Impact of Nutrient density of formula on nutritional intakes in healthy term infants; Influence of home reconstitution.

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This study, is a part of the ***GIRAFFE*** *study (**Growth of Infants who are Formula Fed Exclusively)** promoted and funded by Danone Research Utrecht, The Netherlands*

Study objective

The study is a part of a prospective, double-blind RCT investigating the nutritional efficacy and suitability of hypo-allergenic formula with lowered protein content until 16 weeks of life in healthy term infants.

- Control product: 2.27 g protein /100 kcal (*1.50 g & 66 kcal/dL*)
- Investigational product I: 2.0 g protein /100 kcal (*1.32 g & 66 kcal/dL*)
- Investigational product II: 1.8 g protein /100 kcal (*1.19 g & 66 kcal/dL*)
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- Primary study outcome of the ***GIRAFFE study*** is a weight gain equivalent to the WHO reference values.
- <u>Primary outcome of the present study is the influence of home reconstitution on nutritional intakes and growth</u>

Study design

Diary: adverse events, medication, concomitant food

Measurements of **weight**, **length**, **head circumference**
(arm circumference at 4, 12, 16 & 52 weeks)

Healthy, full-term
aged between
0 and 14 days
exclusively formula fed

Q — Bottle analysis

Q — Bottle analysis

Q — Blood sample

Body composition

3 days food intake

N=156

n=52 Investigational product with a protein content of 1.8 g/100 kcal

n=52 Investigational product with a protein content of 2.0 g/100 kcal

n=52 Control product with a protein content of 2.27 g/100 kcal

Age: baseline | **4 weeks** | 8 weeks | **12 weeks** | 16 weeks | 52 weeks

Study entry & randomisation

Q= *Questionnaire:* ***7 days formula intake****, GI tolerance*

Material and Methods

We calculated:

- Protein content of formulas: N*6.25 as well as the formula density: Fat content/Fat labeled
- Protein and energy intakes at 4 and 12 wks from chemical and labeled values considering the mean volume intake during the corresponding 7 days record.
- Weight gain between 4 and 12 wks in g, g/d, g/kg*d

We compared:

- Protein & energy intakes estimated from chemical analysis to that from labeled values.

We evaluated:

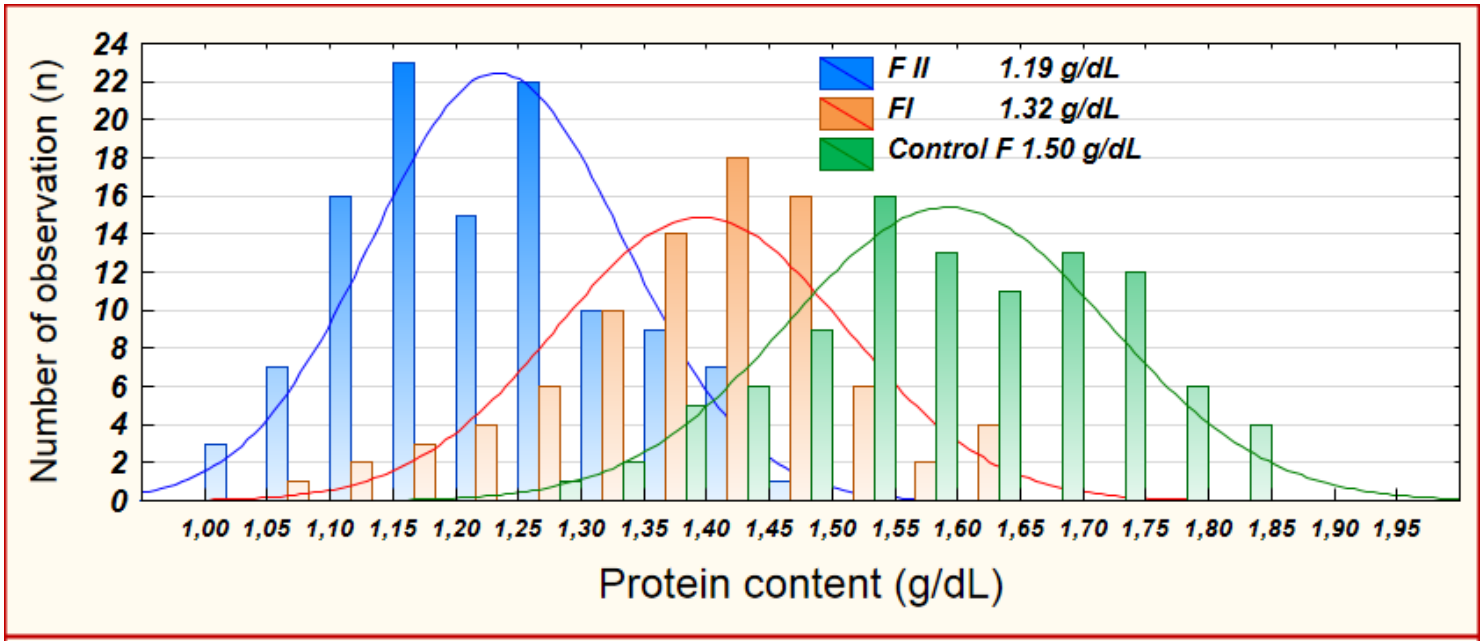
- The relationship between formula intake and the formula density.
- The influence of formula density on weight gain between 4 and 12 wks.

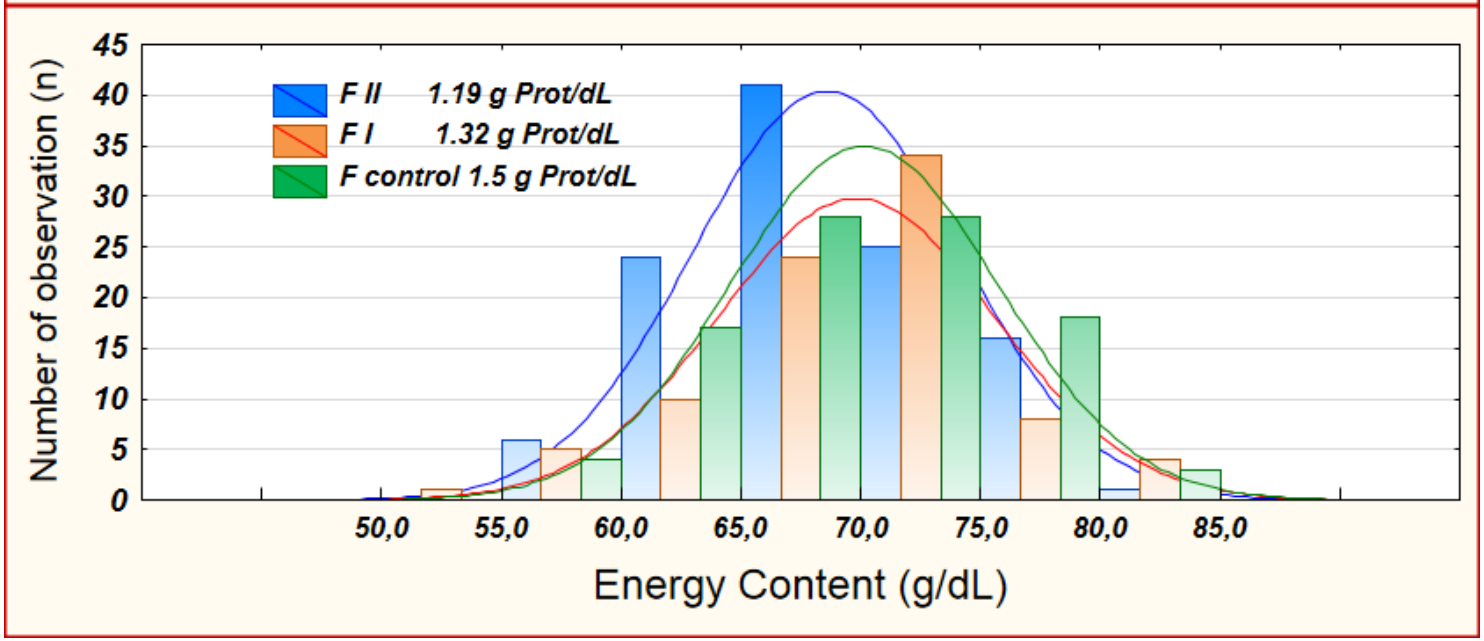
Results

- 207 subjects were included in the GIRAFFE study. Of those, 162 subjects completed the intervention period of 16 weeks (PP).
- In all, 333 bottles were collected and analyzed in our laboratory. In 6 bottled, the results of the fat and the nitrogen contents were discordant, and the results were excluded from the final analysis.
- 7 days formula intakes reported as <100 or >220 ml/kg body weight*day were considered as out of ranges (n=29) and were excluded from the final analysis (n=298).

Paired data at 4 and 12 wks were finally obtained in 129 infants.

Protein and energy content of the home prepared Bottles





n=258

Formula density range (Chem fat/label fat): **(0.87 – 1.14**) at 4wks and **(0.86 - 1.15)** at 12 wks

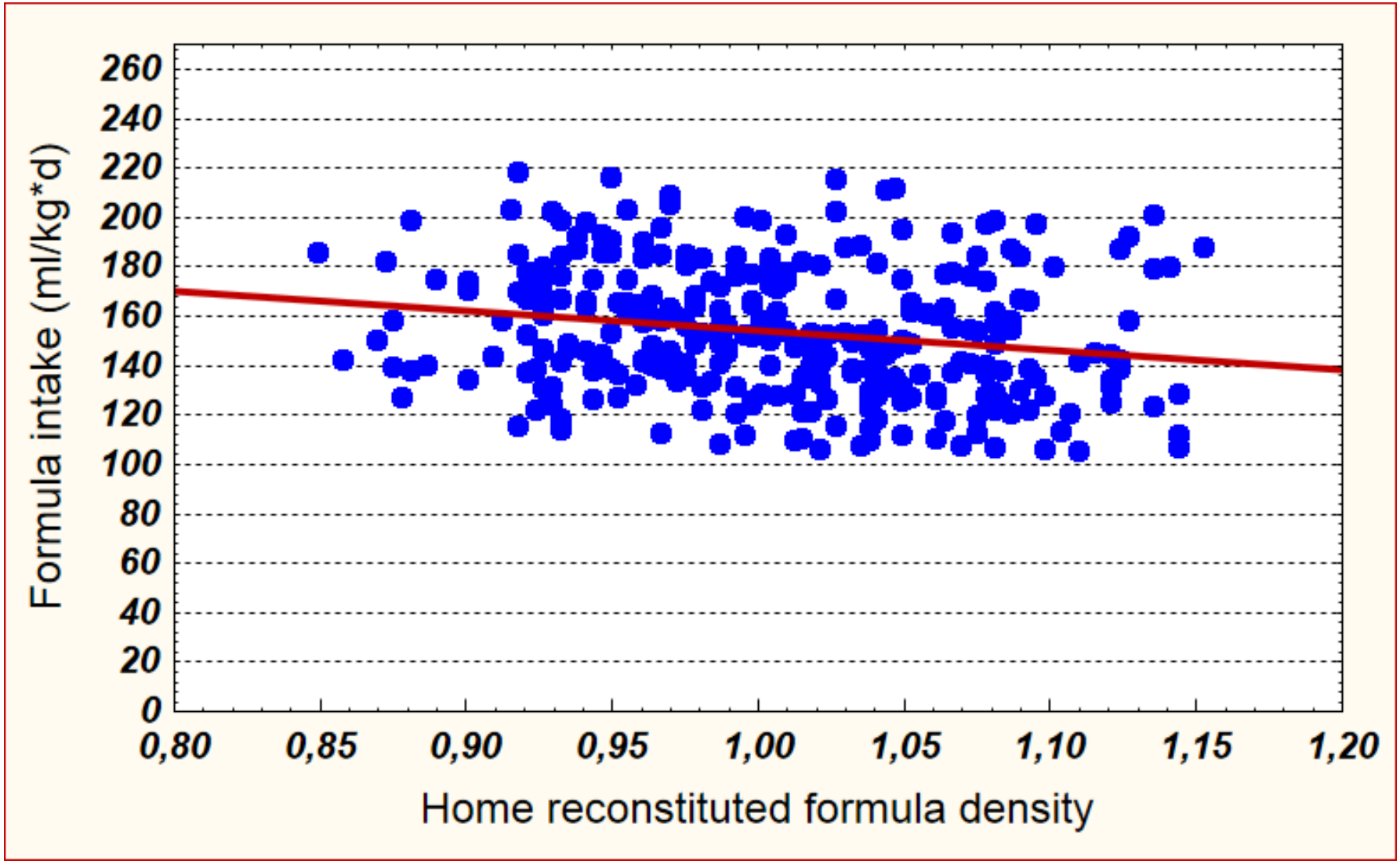
Formula and nutrient intakes at 4 and 12 wks of age

Intakes (/kg*d)	4 weeks N=129	12 weeks N=129	Paired t test
Volume (ml)	168,7 ± 23,0	137,4 ± 19,1	p<0.0001
Protein -Label	2,25 ± 0,40	1,83 ± 0,32	p<0.0001
-Chemical	2,35 ± 0,46 §	1,94 ± 0,36 §	p<0.0001
Fat -Label	5,91 ± 0,81	4,87 ± 0,67	p<0.0001
-Chemical	5,91 ± 0,88	4,81 ± 0,67$	p<0.0001
Energy -Label	111,4 ± 15,2	90,7 ±12,6	p<0.0001
-Chemical	111,4 ± 16,6	91,9 ± 12,7$	p<0.0001
Density* -label	1.00	1.00	
-Chemical (Prot.)	1,042 ± 0,080	1,064 ± 0,087	p=0.001
-Chemical (Fat)	1,002 ± 0,068£	1,016 ± 0,062$	p=0,014
Range	**(0.87 – 1.14)**	**(0.86 - 1.15)**	

$ p<0.05; £ p<0.005; § p<0.0001

* The difference between the calculated fat density and protein density could be the result of a laboratory slight overestimation of the nitrogen content or to the use of an inadequate conversion factor: ***Prot= N*6.25***

Relationship between volume intakes and the formula density

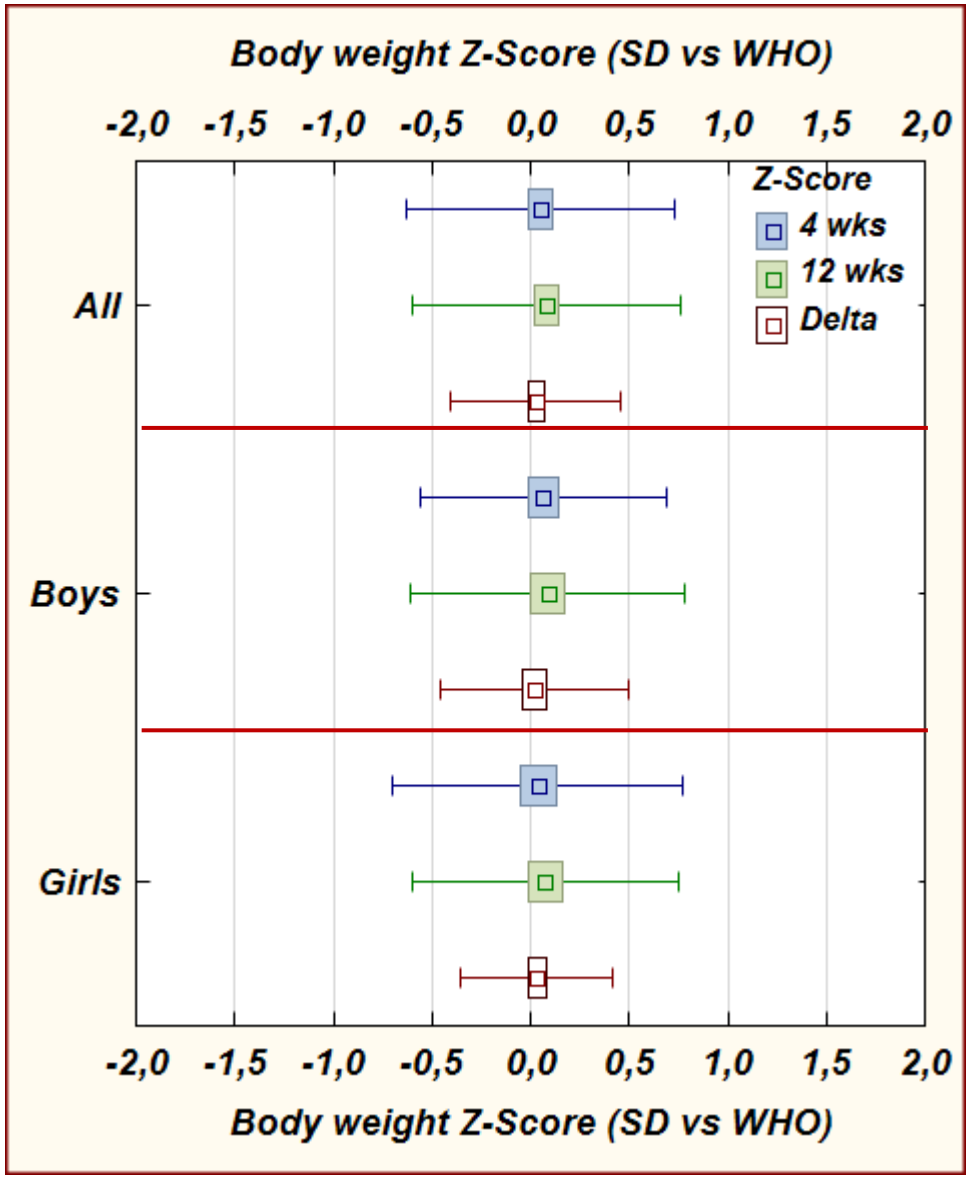


Vol intake (ml/kg*d)= -0.789 * Formula density + 233.2; r=0.20; p= 0.00057; n=298

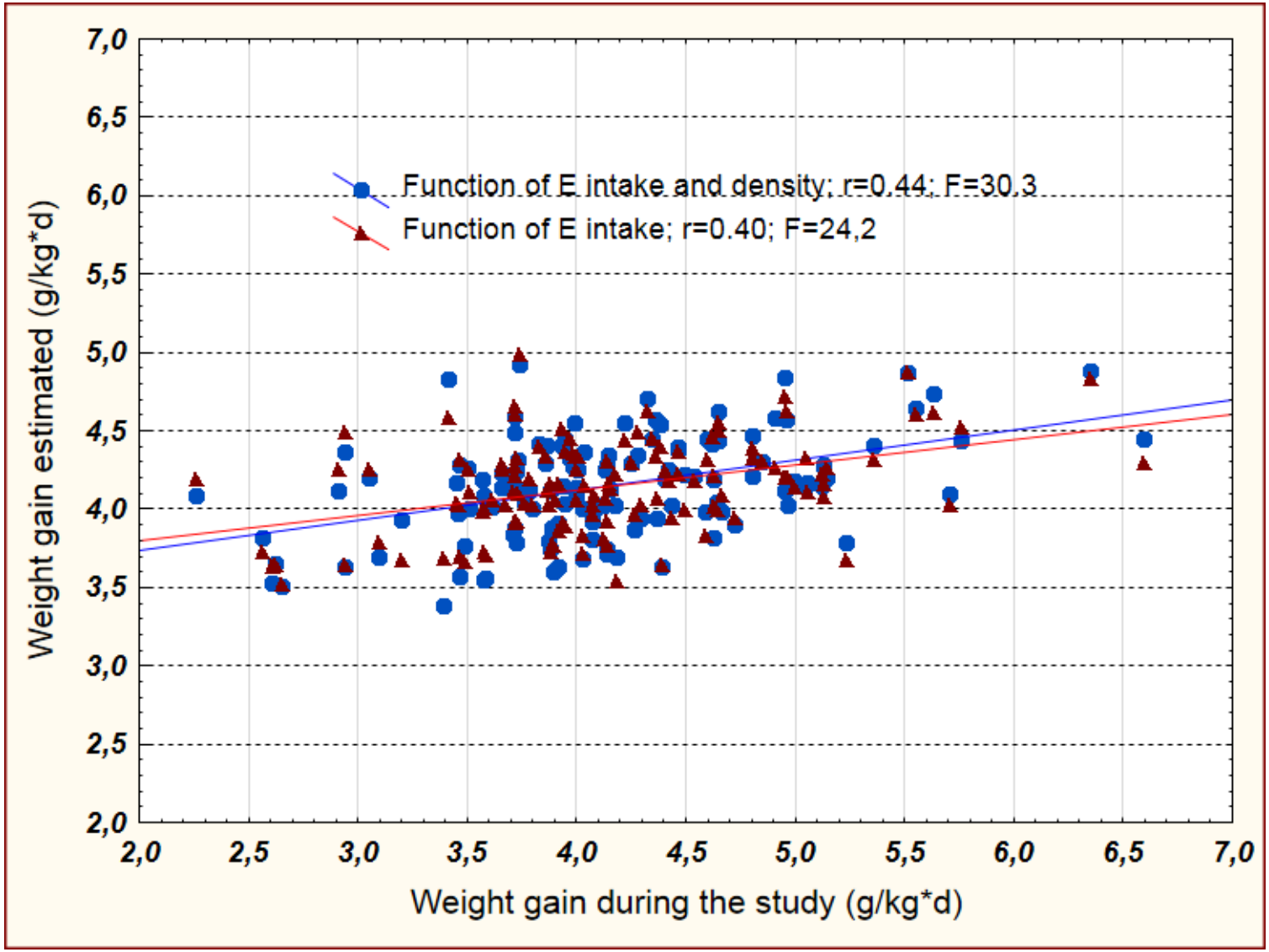
Weight gain during the Study

Weight gain 4 to 12 wks	Girls n=65	Boys n=64	Total n=129
Kg/study	1.59±0.37	1.80±0.40[c]	1,68±0,38
g/d	27.8±5.1	31.5±7.0[c]	29,6±6,4
g/kg*d	3.96±0.64	4.34±0,79[c]	4,15±0,74
Prot g/dl	1.37±0.18	1.46±0,19[c]	1.39±0.18
BW at 4 wks (g)	4,073±0,492	4,323±0,426[c]	4.197±0,475

Body weight Z-Scores compared to WHO Values



Relationship between weight gain and E intake (F=24.2) is improve when and F density is included in the relation (F=30.3)



WG= WG (g/kg*d=O.029*E intake (labelled)+ 2.43* F density – 1.236;
n=129;r=0.44; p E int<O.OOOOO1; p F density=0.026

In conclusion

Our study suggests:

- *The reconstitution procedure at home significantly influences the nutrient density of the studied formulas.*
- *Density of powder formula is an additional factor to volume intake to be considered in nutritional studies. It could also influence the sample size evaluation.*
- *Formula intakes at 4 and 12 wks are inversely related to the formula density.*
- *Weight gain is related to energy intakes but also to formula density that needs to be considered as an additional factor.*

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Reconstitution procedure needs to be take into account in the interpretation of the results in nutritional studies using powder formula in healthy term infants.