Supplemental Table 1: Macronutrient composition of SF and CF

Ingredient	**Study Formula**	**Control Formula**
Energy (kcal/oz)	20	20
Protein (g/100kcal)	2.0	2.0
Whey:casein ratio	80:20	60:40
Partially hydrolyzed proteins?	Yes	No
Intact proteins?	Yes	Yes
Fat (g/100kcal)	5.6	5.3
Carbohydrate (g/100kcal)	10	11.3
Prebiotic (g/L)	4 GOS	2 GOS 2 PDX

Supplemental Table 2. Participant Characteristics by Feeding Group in the ITT population

	Study Formula (n=106)	**Commercial Formula** (n=105)	**Human Milk** (n=100)
Sex			
Male	52 (49)	51 (49)	45 (45)
Female	54 (51)	54 (51)	55 (55)
Race			
White	77 (73)	77 (73)	87 (87)
Black	25 (24)	24 (23)	8 (8)
Asian	0	0	1 (1)
More than one race	4 (4)	4 (4)	4 (4)
Ethnicity			
Hispanic or Latino	17 (16)	15 (14)	20 (20)
Non-Hispanic	89 (84)	90 (86)	80 (80)
Age at enrollment, days	9 (2, 14)	8 (2, 14)	12 (2, 14)
Weight at enrollment, g	3325 (2590, 4317)	3348 (2665, 4540)	3505 (2673, 4535)
Length at enrollment, cm	50 (47, 54)	50 (47, 54)	51 (47, 55)
Head Circumference at enrollment, cm	35 (33, 37)	35 (33, 37)	36 (33, 38)
Birth weight, g	3343 (2608, 4281)	3265 (2581, 4340)	3430 (2650, 4609)
Birth length, cm	51 (46, 55)	51 (46, 56)	51 (46, 56)
Gestational age at birth, weeks			
37	14 (13)	11 (10)	5 (5)
38	16 (15)	22 (21)	23 (23)
39	59 (56)	50 (48)	55 (55)
40	17 (16)	20 (19)	15 (15)
41	0	2 (2)	2 (2)
Birth mode			
Vaginal	75 (71)	72 (69)	77 (77)
Caesarean section	31 (29)	33 (31)	23 (23)
Maternal age at enrollment, years	28 (18, 39)	27 (15, 41)	29 (20, 41)
Maternal pre-pregnancy BMI, kg/m^2	27 (16, 55)	29 (17, 64)	24 (18, 46)
Highest maternal education level			
Primary school	5 (5)	10 (10)	3 (3)
High school/technical school	61 (58)	56 (53)	31 (31)

College degree or higher	40 (38)	39 (37)	66 (66)
Maternal household income			
<$50,000	50 (47)	44 (42)	34 (34)
$50,000 - $75,000	29 (27)	30 (29)	24 (24)
$75,000 - $100,000	15 (14)	17 (16)	16 (16)
≥$100,000	12 (11)	14 (13)	34 (34)
Maternal smoking during pregnancy	12 (11)	8 (8)	5 (5)
Human milk intake prior to study	36 (34)	33 (31)	100 (100)
Human milk intake prior to study, days	4 (1, 14)	3 (1, 14)	12 (2, 14)

Categorical variables summarized by frequency (percent) and continuous variables by median (minimum, maximum)

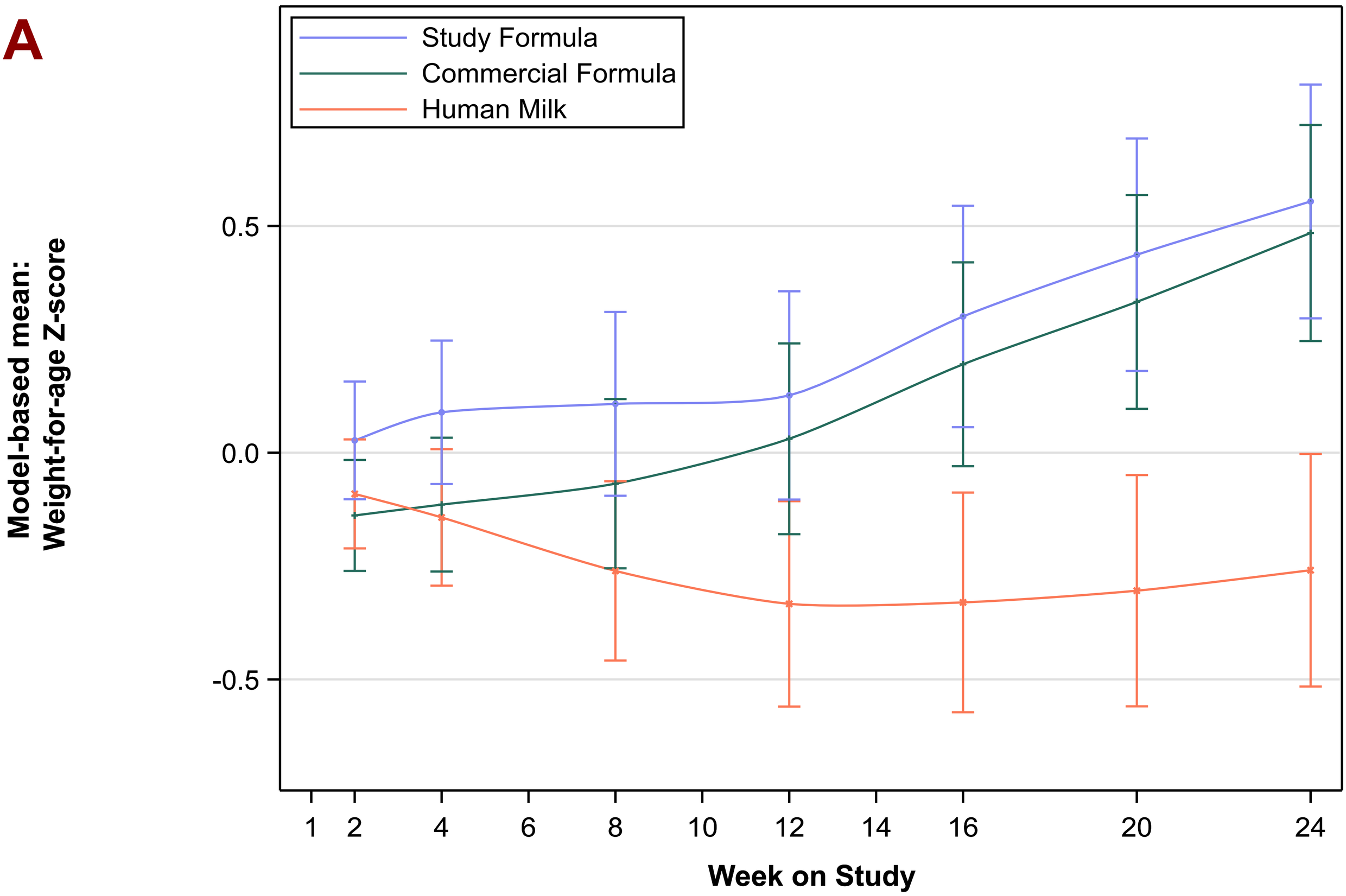
Supplemental Table 3. Participant Characteristics by Feeding Group in the PP population

	Study Formula (n=61)	**Commercial Formula** (n=67)	**Human Milk** (n=57)
Sex			
Male	26 (43)	32 (48)	29 (51)
Female	35 (57)	35 (52)	28 (49)
Race			
White	48 (79)	53 (79)	51 (89)
Black	9 (15)	11 (16)	3 (5)
Asian	0	0	1 (2)
More than one race	4 (7)	3 (4)	2 (4)
Ethnicity			
Hispanic or Latino	52 (85)	58 (87)	50 (88)
Non-Hispanic	9 (15)	9 (13)	7 (12)
Age at enrollment, days	9 (3, 14)	10 (2, 14)	12 (2, 14)
Weight at enrollment, g	3365 (2590, 4317)	3402 (2665, 4540)	3580 (3025, 4535)
Length at enrollment, cm	50 (47, 54)	50 (47, 54)	51 (48, 55)
Head Circumference at enrollment, cm	36 (33, 37)	35 (33, 37)	36 (34, 38)
Birth weight, g	3330 (2720, 4167)	3265 (2722, 4340)	3458 (2760, 4609)
Birth length, cm	51 (47, 55)	51 (46, 56)	51 (46, 56)
Gestational age at birth, weeks			
37	5 (8)	8 (12)	4 (7)
38	12 (20)	12 (18)	13 (23)
39	36 (59)	31 (46)	32 (56)
40	8 (13)	14 (21)	6 (11)
41	0	2 (3)	2 (4)
Birth mode			
Vaginal	48 (79)	46 (69)	45 (79)
Caesarean section	13 (21)	21 (31)	12 (21)
Maternal age at enrollment, years	28 (18, 39)	28 (15, 41)	30 (20, 41)
Maternal pre-pregnancy BMI, kg/m^2	29 (18, 55)	28 (18, 64)	24 (18, 44)
Highest maternal education level			
Primary school	2 (3)	6 (9)	1 (2)
High school/technical school	31 (51)	30 (45)	16 (28)
College degree or higher	28 (46)	31 (46)	40 (70)
Maternal household income			
<$50,000	29 (48)	27 (40)	14 (25)

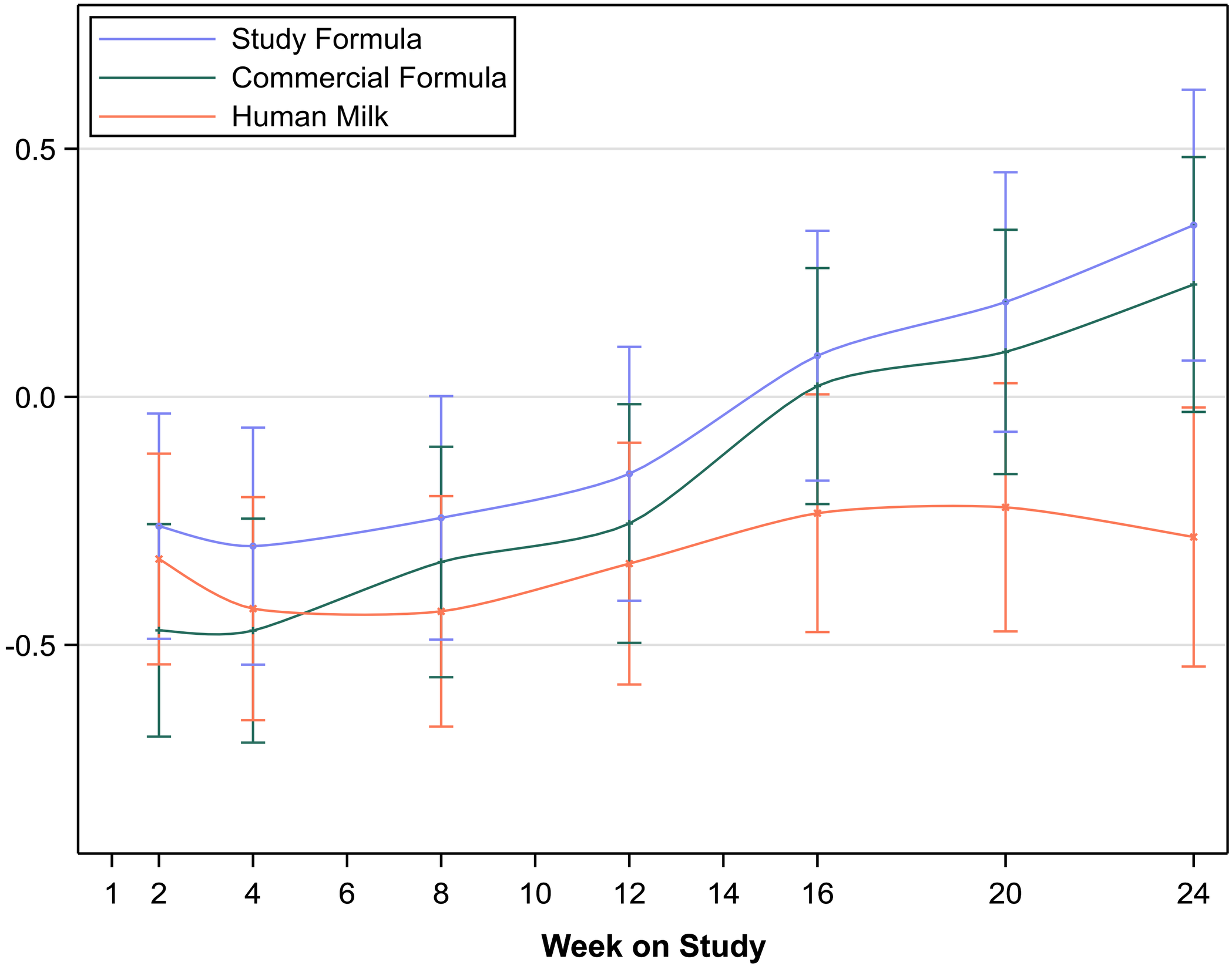
$50,000 - $75,000	17 (28)	16 (24)	15 (26)
$75,000 - $100,000	8 (13)	14 (21)	9 (16)
≥$100,000	7 (12)	10 (15)	19 (33)
Maternal smoking during pregnancy	8 (13)	6 (9)	3 (5)
Human milk intake prior to study	22 (36)	21 (31)	57 (100)
Human milk intake prior to study, days	4 (1, 12)	2 (1, 14)	12 (2, 14)

Categorical variables summarized by frequency (percent) and continuous variables by median (minimum, maximum)

A

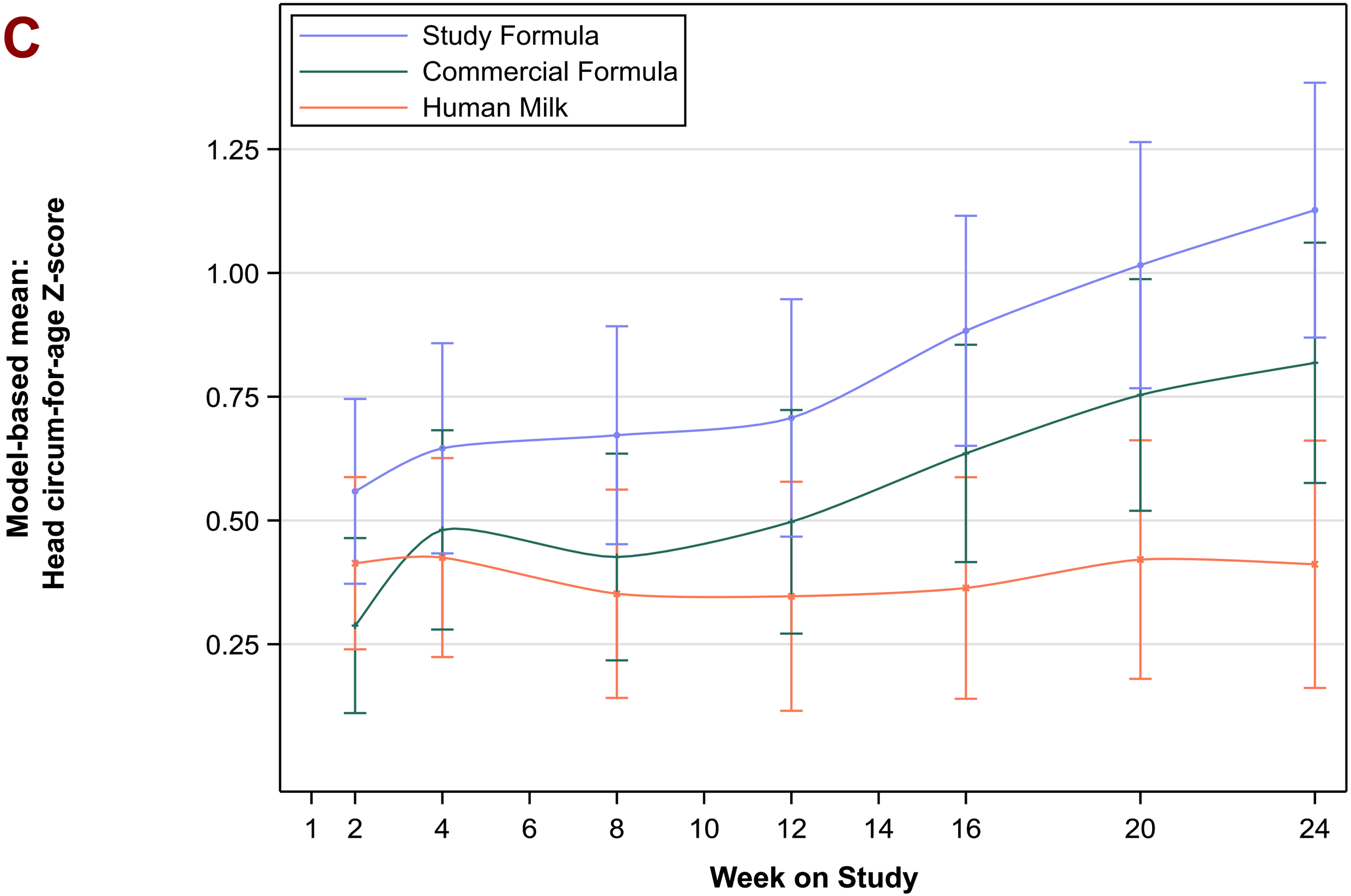

Study Formula
Commercial Formula
Human Milk
Model-based mean:
Weight-for-age Z-score
0.5
0.0
-0.5
1
2
4
6
8
10
12
14
16
20
24
Week on Study

B

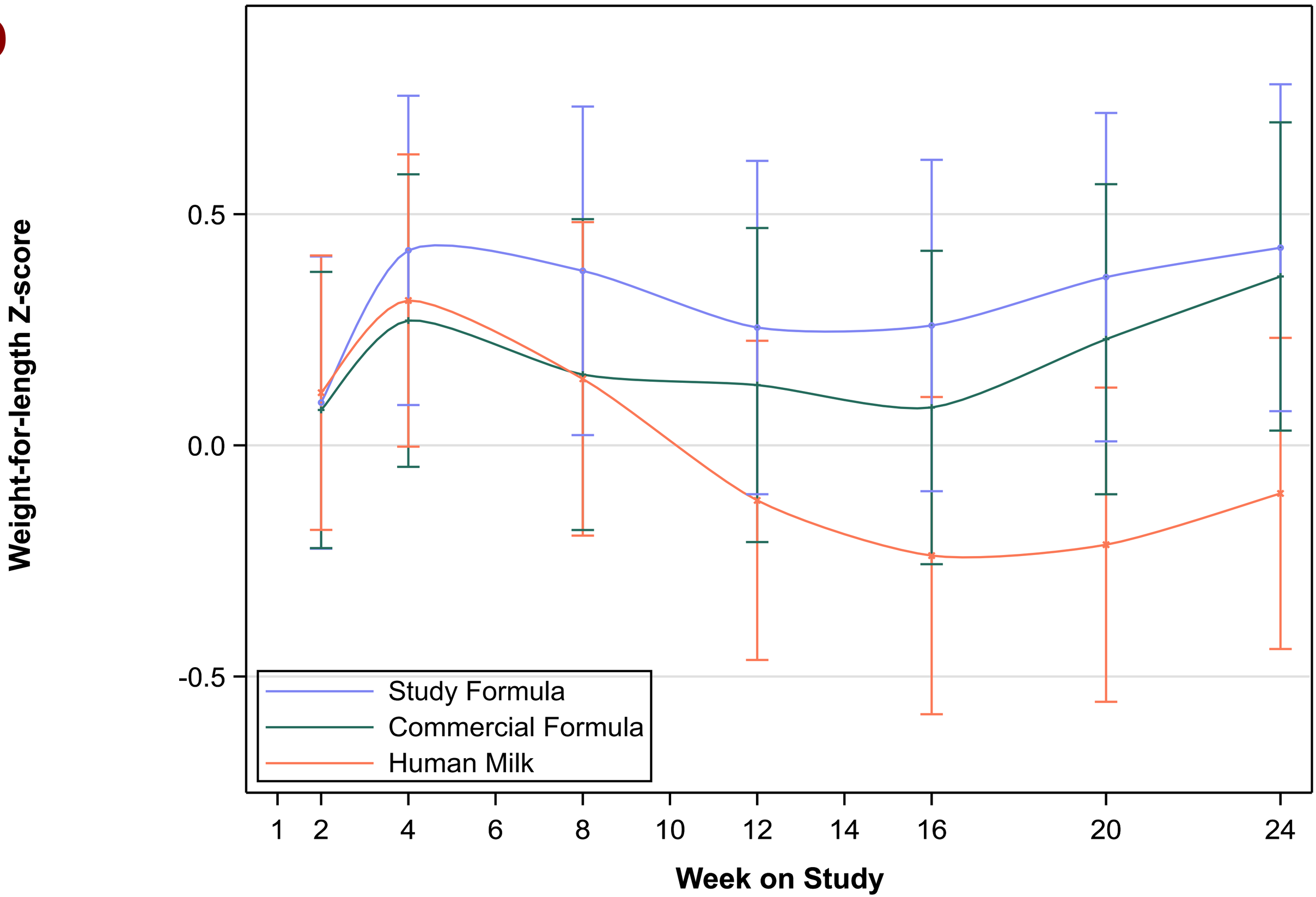


Model-based mean: Length-for-age Z-score

C


Study Formula
Commercial Formula
Human Milk
Model-based mean:
Head circum-for-age Z-score
1.25
1.00
0.75
0.50
0.25
1
2
4
6
8
10
12
14
16
20
24
Week on Study

D


Model-based mean:
Weight-for-length Z-score
0.5
0.0
-0.5
Study Formula
Commercial Formula
Human Milk
1
2
4
6
8
10
12
14
16
20
24
Week on Study

Supplemental Table 4. Adjusted Anthropometrics by Visit by Feeding Group in the PP Population

	Study Formula (n=61)	**Commercial Formula** (n=67)	**Human Milk** (n=57)
Weight (kg)			
Week 2	4.1 (0.04)	4.0 (0.04)	4.1 (0.04)
Week 4	4.7 (0.05)	4.6 (0.05)	4.6 (0.05)[b]
Week 8	5.6 (0.07)	5.5 (0.06)	5.4 (0.07)[b]
Week 12	6.3 (0.08)	6.2 (0.08)	6.0 (0.08)[b]
Week 16	7.0 (0.10)	6.9 (0.09)	6.5 (0.10)[b]
Week 20	7.6 (0.11)	7.5 (0.10)	7.0 (0.11)[b]
Week 24	8.1 (0.11)	8.0 (0.10)	7.4 (0.11)[b]
Weight-for-Age Z-Score			
Week 2	0.03 (0.07)[a]	-0.14 (0.06)	-0.09 (0.06)
Week 4	0.09 (0.08)[a]	-0.11 (0.07)	-0.14 (0.08)[b]
Week 8	0.11 (0.10)	-0.07 (0.09)	-0.26 (0.10)[b]
Week 12	0.13 (0.12)	0.03 (0.11)	-0.33 (0.11)[b]
Week 16	0.30 (0.12)	0.19 (0.11)	-0.33 (0.12)[b]
Week 20	0.44 (0.13)	0.33 (0.12)	-0.30 (0.13)[b]
Week 24	0.55 (0.13)	0.48 (0.12)	-0.26 (0.13)[b]
Weight Gain Velocity (g/d)			
Week 2	43.3 (1.71)[a]	36.6 (1.61)	40.1 (1.70)
Week 4	41.8 (1.50)[a]	37.0 (1.41)	38.0 (1.48)
Week 8	36.7 (1.33)	34.0 (1.26)	33.2 (1.30)
Week 12	32.6 (1.21)	31.2 (1.14)	29.4 (1.17)[b]
Week 16	30.3 (1.12)	29.1 (1.06)	26.6 (1.07)[b]
Week 20	28.5 (1.08)	27.5 (1.02)	24.8 (1.02)[b]
Week 24	26.5 (1.03)	25.9 (0.97)	23.0 (0.96)[b]
Length (cm)			
Week 2	52.8 (0.23)	52.5 (0.21)	52.8 (0.21)
Week 4	54.6 (0.24)	54.3 (0.23)	54.4 (0.22)
Week 8	57.8 (0.25)	57.6 (0.23)	57.4 (0.23)
Week 12	60.6 (0.27)	60.4 (0.25)	60.2 (0.25)
Week 16	63.4 (0.27)	63.3 (0.25)	62.7 (0.26)[b]
Week 20	65.3 (0.28)	65.1 (0.27)	64.3 (0.27)[b]
Week 24	67.4 (0.30)	67.1 (0.28)	65.9 (0.29)[b]
Length-for-Age Z-Score			
Week 2	-0.26 (0.11)	-0.47 (0.11)	-0.33 (0.11)
Week 4	-0.30 (0.12)	-0.47 (0.11)	-0.43 (0.11)
Week 8	-0.24 (0.12)	-0.33 (0.12)	-0.43 (0.12)

Week 12	-0.16 (0.13)	-0.26 (0.12)	-0.34 (0.12)
Week 16	0.08 (0.13)	0.02 (0.12)	-0.23 (0.12)[b]
Week 20	0.19 (0.13)	0.09 (0.12)	-0.22 (0.13)[b]
Week 24	0.35 (0.14)	0.23 (0.13)	-0.28 (0.13)[b]
Length Gain Velocity (mm/d)			
Week 2	1.7 (0.10)	1.4 (0.09)	1.5 (0.10)
Week 4	1.5 (0.06)	1.3 (0.06)	1.3 (0.06)
Week 8	1.3 (0.04)	1.3 (0.04)	1.2 (0.04)
Week 12	1.2 (0.03)	1.2 (0.03)	1.1 (0.03)
Week 16	1.1 (0.03)	1.1 (0.02)	1.1 (0.02)[b]
Week 20	1.1 (0.02)	1.0 (0.02)	1.0 (0.02)[b]
Week 24	1.0 (0.02)	1.0 (0.02)	0.9 (0.02)[b]
Weight-for-Length Z-score			
Week 2	0.09 (0.16)	0.08 (0.15)	0.11 (0.15)
Week 4	0.42 (0.17)	0.27 (0.16)	0.31 (0.16)
Week 8	0.38 (0.18)	0.15 (0.17)	0.14 (0.17)
Week 12	0.25 (0.18)	0.13 (0.17)	-0.12 (0.17)
Week 16	0.26 (0.18)	0.08 (0.17)	-0.24 (0.17)[b]
Week 20	0.36 (0.18)	0.23 (0.17)	-0.21 (0.17)[b]
Week 24	0.43 (0.18)	0.37 (0.17)	-0.10 (0.17)[b]
Head circumference (cm)			
Week 2	37.1 (0.12)[a]	36.8 (0.11)	36.9 (0.11)
Week 4	38.2 (0.13)	38.0 (0.12)	37.9 (0.12)
Week 8	39.8 (0.13)[a]	39.5 (0.13)	39.3 (0.13)[b]
Week 12	41.0 (0.15)	40.8 (0.14)	40.5 (0.15)[b]
Week 16	42.3 (0.15)	42.0 (0.14)	41.6 (0.14)[b]
Week 20	43.2 (0.16)	42.9 (0.15)	42.4 (0.15)[b]
Week 24	44.2 (0.16)	43.7 (0.16)	43.2 (0.16)[b]
Head circumference-for-Age Z-score			
Week 2	0.56 (0.09)[a]	0.29 (0.09)	0.41 (0.09)
Week 4	0.65 (0.11)	0.48 (0.10)	0.43 (0.10)
Week 8	0.67 (0.11)	0.43 (0.11)	0.35 (0.11)[b]
Week 12	0.71 (0.12)	0.50 (0.11)	0.35 (0.12)[b]
Week 16	0.88 (0.12)	0.64 (0.11)	0.36 (0.11)[b]
Week 20	1.02 (0.13)	0.75 (0.12)	0.42 (0.12)[b]
Week 24	1.13 (0.13)	0.82 (0.12)	0.41 (0.13)[b]
Head circumference velocity (mm/d)			
Week 2	1.08 (0.05)[a]	0.86 (0.05)	0.98 (0.05)
Week 4	0.94 (0.03)	0.87 (0.03)	0.87 (0.04)
Week 8	0.75 (0.02)[a]	0.69 (0.02)	0.70 (0.02)
Week 12	0.65 (0.02)	0.61 (0.02)	0.61 (0.02)
Week 16	0.59 (0.01)[a]	0.55 (0.01)	0.55 (0.01)[b]

Week 20	0.55 (0.01)[a]	0.52 (0.01)	0.51 (0.01)[b]
Week 24	0.51 (0.01)[a]	0.48 (0.01)	0.46 (0.01)[b]

Model-based means (SE), Adjusted using previously described factors plus baseline value, maternal education, income level, and maternal pre-pregnancy BMI.

[a] Significant difference between SF and CF, $p < 0.025$

[b] Significant difference between SF and HM, $p < 0.025$

Supplemental Table 5. Serum Amino Acid Concentrations (µmol/l) in a subgroup of the PP Population at Week 16 by Feeding Group

	Study Formula (n= 21)	**Commercial Formula** (n= 28)	**Human Milk** (n= 25)
Alanine	512 (145)	517 (118)	569 (166)
Arginine	112 (23)	127 (33)	127 (22)
Aspartic Acid	61 (30)	54 (28)	137 (70)
Asparagine	70 (16)	64 (11)	60 (18)
Cysteine	7 (8)	5 (7)	6.8 (5.4)
Glutamic Acid	158 (71)	140 (59)	158 (63)
Glutamine	520 (137)	543 (146)	581 (113)
Glycine	369 (166)	335 (128)	473 (266)
Histidine	120 (43)	104 (32)	151 (72)
Isoleucine	105 (24)	97 (20)	89 (29)
Leucine	150 (29)	152 (33)	142 (42)
Lysine	211 (51)	201 (44)	191 (53)
Methionine	32 (8)	33 (8)	27 (7)
Phenylalanine	76 (14)	78 (18)	75 (18)
Proline	207 (38)	221 (61)	252 (53)
Serine	423 (273)	334 (212)	617 (436)
Threonine	282 (88)	234 (70)	221 (83)
Tryptophan	96 (15)	86 (17)	78 (17)
Tyrosine	98 (22)	49 (21)	101 (28)
Valine	237 (33)	243 (47)	209 (58)

Mean (SD)

Supplemental Table 6. Gastrointestinal Tolerance by Visit by Feeding Group in the PP population

	Study Formula (n=61)[c]	**Commercial Formula** (n=67)[c]	**Human Milk** (n=57)[c]
Number of spit-ups per day, mean (SE)			
Week 1	2.2 (0.3)	2.1 (0.3)	2.3 (0.259)
Week 2	2.3 (0.3)	3.0 (0.3)	3.1 (0.304)
Week 4	2.5 (0.3)	2.9 (0.3)	3.6 (0.312)[b]
Week 6	2.7 (0.3)	3.0 (0.3)	3.6 (0.319)
Week 8	2.5 (0.3)[a]	3.4 (0.3)	3.2 (0.322)
Week 10	2.4 (0.3)[a]	3.5 (0.3)	3.1 (0.306)
Week 12	2.5 (0.3)[a]	3.4 (0.3)	3.2 (0.309)
Week 14	2.3 (0.3)[a]	3.2 (0.3)	3.1 (0.303)
Week 16	2.6 (0.3)	3.0 (0.3)	2.9 (0.302)
Week 20	2.4 (0.3)	2.6 (0.3)	2.7 (0.322)
Week 24	2.0 (0.3)	2.3 (0.3)	2.5 (0.299)
Stool Consistency Score, mean (SE)			
Week 1	3.8 (0.1)[a]	3.4 (0.1)	3.9 (0.1)
Week 2	3.8 (0.1)[a]	3.3 (0.1)	3.9 (0.1)
Week 4	3.7 (0.1)[a]	3.4 (0.1)	4.0 (0.1)
Week 6	3.7 (0.1)[a]	3.3 (0.1)	3.9 (0.1)
Week 8	3.7 (0.1)[a]	3.3 (0.1)	3.9 (0.1)
Week 10	3.7 (0.1)[a]	3.2 (0.1)	3.8 (0.1)
Week 12	3.8 (0.1)[a]	3.3 (0.1)	3.8 (0.1)
Week 14	3.6 (0.1)[a]	3.2 (0.1)	3.9 (0.1)
Week 16	3.6 (0.1)[a]	3.3 (0.1)	3.9 (0.1)[b]
Week 20	3.4 (0.1)[a]	3.1 (0.1)	3.8 (0.1)[b]
Week 24	3.3 (0.1)	3.1 (0.1)	3.5 (0.1)
Number of stools per day, mean (SE)			
Week 1	2.8 (0.2)	2.7 (0.2)	5.7 (0.3)[b]
Week 2	2.9 (0.3)	2.5 (0.2)	5.7 (0.3)[b]
Week 4	2.5 (0.3)	2.4 (0.2)	4.7 (0.3)[b]
Week 6	2.2 (0.2)	2.1 (0.2)	3.7 (0.2)[b]
Week 8	2.2 (0.3)	2.2 (0.3)	3.0 (0.3)[b]
Week 10	2.0 (0.2)	2.1 (0.2)	2.8 (0.2)[b]
Week 12	2.1 (0.2)	2.2 (0.2)	2.3 (0.2)
Week 14	2.1 (0.2)	2.0 (0.2)	1.9 (0.2)
Week 16	2.0 (0.2)	1.6 (0.2)	1.3 (0.2)[b]
Week 20	1.8 (0.2)	2.0 (0.2)	1.3 (0.2)
Week 24	1.7 (0.2)	1.8 (0.27)	1.2 (0.2)
Proportion of infants with moderate or excessive gassiness, %			
Week 1	50.8	47.7	34.6
Week 2	60.7	71.6	62.5

Week 4	73.3	74.2	75.0
Week 6	67.2	73.1	73.7
Week 8	63.3	78.5	60.7
Week 10	54.2	69.2	54.4
Week 12	57.6	65.2	50.9
Week 14	50.8	54.5	47.4
Week 16	54.7	67.6	50.0
Week 20	50.8	47.8	42.1
Week 24	52.5	47.6	26.3

[a] Significant difference between SF and CF, $p < 0.025$

[b] Significant difference between SF and HM, $p < 0.025$

[c] Number of participants for each group at each timepoint was variable between 52-71

Supplemental Table 7: Adverse Events by Feeding Group by Body System or Organ Class in the PP Population

	Study Formula (n=61)	**Commercial Formula** (n=67)	**Human Milk** (n=57)
Gastrointestinal disorders	28 (45.9)	28 (41.8)	24 (42.1)
Infections and infestations	21 (34.4)	18 (26.9)	32 (56.1)
Skin and subcutaneous tissue disorders	27 (44.3)	22 (32.8)	20 (35.1)
Respiratory, thoracic and mediastinal disorders	13 (21.3)	15 (22.4)	9 (15.8)
Congenital, familial and genetic disorders	10 (16.4)	5 (7.5)	11 (19.3)
Pregnancy, puerperium and perinatal conditions	7 (11.5)	8 (11.9)	6 (10.5)
Injury, poisoning and procedural complications	8 (13.1)	6 (9.0)	5 (8.8)
General disorders and administration site conditions	2 (3.3)	6 (9.0)	6 (10.5)
Musculoskeletal and connective tissue disorders	2 (3.3)	3 (4.5)	4 (7.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (3.3)	2 (3.0)	2 (3.5)
Metabolism and nutrition disorders	1 (1.6)	2 (3.0)	1 (1.8)
Investigations	2 (3.3)	1 (1.5)	0 (0)
Reproductive system and breast disorders	0 (0)	1 (1.5)	1 (1.8)
Cardiac disorders	0 (0)	0 (0)	1 (1.8)
Endocrine disorders	1 (1.6)	0 (0)	0 (0)
Eye disorders	0 (0)	1 (1.5)	0 (0)
Immune system disorders	1 (1.6)	0 (0)	0 (0)

Number (%)

Supplemental Table 8: Occurrence of Possibly Related Adverse Event for Each System Organ Class and Use of Concomitant Medications of the Alimentary Tract and Metabolism by Feeding Group in the PP Population

	Study Formula (n=61)	**Commercial Formula** (n=67)	**Human Milk** (n= 57)
Possibly Related Adverse Events			
Gastrointestinal disorders[b]	8 (13.1)	6 (9.0)	1 (1.8)
Skin and subcutaneous tissue disorders[c]	2 (3.3)	5 (7.5)	1 (1.8)
Pregnancy, puerperium and perinatal conditions[d]	2 (3.3)	3 (4.5)	0 (0)
Concomitant Medications			
Drugs for all gastrointestinal and metabolism conditions	22 (36.1)	28 (41.8)	34 (59.6)
Drugs for functional gastrointestinal disorders[e]	13 (21.3)	18 (26.9)	12 (21.1)
Drugs for peptic ulcer and gastroesophageal reflux disease (GERD)[f]	4 (6.6)	9 (13.4)	4 (7.0)
Drugs for constipation[g]	2 (3.3)	2 (3.0)	2 (3.5)

Number (%)

[a]Includes all AEs designated by study investigators as "Possibly", "Probably", and "Definitely" related to study formula/human milk intake

[b] Gastrointestinal Disorders includes: Flatulence, Infantile spitting up, Diarrhoea, Gastrooesophageal reflux disease, Abdominal distension, Constipation

[c]Skin and subcutaneous tissue disorders includes: Dermatitis atopic, Seborrhoeic dermatitis

[d]Pregnancy, puerperium and perinatal conditions includes: Neonatal disorder

[e] Simethicone, Gripe water

[f] Famotidine, Ranitidine

[g] Glycerol, Polyethylene glycol, Fructooligosaccharides, Magnesium hydroxide, Prune juice