G-TWYST
GM PLANTS TWO YEAR SAFETY TESTING

Statistical analysis of differential white blood cell counts for G-TwYST studies A and C

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1 Introduction

Statistical analysis of the G-TwYST studies was reported in

Study A: Goedhart & van der Voet (2018a, 2018b 2018c, 2018d and 2018e)

Study B: Goedhart & van der Voet (2017)

Study C: Goedhart & van der Voet (2018f)

Note that for Study A there are separate reports for data acquired after 3, 6, 12 and 24 months as well as a main report. Study B and C were 3 months studies only. These reports lacks a statistical analysis of differential white blood cell counts, or diffWBC for short, for Study A data acquired after 3, 12 and 24 month, and also for study C. This report presents these statistical analysis; it includes, for reasons of completeness, the statistical analysis of diffWBC for study A for 6 months which was already presented in Goedhart & van der Voet (2018c). The reader is referred to the reports listed above for details of the study plans and the statistical methods used. Here only the results of the statistical analysis are presented.

2 Data

2.1 Available diffWBC data for studies A and C

The available files for the diffWBC data for studies A and C are given in Table 1. The number of observations, generally evenly distributed across treatment group, are given in Table 2. For study A in principle the same rats were observed after 3, 6, 12 and 24 months. However due to mortality, especially after 24 months, additional rats were observed.

Table 1 Data files for G-TwYST studies A and C.

Data files differential white blood cell counts Study A	Date	Time	Size (b)
3 months: Diferent WBC GTWYST A-3M database.xlsx	06-03-2018	12:53	33,234
6 months: Differential WBC G-TwYST A - after 6M final 12.12.17.xlsx	12-12-2017	14:17	37,026
12 months: Database Differential WBC GTWYST A - 12M final JT.xlsx	15-06-2018	10:40	33,513
24 months: Database Differential WBC GTWYST A - 24M final JT.xlsx	14-06-2018	11:57	30,358
Data file differential white blood cell counts Study C	**Date**	**Time**	**Size (b)**
3 months: Differential WBC - G-TwYST C 20.3.18.xlsx	20-03-2018	12:01	28,404

Table 2 Number of animals for which diffWBC data are available in studies A and C.

Variable	Males	Females
study A 3 months	200	200
study A 6 months	200	199
study A 12 months	197	202
study A 24 months	154	141
study C	128	128

For each sample 200 cells are classified as a Lymphocyte, Neutrophil, Monocyte, Eosinophil or Basophil. The latter type is rarely found and is not statistically analysed. Occasionally less or more than 200 cell are classified. The data are thus expressed as a percentage of the total number of counted cells. The diffWBC data are thus not independent as the sum of the percentages equals 100.

2.2 Outliers and checking of ANOVA assumptions for study A

Table 3 and Table 4 lists the five smallest and largest values for every diffWBC response variable in study A for Males and Females respectively. Goedhart & van der Voet (2018c) found extreme values for Lymphocytes and Neutrophils for female animal 616 in group NK11- in Study A after 6 months. The same animal also had extreme Lymphocytes and Neutrophils values after 3 months, and these are therefore also considered as outliers. Animal 616 died after 372 days and there are no diffWBC data for this animal after 12 and 24 months.

Table 3 The five smallest and five largest observed diffWBC percentages for every response variable observed in study A for Males. Outliers are listed in yellow.

Smallest five Lymphocytes Males				Largest five Lymphocytes Males			
Animal	Cage	Group	Lymphocytes-03	Animal	Cage	Group	Lymphocytes-03
266	133	NK33-	38.0	9	5	NK33+	85.0
265	133	NK33-	45.5	35	18	NK33+	84.5
40	20	NK33+	50.5	161	81	NK11+	83.0
60	30	NK33+	52.5	231	116	NK33-	83.0
195	98	NK11+	54.0	302	151	Control	83.0
Animal	Cage	Group	Lymphocytes-06	Animal	Cage	Group	Lymphocytes-06
160	80	NK11+	54.0	22	11	NK33+	83.5
196	98	NK11+	54.0	300	150	Control	82.5
222	111	NK33-	54.0	156	78	NK11+	82.0
269	135	NK33-	56.5	296	148	Control	81.5
298	149	Control	56.5	9	5	NK33+	81.0
Animal	Cage	Group	Lymphocytes-12	Animal	Cage	Group	Lymphocytes-12
153	77	NK11+	12.0	35	18	NK33+	78.5
195	98	NK11+	43.5	36	18	NK33+	77.0
81	41	NK11-	44.0	307	154	Control	75.5
202	101	NK11+	44.0	280	140	NK33-	74.5
221	111	NK33-	44.0	283	142	Control	74.5
Animal	Cage	Group	Lymphocytes-24	Animal	Cage	Group	Lymphocytes-24
130	65	NK11-	1.0	174	87	NK11+	86.5
123	62	NK11-	14.0	305	153	Control	83.0
339	170	Control	15.5	22	11	NK33+	81.5
36	18	NK33+	17.0	117	59	NK11-	71.5
59	30	NK33+	18.0	200	100	NK11+	70.0

Smallest five Neutrophils Males				Largest five Neutrophils Males			
Animal	Cage	Group	Neutrophils-03	Animal	Cage	Group	Neutrophils-03
35	18	NK33+	11.5	266	133	NK33-	58.0
79	40	NK11-	11.5	265	133	NK33-	51.5
9	5	NK33+	13.5	40	20	NK33+	45.0
21	11	NK33+	14.0	60	30	NK33+	44.5
143	72	NK11+	14.0	195	98	NK11+	42.0
Animal	Cage	Group	Neutrophils-06	Animal	Cage	Group	Neutrophils-06
22	11	NK33+	14.5	160	80	NK11+	45.0
9	5	NK33+	15.5	196	98	NK11+	43.0
156	78	NK11+	16.0	228	114	NK33-	40.0
80	40	NK11-	16.5	269	135	NK33-	40.0
217	109	NK33-	16.5	222	111	NK33-	39.5
Animal	Cage	Group	Neutrophils-12	Animal	Cage	Group	Neutrophils-12
35	18	NK33+	19.5	153	77	NK11+	81.0

36	18	NK33+	22.0	202	101	NK11+	55.0
80	40	NK11-	24.0	81	41	NK11-	54.0
232	116	NK33-	24.0	195	98	NK11+	54.0
280	140	NK33-	24.0	221	111	NK33-	53.0
Animal	Cage	Group	Neutrophils-24	Animal	Cage	Group	Neutrophils-24
174	87	NK11+	12.0	130	65	NK11-	91.0
305	153	Control	15.0	36	18	NK33+	82.5
22	11	NK33+	17.5	162	81	NK11+	81.0
117	59	NK11-	25.5	327	164	Control	79.5
165	83	NK11+	27.0	123	62	NK11-	78.0

Smallest five Monocytes Males				**Largest five Monocytes Males**			
Animal	Cage	Group	Monocytes-03	Animal	Cage	Group	Monocytes-03
17	9	NK33+	0.5	73	37	NK11-	4.5
27	14	NK33+	0.5	74	37	NK11-	4.0
80	40	NK11-	0.5	89	45	NK11-	4.0
122	61	NK11-	0.5	3	2	NK33+	3.5
149	75	NK11+	0.5	6	3	NK33+	3.5
Animal	Cage	Group	Monocytes-06	Animal	Cage	Group	Monocytes-06
65	33	NK33+	0.0	224	112	NK33-	3.0
71	36	NK11-	0.0	297	149	Control	2.5
89	45	NK11-	0.0	10	5	NK33+	2.0
135	68	NK11-	0.0	28	14	NK33+	2.0
136	68	NK11-	0.0	148	74	NK11+	2.0
Animal	Cage	Group	Monocytes-12	Animal	Cage	Group	Monocytes-12
3	2	NK33+	0.0	8	4	NK33+	3.0
15	8	NK33+	0.0	265	133	NK33-	3.0
16	8	NK33+	0.0	81	41	NK11-	2.0
17	9	NK33+	0.0	196	98	NK11+	2.0
18	9	NK33+	0.0	7	4	NK33+	1.5
Animal	Cage	Group	Monocytes-24	Animal	Cage	Group	Monocytes-24
36	18	NK33+	0.0	334	167	Control	11.0
45	23	NK33+	0.0	317	159	Control	10.5
106	53	NK11-	0.0	139	70	NK11-	10.0
122	61	NK11-	0.0	345	173	Control	10.0
162	81	NK11+	0.0	59	30	NK33+	8.5

Smallest five Eosinophils Males				**Largest five Eosinophils Males**			
Animal	Cage	Group	Eosinophils-03	Animal	Cage	Group	Eosinophils-03
17	9	NK33+	0.0	79	40	NK11-	7.0
27	14	NK33+	0.0	15	8	NK33+	6.0
39	20	NK33+	0.0	290	145	Control	5.5
98	49	NK11-	0.0	55	28	NK33+	5.0
129	65	NK11-	0.0	175	88	NK11+	5.0
Animal	Cage	Group	Eosinophils-06	Animal	Cage	Group	Eosinophils-06
75	38	NK11-	0.0	159	80	NK11+	10.5
141	71	NK11+	0.0	230	115	NK33-	8.0
155	78	NK11+	0.0	245	123	NK33-	6.5
210	105	NK11+	0.0	167	84	NK11+	6.0
249	125	NK33-	0.0	292	146	Control	6.0
Animal	Cage	Group	Eosinophils-12	Animal	Cage	Group	Eosinophils-12
12	6	NK33+	0.0	89	45	NK11-	6.5
15	8	NK33+	0.0	84	42	NK11-	6.0

21	11	NK33+	0.0	153	77	NK11+	6.0
55	28	NK33+	0.0	13	7	NK33+	5.5
77	39	NK11-	0.0	152	76	NK11+	5.0
Animal	Cage	Group	Eosinophils-24	Animal	Cage	Group	Eosinophils-24
22	11	NK33+	0.0	105	53	NK11-	5.0
25	13	NK33+	0.0	190	95	NK11+	5.0
48	24	NK33+	0.0	201	101	NK11+	5.0
61	31	NK33+	0.0	232	116	NK33-	4.0
67	34	NK33+	0.0	243	122	NK33-	4.0

Table 4 The five smallest and five largest observed diffWBC percentages for every response variable observed in study A for Females. Outliers are listed in yellow.

Smallest five Lymphocytes Females				Largest five Lymphocytes Females			
Animal	Cage	Group	Lymphocytes-03	Animal	Cage	Group	Lymphocytes-03
616	558	NK11-	20.0	792	646	Control	87.0
729	615	NK33-	51.0	566	533	NK33+	86.5
571	536	NK11-	51.5	724	612	NK33-	86.0
836	668	Control	52.0	765	633	NK33-	86.0
641	571	NK11+	56.5	845	673	Control	86.0
Animal	Cage	Group	Lymphocytes-06	Animal	Cage	Group	Lymphocytes-06
616	558	NK11-	24.0	513	507	NK33+	83.0
782	641	Control	52.0	795	648	Control	80.0
629	565	NK11-	55.5	514	507	NK33+	78.5
640	570	NK11-	55.5	516	508	NK33+	78.5
709	605	NK11+	57.0	586	543	NK11-	78.5
Animal	Cage	Group	Lymphocytes-12	Animal	Cage	Group	Lymphocytes-12
585	543	NK11-	33.0	711	606	NK33-	91.5
727	614	NK33-	41.5	641	571	NK11+	88.5
815	658	Control	43.0	724	612	NK33-	86.5
643	572	NK11+	46.0	781	641	Control	85.5
825	663	Control	46.0	788	644	Control	85.0
Animal	Cage	Group	Lymphocytes-24	Animal	Cage	Group	Lymphocytes-24
592	546	NK11-	9.0	702	601	NK11+	80.0
671	586	NK11+	11.0	568	534	NK33+	79.5
521	511	NK33+	17.0	567	534	NK33+	79.0
664	582	NK11+	21.0	602	551	NK11-	79.0
831	666	Control	22.0	690	595	NK11+	77.5

Smallest five Neutrophils Females				Largest five Neutrophils Females			
Animal	Cage	Group	Neutrophils-03	Animal	Cage	Group	Neutrophils-03
566	533	NK33+	10.0	616	558	NK11-	73.5
792	646	Control	11.0	729	615	NK33-	47.5
845	673	Control	12.0	571	536	NK11-	43.5
802	651	Control	12.5	680	590	NK11+	40.0
724	612	NK33-	13.0	575	538	NK11-	39.5
Animal	Cage	Group	Neutrophils-06	Animal	Cage	Group	Neutrophils-06
513	507	NK33+	16.5	616	558	NK11-	69.5
795	648	Control	17.0	782	641	Control	45.0
651	576	NK11+	19.0	727	614	NK33-	41.0
808	654	Control	19.0	629	565	NK11-	40.5
626	563	NK11-	19.5	709	605	NK11+	40.0

Statistical analysis of differential white blood cell counts for G-TwYST studies A and C

Animal	Cage	Group	Neutrophils-12	Animal	Cage	Group	Neutrophils-12
711	606	NK33-	3.5	585	543	NK11-	63.5
724	612	NK33-	10.5	727	614	NK33-	56.5
712	606	NK33-	11.0	643	572	NK11+	52.0
641	571	NK11+	11.5	606	553	NK11-	50.5
781	641	Control	12.5	730	615	NK33-	50.5
Animal	Cage	Group	Neutrophils-24	Animal	Cage	Group	Neutrophils-24
568	534	NK33+	17.0	592	546	NK11-	88.0
602	551	NK11-	18.0	521	511	NK33+	81.5
567	534	NK33+	18.5	671	586	NK11+	77.0
702	601	NK11+	19.0	664	582	NK11+	75.0
690	595	NK11+	20.0	771	636	NK33-	75.0

Smallest five Monocytes Females				**Largest five Monocytes Females**			
Animal	Cage	Group	Monocytes-03	Animal	Cage	Group	Monocytes-03
574	537	NK11-	0.0	503	502	NK33+	3.5
514	507	NK33+	0.5	540	520	NK33+	3.5
573	537	NK11-	0.5	577	539	NK11-	3.5
616	558	NK11-	0.5	578	539	NK11-	3.5
653	577	NK11+	0.5	642	571	NK11+	3.5
Animal	Cage	Group	Monocytes-06	Animal	Cage	Group	Monocytes-06
508	504	NK33+	0.0	616	558	NK11-	3.5
513	507	NK33+	0.0	755	628	NK33-	3.0
516	508	NK33+	0.0	714	607	NK33-	2.5
519	510	NK33+	0.0	784	642	Control	2.5
528	514	NK33+	0.0	578	539	NK11-	2.0
Animal	Cage	Group	Monocytes-12	Animal	Cage	Group	Monocytes-12
507	504	NK33+	0.0	799	650	Control	7.0
508	504	NK33+	0.0	552	526	NK33+	5.0
509	505	NK33+	0.0	659	580	NK11+	4.5
510	505	NK33+	0.0	815	658	Control	4.5
512	506	NK33+	0.0	755	628	NK33-	4.0
Animal	Cage	Group	Monocytes-24	Animal	Cage	Group	Monocytes-24
553	527	NK33+	0.0	671	586	NK11+	10.5
630	565	NK11-	0.0	831	666	Control	8.5
631	566	NK11-	0.0	540	520	NK33+	8.0
688	594	NK11+	0.0	618	559	NK11-	7.5
698	599	NK11+	0.0	823	662	Control	7.0

Smallest five Eosinophils Females				**Largest five Eosinophils Females**			
Animal	Cage	Group	Eosinophils-03	Animal	Cage	Group	Eosinophils-03
540	520	NK33+	0.0	826	663	Control	8.5
569	535	NK33+	0.0	836	668	Control	6.5
570	535	NK33+	0.0	555	528	NK33+	6.0
573	537	NK11-	0.0	616	558	NK11-	6.0
576	538	NK11-	0.0	517	509	NK33+	5.0
Animal	Cage	Group	Eosinophils-06	Animal	Cage	Group	Eosinophils-06
508	504	NK33+	0.0	577	539	NK11-	6.0
622	561	NK11-	0.0	517	509	NK33+	5.0
769	635	NK33-	0.0	539	520	NK33+	5.0
507	504	NK33+	0.5	762	631	NK33-	5.0
509	505	NK33+	0.5	796	648	Control	5.0

Animal	Cage	Group	Eosinophils-12	Animal	Cage	Group	Eosinophils-12
522	511	NK33+	0.0	580	540	NK11-	10.5
612	556	NK11-	0.0	598	549	NK11-	6.0
629	565	NK11-	0.0	718	609	NK33-	5.0
641	571	NK11+	0.0	552	526	NK33+	4.5
643	572	NK11+	0.0	711	606	NK33-	4.5
Animal	Cage	Group	Eosinophils-24	Animal	Cage	Group	Eosinophils-24
533	517	NK33+	0.0	527	514	NK33+	4.0
534	517	NK33+	0.0	619	560	NK11-	4.0
535	518	NK33+	0.0	734	617	NK33-	4.0
540	520	NK33+	0.0	748	624	NK33-	4.0
541	521	NK33+	0.0	756	628	NK33-	4.0

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. To circumvent taking the logarithm of zero, 0.5 was added to each Monocytes and Eosinophils observation before taking logs. Grubbs’ outlier test at the 1% level was sequentially applied to the residuals to detect outliers. This resulted in the outliers listed below, and these were presented to the G-TwYST coordinator who confirmed the proposed outlier classifications:

1. Males, Lymphocytes-03, cage 133, group NK33- (p-value 0.000). This cage houses the two animals 266 and 265 with the two smallest Lymphocytes values (38.0 and 45.5, Table 3). These two values are considered to be outliers.
2. Males, Lymphocytes-12, cage 77, group NK11+ (p-values 0.000). This cage houses animal 153 with by far the smallest Lymphocyte value (12.0, Table 3). This value is considered to be an outlier.
3. Males, Lymphocytes-24, cage 65, group NK11- (p-values 0.003). This cage houses animal 130 with by far the smallest Lymphocyte value (1.0, Table 3). This value is considered to be an outlier.
4. Females, Lymphocytes-03, cage 615, group NK33- (p-values 0.003); found after removing the value for animal 616. Cage 615 houses animals 729 and 730 with values 51.0 and 62.5, of which 51.0 is the second smallest (Table 4). These values are not considered to be extreme and are therefore not seen as outliers.
5. Females, Lymphocytes-24, cage 586, group NK11+ (p-values 0.005). The cage mean for this cage is based on a single animal 671 with the second smallest value (11.0, Table 4). This value is not considered to be extreme and is therefore not seen as an outlier.
6. Females, Neutrophils-12, cage 606, group NK33- (p-values 0.000). This cage houses animal 711 with by far the smallest value (3.5, Table 4). This value is considered to be an outlier.
7. Females, Monocytes-03, cage 537, group NK11- (p-values 0.004). This cage houses animal 574 and 573 with two of the smallest values (0.0 and 0.5, Table 4). These values are not considered to be extreme and are therefore not seen as outliers.

Plots of residuals versus fitted values, after removal of the outliers listed above, are given in Figure 1 and Figure 3, while normal probability plots are given in Figure 2 and Figure 4. These residual plots are generally satisfactory implying that the ANOVA assumptions, homogeneity of variance and less importantly normality, are generally fulfilled.

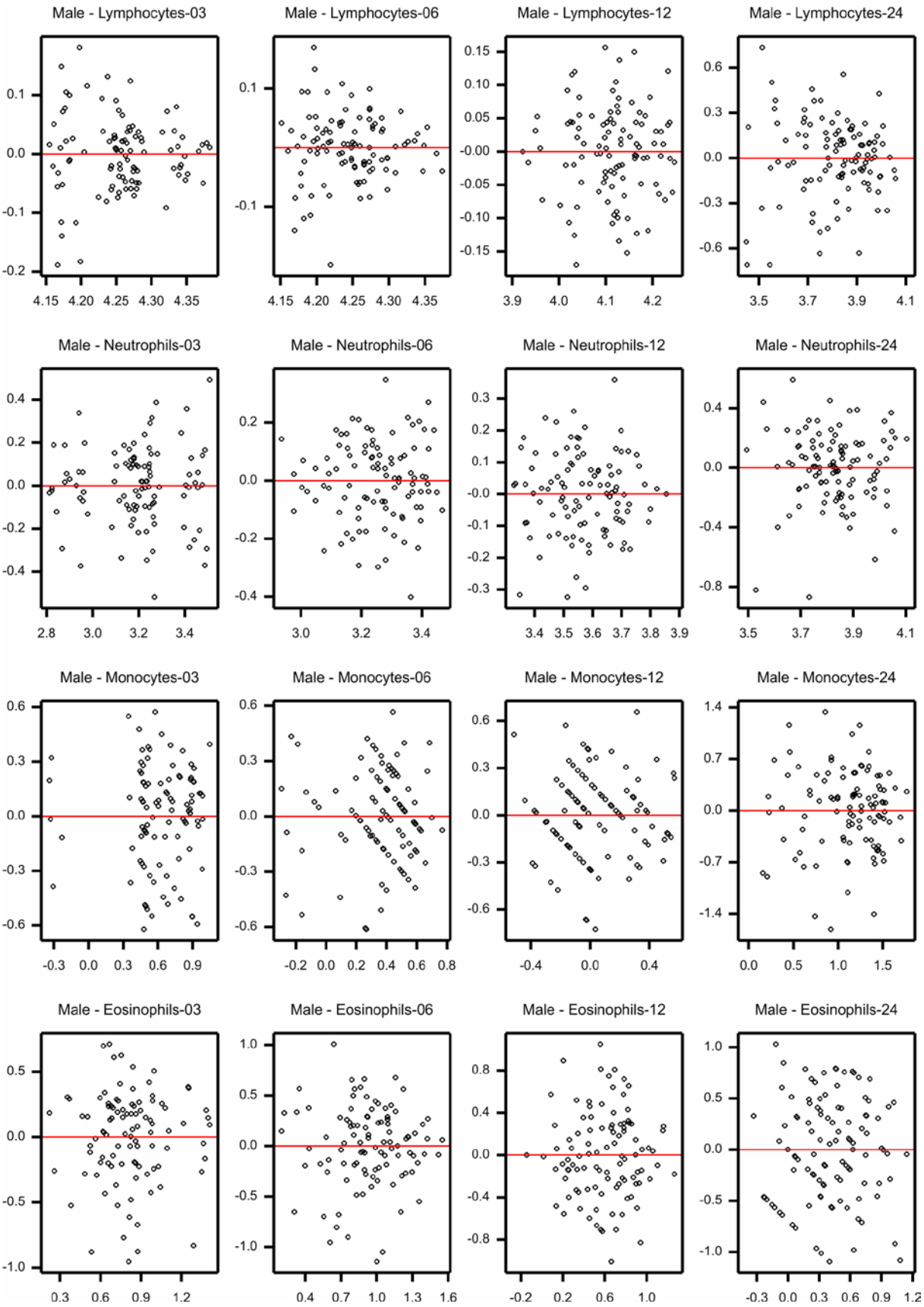

Figure 1 Residuals along the y-axis versus fitted values along the x-axis resulting from an analysis of variance for Study A in Males on log transformed cage means.

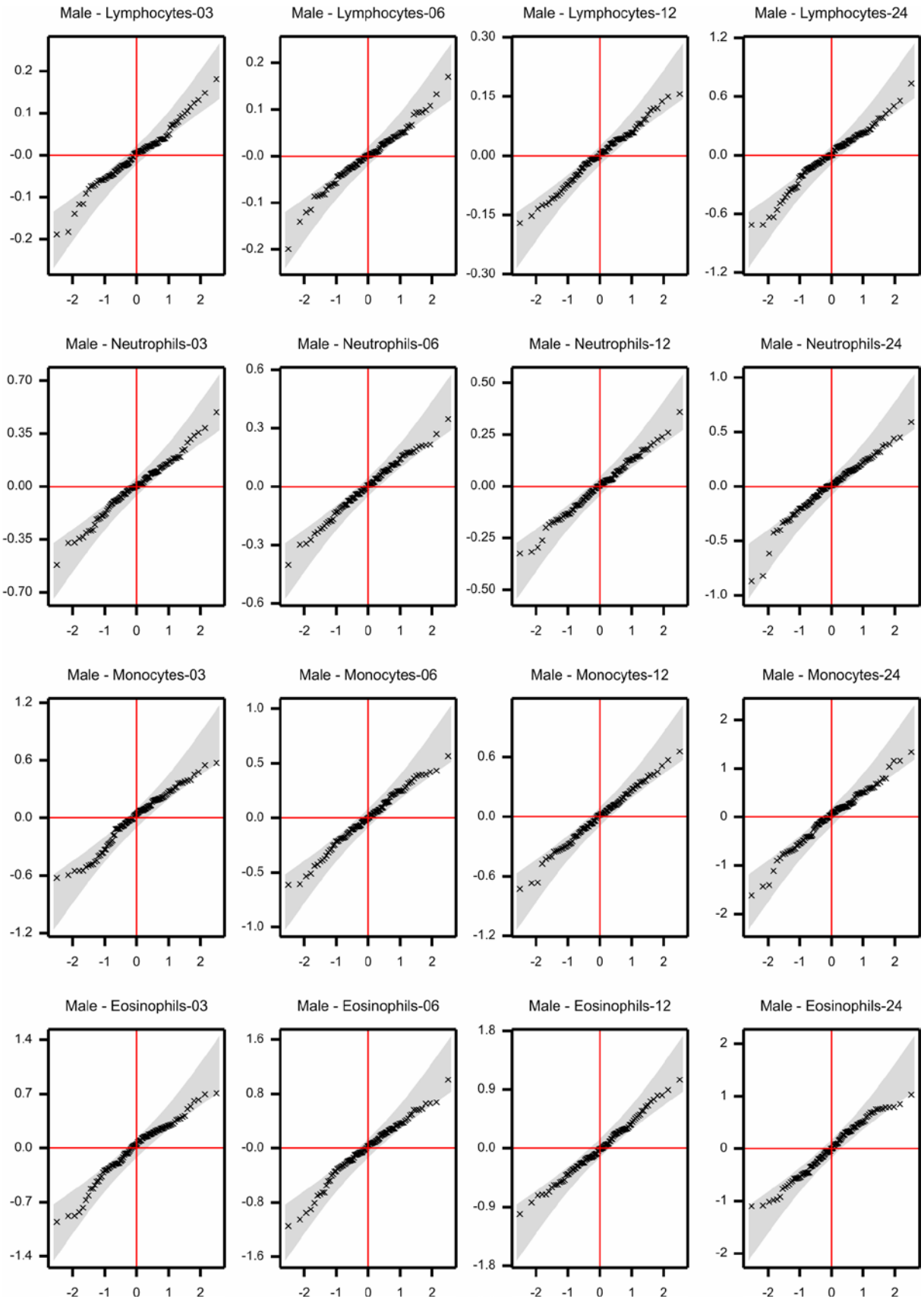

Figure 2 Normal probability plots of residuals resulting from an analysis of variance for Study A in Males on log transformed cage means.

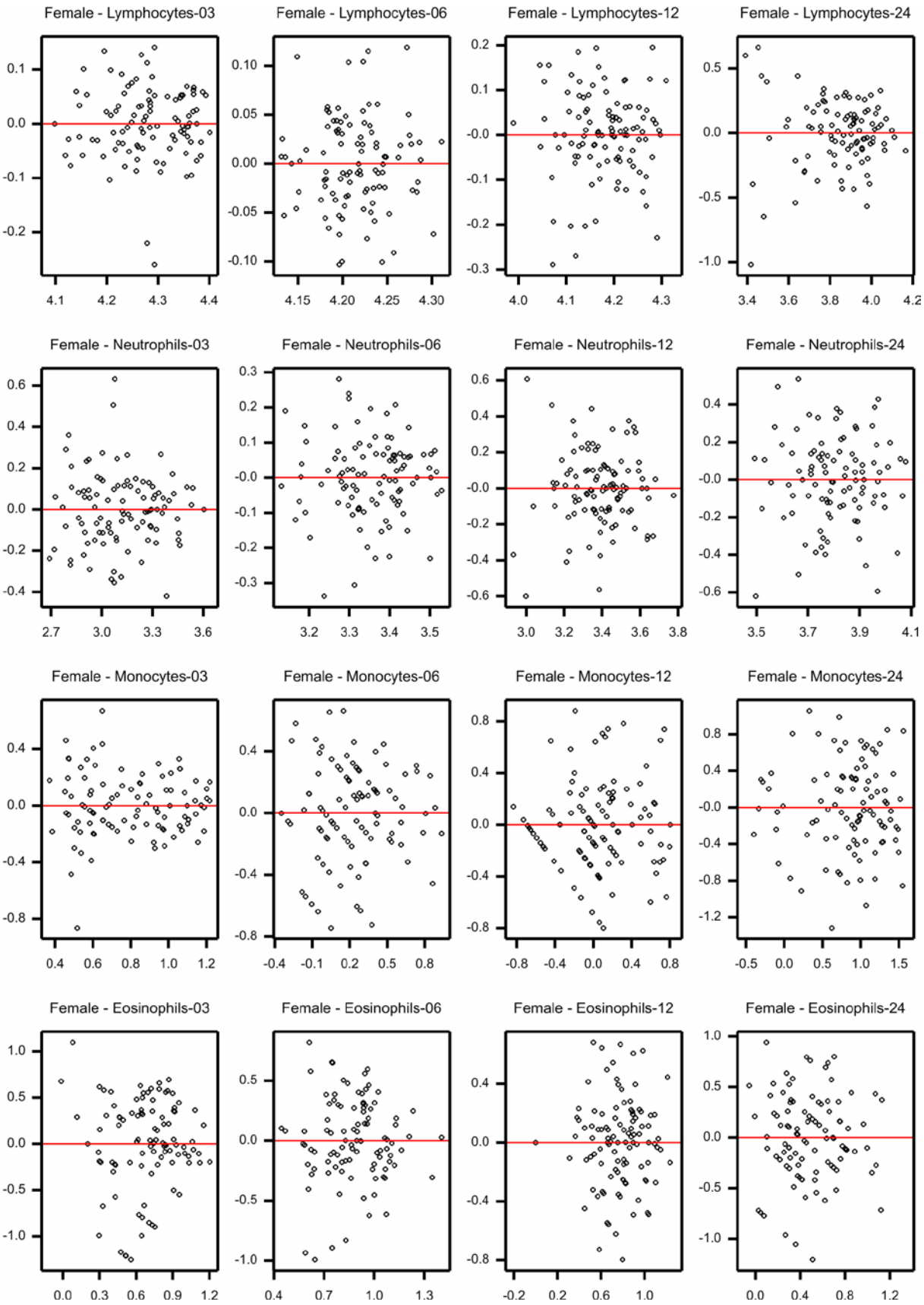

Figure 3 Residuals along the y-axis versus fitted values along the x-axis resulting from an analysis of variance for Study A in Females on log transformed cage means.

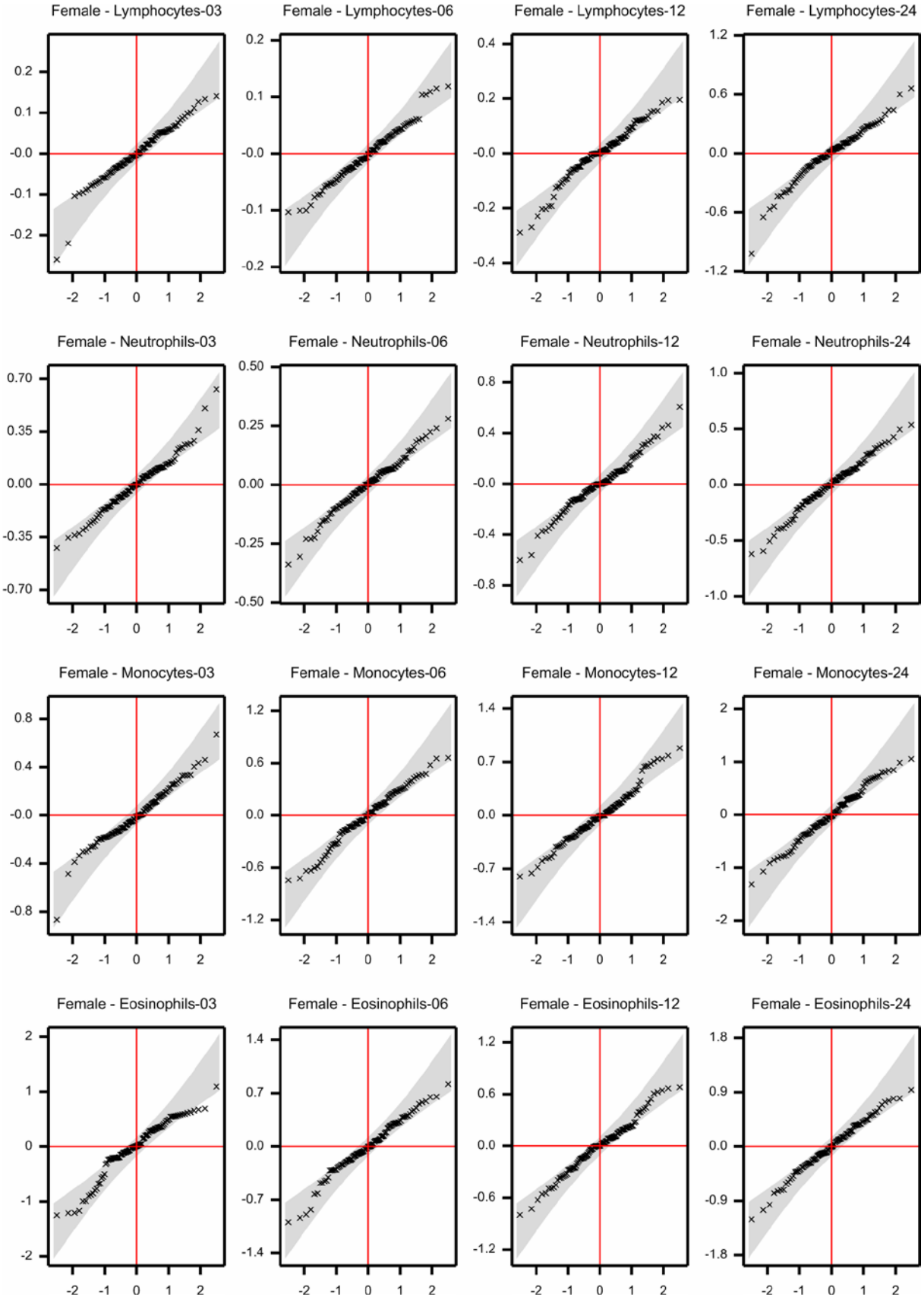

Figure 4 Normal probability plots of residuals resulting from an analysis of variance for Study A in Females on log transformed cage means.

2.3 Outliers and checking of ANOVA assumptions for study C

Data on diffWBC are available for all 256 animals in Study C. Basophils were mainly zero, expect for a count of 1 for two male animals and for one female animal, and Basophils were therefore not statistically analysed. The five smallest and largest values are given in Table 5 and Table 6.

Table 5 The five smallest and five largest observed diffWBC percentages for every response variable observed in study C for Males. No outliers were identified.

Five smallest Males				Five largest Males			
Animal	Cage	Group	Lymphocytes	Animal	Cage	Group	Lymphocytes
21	11	NK50+	20.5	49	25	NK11+/50	99.0
118	59	NK33+	29.5	1	1	NK50-	98.5
102	51	Con33	39.0	76	38	NK11-/50	98.0
109	55	Con33	44.0	3	2	NK50-	97.5
110	55	Con33	44.0	68	34	NK11-/50	97.5
Animal	Cage	Group	Neutrophils	Animal	Cage	Group	Neutrophils
1	1	NK50-	0.0	21	11	NK50+	71.0
2	1	NK50-	0.0	118	59	NK33+	66.0
68	34	NK11-/50	0.0	102	51	Con33	57.0
76	38	NK11-/50	0.0	109	55	Con33	51.0
3	2	NK50-	0.5	110	55	Con33	50.5
Animal	Cage	Group	Monocytes	Animal	Cage	Group	Monocytes
1	1	NK50-	0.0	86	43	NK33-	8.5
2	1	NK50-	0.0	79	40	NK11-/50	6.5
3	2	NK50-	0.0	90	45	NK33-	6.5
4	2	NK50-	0.0	84	42	NK33-	6.0
49	25	NK11+/50	0.0	94	47	NK33-	5.5
Animal	Cage	Group	Eosinophils	Animal	Cage	Group	Eosinophils
6	3	NK50-	0.0	97	49	Con33	11.0
7	4	NK50-	0.0	21	11	NK50+	6.5
8	4	NK50-	0.0	88	44	NK33-	4.5
19	10	NK50+	0.0	2	1	NK50-	4.0
29	15	NK50+	0.0	22	11	NK50+	4.0

Table 6 The five smallest and five largest observed diffWBC percentages for every response variable observed in study C for Females. No outliers were identified.

Five smallest Females				Five largest Females			
Animal	Cage	Group	Lymphocytes	Animal	Cage	Group	Lymphocytes
246	90	Con50	40.0	267	101	NK11-/50	98.5
256	95	NK11+/50	46.0	317	126	NK33+	98.0
245	90	Con50	52.0	221	78	NK50+	97.5
322	128	NK33+	52.0	300	117	Con33	97.0
201	68	NK50-	55.5	299	117	Con33	96.5
Animal	Cage	Group	Neutrophils	Animal	Cage	Group	Neutrophils
221	78	NK50+	0.0	246	90	Con50	56.5
267	101	NK11-/50	0.0	256	95	NK11+/50	53.0
317	126	NK33+	1.0	245	90	Con50	44.0
300	117	Con33	2.0	322	128	NK33+	44.0
308	121	Con33	2.5	277	106	NK11-/50	43.0

Animal	Cage	Group	Monocytes	Animal	Cage	Group	Monocytes
202	68	NK50-	0.0	287	111	NK33-	5.0
214	74	NK50-	0.0	216	75	NK50-	3.5
236	85	Con50	0.0	223	79	NK50+	3.5
241	88	Con50	0.0	246	90	Con50	3.5
243	89	Con50	0.0	273	104	NK11-/50	3.5
Animal	Cage	Group	Eosinophils	Animal	Cage	Group	Eosinophils
212	73	NK50-	0.0	229	82	NK50+	4.5
215	75	NK50-	0.0	201	68	NK50-	4.0
236	85	Con50	0.0	292	113	NK33-	4.0
237	86	Con50	0.0	295	115	NK33-	4.0
246	90	Con50	0.0	235	85	Con50	3.5

The four diffWBC variables were log transformed after which cage means were calculated. Note that Neutrophils, Monocytes and Eosinophils contain zero counts, and therefore for these variables 0.5 was added to each value before taking the logarithm. The log-transformed data were statistically analysed by means of an analysis of variance using the model “Block + Group”, which is according to the randomized block design. Grubbs’ outlier test at the 1% level was applied to the residuals to detect outliers. This resulted in a single outlier for Lymphocytes observed in females (p-value for Grubbs’ test equals 0.009 which is just significant at the 1% level). The outlier was observed for Cage 90 for feeding group Con50 with animals 245 and 246 which had two of the lowest values (40.0 and 52.0, Table 6). These values are not considered to be extreme and are therefore, after consultation of the G-TwYST coordinator, not seen as outliers.

Plots of residuals versus fitted values and normal probability plots are given in Figure 5. These residual plots are generally satisfactory implying that the ANOVA assumptions, homogeneity of variance and less importantly normality, are generally fulfilled. Note that for Neutrophils there is some indication that smaller values are more variable than larger values.

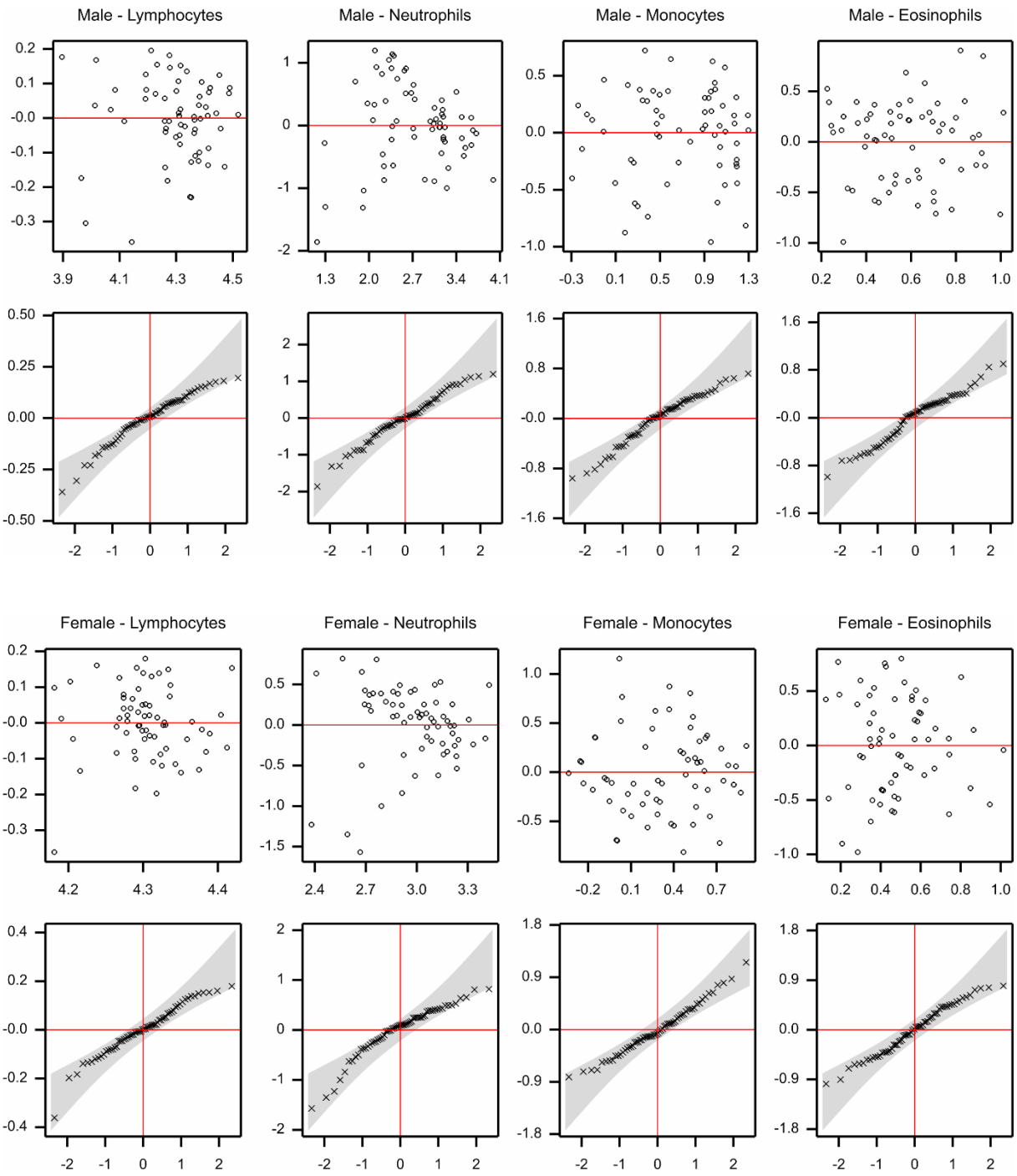

Figure 5 **Residuals along the y-axis versus fitted values along the x-axis resulting from an analysis of variance for Study C on log transformed cage means and normal probability plots for males (top) and females (bottom).**

2.4 Summary tables and figures

Cage means on the original and on the log scale for Study A are given in Appendix 1 and Appendix 2, while Appendix 3 and Appendix 4 present these for Study C. 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 Study A and Table 8 for Study C. These tables were obtained by first calculating cage means and then calculating the summary statistics. Plots of feeding group means of Lymphocytes and Neutrophils versus month for Study A are given in Figure 6.

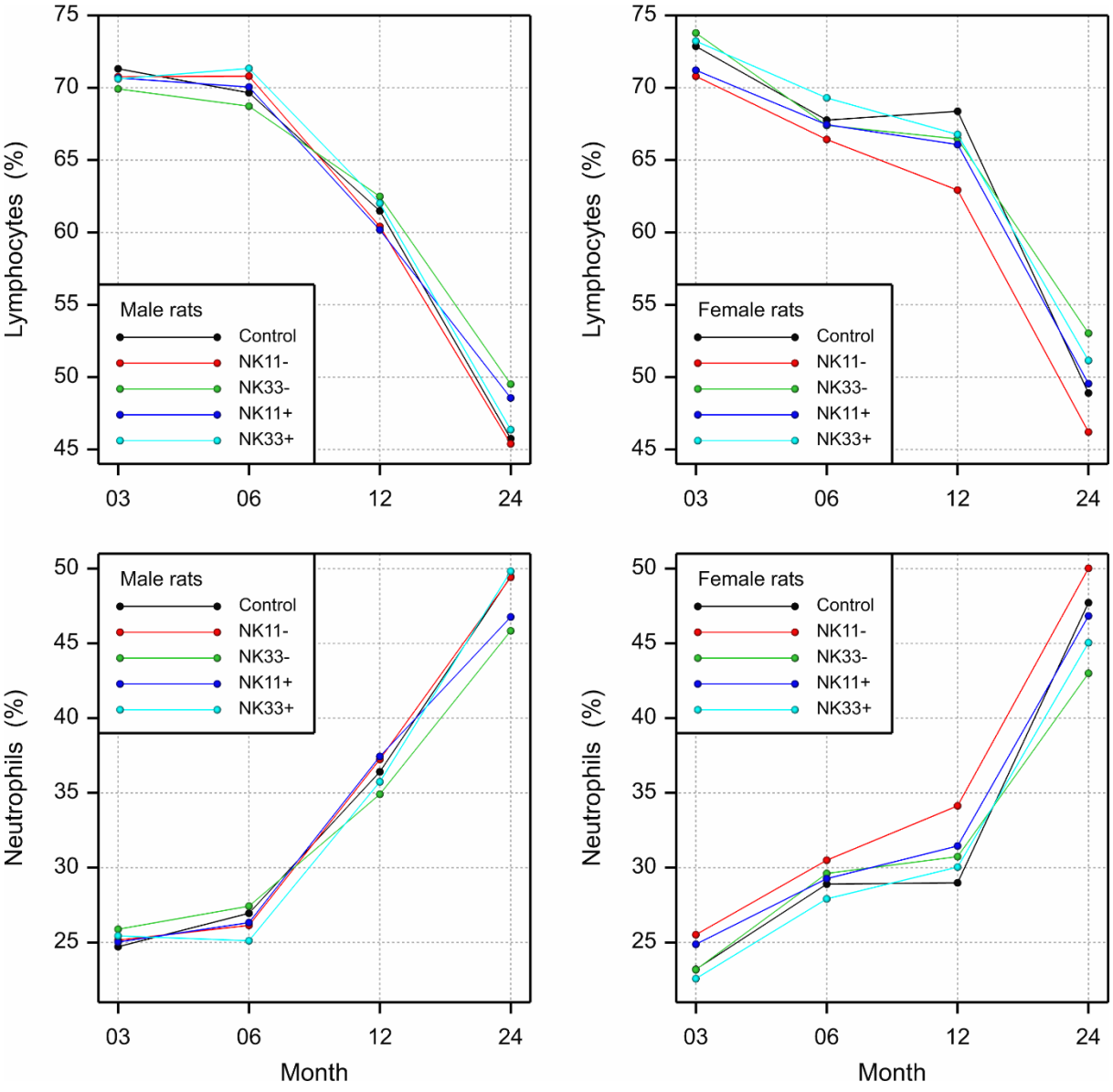

Figure 6 Mean values of Lymphocytes and Neutrophils versus month for each feeding group in Study A for males (left) and females (right).

Table 7 Summary statistics for male and female rats for Study A 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.

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-03	20	71.3	4.1	5.8	20	70.8	5.7	8.0	19	71.4	5.2	7.3	20	70.7	5.9	8.3	20	70.6	8.5	12.0
Lymphocytes-06	20	69.7	5.2	7.5	20	70.8	4.6	6.4	20	68.7	5.3	7.7	20	70.0	6.5	9.3	20	71.3	4.3	6.1
Lymphocytes-12	20	61.5	6.0	9.8	20	60.5	5.3	8.8	20	62.4	6.0	9.6	21	60.2	9.6	15.9	20	62.0	5.5	8.9
Lymphocytes-24	21	47.1	14.7	31.2	23	45.1	12.0	26.7	21	49.6	7.8	15.6	23	48.8	12.5	25.5	19	46.2	15.0	32.5
Neutrophils-03	20	24.7	4.2	16.9	20	25.1	5.7	22.6	20	25.9	8.5	32.7	20	25.0	6.0	23.8	20	25.4	8.4	33.0
Neutrophils -06	20	27.0	4.9	18.0	20	26.1	4.0	15.4	20	27.4	5.3	19.3	20	26.3	5.8	22.0	20	25.1	4.0	15.9
Neutrophils -12	20	36.4	5.8	15.8	20	37.1	5.5	14.9	20	35.0	6.0	17.2	21	37.3	9.0	24.2	20	35.7	5.6	15.6
Neutrophils -24	21	48.2	13.6	28.2	23	49.7	11.5	23.0	21	45.6	8.2	18.1	23	46.6	12.6	27.0	19	50.0	14.4	28.8
Monocytes -03	20	1.9	0.5	24.1	20	2.2	0.8	36.0	20	2.0	0.7	36.2	20	2.1	0.8	41.0	20	2.0	0.6	31.7
Monocytes -06	20	1.2	0.5	40.9	20	0.9	0.4	43.7	20	1.1	0.5	46.9	20	1.0	0.5	50.3	20	1.0	0.4	35.3
Monocytes -12	20	0.5	0.3	63.3	20	0.6	0.4	61.1	20	0.7	0.4	62.3	21	0.7	0.4	61.3	20	0.7	0.5	73.6
Monocytes -24	21	3.5	2.8	80.8	23	3.7	2.1	57.4	21	3.2	1.7	53.6	23	3.2	1.6	51.5	19	2.8	2.3	79.9
Eosinophils -03	20	2.1	1.0	47.6	20	1.8	1.1	62.4	20	2.2	0.9	42.9	20	2.2	1.0	44.3	20	2.0	1.0	53.1
Eosinophils -06	20	2.2	1.2	54.5	20	2.2	1.3	60.4	20	2.8	1.2	45.3	20	2.6	1.7	62.6	20	2.5	0.8	33.5
Eosinophils -12	20	1.6	1.1	68.0	20	1.8	1.1	61.1	20	1.9	0.7	39.5	21	1.8	1.4	75.6	20	1.6	0.8	50.5
Eosinophils -24	21	1.2	0.9	78.0	23	1.4	1.0	71.1	21	1.6	0.8	50.8	23	1.4	1.2	83.1	19	1.0	1.0	100.1

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-03	20	72.9	7.5	10.3	20	71.9	7.2	10.0	20	73.8	6.7	9.1	20	71.2	6.5	9.2	20	73.2	7.0	9.6
Lymphocytes-06	20	67.7	4.3	6.3	20	67.5	4.3	6.4	20	67.4	3.9	5.8	20	67.5	3.5	5.2	20	69.3	4.5	6.5
Lymphocytes-12	20	68.4	7.4	10.8	21	62.8	6.4	10.3	22	66.5	9.0	13.6	21	66.2	6.7	10.1	20	66.7	6.6	9.9
Lymphocytes-24	17	49.6	14.3	28.8	17	46.7	11.6	24.9	20	52.9	8.1	15.2	22	47.3	13.5	28.6	22	50.0	13.2	26.4
Neutrophils-03	20	23.2	6.4	27.7	20	24.4	7.1	28.9	20	23.2	6.6	28.7	20	24.9	6.0	24.1	20	22.6	6.4	28.5
Neutrophils -06	20	29.0	4.3	14.7	20	29.5	4.1	13.8	20	29.6	4.1	14.0	20	29.3	3.8	12.9	20	27.9	4.3	15.5
Neutrophils -12	20	29.0	7.3	25.3	21	34.3	6.5	18.8	22	30.7	9.1	29.6	21	31.3	6.9	22.2	20	30.1	6.1	20.1
Neutrophils -24	17	46.8	13.9	29.6	17	49.8	10.9	22.0	20	42.9	8.5	19.9	22	48.8	11.7	24.1	22	46.2	13.4	29.0

Monocytes -03	20	1.9	0.7	37.6	20	1.7	0.7	41.5	20	1.7	0.6	34.2	20	2.0	0.9	42.7	20	2.0	0.7	36.2
Monocytes -06	20	1.1	0.6	53.7	20	0.9	0.6	75.4	20	1.0	0.6	60.7	20	0.9	0.4	38.6	20	0.7	0.4	59.1
Monocytes -12	20	0.7	0.9	128.0	21	0.8	0.6	72.9	22	0.9	0.7	73.1	21	0.8	0.9	104.5	20	1.0	0.9	91.6
Monocytes -24	17	2.3	2.2	94.4	17	2.2	1.4	66.0	20	2.4	1.4	59.8	22	2.7	2.5	90.0	22	2.4	1.6	66.1
Eosinophils -03	20	2.1	1.2	59.0	20	2.0	1.2	61.8	20	1.3	0.8	60.5	20	1.9	0.8	42.1	20	2.2	1.1	50.5
Eosinophils -06	20	2.2	0.8	33.9	20	2.2	0.9	38.7	20	2.0	1.0	49.6	20	2.3	0.8	33.0	20	2.1	1.2	58.0
Eosinophils -12	20	1.9	0.7	36.0	21	2.2	1.2	57.2	22	1.9	1.0	53.6	21	1.6	0.6	34.9	20	2.2	0.7	33.6
Eosinophils -24	17	1.2	0.7	53.8	17	1.4	0.9	68.0	20	1.8	1.1	61.3	22	1.2	0.7	60.6	22	1.4	0.8	60.1

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

diffWBC	**Con50**			**NK11-/50**			**NK50-**			**NK11+/50**			**NK50+**			**Con33**			**NK33-**			**NK33+**		
Male (N=8)	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV
Lymphocytes	78.1	8.9	11.3	79.4	10.7	13.5	82.7	12.6	15.2	74.4	10.7	14.4	73.8	12.4	16.8	67.0	11.4	17.0	74.1	10.7	14.4	71.9	12.9	18.0
Neutrophils	18.8	8.8	47.0	17.1	9.6	56.1	14.2	12.3	86.0	22.0	9.5	43.4	22.4	11.1	49.4	29.2	10.4	35.5	21.3	9.5	44.6	24.4	12.5	51.3
Monocytes	1.97	0.59	29.9	2.03	1.80	88.6	1.62	1.10	67.8	2.09	1.48	70.5	2.00	1.19	59.4	1.62	1.22	74.9	2.78	1.63	58.5	1.78	0.83	46.5
Eosinophils	1.16	0.42	36.4	1.47	0.75	51.0	1.47	0.83	56.4	1.50	0.50	33.3	1.84	1.47	79.7	2.19	2.06	94.4	1.84	0.74	40.3	1.87	0.69	37.0

diffWBC	**Con50**			**NK11-/50**			**NK50-**			**NK11+/50**			**NK50+**			**Con33**			**NK33-**			**NK33+**		
Female (N=8)	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV	Mean	Sd	CV
Lymphocytes	72.7	11.4	15.7	74.0	7.4	10.0	76.4	7.0	9.2	72.4	1.8	2.4	74.8	9.7	12.9	80.5	8.3	10.3	73.8	6.8	9.2	73.2	7.5	10.2
Neutrophils	24.8	10.7	43.3	23.0	7.1	31.0	21.0	7.1	33.6	25.3	2.5	10.1	21.9	9.4	43.2	17.4	7.6	43.5	23.1	7.7	33.2	24.4	7.4	30.3
Monocytes	1.16	1.00	86.4	1.41	1.07	76.0	1.31	0.74	56.5	1.09	0.93	84.6	1.34	0.79	58.8	0.88	0.76	86.4	1.53	0.90	58.8	0.97	0.78	80.9
Eosinophils	1.38	0.78	56.7	1.53	0.69	44.9	1.25	0.61	49.0	1.19	0.88	74.4	1.94	0.85	44.0	1.16	0.65	56.5	1.50	1.07	71.3	1.44	0.94	65.6

3 Statistical analysis

3.1 Equivalence testing for study A using historical data

Figure 7 displays, for the diffWBC endpoints, the ratio of the residual variance in the current G-TwYST study A as a percentage of the residual variance in the historical GRACE study. This indicates that the 12 and 24 month data are in general more variable than those observed after 3 and 6 months. It also shows that even after 3 and 6 months the Lymphocytes data in G-TwYST Study A is (much) more variable than in GRACE resulting in a less useful equivalence analysis.

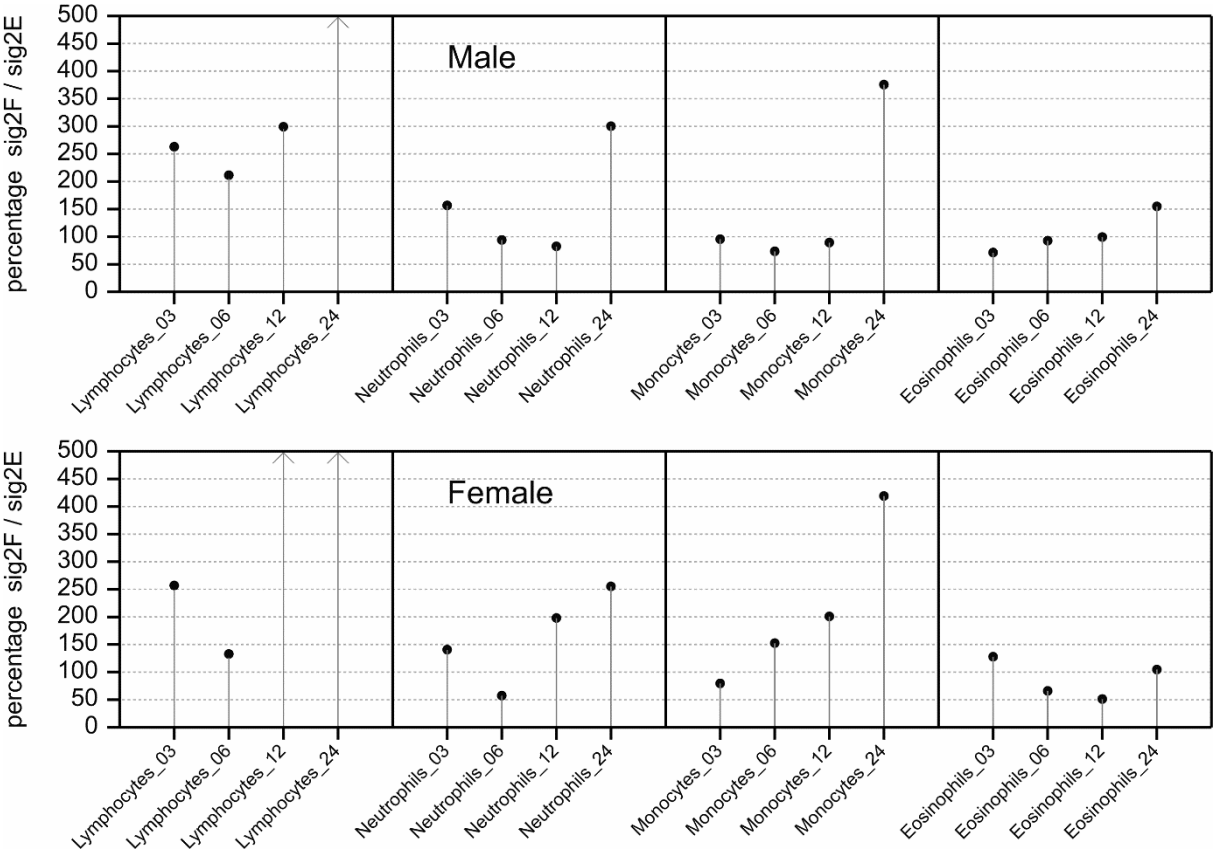

Figure 7 Residual variance (sig2F or σ_F^2) in the current G-TwYST A study as a percentage of the residual variance (sig2E or σ_E^2) in the historical GRACE studies for males (top panel) and females (bottom panel) that survived for 24 months.

Preliminary regulatory values $\alpha = 0.05$, $\beta = 0.20$ and $n_0 = 20$ were employed, where n_0 is similar to the number of cages for the diffWBC endpoints (Table 7). The DWE intervals showing the main results of the equivalence tests are given in Figure 8 and Figure 9. 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 Figure 10 and Figure 11, and also in Table 9. For most cases where the residual variance in G-TwYST is 150% or larger than in the reference data there was a failure to prove equivalence, but equivalence was still more likely than not in all cases but one (Females, Control vs. NK11-, N-12). In all cases where the residual variance was less than 150% compared to the reference data equivalence could be established, except for Eosinophils-03 for Females Control vs NK33-.

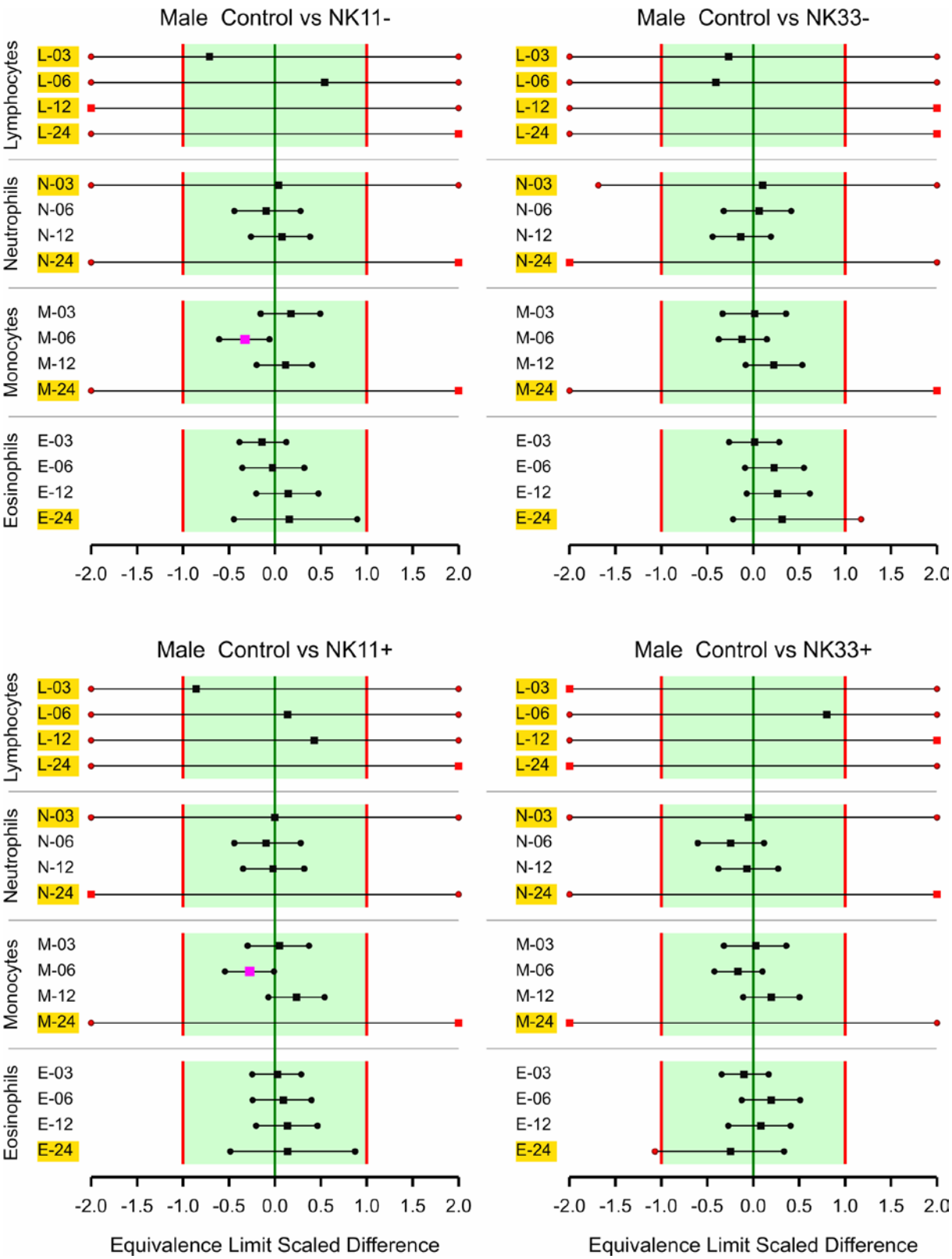

Figure 8 **Equivalence testing of GM feeding groups versus the control feed for males in study A. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed (see also Table 9). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (variance ratio VR>150%). Fuchsia coloured symbols denote a significant difference.**

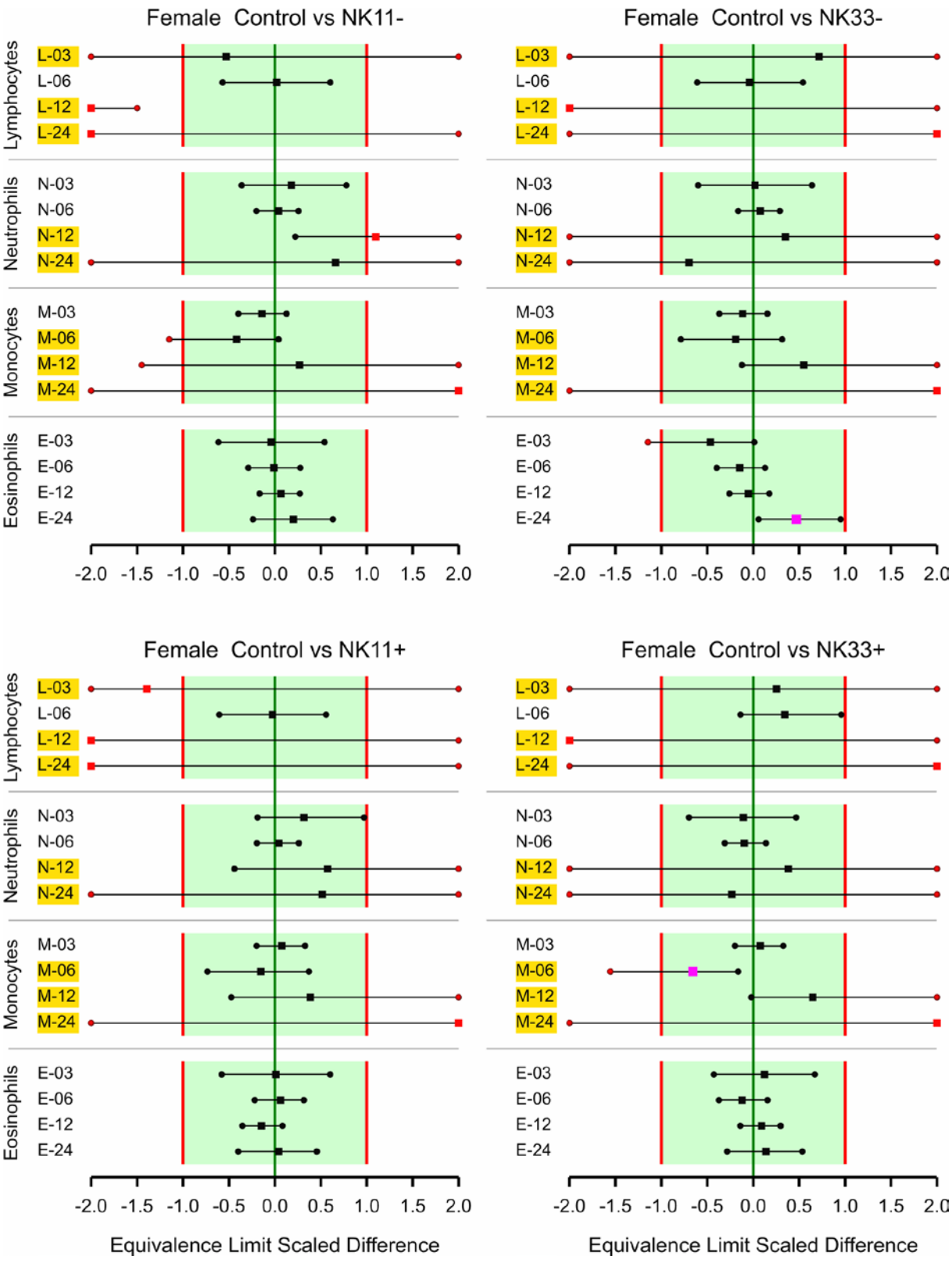

Figure 9 **Equivalence testing of GM feeding groups versus the control feed for females in study A. For estimates (square symbols) on the left of zero the GM feed has a smaller mean than the control feed (see also Table 9). Endpoints labelled with a golden background have a large residual variance compared to the historical studies (variance ratio VR>150%). Fuchsia coloured symbols denote a significant difference.**

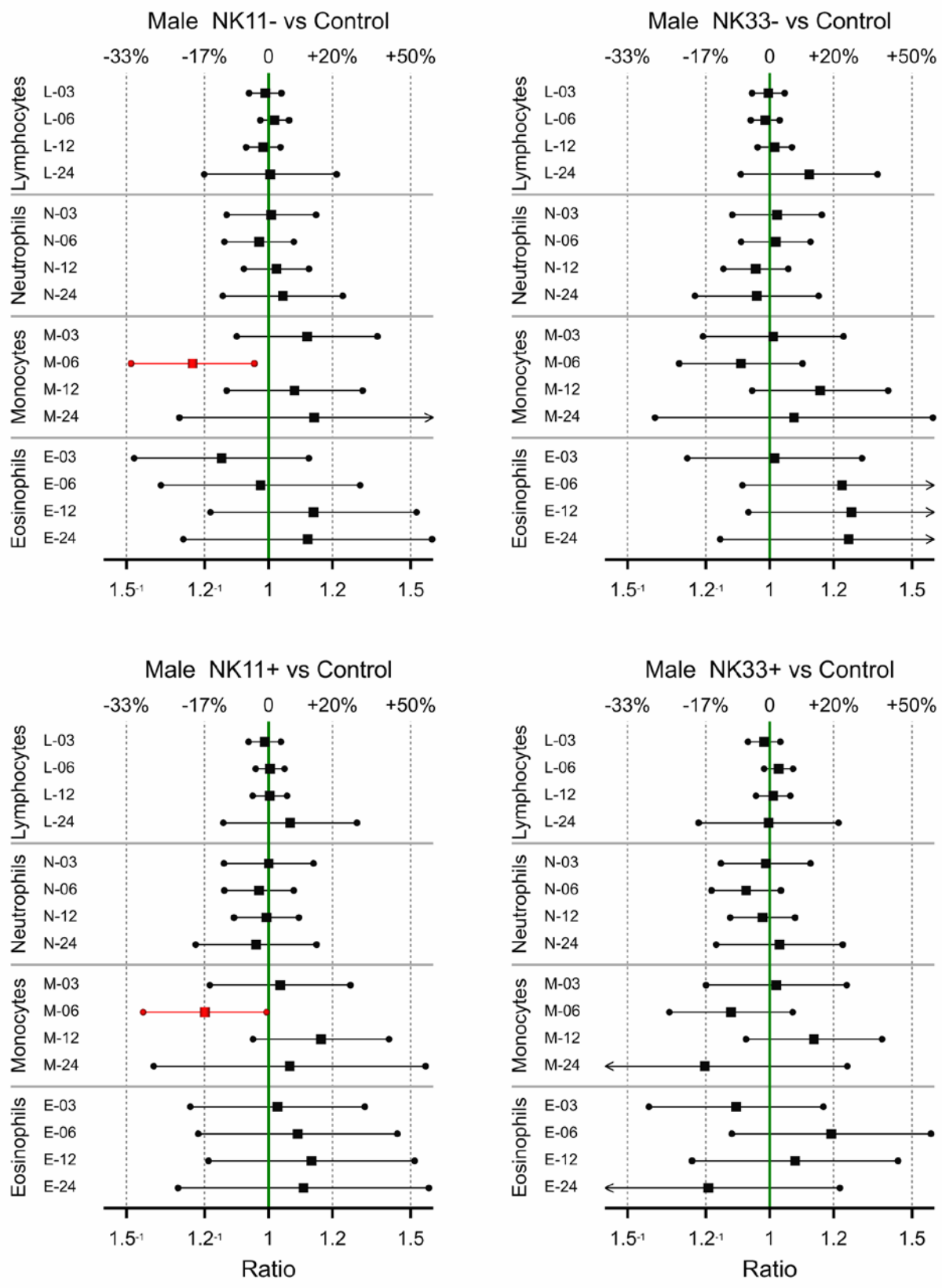

Figure 10 95% confidence intervals for the four comparisons for males in Study A. Intervals that do not encompass the ratio=1 line are given in red, these represent significant differences at the 5% level.

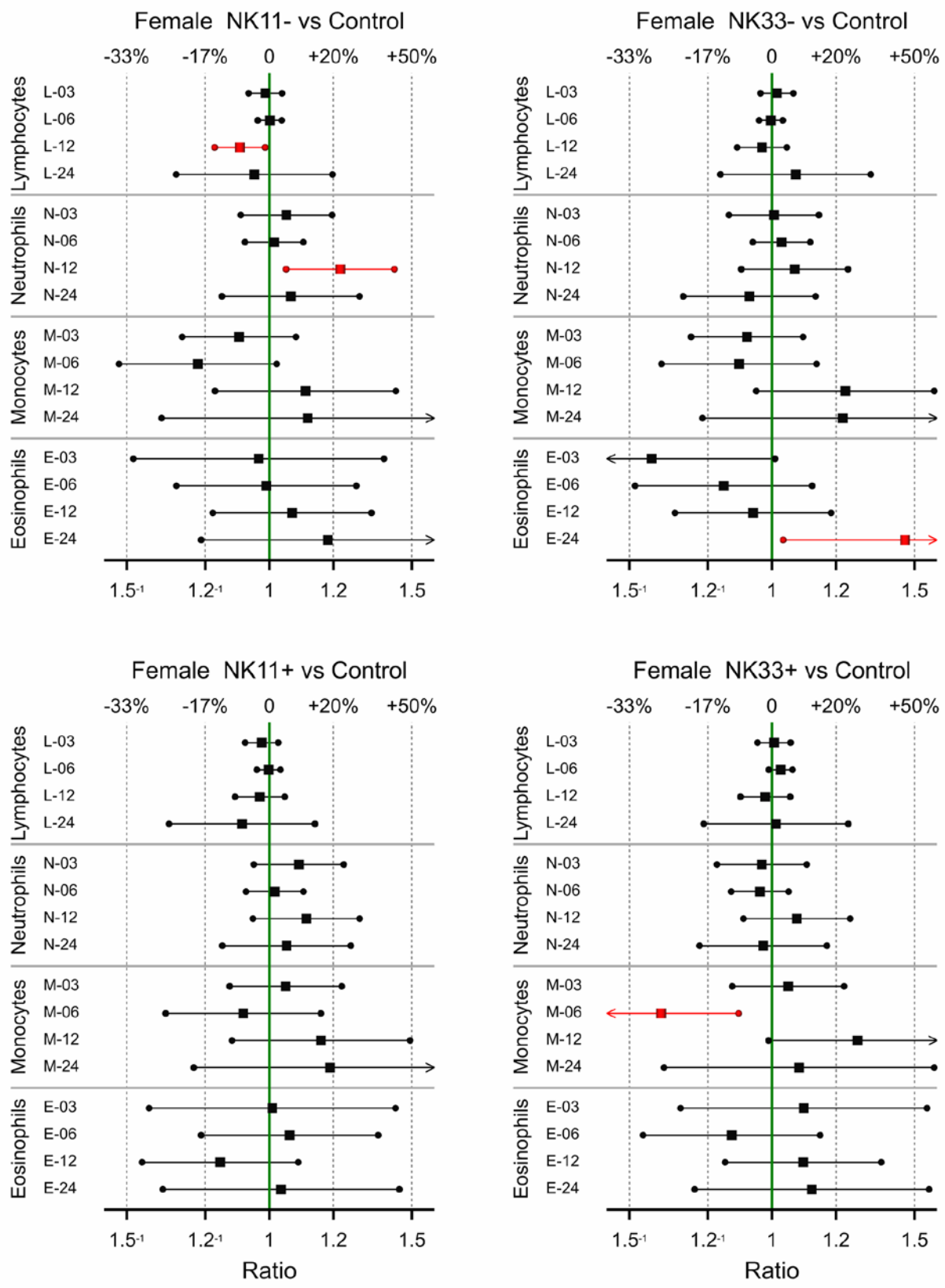

Figure 11 95% confidence intervals for the four comparisons for females in Study A. Intervals that do not encompass the ratio=1 line are given in red, these represent significant differences at the 5% level.

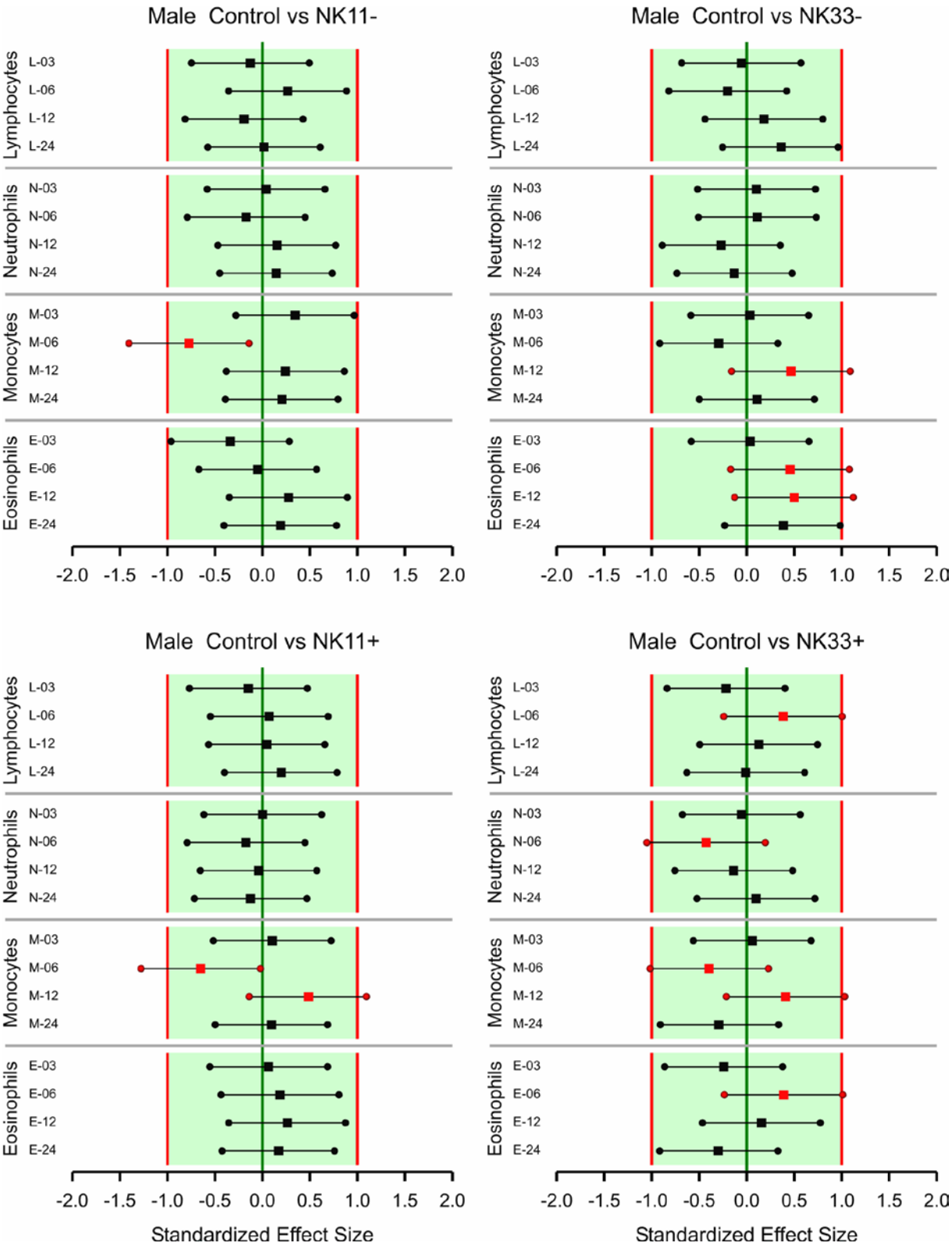

Figure 12 Confidence intervals for Standardized Effect Sized (SES) for male rats in Study A. Intervals that extend beyond the interval (-1,1) are given in red.

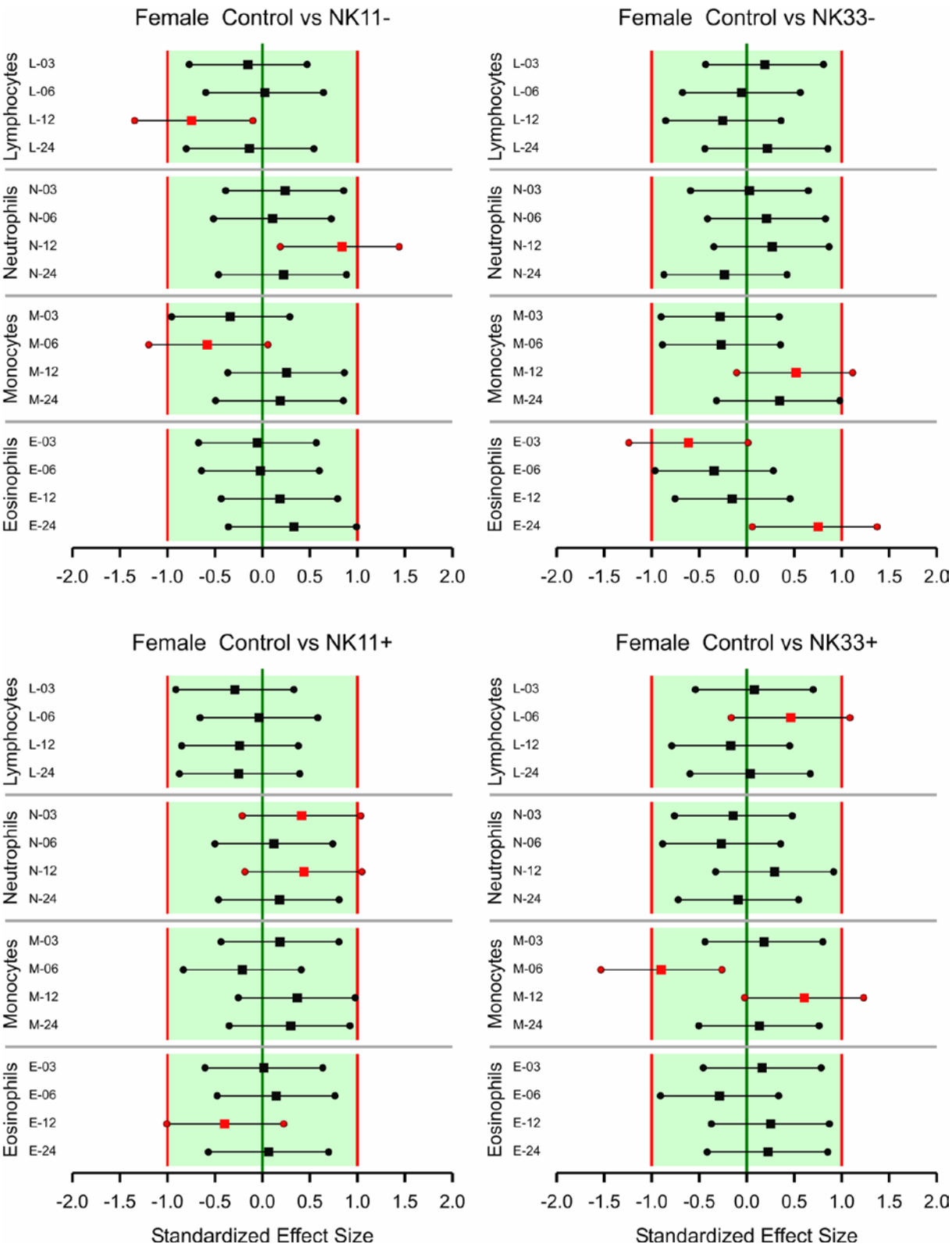

Figure 13 Confidence intervals for Standardized Effect Sized (SES) for female rats in Study A. Intervals that extend beyond the interval (-1,1) are given in red.

Table 9 95% Confidence interval plus estimate for the ratio Δ of the GMO feeds versus the Control feed for Study A. Intervals are based on an ANOVA with 5 feeding groups. Ratios with corresponding 95% confidence 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%.

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-03	0.946	0.991	1.037	0.950	0.996	1.043	0.945	0.989	1.036	0.940	0.984	1.030
Lymphocytes-06	0.977	1.018	1.060	0.947	0.987	1.028	0.964	1.005	1.047	0.984	1.025	1.068
Lymphocytes-12	0.938	0.985	1.034	0.966	1.014	1.065	0.956	1.004	1.054	0.962	1.010	1.061
Lymphocytes-24	0.832	1.005	1.214	0.921	1.119	1.360	0.879	1.064	1.287	0.816	0.997	1.217
Neutrophils-03	0.887	1.008	1.145	0.899	1.021	1.160	0.881	1.000	1.137	0.870	0.989	1.123
Neutrophils -06	0.882	0.973	1.075	0.922	1.018	1.124	0.881	0.973	1.074	0.847	0.935	1.032
Neutrophils -12	0.932	1.023	1.122	0.876	0.961	1.054	0.906	0.994	1.091	0.893	0.980	1.075
Neutrophils -24	0.878	1.041	1.235	0.808	0.964	1.150	0.812	0.965	1.147	0.858	1.028	1.231
Monocytes -03	0.913	1.116	1.364	0.827	1.010	1.234	0.846	1.034	1.263	0.834	1.019	1.245
Monocytes -06	0.676	0.805	0.960	0.773	0.921	1.098	0.699	0.834	0.994	0.751	0.895	1.067
Monocytes -12	0.887	1.077	1.308	0.951	1.154	1.401	0.956	1.161	1.410	0.934	1.134	1.377
Monocytes -24	0.776	1.139	1.672	0.721	1.072	1.593	0.721	1.062	1.565	0.554	0.831	1.247
Eosinophils -03	0.682	0.875	1.122	0.791	1.014	1.301	0.800	1.026	1.316	0.708	0.909	1.165
Eosinophils -06	0.736	0.978	1.299	0.925	1.229	1.633	0.818	1.087	1.444	0.897	1.192	1.583
Eosinophils -12	0.847	1.137	1.525	0.941	1.263	1.694	0.843	1.131	1.517	0.801	1.075	1.442
Eosinophils -24	0.784	1.118	1.594	0.868	1.252	1.806	0.772	1.105	1.580	0.577	0.839	1.221

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-03	0.943	0.989	1.037	0.968	1.014	1.063	0.934	0.979	1.026	0.960	1.006	1.054
Lymphocytes-06	0.968	1.001	1.036	0.964	0.997	1.031	0.965	0.998	1.032	0.991	1.025	1.060
Lymphocytes-12	0.856	0.920	0.988	0.906	0.972	1.043	0.907	0.973	1.045	0.914	0.981	1.053
Lymphocytes-24	0.767	0.958	1.197	0.864	1.070	1.325	0.752	0.925	1.139	0.824	1.012	1.242
Neutrophils-03	0.922	1.050	1.195	0.885	1.006	1.143	0.957	1.087	1.236	0.855	0.972	1.104
Neutrophils -06	0.933	1.014	1.102	0.947	1.027	1.115	0.936	1.016	1.102	0.890	0.966	1.048
Neutrophils -12	1.049	1.224	1.428	0.917	1.067	1.242	0.955	1.111	1.293	0.922	1.073	1.249
Neutrophils -24	0.874	1.063	1.293	0.777	0.938	1.132	0.875	1.050	1.261	0.814	0.976	1.169
Monocytes -03	0.781	0.918	1.079	0.795	0.932	1.092	0.894	1.048	1.229	0.893	1.047	1.228

Monocytes -06	0.652	0.816	1.021	0.730	0.911	1.135	0.745	0.929	1.158	0.585	0.730	0.910
Monocytes -12	0.857	1.108	1.433	0.956	1.232	1.587	0.899	1.159	1.492	0.990	1.276	1.643
Monocytes -24	0.736	1.115	1.689	0.821	1.223	1.824	0.807	1.189	1.752	0.736	1.080	1.586
Eosinophils -03	0.679	0.970	1.385	0.500	0.710	1.009	0.710	1.009	1.432	0.771	1.095	1.555
Eosinophils -06	0.768	0.992	1.281	0.678	0.872	1.121	0.824	1.060	1.363	0.693	0.892	1.147
Eosinophils -12	0.851	1.067	1.337	0.759	0.947	1.183	0.696	0.869	1.086	0.875	1.093	1.364
Eosinophils -24	0.824	1.181	1.694	1.032	1.460	2.065	0.739	1.034	1.447	0.803	1.120	1.563

Table 10 Means and coefficient of variation (CV) for study A. 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.

diffWBC	**Control**		**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Males	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
Lymphocytes-03	71.31	5.8	70.76	8.0		71.40	7.3		70.68	8.3		70.61	12.0	
Lymphocytes-06	69.65	7.5	70.80	6.4		68.72	7.7		70.05	9.3		71.34	6.1	
Lymphocytes-12	61.49	9.8	60.50	8.8		62.35	9.6		61.33	12.6		62.03	8.9	
Lymphocytes-24	47.07	31.2	45.97	23.5		49.61	15.6		48.79	25.5		46.18	32.5	
Neutrophils-03	24.71	16.9	25.15	22.6		25.88	32.7		25.02	23.8		25.44	33.0	
Neutrophils -06	26.95	18.0	26.14	15.4		27.43	19.3		26.33	22.0		25.11	15.9	
Neutrophils -12	36.41	15.8	37.12	14.9		35.05	17.2		37.26	24.2		35.70	15.6	
Neutrophils -24	48.24	28.2	49.72	23.0		45.58	18.1		46.63	27.0		50.00	28.8	
Monocytes -03	1.887	24.1	2.200	36.0		2.012	36.2		2.075	40.8		1.988	31.7	
Monocytes -06	1.200	40.9	0.899	43.7	tw	1.100	46.9		0.987	50.3	tw	1.025	35.3	
Monocytes -12	0.526	63.3	0.600	61.1		0.688	62.3		0.702	61.3		0.687	73.6	
Monocytes -24	3.488	80.8	3.717	57.4		3.167	53.6		3.163	51.5		2.842	79.9	
Eosinophils -03	2.087	47.6	1.887	56.4		2.187	42.9		2.225	44.3		1.962	53.1	
Eosinophils -06	2.200	54.5	2.161	60.4		2.750	45.3		2.638	62.6		2.525	33.5	
Eosinophils -12	1.575	68.0	1.762	61.1		1.887	39.5		1.798	75.6		1.575	50.5	
Eosinophils -24	1.202	78.0	1.424	71.1		1.643	50.8		1.413	83.1		0.974	100.1	

Statistical analysis of differential white blood cell counts for G-TwYST studies A and C

diffWBC	Control		NK11-			NK33-			NK11+			NK33+		
Females	Mean	CV	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig	Mean	CV	Sig
Lymphocytes-03	72.86	10.3	71.88	10.0		73.79	9.1		71.21	9.2		73.23	9.6	
Lymphocytes-06	67.67	6.3	67.46	6.4		67.40	5.8		67.45	5.2		69.30	6.5	
Lymphocytes-12	68.38	10.8	62.75	10.3	tw	66.51	13.6		66.21	10.1		66.70	9.9	
Lymphocytes-24	49.65	28.8	46.68	24.9		52.92	15.2		47.27	28.6		49.99	26.4	
Neutrophils-03	23.20	27.7	24.44	28.9		23.18	28.7		24.88	24.1		22.57	28.5	
Neutrophils -06	28.97	14.7	29.54	13.8		29.61	14.0		29.26	12.9		27.91	15.5	
Neutrophils -12	28.96	25.3	34.32	18.8	dw	30.83	28.0		31.31	22.2		30.15	20.1	
Neutrophils -24	46.84	29.6	49.76	22.0		42.89	19.9		48.77	24.1		46.18	29.0	
Monocytes -03	1.875	37.6	1.716	41.5		1.725	34.2		2.025	42.7		1.975	36.2	
Monocytes -06	1.125	53.7	0.851	75.4		1.012	60.7		0.938	38.6		0.662	59.1	dTW
Monocytes -12	0.738	128.0	0.774	72.9		0.943	73.1		0.833	104.5		0.988	91.6	
Monocytes -24	2.279	94.4	2.176	66.0		2.375	59.8		2.739	90.0		2.420	66.1	
Eosinophils -03	2.063	59.0	1.964	61.8		1.312	60.5		1.875	42.1		2.200	50.5	
Eosinophils -06	2.238	33.9	2.213	38.7		1.975	49.6		2.337	33.0		2.125	58.0	
Eosinophils -12	1.925	36.0	2.155	57.2		1.886	53.6		1.643	34.9		2.162	33.6	
Eosinophils -24	1.235	53.8	1.382	68.0		1.812	61.3	t	1.216	60.6		1.409	60.1	

3.2 Classical statistical analysis for Study A

Table 10 presents the results of the t-tests, of Dunnett's tests and of Wilcoxon tests for the diffWBC endpoints for males and females. These result from a classical analysis of variance, according to the randomized block design, which is performed on the cage means after log transforming the data. 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 and in Figure 10 and Figure 11. Exact p-values for the classical tests are given in Appendix 5.

Results of the Shapiro-Wilks test for normality and Bartlett's and Levene's test for homogeneity of variance are given in Appendix 6. Bartlett's' homogeneity test is significant at the 5% level for males for 3 variables (Lymphocytes-03, Lymphocytes-24 and Neutrophils-24) and for females for 2 variables (Lymphocytes-24 and Eosinophils-06). Levene's homogeneity test is significant for male variable Lymphocytes-03, and for no females variables. This implies that the important assumption of homogeneity of variance is generally fulfilled. For these significant cases, one might resort to Wilcoxon's' test instead of the t-test.

3.3 Standardized effect sizes for Study A

SES 95% confidence intervals are given in Figure 12 and Figure 13. The number of intervals that extend outside the -/+ 1 SD limits equals 23 out of 128 (18%).

3.4 Equivalence testing for study C using historical data

Figure 14 displays the ratio of the residual variance in the current G-TwYST study C as a percentage of the residual variance in the historical GRACE study. This indicates that, except for Eosinophils, the G-TwYST data are much more variable than the Grace data, resulting in a less useful equivalence analysis.

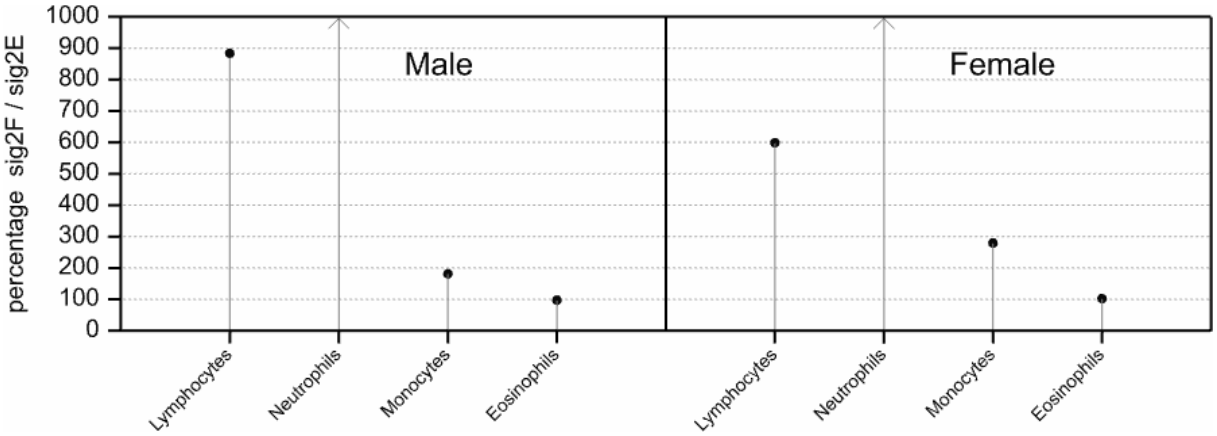

Figure 14 Residual variance (sig2F or σ_F^2) in the current G-TwYST C study as a percentage of the residual variance (sig2E or σ_E^2) in the historical GRACE studies.

Preliminary regulatory values $\alpha = 0.05$, $\beta = 0.20$ and $n_0 = 8$ were employed, where n_0 is equal to the number of cages for the diffWBC endpoints (Table 8). The intervals showing the main results of the equivalence tests are given in Figure 15; Figure 16 provides an alternative representation of the same intervals. 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 11 and Table 12, and also in Figure 17.

Table 11 95% Confidence interval plus estimate for the ratio Δ of the GMO feeds with 50% maize inclusion rate versus the corresponding non-GM control feed for study C. Ratios with corresponding 95/99% intervals that do not encompass the value 1 are coloured yellow/gold; this is equivalent to a significant difference according to a 5/1% t-test.

diffWBC	NK11-/50 vs Con50			NK50- vs Con50			NK11+/50 vs Con50			NK50+ vs Con50		
Males	low	ratio	upp	low	ratio	upp	low	ratio	upp	low	ratio	upp
Lymphocytes	0.89	1.02	1.16	0.92	1.05	1.20	0.83	0.95	1.09	0.80	0.92	1.05
Neutrophils	0.35	0.74	1.55	0.19	0.40	0.84	0.56	1.17	2.46	0.60	1.26	2.66
Monocytes	0.53	0.82	1.27	0.48	0.75	1.17	0.58	0.90	1.40	0.64	1.00	1.55
Eosinophils	0.68	1.08	1.71	0.63	1.01	1.60	0.70	1.12	1.78	0.76	1.21	1.93

diffWBC	NK11-/50 vs Con50			NK50- vs Con50			NK11+/50 vs Con50			NK50+ vs Con50		
Females	low	ratio	upp	low	ratio	upp	low	ratio	upp	low	ratio	upp
Lymphocytes	0.91	1.03	1.15	0.94	1.06	1.19	0.89	1.00	1.12	0.92	1.04	1.16
Neutrophils	0.46	0.81	1.40	0.48	0.83	1.44	0.56	0.98	1.70	0.42	0.73	1.26
Monocytes	0.70	1.12	1.80	0.69	1.10	1.78	0.56	0.91	1.46	0.75	1.21	1.94
Eosinophils	0.68	1.12	1.86	0.60	0.99	1.64	0.57	0.95	1.56	0.90	1.48	2.44

Table 12 95% Confidence interval plus estimate for the ratio Δ of the feeds with 50% maize inclusion rate versus the corresponding 33% inclusion rate for study C, and for the GM 33% feeds versus the non-GM 33% feed. Ratios with corresponding 95/99% intervals that do not encompass the value 1 are coloured yellow/gold; this is equivalent to a significant difference according to a 5/1% t-test.

diffWBC	Con50 vs Con33			NK50- vs NK33-			NK50+ vs NK33+			NK33- vs Con33			NK33+ vs Con33		
Males	low	ratio	upp	low	ratio	upp	low	ratio	upp	low	ratio	upp	low	ratio	upp
Lymphocytes	1.04	1.19	1.36	0.97	1.11	1.27	0.89	1.02	1.16	0.98	1.12	1.28	0.94	1.07	1.22
Neutrophils	0.29	0.60	1.27	0.16	0.33	0.70	0.52	1.08	2.28	0.34	0.72	1.52	0.33	0.70	1.48
Monocytes	0.81	1.26	1.96	0.44	0.68	1.05	0.75	1.16	1.81	0.90	1.40	2.17	0.70	1.08	1.68
Eosinophils	0.51	0.81	1.29	0.48	0.76	1.20	0.56	0.90	1.43	0.68	1.08	1.72	0.69	1.09	1.74

diffWBC	Con50 vs Con33			NK50- vs NK33-			NK50+ vs NK33+			NK33- vs Con33			NK33+ vs Con33		
Females	low	ratio	upp	low	ratio	upp	low	ratio	upp	low	ratio	upp	low	ratio	upp
Lymphocytes	0.80	0.90	1.00	0.92	1.04	1.16	0.91	1.03	1.15	0.82	0.91	1.03	0.81	0.90	1.01
Neutrophils	0.95	1.65	2.88	0.52	0.91	1.58	0.47	0.82	1.42	0.87	1.51	2.62	0.84	1.47	2.55
Monocytes	0.75	1.21	1.94	0.59	0.95	1.53	0.81	1.31	2.11	0.87	1.40	2.25	0.69	1.11	1.79
Eosinophils	0.65	1.07	1.76	0.58	0.95	1.57	0.88	1.46	2.40	0.68	1.12	1.84	0.66	1.08	1.79

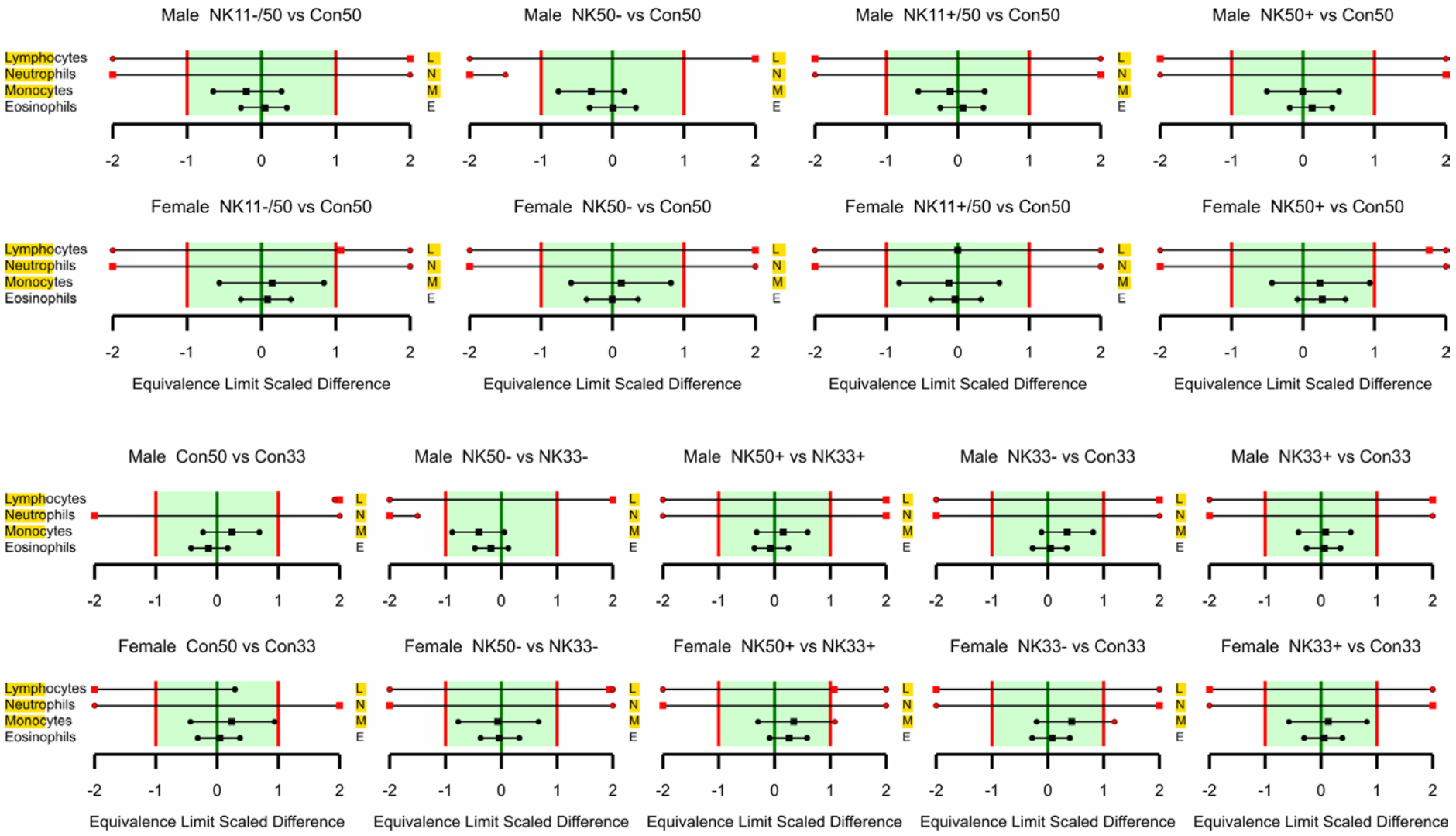

Figure 15 Equivalence testing of GM feeding groups versus the control feed for males in study C. Endpoints labelled with a golden background have a large residual variance compared to the historical studies (VR>150%). Fuchsia coloured symbols denote a significant difference.

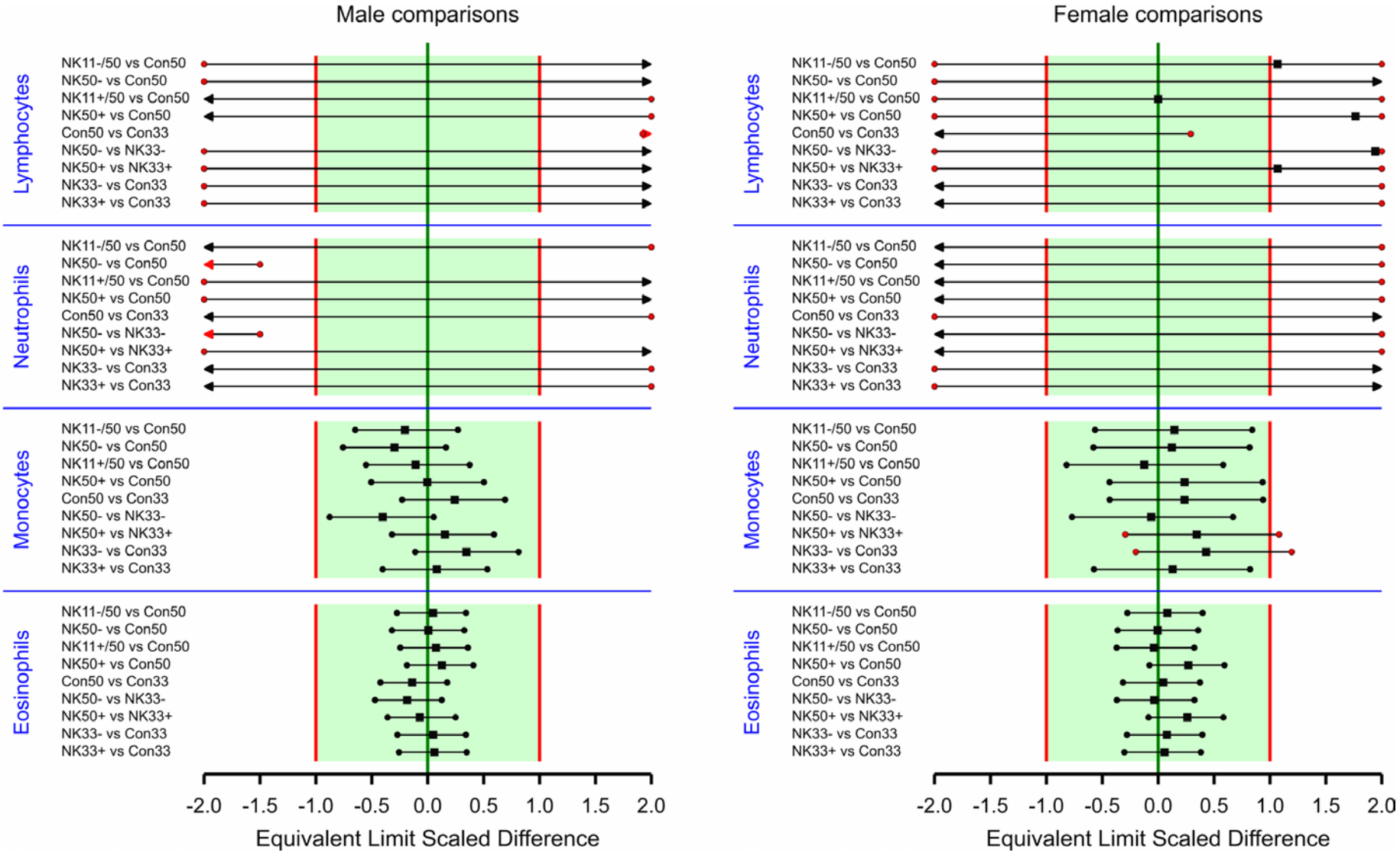

Figure 16 Equivalence testing of GM feeding groups versus the control feed for males in study C; alternative representation of the intervals in Figure 15.

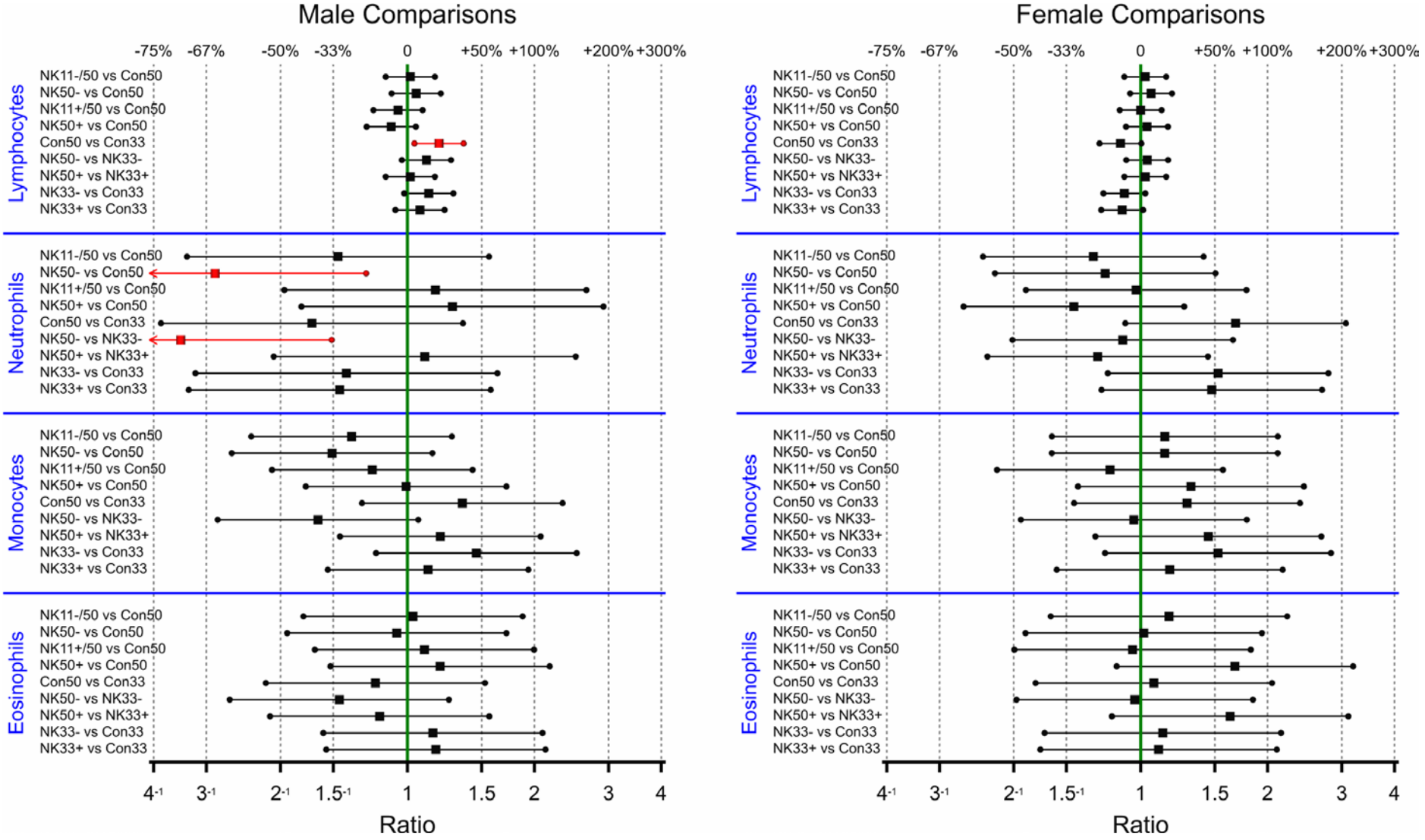

Figure 17 95% confidence intervals for the nine comparisons in Study C. Intervals that do not encompass the ratio=1 line are given in red, these represent significant differences at the 5% level.

3.5 Classical statistical analysis for Study C

Table 13 presents the results of the t-tests, of Dunnett's tests and of Wilcoxon tests for the study C diffWBC endpoints for males and females. These result from a classical analysis of variance, according to the randomized block design, which is performed on the cage means after log transforming the data. For ease of interpretation results are expressed as means on the original scale, rather than on the log scale. Note however that 95% confidence intervals on the ratio scale are given in Table 11 and Table 12, and also in Figure 17. Exact p-values for the classical tests are given in Appendix 5

Results of the Shapiro-Wilks test for normality and Bartlett's and Levene's test for homogeneity of variance are given in Appendix 6. Bartlett's' homogeneity test is significant at the 5% level for male variable Neutrophils and for females variables Lymphocytes and Neutrophils. Levene's homogeneity test is significant for male variables Neutrophils and Monocytes, and for no female variables. For these significant cases, one might resort to Wilcoxon's' test instead of the t-test.

3.6 Standardized effect sizes for Study C

SES 95% confidence intervals are given in Figure 18. The SES interval lies completely within the (-1,1) interval only when the difference between the group means is very close to zero.

Table 13 Means per feeding group and results of statistical tests for nine comparisons for Study C. Significant difference 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. See text.

diffWBC	Means								NK11-Con50	NK50-Con50	NK11+Con50	NK50+Con50	Con50 Con33	NK50-NK33-	NK50+NK33+	NK33-Con33	NK33+Con33
Males	Con50	NK11-	NK50-	NK11+	NK50+	Con33	NK33-	NK33+									
Lymphocytes	78.09	79.41	82.66	74.41	73.78	67.00	74.09	71.94					tW				
Neutrophils	18.75	17.06	14.25	22.00	22.38	29.19	21.28	24.41		t				T			
Monocytes	1.969	2.031	1.625	2.094	2.000	1.625	2.781	1.781									
Eosinophils	1.156	1.469	1.469	1.500	1.844	2.188	1.844	1.875									

diffWBC	Means								NK11-Con50	NK50-Con50	NK11+Con50	NK50+Con50	Con50 Con33	NK50-NK33-	NK50+NK33+	NK33-Con33	NK33+Con33
Females	Con50	NK11-	NK50-	NK11+	NK50+	Con33	NK33-	NK33+									
Lymphocytes	72.72	74.03	76.41	72.44	74.84	80.53	73.84	73.16									
Neutrophils	24.75	23.03	21.00	25.28	21.88	17.44	23.12	24.44									
Monocytes	1.156	1.406	1.312	1.094	1.344	0.875	1.531	0.969									
Eosinophils	1.375	1.531	1.250	1.188	1.938	1.156	1.500	1.438									

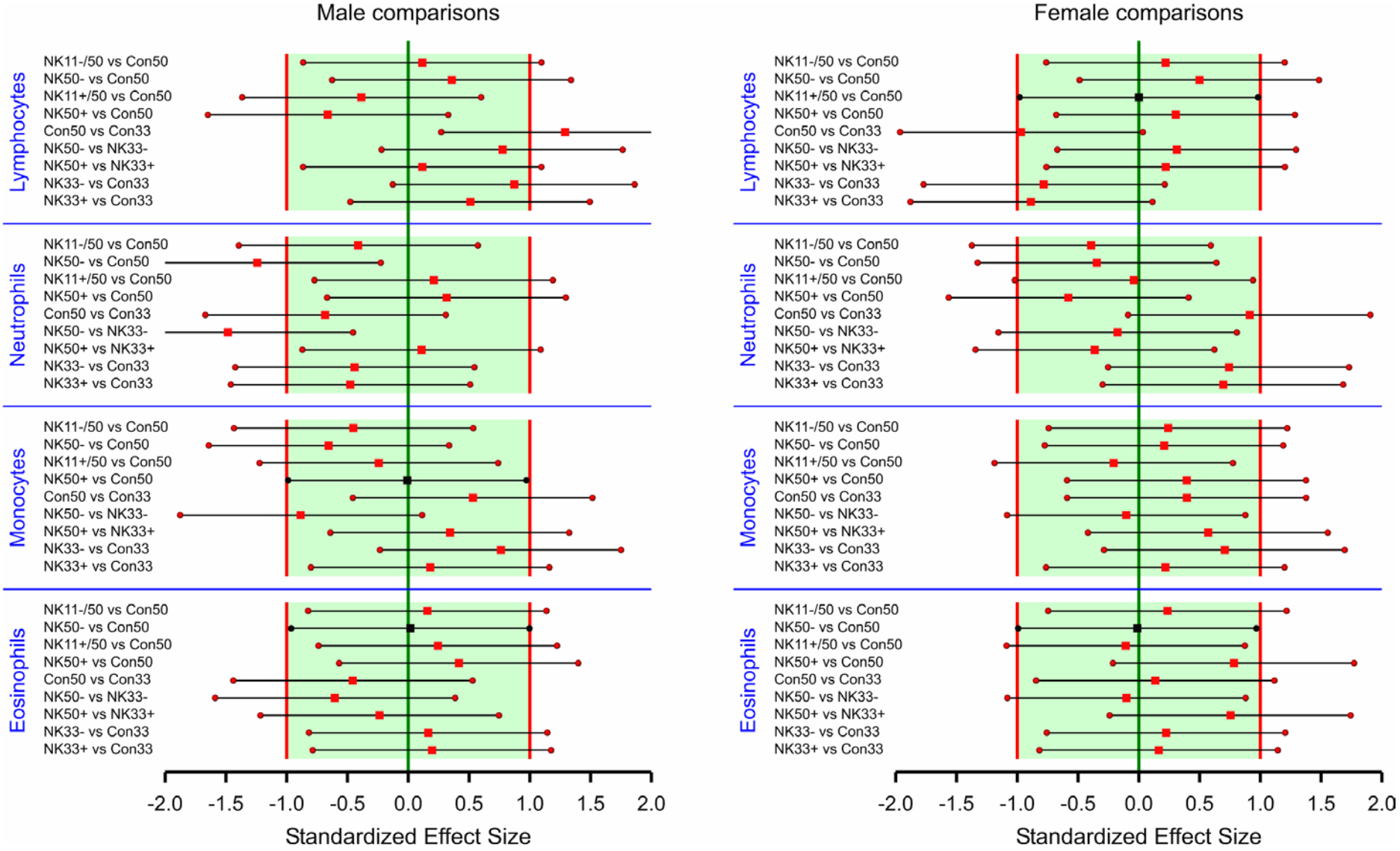

Figure 18 Confidence intervals for Standardized Effect Sized (SES) for Study C. Intervals that extend beyond the interval (-1,1) are given in red.

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List of Tables

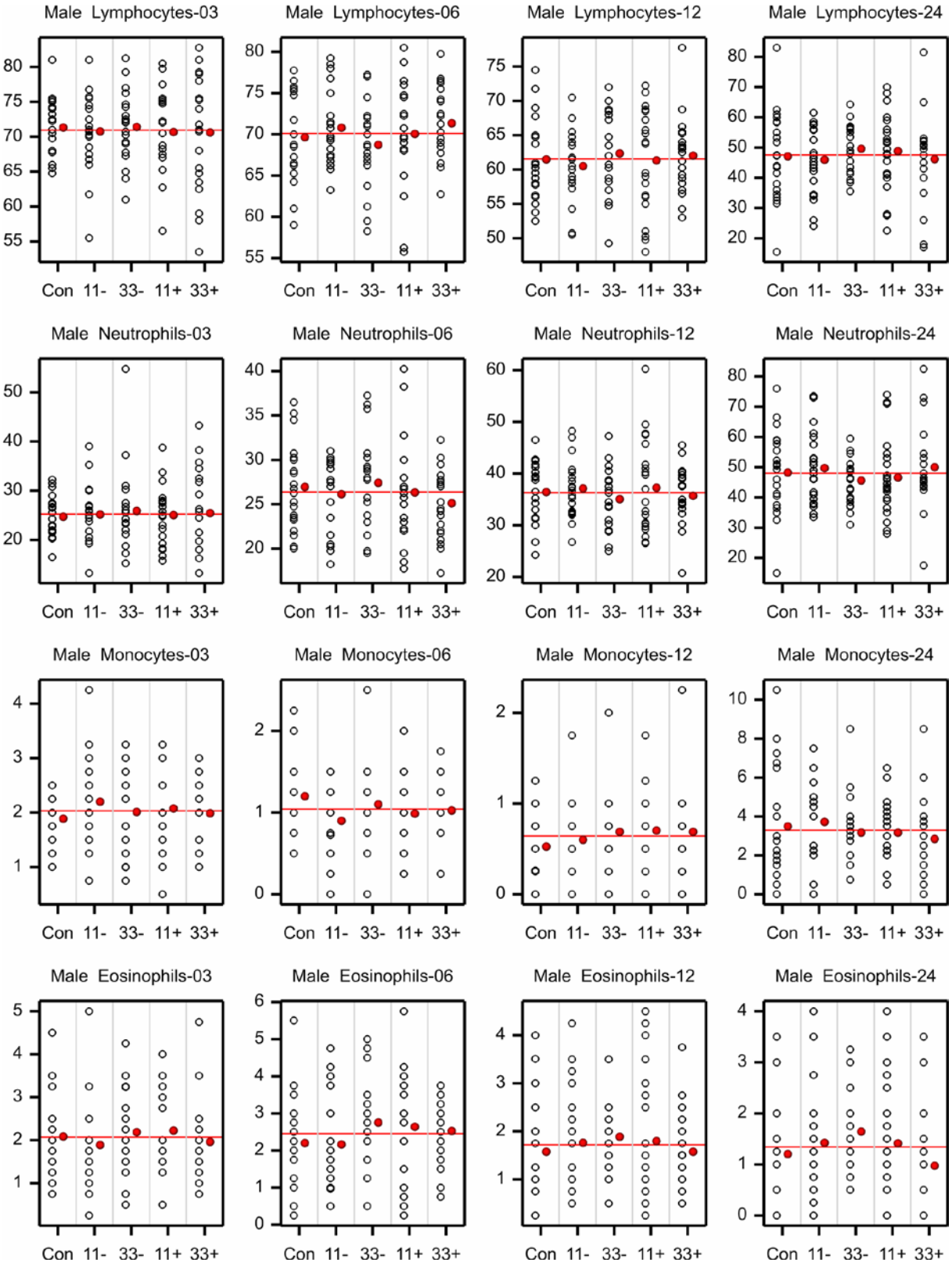
Table 12 95% Confidence interval plus estimate for the ratio Δ of the feeds with 50% maize inclusion rate versus the corresponding 33% inclusion rate for study C, and for the GM 33% feeds versus the non-GM 33% feed. Ratios with corresponding 95/99% intervals that do not encompass the value 1 are coloured yellow/gold; this is equivalent to a significant difference according to a 5/1% t-test.

Table 13 Means per feeding group and results of statistical tests for nine comparisons for Study C. Significant difference 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. See text.

List of Figures

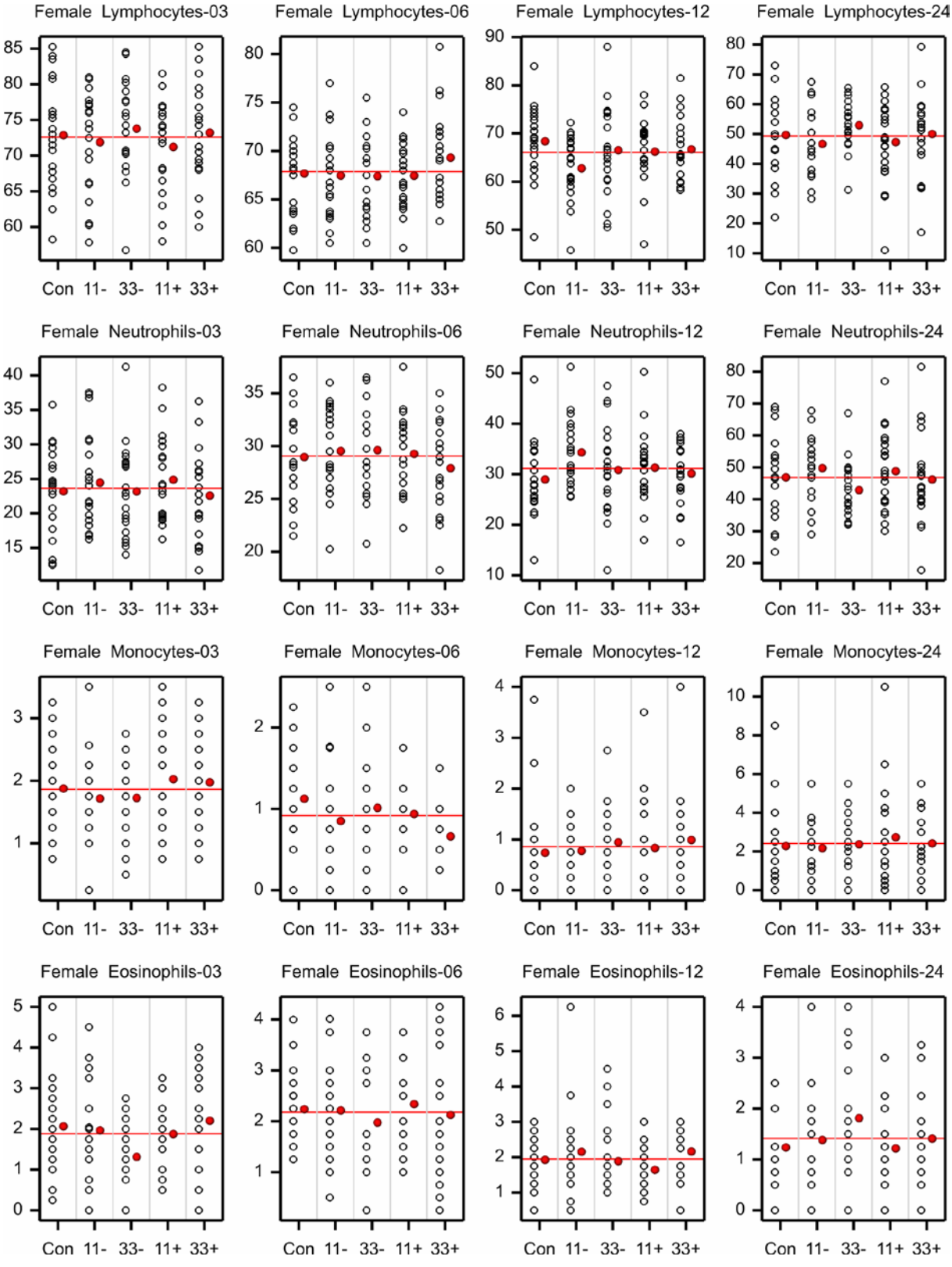
Appendix 1. Graphs of cage means on the original scale for study A

Red symbols denote means for feeding groups while the red line denotes the overall mean. Note that observations might overlap.



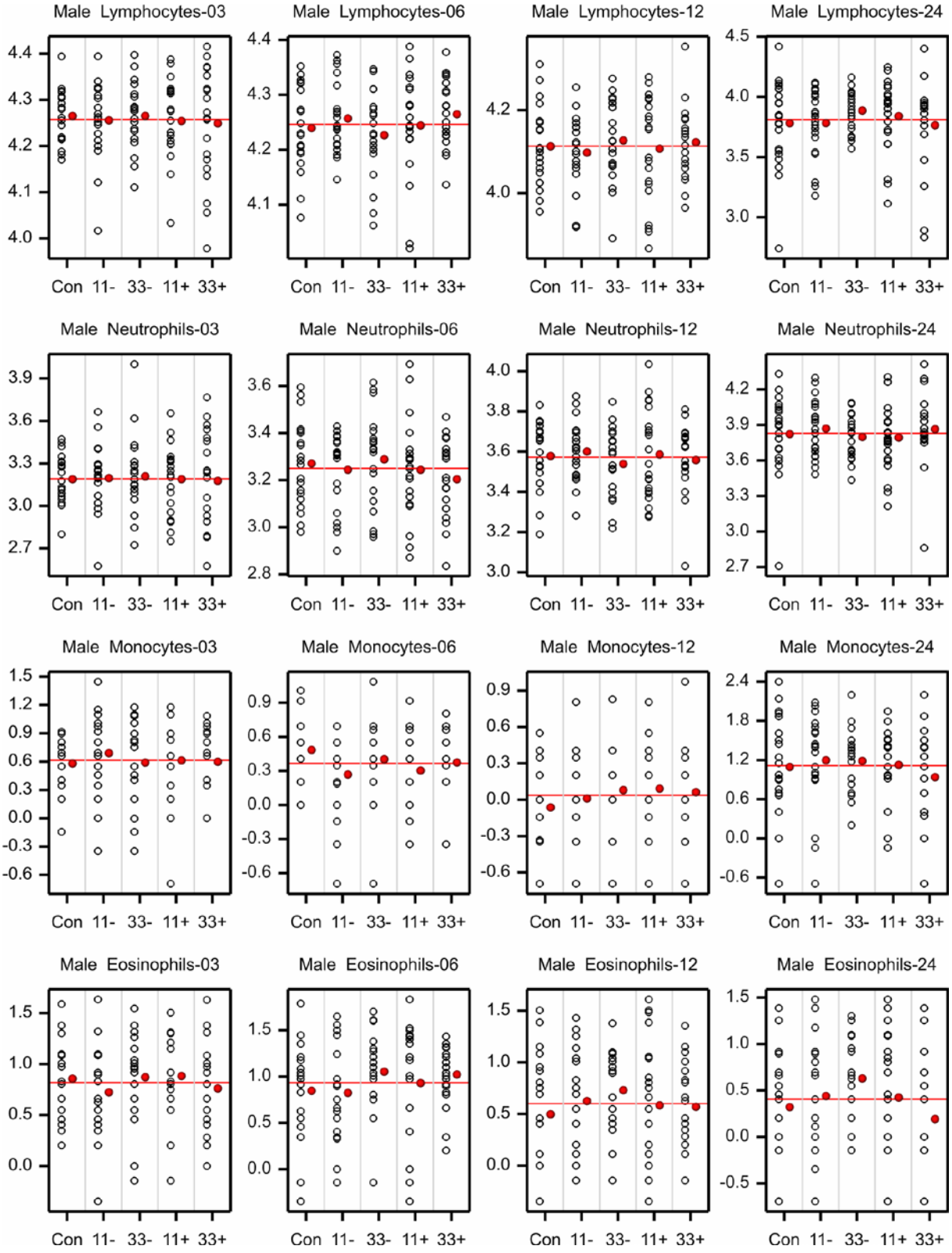
Appendix 1. Graphs of cage means on the original scale for study A(continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean. Note that observations might overlap.



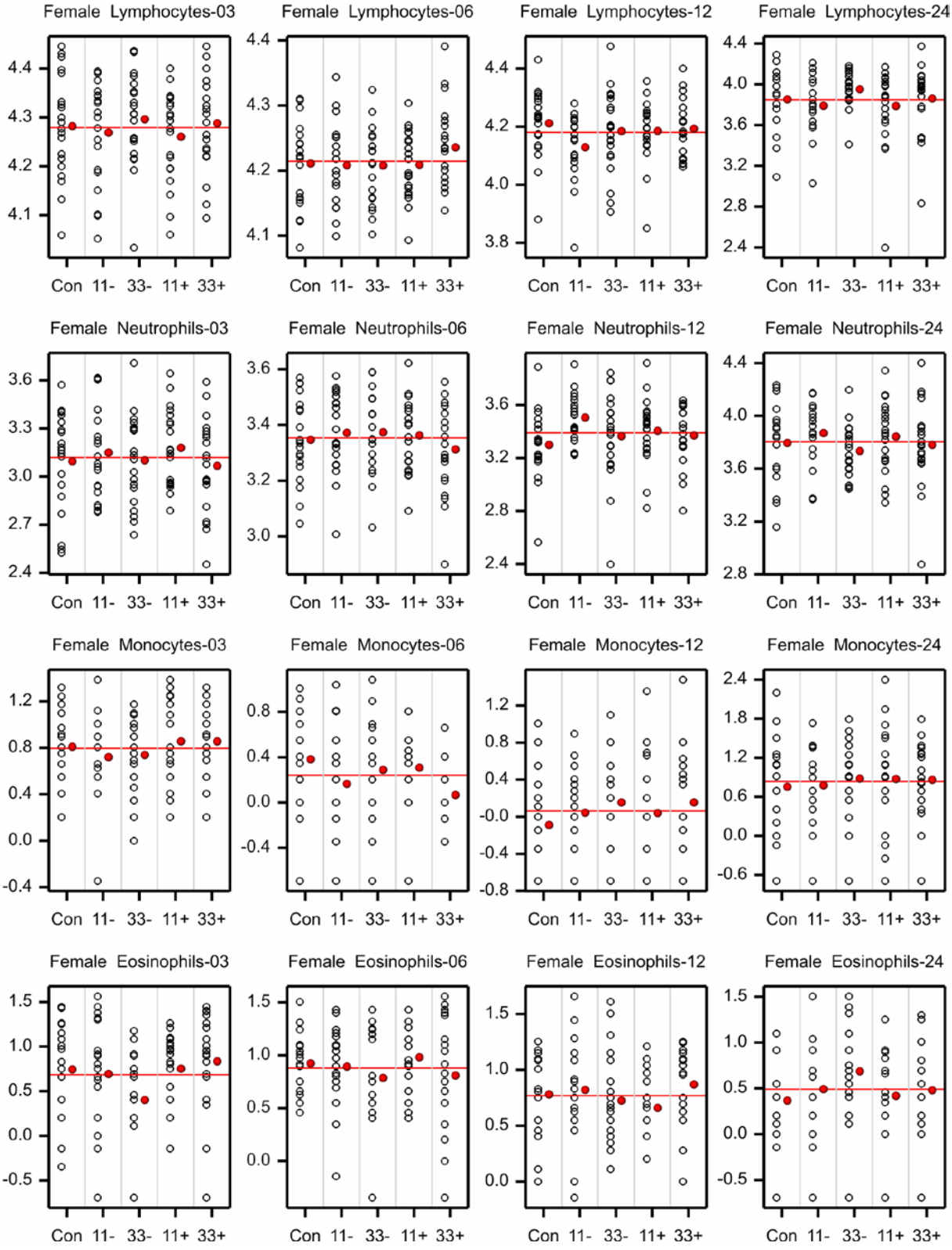
Appendix 2. Graphs of cage means on the log scale for study A

Red symbols denote means for feeding groups while the red line denotes the overall mean. Note that observations might overlap.



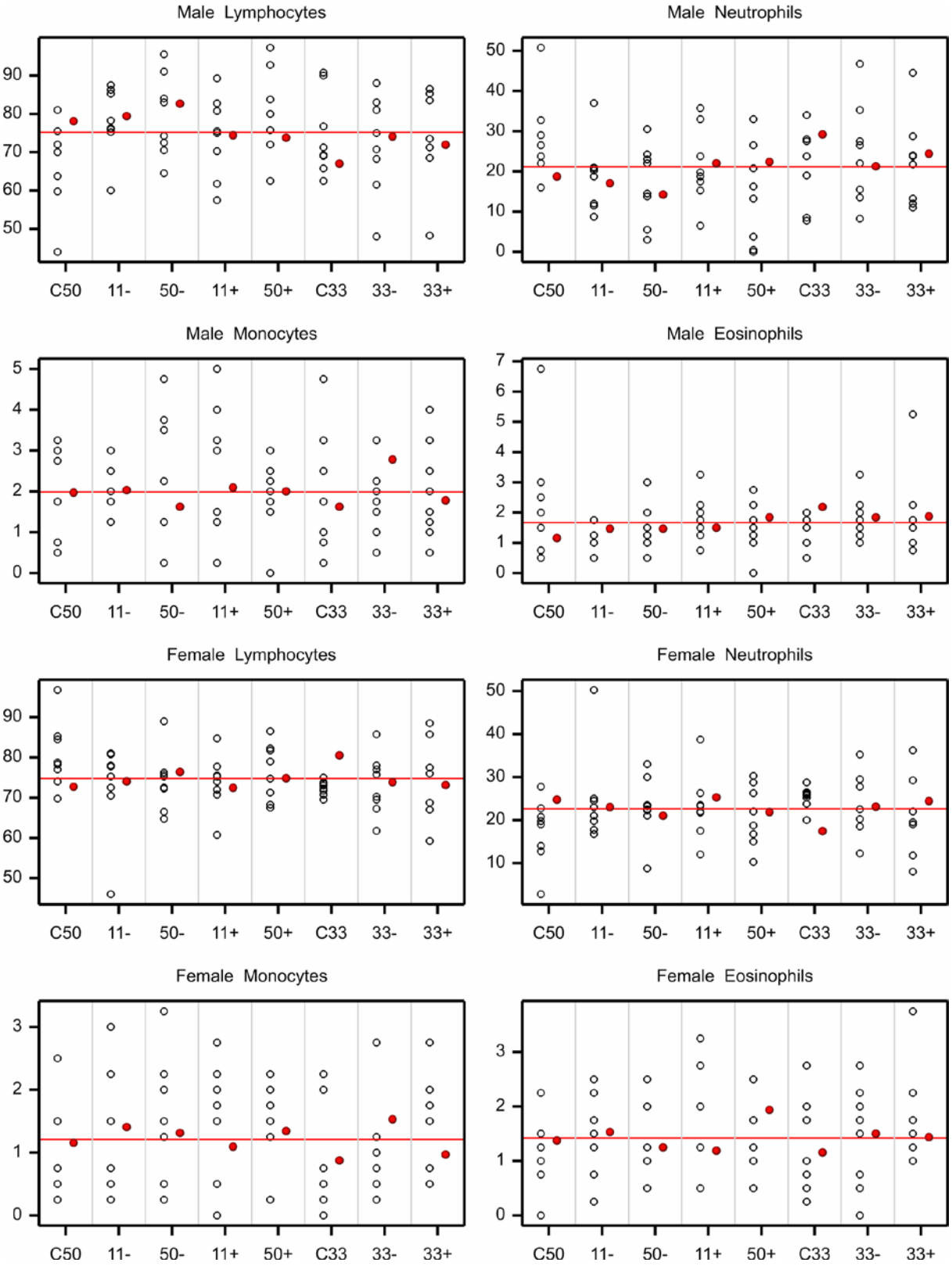
Appendix 2. Graphs of cage means on the log scale for study A(continued)

Red symbols denote means for feeding groups while the red line denotes the overall mean. Note that observations might overlap.



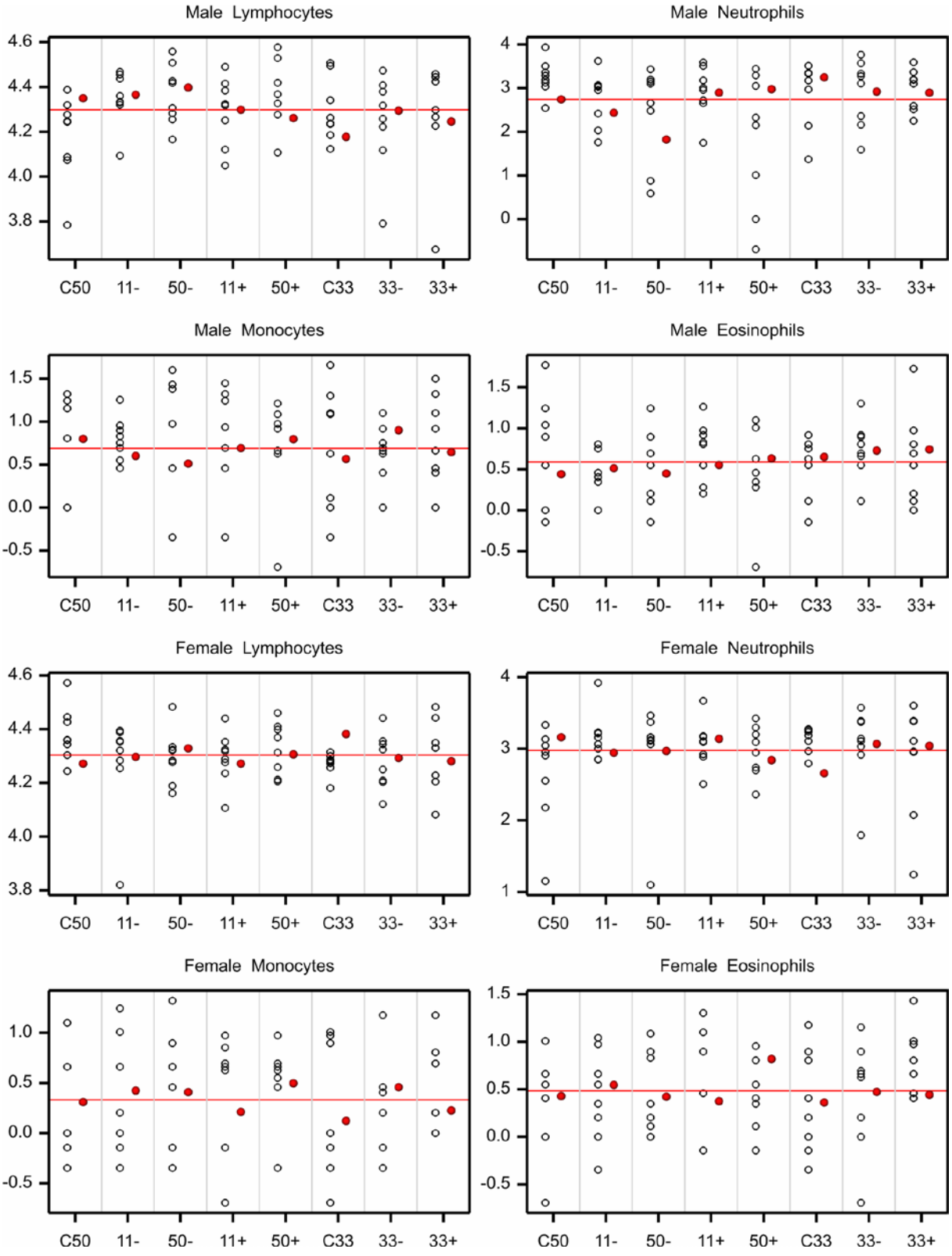
Appendix 3. Graphs of cage means on the original scale for study C

Red symbols denote means for feeding groups while the red line denotes the overall mean. Note that observations might overlap.



Appendix 4. Graphs of cage means on the log scale for study C

Red symbols denote means for feeding groups while the red line denotes the overall mean. Note that observations might overlap.



Appendix 5. P-values for difference tests for studies A and C

A diffWBC	NK11-			NK33-			NK11+			NK33+		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Lymphocytes-03	0.983	0.687	0.869	0.999	0.860	0.829	0.972	0.642	0.732	0.896	0.491	0.812
Lymphocytes-06	0.816	0.403	0.177	0.920	0.527	0.388	0.998	0.823	0.956	0.561	0.229	0.133
Lymphocytes-12	0.928	0.540	0.522	0.943	0.567	0.452	1.000	0.885	0.596	0.984	0.689	0.756
Lymphocytes-24	1.000	0.956	0.869	0.606	0.254	0.196	0.917	0.522	0.860	1.000	0.973	0.782
Neutrophils-03	1.000	0.902	0.869	0.993	0.746	0.869	1.000	0.994	0.898	0.999	0.860	0.784
Neutrophils-06	0.953	0.588	0.644	0.990	0.725	0.522	0.951	0.584	0.648	0.466	0.180	0.177
Neutrophils-12	0.968	0.630	0.784	0.809	0.397	0.312	1.000	0.898	0.701	0.978	0.664	0.825
Neutrophils-24	0.971	0.637	0.784	0.981	0.678	0.304	0.983	0.684	0.860	0.994	0.761	0.818
Monocytes-03	0.648	0.278	0.237	1.000	0.921	0.794	0.992	0.744	0.732	0.999	0.853	0.837
Monocytes-06	0.056	0.017	0.028	0.759	0.355	0.266	0.134	0.043	0.042	0.534	0.214	0.144
Monocytes-12	0.861	0.448	0.393	0.391	0.145	0.141	0.355	0.129	0.248	0.505	0.199	0.162
Monocytes-24	0.904	0.503	0.452	0.990	0.729	0.966	0.994	0.758	0.490	0.773	0.367	0.579
Eosinophils-03	0.661	0.287	0.507	1.000	0.912	0.794	0.999	0.838	0.632	0.858	0.446	0.641
Eosinophils-06	1.000	0.874	1.000	0.407	0.152	0.198	0.940	0.561	0.546	0.548	0.222	0.191
Eosinophils-12	0.799	0.388	0.260	0.329	0.118	0.142	0.821	0.408	0.926	0.967	0.626	0.455
Eosinophils-24	0.924	0.533	0.408	0.554	0.225	0.167	0.949	0.581	0.820	0.759	0.356	0.065
A diffWBC	**NK11-**			**NK33-**			**NK11+**			**NK33+**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Lymphocytes-03	0.971	0.637	0.352	0.934	0.550	0.701	0.768	0.361	0.452	0.997	0.799	0.898
Lymphocytes-06	1.000	0.939	0.953	0.999	0.863	0.920	1.000	0.910	0.869	0.397	0.147	0.076
Lymphocytes-12	0.076	0.023	0.020	0.842	0.428	0.452	0.863	0.450	0.546	0.956	0.596	0.812
Lymphocytes-24	0.985	0.703	0.850	0.916	0.532	0.146	0.859	0.458	0.330	1.000	0.912	0.940
Neutrophils-03	0.872	0.460	0.293	1.000	0.929	0.985	0.499	0.195	0.245	0.976	0.655	0.701
Neutrophils-06	0.992	0.740	0.595	0.910	0.511	0.430	0.987	0.706	0.701	0.816	0.403	0.277
Neutrophils-12	0.038	0.011	0.011	0.812	0.399	0.388	0.448	0.171	0.090	0.760	0.355	0.475
Neutrophils-24	0.919	0.537	0.791	0.893	0.499	0.244	0.950	0.593	0.229	0.996	0.786	0.860
Monocytes-03	0.674	0.294	0.309	0.788	0.378	0.629	0.940	0.561	0.508	0.943	0.566	0.575
Monocytes-06	0.222	0.075	0.084	0.813	0.400	0.681	0.907	0.506	0.260	0.020	0.006	0.003
Monocytes-12	0.843	0.429	0.451	0.298	0.105	0.182	0.602	0.250	0.164	0.180	0.059	0.145
Monocytes-24	0.954	0.602	0.733	0.692	0.317	0.273	0.772	0.377	0.639	0.982	0.689	0.834

Eosinophils-03	0.999	0.866	0.965	0.171	0.056	0.153	1.000	0.962	1.000	0.961	0.608	0.601
Eosinophils-06	1.000	0.948	1.000	0.652	0.281	0.235	0.974	0.648	0.481	0.776	0.367	0.588
Eosinophils-12	0.944	0.569	0.571	0.968	0.630	0.644	0.533	0.213	0.107	0.843	0.429	0.360
Eosinophils-24	0.750	0.360	0.193	0.101	0.033	0.216	0.999	0.843	0.691	0.894	0.499	0.589

C: diffWBC	**NK11-/50 vs Con50**			**NK50- vs Con50**			**NK11+/50 vs Con50**			**NK50+ vs Con50**		
Males	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Lymphocytes	0.998	0.818	0.641	0.884	0.478	0.250	0.856	0.444	0.547	0.486	0.191	0.250
Neutrophils	0.825	0.413	0.547	0.055	0.016	0.148	0.981	0.676	0.742	0.922	0.531	0.547
Monocytes	0.777	0.371	0.547	0.497	0.196	0.383	0.968	0.629	0.844	1.000	0.987	0.945
Eosinophils	0.993	0.754	0.844	1.000	0.973	0.933	0.967	0.628	0.742	0.820	0.409	0.641
C: diffWBC	**NK11-/50 vs Con50**			**NK50- vs Con50**			**NK11+/50 vs Con50**			**NK50+ vs Con50**		
Females	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox	Dunnet	t-test	Wilcox
Lymphocytes	0.977	0.661	0.742	0.712	0.322	0.742	1.000	0.999	0.250	0.931	0.546	0.547
Neutrophils	0.848	0.436	1.000	0.896	0.493	0.547	1.000	0.935	1.000	0.600	0.251	0.383
Monocytes	0.968	0.632	0.933	0.981	0.679	0.553	0.982	0.680	0.383	0.846	0.434	0.461
Eosinophils	0.971	0.639	0.528	1.000	0.980	0.844	0.998	0.829	0.674	0.341	0.124	0.195

C: diffWBC	**Con50 vs Con33**			**NK50- vs NK33-**			**NK50+ vs NK33+**			**NK33- vs Con33**			**NK33+ vs Con33**		
Males	Dunn	t-test	Wlcx	Dunn	t-test	Wlcx	Dunn	t-test	Wlcx	Dunn	t-test	Wlcx	Dunn	t-test	Wlcx
Lymphocytes		0.013	0.008		0.127	0.055		0.818	0.945	0.154	0.087	0.195	0.493	0.312	0.742
Neutrophils		0.178	0.078		0.005	0.055		0.828	0.844	0.583	0.381	0.313	0.536	0.344	0.547
Monocytes		0.292	0.250		0.083	0.109		0.496	0.735	0.229	0.134	0.313	0.909	0.719	0.800
Eosinophils		0.365	0.674		0.232	0.547		0.639	0.624	0.924	0.744	0.844	0.895	0.697	1.000
C: diffWBC	**Con50 vs Con33**			**NK50- vs NK33-**			**NK50+ vs NK33+**			**NK33- vs Con33**			**NK33+ vs Con33**		
Females	Dunn	t-test	Wlcx	Dunn	t-test	Wlcx	Dunn	t-test	Wlcx	Dunn	t-test	Wlcx	Dunn	t-test	Wlcx
Lymphocytes		0.058	0.250		0.534	0.148		0.659	0.641	0.214	0.124	0.109	0.145	0.082	0.195
Neutrophils		0.074	0.109		0.728	0.461		0.471	0.742	0.246	0.144	0.250	0.288	0.171	0.383
Monocytes		0.433	0.461		0.836	0.844		0.259	0.195	0.276	0.164	0.148	0.871	0.664	0.834
Eosinophils		0.787	0.461		0.840	0.844		0.137	0.078	0.864	0.655	0.726	0.925	0.745	0.834

Appendix 6. Tests for normality and homogeneity of variance for studies A and C

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.

Study A: Male diffWBC	SW Control	SW NK11-	SW NK33-	SW NK11+	SW NK33+	SW residual	Bartlett	Levene
Lymphocytes-03	0.548	0.096	0.998	0.430	0.266	0.155	0.019	0.013
Lymphocytes-06	0.561	0.284	0.509	0.066	0.925	0.199	0.268	0.713
Lymphocytes-12	0.879	0.502	0.567	0.089	0.575	0.754	0.366	0.072
Lymphocytes-24	0.177	0.044	0.622	0.043	0.003	0.077	0.004	0.116
Neutrophils-03	0.648	0.404	0.189	0.735	0.629	0.639	0.077	0.058
Neutrophils-06	0.715	0.007	0.272	0.668	0.728	0.867	0.790	0.962
Neutrophils-12	0.323	0.989	0.736	0.271	0.028	0.917	0.450	0.108
Neutrophils-24	0.010	0.805	0.583	0.500	0.005	0.006	0.050	0.724
Monocytes-03	0.116	0.528	0.202	0.045	0.074	0.025	0.178	0.196
Monocytes-06	0.394	0.021	0.031	0.087	0.050	0.633	0.409	0.343
Monocytes-12	0.050	0.486	0.224	0.504	0.178	0.888	0.756	0.500
Monocytes-24	0.885	0.011	0.872	0.068	0.332	0.202	0.066	0.105
Eosinophils-03	0.788	0.958	0.139	0.260	0.796	0.009	0.938	0.899
Eosinophils-06	0.392	0.433	0.198	0.108	0.041	0.076	0.110	0.056
Eosinophils-12	0.286	0.571	0.164	0.301	0.707	0.974	0.263	0.111
Eosinophils-24	0.467	0.476	0.203	0.241	0.207	0.139	0.505	0.430
Study A: Female diffWBC	**SW Control**	**SW NK11-**	**SW NK33-**	**SW NK11+**	**SW NK33+**	**SW residual**	**Bartlett**	**Levene**
Lymphocytes-03	0.844	0.046	0.262	0.350	0.818	0.002	0.981	0.939
Lymphocytes-06	0.493	0.902	0.851	0.869	0.371	0.336	0.878	0.913
Lymphocytes-12	0.164	0.027	0.756	0.016	0.311	0.013	0.585	0.630
Lymphocytes-24	0.425	0.358	0.018	0.000	0.003	0.018	0.018	0.214
Neutrophils-03	0.117	0.139	0.663	0.587	0.949	0.121	0.862	0.877
Neutrophils-06	0.657	0.258	0.734	0.794	0.476	0.430	0.911	0.948
Neutrophils-12	0.193	0.705	0.096	0.304	0.077	0.222	0.133	0.476
Neutrophils-24	0.490	0.093	0.680	0.850	0.079	0.565	0.228	0.492

Monocytes-03	0.576	0.095	0.261	0.339	0.759	0.043	0.838	0.707
Monocytes-06	0.325	0.609	0.776	0.002	0.049	0.297	0.200	0.077
Monocytes-12	0.085	0.700	0.363	0.126	0.403	0.092	0.748	0.679
Monocytes-24	0.986	0.563	0.265	0.426	0.259	0.780	0.619	0.507
Eosinophils-03	0.049	0.281	0.029	0.014	0.014	0.000	0.581	0.709
Eosinophils-06	0.719	0.174	0.032	0.301	0.594	0.140	0.044	0.053
Eosinophils-12	0.133	0.302	0.333	0.414	0.019	0.377	0.436	0.479
Eosinophils-24	0.214	0.784	0.172	0.076	0.184	0.785	0.992	0.966

C: diffWBC											
Males	**Con50**	**NK11-/50**	**NK50-**	**NK11+/50**	**NK50+**	**Con33**	**NK33-**	**NK33+**	**Residual**	**Bartlett**	**Levene**
Lymphocytes	0.071	0.846	0.541	0.281	0.005	0.198	0.737	0.197	0.033	0.500	0.887
Neutrophils	0.429	0.029	0.300	0.016	0.518	0.875	0.386	0.386	0.409	0.006	0.001
Monocytes	0.926	0.065	0.015	0.647	0.938	0.012	0.136	0.632	0.077	0.064	0.003
Eosinophils	0.333	0.966	0.193	0.087	0.486	0.438	0.678	0.794	0.138	0.194	0.145
C: diffWBC											
Females	**Con50**	**NK11-/50**	**NK50-**	**NK11+/50**	**NK50+**	**Con33**	**NK33-**	**NK33+**	**Residual**	**Bartlett**	**Levene**
Lymphocytes	0.001	0.480	0.498	0.044	0.830	0.745	0.721	0.915	0.063	0.045	0.387
Neutrophils	0.036	0.000	0.859	0.044	0.077	0.072	0.538	0.022	0.001	0.004	0.164
Monocytes	0.283	0.310	0.040	0.172	0.321	0.024	0.018	0.406	0.672	0.929	0.613
Eosinophils	0.898	0.189	0.924	0.766	0.688	0.215	0.173	0.458	0.321	0.762	0.536