everidis®
HEALTH SCIENCES

CLINICAL TRIALS

A **Great Start** to **Life!**

L. reuteri* Protectis®– A Proven & Safe Probiotic for Mom & Baby

for Healthcare Professionals

Contents

INTRODUCTION

L. reuteri Protectis Promoting a Healthy GI Microbiota*

The *first* 1,000 days of life – the period from conception to 2 years of age – **represents a *critical* period for baby's developing microbiota.**[1]

L. reuteri Protectis is:

An Intergenerational Probiotic

Passed from generation to generation during childbirth and breastfeeding, ***L. reuteri*** **is an indigenous probiotic** whose *natural* habitat is the human body.[2]

Significant for Health*

L. reuteri* has co-evolved with humans** since the beginning of time.[2,3] Humans have a **symbiotic relationship with *L. reuteri that is *significant* for health.*[2]

Proven & Safe*

More than 150 clinical trials have shown the **safety & health-promoting effects** of ***L. reuteri*** **Protectis.***

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

SECTION 1

L. reuteri Protectis Gastrointestinal Health Clinical Trials

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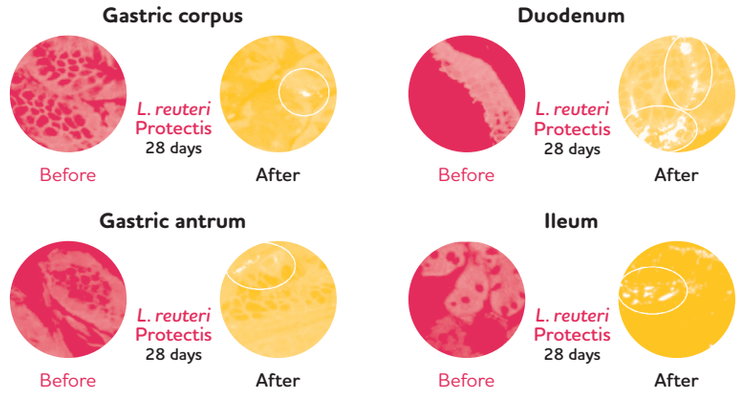
Colonizes the Entire **GI Tract***[4]



***L. reuteri* Protectis** colonies on biopsy specimens taken before and after supplementation.

Promotes a Healthy Microbiota in **Colicky Babies***[5]

< Significantly ***reduced*** ***E. coli*** in colicky infants (p=0.001)

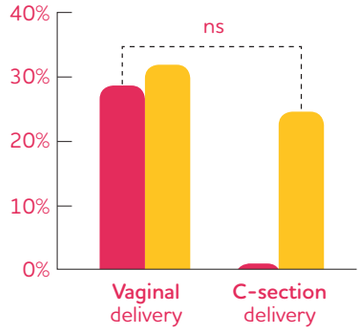
> Significantly ***increased*** **lactobacilli** in colicky infants (p=0.002)

Study design:
R, C, DB.

Intervention:
***L. reuteri* Protectis** once daily for 21 days in 50 colicky infants (age 2-16 weeks). **Savino, et al 2010.**

Promotes a Healthy Microbiota in **Babies Born Via C-Section***[6]

Proportion of **Bifidobacterium** in microbiota at **2 weeks** of age



Formula + *L. reuteri*
Control formula

Study design:
MC, DB, C, R.

Intervention:
Formula containing ***L. reuteri* Protectis**, equivalent to the standard dose, for the first 6 months of life in 40 infants (age <72 hours) delivered via C-section and vaginally. **Rodenas, et al 2016.**

C = Controlled DB = Double blind MC = Multicenter R = Randomized

Helping baby
experience fewer
GI symptoms.*

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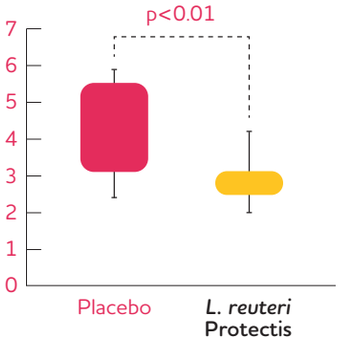
Improves Gastrointestinal **Motility***[7]

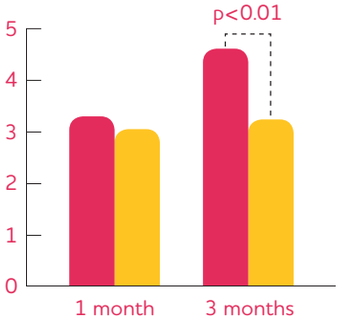


L. reuteri
Placebo

Study design:
R, DB, PC, PG.

Intervention:
L. reuteri Protectis once daily for 30 days in 42 infants (age <4 months). **Indrio, et al 2011.**

Reduces the Frequency of **Regurgitation***[8]

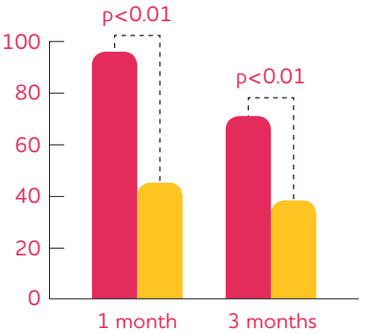


L. reuteri
Placebo

Study design:
MC, DB, PC, R.

Intervention:
L. reuteri Protectis once daily for 3 months in 589 full-term newborns (age <1 week). **Indrio, et al 2014.**

Reduces the Incidence of **Colic***[8]



L. reuteri
Placebo

Study design:
MC, DB, PC, R.

Intervention:
L. reuteri Protectis once daily for 3 months in 589 full-term newborns (age <1 week). **Indrio, et al 2014.**

DB = Double blind **MC** = Multicenter **PC** = Placebo controlled **PG** = Parallel group **R** = Randomized

CRITICAL QUESTION

Are Babies **Born** *with Colic?*

Infant colic impacts the ***whole*** **family.**

Besides baby's presumed suffering, **colic is linked to maternal anxiety and depression,** *disrupts* the establishment of the mother-baby bond, *interferes* with breastfeeding and *contributes* to family dysfunction.[9, 10]

It is known that the **GI microbiota** is associated with infant colic, as babies with colic have *lower* levels of **lactobacilli** and *higher* levels of ***E. coli*** compared to non-colicky infants.[5]

It has been shown that **alterations** in the bacterial composition of the **maternal GI microbiota** can affect the development and function of **baby's GI tract.**[11] ***Could colic be the result of a disrupted maternal GI microbiota?***

The mother's microbiota is important for **baby's health.**

Maternal Antibiotic Use

It has been shown that exposure to antibiotics during pregnancy or delivery is associated with **infantile colic.** It is thought that maternal antibiotic exposure may *disrupt* the initial colonization of maternal microbes and thus be causally related to the development of colic.[10]

Prenatal Probiotic Supplementation

It is known that the probiotic ***L. reuteri*** is an effective treatment **for infantile colic,** but ***can colic be prevented?****
Studies now show that **prenatal supplementation** with probiotics **can *prevent*** the occurrence and ***reduce* the severity** of infantile colic.*[12, 13]

The Meconium Microbiome

In addition, the **microbiome** of the first-pass meconium has been associated with **colic.** Infants who subsequently developed colic had a *lower* abundance of **lactobacilli** in their the first-pass meconium than non-colicky infants.[14]

The *Most* Clinically Studied Probiotic for **Colic**

Eight
Colic Treatment Studies[5, 15-21]

- ***Significant*** **reduction** in daily crying & fussing, ***improved*** the well-being of mom and baby, high parental satisfaction rate*

Two
Colic Prevention Studies[8, 22]

- ***Significant*** **reduction** in daily inconsolable crying time, ***reduced*** formula use, ***improved*** breastfeeding rates, saved families money*

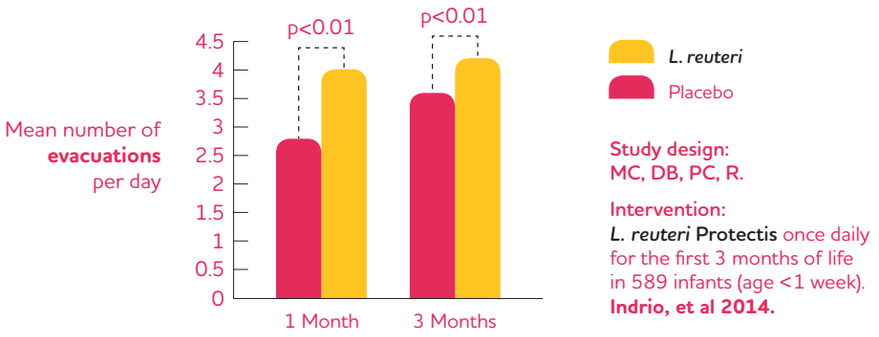
Nine
Meta-Analyses[23-31]

- ***L. reuteri*** **DSM 17938** is the ***only*** probiotic proven effective in infantile colic, especially in exclusively or predominantly breastfed infants*

Four
International Clinical Guidelines[32-35]

- ***Supports*** **the use of *L. reuteri* Protectis** for functional gastrointestinal disorders in infants*

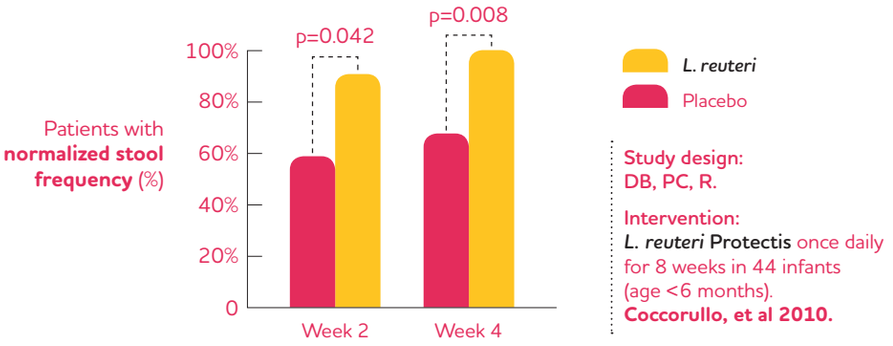
Promotes Regular **Bowel Movements***[8]



Study design:
MC, DB, PC, R.

Intervention:
L. reuteri **Protectis** once daily for the first 3 months of life in 589 infants (age <1 week).
Indrio, et al 2014.

Increases Stool Frequency in **Constipated Infants***[36]



Study design:
DB, PC, R.

Intervention:
L. reuteri **Protectis** once daily for 8 weeks in 44 infants (age <6 months).
Coccorullo, et al 2010.

DB = Double blind **MC** = Multicenter **PC** = Placebo controlled **R** = Randomized

SECTION 2

L. reuteri Protectis
Immune Health
Clinical Trials

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More
healthy days
for baby.*

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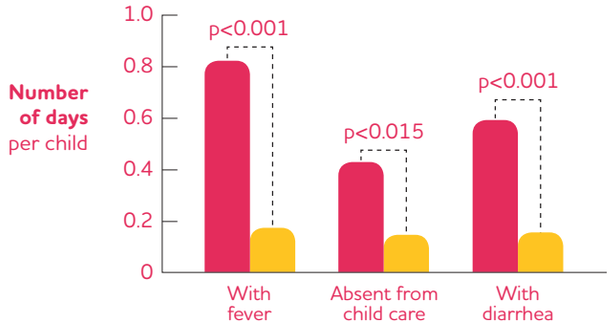
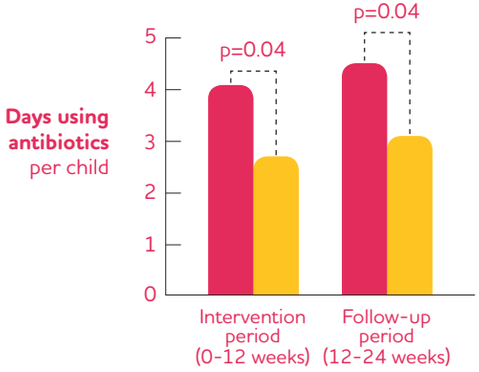
Fewer Days with Fever, Diarrhea and **Less Absence** from **Day Care***[37]



Study design:
R, DB, PC.

Intervention:
***L. reuteri* Protectis** once daily for 12 weeks in 201 formula fed babies (age 4-10 months).
Weizman, et al 2005.

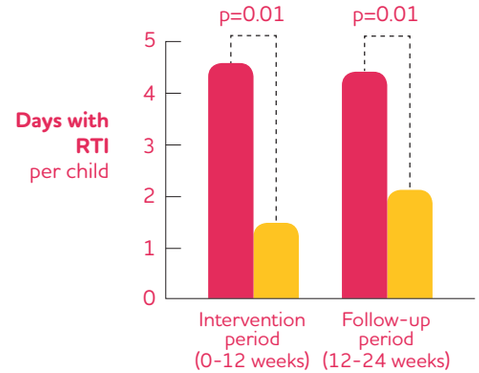
Fewer Days on **Antibiotics***[38]



Study design:
R, DB, PC.

Intervention:
***L. reuteri* Protectis** once daily for 3 months with a follow-up at 6 months in 336 healthy children (age 6-36 months).
Gutiérrez, et al 2014.

Fewer Days with **Respiratory Tract Infections***[38]



Study design:
R, DB, PC.

Intervention:
***L. reuteri* Protectis** once daily for 3 months with a follow-up at 6 months in 336 healthy children (age 6-36 months).
Gutiérrez, et al 2014.

DB = Double blind **PC** = Placebo controlled **R** = Randomized

CRITICAL QUESTION

Does the Mother's Microbiota ***Influence*** *the Development of* ***Allergic Disease?***

Allergic diseases including atopic dermatitis, food allergy, rhinitis, and asthma typically manifest in early childhood. Although genetic factors play a role, **changes in the genotype cannot explain the rapid *increase* in the prevalence of allergy** in affluent countries.

Microbial contact in early life is *essential* for the **development and maturation of the immune system.**[39] *Is our modern lifestyle affecting the transmission and composition of* ***baby's microbiota*** *and thus giving rise to allergic disease?*[39,40]

Maternal Family Life

Exposure to a traditional farm environment during **pregnancy** demonstrates ***stronger*** **protection** against allergy development in baby than postnatal exposure alone.[41-43]

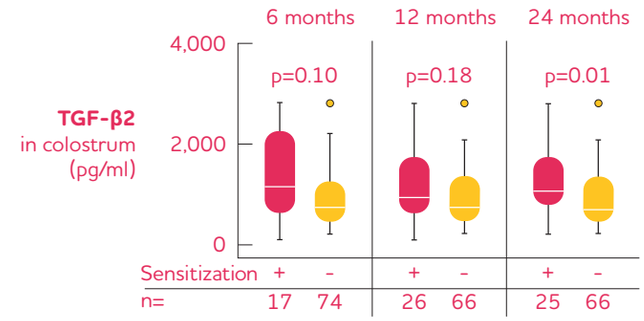
Maternal Antibiotic Exposure

Antibiotic use during pregnancy is associated with an ***increased*** **risk of allergy** and **asthma development.**[41,44]

Prenatal Probiotic Supplementation

Pre- and postnatal probiotic use is necessary to *reduce* the **risk of atopic dermatitis in infants** as supplementation to the baby alone seems to be *ineffective.*[41,45-47]

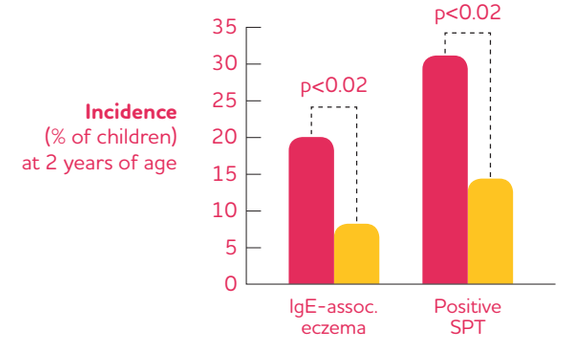
Less Sensitization at **2 Years of Age***[48]



Study design:
DB, PC, AP.

Intervention:
L. reuteri **Protectis** once daily from gestational week 36 until delivery in 109 pregnant women in families with a history of allergic disease, followed by the same dose in the infants for 12 months, with follow-up at 2 years.
Bottcher, et al 2014.

Reduced IgE-associated Eczema at **2 Years of Age***[49]



Study design:
DB, R, PC.

Intervention:
L. reuteri **Protectis** once daily from gestational week 36 until delivery in 188 pregnant women in families with a history of allergic disease, followed by the same dose in the infants for 12 months, with follow-up at 2 years.
Abrahamsson, et al 2013.

AP = Allergy prevention **DB** = Double blind **PC** = Placebo controlled **R** = Randomized

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