Microbiote

Y a t'il aujourd'hui des conséquences thérapeutiques de l'évolution des connaissances ?

Marc Bellaïche
Robert Cohen

Parmi les propositions suivantes concernant les probiotiques lesquelles vous paraissent démontrées ?

1. Réduction de la diarrhée liée aux antibiotiques
2. Amélioration des symptômes de la maladie de Crohn
3. Amélioration des symptômes de l'intestin irritable
4. Amélioration des symptômes des gastro-entérites

Parmi les propositions suivantes concernant les probiotiques lesquelles vous paraissent démontrées ?

1. Réduction des infections ORL
2. Réduction du nombre de jours de traitement antibiotique
3. Réduction de l'absentéisme en collectivité
4. Réduction des infections digestives

Parmi les propositions suivantes concernant les probiotiques lesquelles vous paraissent démontrées ?

1. Réduction du risque d'infection nosocomiale
2. Réduction du risque d'entérocolite
3. Septicémies liées aux germes contenus dans les probiotiques
4. Meilleure réponse vaccinale

Liens d'interets

danone, nestlé, picot, mead johnson, pediact, laudavie, biocodex, sodilac, pileje

Docteur, j'en peux plus, mon Djibril, 2 mois,il rote, il péte, il dort pas, il régurgite, il a mal, il hurle, il mange bien puis pas bien. On est sous « lait sans lait », eaux de chaud, IPP, anti acides. On a fait 6 séances d'ostéopathie. La maman vous implore à l'aide ….

A. Je prescris double dose d'IPP
B. Je prescris des amino-acides
C. Je prescris un abonnement chez le psy
D. Je demande à la grand-mère de s'en occuper
E. Et si je prescrivais des probiotiques, comme la mère me le demande !!!…

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(IN)FORMATION sur les probiotiques

Gérer ambiguïté de l'aspect médical et de l'aspect commercial

La Visite Médicale partage avec les Valeurs Médicales le même concept

Un art qui obéit à des normes très strictes

Visiteurs qui débarquent d'un autre temps

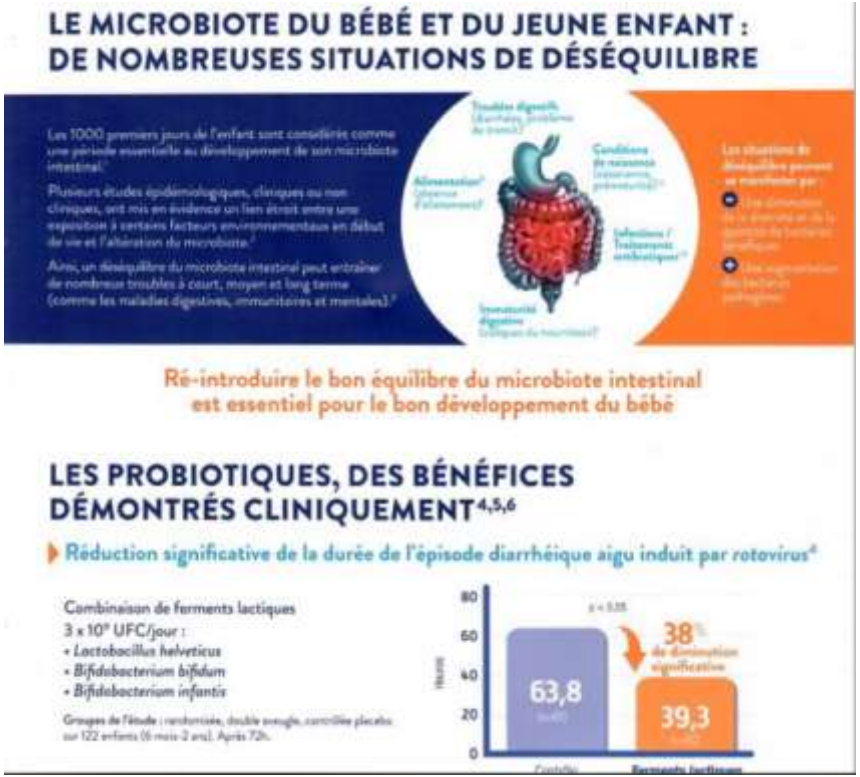
HIATUS entre le VM et le MT

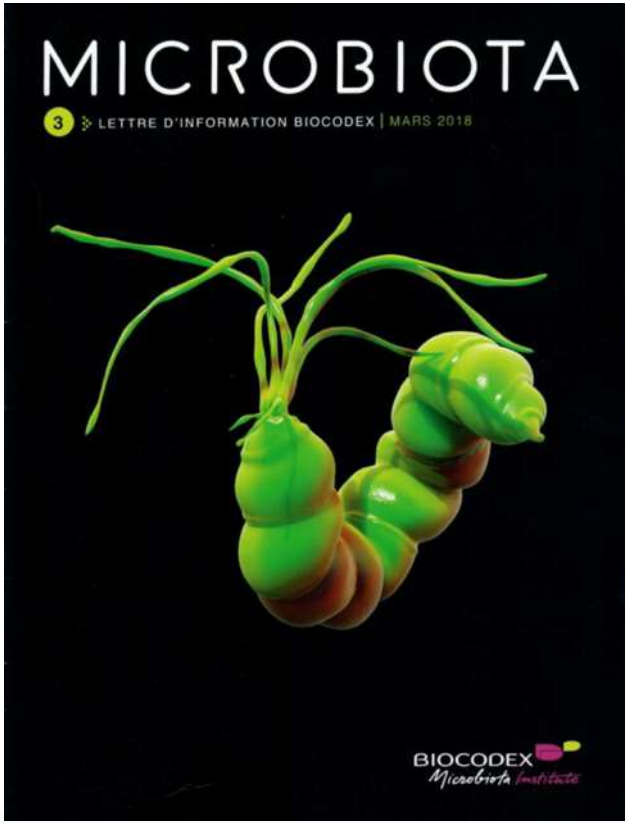
Visuellement au **M**ieux

Médecin aux **T**raits tirés

Microbiote


BIOSTIME INSTITUTE
NUTRITION & CARE
GENEVA
LES PROBIOTIQUES : DES BÉNÉFICES DÉMONTRÉS PAR DES ÉTUDES CLINIQUES[1,2,3]
Synthèse des résultats des études
1. Canani et al. Efficacy of a synbiotic supplementation in the prevention of common winter diseases in children: a randomized, double-blind, placebo-controlled pilot study. Ther Adv Respir Dis. 2010 ;4(5):271-278.
2. Stojanovic et al. Experimental study (consort compliant): Optimal time period to achieve the effects on synbiotic-controlled wheezing and respiratory infections in young children. Srp Arh Celok Lek. 2010 ;144(1-2):38-45.
3. Cui et al. The treatment of 62 cases of rotavirus gastroenteritis by probiotics. Chinese J. of General Med. 2003 ;5(5):53-54.
Ce document est une synthèse de données scientifiques fournie à titre d'information sur la base d'études scientifiques publiées.
Ce document n'a pas de caractère commercial.
Il est réservé exclusivement à l'usage du corps médical et paramédical.


LE MICROBIOTE DU BÉBÉ ET DU JEUNE ENFANT : DE NOMBREUSES SITUATIONS DE DÉSÉQUILIBRE
Les 1000 premiers jours de l'enfant sont considérés comme une période essentielle au développement de son microbiote intestinal.
Plusieurs études épidémiologiques, cliniques ou non cliniques, ont mis en évidence un lien étroit entre une exposition à certains facteurs environnementaux en début de vie et l'altération du microbiote.
Ainsi, un déséquilibre du microbiote intestinal peut entraîner de nombreux troubles à court, moyen et long terme (comme les maladies digestives, immunitaires et mentales).
Troubles digestifs
Conditions de naissance
Alimentation
Infections / Traitements antibiotiques
Immaturité digestive
Les situations de déséquilibre peuvent se manifester par :
Ré-introduire le bon équilibre du microbiote intestinal est essentiel pour le bon développement du bébé
LES PROBIOTIQUES, DES BÉNÉFICES DÉMONTRÉS CLINIQUEMENT[4,5,6]
Réduction significative de la durée de l'épisode diarrhéique aigu induit par rotavirus[4]
Combinaison de ferments lactiques
3 x 10⁹ UFC/jour :
• Lactobacillus helveticus
• Bifidobacterium bifidum
• Bifidobacterium infantis
Groupes de l'étude : randomisée, double aveugle, contrôlée placebo sur 122 enfants (6 mois-2 ans). Après 72h.
p = 0,05
38 % de diminution significative
63,8
39,3
Heure
80
60
40
20
0
Contrôle
Ferments lactiques


MICROBIOTA
3 LETTRE D'INFORMATION BIOCODEX | MARS 2018
BIOCODEX
Microbiota Institute


SYNTHÈSE
TRAITEMENT ANTIBIOTIQUE CHEZ LE NOURRISSON : CONSÉQUENCES À COURT ET À LONG TERMES SUR LE MICROBIOME

LA REVUE DES
MICROBIOTES

Le premier journal français consacré aux microbiotes et à leurs répercussions en santé humaine

L'impact médical de ces micro-organismes vous intéresse ?

La revue des Microbiotes présente les dernières actualités dans la recherche sur les microbiotes, analysées et commentées par notre comité rédactionnel pluridisciplinaire.

La revue des Microbiotes, c'est :

- Une plume indépendante, au service de l'information scientifique
- Pour chaque numéro, 24 pages dédiées à la connaissance des microbiotes :
  - Dossiers thématiques (Microbiotes et allergies, Microbiote et obésité...)
  - Commentaires d'abstracts des derniers congrès
  - Des interviews d'experts
  - Des focus sur les publications récentes...
- 3 numéros par an : mars, juin, octobre
- Pour plus de renseignements : **abonnement@microbiotes.com**

Composition du comité rédactionnel :

- **Pr Jacques Amar,** cardiologue, CHU Toulouse, Consultant scientifique de VAIOMER, Labège.
- **Dr Marc Bellaiche,** pédiatre, Service des maladies digestives de l'enfant, Hôpital Robert Debré, Paris.
- **Dr Jean-Marc Bohbot,** infectiologue, Institut Alfred Fournier, Paris.
- **Pr Stanislas Bruley des Varannes,** gastro-entérologue, Institut des maladies de l'appareil digestif, Nantes.
- **Pr Pierre Desreumaux,** hépato-gastro-entérologue, Directeur du Centre de Recherche sur l'Inflammation (LIRIC) INSERM 995, Lille.
- **Dr Philippe Gérard,** microbiologiste, INRA, MICALIS UMR 1319, Jouy-en-Josas.
- **Dr Cyrille Hoarau,** immunologiste et allergologue, Unité transversale d'allergologie et immunologie clinique, CHRU, Tours.
- **Dr Alexis Mosca,** pédiatre, Service des maladies digestives de l'enfant, Hôpital Robert Debré, Paris.
- **Pr Bruno Pot,** PhD, microbiologiste, Institut Pasteur de Lille, CNRS, Lille.
- **Pr Patrick Vermersch,** neurologue, Service neurologie, CHRU, Lille.

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Microbiote

LA NAISSANCE DE NOTRE MICROBIOTE

10/09/2018

Microbiote : les probiotiques de l'alimentation, pas si bénéfiques que ça

Très en vogue, les probiotiques de l'alimentation ne seraient pas aussi efficaces qu'on le croit, suggèrent deux nouvelles études parues dans la revue Cell.

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10/09/2018

Microbiote : les probiotiques de l'alimentation, pas si bénéfiques que ça

Très en vogue, les probiotiques de l'alimentation ne seraient pas aussi efficaces qu'on le croit, suggèrent deux nouvelles études parues dans la revue Cell.

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Le dossier | Parole d'expert | Vidéo

LE DOSSIER

Probiotiques : quelle efficacité ?

Microbiote

LE FIGARO

Digestion : les probiotiques sont-ils efficaces ?

Réagir Recommander

SANTÉ - Deux études sèment le doute sur la capacité de ces bactéries à rééquilibrer la flore intestinale, même si elles sont bénéfiques lors de la prise d'antibiotiques.

Des bactéries réduisent les risques d'infections mortelles des nouveaux-nés

Réactions (13) Recommander

FIGARO SANTÉ Une étude réalisée en Inde montre que des probiotiques donnés après la naissance réduisent spectaculairement le risque de septicémie.

Maladie de Crohn : quand nos excréments viennent au secours des malades

FUTURA SANTÉ Explorer Vidéos Photos Experts Forum Promos

Le dossier Parole d'expert Vidéo

LE DOSSIER

Probiotiques : quelle efficacité ?

M Sciences

Sciences Vidéos Archéologie Astronomie Biologie Cerveau Géophysique Les défis de la science

> Découvrir l'application

ARTICLE SÉLECTIONNÉ DANS LA MATINALE DU 18/07/2018

Alerte mondiale à la fausse science

Des dizaines de revues scientifiques produisent et éditent des études peu scrupuleuses se retrouvant ensuite dans des banques de données servant de base à des experts.

Medscape Infectious Diseases

Perspective > Medscape Gastroenterology

Microbiome Profiling: Big Business, but What About the Data?

John Watson

TFI

Candidose

C. difficile

Susceptibilité aux infections digestives

Susceptibilité aux infections extra-digestives

Allergies

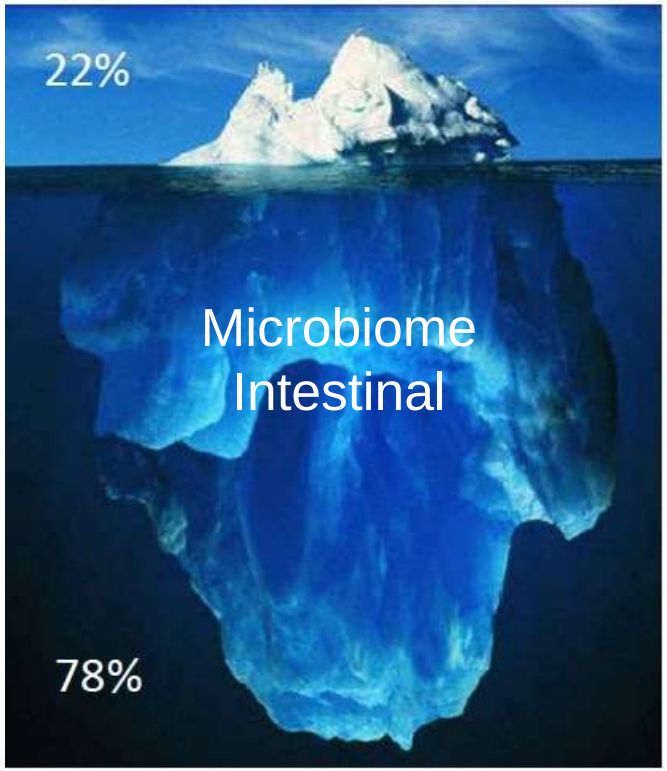
Maladie neuro-psychiatrique (Autisme)

Obésité

Diabète de type 2

Maladies auto-immunes (Maladie de Crohn Arthrite Juvénile)

Un nouvel organe (re)découvert !



Espèces cultivables

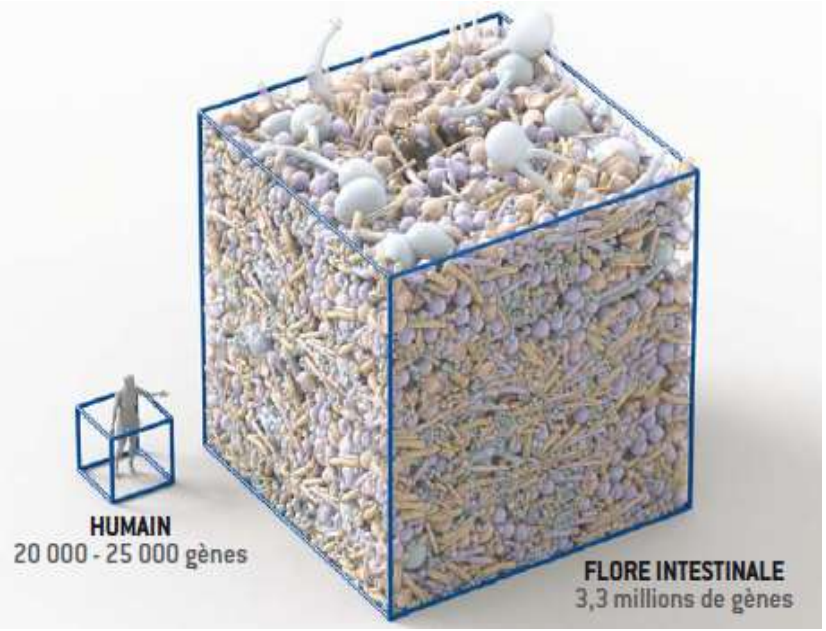
Espèces non cultivables

ARN 16s

Un noyau commun à l'espèce humaine

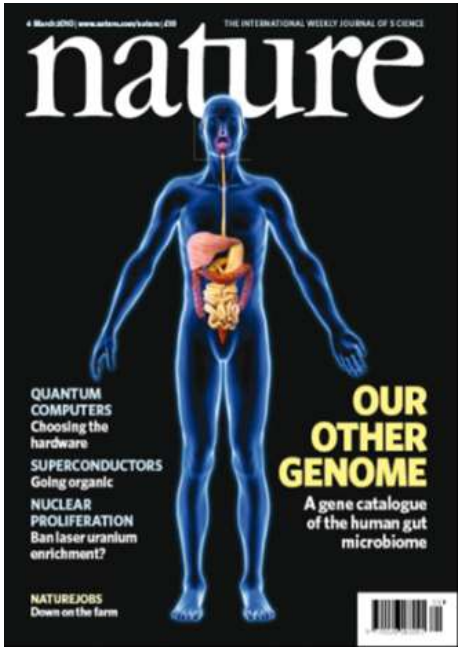
Eckburg, Science, 2005
Qin, Nature, 2010

- **Plus de 3000 espèces différentes**
- **57 espèces communes à > 90% des individus**
- **Mais une grande variabilité inter individuelle**



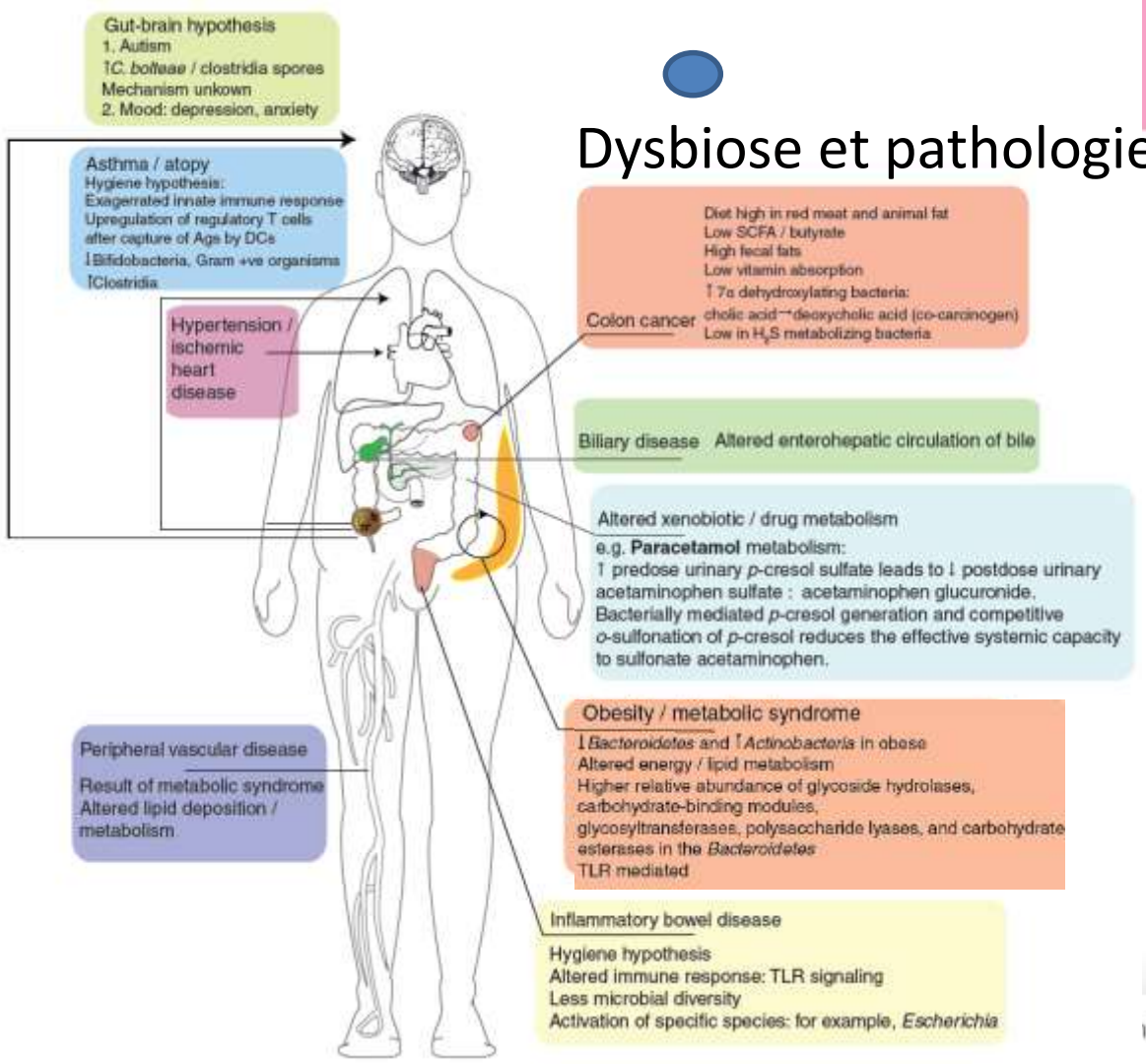
Microbiote, microbiome, métagénome

- Microbiote = ensemble des micro-organismes vivants dans un environnement spécifique
  - ***Association mutualiste***
- Microbiome = ensemble des gènes du microbiote
- Métagénome = ensemble des gènes présents dans un environnement spécifique
- Métagénomique = technique permettant d'analyser l'ensemble des gènes dominants d'un écosystème
  - ***MetaHIT***
  - ***Human Microbiome Project***



Qin, Nature 2010

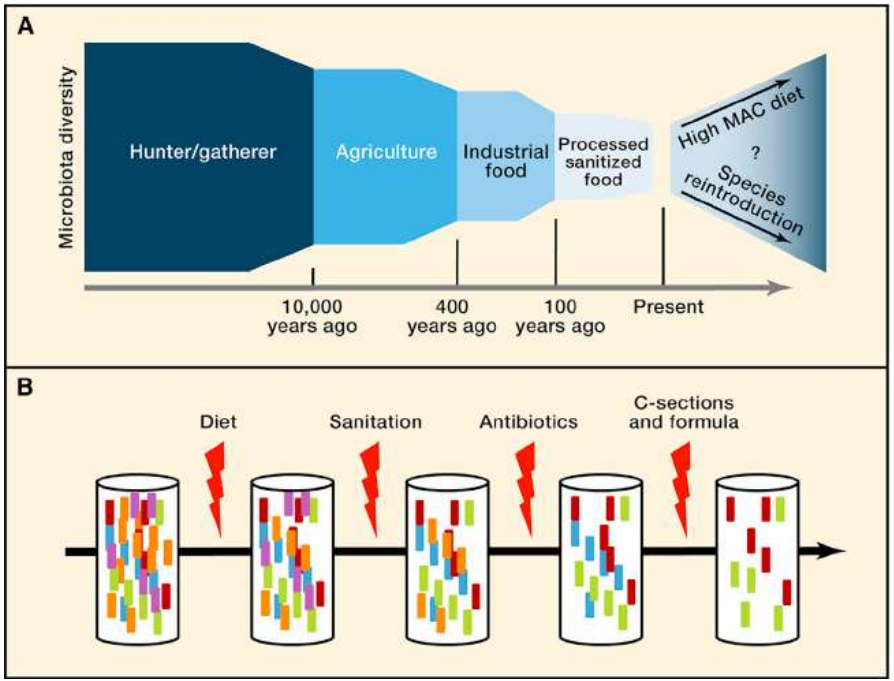
Dysbiose et pathologie humaine



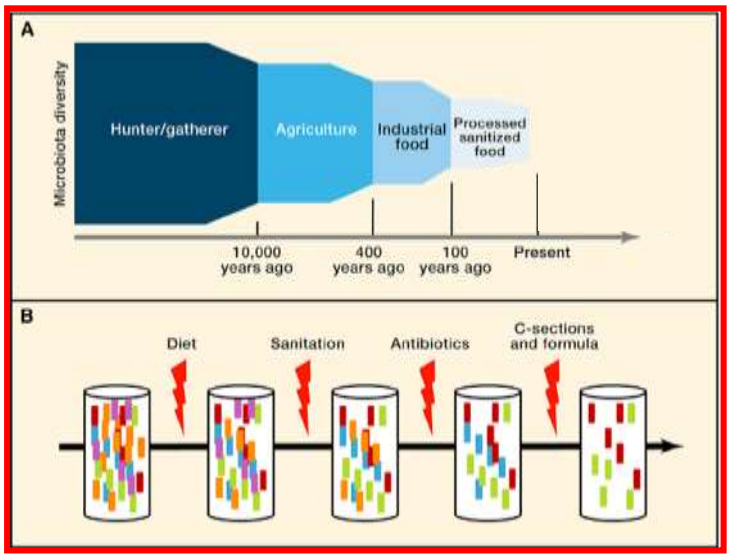
Kinross *et al*.
Genome Medicine 2011

Pourquoi une dysbiose ?

Une perte de diversité progressive



Sonnenburg, Cell Metabolism, 2014



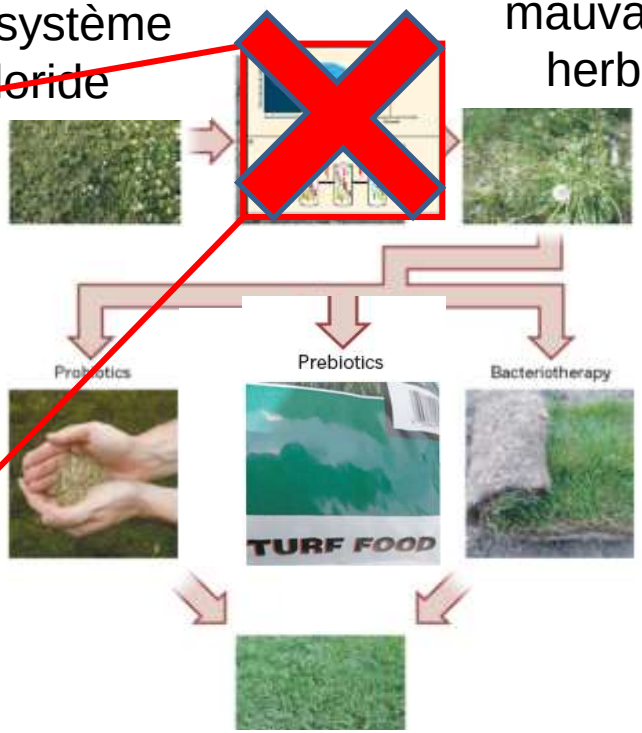
IPP ?

d'après Lozupone, Nature, 2012

ΙΠΠΟΚΡΑΤΟΥΣ
ΟΡΚΟΣ
HIPPOCRATIS
IVSIVRANDVM

écosystème floride

mauvaises herbes



écosystème restauré

d'après Lozupone, Nature, 2012

Primum non nocere

Sonnenburg, Cell Metabolism, 2014

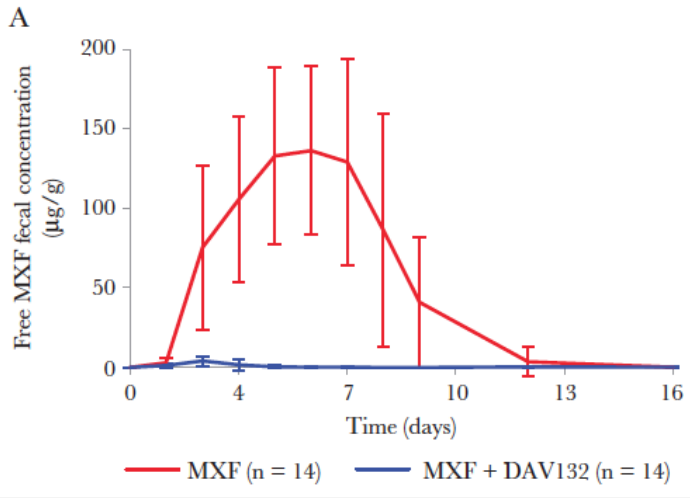
The Journal of Infectious Diseases
MAJOR ARTICLE

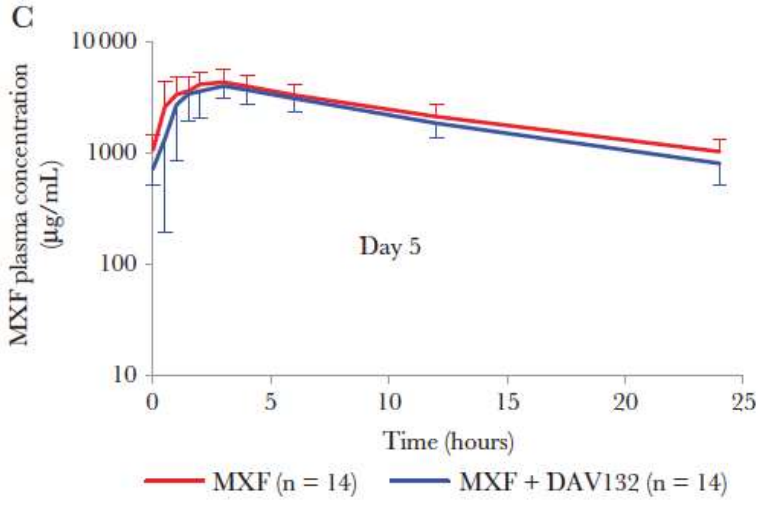
Protection of the Human Gut Microbiome From Antibiotics

Jean de Gunzburg,[1,a] Amine Ghozlane,[2,a] Annie Ducher,[1,a] Emmanuelle Le Chatelier,[2,a] Xavier Duval,[3,4,5] Etienne Ruppé,[2,b] Laurence Armand-Lefevre,[3,4,5] Frédérique Sablier-Gallis,[1] Charles Burdet,[4,5] Loubna Alavoine,[3] Elisabeth Chachaty,[6] Violaine Augustin,[1] Marina Varastet,[1] Florence Levenez,[2] Sean Kennedy,[2,b] Nicolas Pons,[2] France Mentré,[4,5,c] and Antoine Andremont[3,4,5,c]

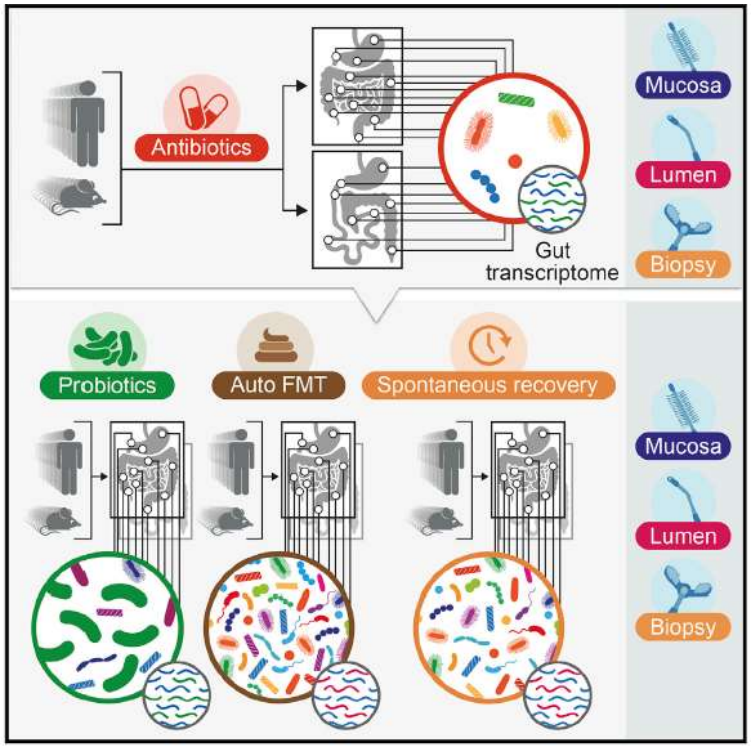
De Gunzburg, The Journal of Infectious Diseases. 2018;00:1–36

MXF = Moxifloxacin



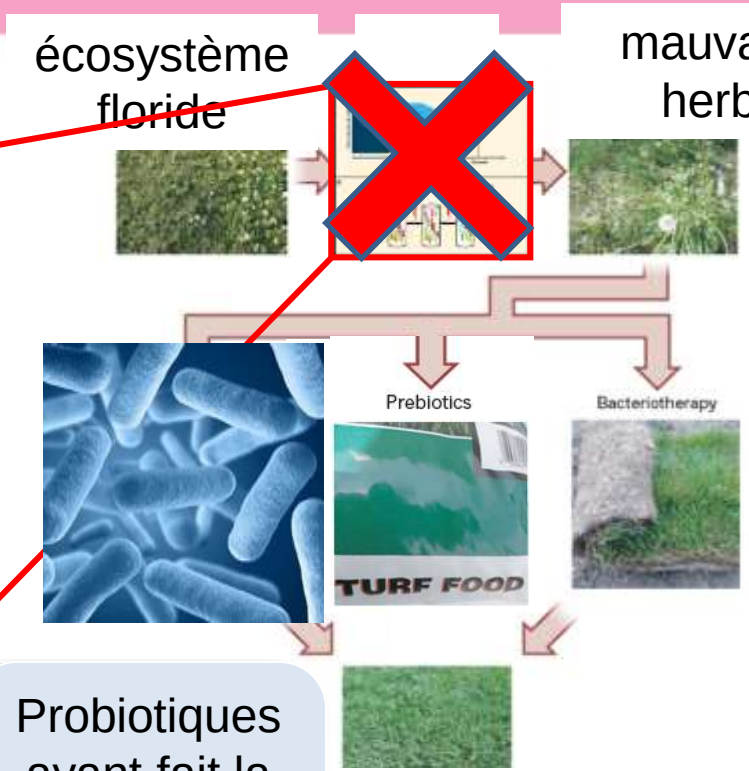


Probiotics perturb rather than aid in microbiota recovery back to baseline after antibiotic treatment in humans



Suez et al., 2018, Cell 174, 1406–1423

Primum non nocere

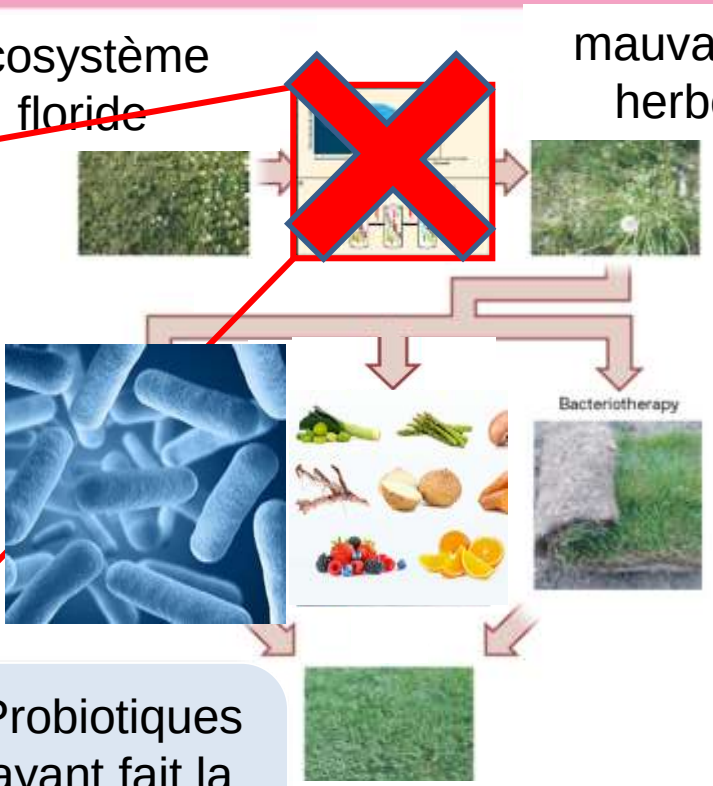


Probiotiques ayant fait la preuve de leur efficacité

d'après Lozupone, Nature, 2012

ΙΠΠΟΚΡΑΤΟΥΣ
ΟΡΚΟΣ
HIPPOCRATIS
IVSIVRANDVM

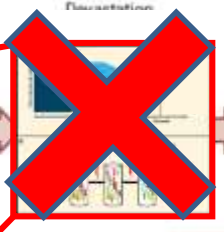
Primum non nocere



d'après Lozupone, Nature, 2012

Primum non nocere

écosystème floride



mauvaises herbes

d'après Lozupone, Nature, 2012

écosystème restauré

Probiotiques ayant fait la preuve de leur efficacité

En cas de colite à *C. difficile* récidivante

Microbiote


Oh! C'est gentil cette glace au café chocolat...
Euh... C'est votre greffe de matières fécales...
...pour votre colopathie aiguë!
Pinel

500 CLINICAL AND SYSTEMATIC REVIEWS nature publishing group

REVIEW

Fecal Microbiota Transplantation for *Clostridium difficile* Infection: Systematic Review and Meta-Analysis

Zain Kassam, MD, FRCPC[1], Christine H. Lee, MD, FRCPC, FIDSA[2,3,4], Yuhong Yuan, MD, PhD[1,5] and Richard H. Hunt, MB, FRCP, FRCPC, MACG, AGAF[1,5]

RESULTS: Eleven studies with a total of 273 CDI patients treated with FMT were identified; no RCTs were found as none have been published. Two-hundred and forty-five out of 273 patients experienced clinical resolution (UPR 89.7%; WPR 89.1% (95% CI 84 to 93%)). There was no statistically significant heterogeneity between studies (Cochran *Q* test *P*=0.13, *I*²=33.7%). *A priori* subgroup analysis suggested that lower gastrointestinal FMT delivery (UPR 91.4%; WPR 91.2% (95% CI 86 to 95%)) led to a trend towards higher clinical resolution rates than the upper gastrointestinal route (UPR 82.3%; WPR 80.6% (95% CI 69–90%)) (proportion difference of WPR was 10.6% (95% CI –0.6 to 22%)). No difference in clinical outcomes was detected between anonymous vs. patient selected donors. There were no reported adverse events associated with FMT and follow-up was variable from weeks to years.

CONCLUSIONS: FMT holds considerable promise as a therapy for recurrent CDI but well-designed, RCTs and long-term follow-up registries are still required. These are needed to identify the right patient, efficacy and safety profile of FMT before this approach can be widely advocated.

Do It Yourself …http://thepowerofpoop.com/epatients/fecal-transplant-instructions/

https://www.youtube.com/watch?v=WEMnRC22oOs

TMF Koala

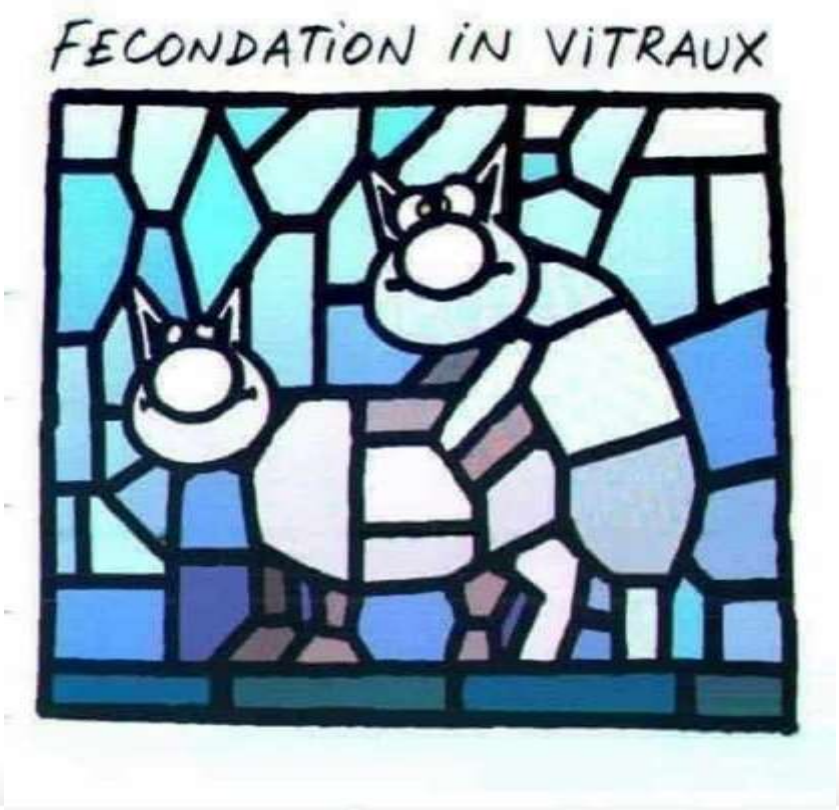
News, by SARA REARDON 14 JUNE 2018, VOL 558, NATURE

Situations cliniques avec recommandation des sociétés savantes internationales sur la prescription de modulateur de microbiote précisant un nom spécifique, une dose et une durée de traitement ?

Oui **Non**

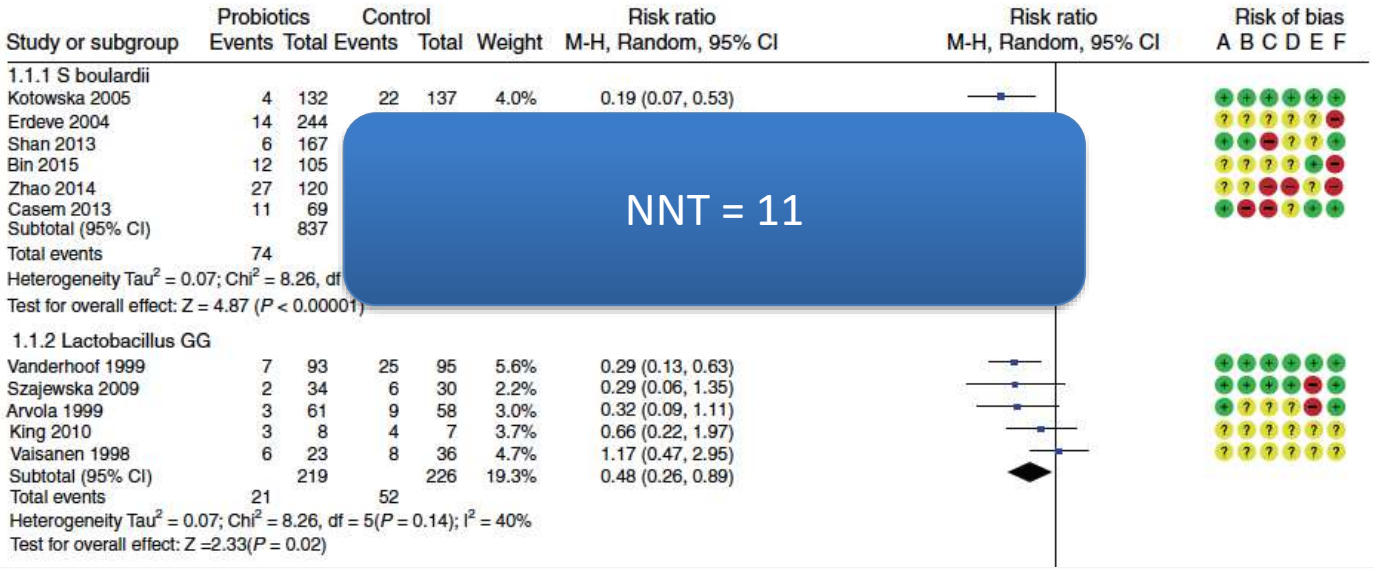
Situations c **mandation des sociétés** **nales sur la prescription** **re précisant un nom spéc** **ne durée de**

Oui **Non**


FECONDATION IN VITRAUX

Probiotics for the Prevention of Antibiotic-Associated Diarrhea in Children

JPGN • Volume 62, Number 3, March 2016



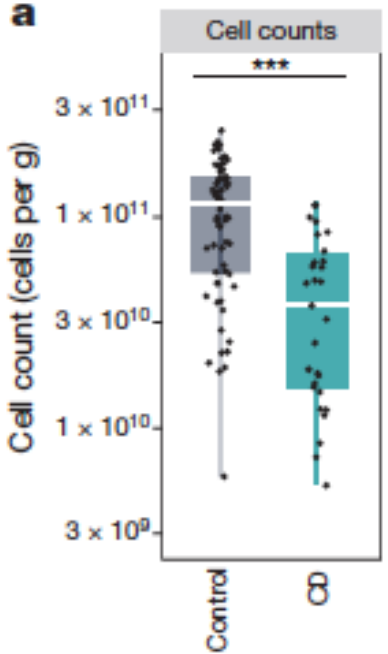
Probiotics for the Prevention of Antibiotic-Associated Diarrhea in Children

JPGN • Volume 62, Number 3, March 2016

RECOMMENDATION. If the use of probiotics for preventing AAD in children is considered, the WG recommends using *L rhamnosus* GG.
QUALITY OF EVIDENCE: Moderate.
STRENGTH OF RECOMMENDATION: Strong

RECOMMENDATION. If the use of probiotics for preventing AAD in children is considered, the WG recommends using *S boulardii* for preventing AAD in children.
QUALITY OF EVIDENCE: Moderate.
STRENGTH OF RECOMMENDATION: Strong.

Quantitative microbiome alterations in Crohn's disease



Vandeputte et al. Nature, 2017

ORIGINAL ARTICLE

Identification of an anti-inflammatory protein from *Faecalibacterium prausnitzii*, a commensal bacterium deficient in Crohn's disease

E Quévrain,[1,2,3] M A Maubert,[1,2,3,4] C Michon,[5,6] F Chain,[5,6] R Marquant,[1,3,7] J Tailhades,[1,3,7] S Miquel,[5,6] L Carlier,[1,3,7] L G Bermúdez-Humarán,[5,6] B Pigneur,[1,2,3] O Lequin,[1,3,7] P Kharrat,[5,6] G Thomas,[1,2,3] D Rainteau,[1,2,3,4] C Aubry,[5,6] N Breyner,[5,6] C Afonso,[8] S Lavielle,[1,3,7] J-P Grill,[1,2,3] G Chassaing,[1,3,7] J M Chatel,[5,6] G Trugnan,[1,2,3,4] R Xavier,[9] P Langella,[5,6] H Sokol,[1,2,3,5,10] P Seksik[1,2,3,10]

What are the new findings?

- *F. prausnitzii* produces bioactive peptides derived from a single 15 kDa protein (ZP05614546.1) of unknown function named microbial anti-inflammatory molecule (MAM).
- MAM expression in epithelial cell lines is able to block the NF-κB pathway.
- *Lactococcus lactis* harbouring a MAM-cDNA encoding plasmid is able to alleviate dinitrobenzene sulfonic acid-colitis in mice.

Journal of Crohn's and Colitis (2014) 8, 1179–1207

Available online at www.sciencedirect.com

ScienceDirect

ELSEVIER

CONSENSUS/GUIDELINES

Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease

3.7. Probiotics

Statement 21

Probiotics are not recommended for maintenance of remission [EL3 (pediatrics) EL2 (adults)] 96% agreement

Evidence suggests that probiotics may be effective in reducing inflammation in experimental colitis models, and

VSL#3 Improves Symptoms in Children with Irritable Bowel Syndrome: A Multicenter, Randomized, Placebo-Controlled, Double-Blind, Crossover Study

- 59 enfants de 4-18 ans
- VSL#3 vs placebo - 6 sem
- 2 sem wash out
- Switch 6 sem

TABLE 2. Baseline characteristics of the 59 patients

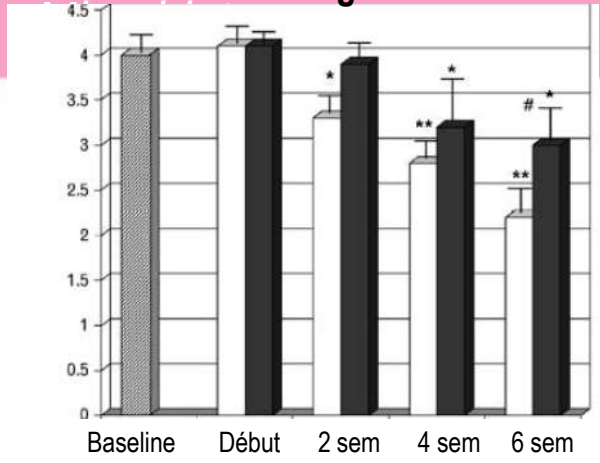
Age (mean, range), y	12.5 (5–18)
Sex (no. girls, percentage)	28, 47%
Predominant type of IBS (no. of patients)	
Constipation	16
Diarrhea	20
Mixed/alternating pattern	23
Abdominal pain severity score at baseline	2.7 ± 0.9
Abdominal bloating/gassiness	2.9 ± 1.0
Stool changes (constipation or diarrhea)	2.8 ± 0.8
Family assessment of disruption	2.2 ± 0.4

Values are mean ± SD (range). Scores are in a 5-point scale, 0–4. IBS = irritable bowel syndrome.

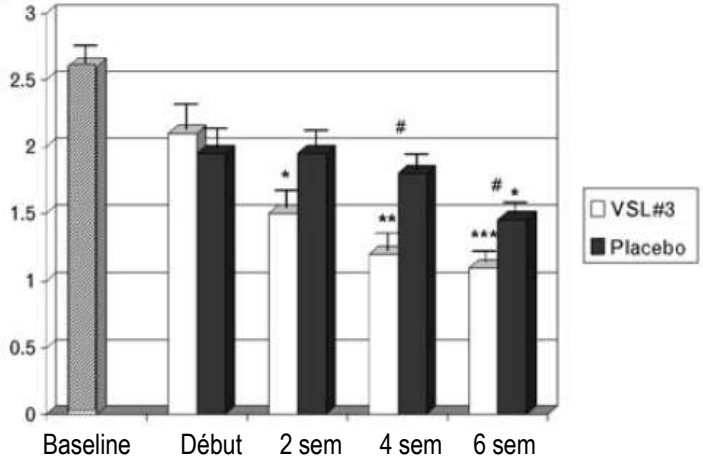
Guandalini S, JPGN 2010

VSL#3
Vivomixx*

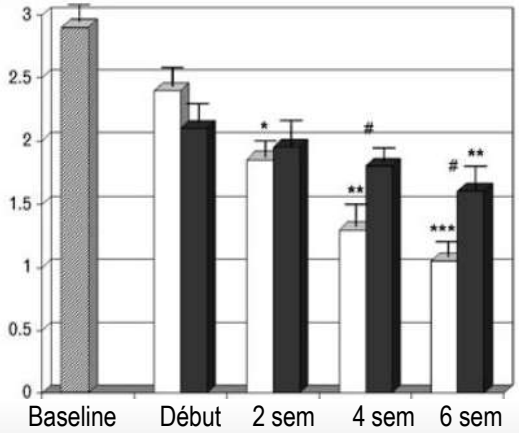
Score global



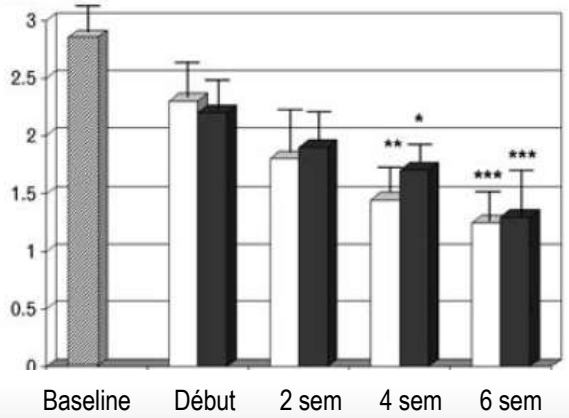
Douleurs abdominales



Ballonnement



Consistance des selles



* vs début ; ♯placebo vs VSL#3

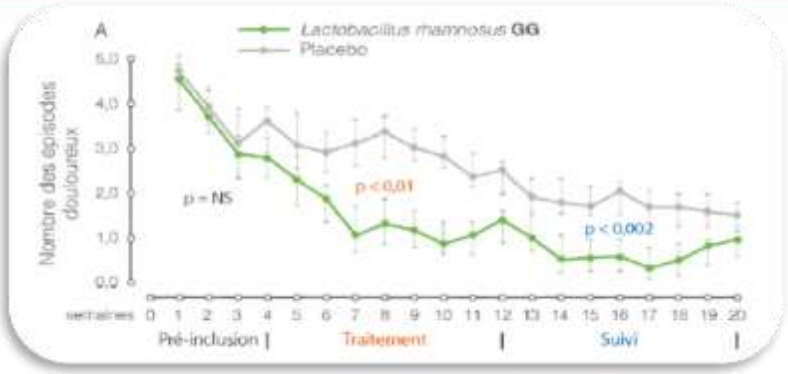
A Randomized Controlled Trial of *Lactobacillus* GG in Children With Functional Abdominal Pain

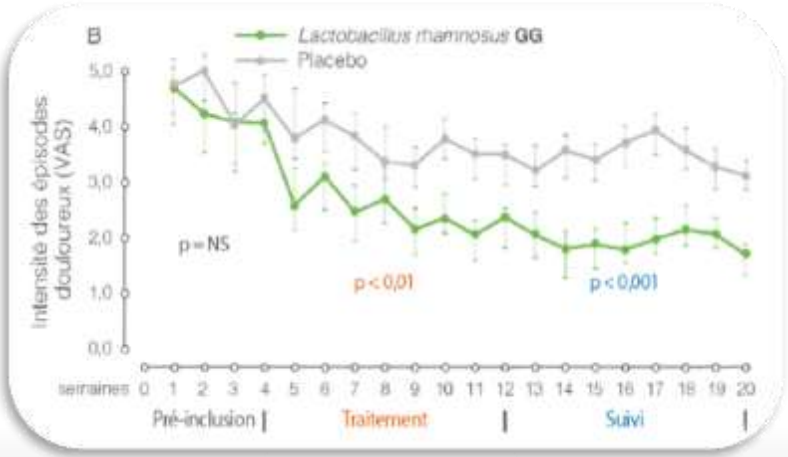
- 141 enfants ; multi-centrique
- Douleurs abdo (FAP, IBS)
- LGG ($3x10^9$ CFU, x 2/j) vs placebo
- 8 sem + 8 sem de suivi

Francavilla R, Pediatrics 2010

Microbiote

LGG Probiolog*





- LGG ↓ fréquence et sévérité des douleurs ($p < 0,01$)
- LGG améliore la perméabilité intestinale (IBS)

Lactobacillus reuteri DSM 17938 for the Management of Functional Abdominal Pain in Childhood: A Randomized, Double Blind, Placebo-Controlled Trial

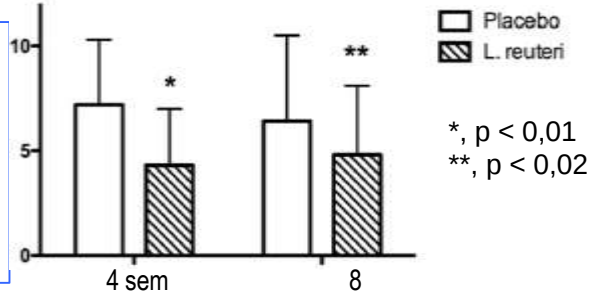
- 93 enfants de 6-15 ans
- FAP (Rome III)
- *L reuteri* DSM 17938 ($1x10^8$ CFU/j) vs placebo
- 4 sem + 4 sem de suivi

Lactobacillus reuteri DSM 17938 Biogaia*

Table. Baseline characteristics

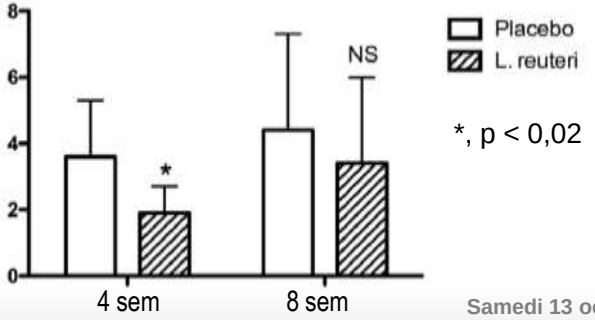
	L reuteri (n = 47)	Placebo (n = 46)
Age (y)	12.2 ± 2.8	11.7 ± 3.2
Sex (male/female)	28/19	25/21
Body weight (kg)	44 ± 11	42 ± 14
Duration of symptoms (y)	1.8 ± 1.4	2.2 ± 1.9
Drug use for abdominal pain (n)	13	16
School absenteeism because of pain (n)	7	9
Self-reported frequency (episodes/wk)	4.2 ± 1.7	3.8 ± 2.1
Self-reported severity, Hicks score	6.8 ± 3.3	7.1 ± 2.8

Intensité des DA



sem

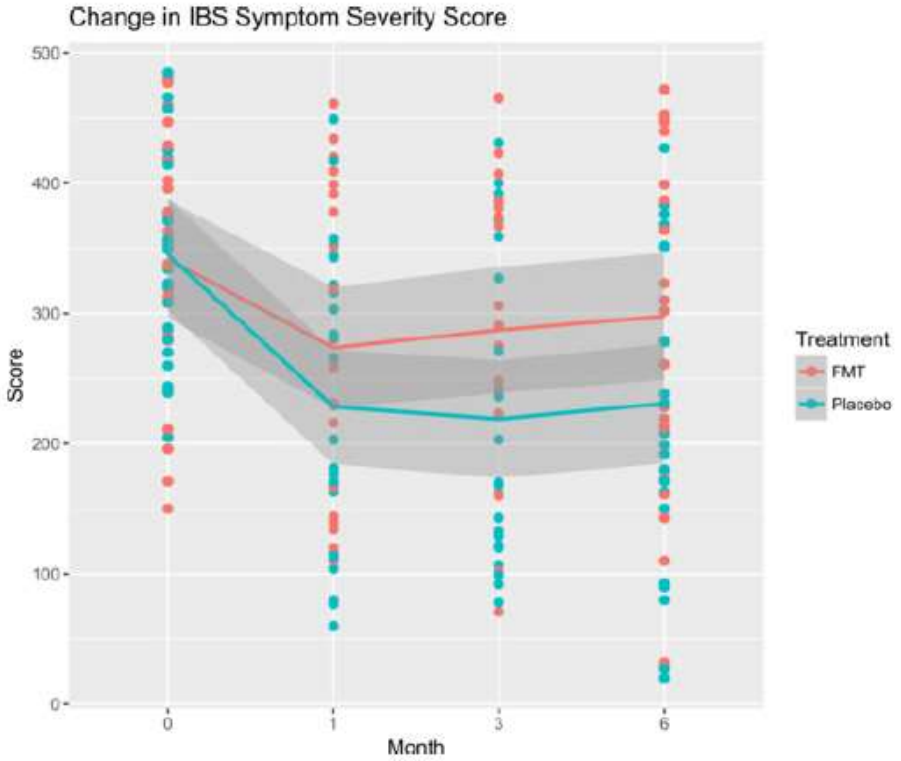
Fréquence des DA



Weizman Z, J Pediatr 2016

Faecal microbiota transplantation alters gut microbiota in patients with irritable bowel syndrome: results from a randomised, double-blind placebo-controlled study

Sofie Ingdam Halkjær,[1] Alice Højer Christensen,[2] Bobby Zhao Sheng Lo,[1] Patrick Denis Browne,[3] Stig Günther,[2] Lars Hestbjerg Hansen,[3] Andreas Munk Petersen[1]



Halkjær SI, et al. Gut 2018

Gastroenterology 2016;150:1456–1468

Childhood Functional Gastrointestinal Disorders: Child/ Adolescent

Jeffrey S. Hyams,[1,*] **Carlo Di Lorenzo**,[2,*] Miguel Saps,[2] Robert J. Shulman,[3] Annamaria Staiano,[4] and Miranda van Tilburg[5]

together. There are data supporting the utility of probiotics.[49,50] One small prospective, double-blind trial in

CLINICAL GUIDELINES

European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases Evidence-Based Guidelines for the Management of Acute Gastroenteritis in Children in Europe: Update 2014

Guarino et al. JPGN 2014;59: 132–152

Use of Probiotics for Management of Acute Gastroenteritis: A Position Paper by the ESPGHAN Working Group for Probiotics and Prebiotics

Szajewska et al.,JPGN 2014;58: 531–539

Etudes disponibles

TABLE 1. Probiotics for treating acute gastroenteritis

Probiotics with a positive recommendation	QoE	Recommendation
Lactobacillus GG	Low	Strong
Saccharomyces boulardii	Low	Strong
L reuteri DSM 17938	Very low	Weak
L acidophilus LB (heat-inactivated)	Very low	Weak

Réduisent la diarrhée d'une journée !!

Guarino et al. JPGN 2014;59: 132–152

ORIGINAL STUDIES

Probiotics and Prebiotics in Preventing Episodes of Acute Otitis Media in High-risk Children: A Randomized, Double-blind, Placebo-controlled Study

Robert Cohen, MD,† Elvira Martin, MD,* France de La Rocque, MD,* Franck Thollot, MD,‡ Sophie Pecquet, MD,§ Andreas Werner, MD,‡ Michel Boucherat, MD,*† Emmanuelle Varon, MD,¶*

TABLE 2. Characteristics of AOM Episodes, Lower Respiratory Tract Infections, Antibiotic Courses During the 12-month Follow-up and Main Adverse Events (Intent-to-treat Population)

(*Pediatr Infect Dis J* 2013;32: 810–814)

	Control Group N = 112	Treatment Group N = 112	*P*
AOM			
No. of episodes	237	249	0.797*
No. of episodes with Paradise criteria	161	160	0.39†
No. of episodes diagnosed by investigators	167	167	0.42†
No. of episodes diagnosed by other physicians	70	82	
No. (%) of patients with ≥1 episodes of AOM	80 (71.4)	80 (71.4)	0.8‡
No. (%) of patients with recurrent AOM	34 (30.4)	34 (30.4)	0.889‡
No. of lower respiratory tract infections	121	107	0.625*
Antibiotic courses, no.	280	291	0.756*
For AOM	226	242	0.45†
For other reasons	54	49	
No. of children with gastrointestinal symptoms	46	52	0.412†
No. of children with allergic or dermatologic diseases	23	15	0.15†

European Journal of Pediatrics
July 2018, Volume 177, Issue 7, pp 979–994 | Cite as

Probiotics for respiratory tract infections in children

What is known:

• *Previously published systematic reviews have suggested that probiotics may have a preventive effect on respiratory infections, but limited data exist on strain specific effects.*

What is new:

• *This systematic review showed that use of Lactobacillus rhamnosus GG modestly reduces the duration of respiratory tract infections.*

PEDIATRICS Volume 140, number 2, August 2017

Probiotics and Child Care Absence Due to Infections: A Randomized Controlled Trial

Rikke Pilmann Laursen, MSc, Anni Larnkjær, PhD, Christian Ritz, PhD, Hanne Hauger, MSc, Kim Fleischer Michaelsen, DMSc, Christian Mølgaard, PhD

METHODS: The ProbiComp study was a randomized, double-blind, placebo-controlled study. A total of 290 infants were randomly allocated to receive a placebo or a combination of *Bifidobacterium animalis* subsp *lactis* and *Lactobacillus rhamnosus* in a dose of 10^9 colony-forming units of each daily for a 6-month intervention period. Absence from child care, occurrence of infant symptoms of illness, and doctor visits were registered by the parents using daily and weekly Web-based questionnaires.

RESULTS: Median absence from child care was 11 days (interquartile range: 6–16). Intention-to-treat analysis showed no difference between the probiotics and placebo groups ($P = .19$). Additionally, there was no difference in any of the secondary outcomes between groups; the number of children with doctor-diagnosed upper or lower respiratory tract infections, the number of doctor visits, antibiotic treatments, occurrence and duration of diarrhea, and days with common cold symptoms, fever, vomiting, or caregivers' absence from work.

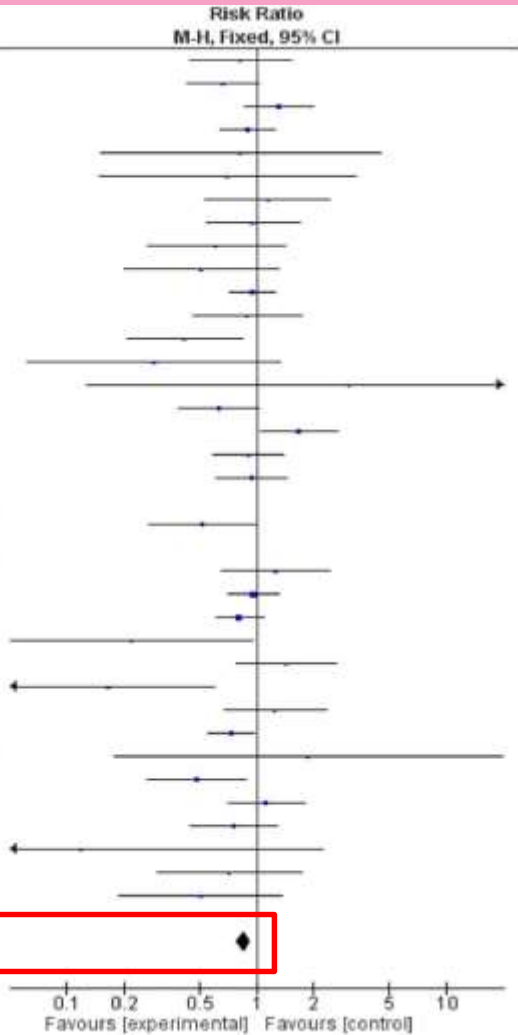
Prévention des infections nosocomiales (LOS)

- 37 études RC éligibles dans la méta-analyse de 2016
- *Lactobacillus* faisant partie des probiotiques dans 21 études *Bifidobacterium* dans 22
- Un total de 9 416 enfants inclus
- Infection nosocomiale = Critère de jugement principal dans 9 études seulement

Rao SC, Athalye-Jape GK, Deshpande GC et al. Pediatrics 2016

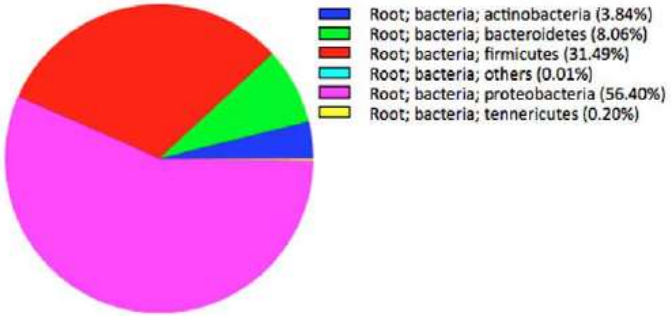
Study or Subgroup	Probiotics Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Al Hosni 2012	13	50	16	51	2.1%	0.83 [0.45, 1.54]
Awad 2010	18	36	12	16	2.2%	0.67 [0.43, 1.03]
Bin-Nun 2005	31	72	24	73	3.1%	1.31 [0.86, 2.00]
Braga 2011	40	119	42	112	5.7%	0.90 [0.63, 1.27]
Chrzanowska Liszewsk 2012	2	21	3	26	0.4%	0.83 [0.15, 4.49]
Costalos 2003	3	51	3	36	0.5%	0.71 [0.15, 3.30]
Dani 2002	14	295	12	290	1.6%	1.15 [0.54, 2.44]
Demirel 2013	20	135	21	136	2.8%	0.96 [0.55, 1.69]
Dilli 2015A	8	100	13	100	1.7%	0.62 [0.27, 1.42]
Dutta 2015	10	114	6	35	1.2%	0.51 [0.20, 1.31]
Fernandez-Carrocera 2013	42	75	44	75	5.8%	0.95 [0.72, 1.26]
Hays 2015	25	145	10	52	1.9%	0.90 [0.46, 1.74]
Hikaru 2012	10	108	22	100	3.0%	0.42 [0.21, 0.84]
Hua 2014	2	119	8	138	1.0%	0.29 [0.06, 1.34]
Kitajima 1997	1	45	0	46	0.1%	3.07 [0.13, 73.32]
Lin 2005	22	180	36	187	4.6%	0.63 [0.39, 1.04]
Lin 2008	40	217	24	217	3.2%	1.67 [1.04, 2.67]
Manzoni 2006	19	39	22	41	2.8%	0.91 [0.59, 1.40]
Mihatsch 2010	28	91	29	89	3.9%	0.94 [0.61, 1.45]
Millar 1993	0	10	0	10		Not estimable
Oncel and Sari 2014	13	200	25	200	3.3%	0.52 [0.27, 0.99]
Partty 2013	0	31	0	32		Not estimable
Patole 2014	17	74	12	86	1.7%	1.26 [0.65, 2.45]
Pips 2014	73	650	77	660	10.0%	0.96 [0.71, 1.30]
ProPrems 2013	72	548	89	551	11.7%	0.81 [0.61, 1.08]
Ren Y 2010	2	35	9	35	1.2%	0.22 [0.05, 0.96]
Rojas 2012	24	372	17	378	2.2%	1.43 [0.78, 2.63]
Romeo 2011	3	166	9	83	1.6%	0.17 [0.05, 0.60]
Rouge 2009	15	45	13	49	1.6%	1.26 [0.67, 2.34]
Roy 2014	31	56	42	56	5.5%	0.74 [0.56, 0.98]
Saengtawesin 2014	2	31	1	29	0.1%	1.87 [0.18, 19.55]
Samanta 2009	13	91	28	95	3.6%	0.48 [0.27, 0.88]
Sari 2010	29	110	26	111	3.4%	1.13 [0.71, 1.78]
Serce 2013	19	104	25	104	3.3%	0.76 [0.45, 1.29]
Stratiki 2007	0	41	3	34	0.5%	0.12 [0.01, 2.23]
Tewari 2015	8	123	11	121	1.5%	0.72 [0.30, 1.72]
Totsu 2014	6	153	10	130	1.4%	0.51 [0.19, 1.36]
Total (95% CI)		**4852**		**4564**	**100.0%**	**0.86 [0.78, 0.94]**
Total events	675		744			

Heterogeneity: Chi² = 52.18, df = 34 (P = 0.02); I² = 35%
Test for overall effect: Z = 3.38 (P = 0.0007)



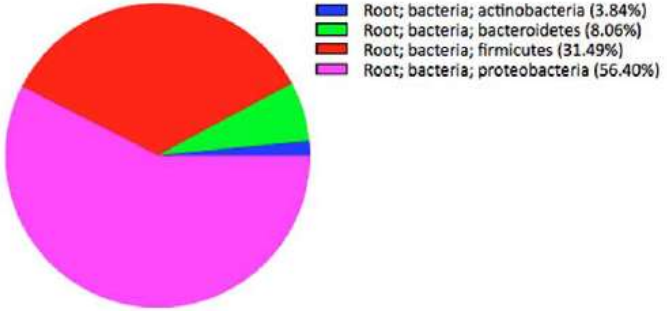
Microbiote et ECUN

Controls, one week before diagnosis

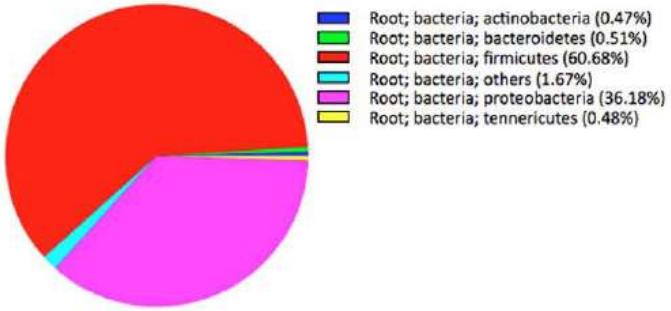


Controls, <72h of diagnosis

n = 9

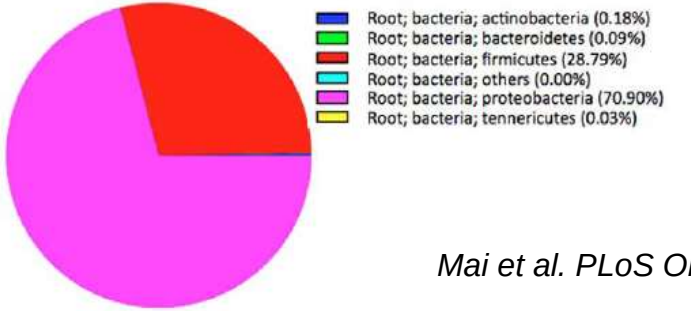


Cases, one week before diagnosis



Cases, <72h of diagnosis

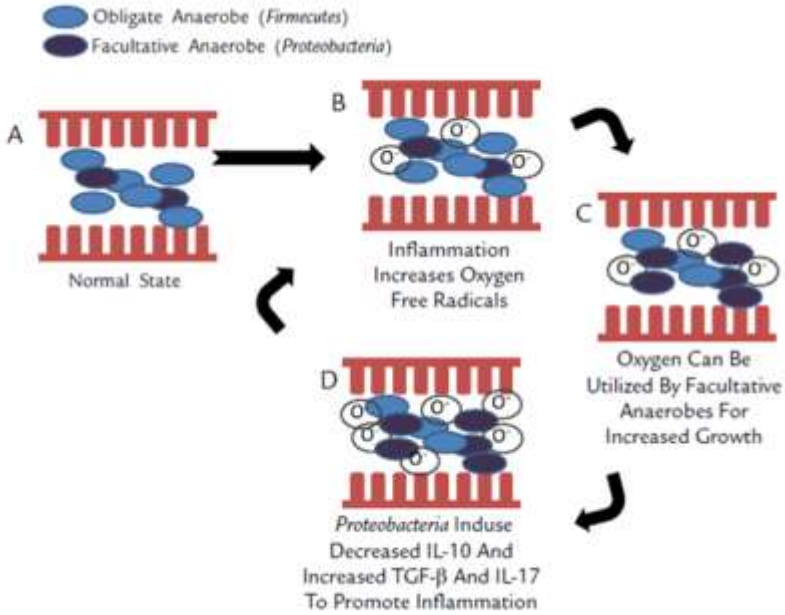
n = 9



Mai et al. PLoS ONE, 2011

Development of the Neonatal Intestinal Microbiome and Its Association With Necrotizing Enterocolitis

Timothy G. Elgin, MD; Stacy L. Kern, MD; and Steven J. McElroy, MD



Clin Ther 2016

Probiotics Reduce All-Cause Mortality and Necrotizing Enterocolitis: It Is Time to Change Practice

PEDIATRICS Volume 125, Number 5, May 2010

Nonadministration of Routine Probiotics Unethical—Really?
Josef Neu and Jonathan Shuster
Pediatrics 2010;126;e740

Probiotics: Are We Ready for Routine Use?

PEDIATRICS Volume 125, Number 5, May 2010

A Cautionary Note on Instituting Probiotics Into Routine Clinical Care for Premature Infants. *Pediatrics.* 2010;126(3):e741–e742
Pediatrics 2010;126;1052

Bifidobacterium breve BBG-001 in very preterm infants: a randomised controlled phase 3 trial

Lancet 2016; 387: 649–60

*Kate Costeloe, Pollyanna Hardy, Edmund Juszczak, Mark Wilks, Michael R Millar, on behalf of The Probiotics in Preterm Infants Study Collaborative Group**

1315 préma (23→30 S), 24 hôpitaux anglais, double aveugle, *Bifidobacterium breve*			
	650	660	
EUN	61 (9%)	66 (10%	RR 0.93 IC95% 0,67-1,30)
Sepsis	73 (11%)	77 (12%)	RR 0.97 IC95% 0,79-1,29)
Décès	54 (8%)	56 (9%)	RR 0.93 IC95% 0,67-1,30)

Cochrane Database of Systematic Reviews

Probiotics for prevention of necrotizing enterocolitis in preterm infants

Cochrane Systematic Review - **Intervention** | Version published: 10 April 2014 see what's new

New search 537 View article information

Khalid AlFaleh | Jasim Anabrees

View authors' declarations of interest

- 24 études…>5000 prématurés < 1500 gr
  5529 enfants
- Grande variabilité
  - Critères d'inclusion
  - Critères diagnostiques
  - Mode d'alimentation
  - Type de pro-biotique

EUN = RR 0,43 IC95% 0,33-56

Décès = RR 0,65 IC95% 0,52-0,81

Ce qui a l'air de marcher c'est : ….

Lactobacilles seuls ou avec bifidobacterium

Cochrane Database of Systematic Reviews

Probiotics for prevention of necrotizing enterocolitis in preterm infants

Cochrane Systematic Review - **Intervention** | Version published: 10 April 2014 see what's new

New search | 537 | View article information

Khalid AlFaleh | Jasim Anabrees

4/20 atteignent la significativité
Petites études +++

Review: Probiotics for prevention of necrotizing enterocolitis in preterm infants
Comparison: 1 Probiotics versus control (all infants)
Outcome: 1 Severe necrotising enterocolitis (stage II-III)

Study or subgroup	Probiotics n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Al-Hosni 2012	2/50	2/51		1.2 %	1.02 [0.15, 6.96]
Bin-Nun 2005	1/72	10/73		6.2 %	0.10 [0.01, 0.77]
Braga 2011	0/119	4/112		2.9 %	0.10 [0.01, 1.92]
Costalos 2003	5/51	6/36		4.4 %	0.59 [0.19, 1.78]
Dani 2002	4/295	6/290		5.0 %	0.49 [0.15, 1.61]
Demirel 2013	6/135	7/136		4.3 %	0.86 [0.30, 2.50]
Fernández-Carrocera 2013	6/75	12/75		7.5 %	0.50 [0.20, 1.26]
Kitajima 1997	0/45	0/46			Not estimable
Lin 2005	2/150	10/157		6.1 %	0.21 [0.05, 0.94]
Lin 2006	4/217	14/217		6.7 %	0.29 [0.10, 0.85]
Manzoni 2006	1/39	3/41		1.8 %	0.35 [0.04, 3.23]
Manzoni 2009	0/151	10/166		6.2 %	0.05 [0.00, 0.90]
Mihatsch 2010	2/91	4/89		2.5 %	0.49 [0.09, 2.60]
Mohan 2006	2/37	1/32		0.7 %	1.73 [0.16, 18.20]
ProPrems 2013	11/548	24/551		14.9 %	0.46 [0.23, 0.93]
Rojas 2012	9/372	15/378		9.3 %	0.61 [0.27, 1.36]
Roug_x00e9_ 2009	2/45	1/49		0.6 %	2.18 [0.20, 23.21]
Samanta 2009	5/91	15/95		9.1 %	0.35 [0.13, 0.92]
Sari 2010	6/110	10/111		6.2 %	0.61 [0.23, 1.61]
Stratiki 2007	0/36	3/31		2.4 %	0.12 [0.01, 2.19]
Total (95% CI)	**2761**	**2768**	◆	**100.0 %**	**0.43 [0.33, 0.56]**

Total events: 66 (Probiotics), 159 (Control)
Heterogeneity: Chi² = 14.67, df = 18 (P = 0.68); I² = 0.0%
Test for overall effect: Z = 6.02 (P < 0.00001)
Test for subgroup differences: Not applicable

0.005 0.1 1 10 200
Favours probiotics Favours control

Cochrane Database of Systematic Reviews

Probiotics for prevention of necrotizing enterocolitis in preterm infants

Cochrane Systematic Review - **Intervention** | Version published: 10 April 2014 see what's

New search 537 View article information

Khalid AlFaleh | Jasim Anabrees

View authors' declarations of interest

- 24 études…>5000 prém
- Grande variabil
  - Cri
  -
  -
  -

56

2-0,81

c'est :

uis ou avec bifidobacterium

Enteral supplementation of probiotics prevents severe NEC and all cause mortality in preterm infants. Our updated review of available evidence strongly supports a change in practice. Head to head comparative studies are required to assess the most effective preparations, timing, and length of therapy to be utilized.

æ

World Allergy Organization-McMaster University Guidelines for Allergic Disease Prevention (GLAD-P): Probiotics

WAO journal
WORLD ALLERGY ORGANIZATION

Recommendation 1

The WAO guideline panel suggests using probiotics in pregnant women at high risk for allergy in their children, because considering all critical outcomes, there is a net benefit resulting primarily from prevention of eczema (conditional recommendation, very low quality evidence).

Recommendation 2

The WAO guideline panel suggests using probiotics in women who breastfeed infants at high risk of developing allergy, because considering all critical outcomes, there is a net benefit resulting primarily from prevention of eczema (conditional recommendation, very low quality evidence).

Recommendation 3

The WAO guideline panel suggests using probiotics in infants at high risk of developing allergies, because considering all critical outcomes, there is a net benefit resulting primarily from prevention of eczema (conditional recommendation, very low quality evidence).

Fiocchi et al. World Allergy Organization Journal (2015)

Diet during pregnancy and infancy and risk of allergic or autoimmune disease: A systematic review and meta-analysis

- We undertook a systematic review of observational and intervention studies of maternal diet during pregnancy and lactation and infant diet during the first year of life to evaluate whether dietary exposures in early life influence risk of allergic or autoimmune disease.
- We found that supplementation with micro-organisms (probiotics) during late pregnancy and breastfeeding may reduce risk of eczema, and fish oil supplementation during pregnancy and breastfeeding may reduce risk of sensitisation to food allergens.
- We found more limited data that longer duration of breastfeeding may reduce risk of eczema and type 1 diabetes mellitus.

Garcia-Larsen et al. (2018) PLoS Med 15(2):e1002507

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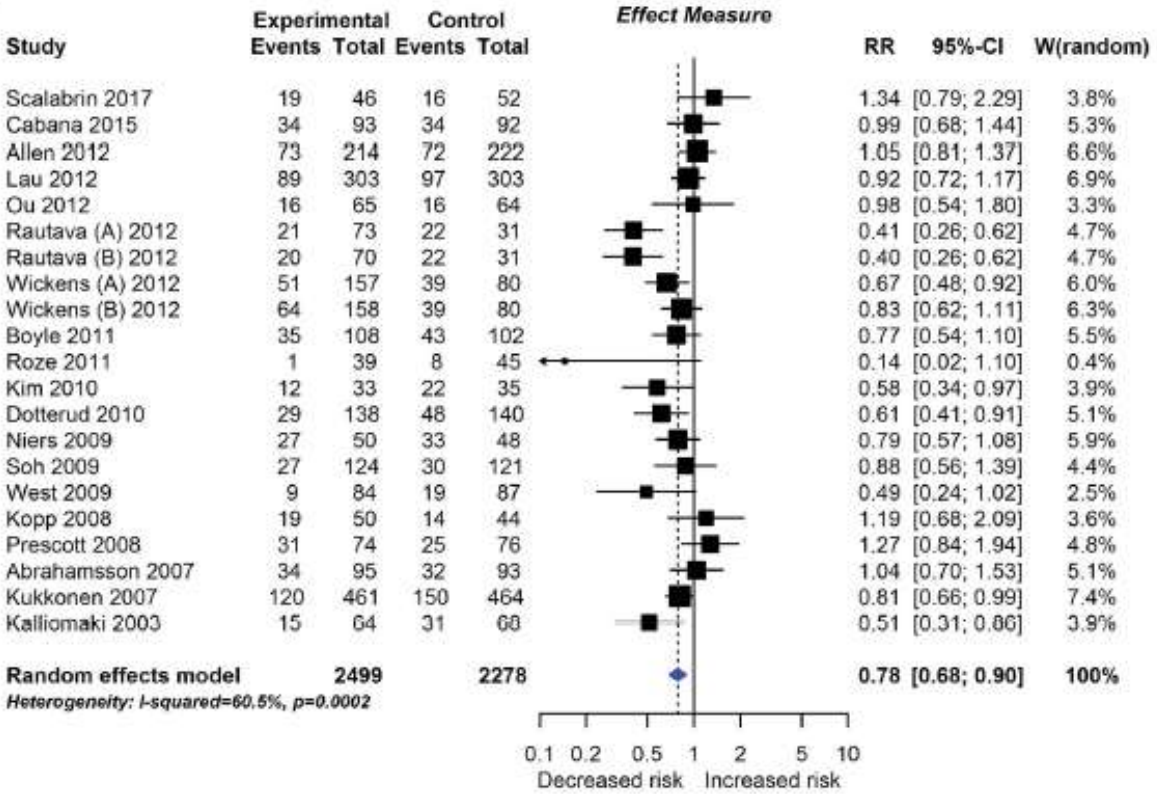
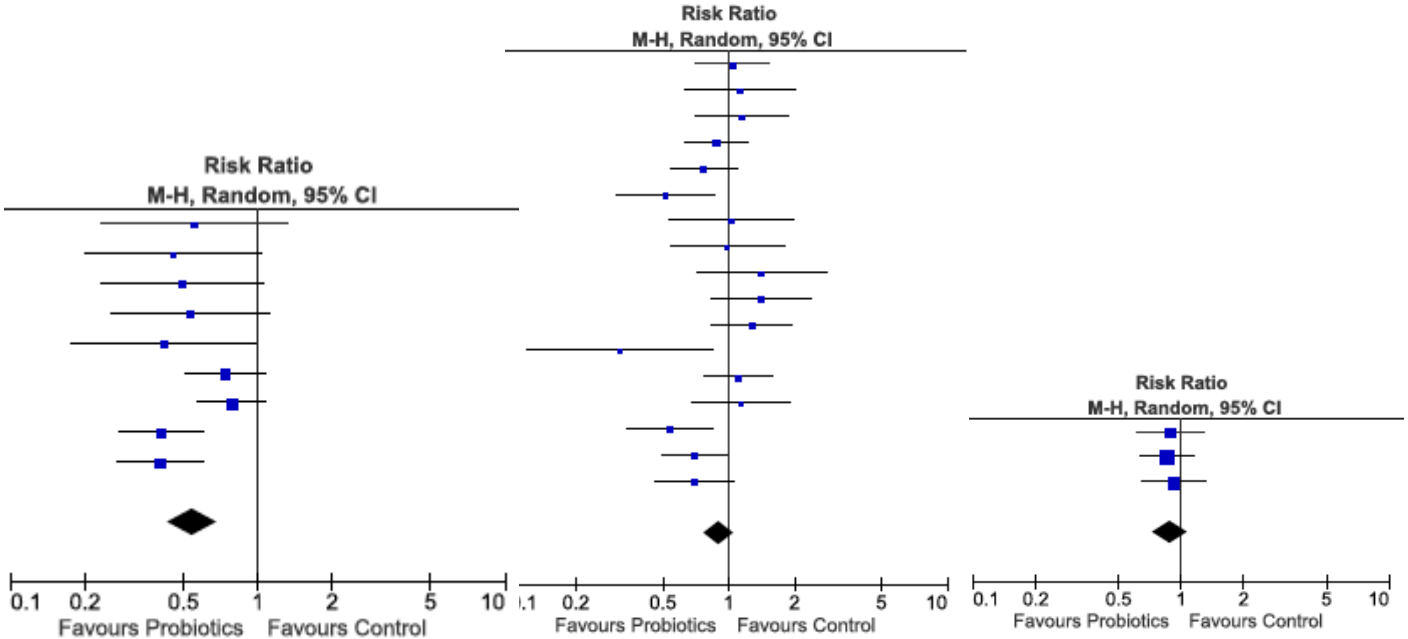


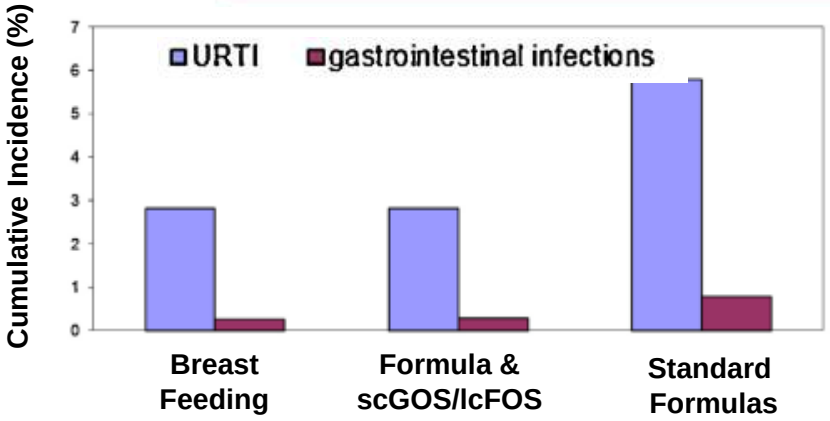
Garcia-Larsen et al. (2018) PLoS Med 15(2):e1002507

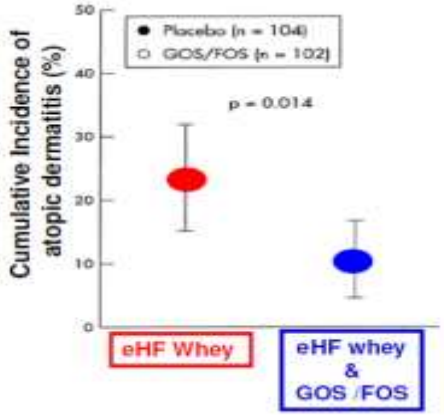
Mieux avec des mixtures !



Mixture Lactobacilles Bifidobactéries

lcFOS/scGOS 1:9 diminue les incidences des infections et de la dermatite atopique



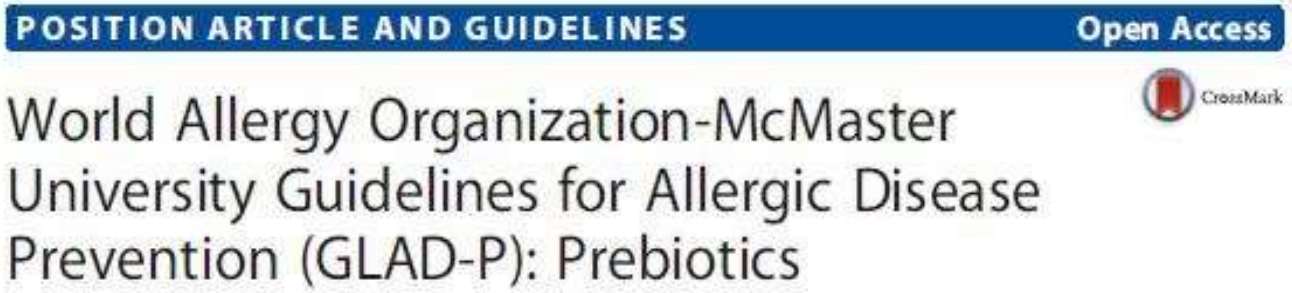


Infections:

- **Diminue l'incidence des infections respiratoires hautes (URTI)**
  Arslanoglu et al. 2007
- **Diminue l'incidence des infections gastro-intestinales**
  Arslanoglu et al. 2007
- **Diminue l'incidence cumulée à 18 mois des URTI et infections gatro-intestinales**
  Ivakhnenko & Nyankovskyy, 2013

Allergie:

- **Diminue l'incidence de la dermatite atopique (AD)**
  - **chez les enfants à risque (historique familial)**
    Moro et al., 2006, Arslanoglu et al. 2008, Arslanoglu et al. 2012
  - **chez les enfants à faible risque (pas d'historique familial))**
    Gruber et al., 2010, Gruber et al., 2015, Ivakhnenko & Nyankovskyy, 2013


POSITION ARTICLE AND GUIDELINES Open Access

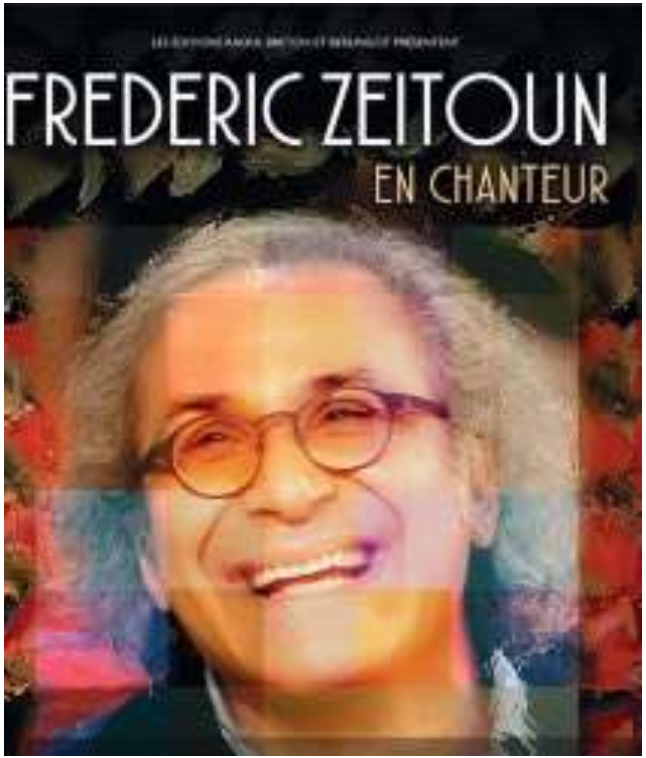
World Allergy Organization-McMaster University Guidelines for Allergic Disease Prevention (GLAD-P): Prebiotics

Le WAO guideline panel suggère l'utilisation d'une supplémentation de prébiotiques chez les enfants non allaités et suggère de ne pas utiliser une supplémentation de prébiotiques chez les enfants allaités.

Ces deux recommandations sont conditionnelles et basées sur un niveau de certitude d'évidence faible.

Cuello-Garcia et al., World Allergy Organization Journal 9:10, 2016

Alors tu réponds oui ou non ?


FREDERIC ZEITOUN
EN CHANTEUR

Colic treatment : network meta-analysis

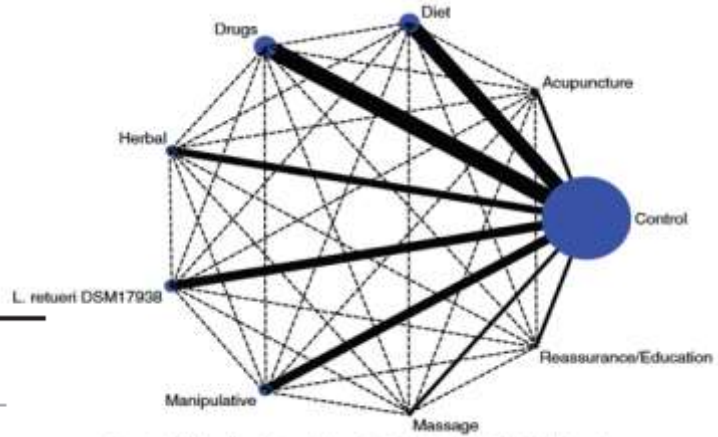


Figure 2. Network meta-analysis of multiple treatments for infantile colic.

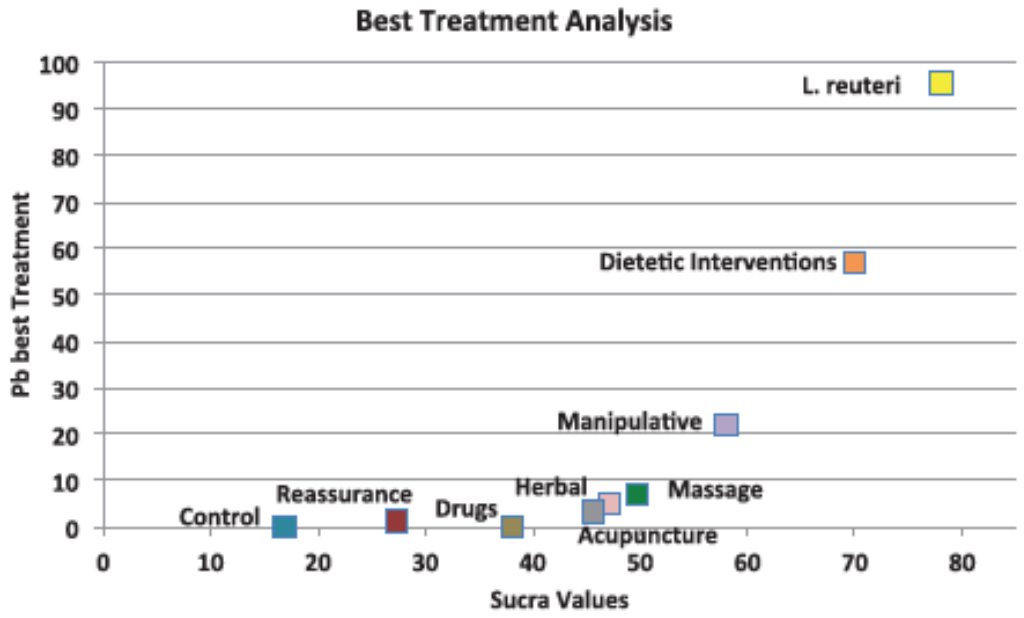


Figure 6. Ranking plot of multiple treatments for infantile colic.

Gutiérrez-Castrellón et al. Medicine (2017)

Le probiotique « de référence » : *L reuteri* DSM17938 protectis

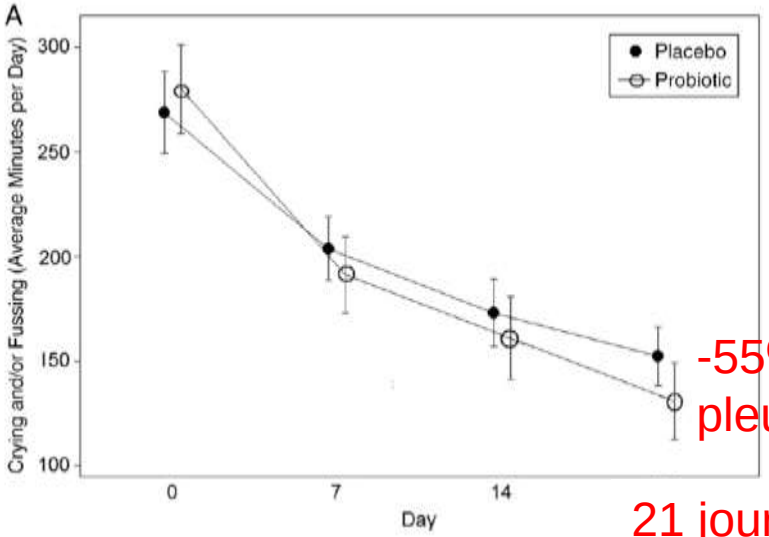
Lactobacillus reuteri to Treat Infant Colic: A Meta-analysis
PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

25.4 minutes de pleurs en moins à **j21**
(de 3.5 à 47.3 min)

4 études, 345 bébés
(174 probiotiques et 171 placebo)

Effet chez ceux allaités mais pas chez ceux au biberon

Sung, Pediatrics, 2018



-55% de pleurs/jour

21 jours

Conclusion : *L reuteri* DSM17938 est efficace et peut être recommandé pour les bébés allaités avec coliques

En prévention

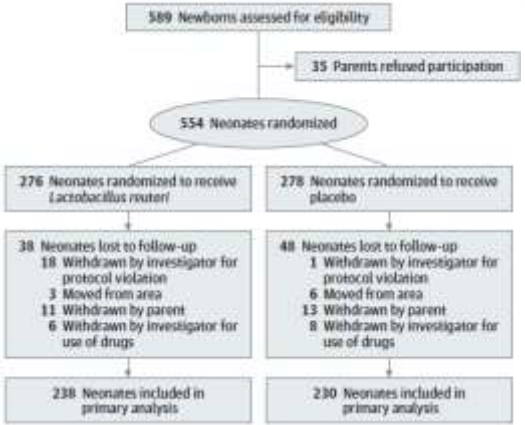


Table 1. Clinical and Demographic Data at Baseline

Characteristic	*Lactobacillus reuteri* DSM 17938 (n = 238)	Placebo (n = 230)	*P* Value
Gestational age, mean (SD), wk	39.4 (19.0)	39.1 (1.4)	.05
Birth weight, mean (SD), g	3378 (413)	3302 (392)	.04
Male/female sex, No. (%)	122 (51.3)/116 (48.7)	120 (52.2)/110 (47.8)	.84
Vaginal/cesarean delivery, No. (%)	159 (66.8)/79 (33.2)	141 (61.3)/89 (38.7)	.21
Breast/formula feeding, No. (%)	132 (55.5)/106 (44.5)	121 (52.6)/109 (47.4)	.53

Indrio et al. JAMA Pediatr. 2014

Table 2. Primary Outcome at 1 Month of Life

Characteristic	Mean (SD) [95% CI]		*P* Value
	Lactobacillus reuteri DSM 17938	Placebo	
Colic, min/d	45 (12) [43.5-46.5]	96 (34) [91.6-100.4]	<.01
Regurgitation, No./d	2.7 (1.5) [2.5-2.9]	3.3 (2.3) [3.0-3.6]	.35
Evacuation, No./d	4.01 (1.1) [3.9-4.1]	2.8 (0.6) [2.7-2.9]	<.01

Table 3. Primary Outcome at 3 Months of Life

Characteristic	Mean (SD) [95% CI]		*P* Value
	Lactobacillus reuteri DSM 17938	Placebo	
Colic, min/d	37.7 (33.8) [33.4-42.0]	70.9 (51.9) [64.2-77.6]	<.01
Regurgitation, No./d	2.9 (1.1) [2.7-3.0]	4.6 (3.2) [4.2-5.0]	
Evacuation, No./d	4.2 (1.8) [4.0-4.4]	3.6 (1.8) [3.4-3.8]	

Indrio et al. JAMA Pediatr. 2014

Associé à la Vitamine D : une bonne idée …

Endpoint	*Lactobacillus reuteri* + vitamin D3 (n=51)	Vitamin D3 (n=54)	Relative Risk (95% CI)	Chi^2 (*P*-value)	NNT[1]
Primary endpoints					
Use of cimetropium bromide	1	24	0.04 (0.01-0.31)	23.806 (<0.0001)	2.35
Use of simethicone	11	48	0.24 (0.14-0.41)	45.592 (<0.0001)	1.49
Secondary endpoint					
Use of infant formula in the first three months	7	20	0.37 (0.17-0.80)	6.291 (0.0121)	4.29
	Lactobacillus reuteri + vitamin D3 (average ± SD)	Vitamin D3 (average ± SD)	t value (df)	*P*-value	
Phone calls for each infant[2]	5.04±2.64	8.40±3.58	5.448 (103)	<0.0001	-
Visits for each infant[2]	2.66±1.77	4.98±1.89	6.483 (103)	<0.0001	-

[1] NNT = number needed to treat.
[2] Average ± standard deviation.

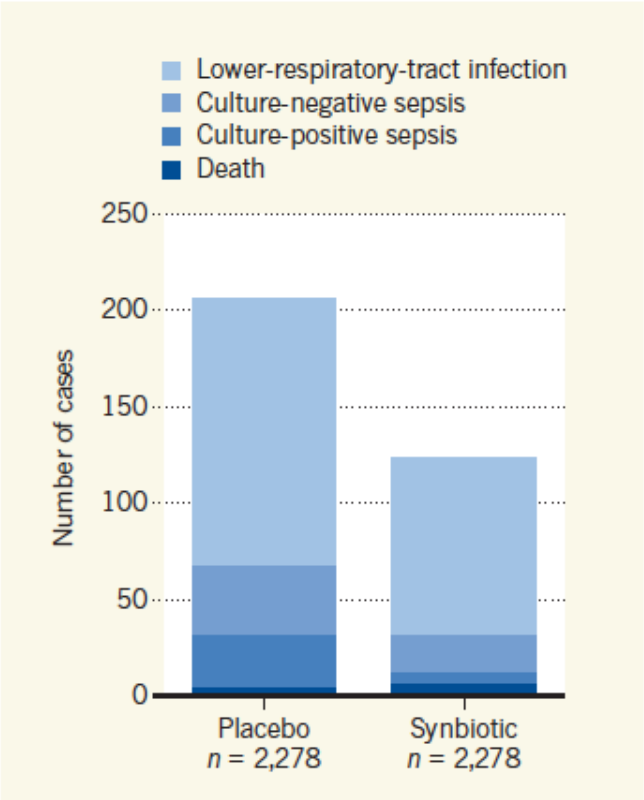
Savino, Beneficial Microbes

Recos USA C Diff 2018

Clinical Definition	Recommended Treatment	Pediatric Dose	Maximum Dose	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	• Metronidazole × 10 days (PO), OR • Vancomycin × 10 days (PO)	• 7.5 mg/kg/dose tid or qid • 10 mg/kg/dose qid	• 500 mg tid or qid • 125 mg qid	Weak/Low Weak/Low
Initial episode, severe/ fulminant	• Vancomycin × 10 days (PO or PR) with or without metronidazole × 10 days (IV)[a]	• 10 mg/kg/dose qid • 10 mg/kg/dose tid	• 500 mg qid • 500 mg tid	Strong/Moderate Weak/Low
First recurrence, non-severe	• Metronidazole × 10 days (PO), OR • Vancomycin × 10 days (PO)	• 7.5 mg/kg/dose tid or qid • 10 mg/kg/dose qid	• 500 mg tid or qid • 125 mg qid	Weak/Low
Second or subsequent recurrence	• Vancomycin in a tapered and pulsed regimen[b], OR • Vancomycin for 10 days followed by rifaximin[c] for 20 days, OR • Fecal microbiota transplantation	• 10 mg/kg/dose qid • Vancomycin: 10 mg/kg/dose qid; rifaximin: no pediatric dosing • …	• 125 mg qid • Vancomycin: 500 mg qid; rifaximin: 400 mg tid • …	Weak/Low Weak/Low Weak/Very low

McDonald et al. Clinical Infectious Diseases, 2018

Prévention des infections du nouveau-né par symbiotiques



- 4 556 nouveau-nés (j2-4)
- RCT contre placebo
- *Lactobacillus plantarum* + fructo-oligosaccharide
- Donné pendant 7 jours
- Suivi 2 mois

Panigrahi et al. Nature, 2017

Je met un probiotique dans une bonne indication et ça marche pas ?

La bonne formule ?

Randomised controlled trial demonstrates that fermented infant formula with short-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides reduces the incidence of infantile colic

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Keywords
Fermented formula, Gastrointestinal tolerance, Infant formula, Infantile colic, Prebiotic

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Received
1 November 2016; revised 28 November 2016; accepted 17 March 2017.

DOI:10.1111/apa.13844

ABSTRACT

Aim: We examined the effects on gastrointestinal (GI) tolerance of a novel infant formula that combined specific fermented formula (FERM) with short-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides (scGOS/lcFOS), with a 9:1 ratio and concentration of 0.8 g/100 mL.

Methods: This prospective, double-blind, randomised, controlled trial comprised 432 healthy, term infants aged 0–28 days whose parents decided to not start, or discontinued, breastfeeding. Infant formula with scGOS/lcFOS+50%FERM, scGOS/lcFOS+15%FERM, 50%FERM and scGOS/lcFOS were tested. Parents completed standardised seven-day diaries on GI symptoms, crying, sleeping and stool characteristics each month until the infants were 17 weeks.

Results: All the formulas were well tolerated. At four weeks, the overall incidence of infantile colic was significantly lower (8%) with scGOS/lcFOS+50%FERM than scGOS/lcFOS (20%, $p = 0.034$) or 50%FERM (20%, $p = 0.036$). Longitudinal modelling showed that scGOS/lcFOS+50%FERM-fed infants also displayed a persistently lower daily crying duration and showed a consistent stool-softening effect than infants who received formula without scGOS/lcFOS.

Conclusion: The combination of fermented formula with scGOS/lcFOS was well tolerated and showed a lower overall crying time, a lower incidence of infantile colic and a stool-softening effect in healthy term infants. These findings suggest for the first time that a specific infant formula has a preventive effect on infantile colic in formula-fed infants.

POSITION PAPER

Supplementation of Infant Formula With Probiotics and/or Prebiotics: A Systematic Review and Comment by the ESPGHAN Committee on Nutrition

JPGN 2011;52: 238–250

- **On the basis of this review, available scientific data suggest that the administration of currently evaluated probioticand/or prebiotic supplemented formula to healthy infants does not raise safety concerns with regard to growth and adverse effects**
- **At present, there is insufficient data to recommend the routine use of probiotic- and/or prebiotic-supplemented formulae.**

Update 2017 …

Some beneficial clinical effects are possible; however, there is no existing robust evidence to recommend their routine use.

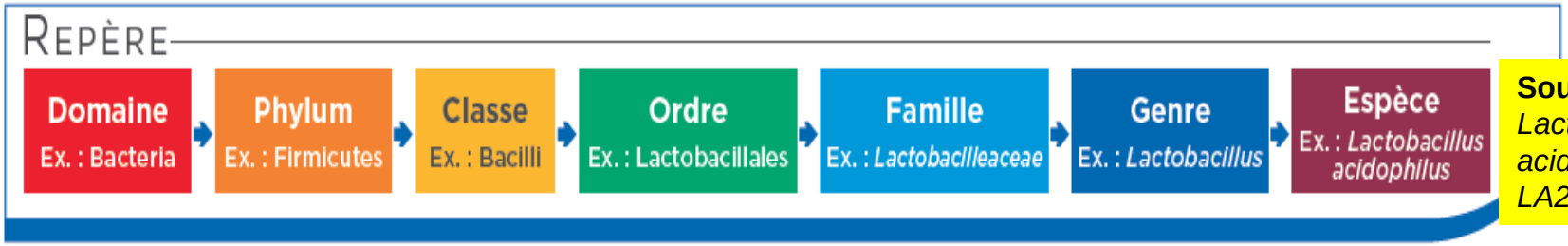
Skórka, Beneficial Microbes, 2017

La bonne souche à bonne dose ?

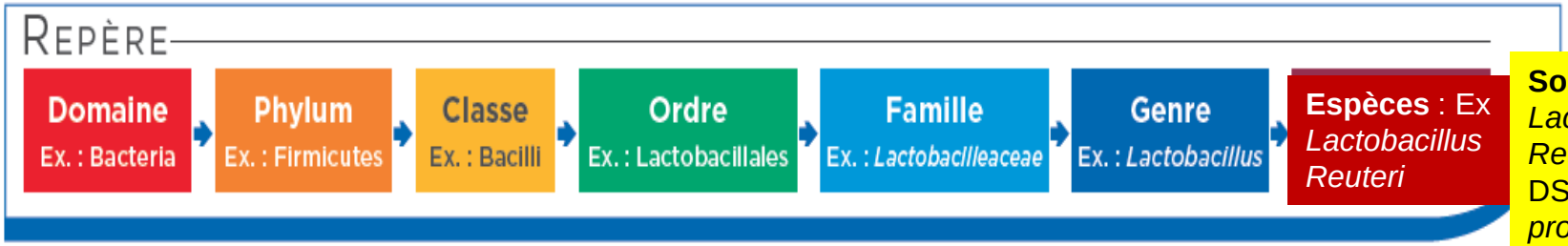
Commercial Probiotic Products: A Call for Improved Quality Control. A Position Paper by the ESPGHAN Working Group for Probiotics and Prebiotics

- Our review provides evidence on the inadequate quality of commercial probiotic products, with regard to microorganism specification, their numbers, functional properties, and the presence of contaminating microorganisms.

JPGN 2017;65: 117–124



Souches: Ex *Lactobacillus acidophilus LA201*



Souches: Ex *Lactobacillus Reuteri* DSM17938 *protectis*

Cavalier smith Biol Rev Camb Philos Soc 1998;73:203-66

La génétique de résistance ?

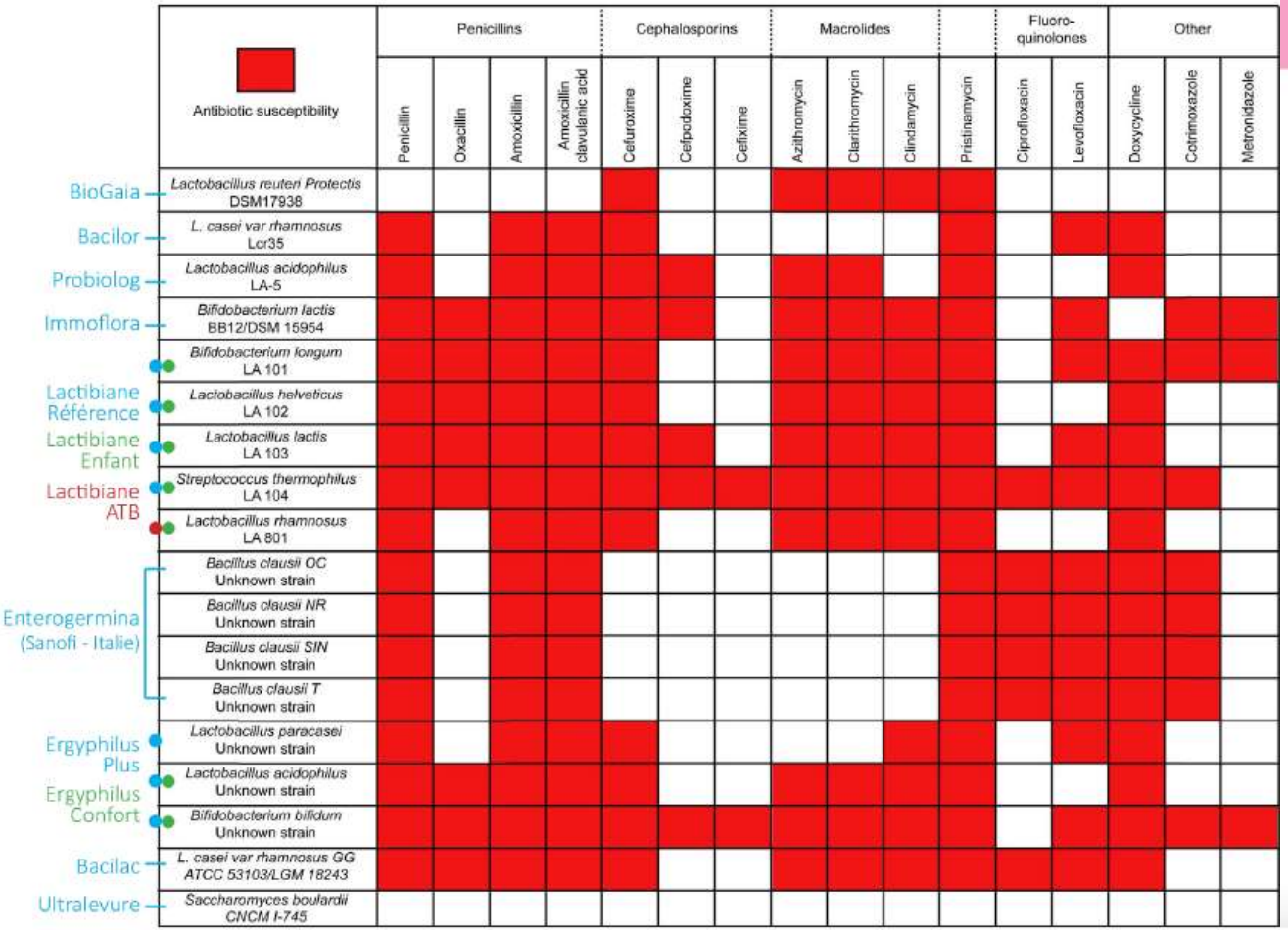
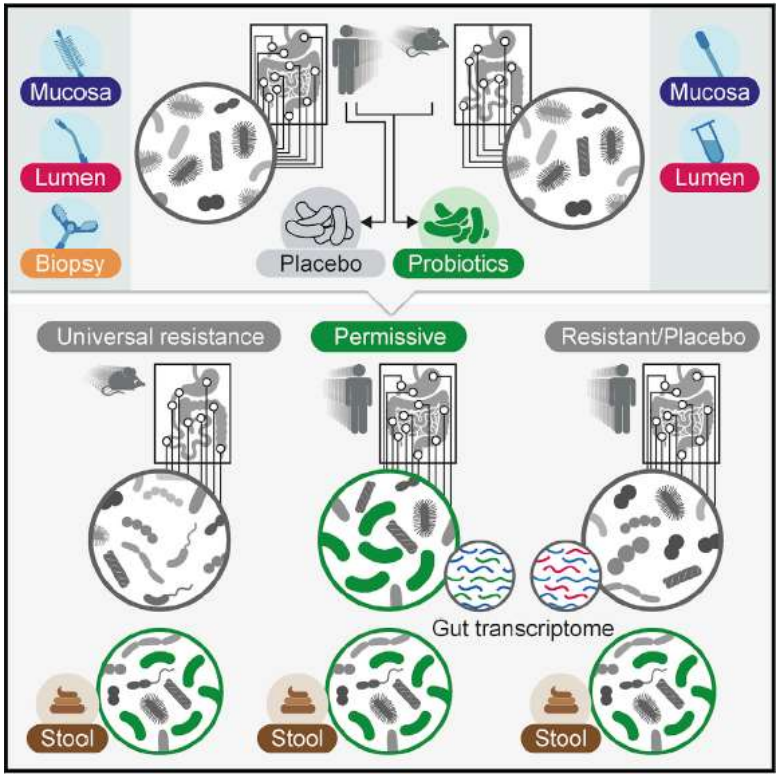


Fig. 1. Map of the antibiotic susceptibility of each probiotic strain.
Carte de sensibilité aux antibiotiques de chaque probiotique.

Personalized probiotics

25 volontaires
Echantillon microbiote prélevé en endoscopie.
Puis probiotiques ou placebo
Second cycle d'endoscopie
- Colonisation ok dits "persistants"
- Expulsion des bonnes bactéries : participants "résistants"

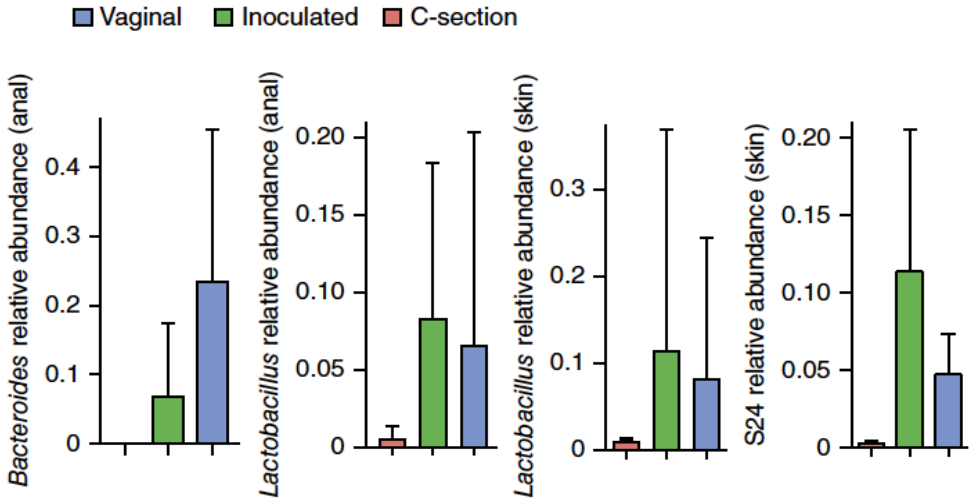


Zmora et al., 2018, Cell 174, 1388–1405

La bonne voie d'administration ?

nature medicine

« Vaginal seeding »



Nat Med. 2016 Mar;22(3):250-3

Microbiote

Take home 4 messages

Protéger son microbiote

Prévenir une dysbiose

Les probiotiques c'est pas automatique

Choisir la souche adaptée, c'est systématique !!!

Ce qui est simple est faux, ce qui est compliqué est inutilisable

Paul Valéry

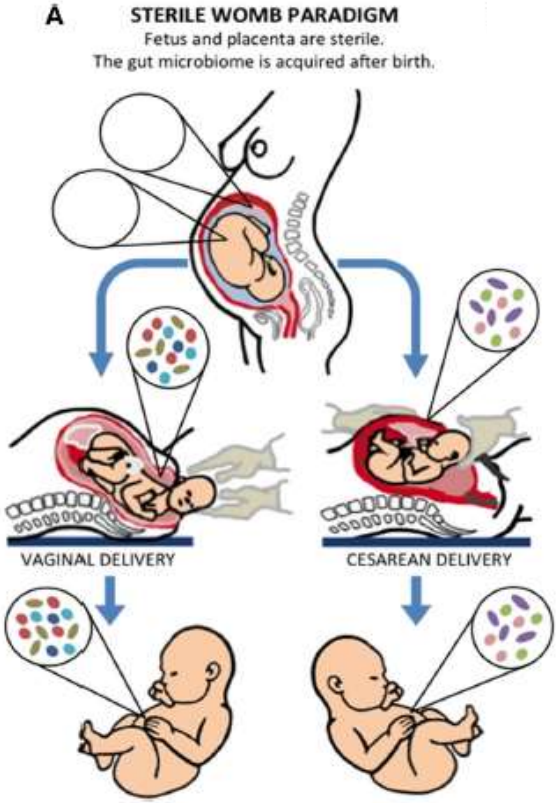
Un microbiote anténatal ?

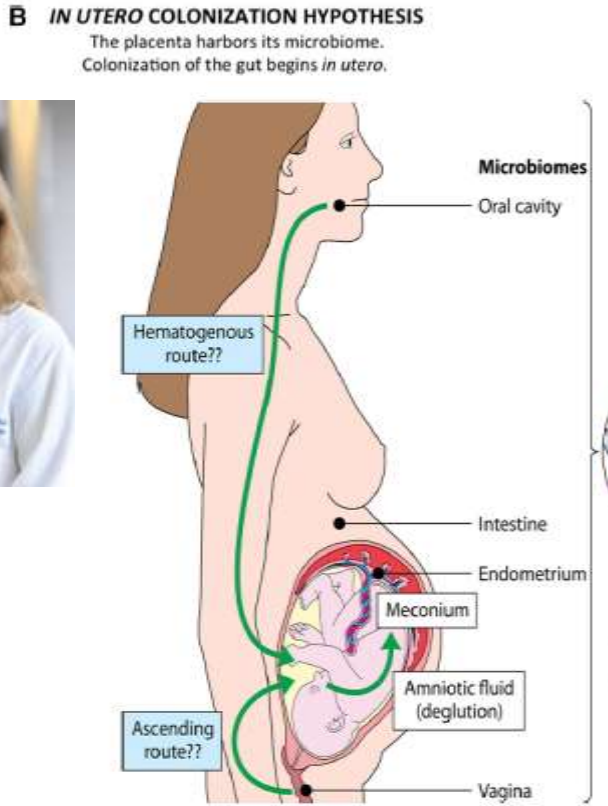
- **Placenta**
  Stout, Am. J. Obstet. Gynecol, 2013
  Aagaard, Sci Transl Med, 2014
- **Sang de cordon**
  Jiménez, Curr. Microbiol, 2005
- **Liquide amniotique**
  DiGiulio, Semin Fetal Neonatal Med, 2012
  Collado, Sci. Rep, 2016
- **Méconium avant alimentation <2h**
  Ardissone, PLoS One, 2014
  Hansen, Plos One, 2015

Microbiote anténatal : 2 visions

Henri Tissier
(1866-1926)

Kjersti M. Aagaard





Perez Munoz, Microbiome, 2017

Voie d'administration ?

Anodin ?

Activité universelle ou interindividuelle ?

Préventif ou curatif ?

Microbiote et coliques

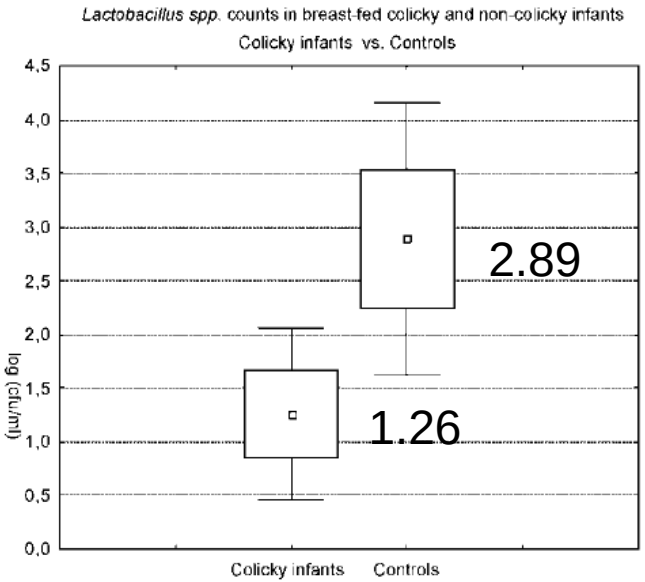
- **Objectif**
  - **Analyse de la flore fécale de nourrissons présentant des coliques vs sans coliques**
- **Méthode**
  - **N=71 (42 avec coliques ou 29 contrôle)**
  - **âgés de 15 à 60 jours**
  - **allaitement maternel exclusif**

Table 1. Clinical characteristics (mean ± SD) of the study population.

	Colicky ($n = 42$)	Non-colicky ($n = 29$)	Statistical analysis
Gender (M/F)	20/22	15/14	n.s.
Age at the study entry (wk)	3.1 ± 0.5	3.3 ± 0.6	n.s.
Type of delivery (vaginal birth/Caesarean section)	25/17	16/13	n.s.
Number of siblings (firstborns/others)	35/7	23/6	n.s.
Birthweight (g)	3304.14 ± 349.8	3280.56 ± 321.5	n.s.
Race (caucasoid/others)	38/4	25/4	n.s.
Crying time/day (min/d)	297 ± 33.6	102 ± 32.3	$p = 0.00$
			CI 95%: 179.01–210.99

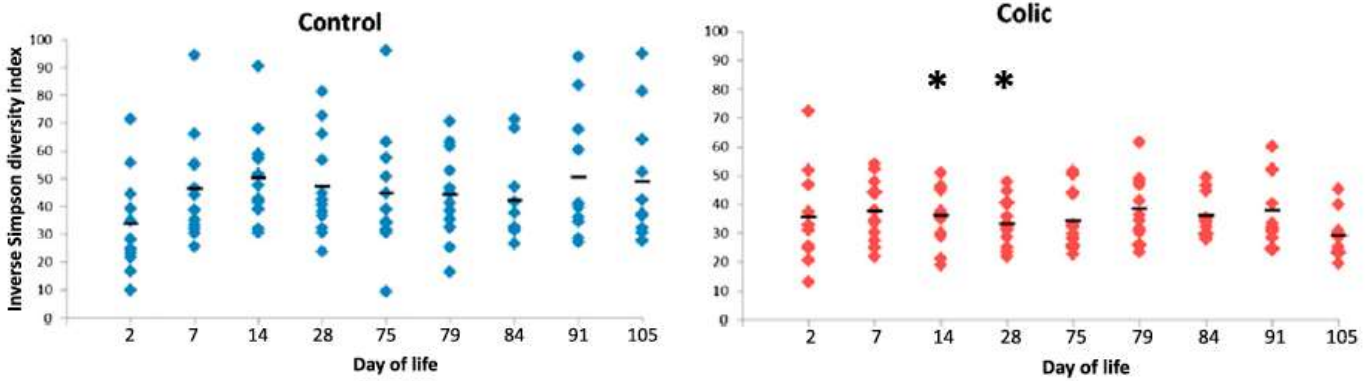
Savino et al. Intestinal microflora in breastfed colicky and non-colicky infants. Acta Paediatrica 2004; 93:825-829

Résultats



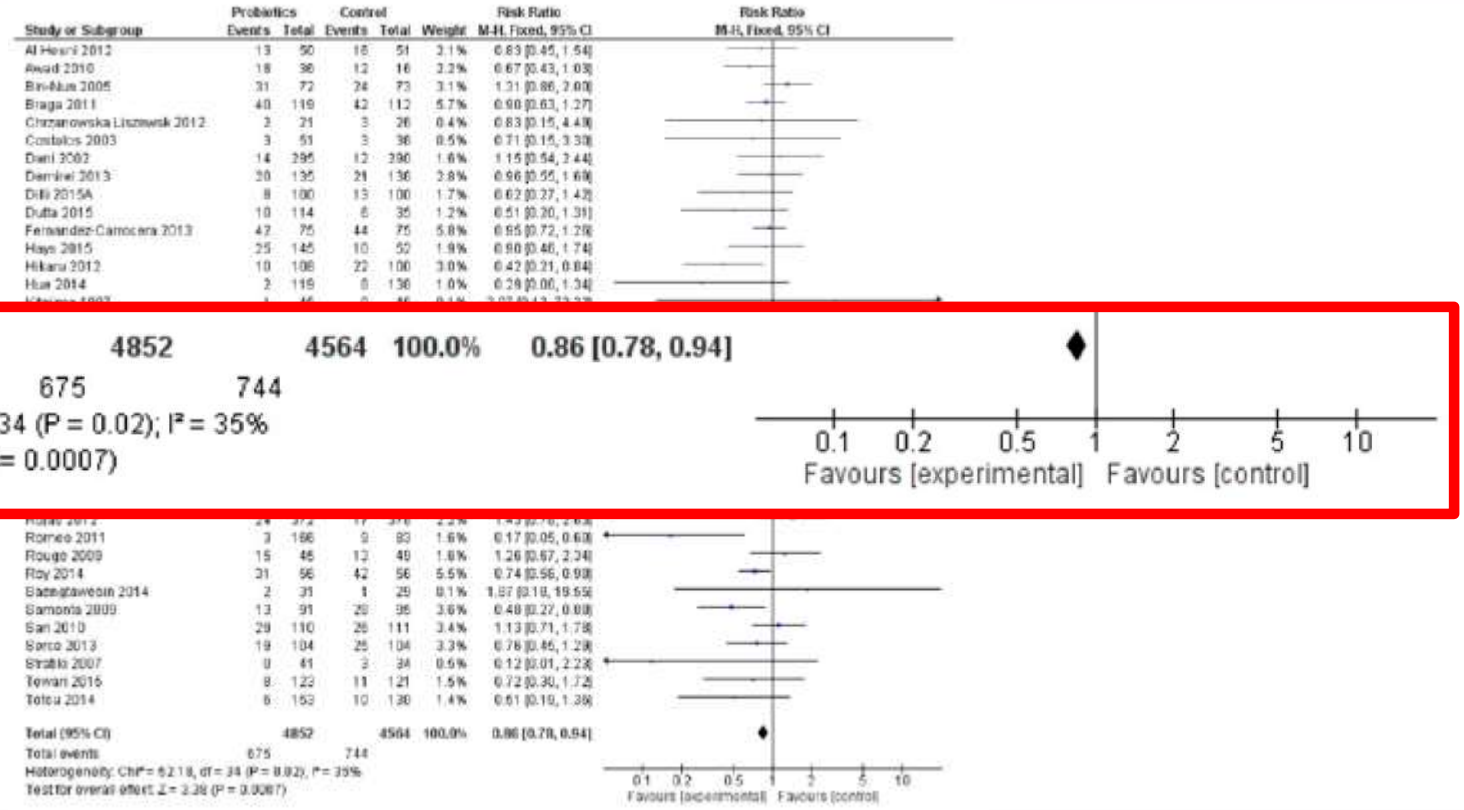
- Les nourrissons sans coliques présentent plus souvent de lactobacilles dans leur flore: 44% vs 19% (p=0.044)
- Et les nourrissons sans coliques ont une flore plus riche en lactobacilles (p=0.029)

Coliques et diversité microbienne



de Weerth, Pediatrics, 2013

Microbiote **Prévention du sepsis chez le prématuré**



Samedi 13 octobre 2018

Rao SC, et al. Probiotic Supplementation and Late-Onset Sepsis in Preterm Infants: A Meta-analysis. Pediatrics. 2016;137(3):e20153684

Crying Time and RORγ/FOXP3 Expression in *Lactobacillus reuteri DSM 17938*–Treated Infants with Colic: A Randomized Trial

Savino F, J Pediatr 2018

- Etude randomisée contrôlée
- *L reuteri* DSM 17938 (10^8 CFU) vs placebo, 30 jours
- Critères de Wessel modifiés

Table I. Baseline characteristics of the study population

	L reuteri (n = 32)	Placebo (n = 28)	*P* value
Mean age (d ± SD)	47.90 ± 25.78	46.11 [illegible]	
Sex			
Female, n (%)			
Male n (%)			.795†
Birth [illegible]		3085 ± 354.63	.521*
	38.21 ± 1.73	38.60 ± 1.92	.453*
[illegible], n (%)	25 (78.13)	24 (85.71)	.529†
Foreign, n (%)	5 (15.63)	4 (14.29)	1.000†
Mixed, n (%)	2 (6.25)	0	.494†
Feeding			
Exclusive breast milk, n (%)	28 (87.50)	22 (78.50)	.301†
Predominant breast milk, n (%)	4 (12.50)	6 (21.50)	.301†

Pas de différences sur les caractéristiques des groupes

Résultats

Durée moyenne (min/j)	*L reuteri* (n=32)	Placebo (n=32)	p value	IC 95%
J0	299,66 ± 27,55	305,41 ± 30,09	0,190	-9,85;12,20
J14	118,32 ± 21,12	226,31 ± 19,77	0,026	-25,02;-12,32
J21	95,11 ± 16,34	187,68 ± 31,88	0,009	-38,52;-46,12
J30	74,67 ± 25,04	147,85 ± 37,99	0,001	-87,32;-59,15

Diminution (médiane) de la calprotectine (p=0,0001) :

- *L reuteri* = 541 µg/g (J0) à 165 µg/g (J30)
- Placebo = 361 µg/g (J0) à 182 µg/g (J30)

Augmentation (médiane) du % des *Lactobacillus* (p=0,049) :

- *L reuteri* = 9,49% (J0) à 23,06% (J30)
- Placebo = 16,01% (J0) à 16,52% (J30)