Saccharomyces boulardii CNCM I-745®

Florastor®

ALL-IN-1 PROBIOTIC - PROBIOTIQUE TOUT-EN-1

Why should you recommend Florastor ?

March 27th 2025

Sponsored by Biocodex Canada Inc

Andy is a private practice dietitian and multi-time published author from Toronto, Canada where he graduated from the University of Toronto School Of Public Health with a master's in public health nutrition in 2014.

Since then Andy's career has taken him through the research and education department of Diabetes Canada and eventually into the world of private practice, writing and social media where he now balances working with clients one on one with an insatiable desire for learning and sharing nutrition science to a broader audience

AGENDA

1. Biocodex & Florastor introductions
2. *S. Boulardii* Unique mechanisms of action
3. When should I recommend Florastor ?
   Prevention and treatment
4. Antibiotic Associated Dysbiosis &
   Antibiotic Associated Diarrhea
5. Scientific guidelines

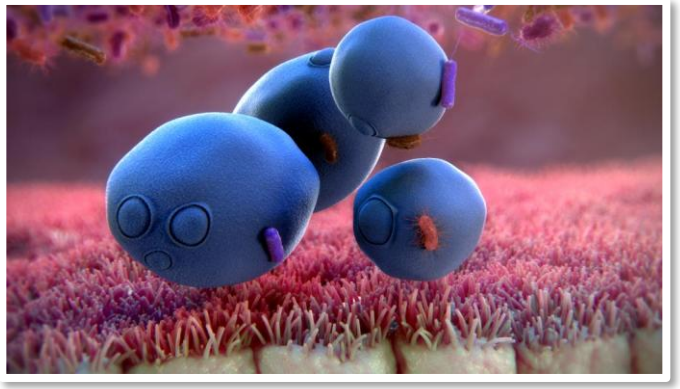
Biocodex & Florastor introductions

Who is Biocodex?

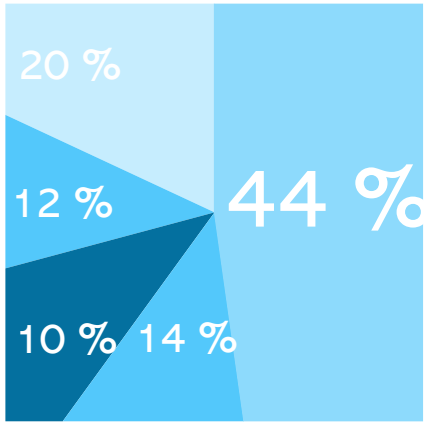
Family-owned multinational pharmaceutical company founded in France in 1953 with a specialization in gastroenterology thanks to a unique probiotic:

The yeast *Saccharomyces boulardii* CNCM I-745®:

- 1st probiotic in the world in its category
- has made it possible to treat 460 MILLION patients since its commercialization.



Portfolio development in new therapeutic areas



44% GASTROENTEROLOGY
14% NEUROLOGY
10% PAIN MANAGEMENT
12% GENERAL MEDICINE
20% WOMEN'S HEALTH

Gastroenterology
Saccharomyces boulardii
CNCM I-175®
Symbiosys®

Women's Health
Saforelle®
Mucogyne®
Physioflor®

Orphan diseases
Diacomit®

Pain
Otipax®
Acupan®

General medicine
Melaxose®
Dolenio®

BIOCODEX Canada Florastor

Saccharomyces boulardii discovery

A yeast sold worldwide

Saccharomyces boulardii **CNCM I-745®**

17 brand names in 130 countries

IN CLASS #1 WORLDWIDE*

TIQVIA MIDAS® Q1 2023 release & IQVIA Consumer Health Customized Insights Q1 2023 release of quarterly sales data for the time period January 2022 to December 2022 reflecting estimates of real-world activity. Copyright IOVIA. All rights reserved.

Who is Florastor?

Florastor is an **all-in-1 probiotic** that helps support gastrointestinal health and could promote a healthy gut flora.

Who is Florastor?

» Florastor is different from the many other probiotics because it's a **yeast**, other probiotics are mainly bacteria
» This yeast is naturally derived. It comes from **tropical fruits** : mangosteen and lychee fruit skin

Saccharomyces boulardii **CNCM I-745®**

» The yeast is called Saccharomyces boulardii
» Florastor is made from a **unique and specific strain** of this yeast the CNCM I-745

Florastor, a natural, convenient and resistant probiotic

NATURAL

Yeast derived from mangosteen and lychee

Vegetarian

Gluten-free

GMO-free

CONVENIENT

No refrigeration needed

Sachet powder / capsule / vial formats

Can be taken anytime during the day, and even **while taking antibiotics**

RESISTANT

Can **withstand the harsh stomach environment**

Yeast 10X larger than bacterial cells **covering a larger intestinal area**

Florastor, an all-in-1 probiotic

Daily Gut support

» Helps support gut health on a daily basis

» Helps prevent the risk of antibiotic-associated diarrhea, acute diarrhea and traveler's diarrhea

Children 3+ months

» Helps support children's gut health and could promote a favorable gut flora

» Helps treat acute diarrhea and prevent antibiotic-associated diarrhea

Double concentration

» Helps reduce recurrent diarrhea associated with *Clostridium difficile* when used as an adjunct to antibiotics

» Is complementary to antibiotic therapy in patients with H. Pylori infections

Gut & Immune Support

» Helps support the immune system

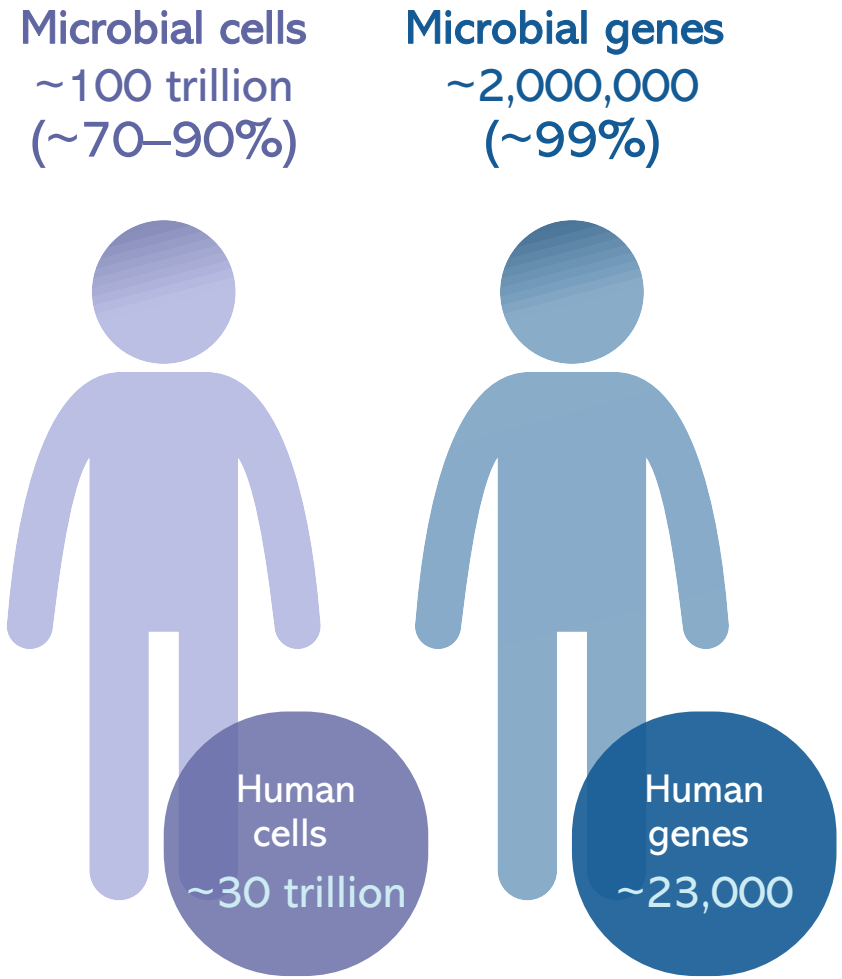
» Helps maintain healthy bones, hair, nails and skin

Gut Microbiota Reminder

Microbiota

Microbiome:
the collective genomes of the micro-organisms in a particular environment

Microbiota:
the community of micro-organisms themselves



Adapted from https://www.Amnh.Org/explore/science-topics/microbiome-health/meet-your-microbiome

The roles & functions of the gut microbiota

1. METABOLIC ROLE	2. BARRIER ROLE	3. DEFENSIVE ROLE	4. MAINTENANCE ROLE	5. GUT-BRAIN AXIS
Impacts on: • Fermentation of **NON DIGESTIBLE CARBOHYDRATES** • Synthesis of **VITAMINS**	Is a key determinant of a **PHYSIOLOGICAL COLONIC BARRIER**	**70 % OF THE IMMUNE SYSTEM** resides in the gut	• Modulates the number and function of goblet cells: impact on **MUCUS PRODUCTION** • Influences the **MOTILITY** and intestinal peristalsis	• Can regulate **FEELINGS OF SATIETY** • May influence responses to **PHYSICAL AND PSYCHOLOGICAL STRESS**

Rowland I, Gibson G, Heinken A, et al. Gut microbiota functions: metabolism of nutrients and other food components. European Journal of Nutrition. 2018;57(1):0. doi:10.1007/s00394-017-1445-8 / Tomas J, Sansonetti P. Host-microbiota dialog: interactions between the microbiota and the intestinal epithelium. In: Marteau P, Dore J, eds. Gut Microbiota: A Full-Fledged Organ. Paris: John Libbey Eurotext; 2017:55-64.

S. BOULARDII
Unique mechanisms of action

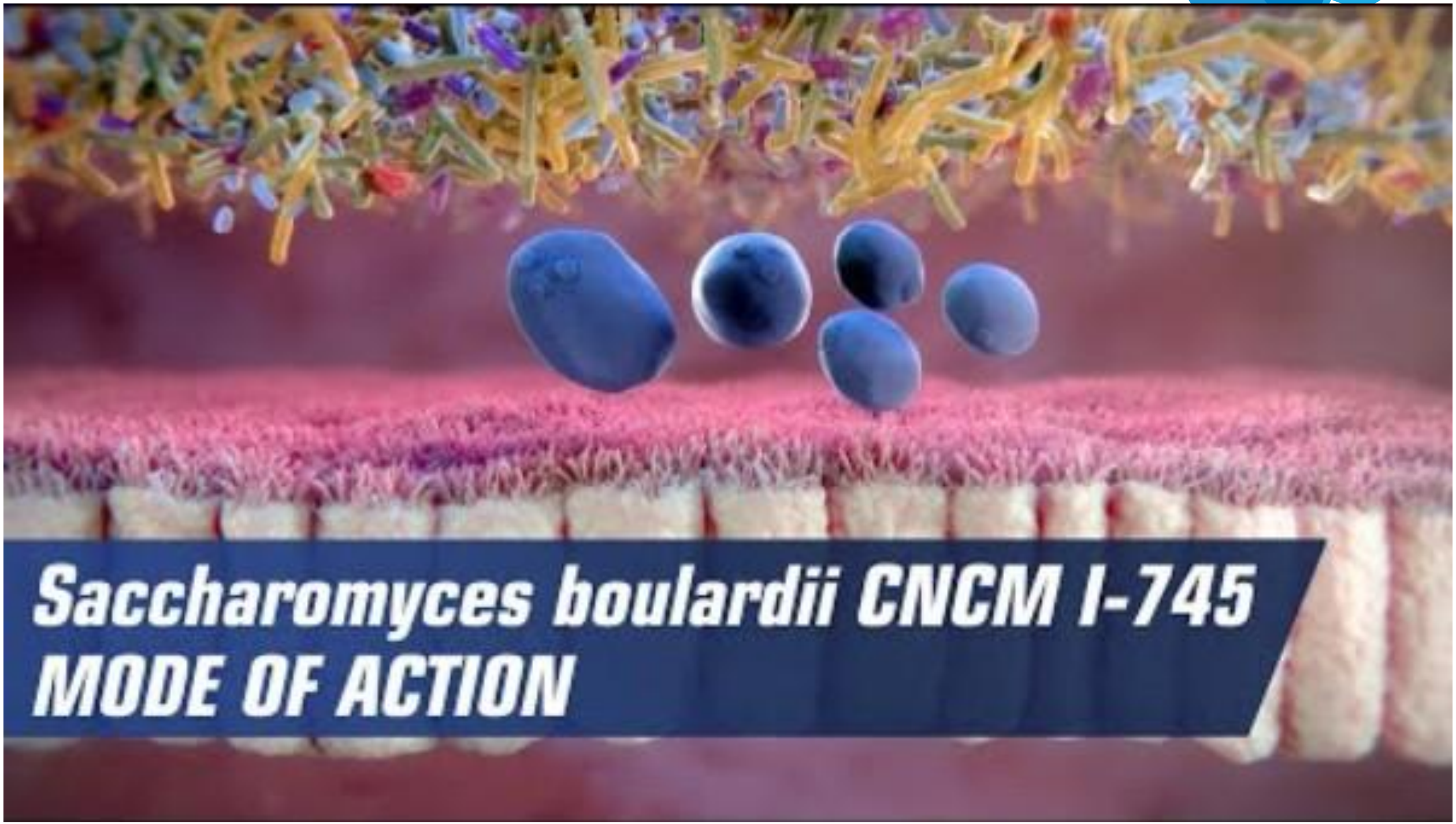
Comparative features of bacterial and yeast probiotics

S. boulardii CNCM I-745 possesses several features that make it suited to be a unique probiotic. It is **naturally non susceptible to antibiotics**, can **survive at low pH**, and **does not permanently colonize the gut**, meaning it does not disturb the microbiota composition3.

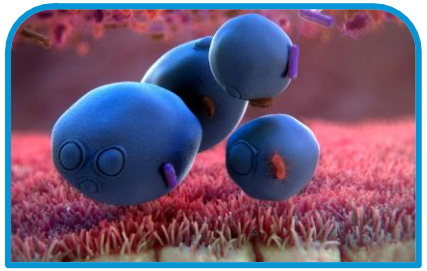
ACTION/PROPERTY	BACTERIA	YEAST
Presence in the human microbiota	99%	<1%
Cell size	1 µm	10 µm
Cell wall composition	Peptidoglycan, LPS, LTA...	Mannose, chitin...
Growth conditions pH	6.5-7.5	2-7
Growth conditions temperature (C°)	10-80	20-30
Resistance to antibiotics	No	Yes
Transmission of genetic material	Yes	No

LPS: lipopolysaccharide; LTA: lipoteichoic acid.

Neut, C., Mahieux, S. & Dubreuil, L. J. Antibiotic susceptibility of probiotic strains: Is it reasonable to combine probiotics with antibiotics? Médecine et Maladies Infectieuses 47, 477–483 (2017). / Edwards-Ingram, L. et al. Genotypic and Physiological Characterization of Saccharomyces boulardii , the Probiotic Strain of Saccharomyces cerevisiae. Appl Environ Microbiol 73, 2458–2467 (2007). / Moré, M. I. & Swidsinski, A. Saccharomyces boulardii CNCM I-745 supports regeneration of the intestinal microbiota after diarrheic dysbiosis – a review. Clin Exp Gastroenterol 8, 237–255 (2015). / Czerucka, D., Piche, T. & Rampal, P. Review article: yeast as probiotics – Saccharomyces boulardii. Aliment Pharmacol Ther 26, 767–778 (2007).


Saccharomyces boulardii CNCM I-745
MODE OF ACTION

S. boulardii Unique mechanisms of action



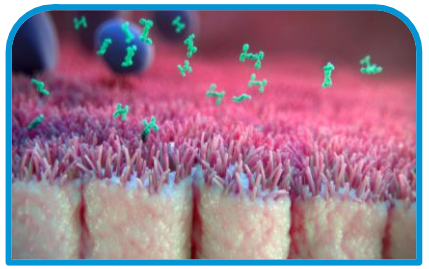
LUMINAL ACTION

METABOLIC ACTION: increases Short-Chain Fatty Acids feeding the intestinal epithelia cells **promoting overall gut health.**

ANTI-TOXIN ACTION : produces proteins that degrade and **destroy harmful toxins** that can lead to water secretion and diarrhea.

ANTI-MICROBIAL ACTION: helps prevent harmful bacteria from invading the intestinal epithelia by causing the bacteria to adhere to it's cell walls. And, unlike other probiotics, *S. boulardii* does not colonize in the intestines, so those **harmful bacteria are then flushed out the digestive system.**

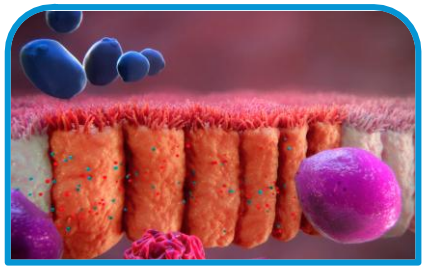
FLORA MODULATION: promotes **normalization of the intestinal flora that have been depleted by antibiotics**.



TROPHIC ACTION

DIGESTIVE ACTION: increases polyamine levels which promotes the maturation of enterocytes and **stimulates the production of digestive enzymes**. This enhances the **absorption of water and nutrients.**

IMMUNE STIMULATION: **stimulates the production of IgA**, the body's most common antibody that protects against bacterial and viral infections.



MUCOSAL ACTION

Decreases the secretion of pro-inflammatory cytokines to help **protect against gut inflammation**

Czerucka D, Rampal P. Diversity of Saccharomyces boulardii CNCM I-745 mechanisms of action against intestinal infections. World journal of gastroenterology. 2019;25(18):2188-2203. doi:10.3748/wjg.v25.i18.2188. / More MI, Swidsinski A. Saccharomyces boulardii CNCM I-745 supports regeneration of the intestinal microbiota after diarrheic dysbiosis - A review. Clinical and Experimental Gastroenterology. 2015;8:237-255. doi:10.2147/CEG.S85574. / Joly F et al. Saccharomyces boulardii CNCM I-745. In: Marteau P, Dore J, eds. Gut Microbiota: A Full-Fledged Organ. Paris: John Libbey Eurotext; 2017:305-350. / Buts, J.P., Bernasconi, P., Van Craynest, M.P., Maldague, P., & De Meyer, R. (1986). Response of human and rat small intestinal mucosa to oral administration of Saccharomyces boulardii. Pediatric Research, 20, 192-196.

When should I recommend Florastor ?
Prevention and treatment

Prevention & Treatment

PREVENTION

Antibiotic-Associated Diarrhea: S. boulardii CNCM I-745 has shown efficacy in preventing antibiotic-associated diarrhea, a common consequence of antibiotic use, which disrupts the balance of gut microbiota.

Antibiotic-Associated Dysbiosis : S. boulardii CNCM I-745 plays a role in preventing dysbiosis by restoring balance and promoting the growth of beneficial bacteria following antibiotic treatment.

***Clostridium difficile* Infection** : One of the most severe forms of antibiotic-associated complications is CDI, where S. boulardii CNCM I-745 helps reduce recurrence rates by neutralizing the harmful effects of the pathogen's toxins.

***Helicobacter pylori* :** Eradication Therapy: S. boulardii CNCM I-745 serves as an adjunct therapy, reducing the adverse effects of antibiotics and maintaining gut health, thereby improving the success rate of eradication and minimizing side effects like diarrhea.

Travelers' diarrhea : Significant reduction in the risk of TD was observed in the latest meta-analysis by McFarland.

TREATMENT

Acute Diarrhea (AD): Traditionally, *S. boulardii* CNCM I-745 was used for its ability to treat AD, helping to restore intestinal balance. This probiotic yeast exerts its therapeutic action by **inhibiting pathogens**, **reducing inflammation**, and **enhancing the gut's natural defense mechanisms**.

Szajewska, H. & Kołodziej, M. Systematic review with meta-analysis: Saccharomyces boulardii in the prevention of antibiotic-associated diarrhoea. Aliment Pharmacol Ther 42, 793–801 (2015). / Zhao, Y. et al. Saccharomyces boulardii Combined With Quadruple Therapy for Helicobacter pylori Eradication Decreased the Duration and Severity of Diarrhea: A Multi-Center Prospective Randomized Controlled Trial. Front. Med. 8, 776955 (2021). / Kabbani, T. A. et al. Prospective randomized controlled study on the effects of Saccharomyces boulardii CNCM I-745 and amoxicillin-clavulanate or the combination on the gut microbiota of healthy volunteers. Gut Microbes 8, 17–32 (2017). / Waitzberg, D. et al. Can the Evidence-Based Use of Probiotics (Notably Saccharomyces boulardii CNCM I-745 and Lactobacillus rhamnosus GG) Mitigate the Clinical Effects of Antibiotic-Associated Dysbiosis? Adv Ther 41, 901–914 (2024). / Czerucka, D., Piche, T. & Rampal, P. Review article: yeast as probiotics – Saccharomyces boulardii. Aliment Pharmacol Ther 26, 767–778 (2007). / McFarland, L. V. et al. A randomized placebo-controlled trial of Saccharomyces boulardii in combination with standard antibiotics for Clostridium difficile disease. JAMA 271, 1913–1918 (1994). / Seddik, H. et al. Saccharomyces boulardii CNCM I-745 plus sequential therapy for Helicobacter pylori infections: a randomized, open-label trial. Eur J Clin Pharmacol 75, 639–645 (2019). / Zhou, B., Chen, L., Li, B., Wan, L. & Ai, Y. Saccharomyces boulardii as an adjuvant therapy for Helicobacter pylori eradication: A systematic review and meta-analysis with trial sequential analysis. Helicobacter 24, e12651 (2019). / Altcheh, J. et al. Randomized, direct comparison study of Saccharomyces boulardii CNCM I-745 versus multi-strained Bacillus clausii probiotics for the treatment of pediatric acute gastroenteritis. Medicine 101, e30500 (2022)./ McFarland, L. V. Systematic review and meta-analysis of Saccharomyces boulardii in adult patients. World J Gastroenterol 16, 2202–2222 (2010).

Role of S. boulardii
Antibiotic-Associated Dysbiosis

Antibiotics and gut microbiota. Composition

Antibiotics induce changes on gut microbiota:

- Affecting gut microbiota diversity and the recovery capability
- Inducing alteration in abundance of certain taxa
- The changes in the gut microbiota induced by different classes of antibiotics vary according to:
  - drug spectrum
  - administration route
  - host characteristic and state

Commonly observed microbiota changes by main antibiotic classes

Glycopeptide antibiotic

- *Adlercreutzia*↓
- *Akkermansia muciniphila*↑
- *Barnesiella*↓
- *Clostridium XIVa*↓
- *Eggerthella*↓
- *Enterococcus*↓
- *Escherichia coli* ↑↓
- *Escherichia/Shigella*↑
- *Eubacterium hallii*↓
- *Faecalibacterium*↓
- *Haemophilus*↑
- *Oscilibacter*↓
- *Proteus*↑
- *Rikenellacea*↓
- *Serratia*↑

Beta-lactam antibiotic

- *Asaccharobacter*↓
- *Butyricicoccus*↓
- *Butyricimous*↓
- *Coprobacillus*↓
- *Eubacterium rectale*↓
- *Gemellales*↓
- *Klebsiella*↑
- *Propionibacterium freudenreichi*↑
- *Pseudomonas*↑
- *Roseburia inulinivorans*↓
- *Ruminococcus bromii*↓
- *Streptococcus thermophilus*↑

- *Alistipes*↓
- *Bacteroides*↓
- *Dorea*↓
- *Feacalibacterium prausnitizii*↓
- *Parabacteroides*↓
- *Prevotella*↓

- *Bifidobacterium*↓
- *Lactobacillus*↓

- *Enterococcus*↑
- *Papillibacter*↓

- *Subdoligranulum*↑
- *Moryella*↑

Quinolone antibiotic

- *Anaerostipes*↓
- *Bacteroides*↑
- *Christensenella*↓
- *Collinsella*↓

- *Eggerthella*↑
- *Parabacteroides*↑
- *Streptococcus*↑

Macrolide antibiotic

Adapted from: Duan, H., Yu, L., Tian, F., Zhai, Q., Fan, L., & Chen, W. (2020). Antibiotic-induced gut dysbiosis and barrier disruption and the potential protective strategies. Critical Reviews in Food Science and Nutrition, 1-26.

Protection of the gut microbiota

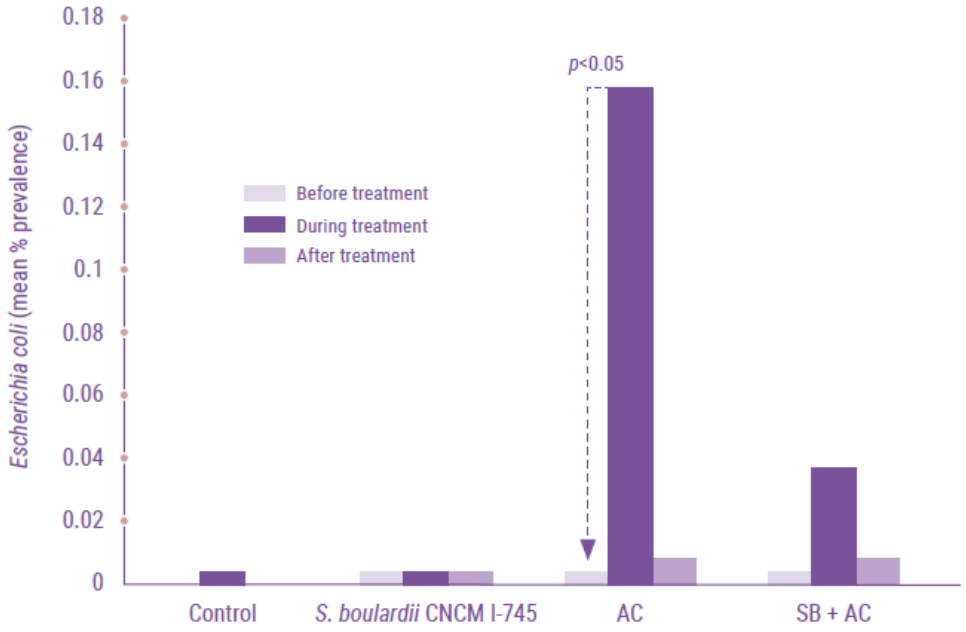


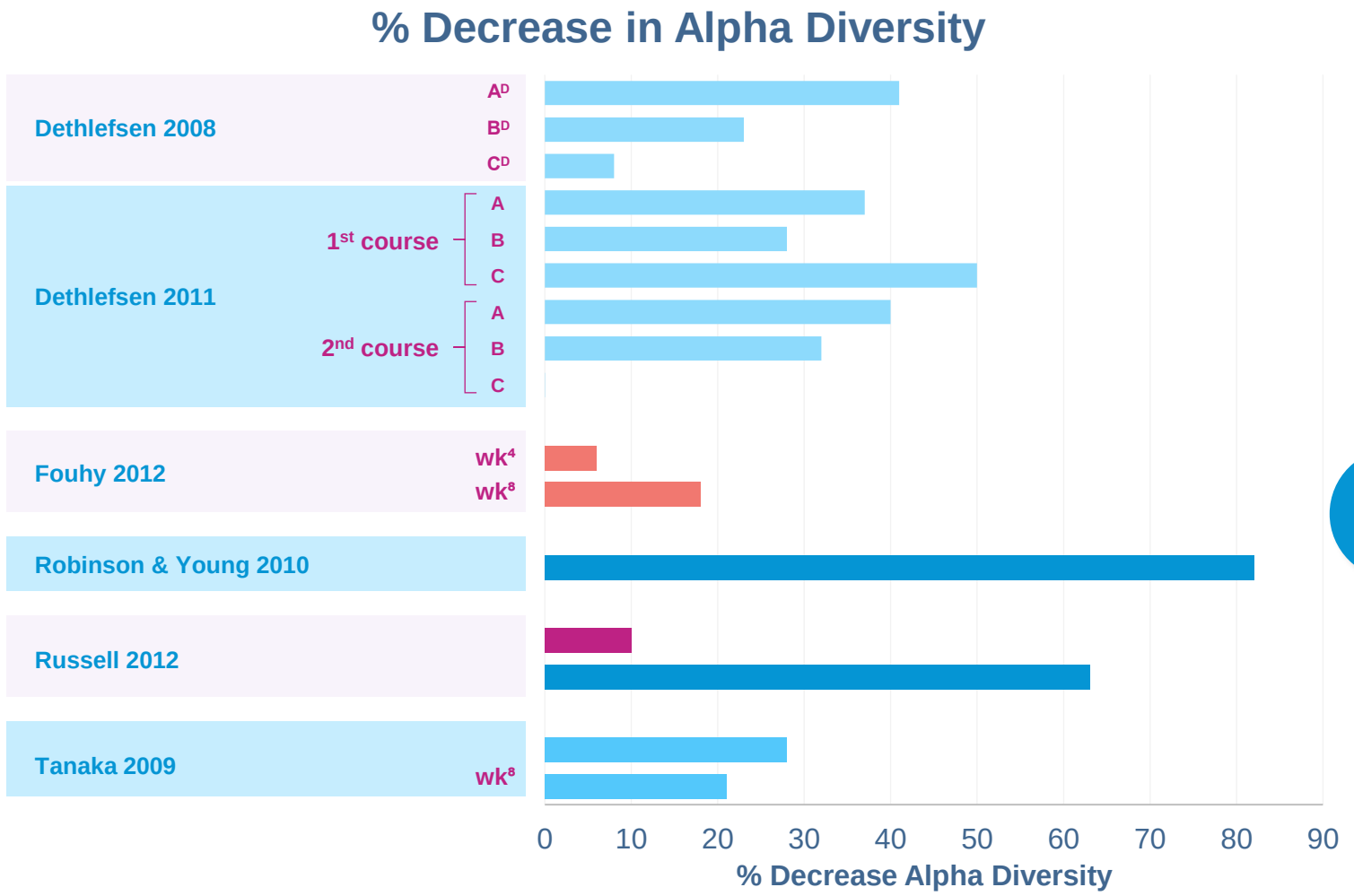
Figure 29: Prevalence of *Escherichia coli* during *S. boulardii* CNCM I-745 and amoxicillin-clavulanate treatment. (Adapted from Kabbani TA *et al.*, 2017 [37]).

SB: *S. boulardii* CNCM I-745; AC: amoxicillin-clavulanate; SB + AC: *S. boulardii* CNCM I-745 + amoxicillin-clavulanate treatment.

- *S. Boulardii* CNCM I-745 administration during antibiotic treatment leads to protection of the gut microbiota diversity by reducing microbiota composition shifts.
- It prevents in the prevalence of some normal beneficial bacteria and prevent the overgrowth of pathogenic *E. coli* associated with diarrhea.

Kabbani, T. A. et al. Prospective randomized controlled study on the effects of Saccharomyces boulardii CNCM I-745 and amoxicillin-clavulanate or the combination on the gut microbiota of healthy volunteers. Gut Microbes 8, 17–32 (2017).

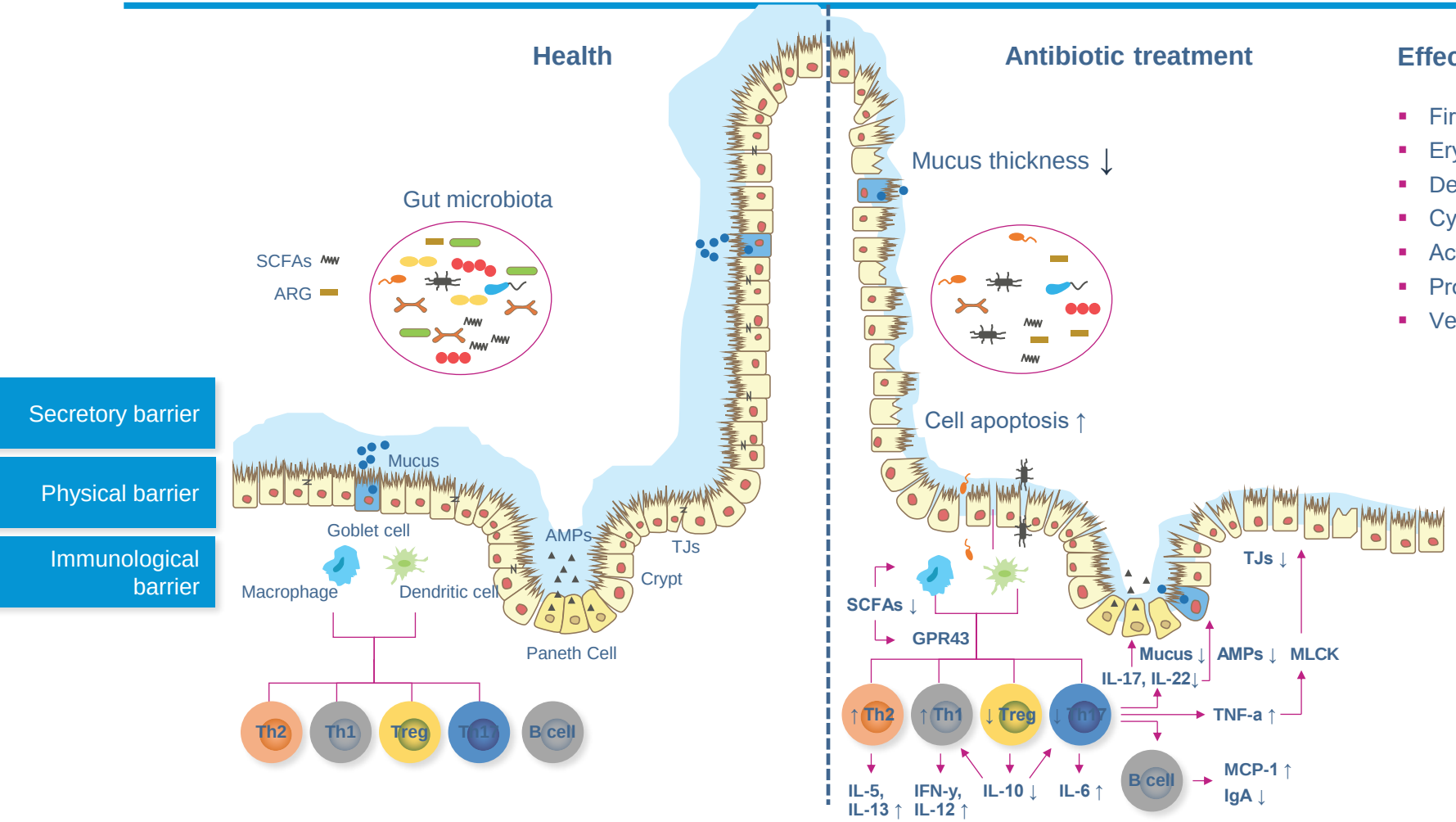
Antibiotics and gut microbiota. Diversity. Example in children



- Current studies report a large range of percent losses of biodiversity after antibiotic exposure suggesting that some subjects may take longer to recover to baseline than others
- The recovery period represents a vulnerable time for the host, since not all members of the microbial community are present to suppress blooms of (potential) pathogens and pathobionts and hence prevent infection.

Adapted from: Vangay et al. Cell host & microbe 17.5 (2015): 553-564.

Antibiotics and gut microbiota. Metabolites and gut barrier



Effects of antibiotics on microbiota diversity

- Firmicutes ↓
- Erysipelotrichia ↓
- Deferribacteres ↓
- Cyanobacteria ↓
- Actinobacteria ↓
- Proteobacteria ↑
- Verrucomicrobia ↑
- Bacteroidetes ↑↓
- Tenericutes ↑↓
- Cytophaga-Flavobacterium-Bacteriodete (CFB) **missing**
- Antibiotic-resistant bacteria ↑

- Reduction in short chain fatty acids
- Disruption of physical barrier
- Disruption of mucus barrier
- Disruption of immunological barrier

Adapted from: Duan, H., Yu, L., Tian, F., Zhai, Q., Fan, L., & Chen, W. (2020). Antibiotic-induced gut dysbiosis and barrier disruption and the potential protective strategies. Critical Reviews in Food Science and Nutrition, 1-26.

Restoration of microbiota. Role of *Saccharomyces boulardii* CNCM I-745

Summary of effects induced by *S. boulardii* CNCM I-745, both during a dysbiotic situation and in the prevention of dysbiosis

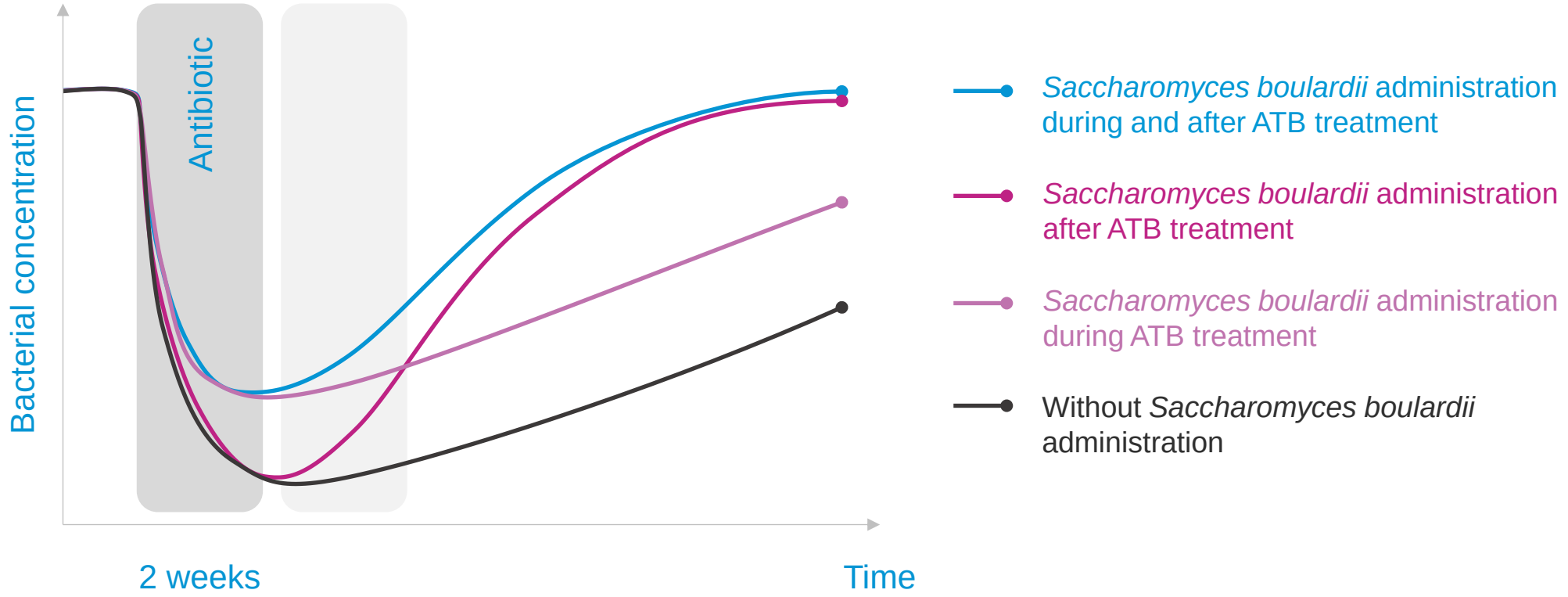
Probiotic creation of a favorable microbiotic environment	Mucus protection; elimination of bacterial toxins, pathogen binding	Possible prebiotic *(substrate for beneficial microbiota)* effect and stimulation of digestive enzymes
Preventive action	▪ Protection against pathogens and their toxins	▪ Stabilization of healthy microbiota; ▪ Improved enzymatic function of mucosal cells
In case of dysbiosis	▪ Protections against pathogens and their toxins; ▪ Regeneration of mucosal cells	▪ Regeneration and stabilization of healthy microbiota; ▪ Improved enzymatic function of mucosal cells

Adapted from: Moré, M. I., & Swidsinski, A. (2015). Saccharomyces boulardii CNCM I-745 supports regeneration of the intestinal microbiota after diarrheic dysbiosis–a review. Clinical and Experimental Gastroenterology, 8, 237.

Florastor

Restoration of microbiota. *Saccharomyces boulardii* CNCM I-745

Proposed impact of *Saccharomyces boulardii* CNCM I-745 on intestinal bacterial populations during antibiotic treatment



Adapted from: Moré, M. I., & Swidsinski, A. (2015). Saccharomyces boulardii CNCM I-745 supports regeneration of the intestinal microbiota after diarrheic dysbiosis–a review. *Clinical and Experimental Gastroenterology*, *8*, 237.

Florastor

Role of *S. boulardii*

Antibiotic Associated Diarrhea

Antibiotic-Associated Diarrhea (AAD). Definition

Antibiotic Associated diarrhea (AAD) is defined as:

Diarrhea occurring in conjunction with antibiotic administration

- Early onset - occurring during antibiotic administration
- Delayed onset - occurring up to 2 months after its discontinuation

Not attributable to any other cause (like infection) or condition (like Irritable Bowel Syndrome)

McFarland, Lynne V. "Antibiotic-associated diarrhea: epidemiology, trends and treatment." (2008): 563-578.

AAD. Risk factors

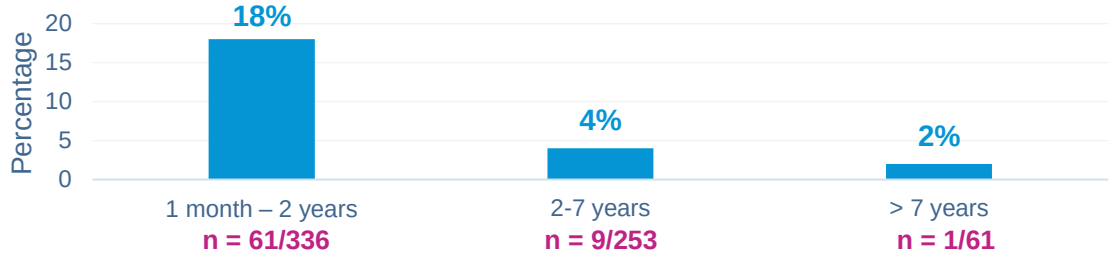
Certain Risk Factors [2]

- **Age**
  - Young children
  - Seniors
- **Hospitalization (more common than outpatients)**
- **History of AAD (patient individual susceptibility)**
- **Antibiotic agent**

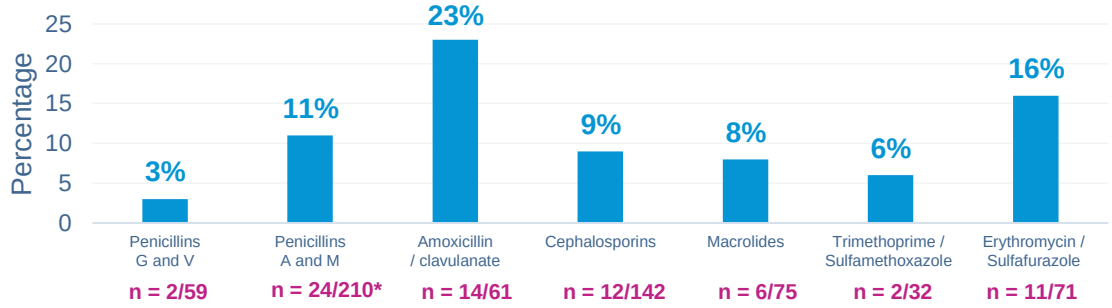
Incidence and Risk Factors of Oral Antibiotic-Associated Diarrhea in an Outpatient Pediatric Population [1]

*Dominique Turck, †Jean-Paul Bernet, †Jacques Marx, †Hélène Kempf, †Patrick Giard,

Incidence of episodes of diarrhea according to age.



Incidence of episodes of diarrhea according to antibiotics prescribed

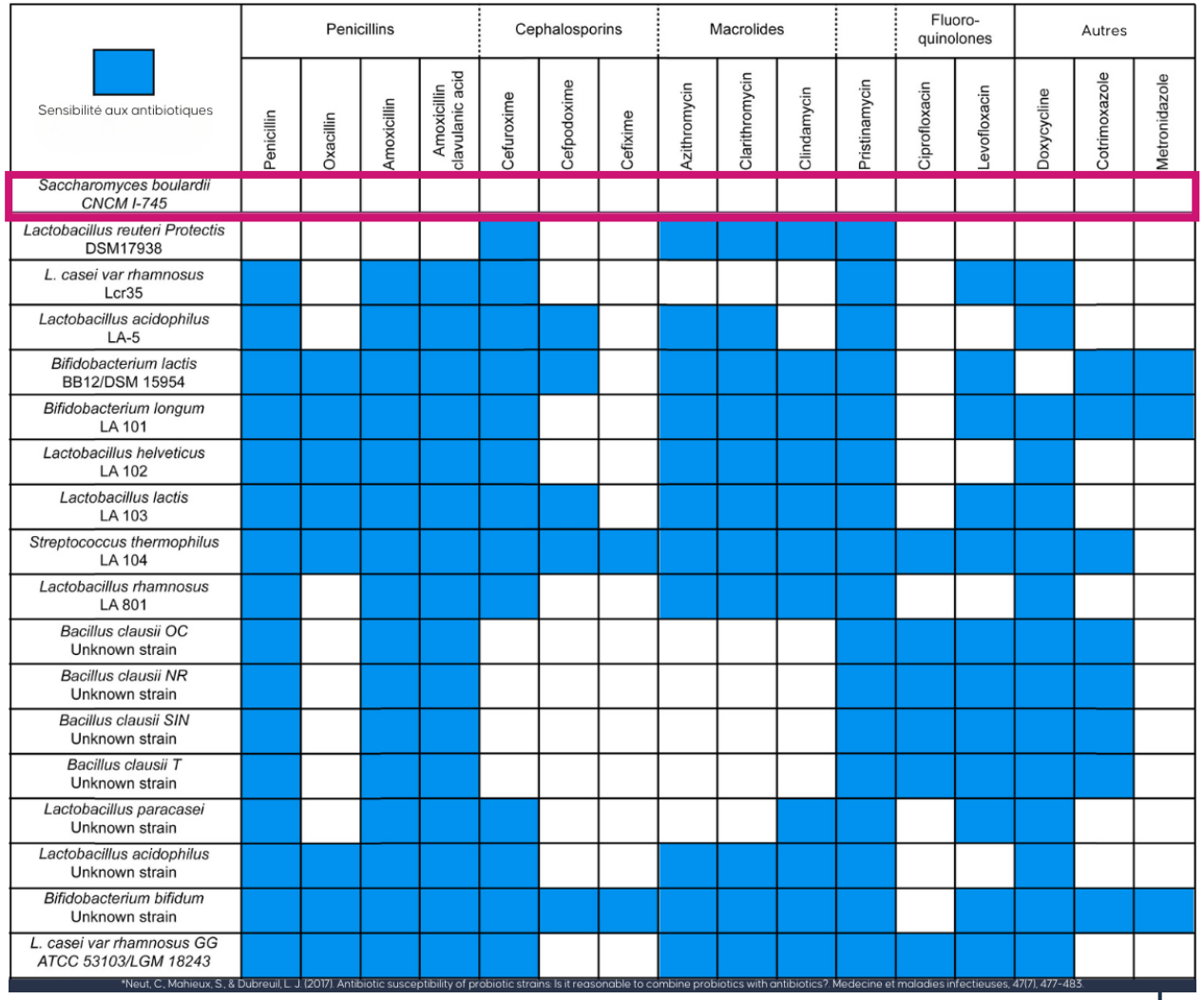


** except Amoxicillin / elavulanate*

1 – Adapted from: Turck et al (2003). JPGN, 37(1), 22-26.
2 - McFarland, Lynne V. "Antibiotic-associated diarrhea: epidemiology, trends and treatment." (2008): 563-578..

S. boulardii CNCM I-745 is naturally non-susceptible to commonly used antibiotics

S. boulardii CNCM I-745 is naturally non-susceptible to commonly used antibiotics, meaning that it **can be administered simultaneously with antibiotics** to counteract the immediate effect on the gut microbiota and occurrence of antibiotic-associated diarrhea.

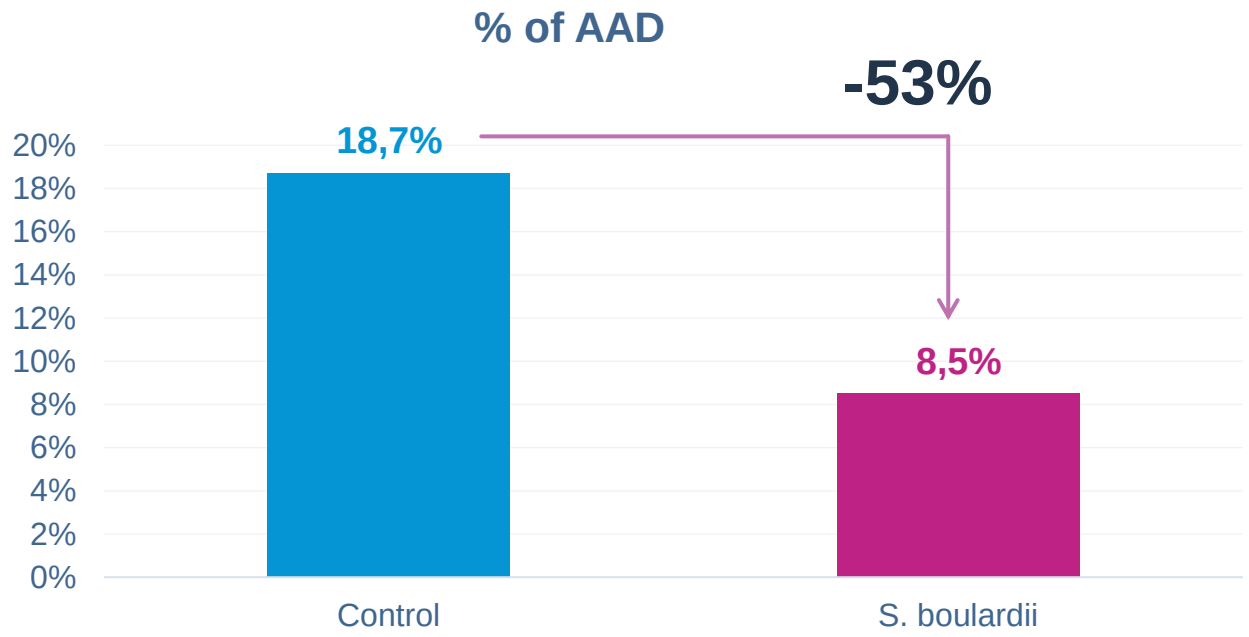


Adapted from: C. Neut, S. Mathieux, L.J. Dubreuil* Inserm, U995, Lille inflammation research international center (LIRIC), university of Lille, 59006 Lille, France;
Received 14 October 2016; accepted 6 July 2017

Florastor

Probiotics for AAD prevention. *Saccharomyces boulardii*

Systematic review with meta-analysis: *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhea



- 21 RCTs (4780 patients) were included, in adults and children
- Administration of *Saccharomyces boulardii* is effective in reducing AAD by 53% *(RR: 0.47, 95% CI: 0.38–0.57, random effect model)*
- *S. boulardii* effectively **reduces** the relative **risk of antibiotic associated diarrhea in children by 57%** and **adults by 51%.**
- For every 10 patients receiving daily *S. boulardii* with antibiotics, one fewer would develop diarrhoea (NNT: 10, 95% CI: 9–13)

Szajewska, H., & Kołodziej, M. (2015). Systematic review with meta-analysis: Saccharomyces boulardii in the prevention of antibiotic-associated diarrhoea. *Alimentary pharmacology & therapeutics*, 42(7), 793-801.

Scientific Guidelines

Scientific organizations guidelines

	WORLD GASTROENTEROLOGY ORGANIZATION (2023)	EUROPEAN SOCIETY FOR PAEDIATRIC GASTROENTEROLOGY HEPATOLOGY AND NUTRITION (2023)	AMERICAN GASTROENTEROLOGICAL ASSOCIATION (2020)
Antibiotic-Associated Diarrhea	In adults: Evidence level 1 to prevent AAD In various clinical settings (hospitalized and outpatients) In children : Evidence level 1 for use of *S. boulardii* to prevent AAD	In children : Strong recommendation for preventing AAD	-
C. difficile	In adults: Prevention of *C. difficile* associated diarrhea (or prevention of recurrence). Evidence level 2	In children : Prevention of *C. difficile* infection in children receiving antibiotic treatment. Low-quality. Conditional recommendation.	In adults: Conditional recommendation, low quality evidence In children : Conditionally recommended S. boulardii for the prevention of *C. difficile* infection in children undergoing antibiotic treatment. Low-quality evidence.
H. Pylori	In children & adults: Evidence level 1 for use of *S. boulardii* in increasing the eradication rate and in reducing gastrointestinal adverse effects associated with H. pylori infection therapies	In children : Recommendation of along with *H. pylori* therapy, *S. boulardii* for increasing the eradication rates and decreasing therapy-related gastrointestinal adverse effects	-
Acute diarrhea	Recommendation for the treatment of acute gastroenteritis. Evidence level 1.	In children : Recommendation in the treatment of acute gastroenteritis.	Probiotic use: Conditional recommendation, moderate quality evidence.

Thank you