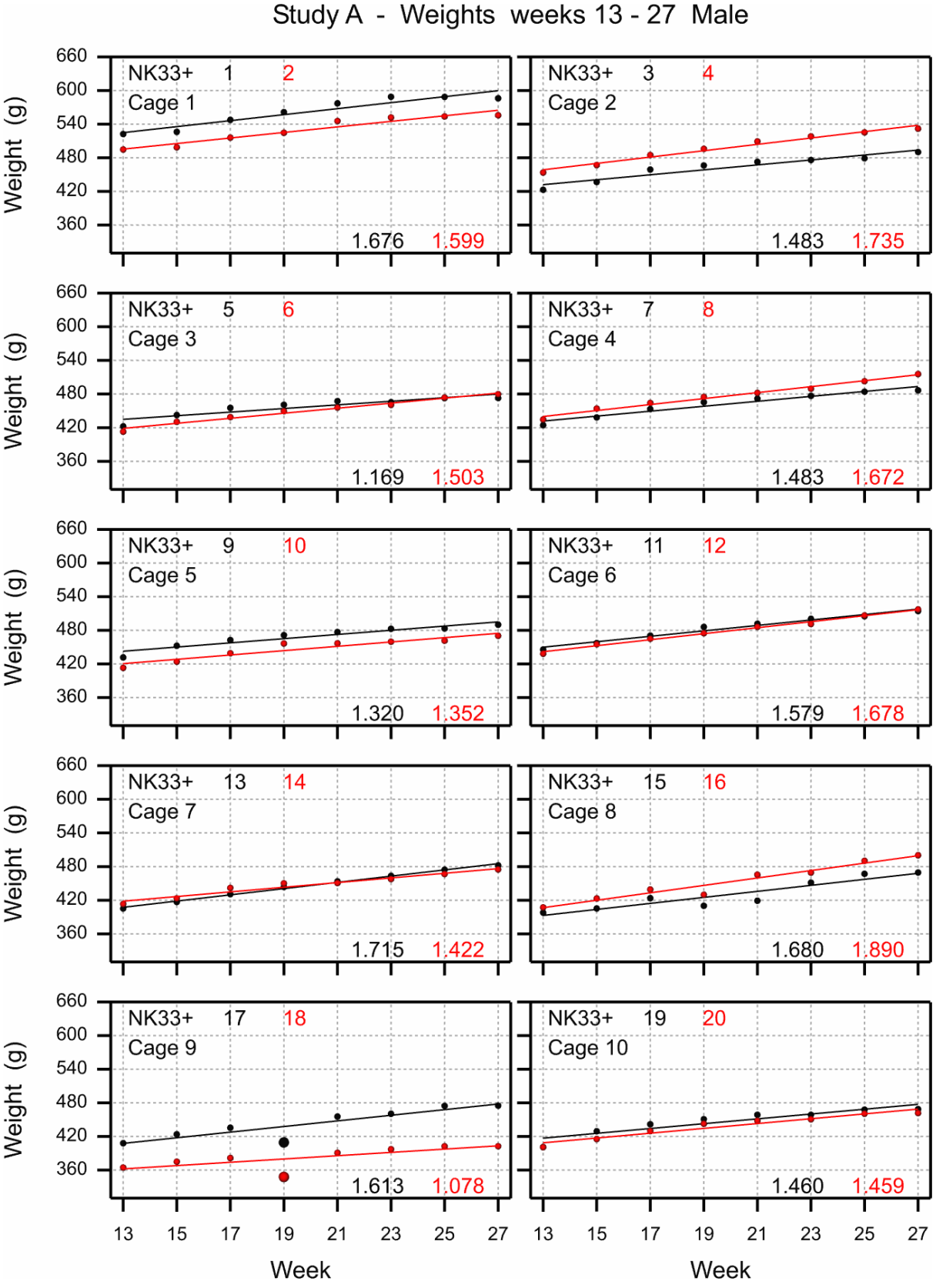
Appendix 1. Growth curves per animal pair (continued)

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.



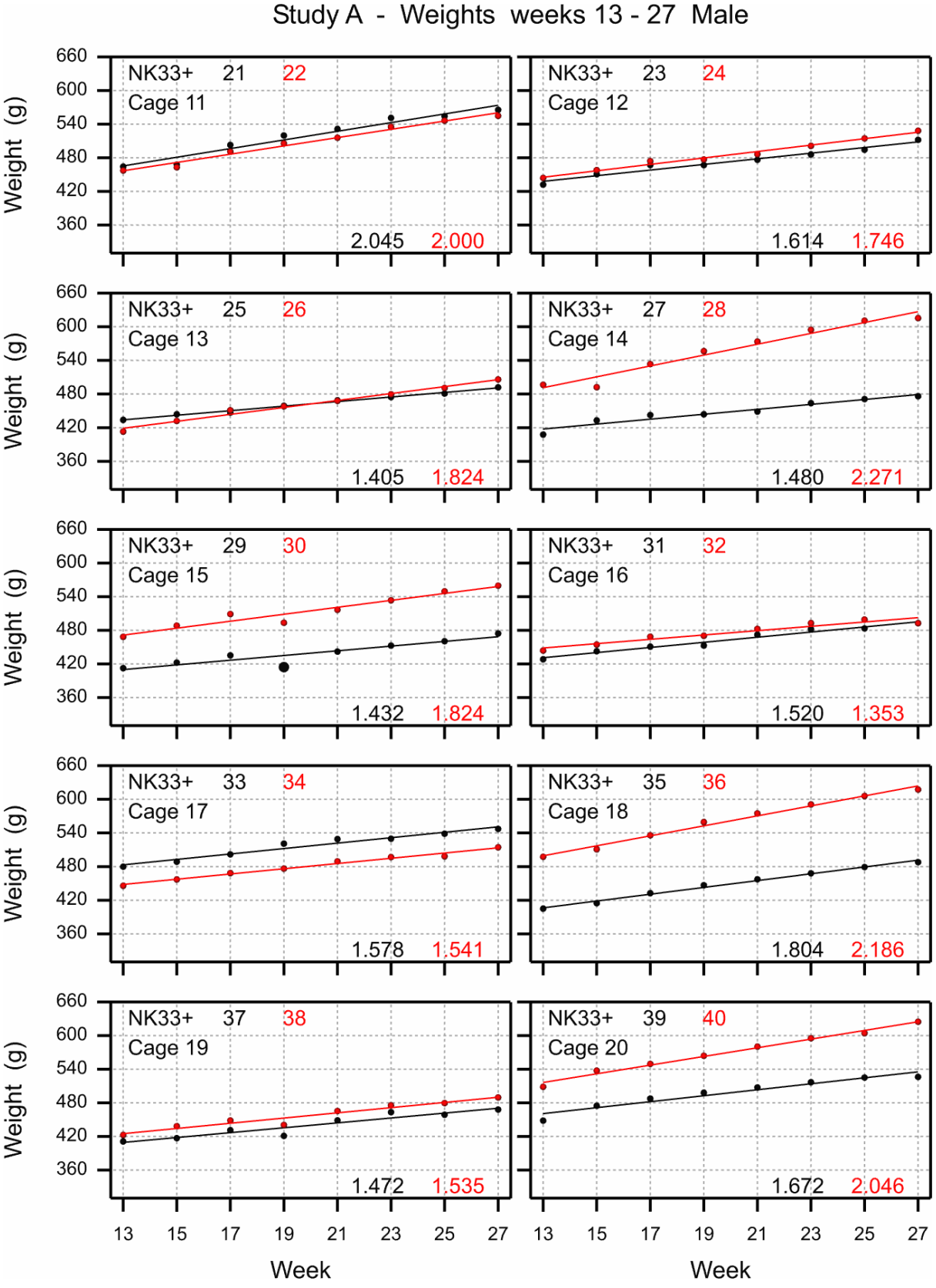
Appendix 1. Growth curves per animal pair (continued)

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.



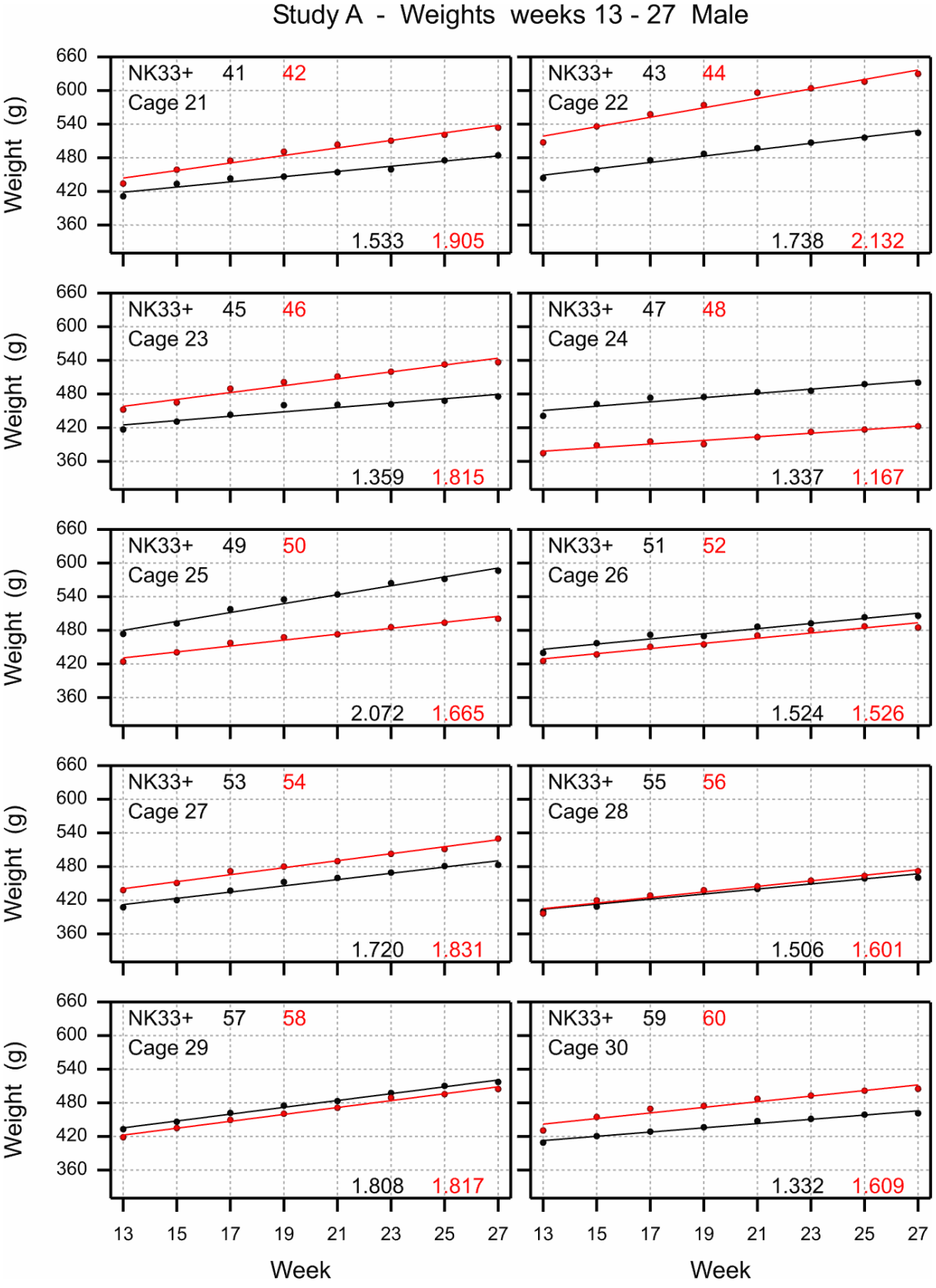
Appendix 1. Growth curves per animal pair (continued)

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.



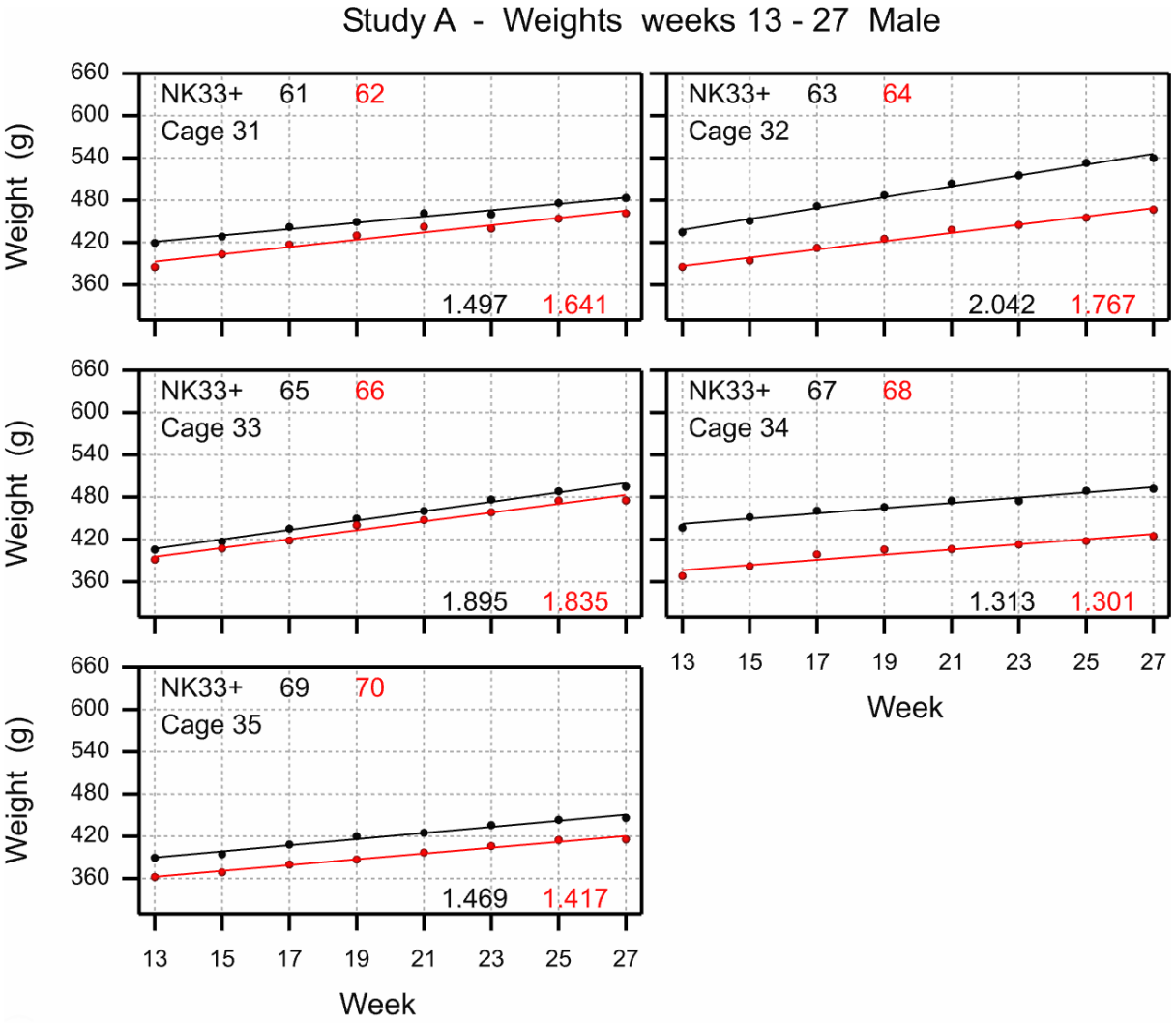
Appendix 1. Growth curves per animal pair (continued)

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.



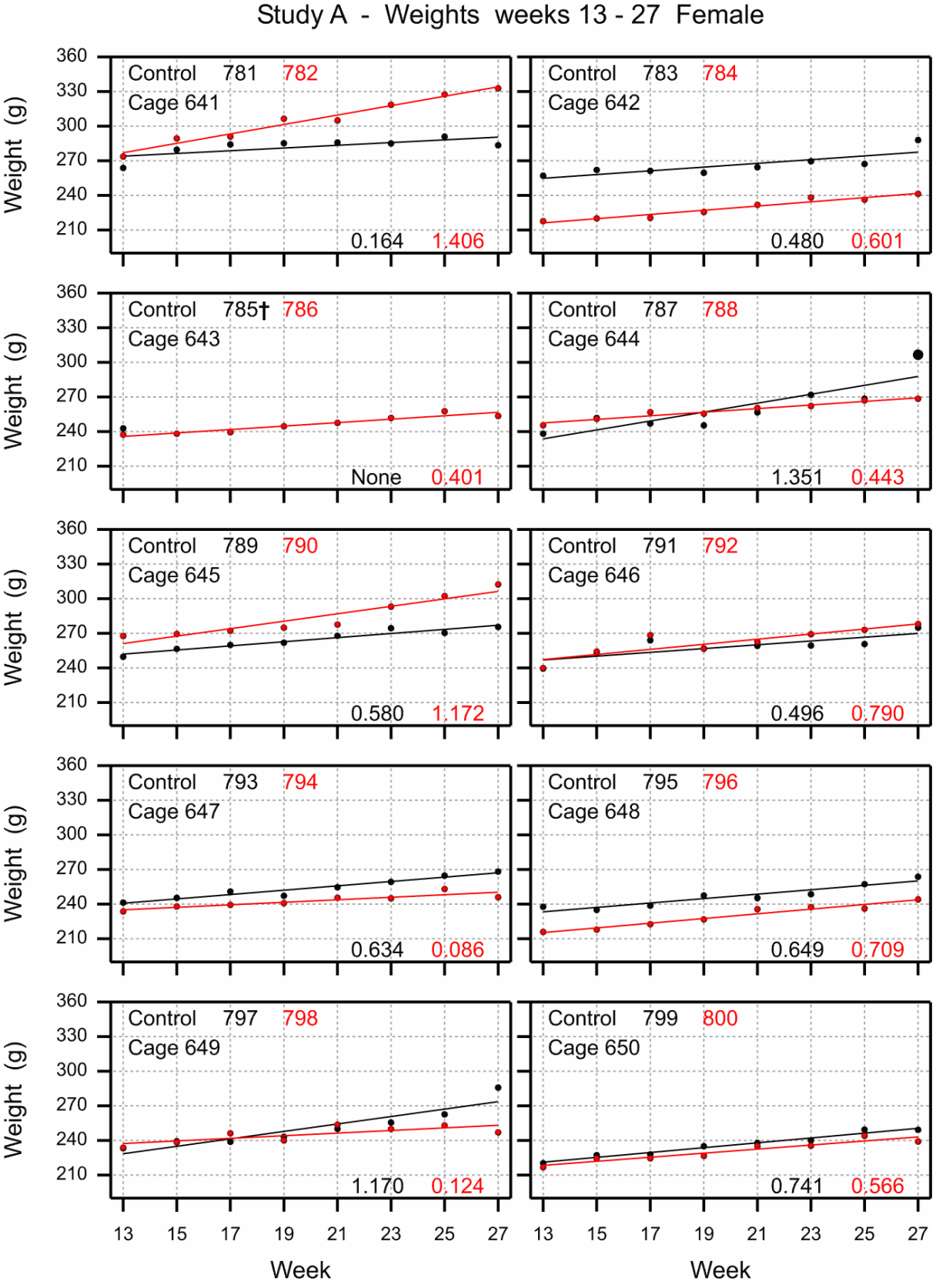
Appendix 1. Growth curves per animal pair (continued)

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.



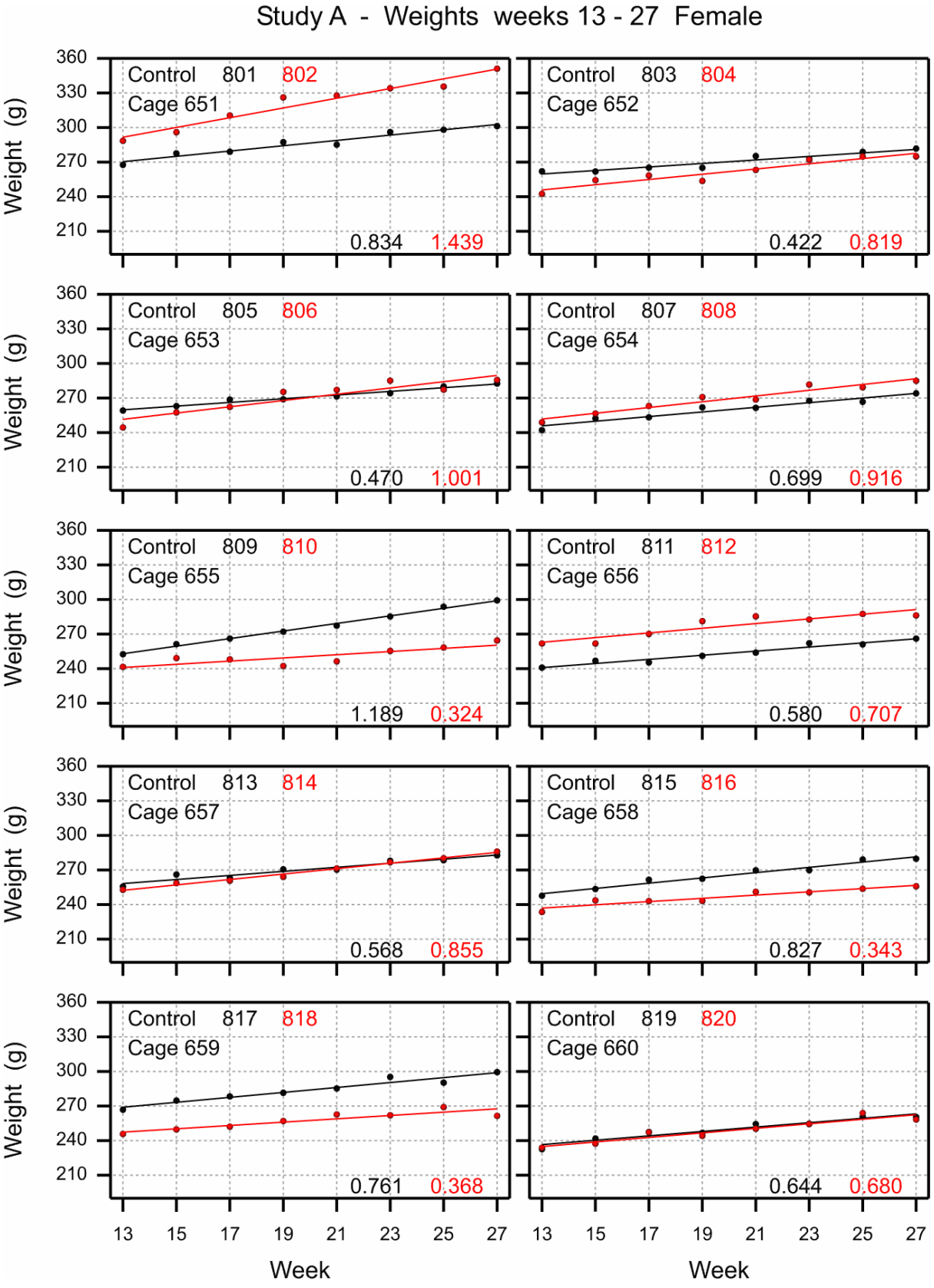
Appendix 1. Growth curves per animal pair (continued)

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.



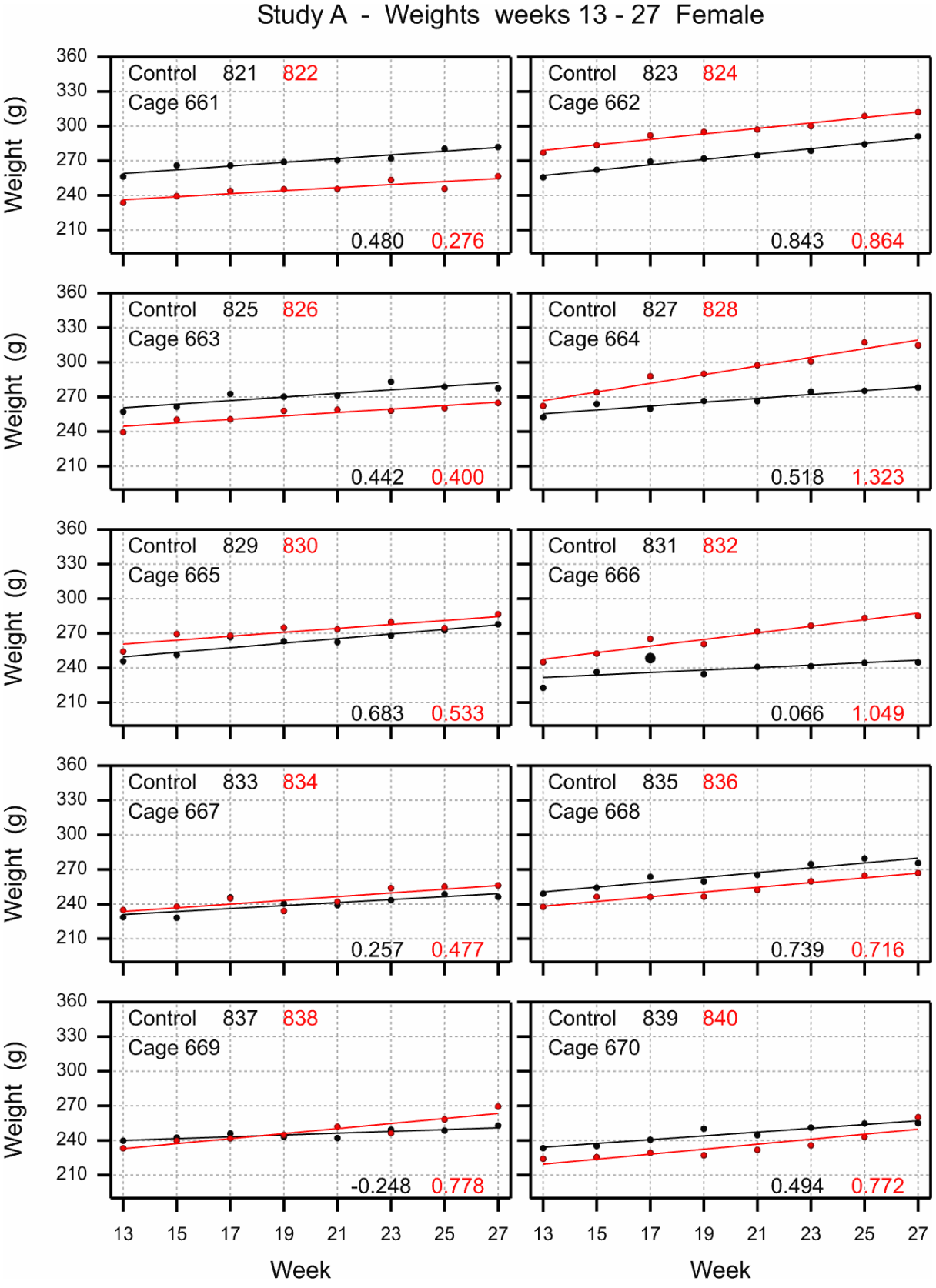
Appendix 1. Growth curves per animal pair (continued)

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.



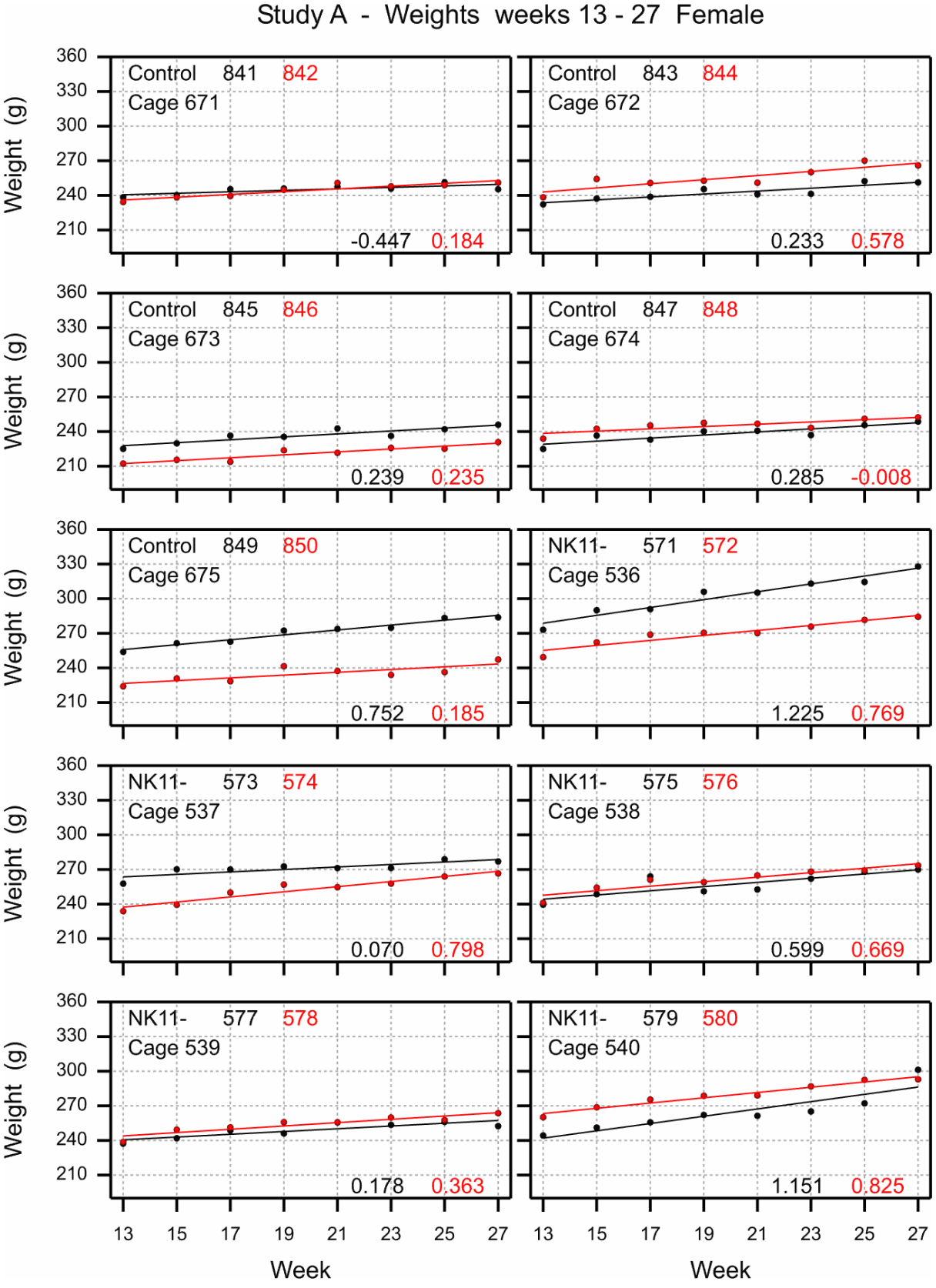
Appendix 1. Growth curves per animal pair (continued)

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.



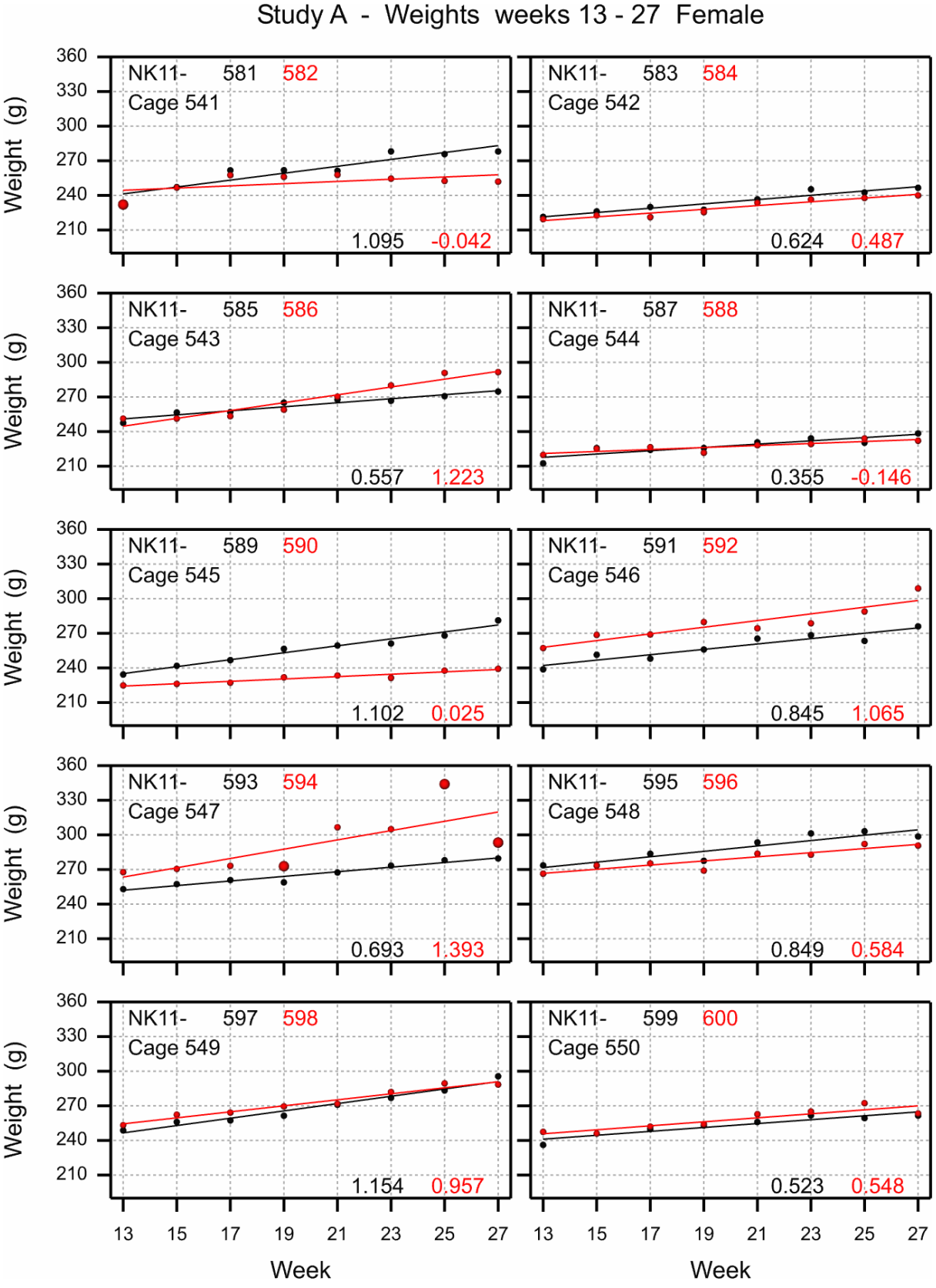
Appendix 1. Growth curves per animal pair (continued)

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.



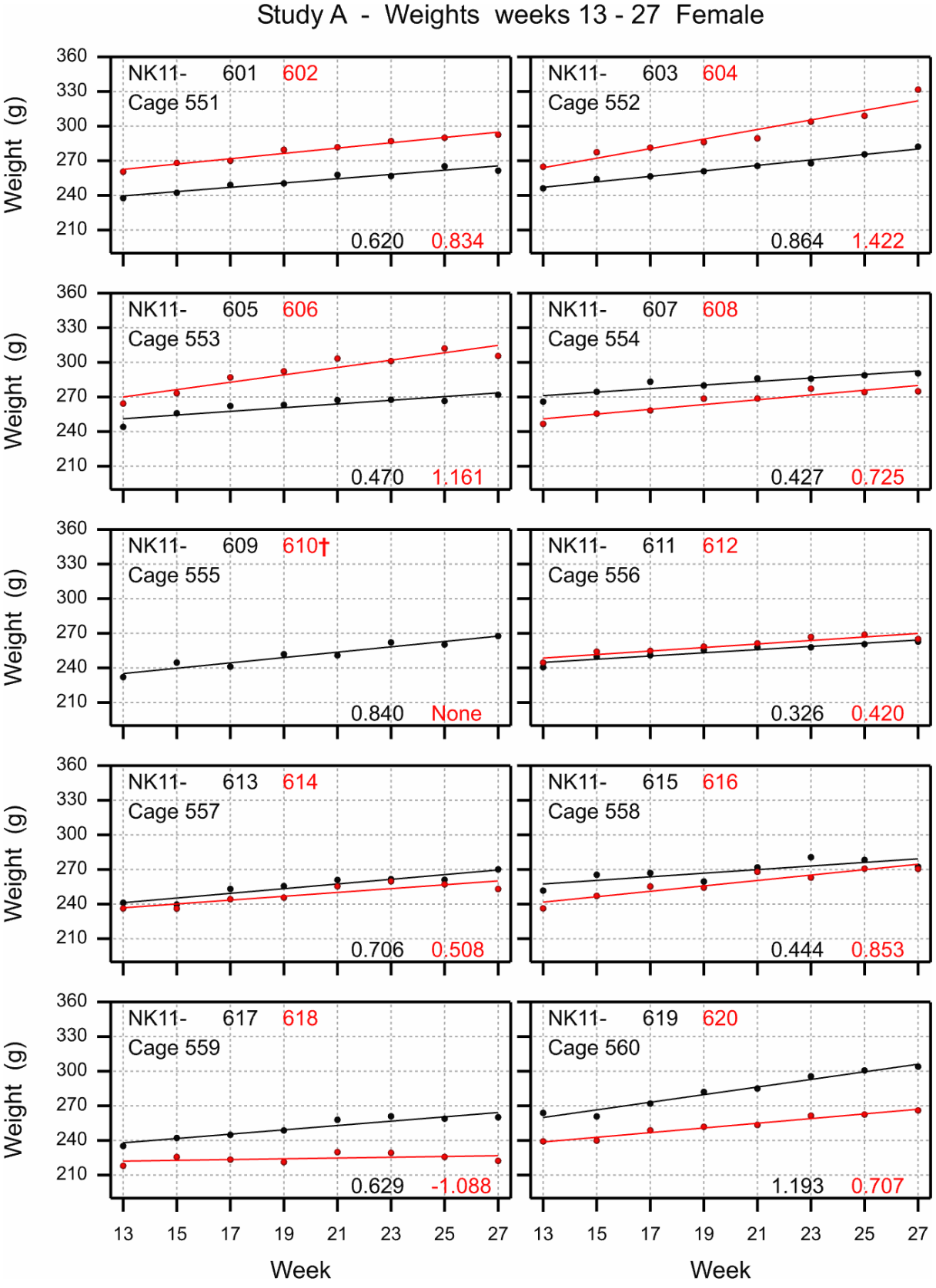
Appendix 1. Growth curves per animal pair (continued)

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.



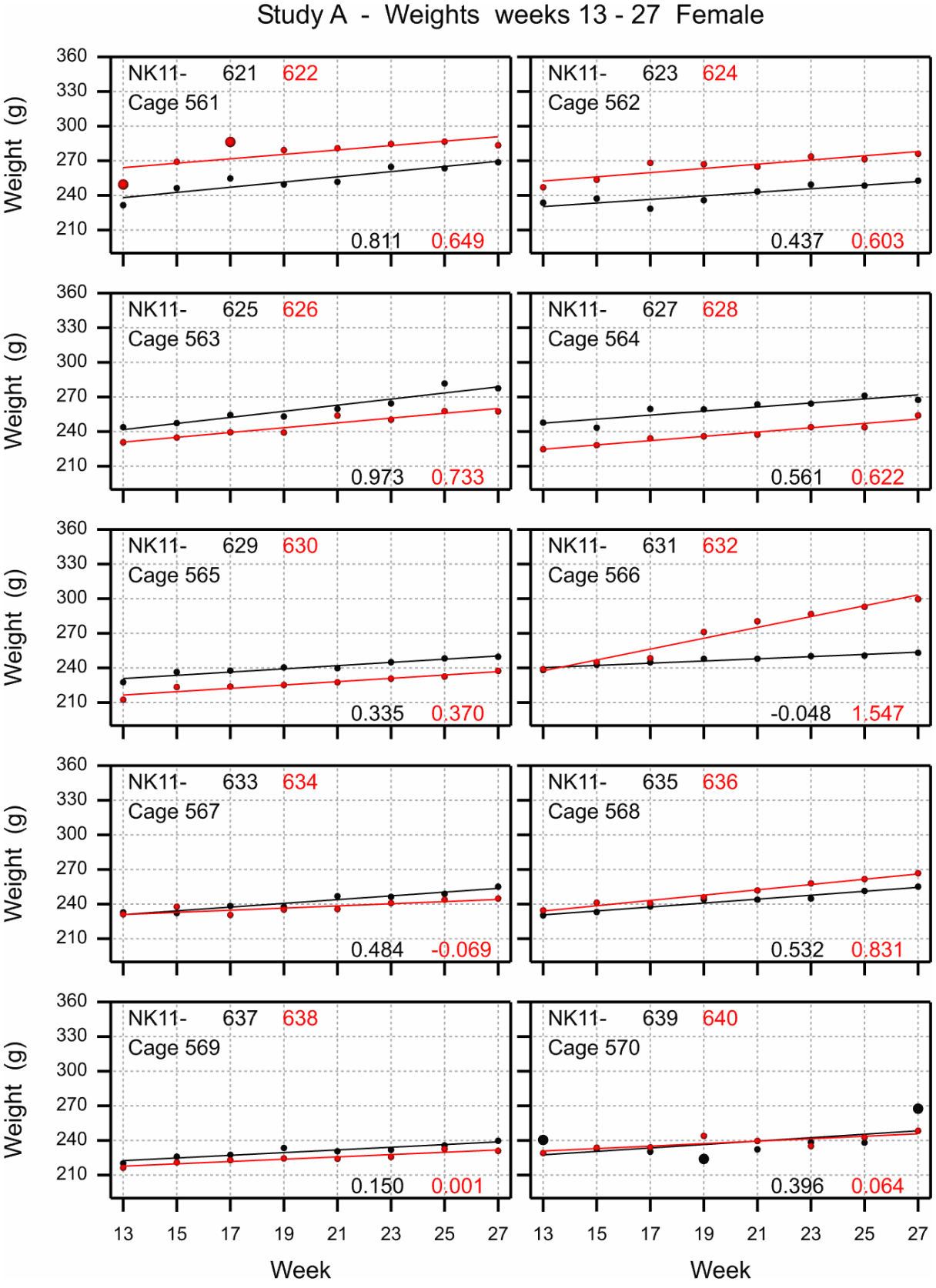
Appendix 1. Growth curves per animal pair (continued)

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.



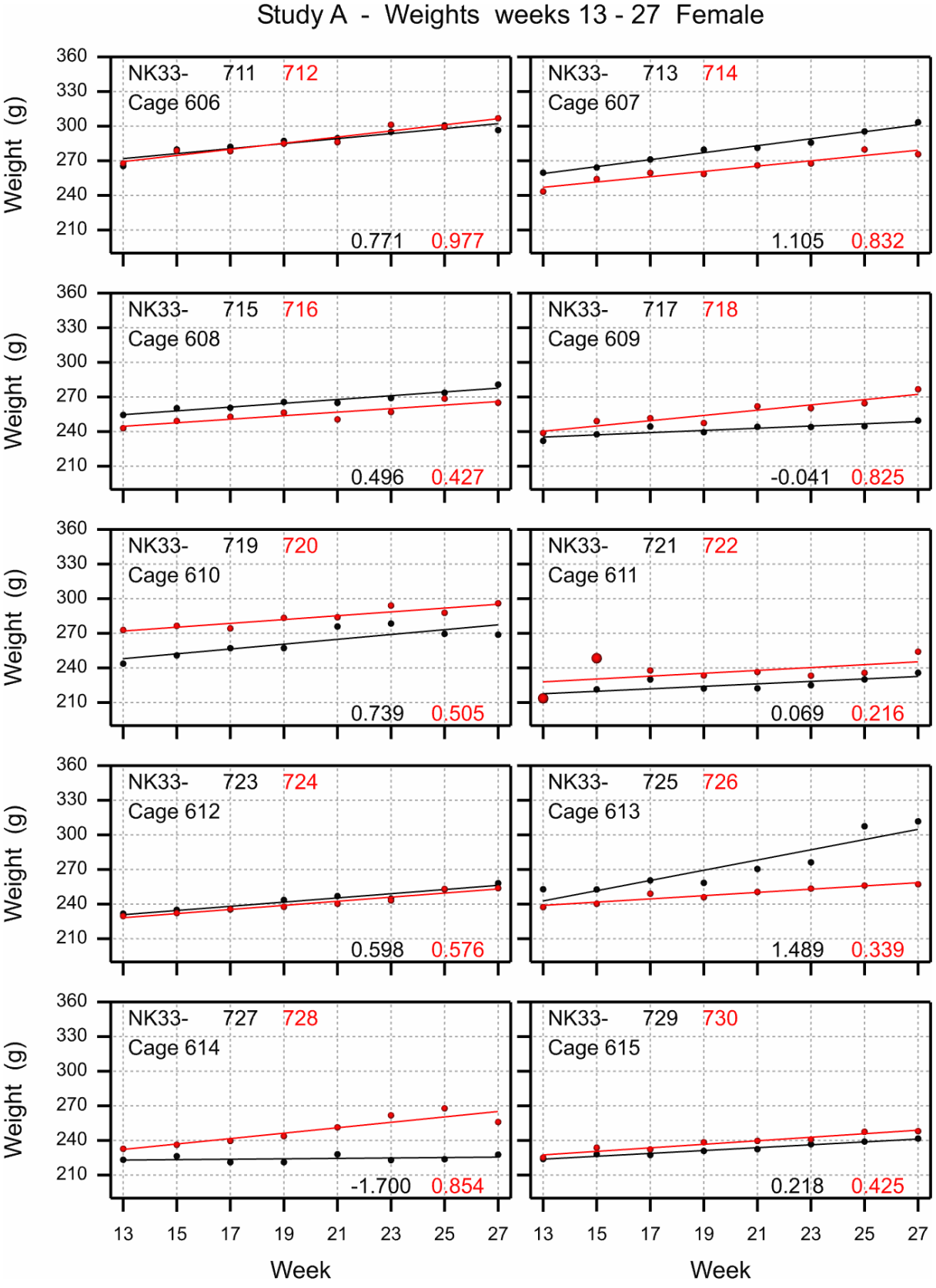
Appendix 1. Growth curves per animal pair (continued)

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.



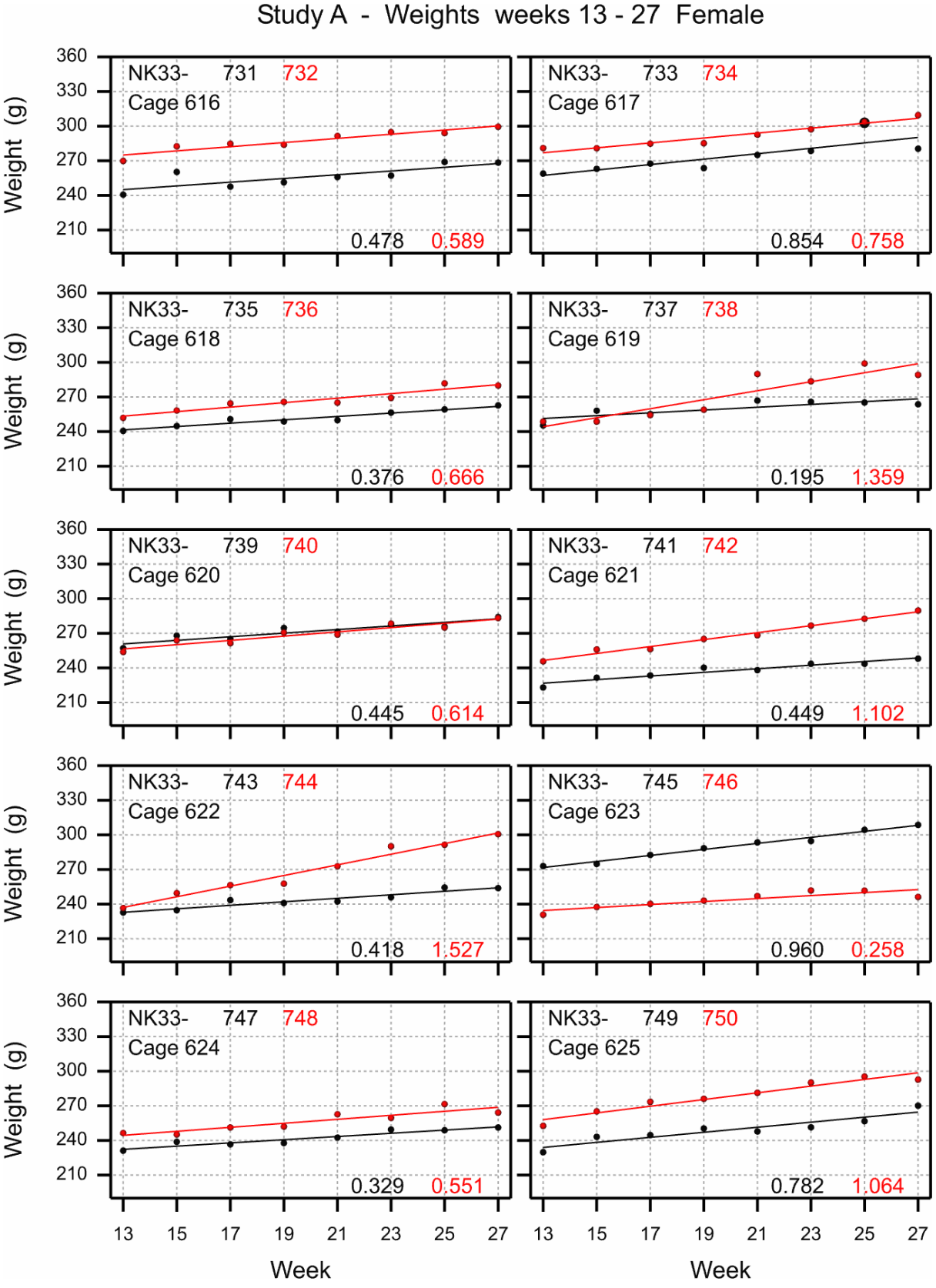
Appendix 1. Growth curves per animal pair (continued)

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.



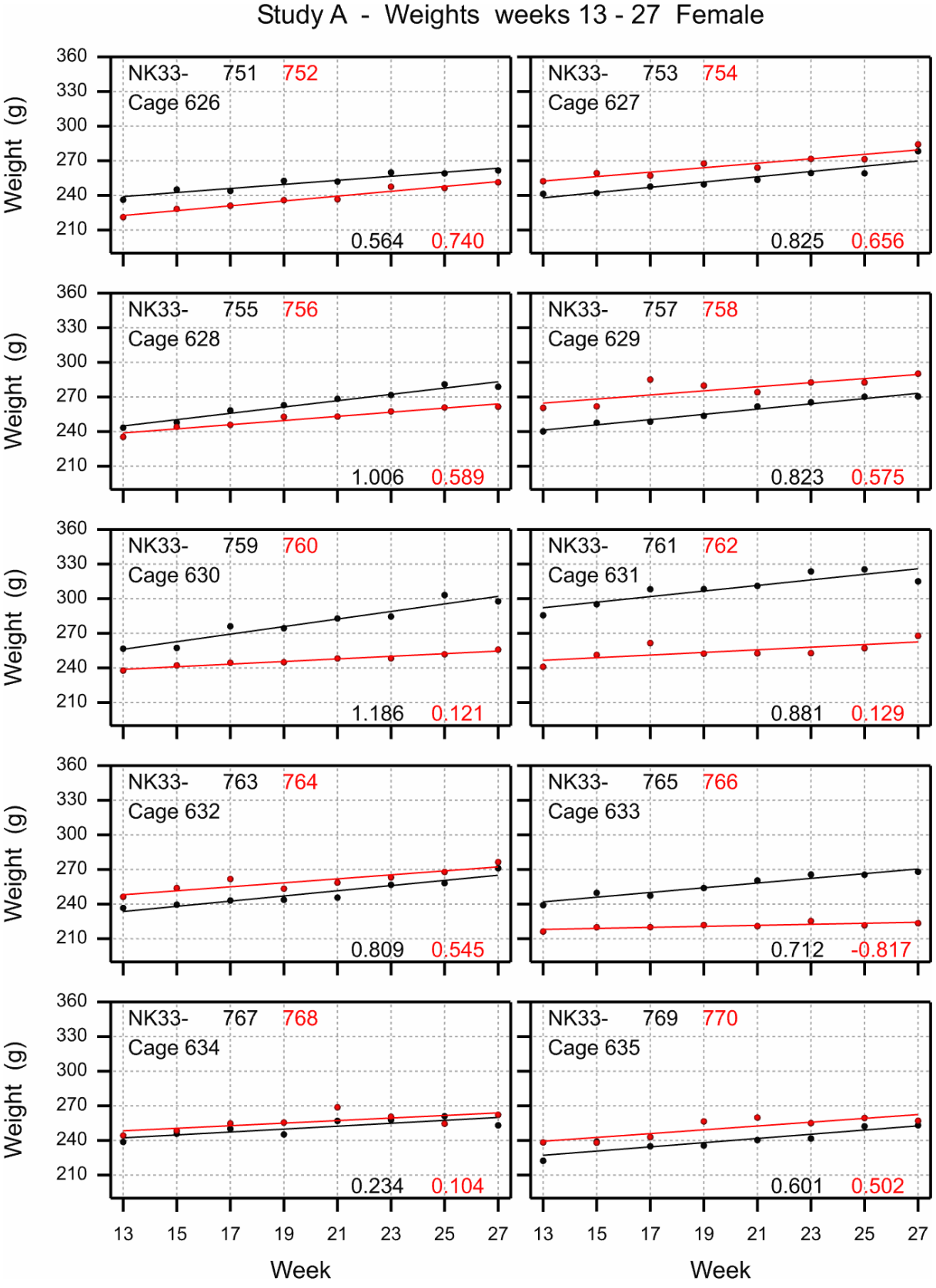
Appendix 1. Growth curves per animal pair (continued)

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.



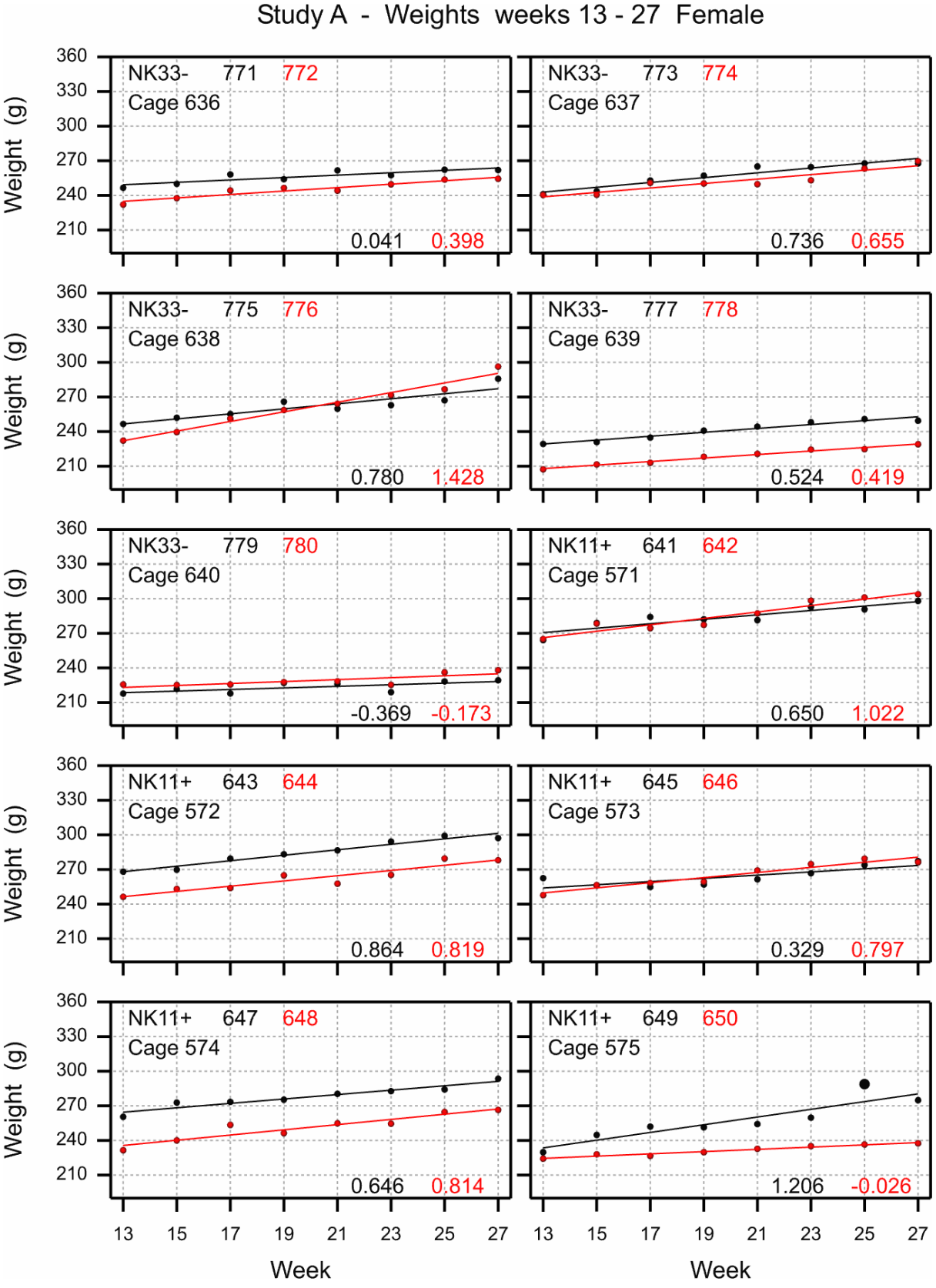
Appendix 1. Growth curves per animal pair (continued)

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.



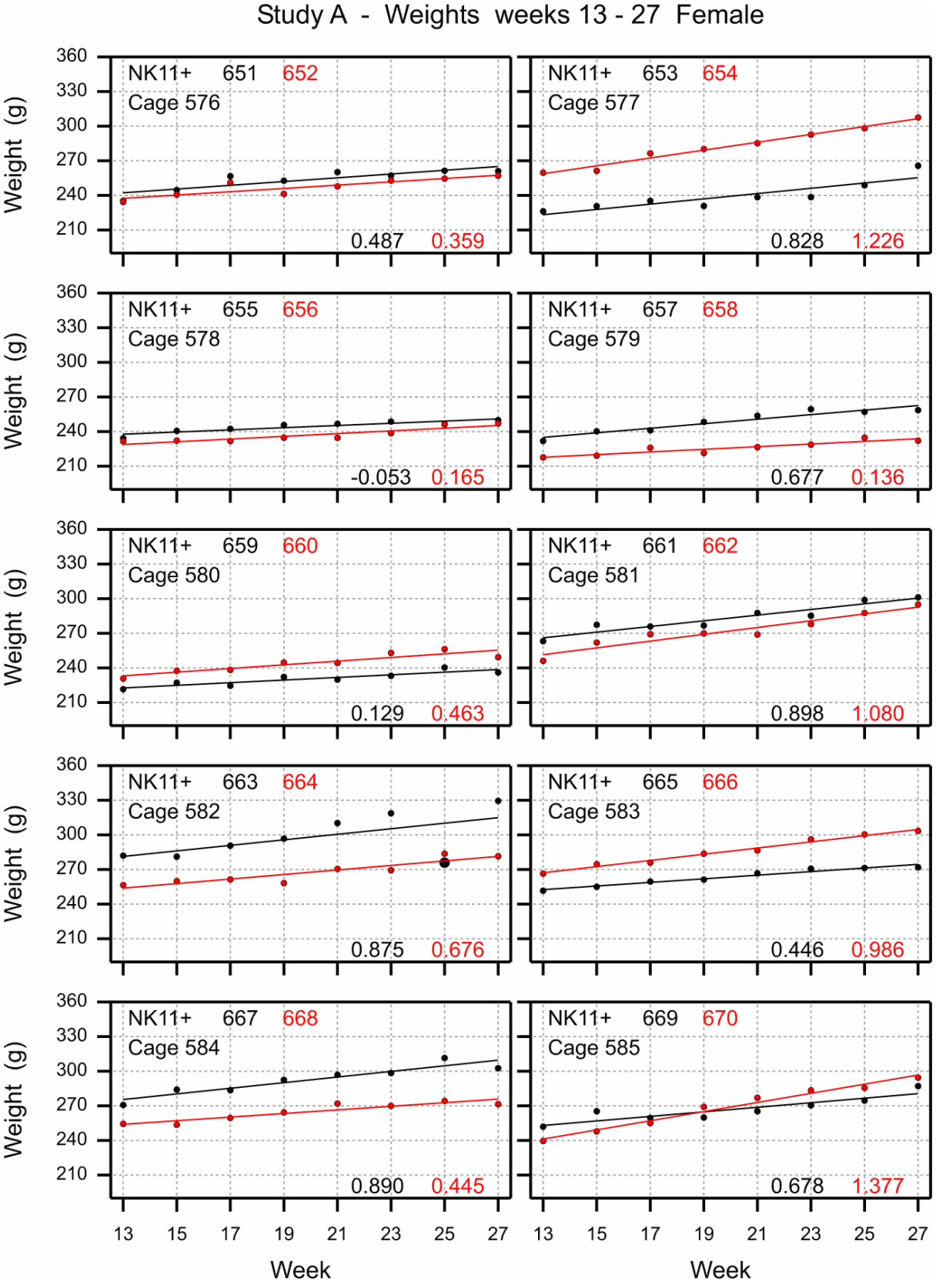
Appendix 1. Growth curves per animal pair (continued)

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.



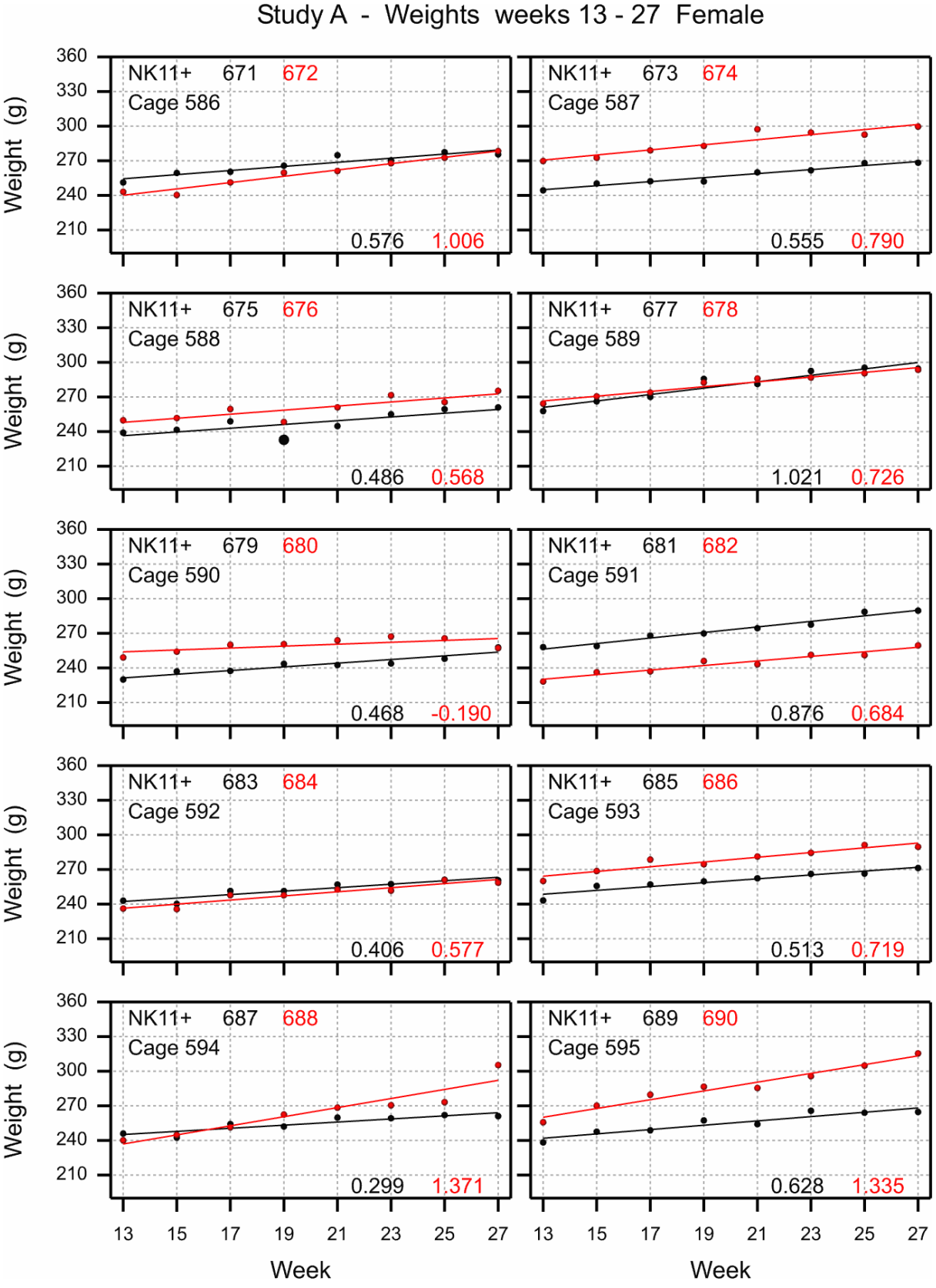
Appendix 1. Growth curves per animal pair (continued)

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.



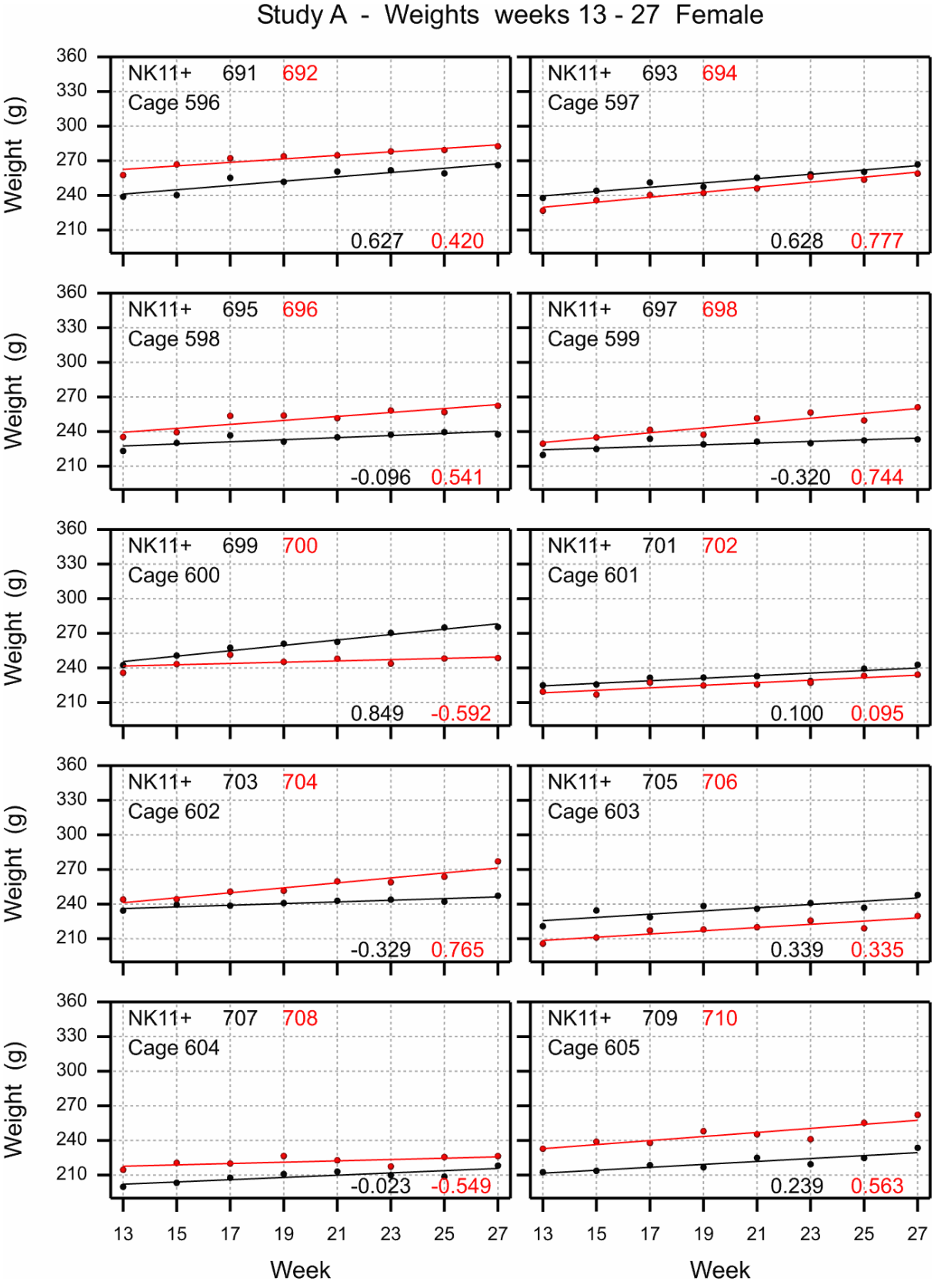
Appendix 1. Growth curves per animal pair (continued)

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.



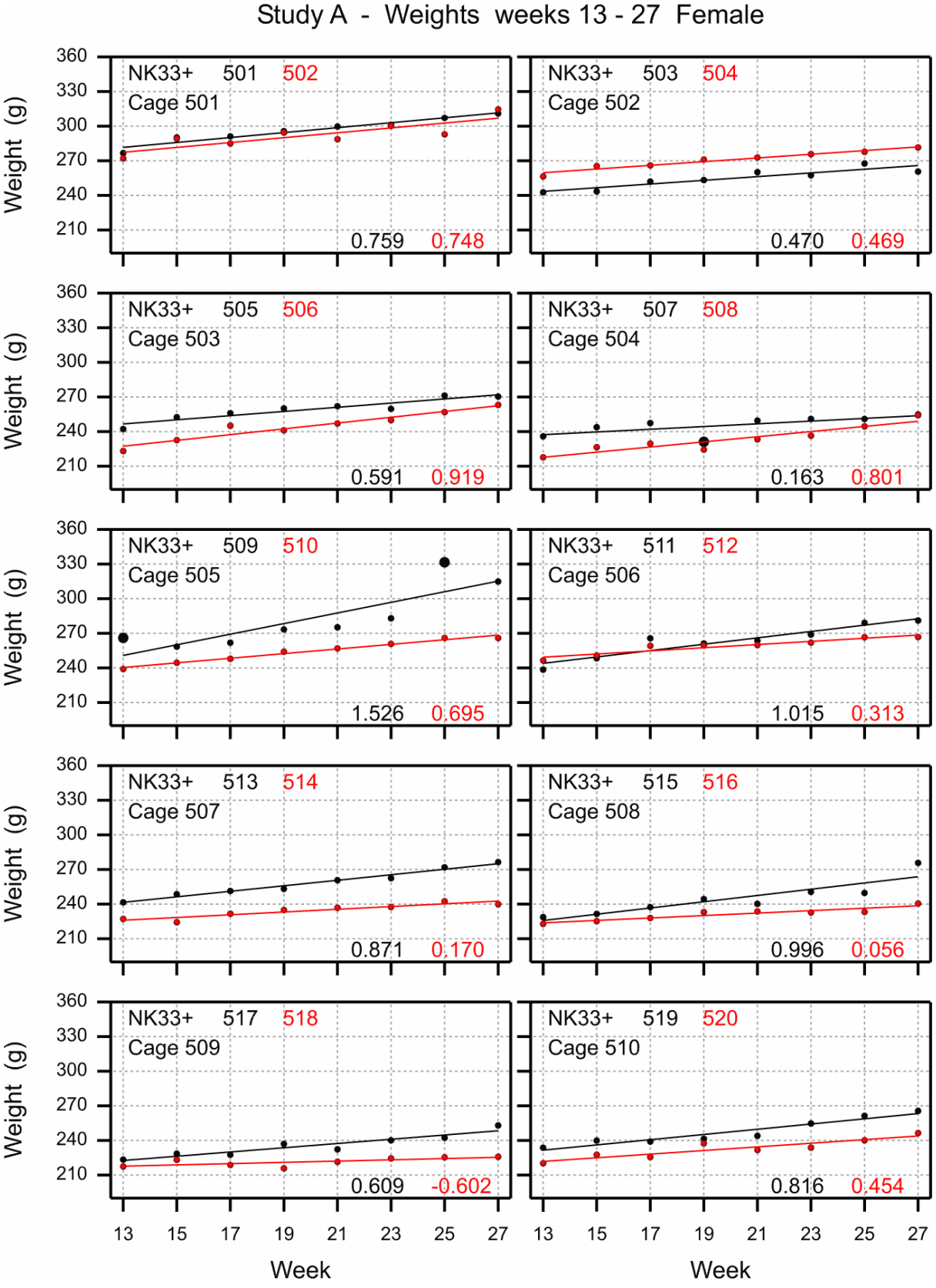
Appendix 1. Growth curves per animal pair (continued)

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.



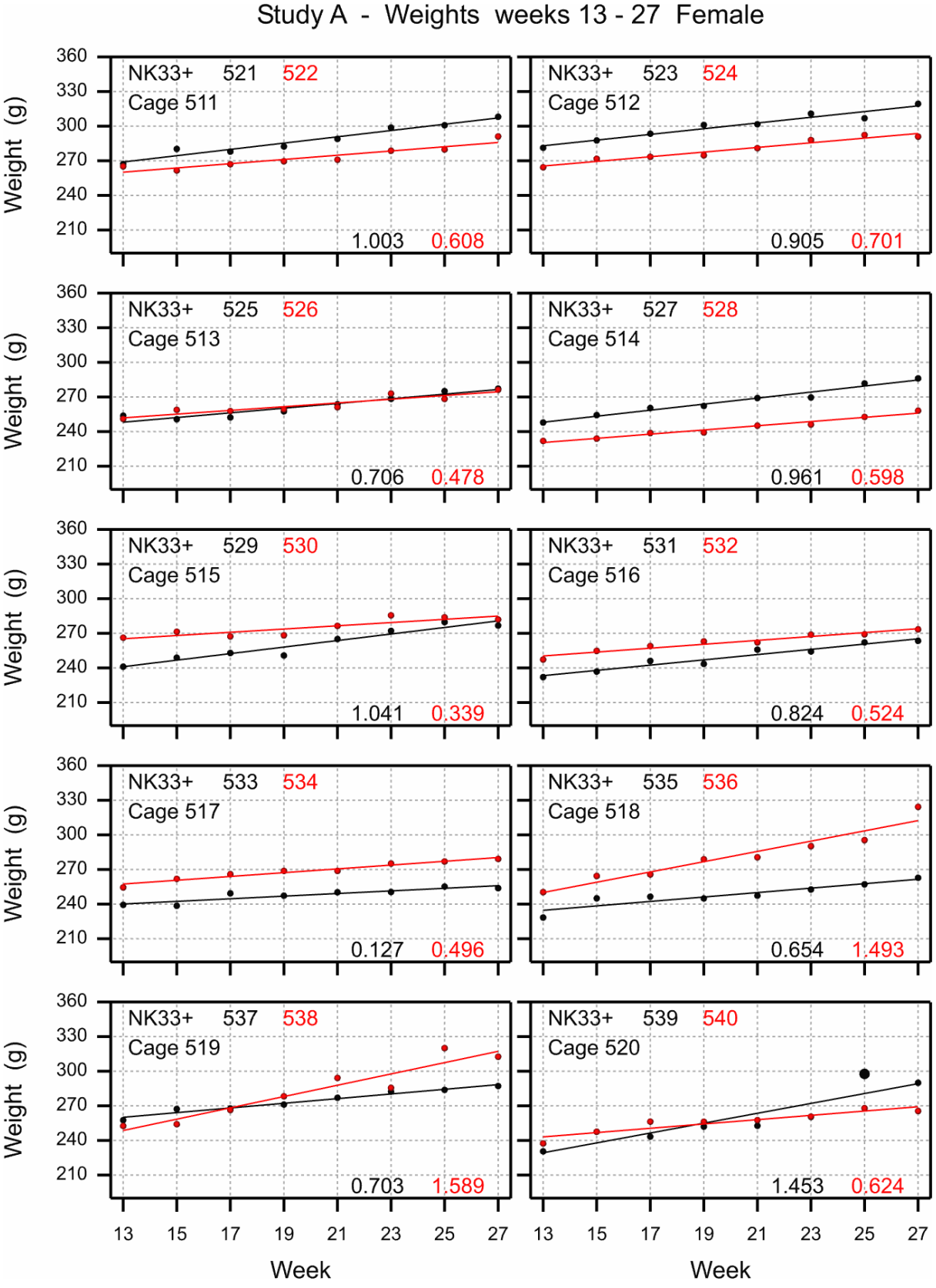
Appendix 1. Growth curves per animal pair (continued)

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.



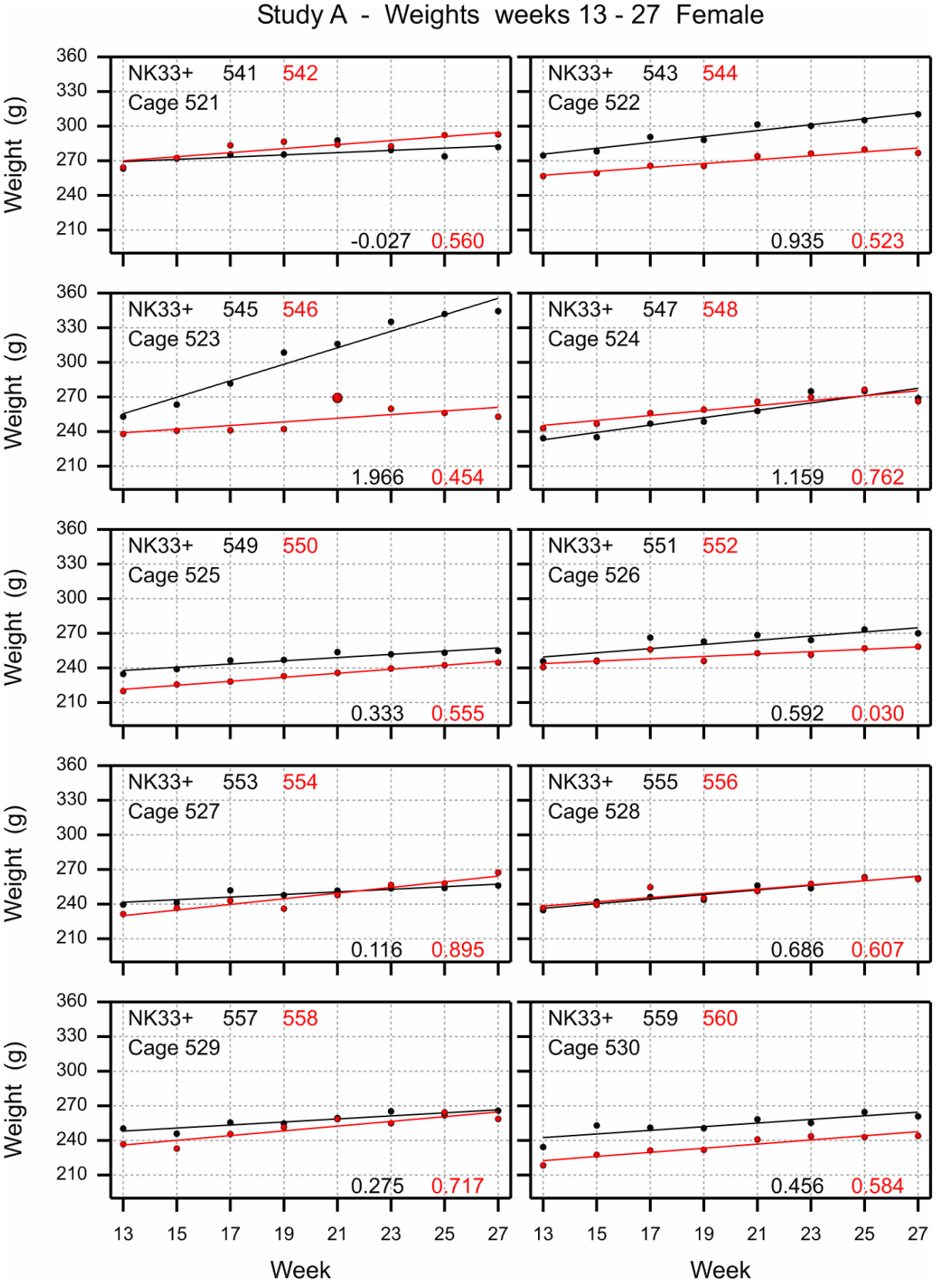
Appendix 1. Growth curves per animal pair (continued)

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.



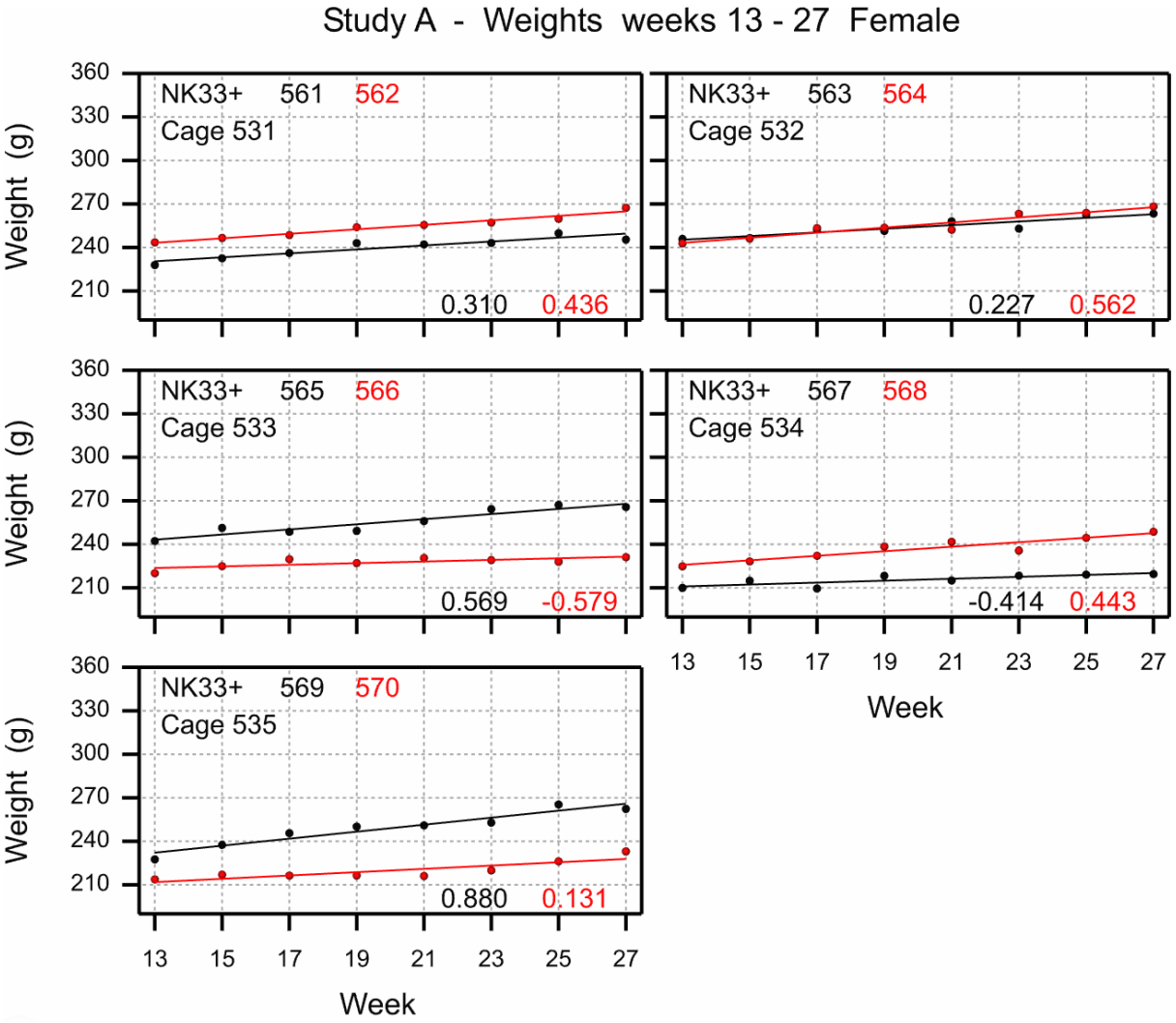
Appendix 1. Growth curves per animal pair (continued)

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.



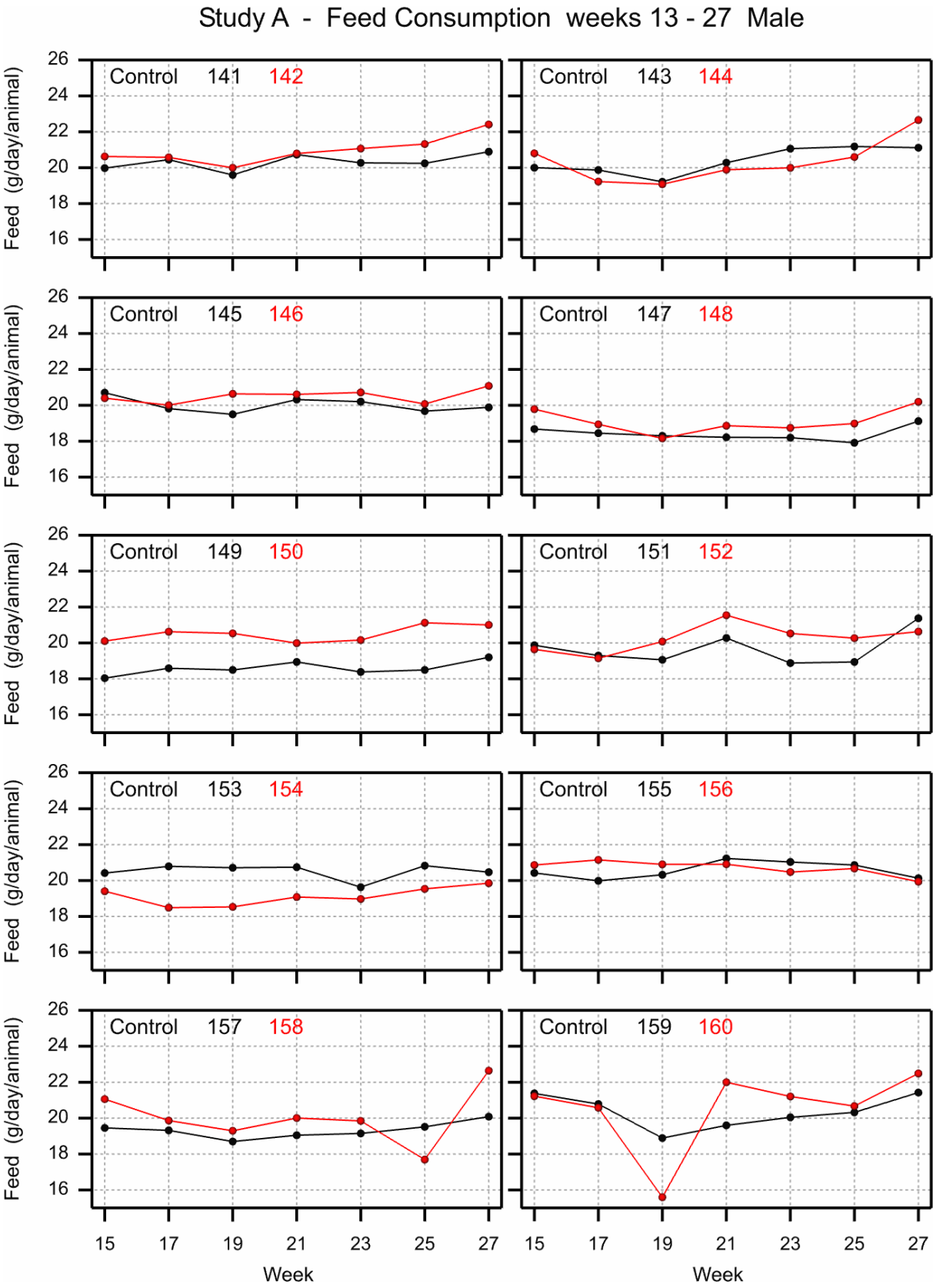
Appendix 1. Growth curves per animal pair (continued)

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.



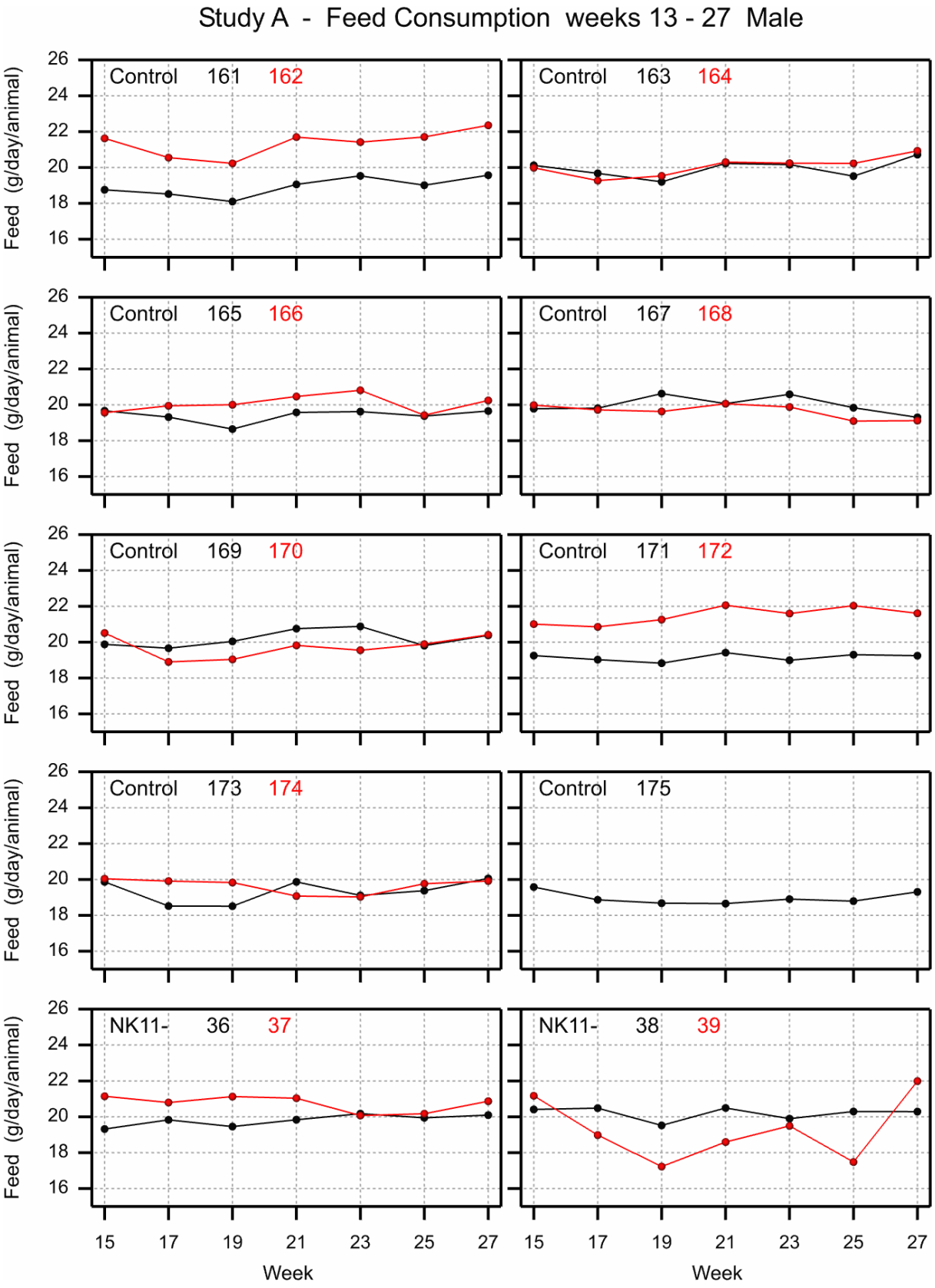
Appendix 2. Feed consumption per cage

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



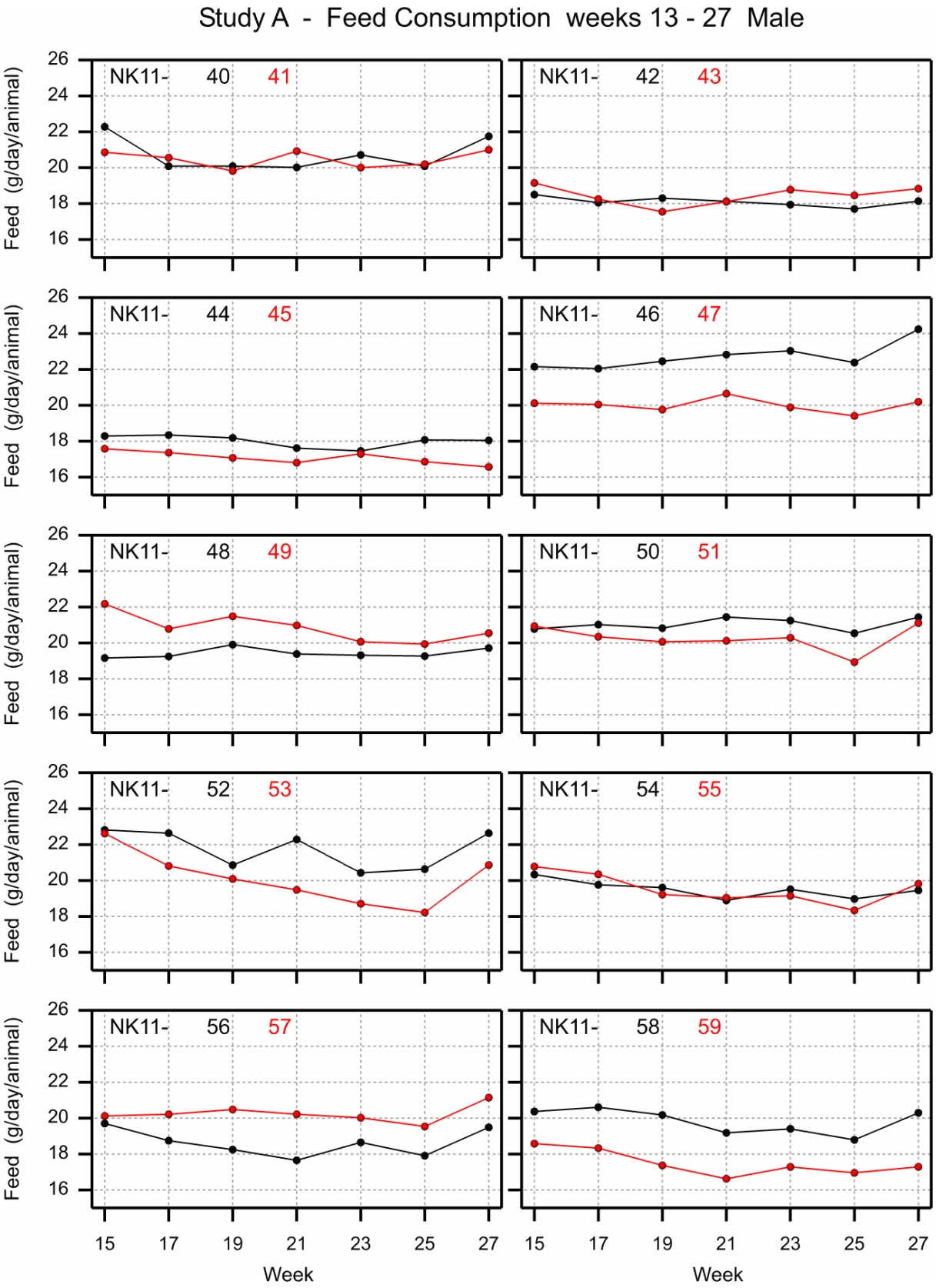
Appendix 2. Feed consumption per cage (continued)

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



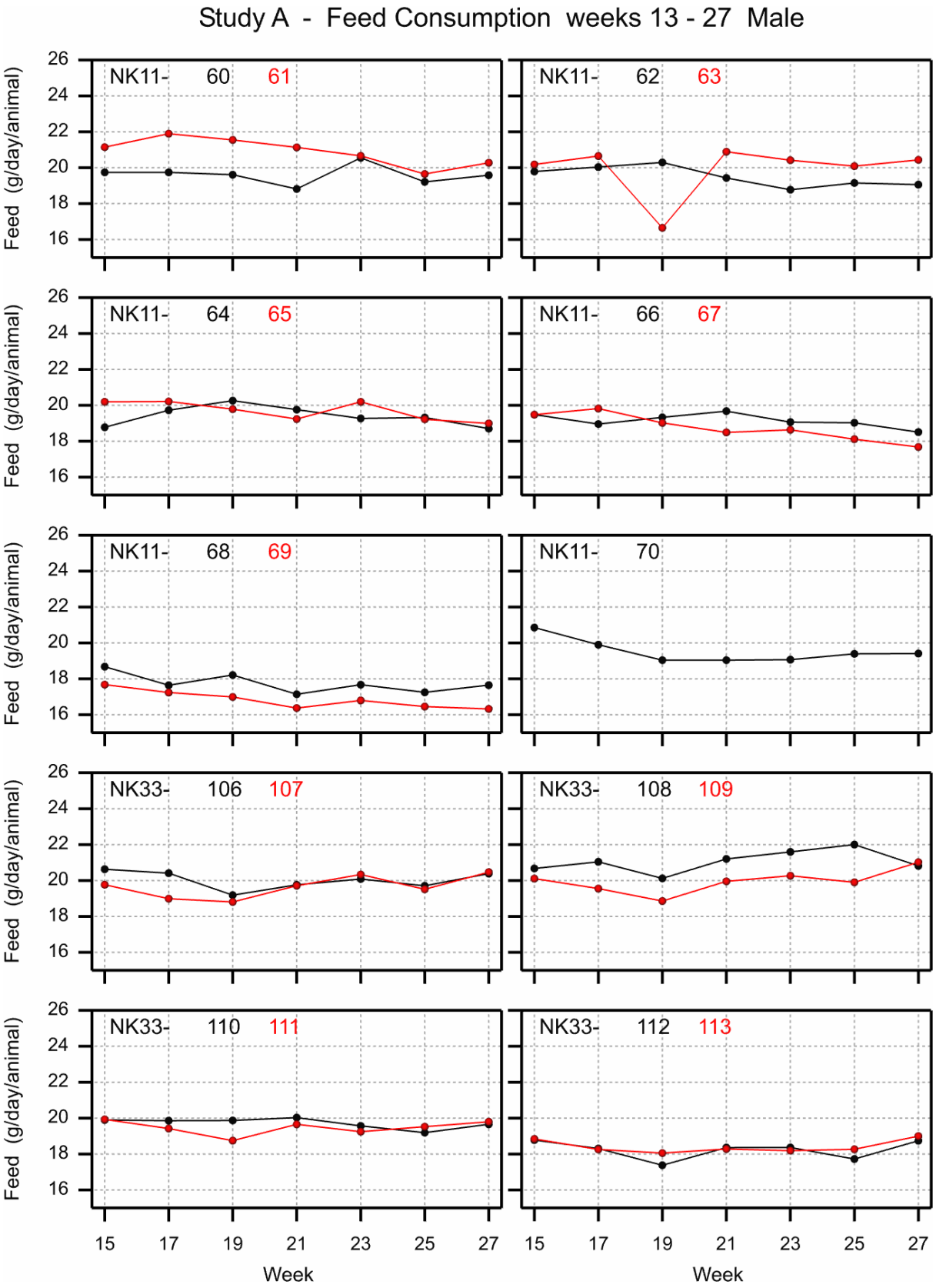
Appendix 2. Feed consumption per cage (continued)

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



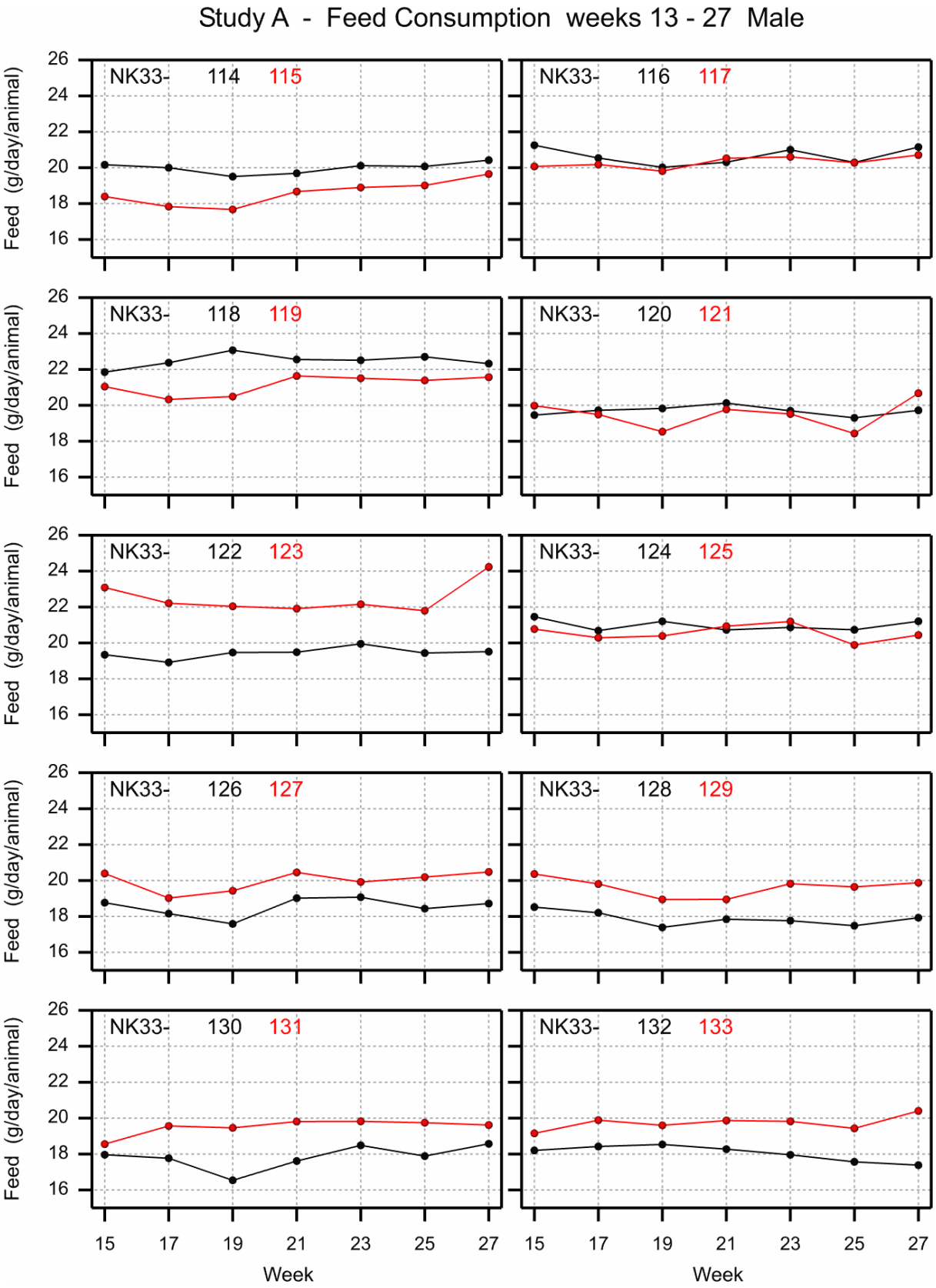
Appendix 2. Feed consumption per cage (continued)

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



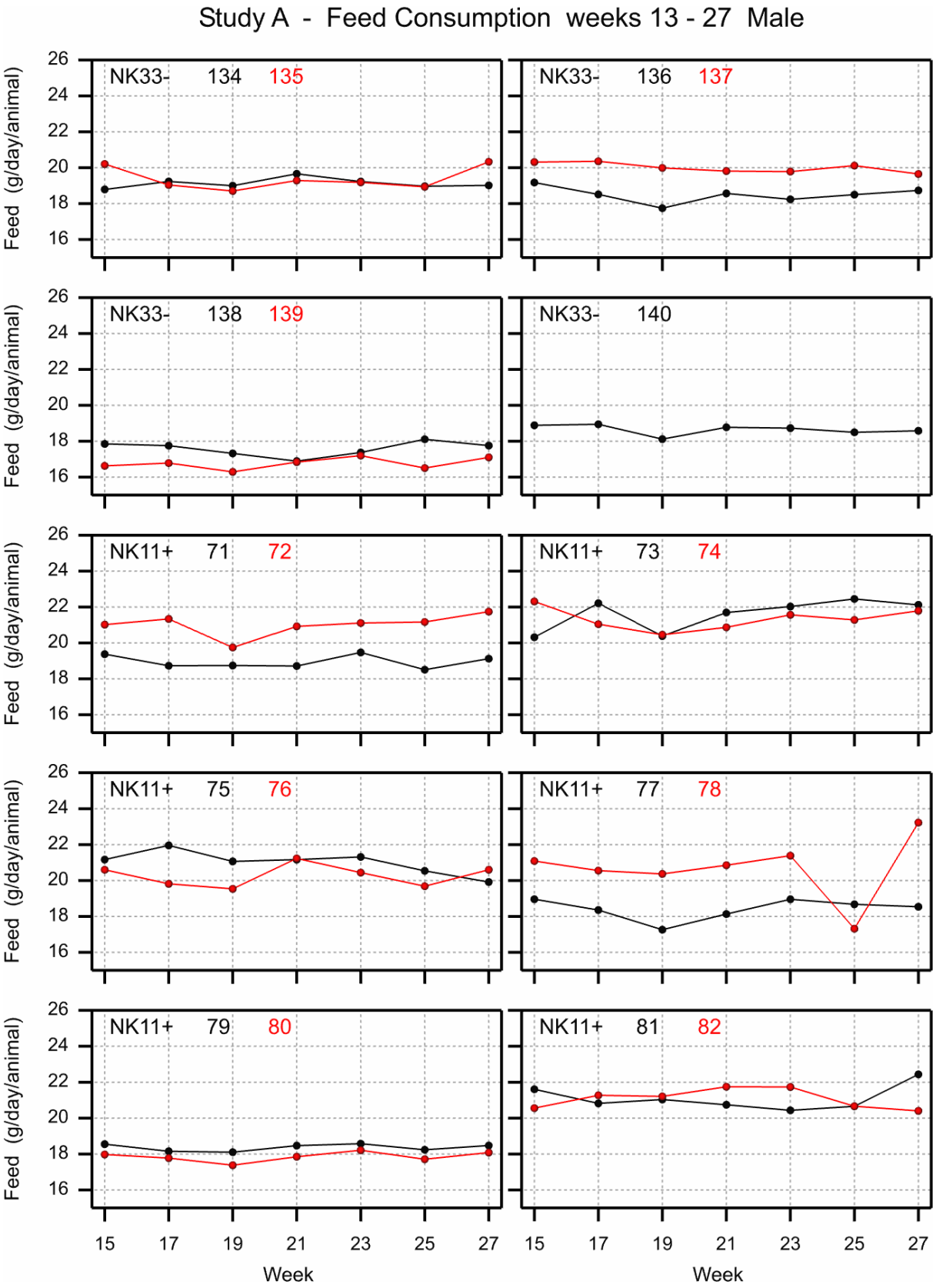
Appendix 2. Feed consumption per cage (continued)

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



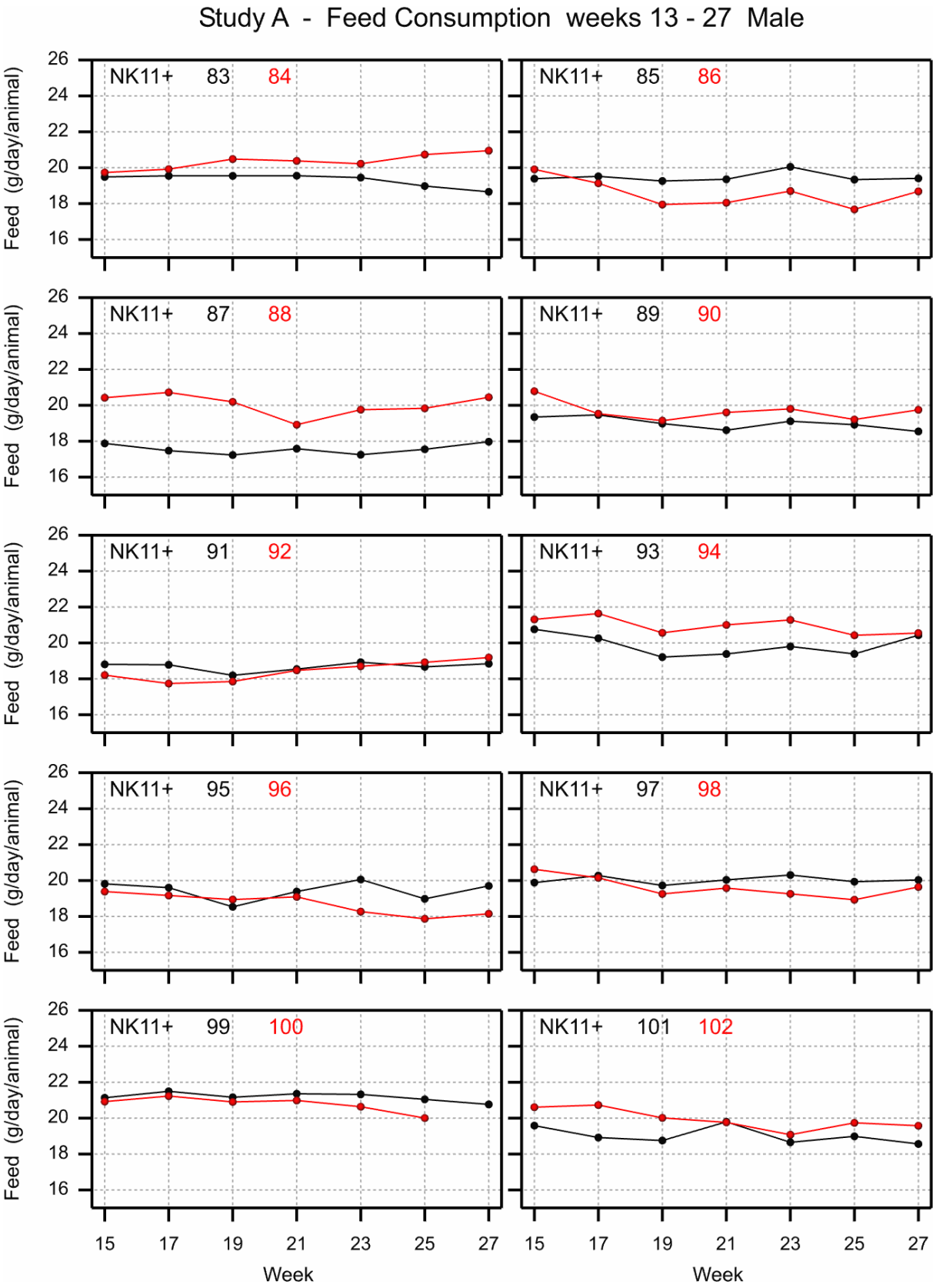
Appendix 2. Feed consumption per cage (continued)

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



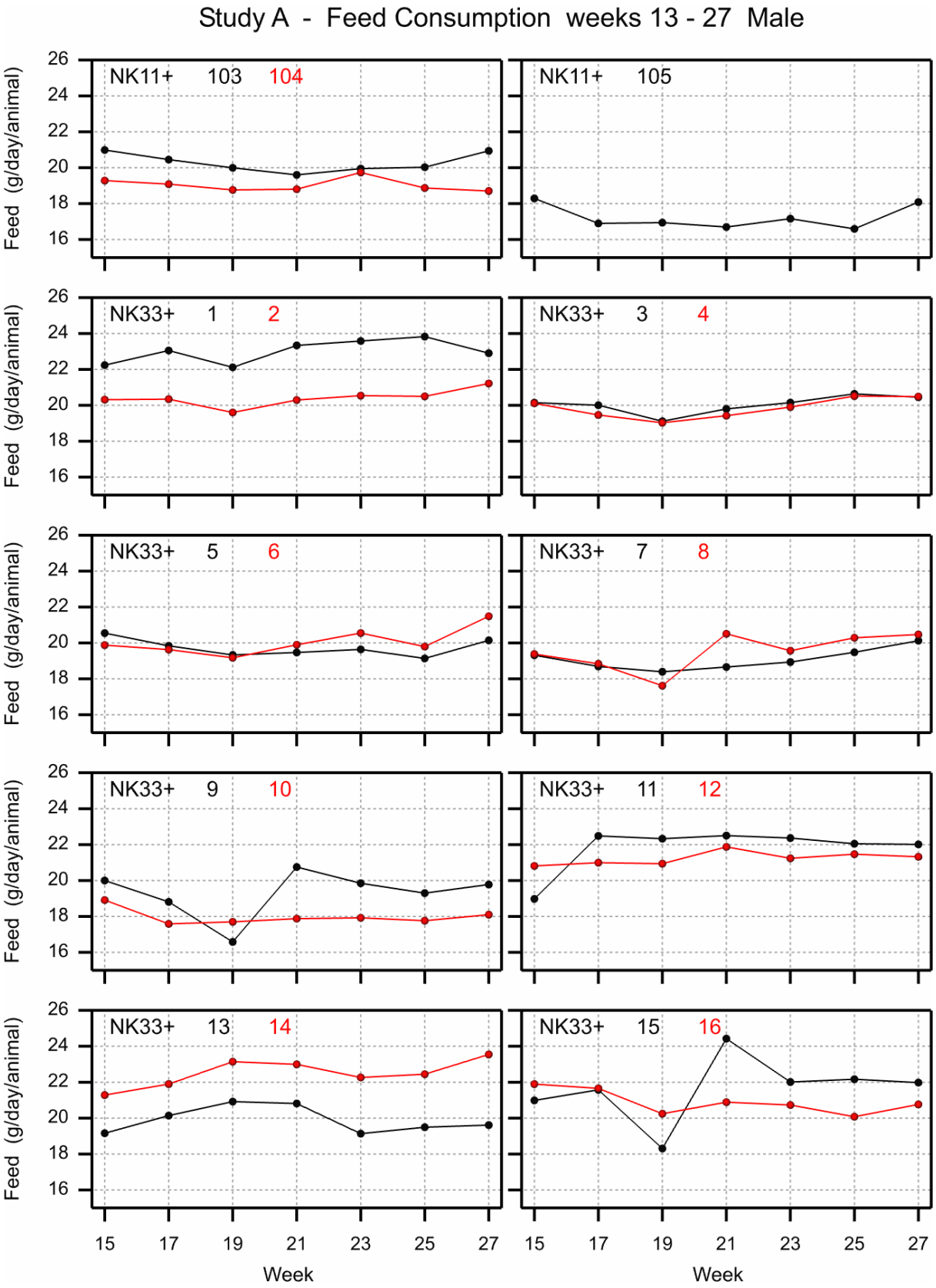
Appendix 2. Feed consumption per cage (continued)

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



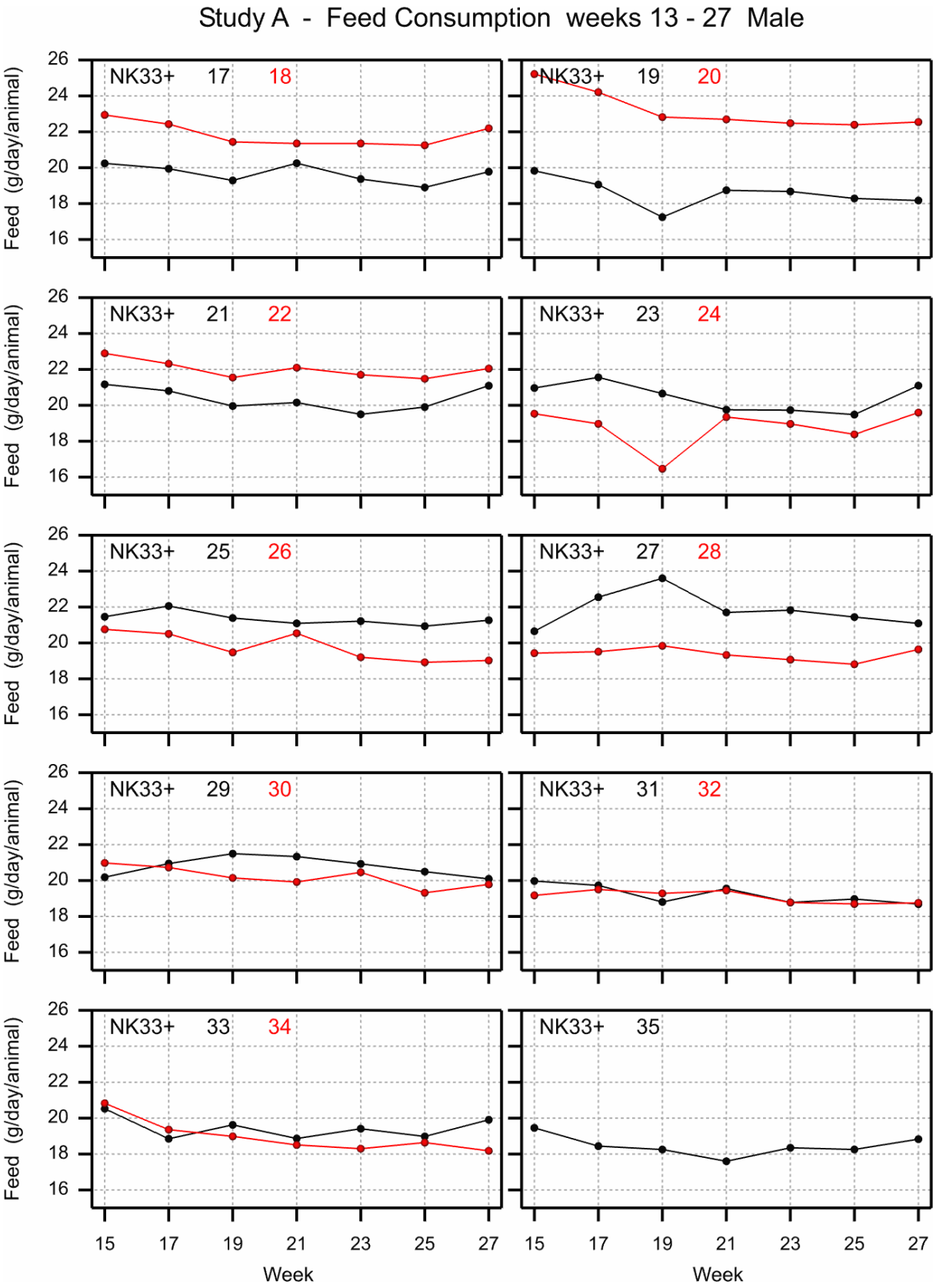
Appendix 2. Feed consumption per cage (continued)

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



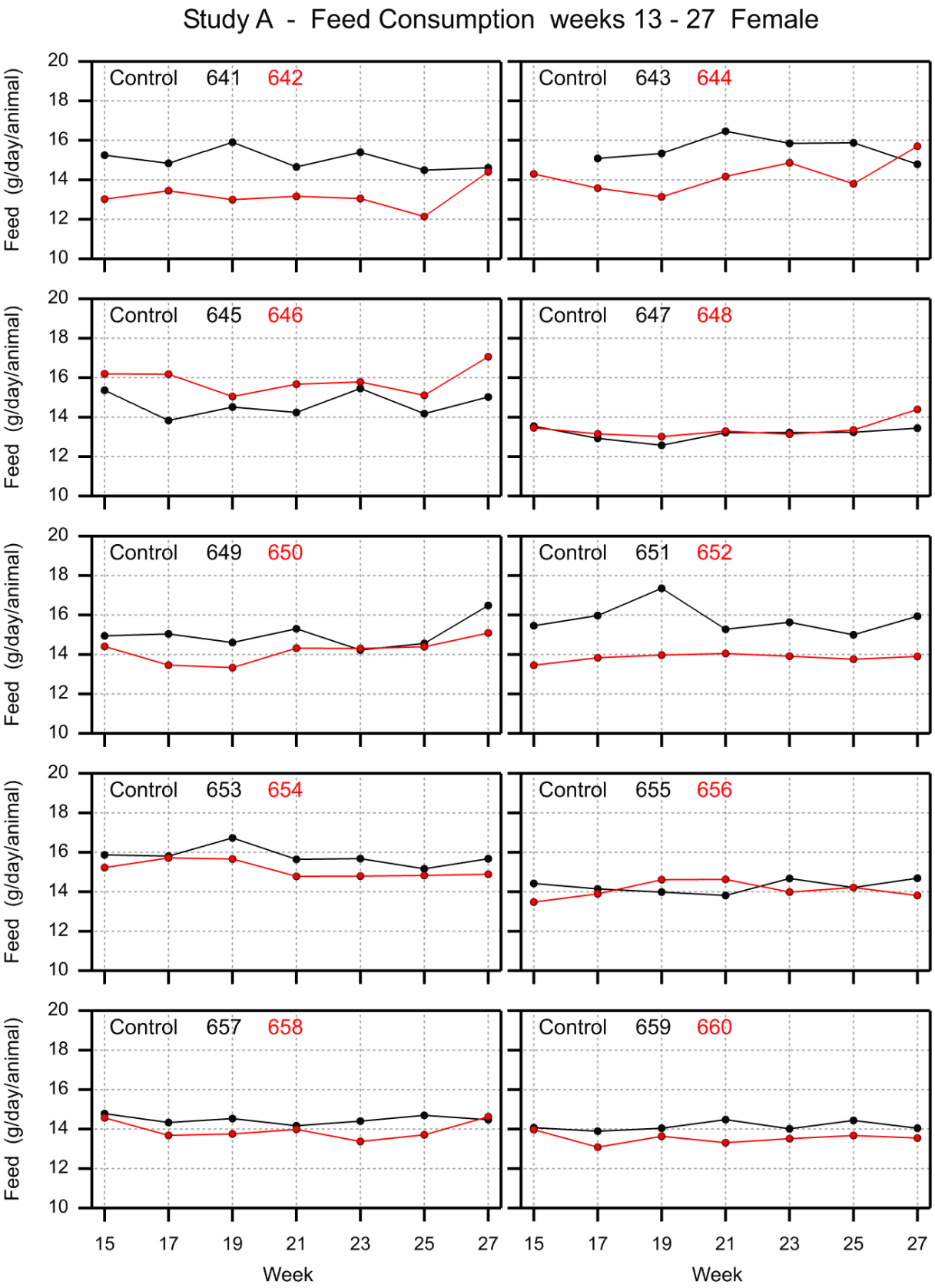
Appendix 2. Feed consumption per cage (continued)

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



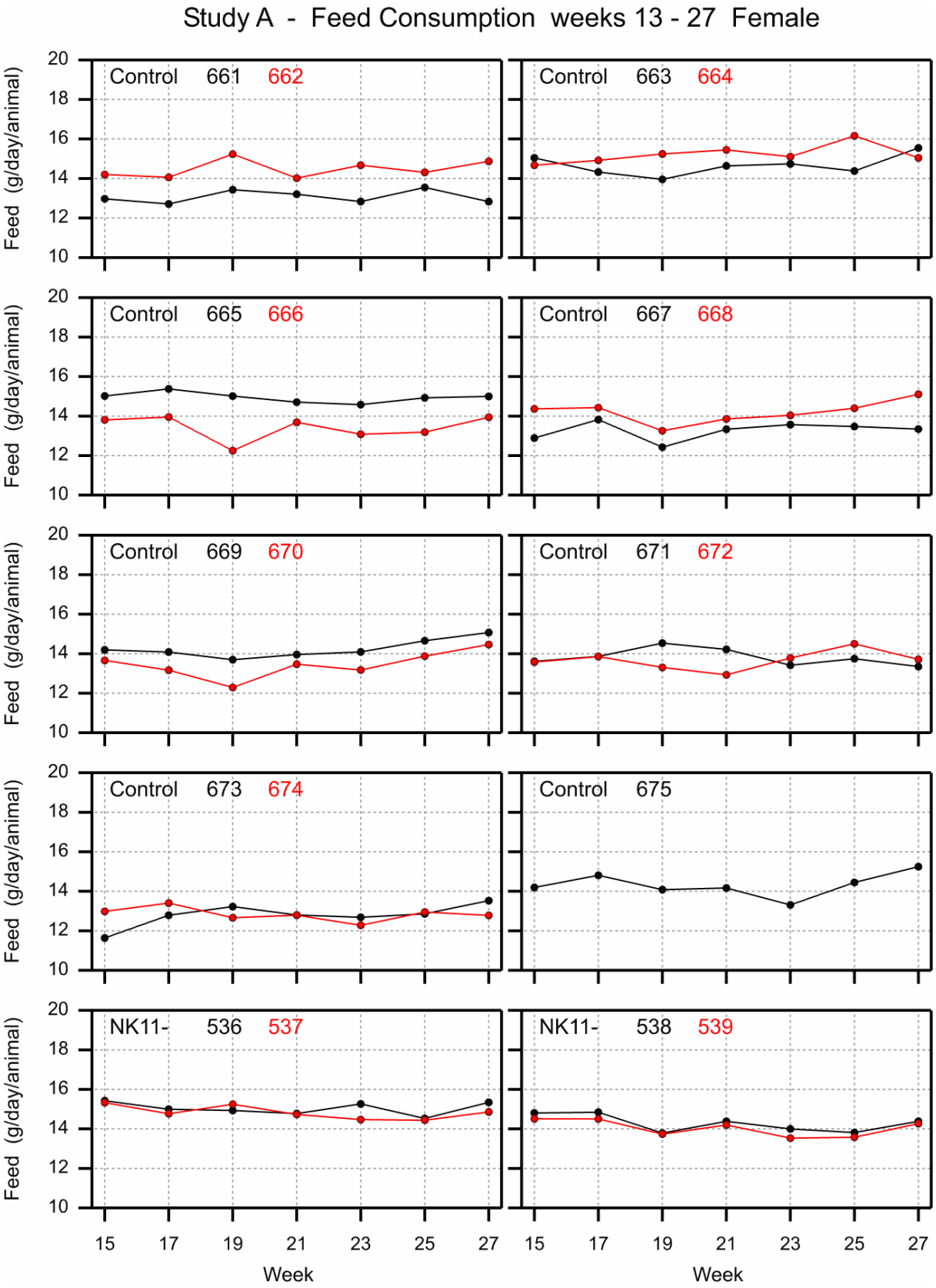
Appendix 2. Feed consumption per cage (continued)

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



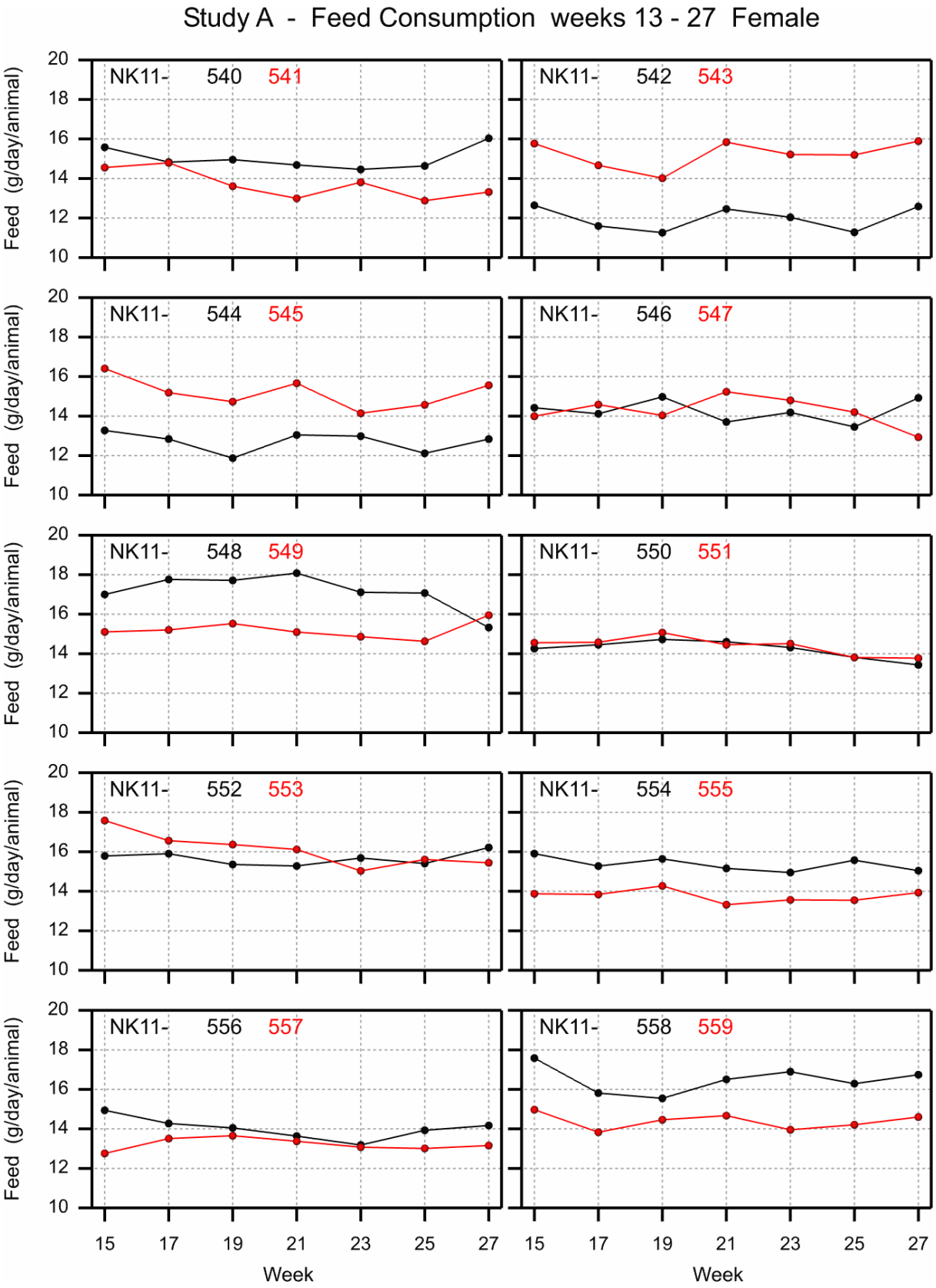
Appendix 2. Feed consumption per cage (continued)

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



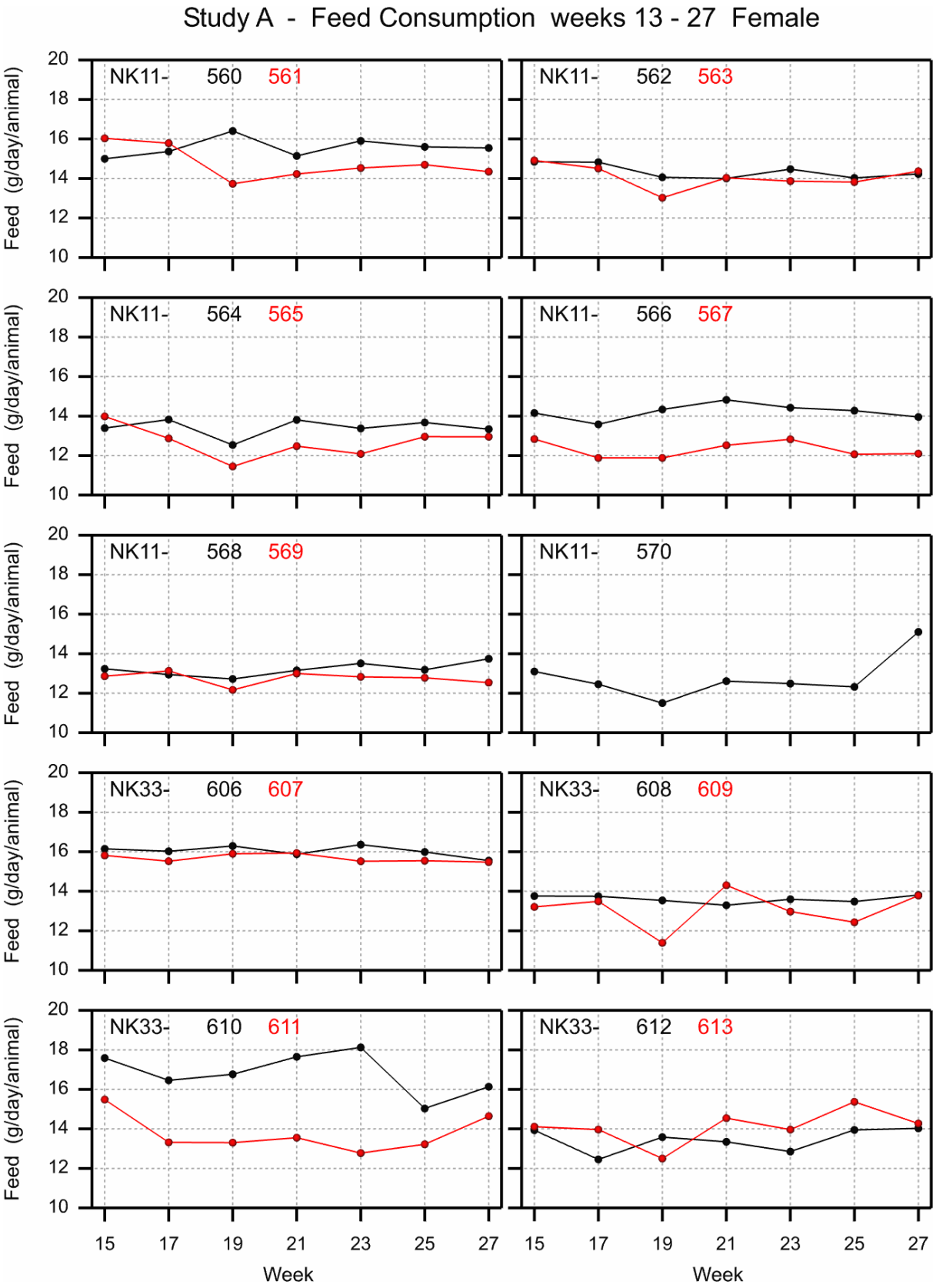
Appendix 2. Feed consumption per cage (continued)

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



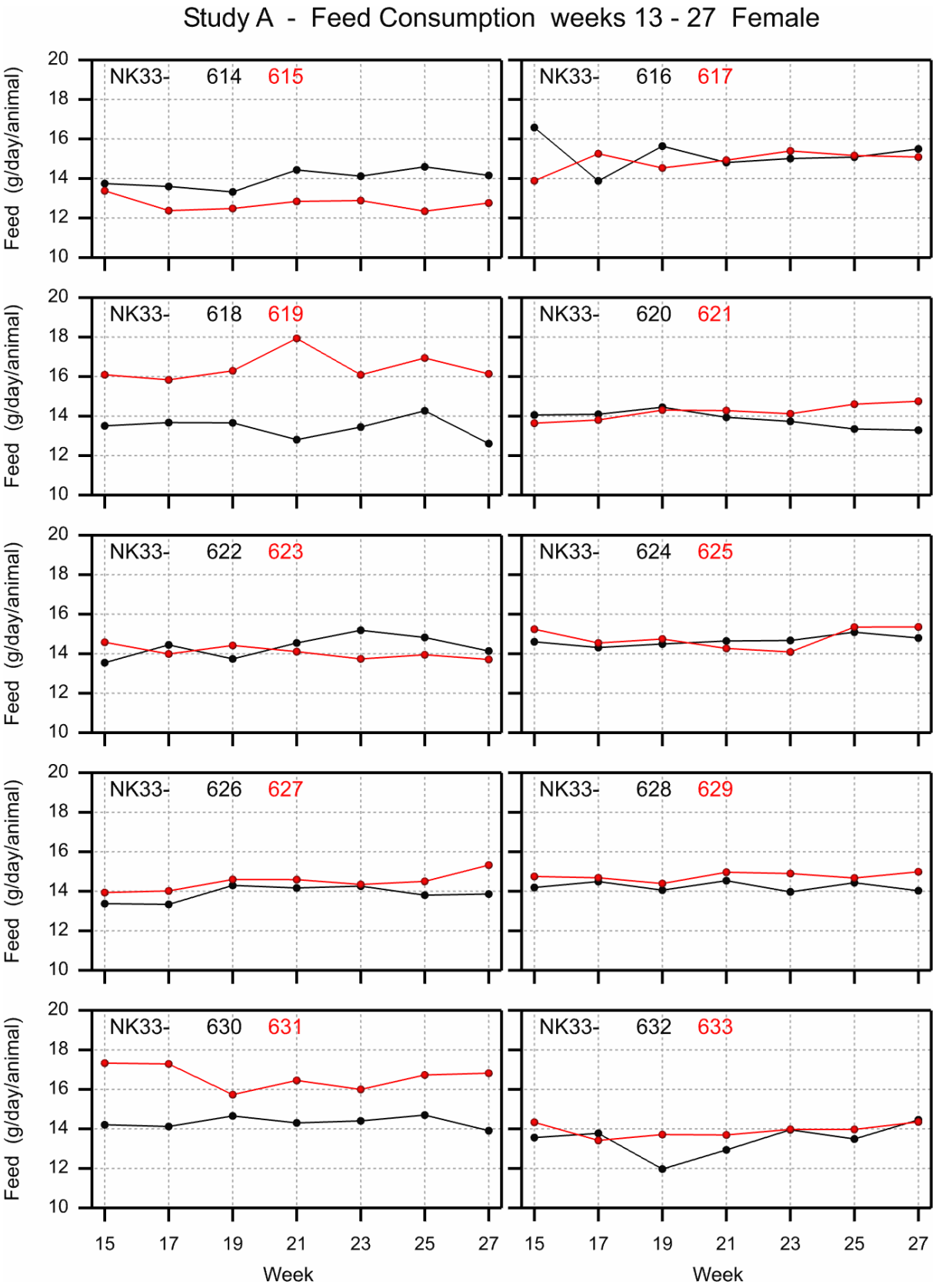
Appendix 2. Feed consumption per cage (continued)

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



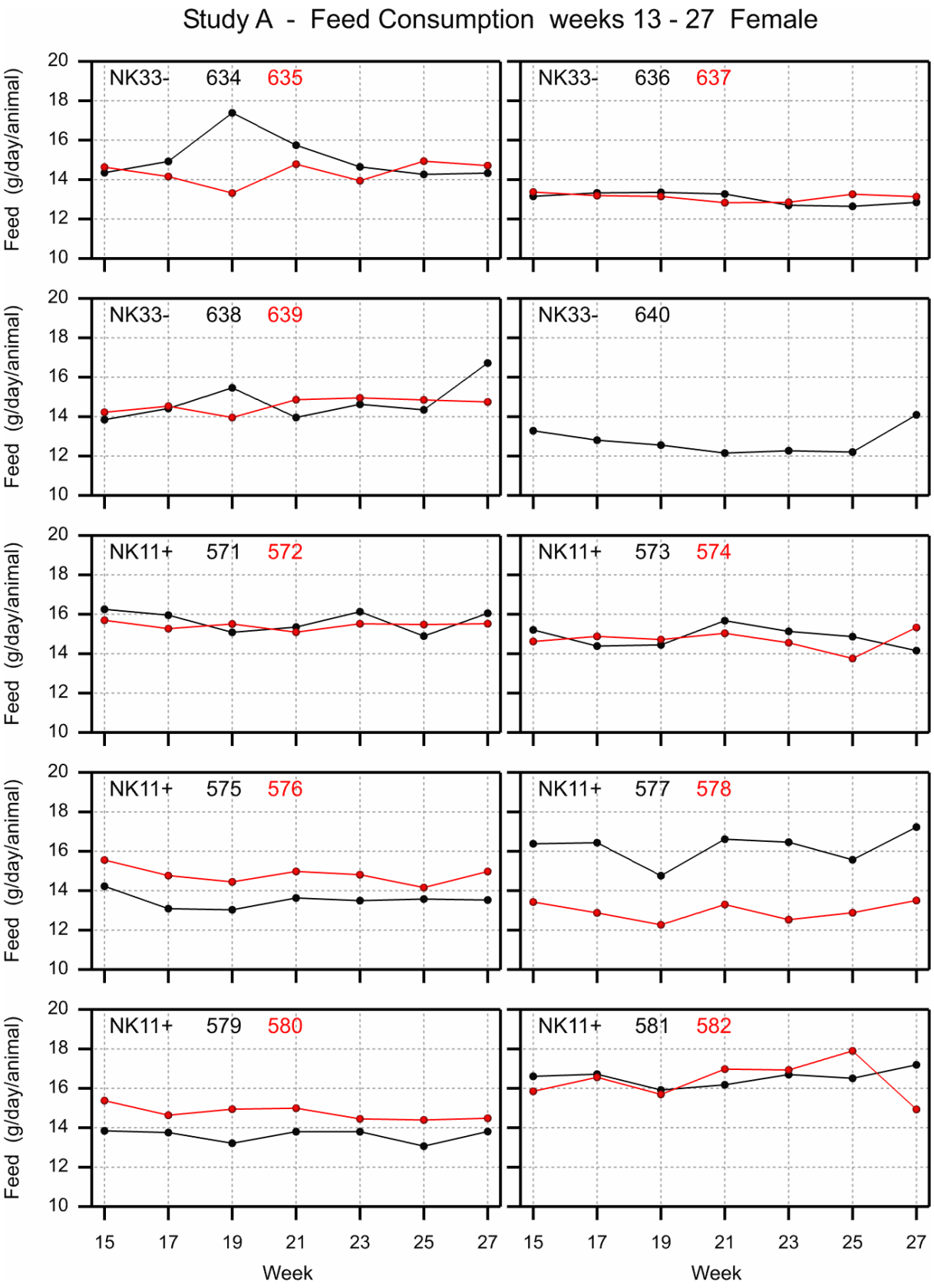
Appendix 2. Feed consumption per cage (continued)

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



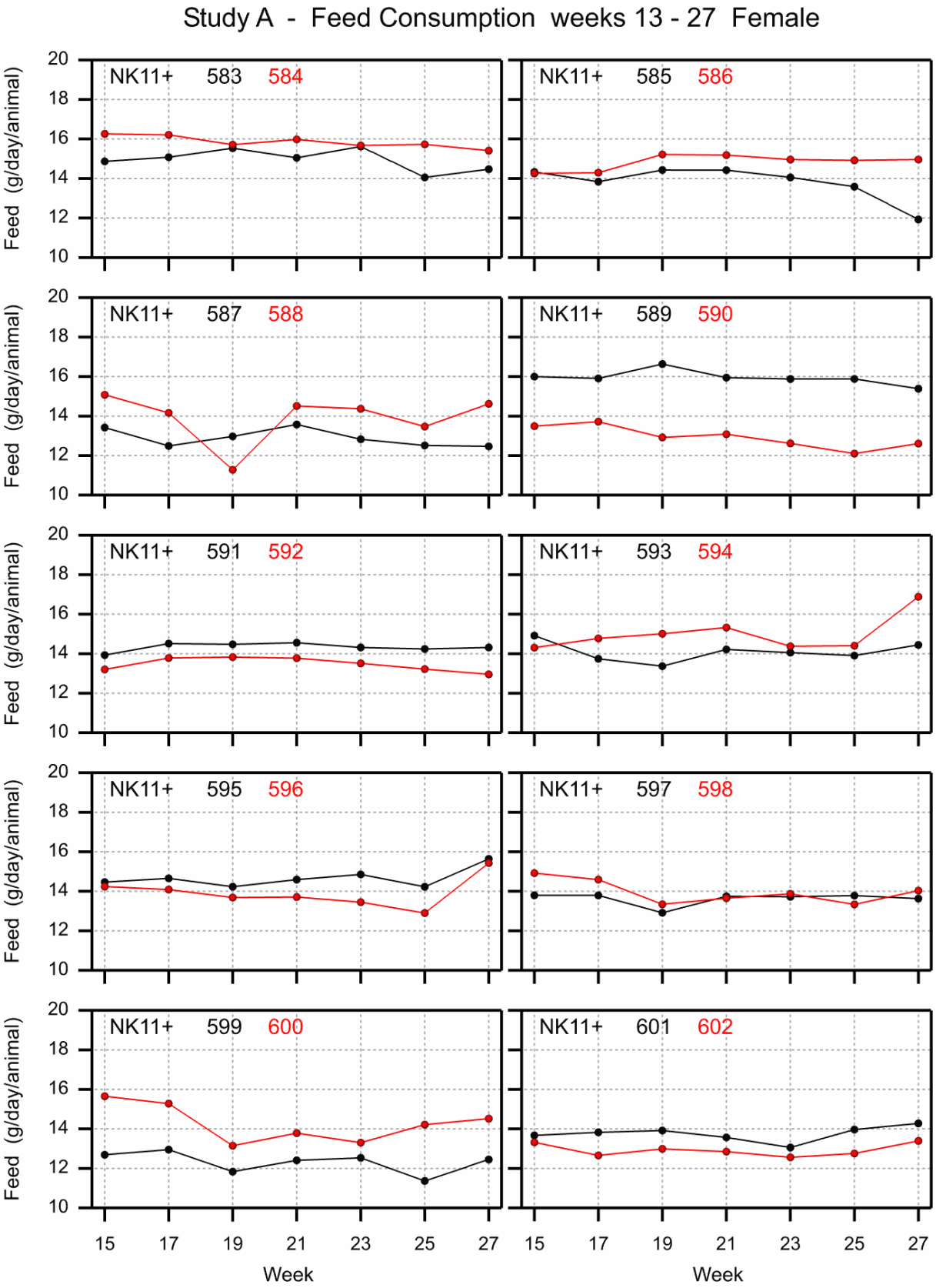
Appendix 2. Feed consumption per cage (continued)

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



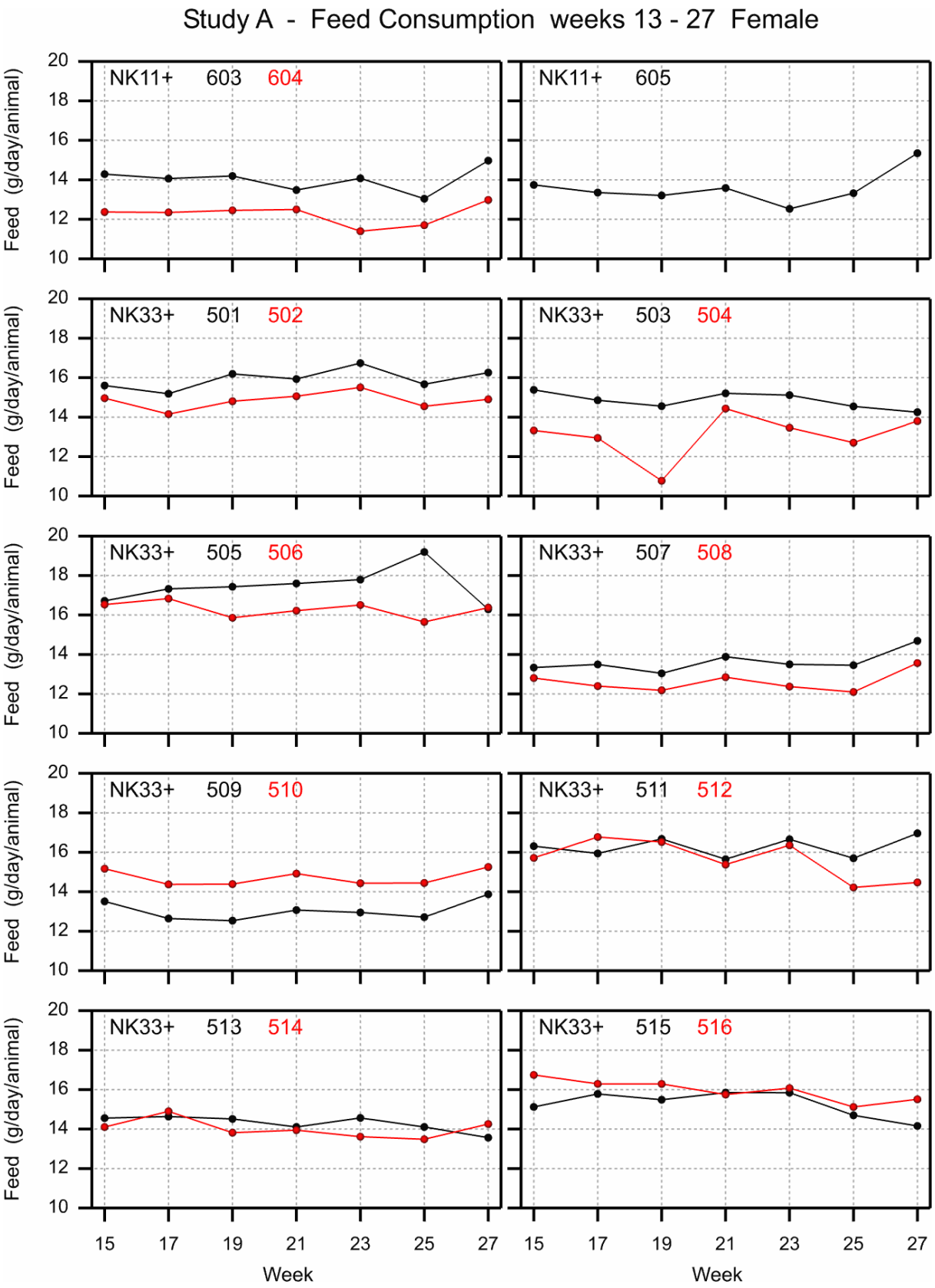
Appendix 2. Feed consumption per cage (continued)

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



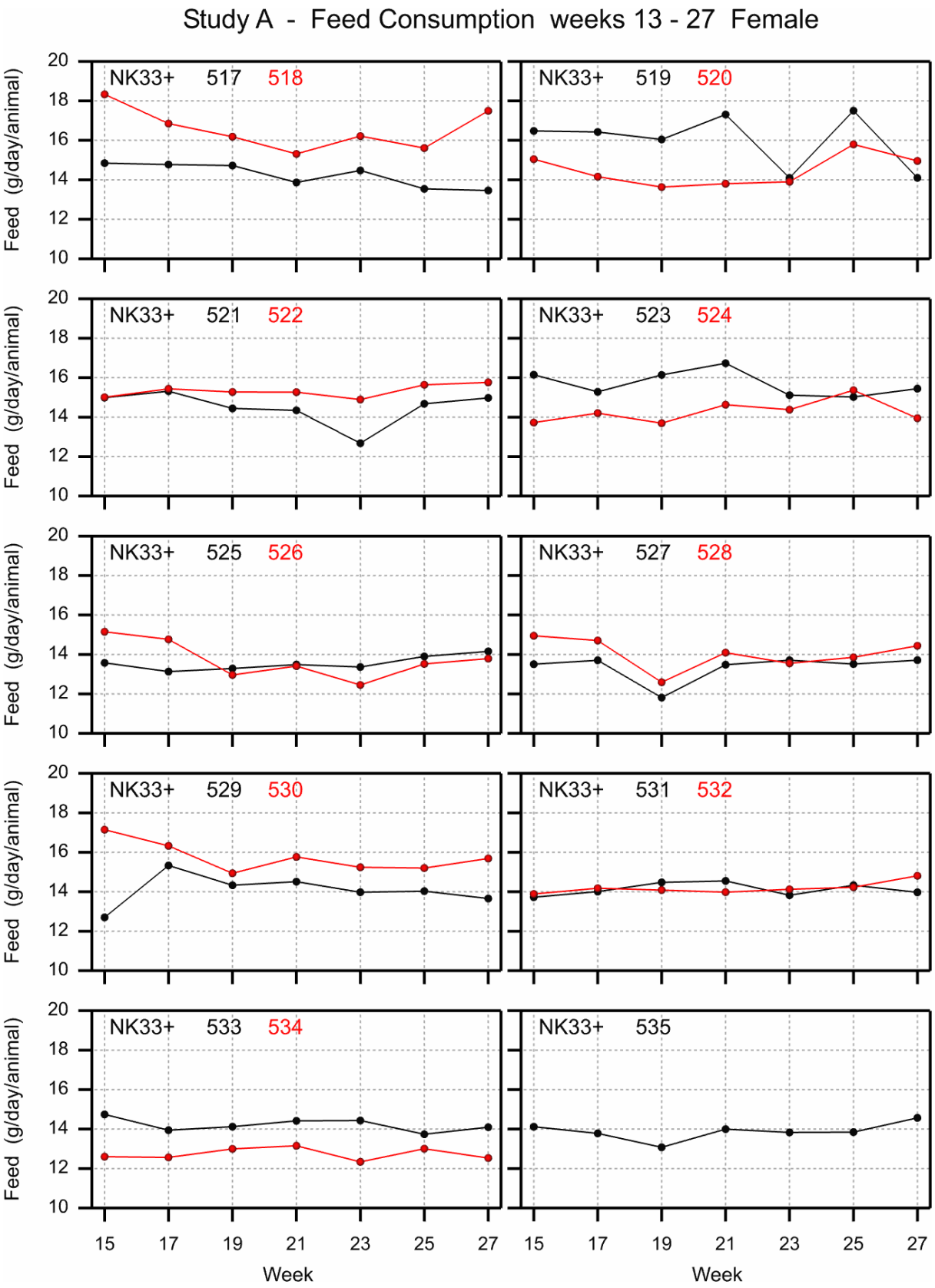
Appendix 2. Feed consumption per cage (continued)

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



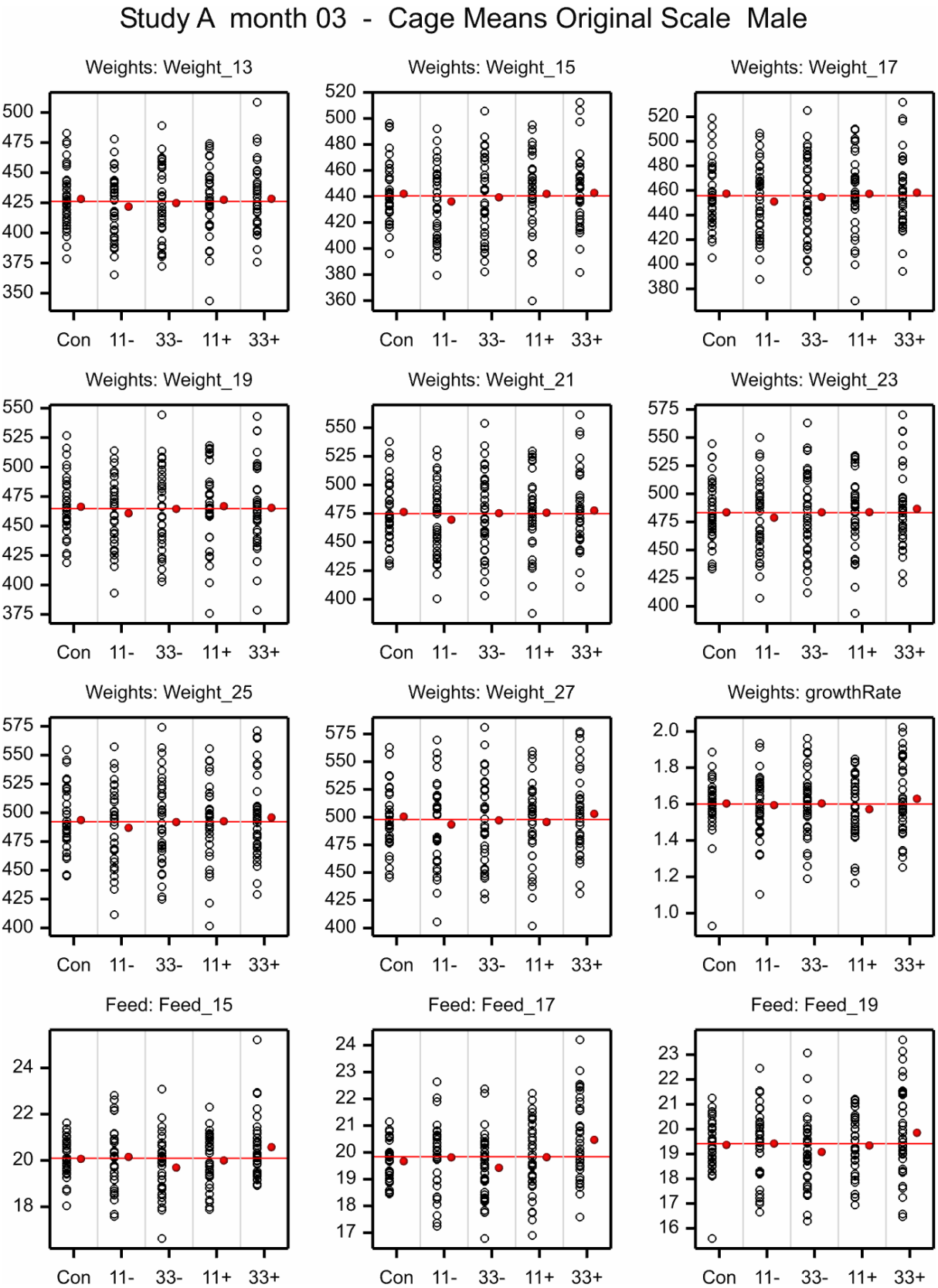
Appendix 2. Feed consumption per cage (continued)

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



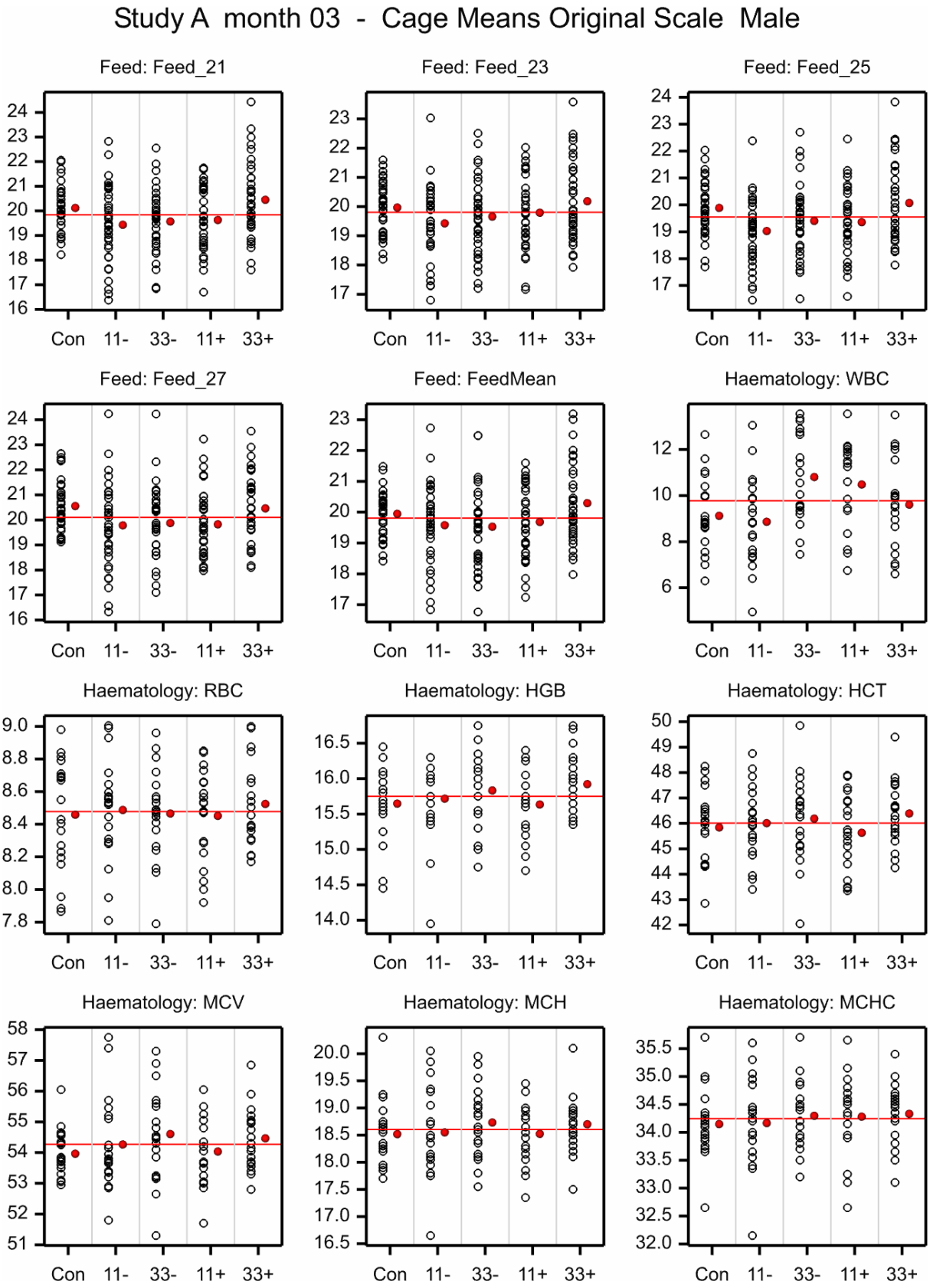
Appendix 3. Graphs of cage means on the original scale

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



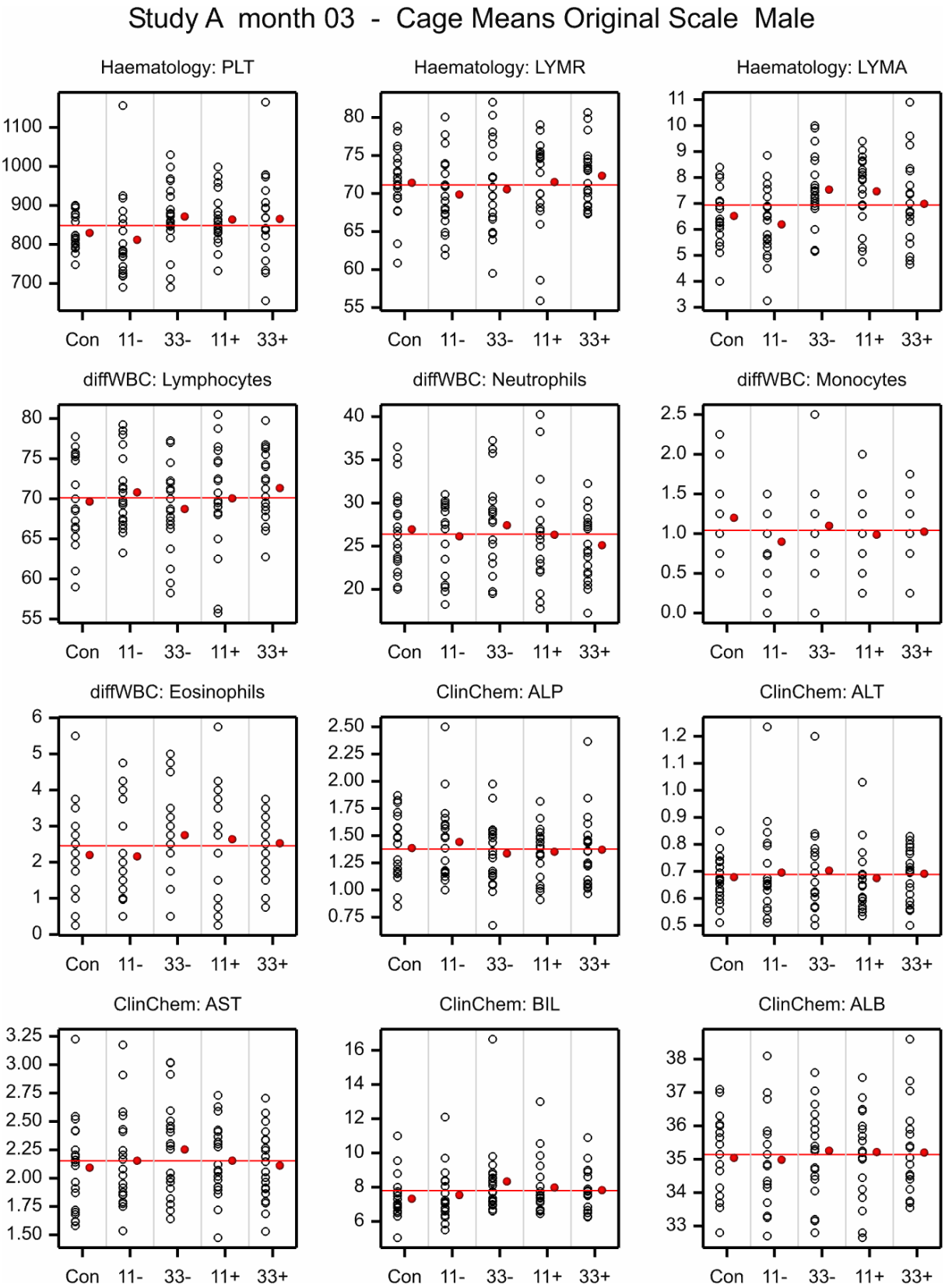
Appendix 3. Graphs of cage means on the original scale (continued)

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



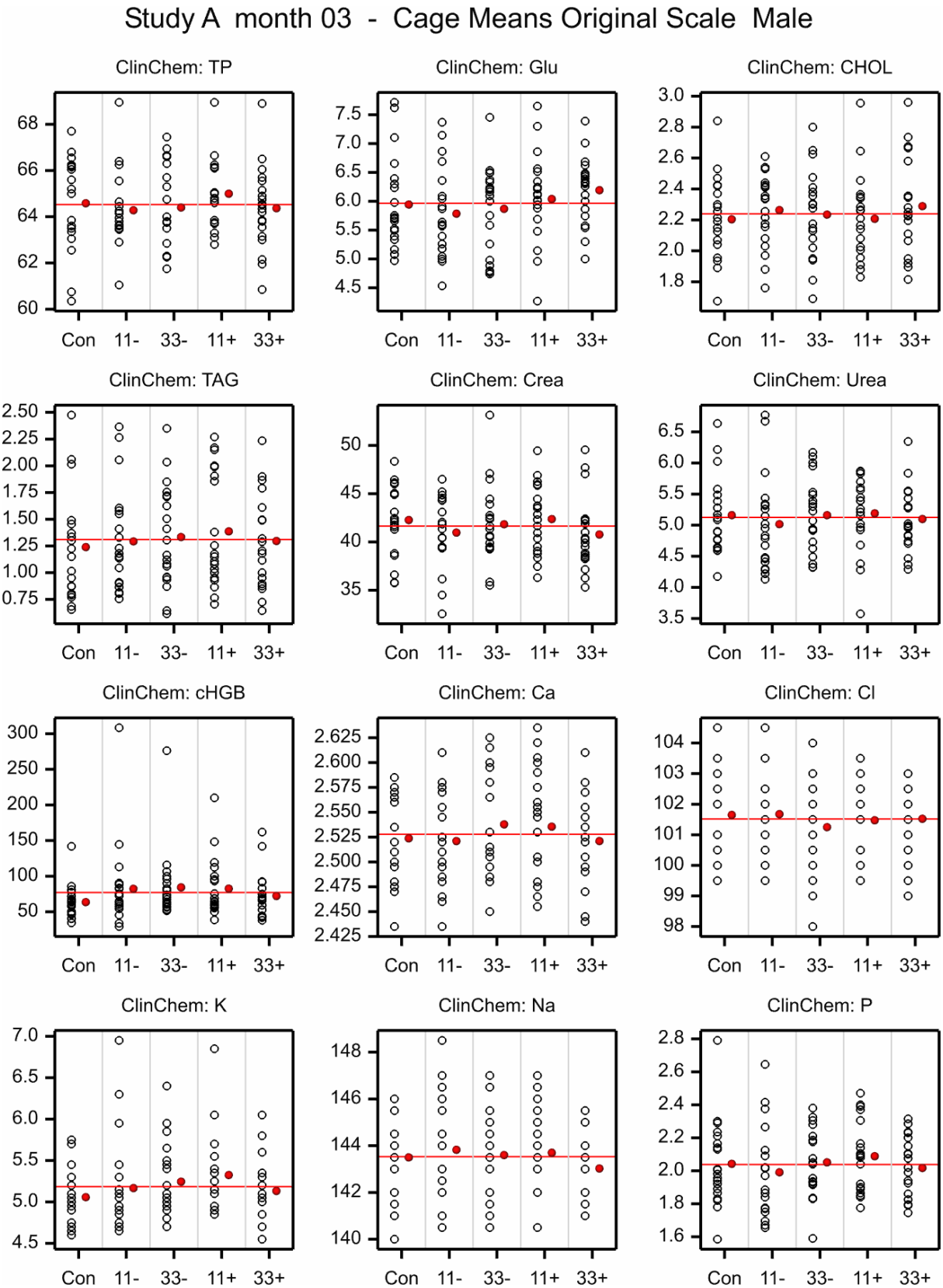
Appendix 3. Graphs of cage means on the original scale (continued)

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



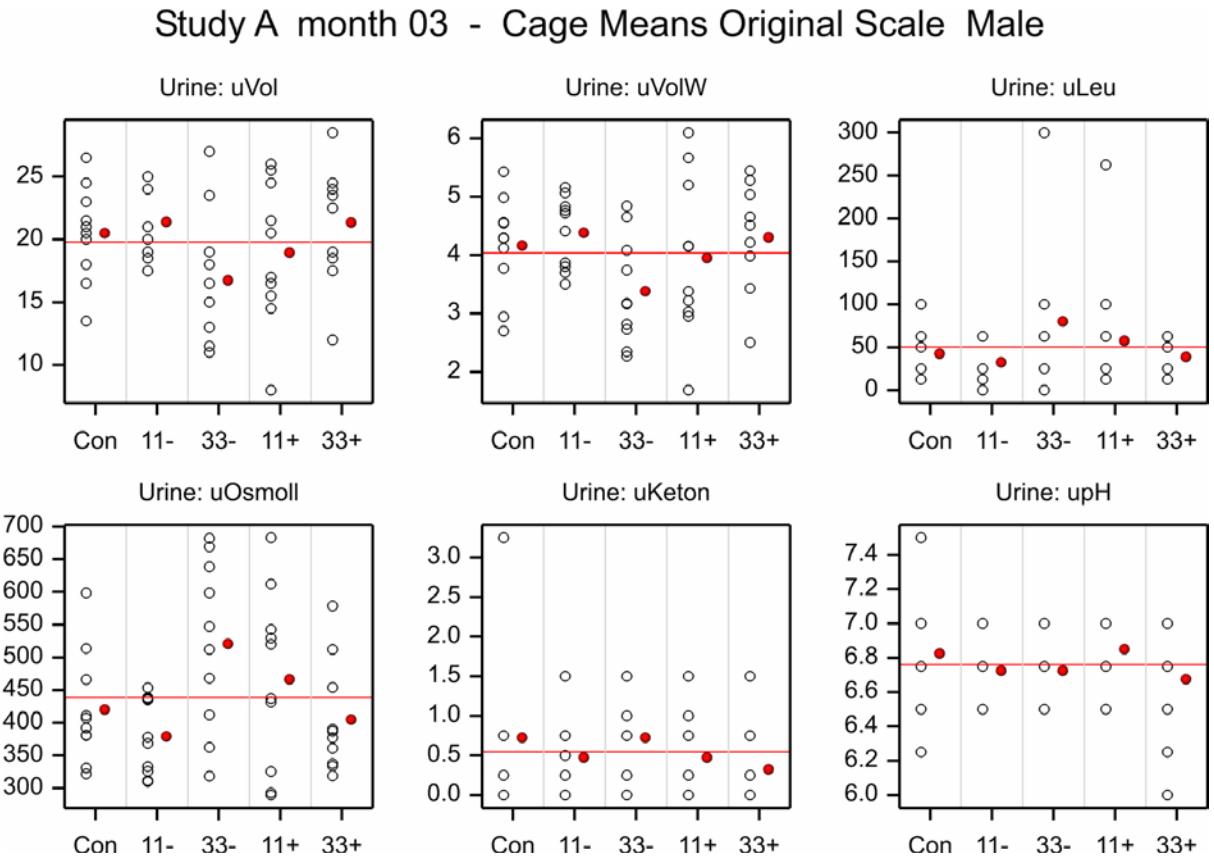
Appendix 3. Graphs of cage means on the original scale (continued)

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



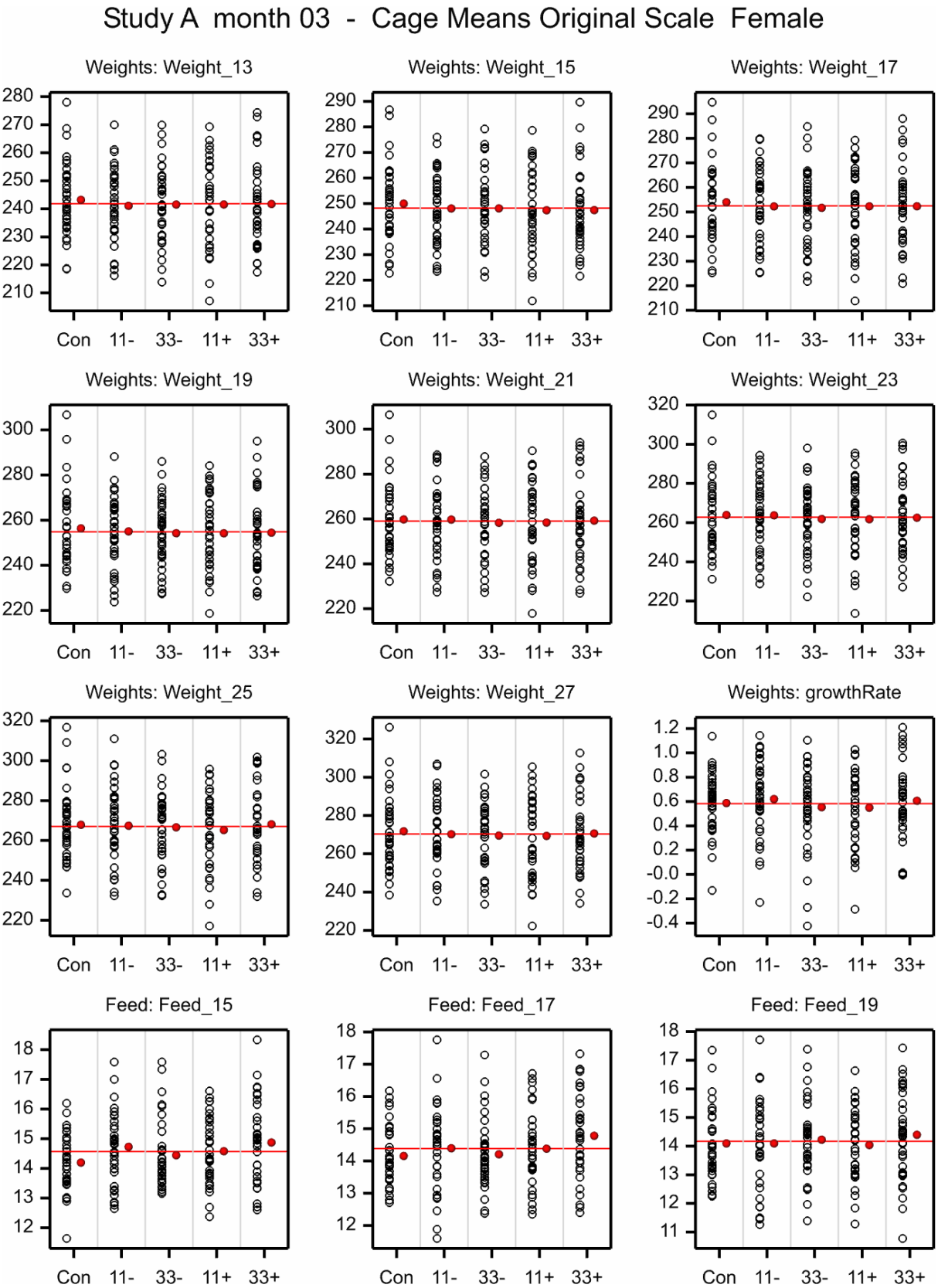
Appendix 3. Graphs of cage means on the original scale (continued)

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



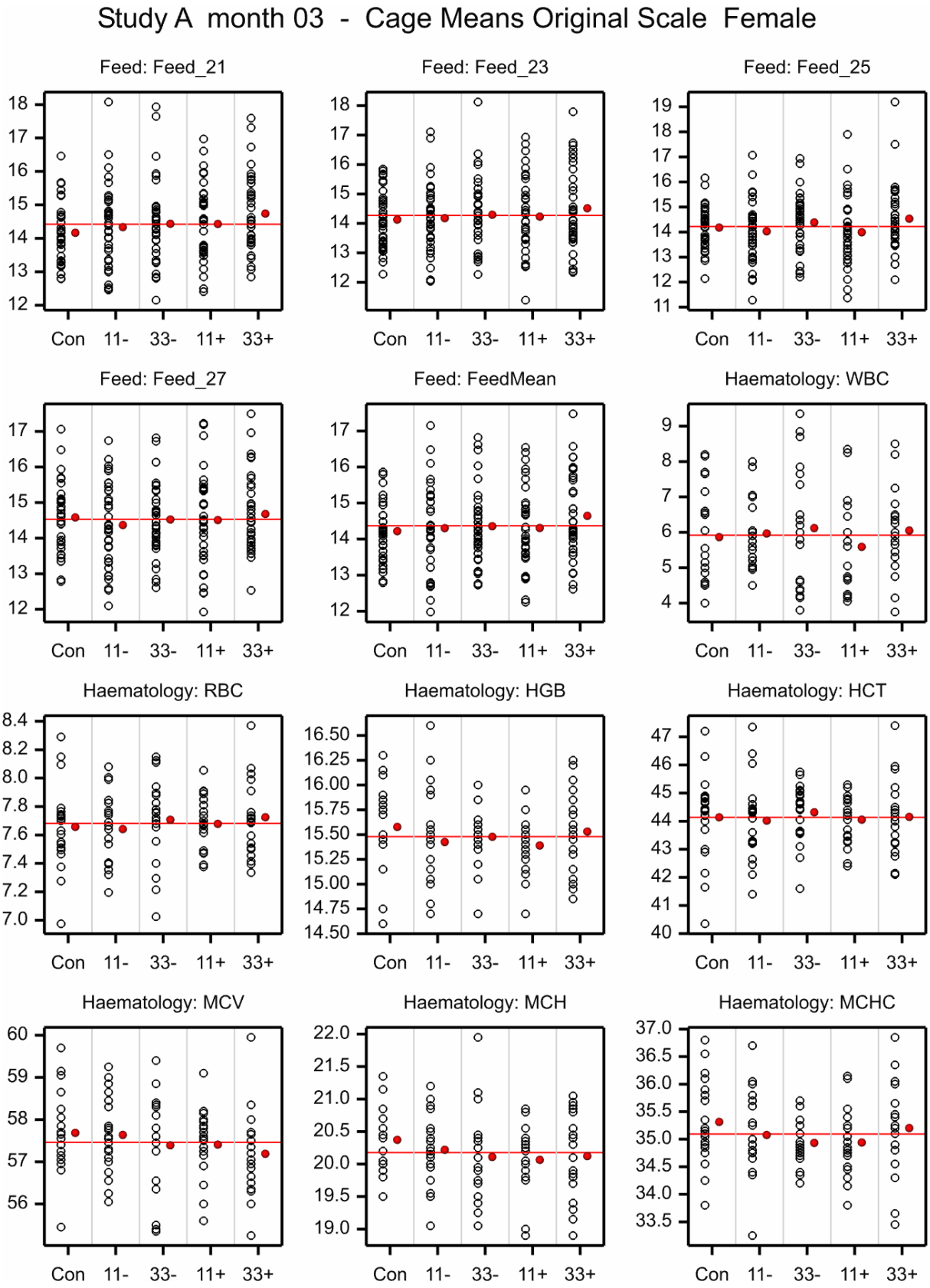
Appendix 3. Graphs of cage means on the original scale (continued)

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



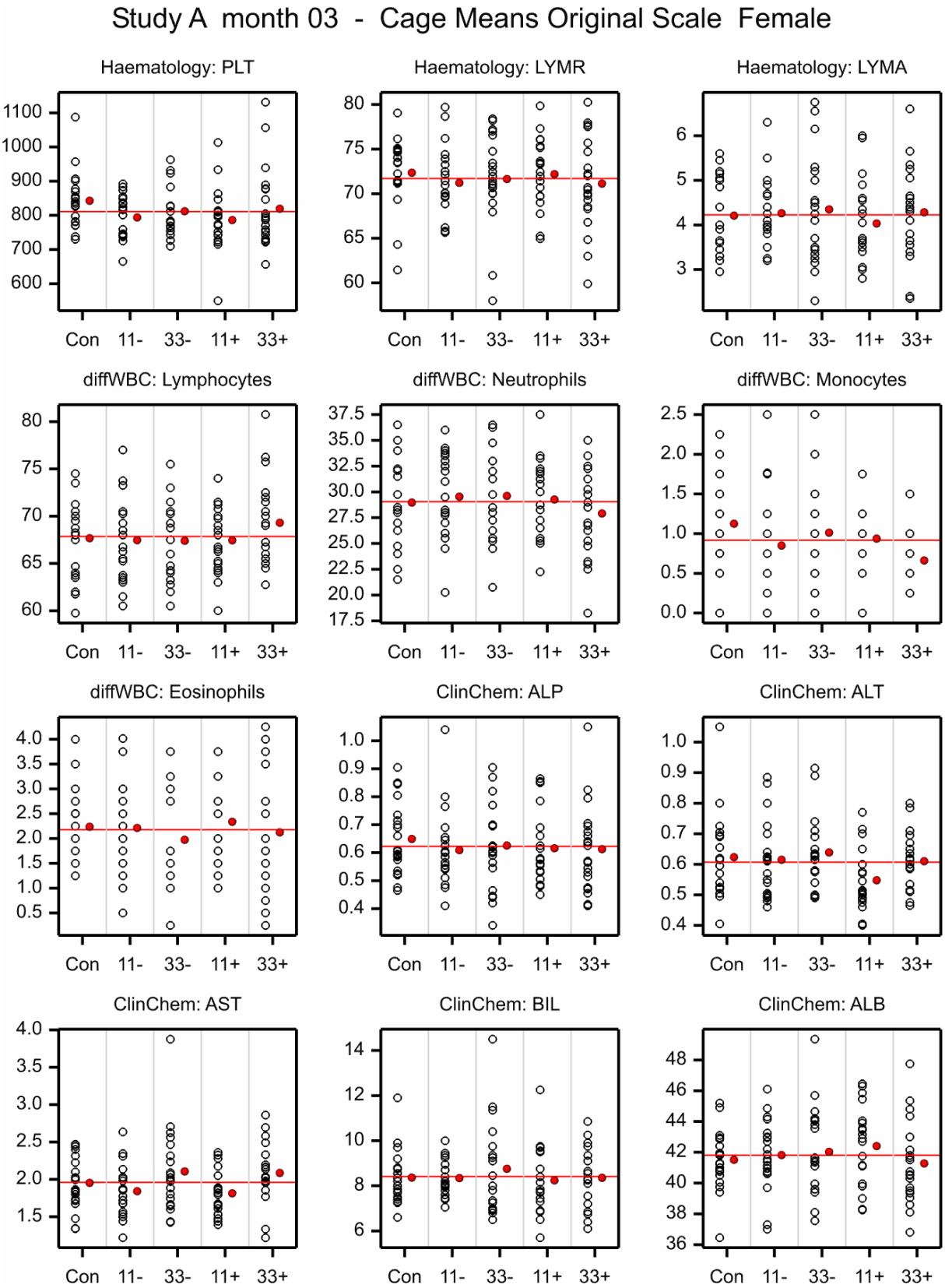
Appendix 3. Graphs of cage means on the original scale (continued)

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



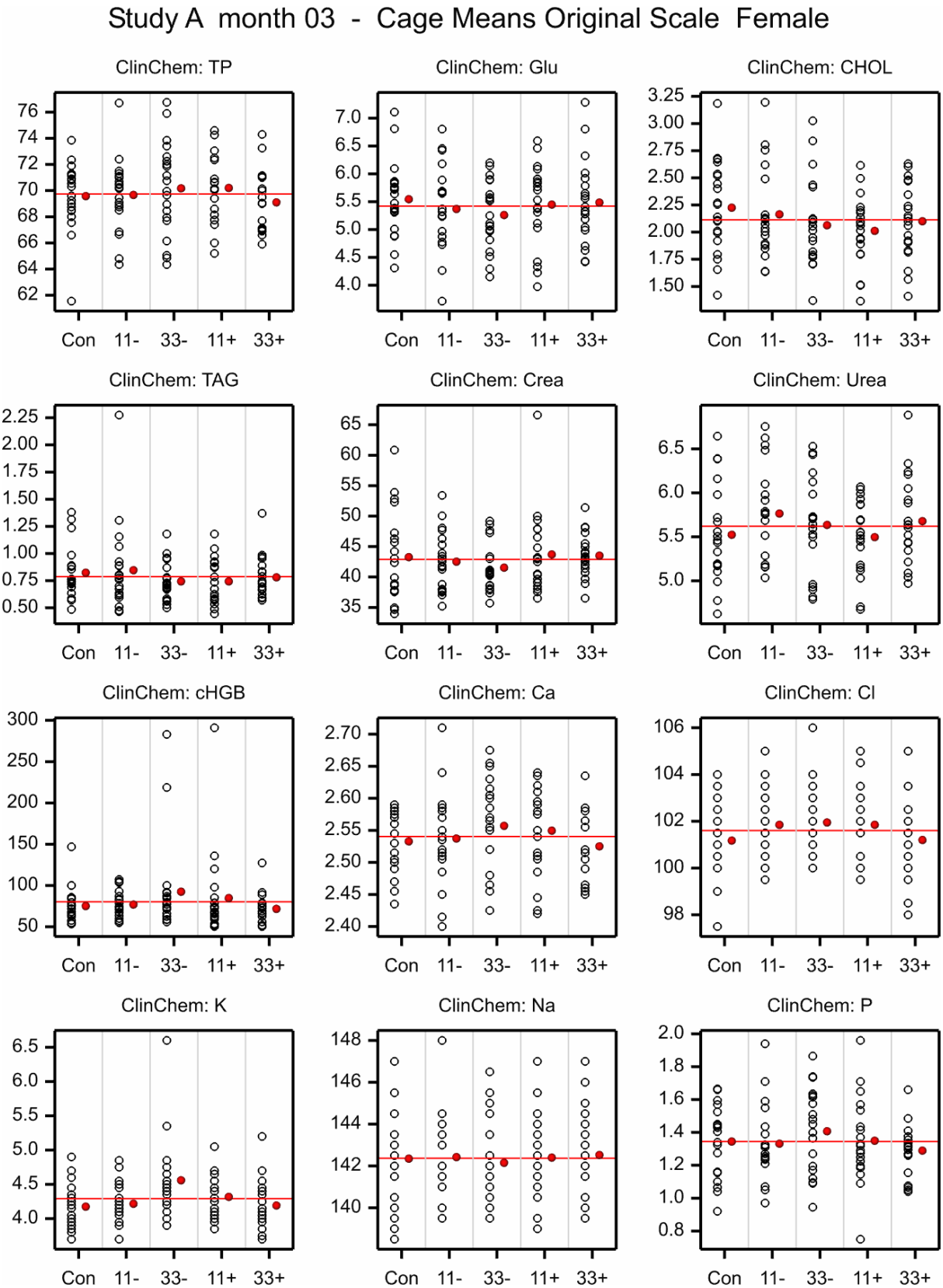
Appendix 3. Graphs of cage means on the original scale (continued)

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



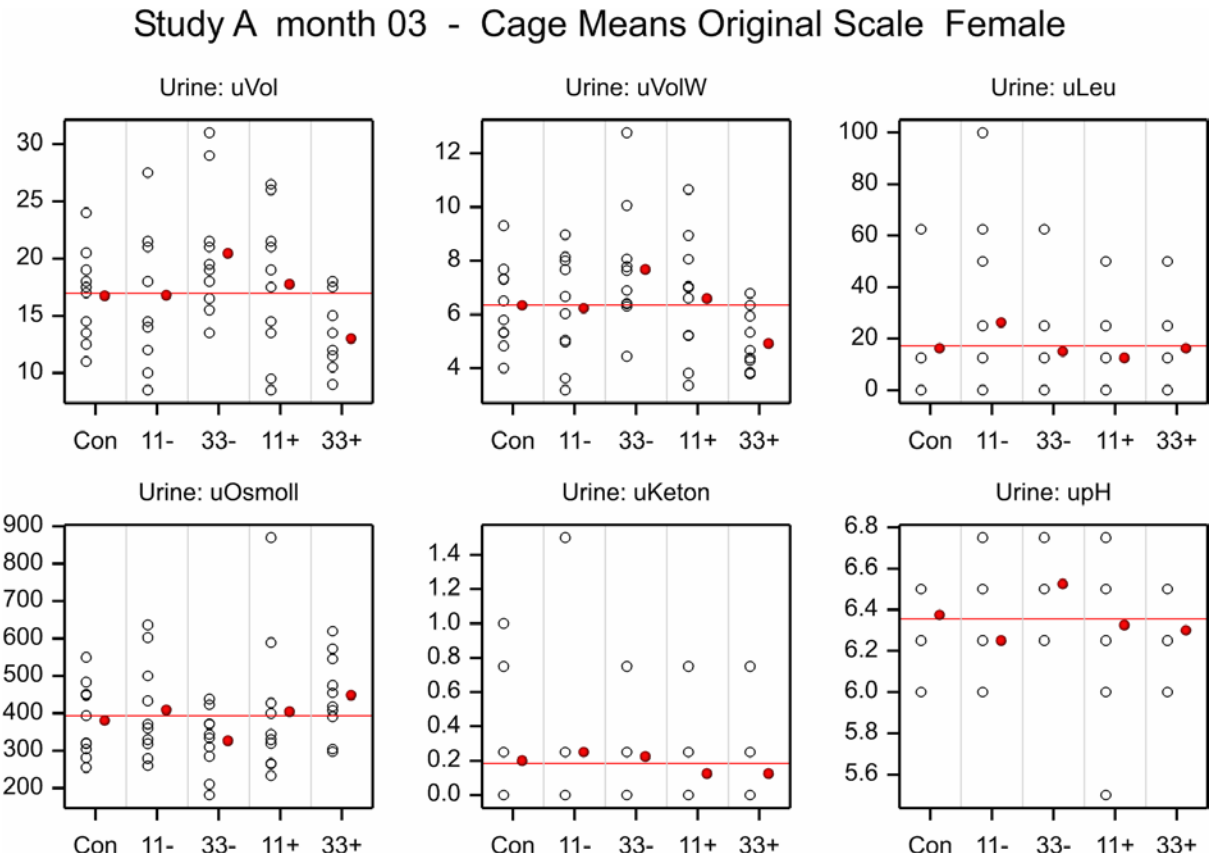
Appendix 3. Graphs of cage means on the original scale (continued)

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



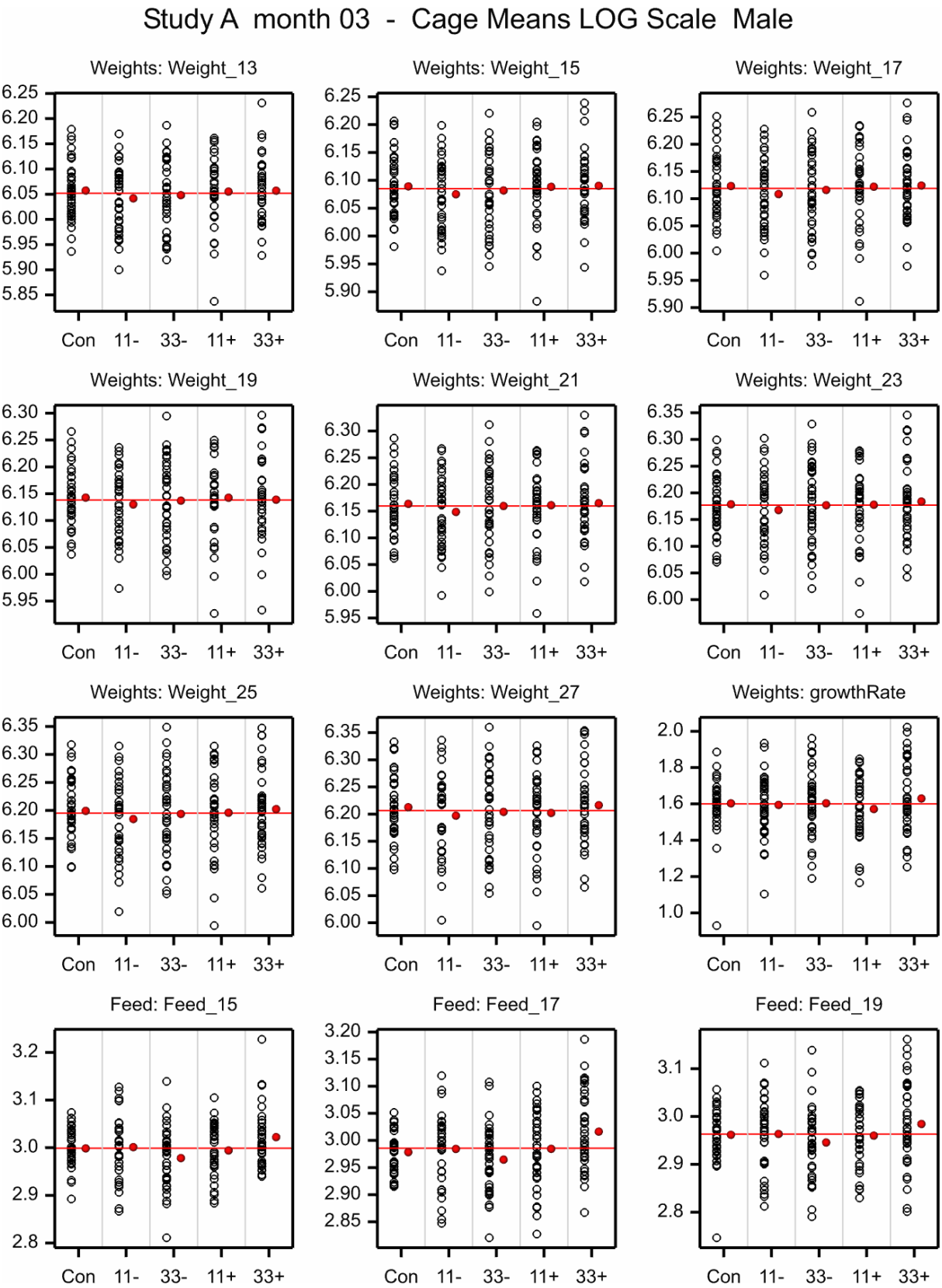
Appendix 3. Graphs of cage means on the original scale (continued)

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



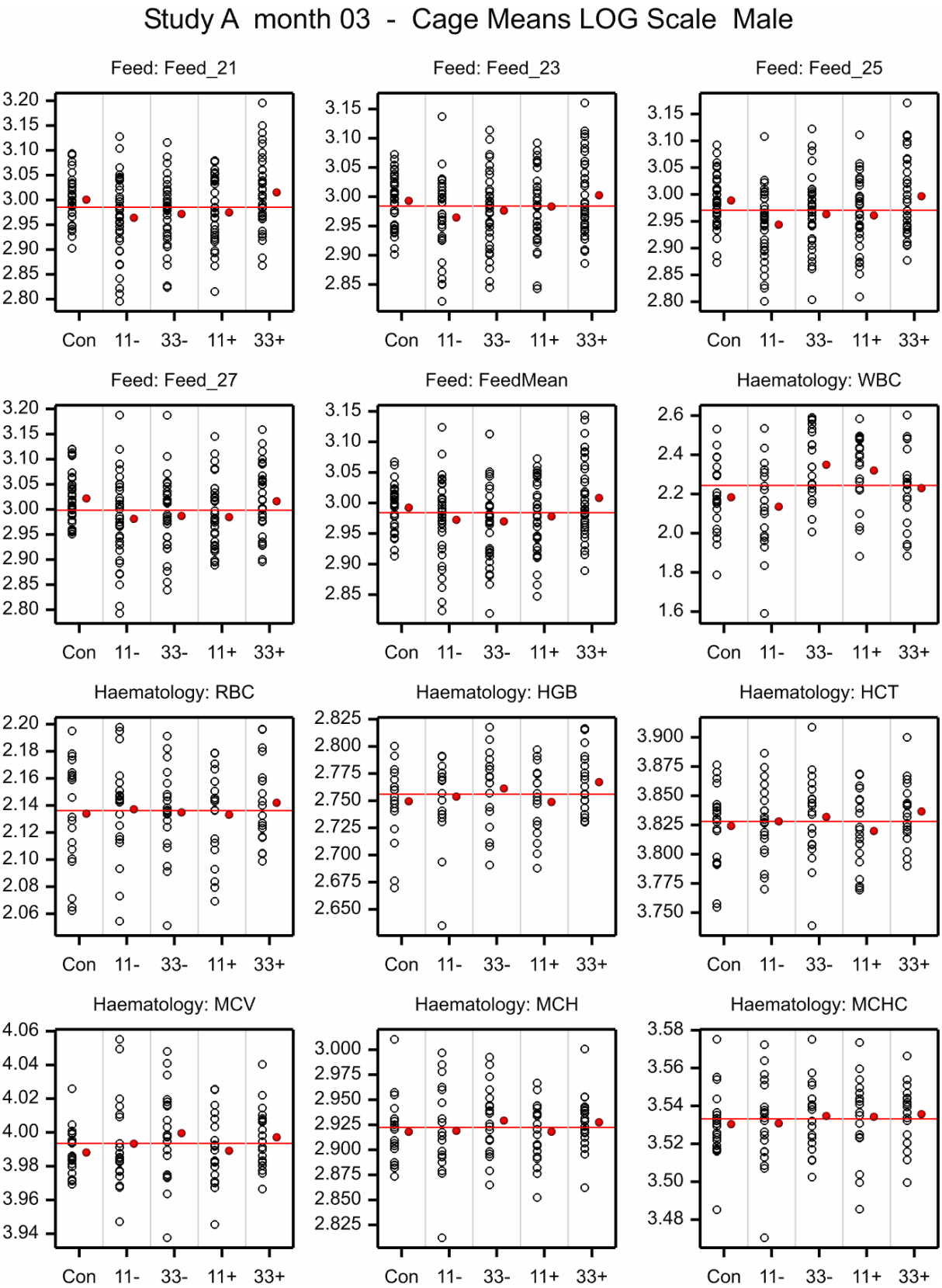
Appendix 4. Graphs of cage means on the log scale

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



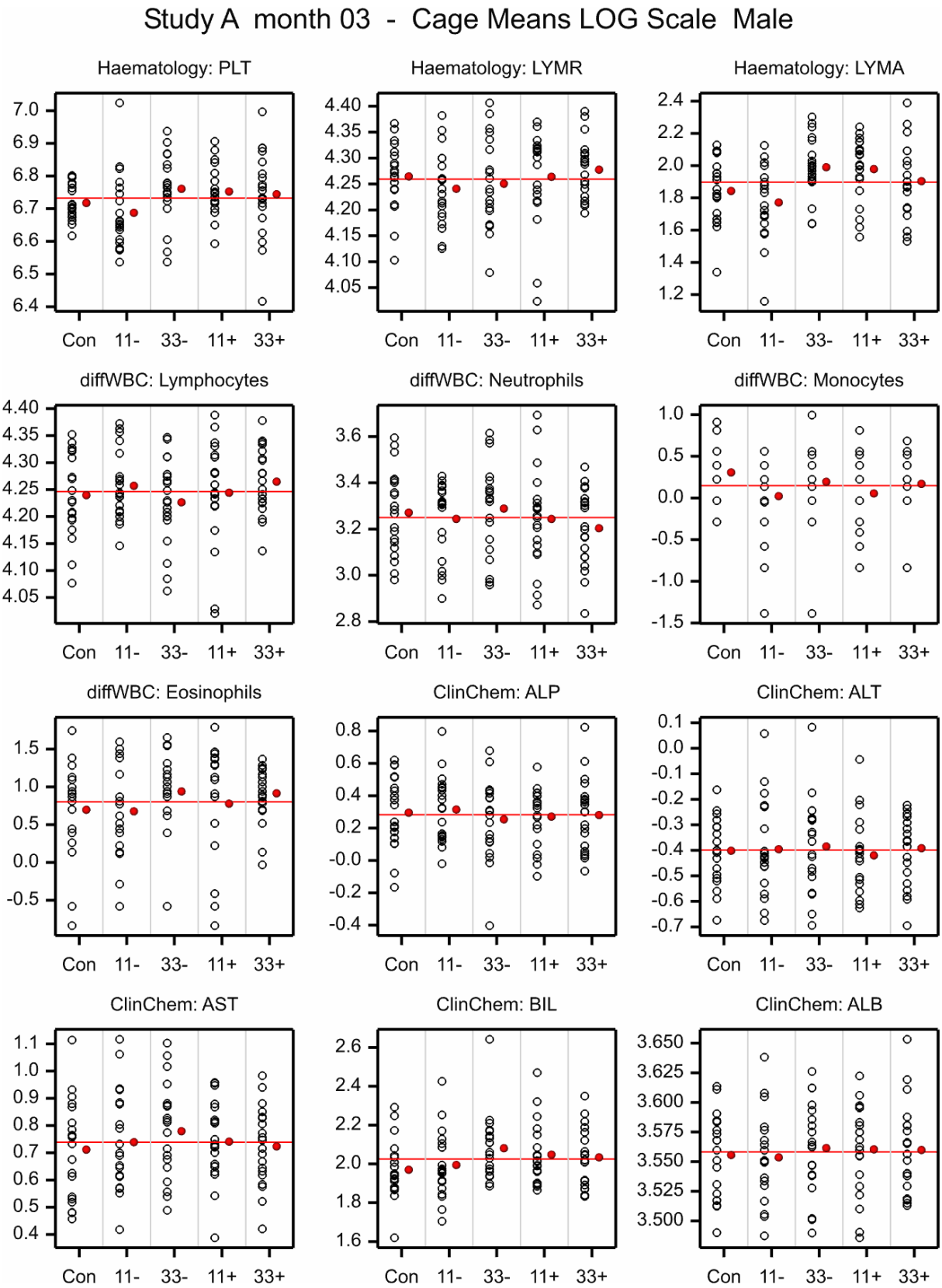
Appendix 4. Graphs of cage means on the log scale (continued)

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



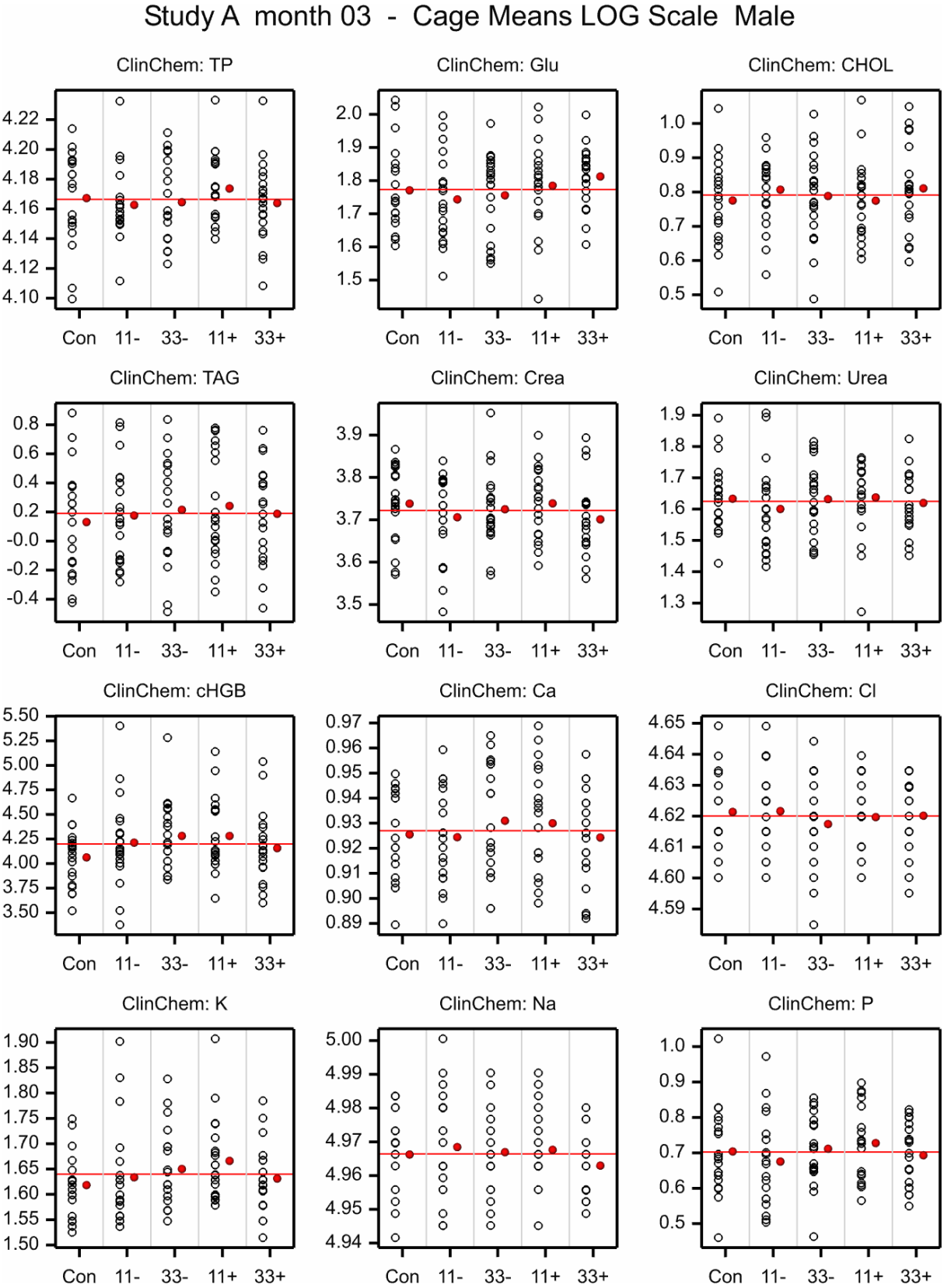
Appendix 4. Graphs of cage means on the log scale (continued)

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



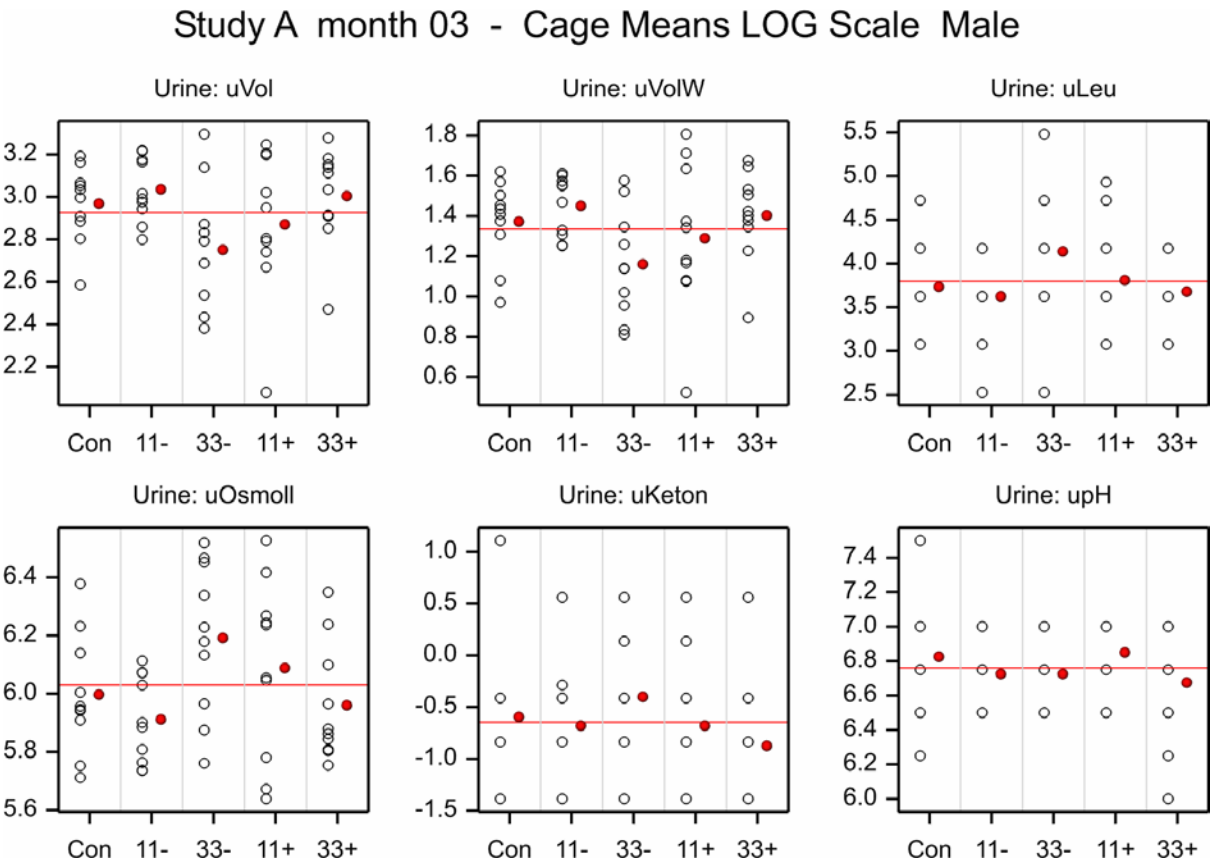
Appendix 4. Graphs of cage means on the log scale (continued)

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



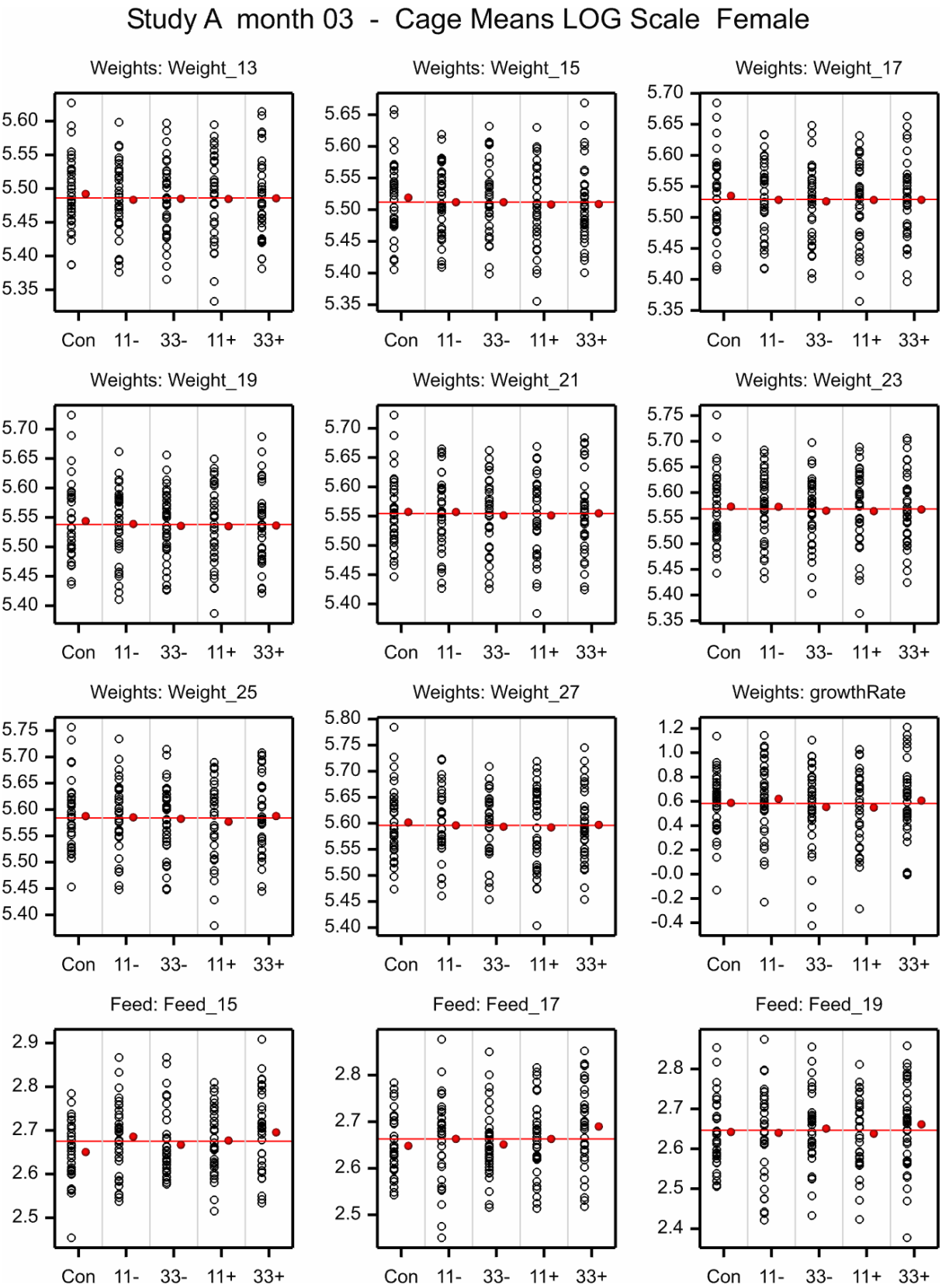
Appendix 4. Graphs of cage means on the log scale (continued)

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



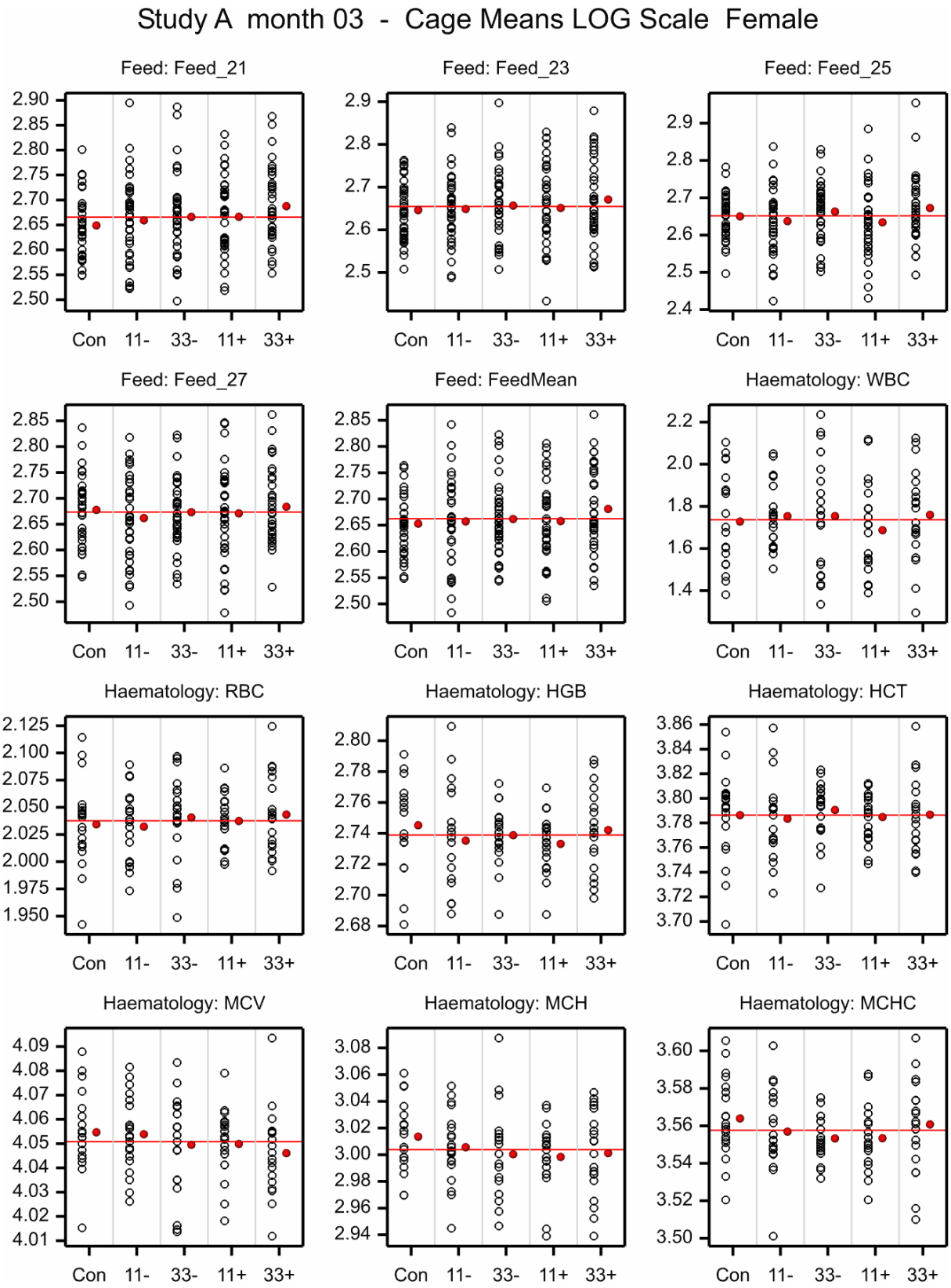
Appendix 4. Graphs of cage means on the log scale (continued)

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



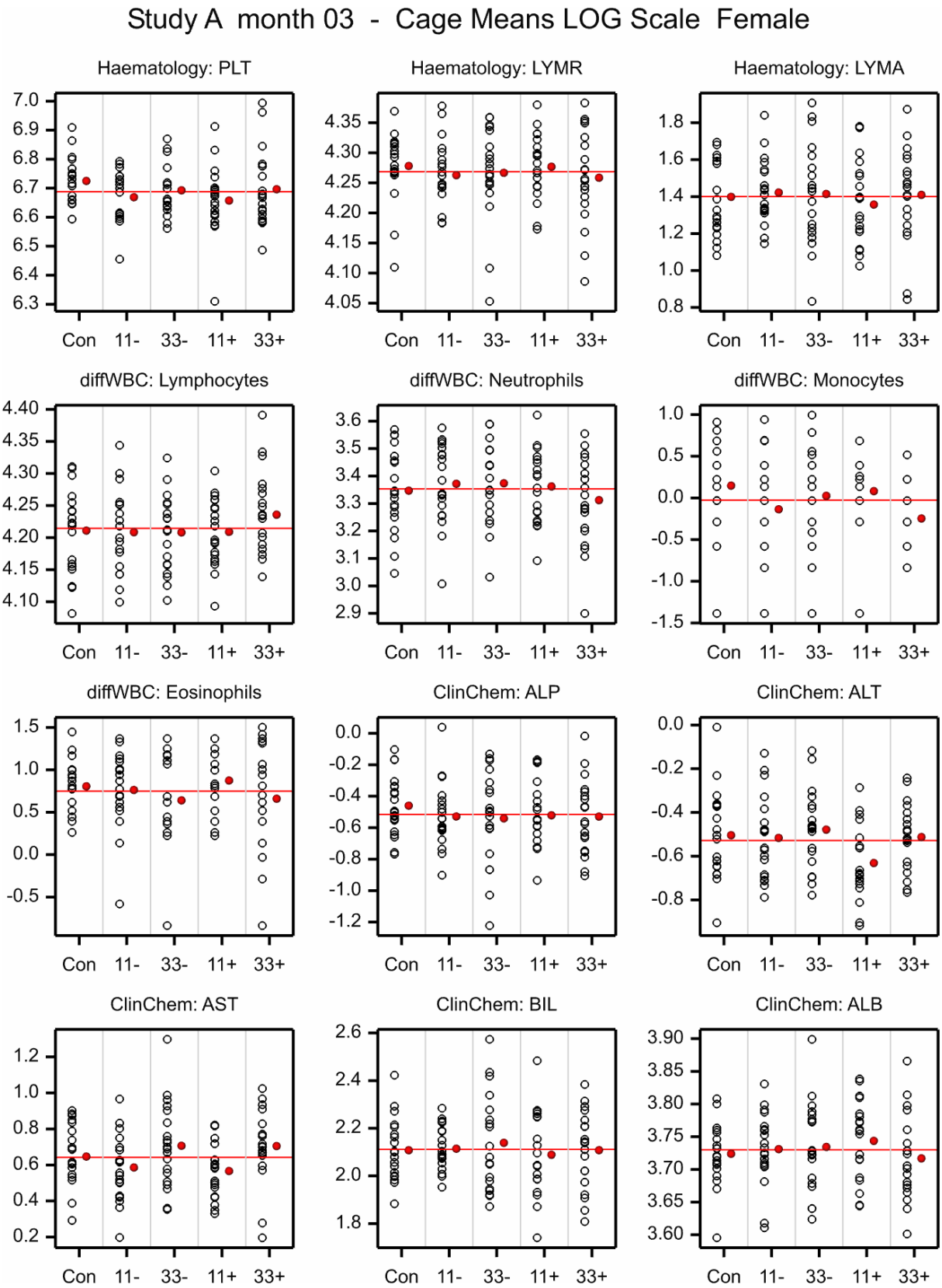
Appendix 4. Graphs of cage means on the log scale (continued)

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



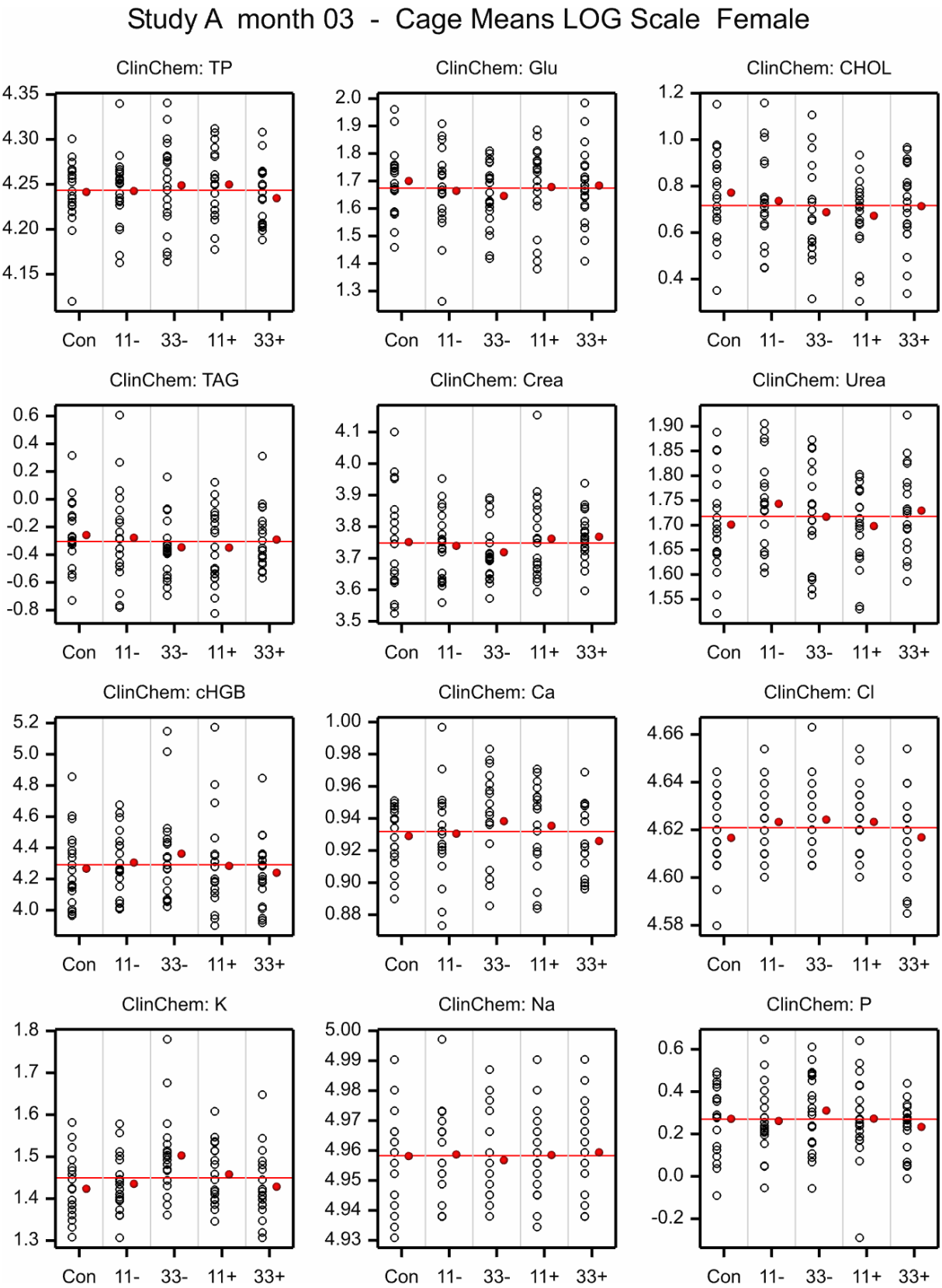
Appendix 4. Graphs of cage means on the log scale (continued)

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



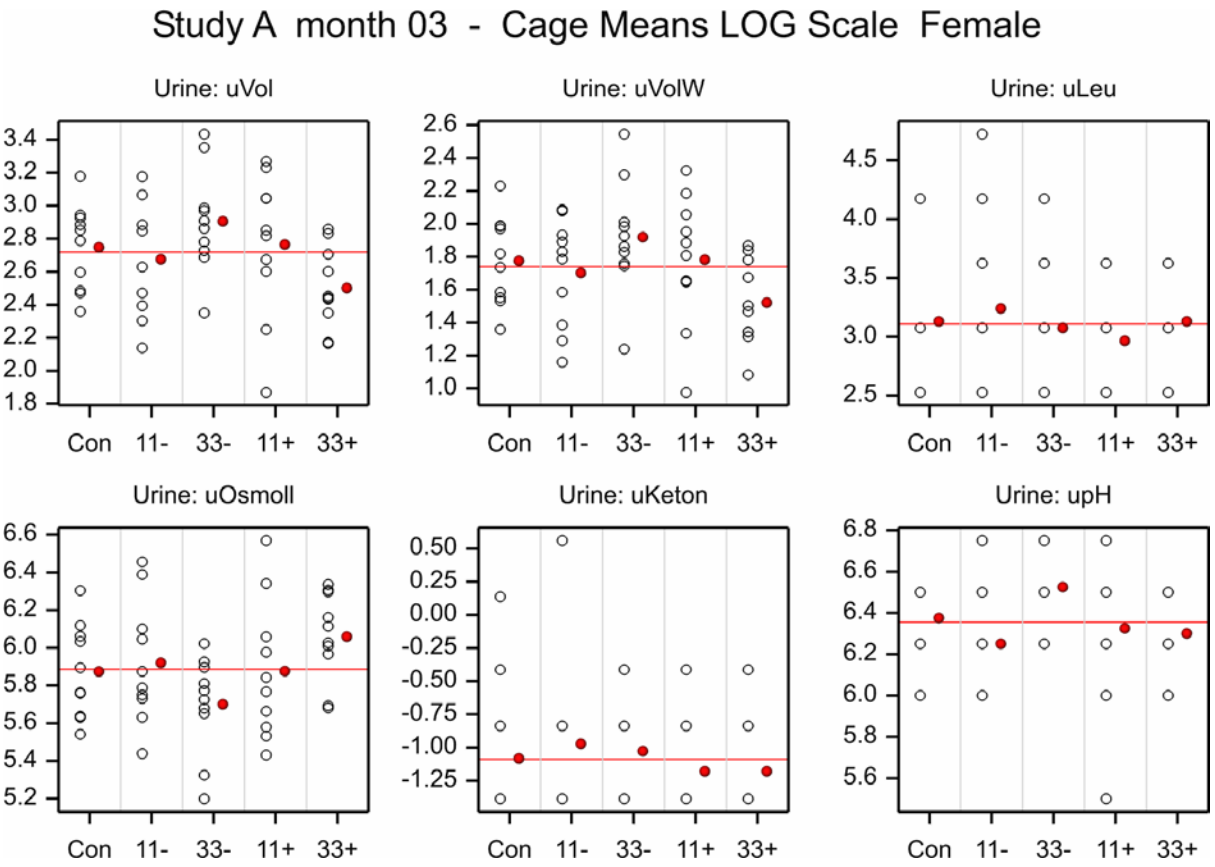
Appendix 4. Graphs of cage means on the log scale (continued)

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



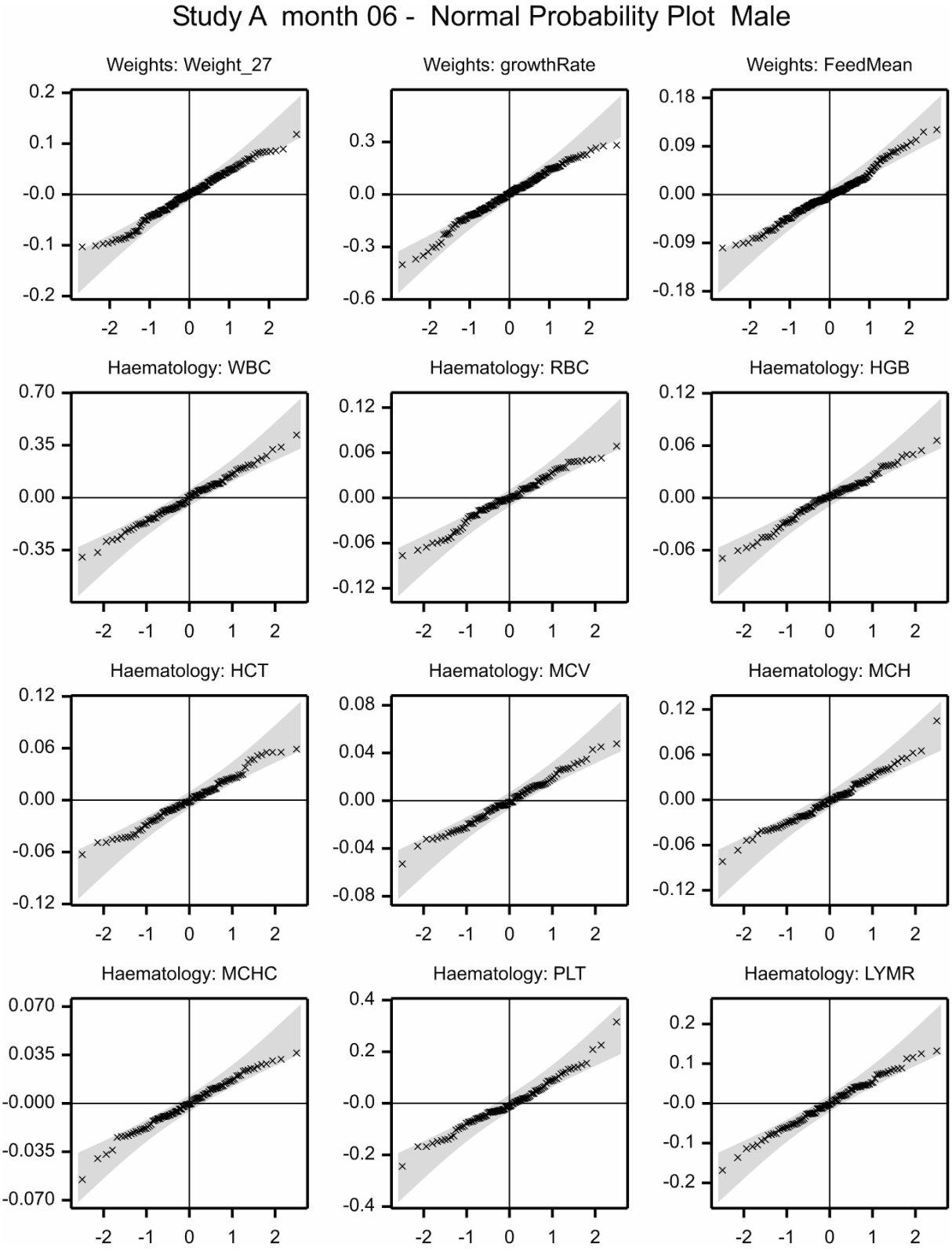
Appendix 4. Graphs of cage means on the log scale (continued)

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



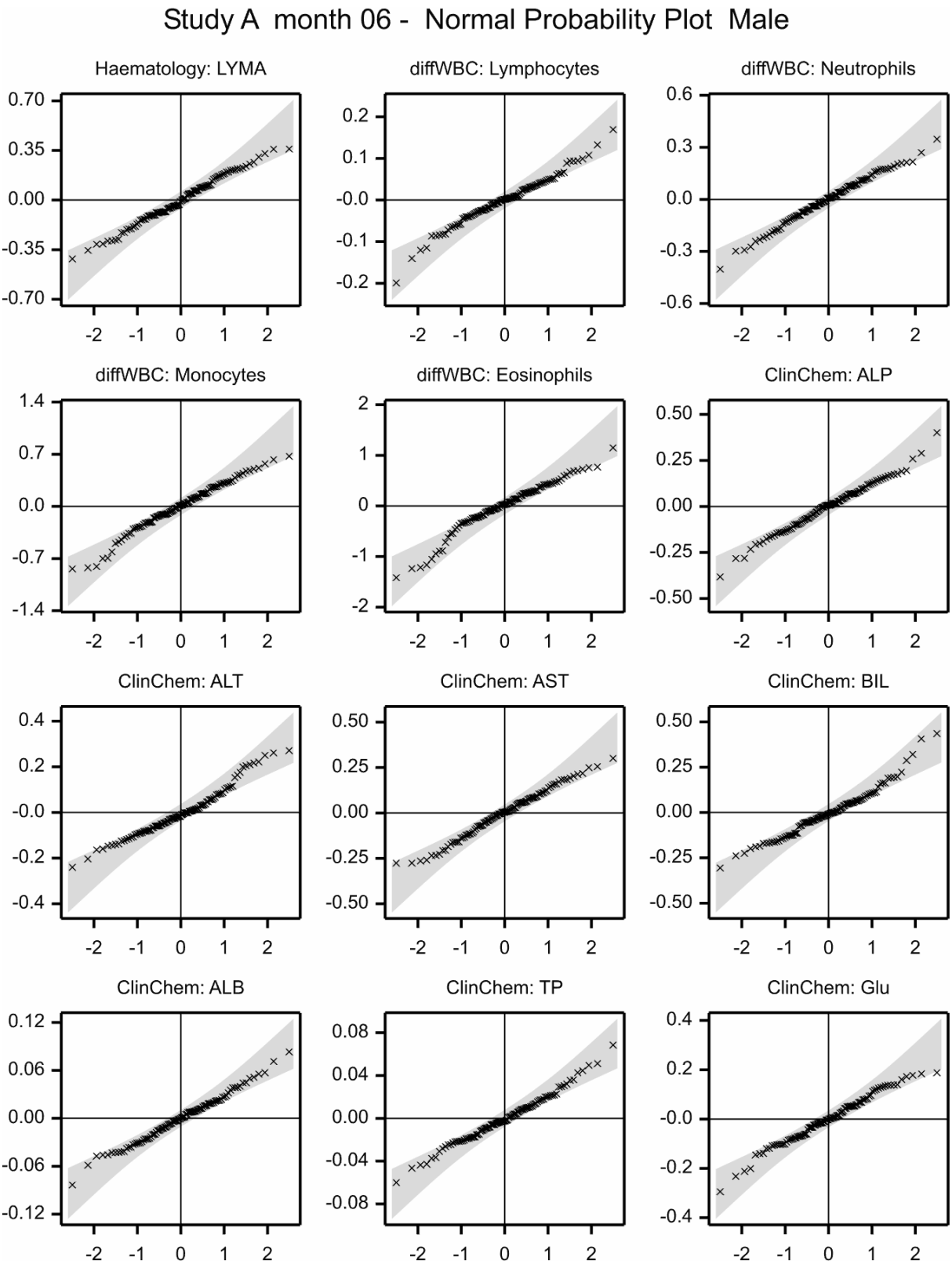
Appendix 5. Normal probability plots of residuals after ANOVA

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



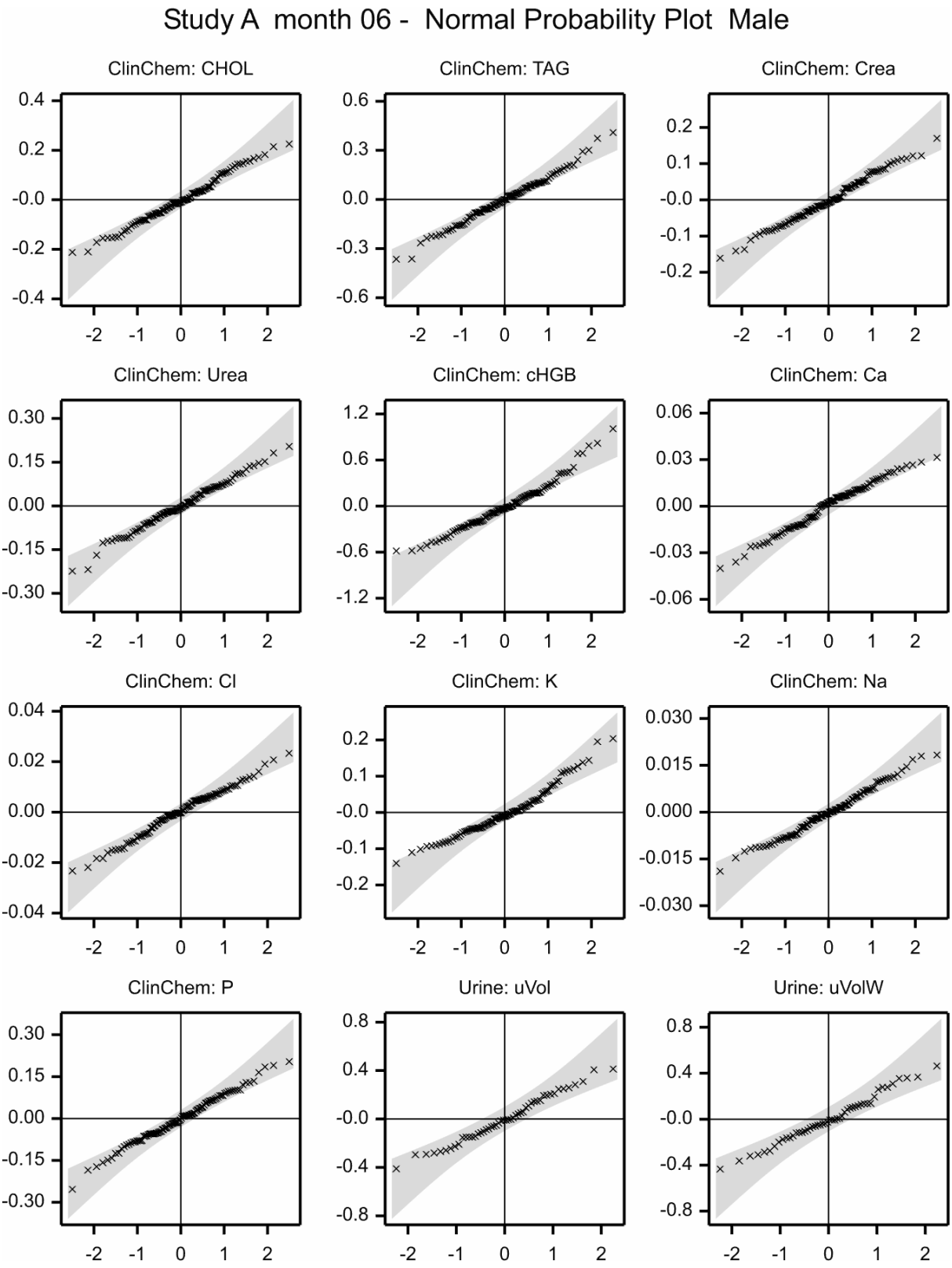
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

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



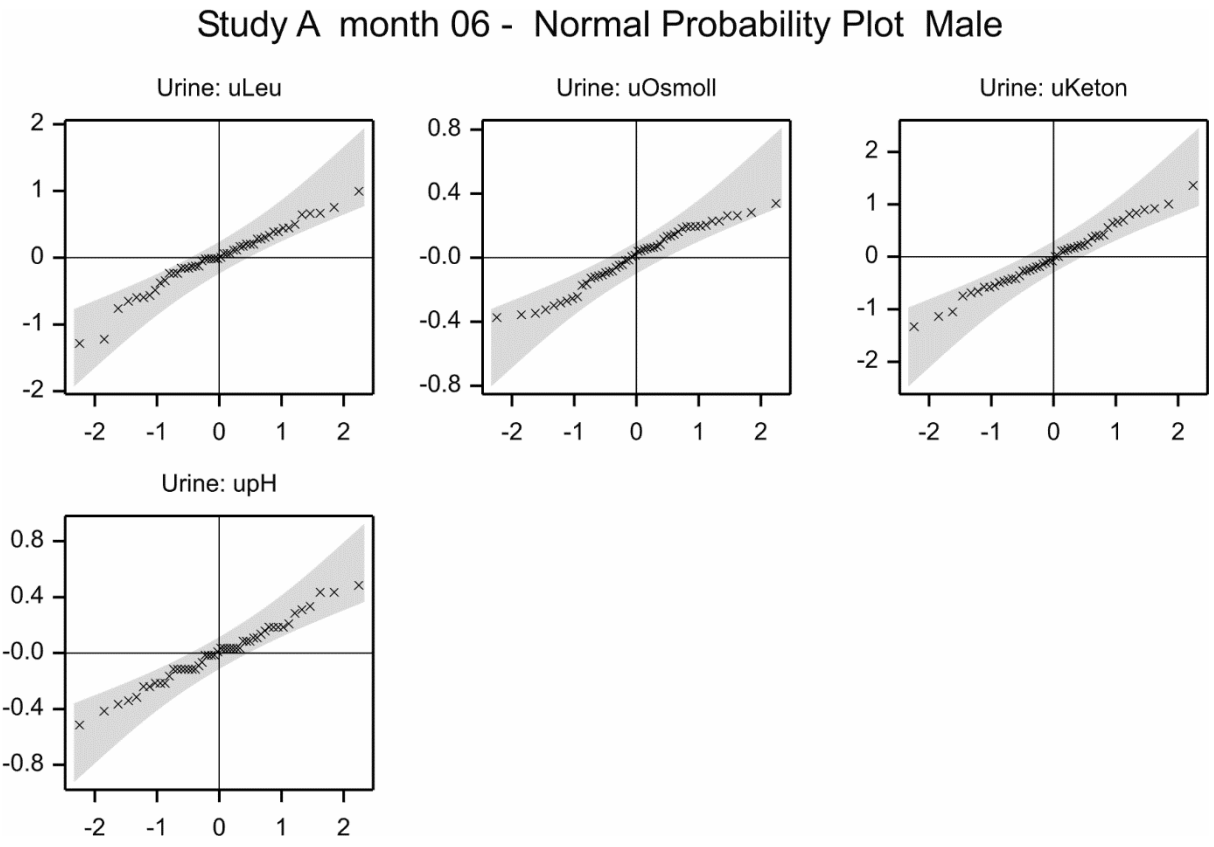
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

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



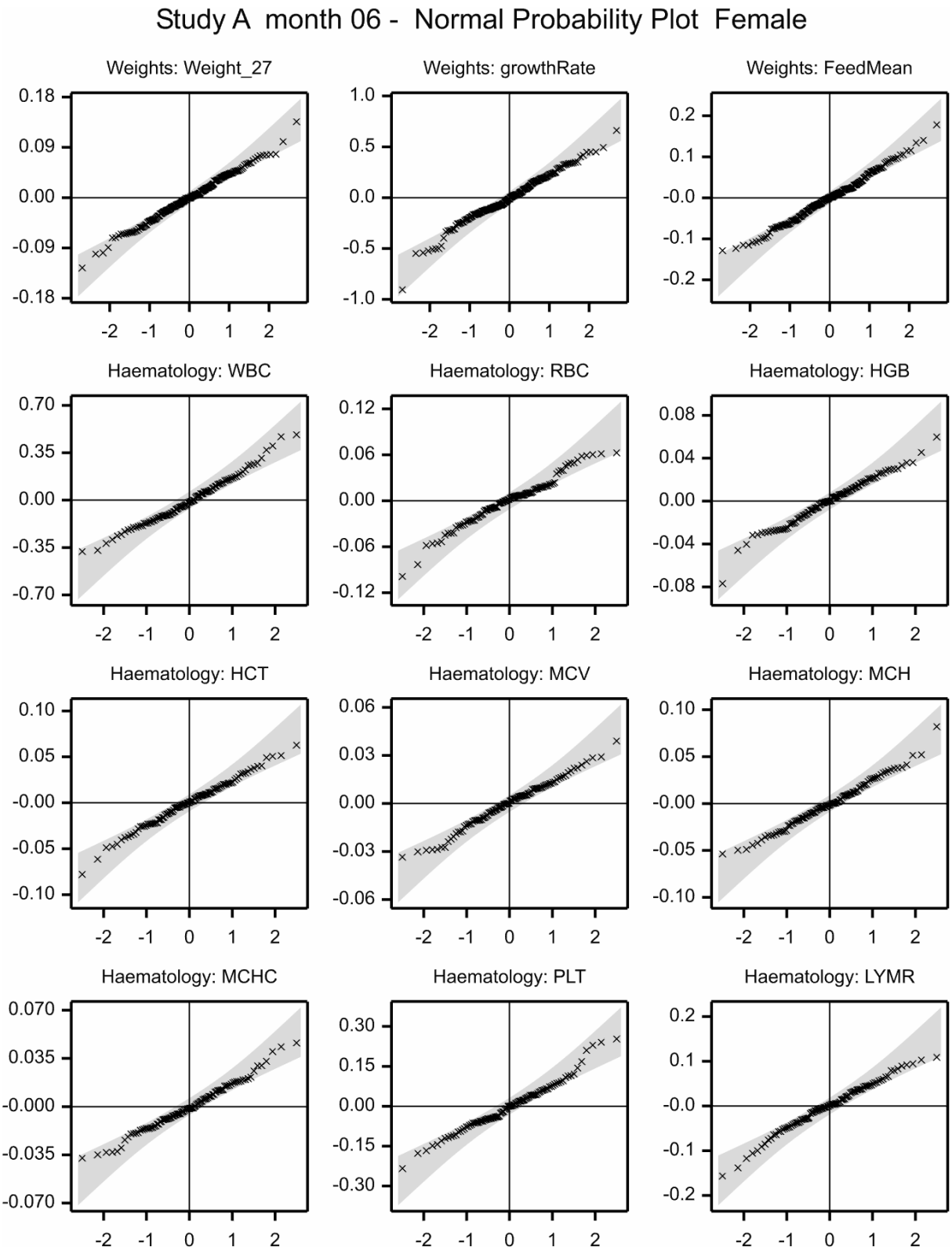
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

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



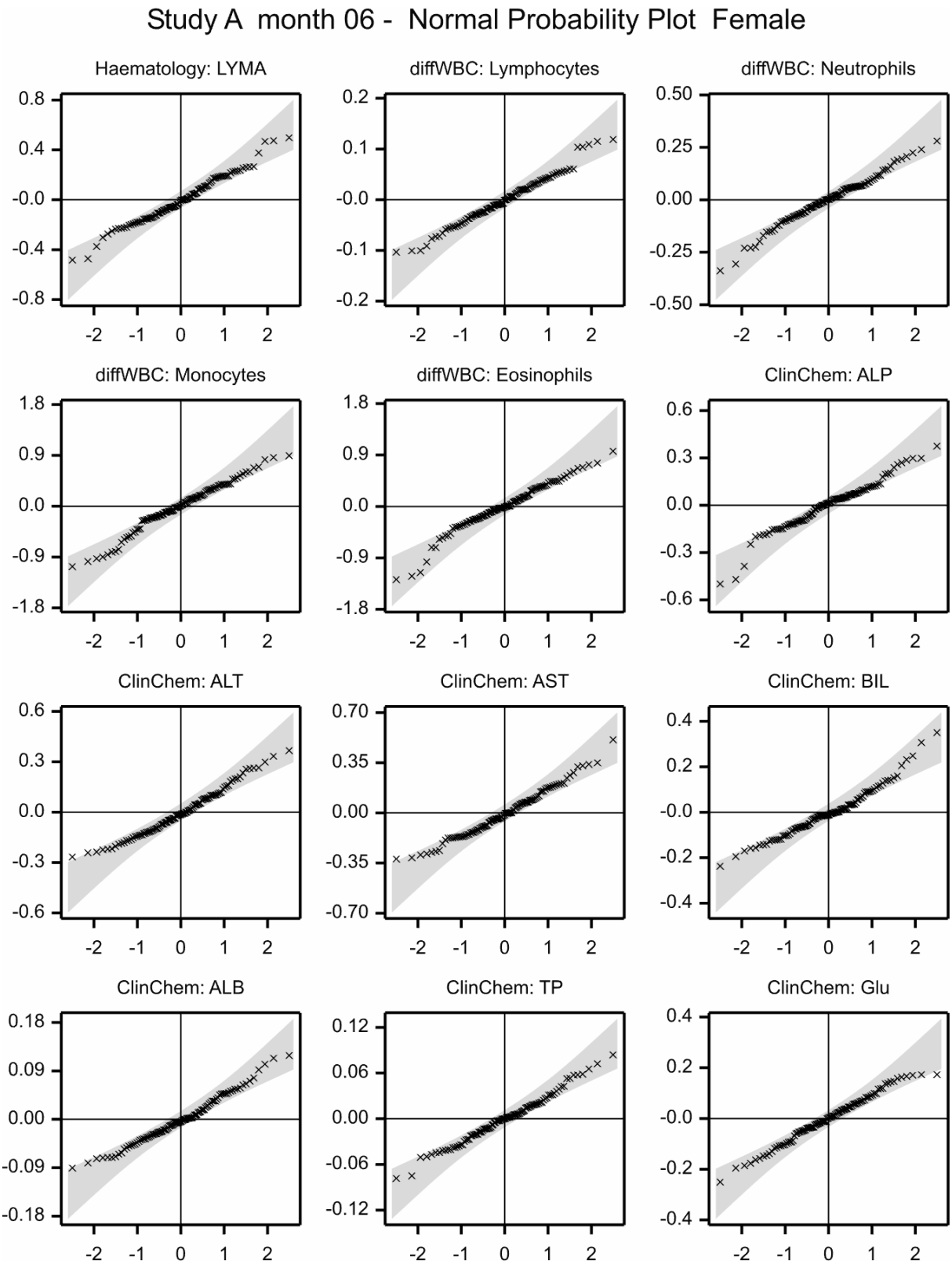
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

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



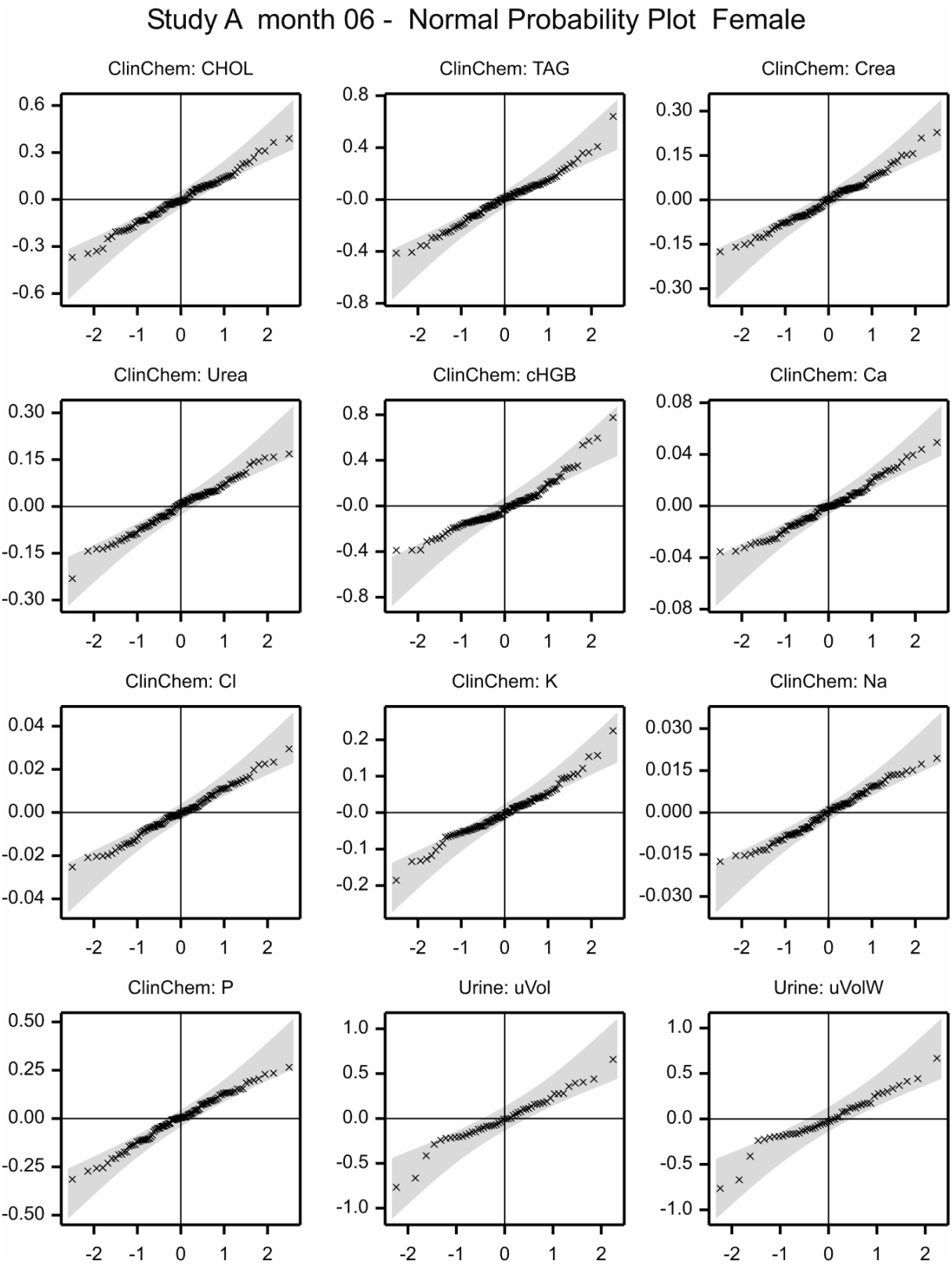
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

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



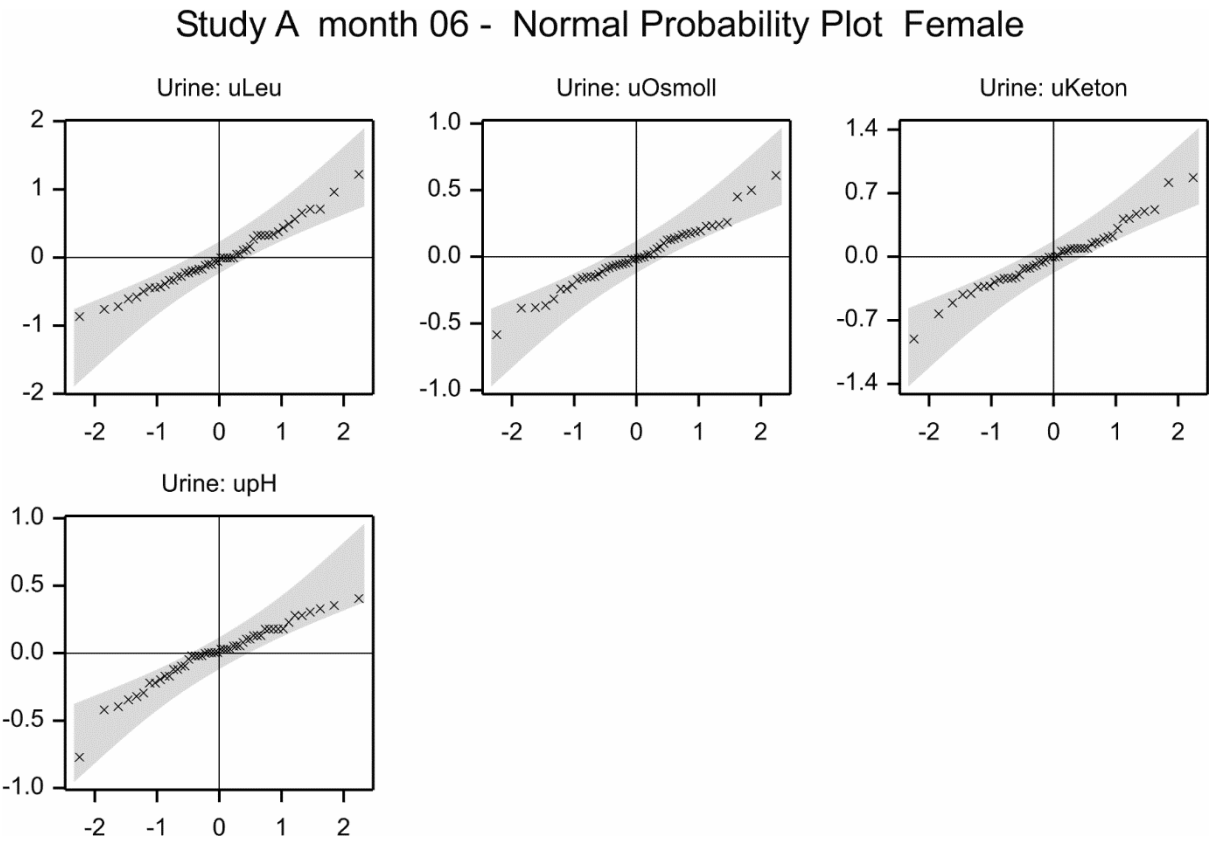
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

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



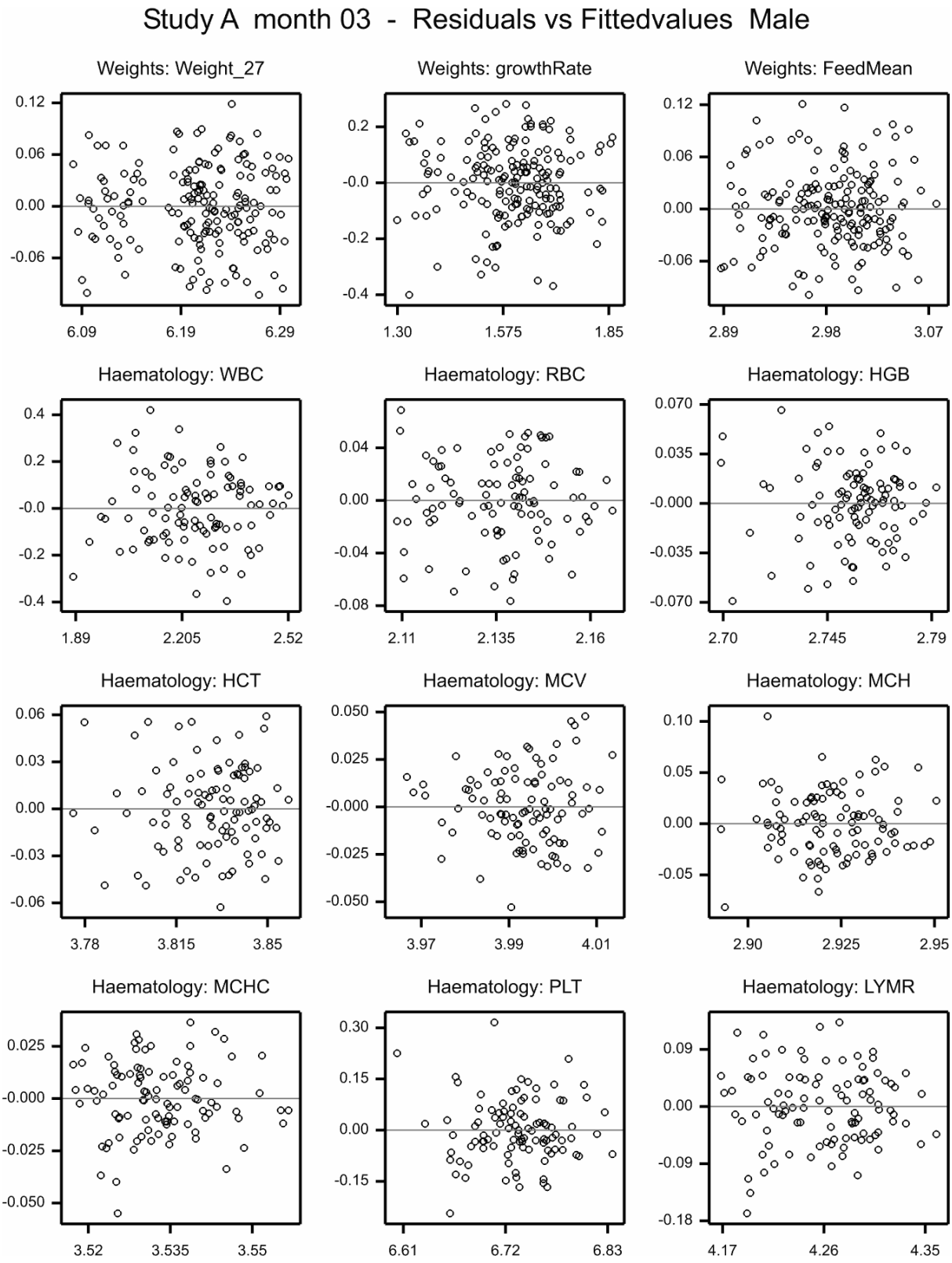
Appendix 5. Normal probability plots of residuals after ANOVA (continued)

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



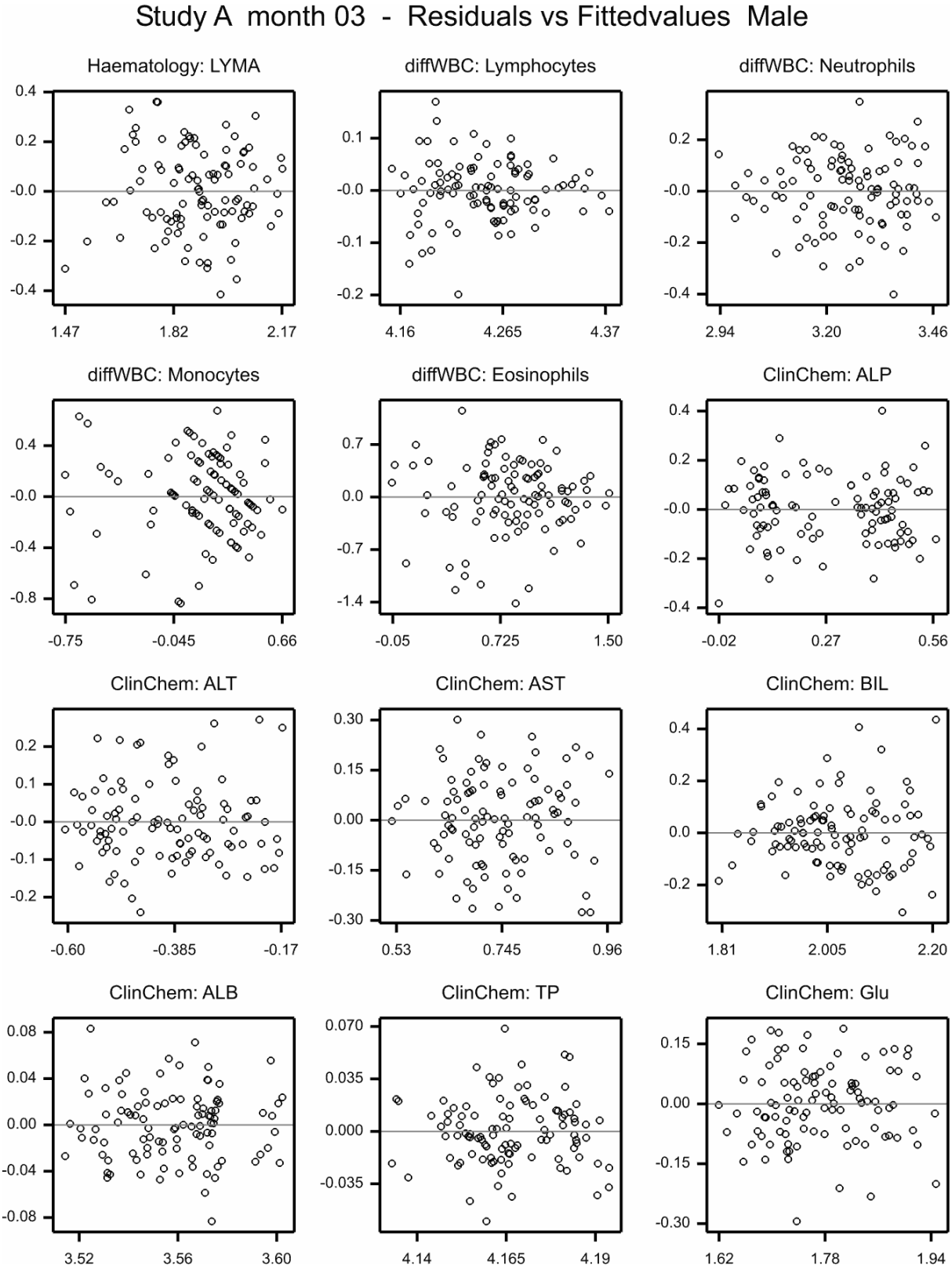
Appendix 6. Graphs of residuals versus fitted values after ANOVA

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



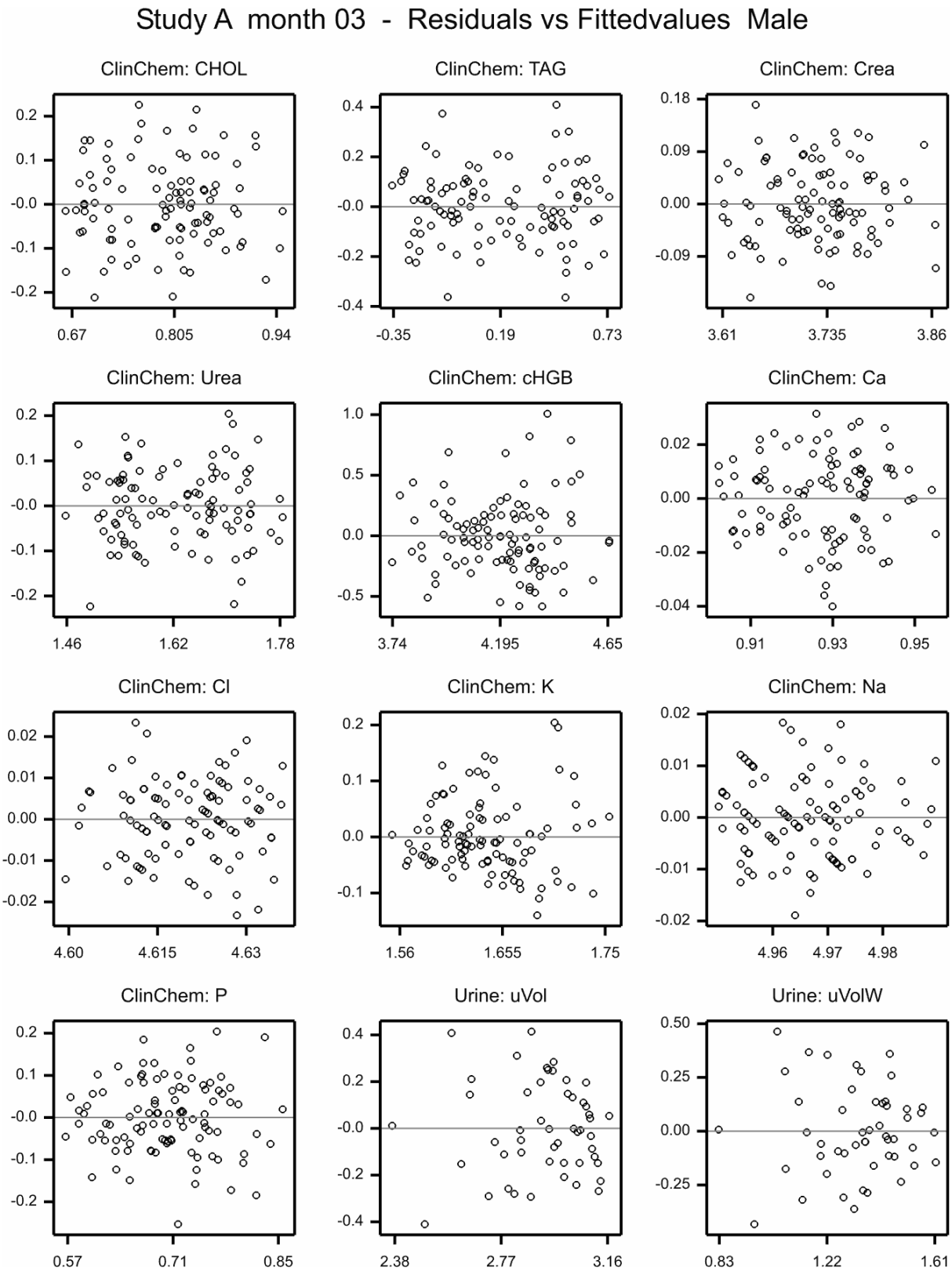
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

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



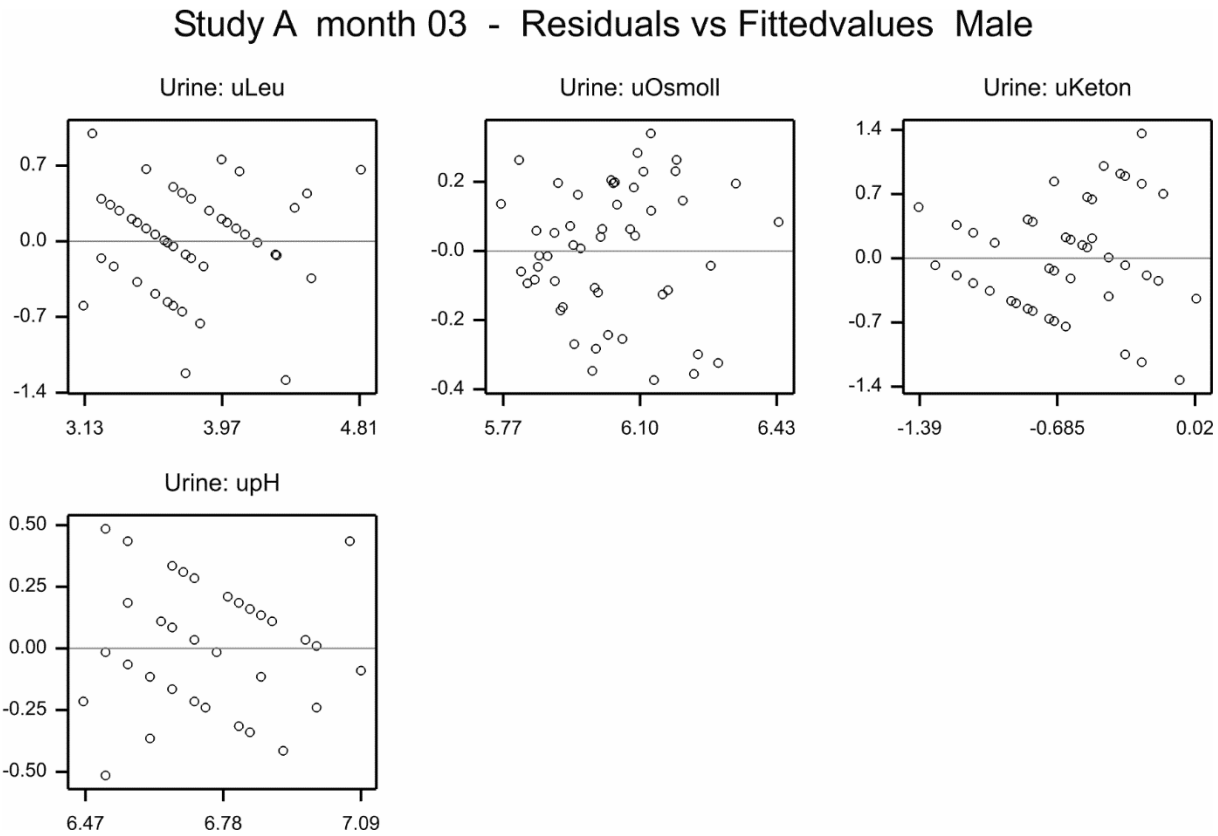
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

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



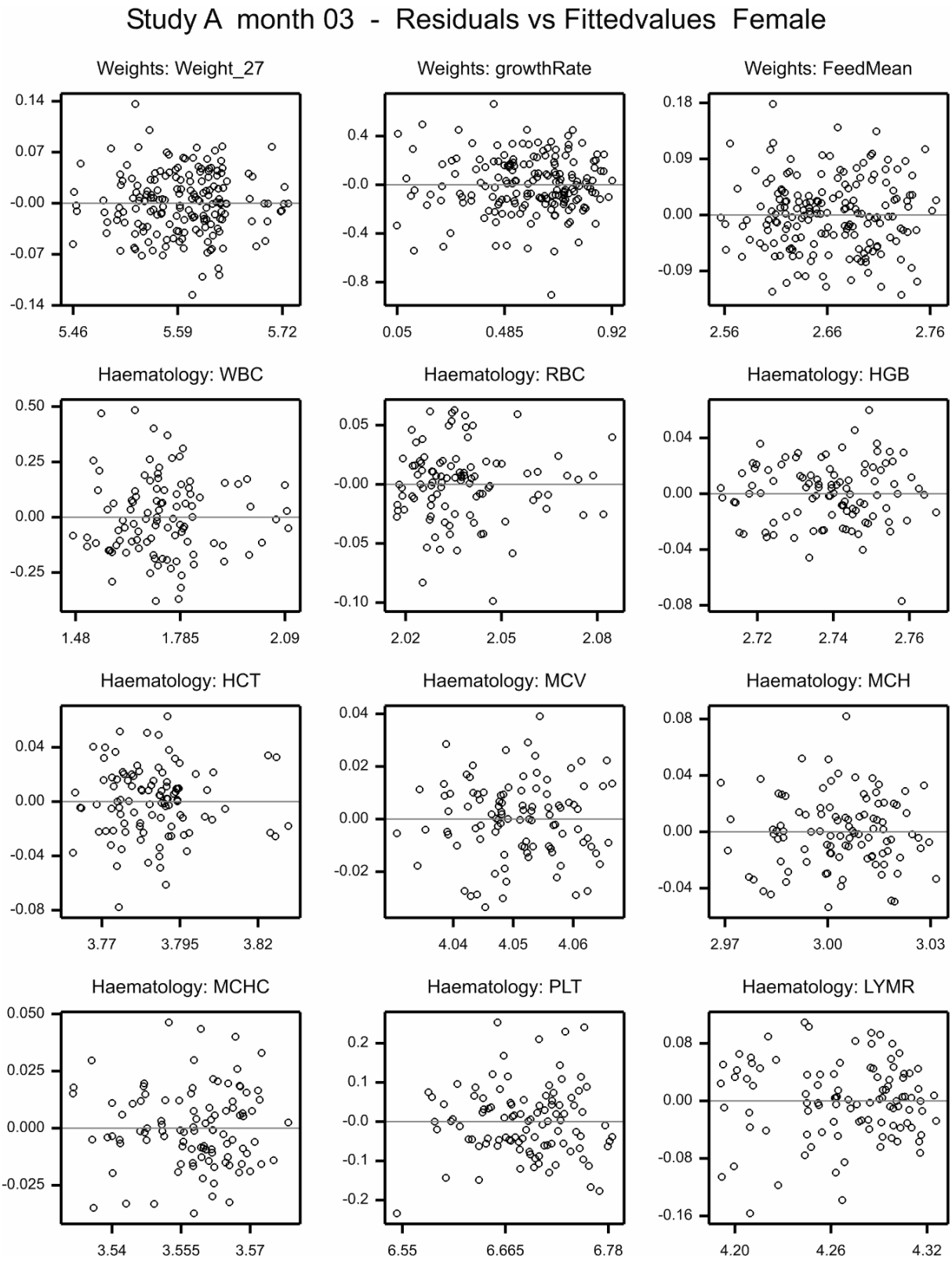
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

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



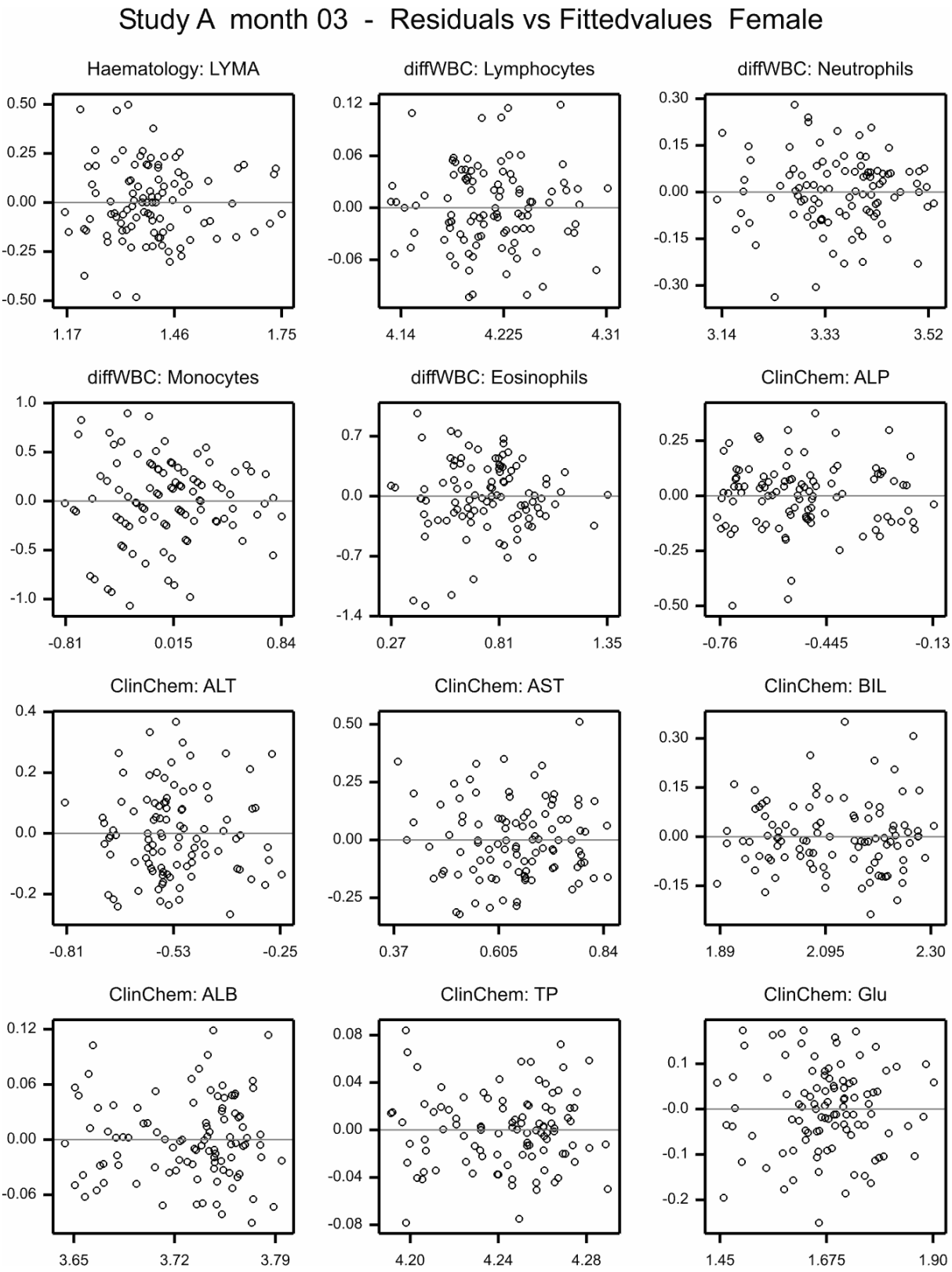
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

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



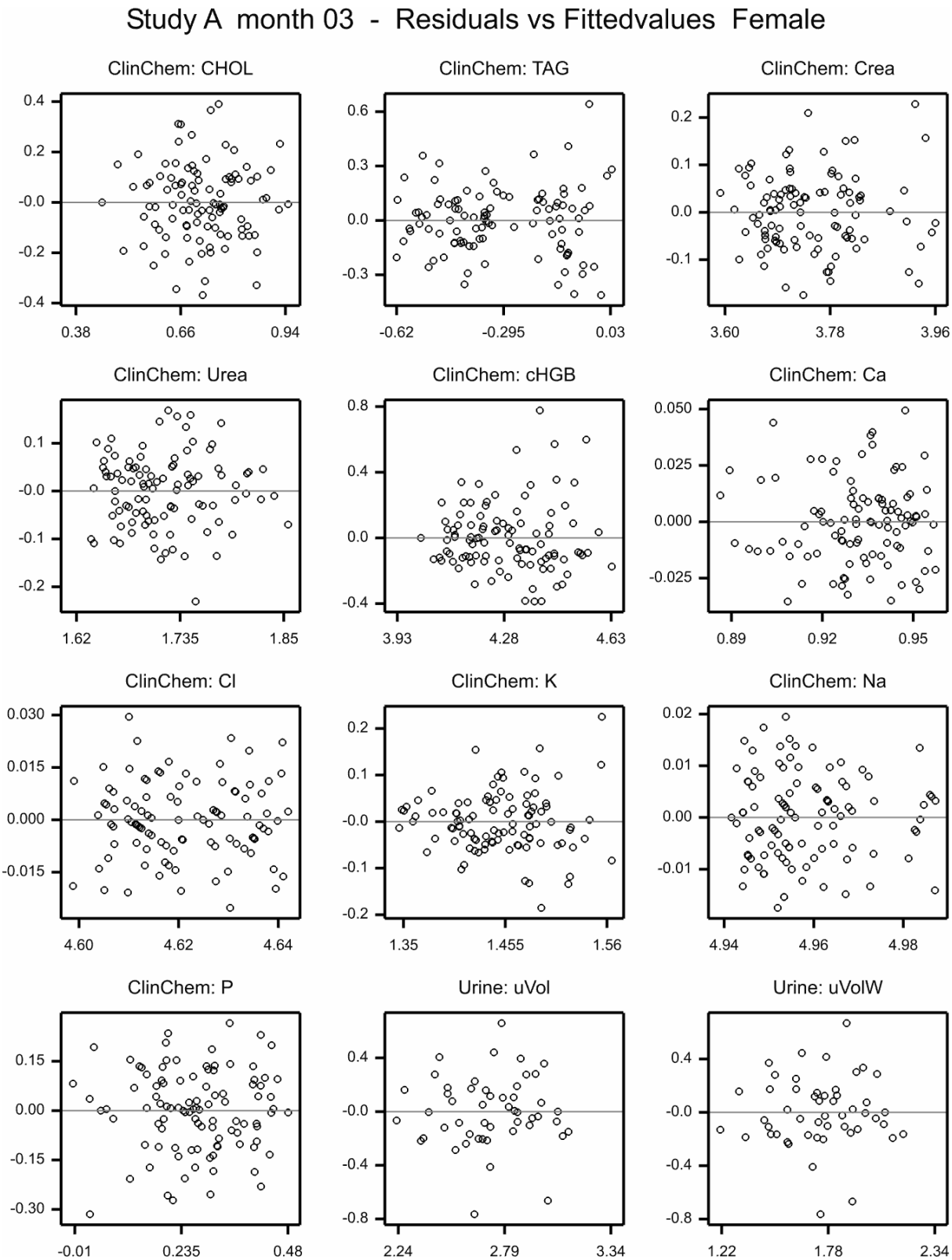
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

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



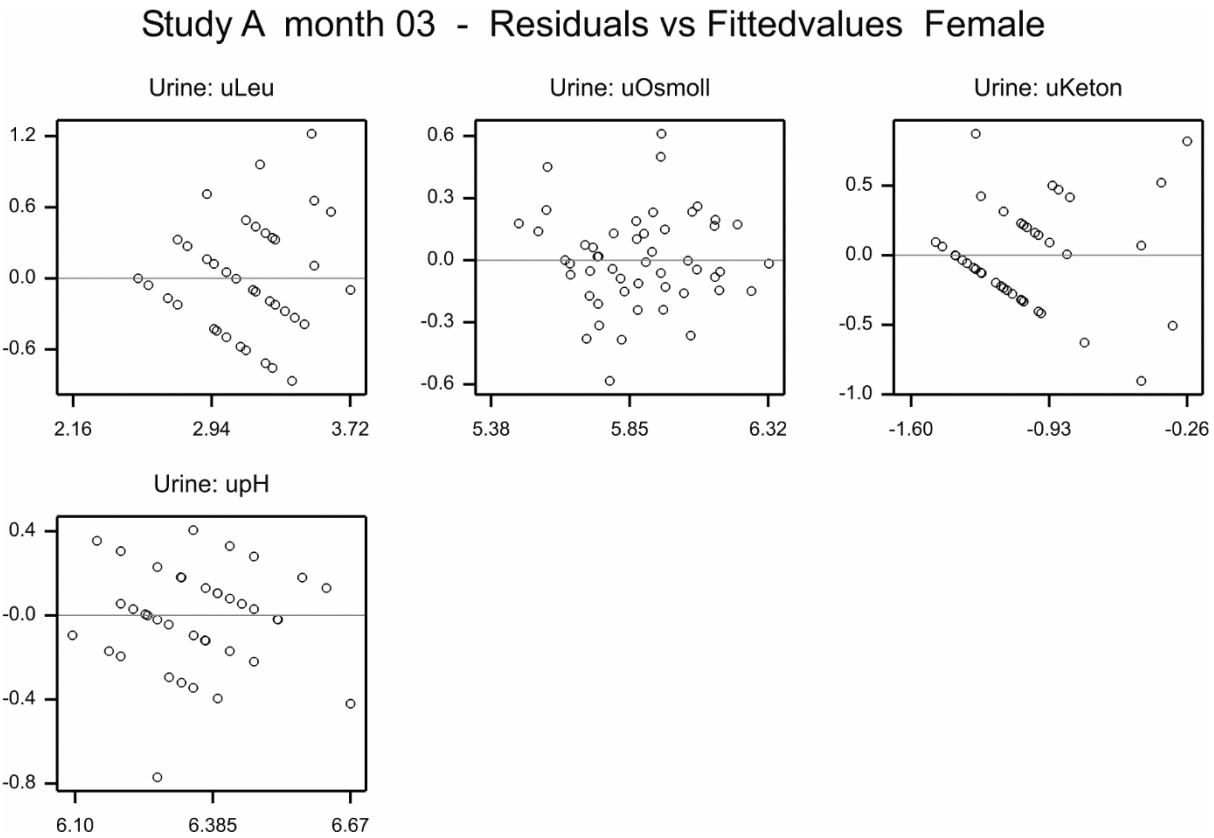
Appendix 6. Graphs of residuals versus fitted values after ANOVA (continued)

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 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_27 and growthRate, 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_27	-0.0156	-0.0087	-0.0106	0.0037	0.3063	-0.0055	-0.0081	-0.0095	-0.0046	0.3063
FeedMean	-0.0200	-0.0226	-0.0143	0.0159	0.5671	0.0044	0.0090	0.0050	0.0282	0.5671
WBC	-0.0481	0.1661	0.1365	0.0466	3.0072	0.0357	0.0258	-0.0411	0.0317	3.0072
RBC	0.0032	0.0010	-0.0008	0.0080	0.0925	-0.0016	0.0063	0.0031	0.0090	0.0925
HGB	0.0043	0.0118	-0.0007	0.0176	0.0471	-0.0086	-0.0065	-0.0121	-0.0031	0.0471
HCT	0.0039	0.0077	-0.0043	0.0124	0.0640	-0.0023	0.0041	-0.0016	0.0003	0.0640
MCV	0.0064	0.0126	0.0022	0.0102	0.0209	-0.0006	-0.0052	-0.0048	-0.0086	0.0209
MCH	0.0010	0.0112	0.0001	0.0095	0.0614	-0.0070	-0.0132	-0.0152	-0.0124	0.0614
MCHC	0.0004	0.0043	0.0039	0.0053	0.0284	-0.0062	-0.0107	-0.0105	-0.0032	0.0284
PLT	-0.0300	0.0435	0.0352	0.0269	0.7755	-0.0577	-0.0323	-0.0676	-0.0284	0.7755
LYMA	-0.0713	0.1475	0.1356	0.0609	3.5482	0.0317	0.0157	-0.0416	0.0109	3.5482
Lymphocytes	0.0174	-0.0131	0.0046	0.0251	0.2152	0.0013	-0.0029	-0.0019	0.0248	0.2152
Neutrophils	-0.0270	0.0175	-0.0273	-0.0673	1.2590	0.0139	0.0271	0.0155	-0.0345	1.2590
Monocytes	-0.2847	-0.1120	-0.2524	-0.1380	17.3790	-0.2697	-0.1222	-0.0660	-0.3943	17.3790
Eosinophils	-0.0199	0.2430	0.0816	0.2185	16.7395	-0.0180	-0.1661	0.0685	-0.1460	16.7395
ALP	0.0196	-0.0415	-0.0240	-0.0142	2.1969	-0.0756	-0.0807	-0.0612	-0.0690	2.1969
ALT	0.0060	0.0167	-0.0182	0.0100	1.9698	-0.0110	0.0254	-0.1273	-0.0083	1.9698
AST	0.0274	0.0677	0.0294	0.0120	2.6691	-0.0447	0.0600	-0.0801	0.0582	2.6691
BIL	0.0249	0.1110	0.0780	0.0640	1.0709	0.0142	0.0312	-0.0190	0.0002	1.0709
ALB	-0.0020	0.0059	0.0048	0.0042	0.1910	0.0056	0.0105	0.0198	-0.0070	0.1910
TP	-0.0046	-0.0027	0.0064	-0.0033	0.0955	-0.0001	0.0074	0.0084	-0.0068	0.0955
Glu	-0.0274	-0.0151	0.0139	0.0417	0.8544	-0.0405	-0.0543	-0.0219	-0.0166	0.8544
CHOL	0.0317	0.0132	-0.0006	0.0354	2.2768	-0.0218	-0.0842	-0.0996	-0.0582	2.2768
TAG	0.0456	0.0845	0.1112	0.0572	3.2769	-0.0146	-0.0887	-0.0913	-0.0327	3.2769
Crea	-0.0323	-0.0134	0.0006	-0.0371	0.6277	-0.0083	-0.0323	0.0107	0.0169	0.6277
Urea	-0.0328	-0.0013	0.0042	-0.0135	0.5733	0.0438	0.0160	-0.0029	0.0284	0.5733
cHGB	0.1501	0.2185	0.2178	0.0940	4.2963	0.0532	0.0961	0.0176	-0.0262	4.2963
Ca	-0.0011	0.0055	0.0045	-0.0012	0.0334	0.0017	0.0092	0.0064	-0.0031	0.0334
Cl	0.0002	-0.0039	-0.0017	-0.0012	0.0119	0.0063	0.0077	0.0067	0.0002	0.0119
K	0.0154	0.0318	0.0479	0.0130	0.4177	0.0168	0.0793	0.0343	0.0049	0.4177
Na	0.0022	0.0007	0.0014	-0.0033	0.0070	0.0011	-0.0014	0.0004	0.0012	0.0070
P	-0.0286	0.0076	0.0237	-0.0107	1.4864	0.0097	0.0387	0.0006	-0.0384	1.4864

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_27	0.961	0.985	1.009	1.063	1.092	1.131	-0.438	-0.174	0.105
FeedMean	0.958	0.980	1.003	1.064	1.094	1.170	-0.472	-0.213	0.035
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	0.851	0.953	1.067	1.456	1.651	2.386	-0.293	-0.090	0.130
RBC	0.981	1.003	1.026	1.088	1.113	1.147	-0.183	0.031	0.224
HGB	0.985	1.004	1.024	1.075	1.097	1.144	-0.166	0.045	0.233
HCT	0.985	1.004	1.024	1.089	1.112	1.148	-0.148	0.037	0.200
MCV	0.992	1.006	1.021	1.012	1.027	1.041	-0.352	0.240	0.932
MCH	0.979	1.001	1.024	1.013	1.039	1.063	-1.405	0.027	1.677
MCHC	0.988	1.000	1.013	1.017	1.029	1.049	-0.461	0.015	0.481
PLT	0.909	0.970	1.036	1.612	1.778	2.031	-0.151	-0.052	0.063
LYMA	0.825	0.931	1.051	1.409	1.598	2.228	-0.386	-0.146	0.105
diffWBC	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
Lymphocytes	0.977	1.018	1.060	1.019	1.066	1.121	-1.032	0.297	2.000
Neutrophils	0.882	0.973	1.075	1.264	1.384	1.600	-0.359	-0.082	0.232
Monocytes	0.598	0.752	0.947	1.544	1.949	3.308	-0.804	-0.413	-0.075
Eosinophils	0.698	0.980	1.377	1.798	2.551	5.365	-0.397	-0.020	0.370
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	0.929	1.020	1.119	1.315	1.431	1.601	-0.211	0.055	0.289
ALT	0.934	1.006	1.084	1.167	1.250	1.375	-0.326	0.026	0.362
AST	0.935	1.028	1.129	1.241	1.353	1.544	-0.229	0.089	0.374
ALB	0.977	0.998	1.020	1.099	1.124	1.160	-0.190	-0.017	0.168
TP	0.980	0.995	1.012	1.073	1.091	1.118	-0.213	-0.052	0.133
Glu	0.908	0.973	1.043	1.288	1.386	1.647	-0.266	-0.081	0.128
CHOL	0.964	1.032	1.106	1.203	1.297	1.618	-0.145	0.115	0.360
TAG	0.943	1.047	1.161	1.844	2.213	4.459	-0.072	0.053	0.171
Crea	0.924	0.968	1.015	1.284	1.364	1.568	-0.237	-0.102	0.047
Urea	0.913	0.968	1.026	1.192	1.278	1.609	-0.349	-0.125	0.106
Ca	0.988	0.999	1.010	1.131	1.161	1.237	-0.076	-0.007	0.067
Cl	0.993	1.000	1.007	1.102	1.124	1.173	-0.057	0.002	0.059
K	0.969	1.016	1.065	1.205	1.264	1.354	-0.138	0.065	0.241
Na	0.997	1.002	1.008	1.112	1.136	1.186	-0.026	0.017	0.054
P	0.914	0.972	1.033	1.159	1.231	1.410	-0.405	-0.132	0.162

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_27	0.967	0.991	1.016	1.063	1.092	1.131	-0.352	-0.097	0.188
FeedMean	0.955	0.978	1.001	1.064	1.094	1.171	-0.506	-0.243	0.008
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	1.055	1.181	1.322	1.458	1.652	2.385	0.092	0.320	0.554
RBC	0.979	1.001	1.024	1.088	1.113	1.147	-0.205	0.009	0.216
HGB	0.992	1.012	1.032	1.075	1.097	1.144	-0.084	0.124	0.311
HCT	0.988	1.008	1.028	1.089	1.112	1.149	-0.112	0.072	0.231
MCV	0.998	1.013	1.027	1.012	1.028	1.042	-0.070	0.472	1.282
MCH	0.989	1.011	1.034	1.013	1.039	1.063	-0.410	0.308	2.000
MCHC	0.992	1.004	1.017	1.017	1.030	1.049	-0.299	0.143	0.569
PLT	0.978	1.044	1.115	1.612	1.778	2.033	-0.039	0.075	0.174
LYMA	1.027	1.159	1.308	1.411	1.598	2.236	0.053	0.305	0.568
diffWBC	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
Lymphocytes	0.947	0.987	1.028	1.019	1.066	1.121	-2.000	-0.226	2.000
Neutrophils	0.922	1.018	1.124	1.264	1.383	1.596	-0.262	0.053	0.338
Monocytes	0.710	0.894	1.125	1.544	1.952	3.276	-0.491	-0.161	0.181
Eosinophils	0.908	1.275	1.791	1.803	2.545	5.263	-0.104	0.251	0.624
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	0.874	0.959	1.053	1.316	1.430	1.599	-0.345	-0.114	0.148
ALT	0.944	1.017	1.096	1.166	1.250	1.374	-0.273	0.073	0.385
AST	0.974	1.070	1.176	1.241	1.353	1.543	-0.089	0.220	0.512
ALB	0.985	1.006	1.028	1.099	1.124	1.159	-0.134	0.050	0.210
TP	0.981	0.997	1.013	1.073	1.091	1.118	-0.198	-0.031	0.154
Glu	0.919	0.985	1.055	1.289	1.386	1.646	-0.234	-0.044	0.167
CHOL	0.946	1.013	1.085	1.204	1.297	1.622	-0.219	0.048	0.294
TAG	0.981	1.088	1.207	1.844	2.214	4.394	-0.024	0.101	0.224
Crea	0.941	0.987	1.034	1.284	1.364	1.571	-0.175	-0.042	0.109
Urea	0.942	0.999	1.059	1.192	1.278	1.611	-0.250	-0.006	0.244
Ca	0.994	1.005	1.017	1.131	1.161	1.236	-0.037	0.036	0.100
Cl	0.989	0.996	1.003	1.102	1.124	1.172	-0.083	-0.033	0.024
K	0.985	1.032	1.082	1.205	1.263	1.353	-0.065	0.135	0.313
Na	0.995	1.001	1.006	1.112	1.136	1.186	-0.037	0.005	0.045
P	0.948	1.008	1.071	1.159	1.231	1.412	-0.268	0.035	0.319

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_27	0.965	0.989	1.014	1.063	1.092	1.132	-0.377	-0.118	0.166
FeedMean	0.963	0.986	1.009	1.064	1.094	1.171	-0.400	-0.153	0.102
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	1.024	1.146	1.283	1.455	1.650	2.403	0.042	0.262	0.490
RBC	0.977	0.999	1.022	1.088	1.113	1.147	-0.217	-0.007	0.210
HGB	0.980	0.999	1.019	1.075	1.097	1.144	-0.216	-0.007	0.208
HCT	0.976	0.996	1.015	1.089	1.112	1.148	-0.202	-0.040	0.145
MCV	0.988	1.002	1.017	1.012	1.028	1.041	-0.577	0.086	0.750
MCH	0.978	1.000	1.023	1.013	1.039	1.063	-1.608	0.007	1.703
MCHC	0.992	1.004	1.016	1.017	1.030	1.049	-0.313	0.130	0.556
PLT	0.970	1.036	1.106	1.613	1.777	2.029	-0.053	0.060	0.158
LYMA	1.015	1.145	1.293	1.410	1.598	2.222	0.031	0.278	0.538
diffWBC	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
Lymphocytes	0.964	1.005	1.047	1.019	1.067	1.120	-2.000	0.079	2.000
Neutrophils	0.881	0.973	1.074	1.264	1.383	1.598	-0.361	-0.083	0.226
Monocytes	0.617	0.777	0.978	1.542	1.951	3.286	-0.745	-0.365	-0.031
Eosinophils	0.772	1.085	1.524	1.803	2.549	5.368	-0.294	0.083	0.431
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	0.889	0.976	1.072	1.314	1.431	1.599	-0.301	-0.066	0.197
ALT	0.911	0.982	1.058	1.167	1.250	1.375	-0.389	-0.080	0.265
AST	0.937	1.030	1.131	1.241	1.353	1.541	-0.221	0.094	0.379
ALB	0.984	1.005	1.026	1.099	1.124	1.159	-0.142	0.040	0.203
TP	0.990	1.006	1.023	1.073	1.091	1.118	-0.112	0.073	0.232
Glu	0.946	1.014	1.087	1.288	1.386	1.647	-0.172	0.042	0.232
CHOL	0.933	0.999	1.071	1.203	1.297	1.615	-0.276	-0.003	0.274
TAG	1.007	1.118	1.240	1.845	2.213	4.419	0.008	0.133	0.261
Crea	0.955	1.001	1.049	1.284	1.363	1.567	-0.153	0.002	0.155
Urea	0.947	1.004	1.065	1.192	1.278	1.615	-0.230	0.015	0.251
Ca	0.993	1.005	1.016	1.131	1.161	1.237	-0.044	0.029	0.093
Cl	0.992	0.998	1.005	1.102	1.124	1.172	-0.065	-0.014	0.044
K	1.001	1.049	1.100	1.205	1.263	1.353	0.004	0.202	0.386
Na	0.996	1.001	1.007	1.112	1.136	1.186	-0.032	0.011	0.048
P	0.963	1.024	1.089	1.159	1.231	1.412	-0.184	0.110	0.381

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_27	0.979	1.004	1.029	1.063	1.092	1.131	-0.248	0.041	0.309
FeedMean	0.993	1.016	1.040	1.064	1.094	1.172	-0.081	0.170	0.421
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	0.936	1.048	1.173	1.455	1.651	2.389	-0.133	0.089	0.292
RBC	0.986	1.008	1.031	1.088	1.113	1.147	-0.136	0.076	0.259
HGB	0.998	1.018	1.038	1.075	1.097	1.144	-0.019	0.186	0.379
HCT	0.993	1.012	1.032	1.089	1.112	1.149	-0.066	0.116	0.277
MCV	0.996	1.010	1.025	1.012	1.028	1.041	-0.171	0.383	1.150
MCH	0.987	1.010	1.033	1.013	1.039	1.063	-0.501	0.261	2.000
MCHC	0.993	1.005	1.018	1.017	1.030	1.050	-0.256	0.178	0.607
PLT	0.962	1.027	1.097	1.613	1.778	2.029	-0.068	0.047	0.145
LYMA	0.942	1.063	1.200	1.411	1.598	2.224	-0.129	0.124	0.362
diffWBC	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Males NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
Lymphocytes	0.984	1.025	1.068	1.019	1.066	1.120	-0.410	0.434	2.000
Neutrophils	0.847	0.935	1.032	1.263	1.383	1.598	-0.491	-0.203	0.098
Monocytes	0.692	0.871	1.096	1.544	1.951	3.297	-0.538	-0.198	0.140
Eosinophils	0.886	1.244	1.748	1.800	2.550	5.276	-0.133	0.225	0.590
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	0.898	0.986	1.082	1.315	1.430	1.602	-0.281	-0.040	0.226
ALT	0.937	1.010	1.088	1.166	1.250	1.373	-0.307	0.044	0.368
AST	0.921	1.012	1.112	1.240	1.353	1.543	-0.285	0.038	0.336
ALB	0.983	1.004	1.026	1.099	1.124	1.159	-0.149	0.035	0.198
TP	0.981	0.997	1.013	1.073	1.091	1.118	-0.202	-0.038	0.148
Glu	0.973	1.043	1.117	1.288	1.386	1.649	-0.083	0.124	0.314
CHOL	0.967	1.036	1.110	1.203	1.297	1.619	-0.129	0.128	0.375
TAG	0.954	1.059	1.175	1.843	2.213	4.398	-0.057	0.068	0.186
Crea	0.919	0.964	1.010	1.284	1.363	1.569	-0.252	-0.117	0.032
Urea	0.930	0.987	1.046	1.191	1.278	1.619	-0.272	-0.051	0.189
Ca	0.988	0.999	1.010	1.131	1.161	1.237	-0.076	-0.008	0.066
Cl	0.992	0.999	1.006	1.102	1.124	1.171	-0.062	-0.011	0.047
K	0.966	1.013	1.062	1.205	1.263	1.353	-0.149	0.055	0.233
Na	0.991	0.997	1.002	1.112	1.136	1.186	-0.063	-0.025	0.017
P	0.930	0.989	1.052	1.158	1.231	1.415	-0.326	-0.049	0.254

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_27	0.972	0.994	1.017	1.097	1.125	1.174	-0.214	-0.046	0.145
FeedMean	0.974	1.004	1.035	1.067	1.108	1.204	-0.269	0.040	0.331
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	0.912	1.036	1.178	1.496	1.698	2.264	-0.174	0.065	0.278
RBC	0.976	0.998	1.021	1.053	1.076	1.123	-0.321	-0.021	0.296
HGB	0.976	0.991	1.008	1.051	1.067	1.095	-0.346	-0.129	0.112
HCT	0.979	0.998	1.017	1.038	1.056	1.091	-0.366	-0.042	0.310
MCV	0.989	0.999	1.010	1.031	1.041	1.055	-0.274	-0.016	0.257
MCH	0.975	0.993	1.011	1.045	1.062	1.085	-0.388	-0.115	0.191
MCHC	0.981	0.994	1.006	1.013	1.026	1.038	-0.797	-0.243	0.271
PLT	0.884	0.944	1.007	1.363	1.465	1.629	-0.299	-0.149	0.016
LYMA	0.898	1.032	1.186	1.433	1.633	2.132	-0.221	0.062	0.319
diffWBC	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11-	lower	esti	upper	lower	median	upper	lower	median	upper
Lymphocytes	0.968	1.001	1.036	1.056	1.092	1.158	-0.404	0.015	0.421
Neutrophils	0.933	1.014	1.102	1.360	1.487	1.853	-0.173	0.034	0.222
Monocytes	0.561	0.764	1.039	1.115	1.421	2.875	-2.000	-0.781	0.099
Eosinophils	0.726	0.982	1.329	2.064	2.717	4.250	-0.313	-0.018	0.292
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	0.831	0.927	1.035	1.192	1.320	1.480	-0.660	-0.270	0.120
ALT	0.892	0.989	1.097	1.576	1.757	2.062	-0.188	-0.019	0.163
AST	0.847	0.956	1.079	1.331	1.482	1.720	-0.385	-0.112	0.193
ALB	0.974	1.006	1.039	1.181	1.225	1.286	-0.130	0.027	0.167
TP	0.977	1.000	1.023	1.157	1.198	1.326	-0.125	-0.001	0.124
Glu	0.897	0.960	1.028	1.289	1.380	1.539	-0.309	-0.124	0.083
CHOL	0.875	0.978	1.094	1.065	1.204	1.387	-2.000	-0.122	0.982
TAG	0.862	0.985	1.127	1.824	2.116	2.808	-0.183	-0.019	0.159
Crea	0.935	0.992	1.052	1.255	1.345	1.670	-0.207	-0.026	0.170
Urea	0.988	1.045	1.105	1.237	1.332	1.730	-0.037	0.144	0.328
Ca	0.988	1.002	1.015	1.124	1.168	1.369	-0.075	0.010	0.090
Cl	0.998	1.006	1.014	1.056	1.068	1.086	-0.025	0.095	0.200
K	0.969	1.017	1.067	1.205	1.268	1.426	-0.128	0.068	0.242
Na	0.995	1.001	1.007	1.054	1.066	1.092	-0.078	0.017	0.101
P	0.923	1.010	1.105	1.166	1.272	1.471	-0.356	0.038	0.408

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_27	0.970	0.992	1.014	1.097	1.125	1.174	-0.234	-0.068	0.121
FeedMean	0.979	1.009	1.040	1.067	1.108	1.204	-0.222	0.082	0.371
Females NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
WBC	0.904	1.026	1.164	1.497	1.698	2.252	-0.193	0.047	0.263
RBC	0.984	1.006	1.029	1.053	1.076	1.123	-0.223	0.082	0.360
HGB	0.978	0.994	1.009	1.051	1.067	1.094	-0.313	-0.097	0.144
HCT	0.986	1.004	1.023	1.038	1.056	1.091	-0.274	0.073	0.389
MCV	0.984	0.995	1.005	1.031	1.041	1.055	-0.363	-0.128	0.138
MCH	0.969	0.987	1.005	1.044	1.062	1.085	-0.497	-0.217	0.083
MCHC	0.977	0.989	1.002	1.013	1.026	1.038	-1.032	-0.420	0.069
PLT	0.908	0.968	1.032	1.363	1.466	1.628	-0.230	-0.084	0.083
LYMA	0.886	1.016	1.165	1.433	1.634	2.136	-0.257	0.031	0.297
diffWBC	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33-	lower	esti	upper	lower	median	upper	lower	median	upper
Lymphocytes	0.964	0.997	1.031	1.056	1.092	1.158	-0.423	-0.032	0.380
Neutrophils	0.947	1.027	1.115	1.361	1.487	1.859	-0.138	0.066	0.247
Monocytes	0.653	0.885	1.198	1.117	1.624	2.850	-2.000	-0.344	2.000
Eosinophils	0.629	0.847	1.141	2.063	2.719	4.267	-0.436	-0.164	0.134
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	0.828	0.922	1.027	1.192	1.320	1.481	-0.681	-0.289	0.098
ALT	0.926	1.026	1.136	1.577	1.758	2.063	-0.136	0.045	0.203
AST	0.943	1.062	1.196	1.331	1.482	1.720	-0.153	0.150	0.427
ALB	0.979	1.011	1.043	1.181	1.225	1.286	-0.106	0.051	0.186
TP	0.985	1.007	1.030	1.157	1.198	1.321	-0.083	0.039	0.148
Glu	0.886	0.947	1.013	1.289	1.380	1.539	-0.355	-0.167	0.041
CHOL	0.824	0.919	1.026	1.065	1.196	1.382	-2.000	-0.474	0.169
TAG	0.802	0.915	1.044	1.827	2.115	2.791	-0.273	-0.116	0.056
Crea	0.914	0.968	1.026	1.255	1.345	1.674	-0.280	-0.104	0.083
Urea	0.962	1.016	1.074	1.238	1.332	1.734	-0.138	0.052	0.226
Ca	0.996	1.009	1.023	1.124	1.168	1.369	-0.025	0.055	0.137
Cl	1.000	1.008	1.016	1.056	1.068	1.086	-0.004	0.115	0.223
K	1.033	1.082	1.135	1.205	1.268	1.420	0.125	0.327	0.527
Na	0.993	0.999	1.005	1.054	1.066	1.093	-0.104	-0.020	0.074
P	0.951	1.039	1.136	1.166	1.272	1.468	-0.217	0.157	0.511

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_27	0.969	0.991	1.013	1.097	1.126	1.174	-0.245	-0.079	0.111
FeedMean	0.975	1.005	1.036	1.067	1.108	1.204	-0.262	0.047	0.338
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	0.846	0.960	1.089	1.497	1.698	2.242	-0.287	-0.076	0.163
RBC	0.981	1.003	1.026	1.053	1.076	1.122	-0.270	0.040	0.328
HGB	0.973	0.988	1.004	1.051	1.067	1.094	-0.401	-0.182	0.057
HCT	0.980	0.998	1.017	1.038	1.056	1.091	-0.365	-0.029	0.326
MCV	0.985	0.995	1.006	1.031	1.041	1.055	-0.354	-0.118	0.144
MCH	0.967	0.985	1.003	1.044	1.062	1.085	-0.537	-0.251	0.046
MCHC	0.977	0.990	1.002	1.013	1.026	1.038	-1.033	-0.418	0.072
PLT	0.877	0.935	0.997	1.363	1.465	1.628	-0.327	-0.175	-0.009
LYMA	0.836	0.959	1.100	1.434	1.635	2.147	-0.334	-0.082	0.197
diffWBC	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK11+	lower	esti	upper	lower	median	upper	lower	median	upper
Lymphocytes	0.965	0.998	1.032	1.056	1.092	1.157	-0.420	-0.021	0.390
Neutrophils	0.936	1.016	1.102	1.361	1.486	1.856	-0.168	0.038	0.225
Monocytes	0.691	0.936	1.268	1.115	1.621	2.855	-2.000	-0.182	2.000
Eosinophils	0.795	1.071	1.442	2.066	2.717	4.295	-0.238	0.067	0.340
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	0.845	0.941	1.048	1.191	1.319	1.478	-0.598	-0.218	0.177
ALT	0.795	0.880	0.975	1.578	1.758	2.059	-0.391	-0.224	-0.044
AST	0.820	0.923	1.039	1.330	1.482	1.719	-0.482	-0.202	0.098
ALB	0.988	1.020	1.053	1.181	1.225	1.286	-0.060	0.097	0.232
TP	0.986	1.008	1.031	1.157	1.198	1.324	-0.079	0.044	0.153
Glu	0.915	0.978	1.046	1.290	1.380	1.539	-0.250	-0.067	0.142
CHOL	0.811	0.905	1.010	1.063	1.195	1.384	-2.000	-0.560	0.063
TAG	0.800	0.913	1.041	1.824	2.116	2.803	-0.275	-0.119	0.054
Crea	0.954	1.011	1.071	1.255	1.345	1.675	-0.161	0.034	0.211
Urea	0.944	0.997	1.054	1.238	1.332	1.733	-0.199	-0.009	0.188
Ca	0.993	1.006	1.020	1.124	1.168	1.368	-0.044	0.038	0.116
Cl	0.999	1.007	1.015	1.056	1.068	1.086	-0.019	0.100	0.206
K	0.987	1.035	1.085	1.205	1.268	1.425	-0.053	0.140	0.319
Na	0.994	1.000	1.006	1.054	1.066	1.092	-0.091	0.005	0.097
P	0.916	1.001	1.093	1.167	1.272	1.468	-0.395	0.004	0.399

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_27	0.973	0.995	1.018	1.097	1.125	1.174	-0.209	-0.038	0.153
FeedMean	0.998	1.029	1.060	1.067	1.108	1.202	-0.022	0.266	0.586
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	0.910	1.032	1.171	1.497	1.699	2.250	-0.182	0.058	0.271
RBC	0.987	1.009	1.032	1.053	1.076	1.123	-0.184	0.121	0.399
HGB	0.981	0.997	1.013	1.051	1.067	1.094	-0.269	-0.047	0.202
HCT	0.982	1.000	1.019	1.038	1.056	1.091	-0.351	0.006	0.358
MCV	0.981	0.991	1.002	1.031	1.041	1.055	-0.453	-0.212	0.046
MCH	0.970	0.988	1.006	1.044	1.062	1.085	-0.484	-0.204	0.097
MCHC	0.985	0.997	1.009	1.013	1.026	1.038	-0.661	-0.125	0.420
PLT	0.912	0.972	1.036	1.362	1.465	1.626	-0.219	-0.074	0.095
LYMA	0.881	1.011	1.159	1.433	1.634	2.144	-0.265	0.022	0.293
diffWBC	Interval for ratio Δ			Interval for EQ limit			Interval for Δ ELSD scale		
Females NK33+	lower	esti	upper	lower	median	upper	lower	median	upper
Lymphocytes	0.991	1.025	1.060	1.056	1.092	1.158	-0.102	0.273	0.669
Neutrophils	0.890	0.966	1.048	1.361	1.487	1.858	-0.267	-0.084	0.119
Monocytes	0.498	0.674	0.913	1.116	1.420	2.857	-2.000	-1.142	-0.191
Eosinophils	0.642	0.864	1.164	2.059	2.718	4.252	-0.416	-0.143	0.156
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	0.838	0.933	1.040	1.192	1.320	1.479	-0.635	-0.246	0.148
ALT	0.895	0.992	1.098	1.575	1.757	2.064	-0.188	-0.015	0.169
AST	0.941	1.060	1.194	1.331	1.482	1.721	-0.159	0.146	0.421
ALB	0.962	0.993	1.025	1.181	1.225	1.286	-0.172	-0.034	0.124
TP	0.971	0.993	1.016	1.157	1.198	1.325	-0.146	-0.036	0.087
Glu	0.920	0.984	1.052	1.289	1.380	1.540	-0.236	-0.050	0.161
CHOL	0.845	0.943	1.053	1.063	1.196	1.386	-2.000	-0.328	0.385
TAG	0.848	0.968	1.104	1.827	2.116	2.803	-0.197	-0.042	0.135
Crea	0.960	1.017	1.077	1.255	1.345	1.674	-0.138	0.054	0.226
Urea	0.974	1.029	1.087	1.237	1.332	1.731	-0.092	0.093	0.270
Ca	0.984	0.997	1.010	1.124	1.168	1.370	-0.095	-0.018	0.066
Cl	0.992	1.000	1.008	1.056	1.068	1.087	-0.119	0.003	0.123
K	0.959	1.005	1.053	1.205	1.268	1.423	-0.181	0.019	0.206
Na	0.995	1.001	1.007	1.054	1.066	1.093	-0.076	0.018	0.103
P	0.881	0.962	1.052	1.166	1.272	1.469	-0.509	-0.157	0.218

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_27	0.539	0.216	0.245	0.896	0.489	0.441	0.813	0.400	0.533	0.995	0.768	0.840
growthRate	0.998	0.812	0.680	1.000	0.987	0.994	0.800	0.387	0.225	0.874	0.462	0.599
FeedMean	0.265	0.091	0.033	0.175	0.057	0.023	0.557	0.226	0.201	0.468	0.180	0.149
Haematology	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
WBC	0.811	0.399	0.409	0.016	0.004	0.015	0.061	0.018	0.064	0.827	0.414	0.430
RBC	0.995	0.774	0.784	1.000	0.933	0.648	1.000	0.945	0.812	0.887	0.480	0.729
HGB	0.978	0.665	0.956	0.568	0.232	0.177	1.000	0.943	0.985	0.224	0.076	0.105
HCT	0.984	0.690	1.000	0.845	0.431	0.330	0.977	0.662	0.701	0.524	0.209	0.216
MCV	0.785	0.380	0.465	0.246	0.086	0.080	0.994	0.759	0.984	0.426	0.163	0.055
MCH	1.000	0.928	0.869	0.717	0.324	0.261	1.000	0.991	0.956	0.814	0.402	0.053
MCHC	1.000	0.944	0.756	0.892	0.486	0.571	0.922	0.529	0.644	0.803	0.391	0.388
PLT	0.772	0.366	0.189	0.489	0.191	0.123	0.664	0.289	0.154	0.831	0.417	0.330
LYMR	0.630	0.268	0.177	0.911	0.512	0.261	1.000	0.975	0.898	0.930	0.543	0.294
LYMA	0.590	0.245	0.189	0.059	0.018	0.048	0.093	0.029	0.123	0.710	0.319	0.388
diffWBC	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Lymphocytes	0.816	0.403	0.177	0.920	0.527	0.388	0.998	0.823	0.956	0.561	0.229	0.133
Neutrophils	0.953	0.588	0.644	0.990	0.725	0.522	0.951	0.584	0.648	0.466	0.180	0.177
Monocytes	0.054	0.016	0.035	0.733	0.335	0.332	0.102	0.032	0.042	0.575	0.236	0.179
Eosinophils	1.000	0.907	0.970	0.421	0.158	0.198	0.970	0.634	0.622	0.515	0.204	0.205
ClinChem	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
ALP	0.981	0.677	0.571	0.787	0.378	0.330	0.961	0.609	0.522	0.994	0.762	0.648
ALT	1.000	0.873	0.927	0.976	0.657	0.956	0.968	0.628	0.522	0.997	0.791	0.841

AST	0.941	0.564	0.729	0.416	0.156	0.202	0.926	0.537	0.245	0.997	0.800	0.648
BIL	0.958	0.600	0.409	0.072	0.022	0.076	0.294	0.104	0.189	0.468	0.181	0.040
ALB	0.999	0.852	0.927	0.952	0.586	0.498	0.977	0.658	0.701	0.985	0.695	0.522
TP	0.945	0.571	0.674	0.991	0.734	0.522	0.840	0.426	0.756	0.982	0.680	0.571
Glu	0.845	0.432	0.231	0.978	0.664	0.596	0.984	0.690	0.784	0.569	0.233	0.076
CHOL	0.767	0.362	0.349	0.986	0.703	0.546	1.000	0.987	0.869	0.696	0.309	0.701
TAG	0.796	0.385	0.097	0.309	0.110	0.245	0.116	0.036	0.024	0.645	0.277	0.261
Crea	0.460	0.177	0.277	0.946	0.574	0.475	1.000	0.979	0.985	0.336	0.121	0.177
Urea	0.634	0.270	0.231	1.000	0.965	0.756	1.000	0.888	0.701	0.974	0.647	0.674
cHGB	0.470	0.182	0.312	0.164	0.054	0.058	0.166	0.054	0.070	0.814	0.402	0.294
Ca	0.999	0.846	0.985	0.721	0.327	0.294	0.833	0.420	0.368	0.998	0.830	0.522
Cl	1.000	0.944	0.809	0.601	0.251	0.177	0.965	0.621	0.852	0.989	0.718	0.955
K	0.915	0.518	0.673	0.473	0.183	0.216	0.146	0.047	0.064	0.951	0.586	0.478
Na	0.837	0.423	0.398	0.997	0.800	0.784	0.961	0.610	0.596	0.576	0.237	0.260
P	0.761	0.357	0.452	0.997	0.807	0.388	0.856	0.444	0.430	0.991	0.729	0.841
Urine	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
uVol	0.909	0.513	0.322	0.123	0.039	0.193	0.738	0.342	0.695	0.990	0.728	0.846
uVolW	0.877	0.471	0.275	0.165	0.054	0.160	0.851	0.441	0.846	0.995	0.777	0.922
uLeu	0.974	0.650	1.000	0.283	0.100	0.175	0.993	0.754	0.461	0.998	0.820	0.796
uOsmoll	0.807	0.398	0.160	0.178	0.059	0.193	0.769	0.366	0.492	0.988	0.715	0.770
uKeton	0.996	0.782	0.599	0.917	0.525	0.396	0.996	0.782	0.722	0.766	0.363	0.438
upH	0.795	0.388	0.254	0.795	0.388	0.279	0.998	0.828	0.903	0.499	0.198	0.396

Weights	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Weight_27	0.968	0.628	0.994	0.884	0.474	0.334	0.818	0.404	0.599	0.983	0.683	0.815
growthRate	0.998	0.812	0.680	1.000	0.987	0.994	0.800	0.387	0.225	0.874	0.462	0.599
FeedMean	0.996	0.778	0.656	0.941	0.562	0.622	0.993	0.747	0.942	0.210	0.070	0.058
Haematology	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
WBC	0.950	0.581	0.595	0.983	0.685	0.648	0.915	0.518	0.622	0.965	0.618	0.349
RBC	1.000	0.890	0.798	0.946	0.573	0.522	0.996	0.783	0.674	0.833	0.418	0.546
HGB	0.668	0.290	0.196	0.830	0.415	0.368	0.363	0.132	0.103	0.985	0.693	0.648
HCT	0.997	0.805	0.738	0.976	0.655	0.784	0.999	0.861	0.729	1.000	0.970	0.702
MCV	1.000	0.906	0.860	0.730	0.332	0.522	0.773	0.365	0.475	0.305	0.108	0.114
MCH	0.863	0.450	0.352	0.403	0.150	0.097	0.278	0.097	0.231	0.459	0.176	0.388
MCHC	0.719	0.324	0.258	0.254	0.087	0.165	0.264	0.091	0.070	0.960	0.606	0.841
PLT	0.240	0.082	0.293	0.709	0.318	0.165	0.123	0.039	0.053	0.790	0.380	0.312
LYMR	0.759	0.354	0.312	0.937	0.555	0.869	1.000	0.946	0.869	0.697	0.309	0.261
LYMA	0.975	0.652	0.541	0.998	0.820	0.784	0.933	0.547	0.430	1.000	0.875	0.571
diffWBC	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Lymphocytes	1.000	0.939	0.953	0.999	0.863	0.920	1.000	0.910	0.869	0.397	0.147	0.076
Neutrophils	0.992	0.740	0.595	0.910	0.511	0.430	0.987	0.706	0.701	0.816	0.403	0.277
Monocytes	0.249	0.085	0.093	0.839	0.424	0.709	0.979	0.666	0.365	0.040	0.012	0.004
Eosinophils	1.000	0.906	1.000	0.635	0.270	0.205	0.974	0.648	0.481	0.729	0.332	0.588
ClinChem	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
ALP	0.453	0.173	0.104	0.381	0.140	0.571	0.621	0.262	0.202	0.520	0.206	0.123
ALT	0.999	0.833	0.623	0.966	0.622	0.674	0.051	0.015	0.021	1.000	0.871	0.898
AST	0.874	0.463	0.568	0.710	0.318	0.202	0.474	0.183	0.040	0.730	0.332	0.231
BIL	0.988	0.713	0.738	0.826	0.412	0.729	0.964	0.617	0.522	1.000	0.995	0.841
ALB	0.991	0.732	0.798	0.912	0.512	0.729	0.544	0.219	0.189	0.978	0.664	0.522
TP	1.000	0.994	0.798	0.912	0.513	0.522	0.872	0.461	0.261	0.933	0.548	0.430
Glu	0.585	0.241	0.275	0.315	0.112	0.123	0.916	0.519	0.648	0.967	0.624	0.674

CHOL	0.986	0.699	0.798	0.359	0.131	0.261	0.222	0.075	0.058	0.674	0.294	0.368
TAG	0.998	0.828	0.541	0.475	0.184	0.114	0.450	0.172	0.040	0.966	0.623	0.475
Crea	0.996	0.780	0.953	0.630	0.267	0.498	0.988	0.712	0.898	0.940	0.561	0.622
Urea	0.342	0.123	0.196	0.942	0.566	0.812	1.000	0.917	0.571	0.695	0.308	0.812
cHGB	0.897	0.491	0.258	0.523	0.208	0.648	0.998	0.817	0.674	0.991	0.730	0.674
Ca	0.997	0.804	0.965	0.447	0.170	0.277	0.742	0.341	0.231	0.973	0.645	0.409
Cl	0.342	0.123	0.108	0.177	0.058	0.064	0.280	0.097	0.154	1.000	0.960	0.911
K	0.893	0.486	0.515	0.005	0.001	0.001	0.403	0.150	0.153	0.999	0.836	0.522
Na	0.990	0.723	0.829	0.976	0.655	0.673	1.000	0.909	0.856	0.984	0.690	0.898
P	0.998	0.830	0.829	0.800	0.388	0.475	1.000	0.989	0.985	0.804	0.391	0.368
Urine	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
uVol	0.808	0.398	0.141	0.615	0.260	0.131	1.000	0.903	0.695	0.236	0.081	0.084
uVolW	0.807	0.396	0.164	0.677	0.298	0.275	1.000	0.961	0.695	0.212	0.071	0.049
uLeu	0.815	0.404	0.430	0.998	0.816	0.943	0.891	0.486	0.829	1.000	1.000	0.577
uOsmoll	0.923	0.533	0.426	0.418	0.158	0.160	1.000	0.987	0.846	0.363	0.133	0.084
uKeton	0.899	0.497	0.583	0.994	0.759	1.000	0.951	0.587	0.892	0.951	0.587	0.410
upH	0.694	0.310	0.187	0.528	0.212	0.124	0.980	0.674	1.000	0.920	0.529	0.407

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_27	0.776	0.685	0.585	0.158	0.641	0.246	0.545	0.378
growthRate	0.000	0.684	0.875	0.167	0.415	0.094	0.573	0.133
FeedMean	0.700	0.478	0.645	0.305	0.436	0.110	0.010	0.059
Male Haematology	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
WBC	0.991	0.946	0.269	0.079	0.540	0.998	0.912	0.971
RBC	0.194	0.401	0.624	0.229	0.256	0.214	0.758	0.548
HGB	0.048	0.001	0.580	0.672	0.388	0.491	0.686	0.908
HCT	0.284	0.970	0.714	0.322	0.917	0.333	0.754	0.820
MCV	0.180	0.085	0.965	0.761	0.821	0.908	0.043	0.171
MCH	0.095	0.536	0.986	0.729	0.267	0.601	0.276	0.285
MCHC	0.153	0.637	0.928	0.462	0.803	0.560	0.543	0.668
PLT	0.223	0.037	0.272	0.522	0.753	0.213	0.003	0.088
LYMR	0.488	0.903	0.790	0.003	0.449	0.951	0.196	0.232
LYMA	0.349	0.385	0.324	0.058	0.832	0.686	0.843	0.819
Male diffWBC	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
Lymphocytes	0.561	0.284	0.509	0.066	0.925	0.199	0.268	0.713
Neutrophils	0.715	0.007	0.272	0.668	0.728	0.867	0.790	0.962
Monocytes	0.374	0.004	0.004	0.037	0.014	0.160	0.196	0.251
Eosinophils	0.111	0.501	0.043	0.043	0.026	0.004	0.063	0.051
Male ClinChem	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
ALP	0.476	0.447	0.386	0.146	0.558	0.895	0.755	0.798
ALT	0.976	0.270	0.621	0.291	0.128	0.015	0.519	0.731
AST	0.408	0.487	0.847	0.541	0.999	0.570	0.742	0.564
BIL	0.203	0.609	0.002	0.027	0.360	0.018	0.964	0.986
ALB	0.416	0.872	0.788	0.527	0.166	0.939	0.998	0.995

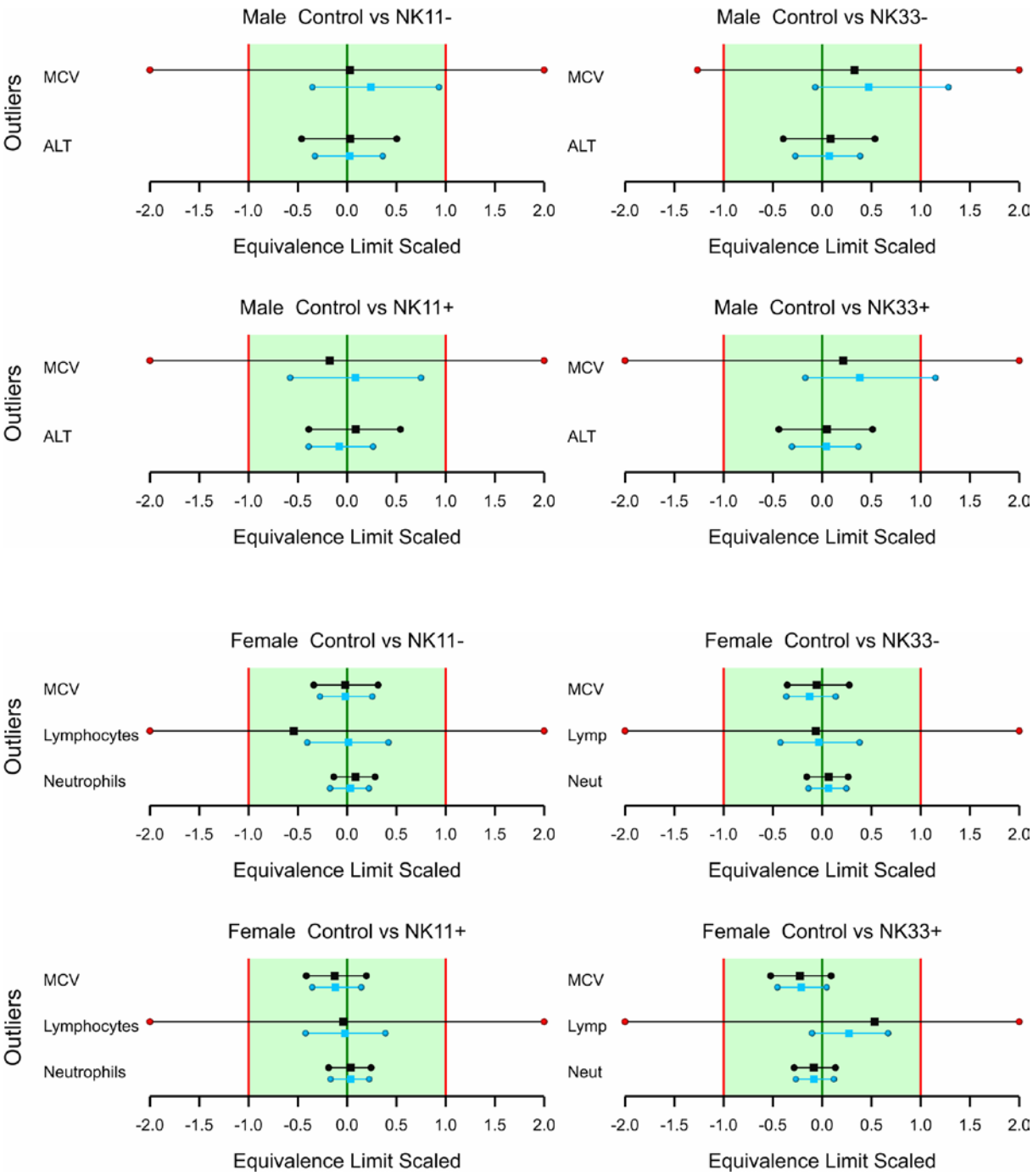
TP	0.185	0.015	0.268	0.240	0.901	0.749	0.742	0.358
Glu	0.114	0.752	0.054	0.461	0.651	0.299	0.529	0.475
CHOL	1.000	0.233	0.991	0.344	0.415	0.578	0.895	0.965
TAG	0.599	0.212	0.716	0.083	0.914	0.852	0.979	0.903
Crea	0.126	0.103	0.269	0.952	0.148	0.743	0.983	0.994
Urea	0.600	0.126	0.332	0.007	0.913	0.872	0.592	0.697
cHGB	0.855	0.184	0.065	0.160	0.217	0.021	0.439	0.839
Ca	0.148	0.687	0.132	0.404	0.586	0.276	0.818	0.460
Cl	0.301	0.499	0.850	0.146	0.192	0.683	0.917	0.894
K	0.375	0.001	0.141	0.010	0.441	0.003	0.287	0.489
Na	0.281	0.492	0.927	0.645	0.193	0.672	0.391	0.228
P	0.484	0.431	0.411	0.244	0.222	0.936	0.476	0.659
Male Urine	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
uVol	0.501	0.328	0.556	0.141	0.148	0.714	0.101	0.240
uVolW	0.239	0.049	0.652	0.558	0.274	0.794	0.088	0.175
uLeu	0.191	0.045	0.048	0.068	0.017	0.234	0.718	0.922
uOsmoll	0.637	0.137	0.589	0.463	0.076	0.101	0.287	0.205
uKeton	0.019	0.184	0.249	0.065	0.011	0.982	0.957	0.838
upH	0.421	0.017	0.036	0.001	0.087	0.866	0.200	0.191

Female Weights	SW Control	SW NK11-	SW NK33-	SW NK11+	SW NK33+	SW residual	Bartlett	Levene
Weight_27	0.808	0.546	0.206	0.294	0.735	0.928	0.886	0.678
growthRate	0.000	0.684	0.875	0.167	0.415	0.094	0.573	0.133
FeedMean	0.419	0.883	0.242	0.633	0.619	0.647	0.391	0.425
Female Haematology	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
WBC	0.202	0.315	0.418	0.229	0.904	0.382	0.234	0.122
RBC	0.462	0.638	0.173	0.584	0.387	0.059	0.312	0.688
HGB	0.382	0.420	0.271	0.916	0.769	0.369	0.049	0.037
HCT	0.174	0.603	0.091	0.330	0.642	0.948	0.089	0.342
MCV	0.427	0.914	0.300	0.547	0.369	0.695	0.631	0.608
MCH	0.770	0.881	0.420	0.088	0.480	0.653	0.580	0.459
MCHC	0.974	0.348	0.690	0.765	0.929	0.502	0.022	0.096
PLT	0.763	0.109	0.321	0.046	0.115	0.152	0.124	0.364
LYMR	0.006	0.339	0.010	0.966	0.729	0.385	0.301	0.591
LYMA	0.057	0.497	0.962	0.382	0.408	0.326	0.323	0.444
Female diffWBC	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
Lymphocytes	0.493	0.902	0.851	0.869	0.371	0.336	0.878	0.913
Neutrophils	0.657	0.258	0.734	0.794	0.476	0.430	0.911	0.948
Monocytes	0.103	0.353	0.438	0.000	0.048	0.123	0.238	0.076
Eosinophils	0.717	0.039	0.015	0.224	0.408	0.019	0.022	0.059
Female ClinChem	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
ALP	0.699	0.196	0.357	0.336	0.936	0.010	0.282	0.390
ALT	0.586	0.319	0.648	0.568	0.690	0.145	0.771	0.730
AST	0.258	1.000	0.598	0.583	0.042	0.271	0.414	0.672
BIL	0.680	0.713	0.269	0.777	0.881	0.019	0.014	0.013
ALB	0.299	0.427	0.553	0.500	0.785	0.260	0.545	0.374
TP	0.015	0.223	0.825	0.786	0.105	0.736	0.522	0.411
Glu	0.525	0.399	0.366	0.066	0.982	0.487	0.759	0.908
CHOL	0.986	0.301	0.639	0.179	0.561	0.874	0.911	0.877
TAG	0.695	0.385	0.423	0.608	0.071	0.291	0.215	0.252
Crea	0.453	0.592	0.074	0.032	0.992	0.584	0.019	0.026

Urea	0.729	0.292	0.254	0.168	0.901	0.671	0.865	0.835
cHGB	0.246	0.467	0.005	0.011	0.173	0.000	0.292	0.788
Ca	0.114	0.690	0.588	0.101	0.247	0.251	0.179	0.336
Cl	0.767	0.738	0.093	0.429	0.786	0.880	0.810	0.719
K	0.598	0.790	0.018	0.571	0.192	0.111	0.568	0.972
Na	0.911	0.176	0.066	0.921	0.483	0.453	0.969	0.981
P	0.272	0.522	0.730	0.139	0.112	0.564	0.281	0.419
Female Urine	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
uVol	0.638	0.776	0.645	0.384	0.479	0.220	0.421	0.447
uVolW	0.779	0.332	0.559	0.754	0.542	0.081	0.694	0.795
uLeu	0.000	0.087	0.074	0.025	0.036	0.649	0.186	0.048
uOsmoll	0.679	0.656	0.247	0.552	0.249	0.661	0.633	0.516
uKeton	0.000	0.001	0.009	0.000	0.000	0.456	0.366	0.659
upH	0.002	0.074	0.017	0.176	0.012	0.046	0.077	0.190

Appendix 11. Statistical analysis of data including outliers

For male animals there are outlying values for MCV (2×), ALT (1×) and BIL (1×), while for females there are outlying values for Lymphocytes (1×), Neutrophils (1×), MCV (1×) and BIL (2×); see Table 6 for a list of outliers. The results of the equivalence tests, using the historical GRACE data, are given below; the black lines are for the analysis including outliers while the blue lines are for the analysis without outliers as in Figure 5 - Figure 8.



Results of the classical analysis without and with outliers are given in the tables below. Note that the top parts of the tables are identical to the values in Table 12 and Table 13.

Without Outliers	Control		NK11-			NK33-			NK11+			NK33+		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
MCV	53.96	1.4	54.27	2.7		54.61	2.7		54.03	2.1		54.46	1.8	
ALT	0.679	12.7	0.695	23.4		0.703	21.8		0.675	17.8		0.691	14.5	
BIL	7.325	17.5	7.543	19.8		8.338	25.8	t	7.985	20.2		7.830	16.4	w
With Outliers	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
MCV	54.22	2.6	54.27	2.7		54.61	2.7		54.03	2.1		54.46	1.8	
ALT	0.679	12.7	0.695	23.4		0.703	21.8		0.721	29.8		0.691	14.5	
BIL	7.325	17.5	8.242	44.2		8.338	25.8	t	7.985	20.2		7.830	16.4	w

Without Outliers	Control		NK11-			NK33-			NK11+			NK33+		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
MCV	57.68	1.7	57.64	1.6		57.39	2.0		57.41	1.4		57.19	1.7	
Lymphocytes	67.67	6.3	67.46	6.4		67.40	5.8		67.45	5.2		69.30	6.5	
Neutrophils	28.97	14.7	29.54	13.8		29.61	14.0		29.26	12.9		27.91	15.5	
BIL	8.365	14.4	8.342	9.3		8.755	23.0		8.242	18.2		8.355	15.7	
With Outliers	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
MCV	57.68	1.7	57.64	1.6		57.58	2.7		57.41	1.4		57.19	1.7	
Lymphocytes	67.67	6.3	66.43	10.1		67.40	5.8		67.45	5.2		69.30	6.5	
Neutrophils	28.97	14.7	30.50	20.2		29.61	14.0		29.26	12.9		27.91	15.5	
BIL	8.365	14.4	8.342	9.3		9.722	45.1		9.292	46.5		8.355	15.7	

Conclusion: for MCV in males and Lymphocytes in females equivalence cannot be established when outliers are included in the analysis. For the classical analysis inclusion of outliers basically makes no difference.