

# Effect of Growing Up Milk containing scGOS/lcFOS/n-3 LCPUFA on the Occurrence of Infections in Young Children attending Day Care Centers

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## Introduction and objectives

Young children attending day care centers are at higher risk for developing respiratory and gastrointestinal infections than children who stay at home (ref 1).

A mixture of short-chain galactooligosaccharides and long-chain fructooligosaccharides (scGOS/lcFOS) has been shown to positively affect the development of the immune system (ref 2, 3).

Adequate dietary n-3 LCPUFA is probably the most limiting factor and most critical to meet the requirements of balanced immune development and function during childhood.

The immune system is constantly developing over lifetime but the 3 first years are the most important. The supplementation of a Growing Up Milk (GUM) with added scGOS/lcFOS/n-3 LCPUFA might contribute to a beneficial effect on the development of the immune system.

In this study we evaluated whether a GUM with added scGOS/lcFOS/n-3 LCPUFA had an effect on the occurrence of infections in healthy young children.

## Subjects and Methods

The study (GIANT) was performed as a randomized double blind controlled parallel multi country intervention trial. The 13 participating study centers were from 5 countries: Poland, Portugal, Malaysia, The Netherlands and Thailand.

**Inclusion criteria:** Healthy subjects between 11 and 29 months of age attending a daycare center.

A total of 907 subjects were screened, 767 were randomized into one of the 2 study groups: an active group, n= 388, receiving GUM with scGOS/lcFOS/n-3 LCPUFA; and a control group n=379, receiving GUM without scGOS/lcFOS/n-3 LCPUFA for a period of 52 weeks, after a 4 week run in period. Subjects were asked to consume 500 ml study product, resulting in a daily intake of 6 g scGOS/lcFOS and 96 mg n-3 LCPUFA.

During intervention, the parents of participating subjects completed a daily diary on compliance of study product intake and occurring illness symptoms. Symptoms were categorized into upper respiratory tract infections (URTI) and gastrointestinal infections (GII) and both were combined as infections.

### Statistical analyses:

Results on the primary parameter were obtained from a Zero-inflated Negative Binomial (ZINB) Regression Model. This model combines two separate parts: A. a (binomial) part whether or not a subject would get an infection and B. a (negative-binomial) part fitting the counts for infections for the subjects.

## Results

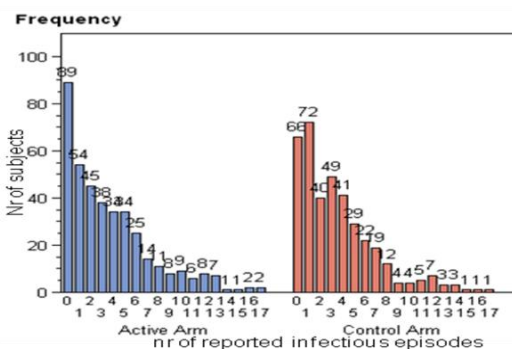


Figure 1. Descriptive statistics for nr of reported episodes during intervention period per arm.

The frequency distribution for the number of reported episodes, showed a skewed distribution in both groups of the ASR (all subjects randomized) population (fig. 1).

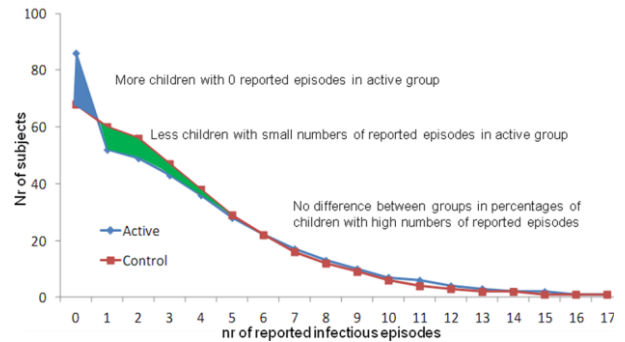


Figure 2. Graph showing nr of subjects with nr of infections for active and control arm, based on prediction from ZINB regression model.

This skewed distribution was taken into account during the analysis phase by using a ZINB regression model (fig. 2).

Model part	p-value
Part A: Yes/No infectious episodes	0.03
Part B : $\geq 1$ infectious episodes	0.17
<b>Overall</b>	<b>0.07</b>

Table 1. Observed p-values for the study arm in the regression model. More subjects in the active group had no infectious episodes and a trend was observed for overall infectious episodes.

Children in the active group compared with the control group had a decreased risk of developing at least one infection ( $p= 0.03$ ). Looking at the total number of infections, the combined model showed a trend towards significance ( $p=0.07$ ) for a reduction in the occurrence of infections in the active group (table 1).

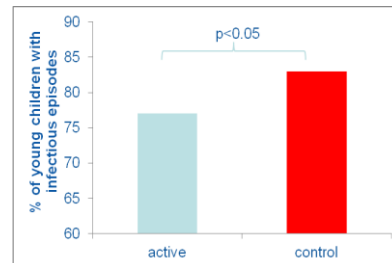


Figure 3. Active group had higher chance of having no infectious episodes in a logistic regression model.

An additional logistic regression analysis was performed in which the chance of having at least one reported episode was modeled against the chance of having no reported episode  $p$ -value  $< 0.05$  (fig 3). This is in line with the results in the binomial part of the ZINB model. Relative risk = 0.93 with a 95% CI 0.87-1.

Furthermore post hoc analyses were performed to check for differences when URTI and GII were analysed separately. No effect was observed, indicating that both contributed to the observed effect.

## Conclusion

- This is the first study in children to show a reduced risk of infection following consumption for 1 year of GUM-supplemented scGOS/lcFOS/n-3 LCPUFA.
- The reduction in the occurrence of infections was of borderline significance.

## References

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