

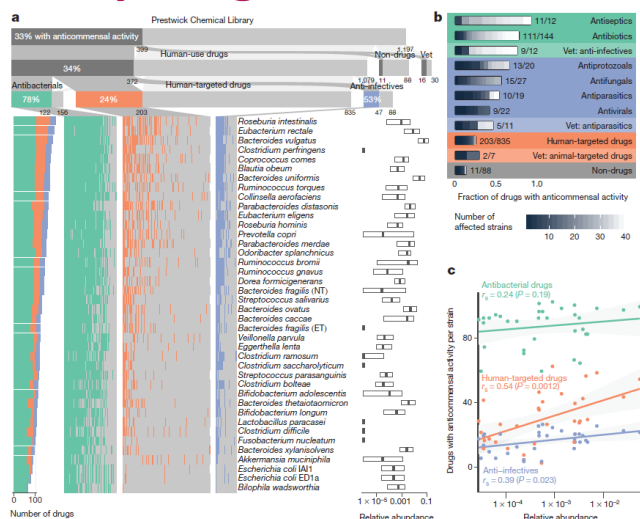
Diarrhea

Natural mechanism of the intestine to quickly eliminate pathogenic germs, toxins, and intolerances.

- **Infections with pathogens**
(e.g., *Salmonella*, *Campylobacter*, *E. coli*, Rotaviruses)
- **Food intolerances**
(e.g., fructose or lactose intolerance, celiac disease)
- **Irritable bowel syndrome**
- **Chronic inflammatory bowel diseases**
- **Medication-related causes**
(e.g., antibiotics, painkillers, chemotherapeutic agents)



Many drugs affect the microbiome



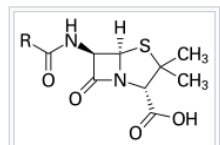
Screening of >1000 non-antibiotic drugs of all therapeutic classes against 40 representative gut bacterial strains

- **24% of the drugs inhibited the growth of intestinal bacteria**
- antibiotic-like side effects
- may promote antibiotic resistance

Antibiotics – a story of success



Alexander Fleming was awarded a Nobel prize for his role in the discovery of penicillin

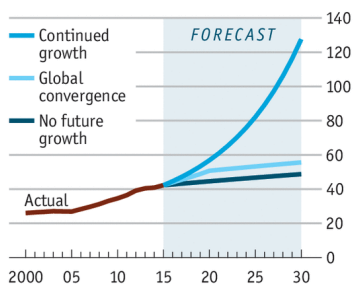


Penicillin, discovered by Alexander Fleming in 1928



Global consumption of antibiotics

2015-30 scenario-based forecasts
Daily dosage, bn



Source: "Global increase and geographic convergence in antibiotic consumption between 2000 and 2015", by Eli Klein et al., Proceedings of the National Academy of Sciences, March 2016

Economist.com

Antibiotics – blessing or curse?

Fast facts:

- most frequently prescribed drugs
- therapy and prevention of infectious diseases

Major problems:

- inappropriate antibiotic use in animals and humans
- widespread use in agriculture and livestock farming
- presence of antibiotic residues in food and aquaculture
→ ecosystem disruption

The problem with antimicrobial resistance

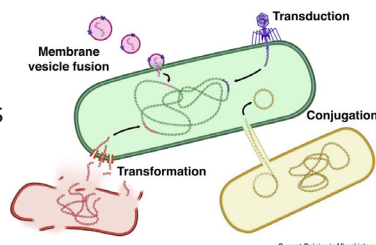
Annual attributable mortality due to antibiotic-resistant infections in the EU alone is estimated to number over 30 000 deaths.

Resistance mechanisms:

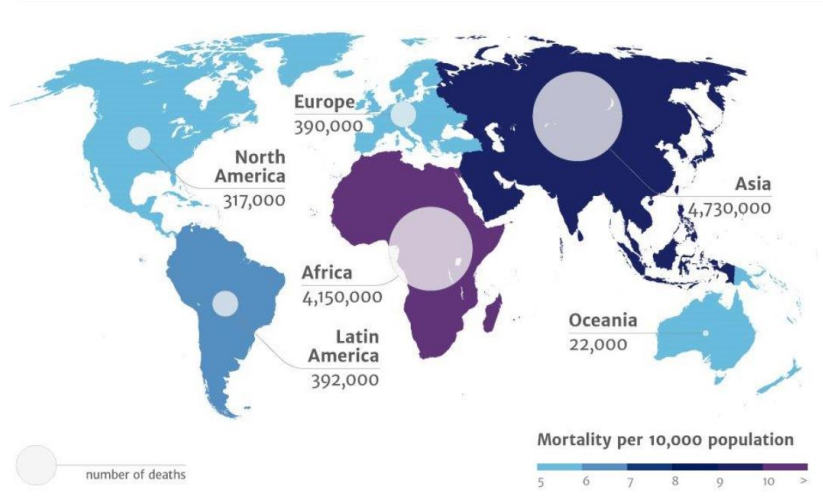
- mutations of chromosomal genes
- acquisition of antibiotic resistance genes (ARGs) via **horizontal gene transfer (HGT)**

HGT can occur in any environment with high bacterial loads

- soil, wastewater treatment plants, ...
- **gut microbiome of humans and animals**
"gut resistome"



Deaths due to antimicrobial resistance by 2050



Source: The Review on Antimicrobial Resistance, 2014

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How do antibiotics affect the gut microbiome?

Antibiotics – k.o. for the intestinal microbiome

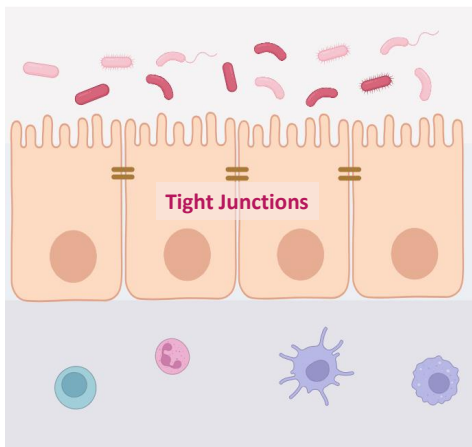
often necessary and lifesaving, but...

- **destroy** not only pathogens but also **crucial gut bacteria** → **dysbiosis!**
- **severe disturbance** of the intestinal ecosystem



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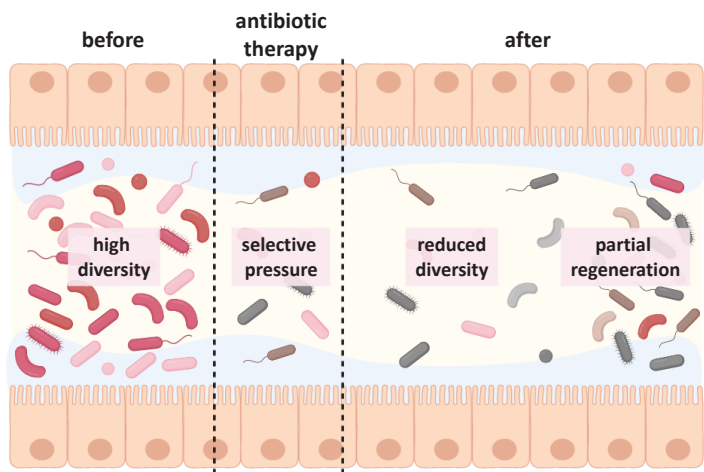
The intestinal barrier



- 1. LEVEL
gut bacteria & mucus
- 2. LEVEL
intestinal mucosa
- 3. LEVEL
submucosa & immune system

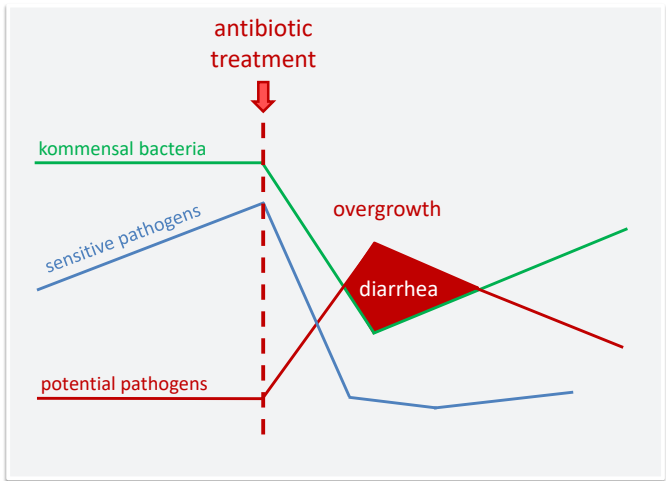
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Antibiotics – k.o. for the intestinal microbiome



Steyer GE, Pfeifer J. Multispezies Probiotika und Antibiotika: Review zur klinischen Evidenz bei der Prävention Antibiotika-Assozierter Diarrhoe (AAD) und Clostridium difficile-Infektionen (CDI). OM & Ernährung. 2013;144:F34-F38.
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Antibiotic-associated diarrhea (AAD)



Antibiotic-associated diarrhea (AAD)

Definition:

- Diarrhea occurring during or up to 2 months after antibiotic therapy

Incidence:

- 5 – 25 %

High risk:

- children and elderly
- immunosuppressed patients

Clinically relevant:

- infection with *Clostridioides difficile* can cause irreversible damage



Clostridioides (Clostridium) difficile

One of the most common **hospital-acquired pathogens**

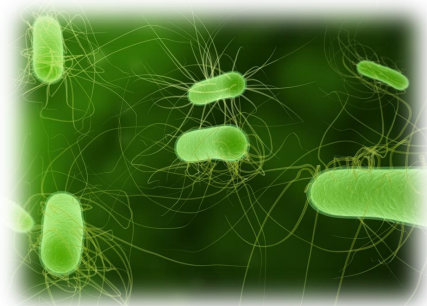
- affects 20-40% of all hospitalized patients

Produces **toxin A** and **toxin B**

- severe inflammation of the colon
- life-threatening diarrhea

Spores ensure survival

- highly resistant
- recurrent infections



C. difficile Infection

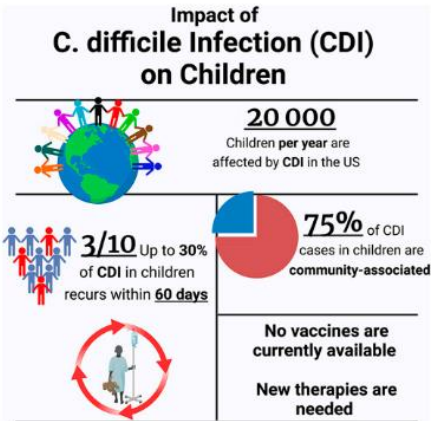
3-5% of adults (80% of newborns) are carriers

Risk factors:

- Antibiotics
- Chemotherapy
- Age (children, >65 years)
- Severe surgical procedures
- Comorbidities such as severe liver or kidney failure
- Immunosuppression

Consequences:

- Increased length of hospital stays (7-30 days)
- Increased costs (54% increase)
- Mortality



Frequent antibiotic therapies in children increase the risk of

Allergies

- atopic dermatitis
- allergic asthma
- food allergies and intolerances

Autoimmune disease

- rheumatoid arthritis
- multiple sklerosis

Overweight

Inflammatory bowel disease

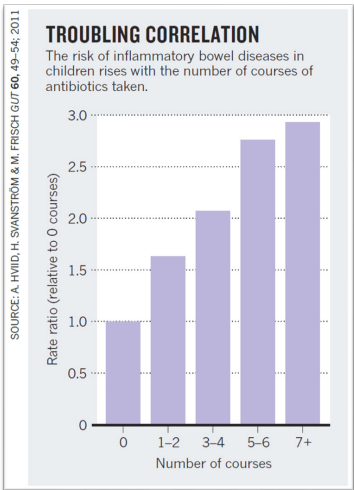


Vangay P, Ward T, Gerber JS, Knights D. Antibiotics, pediatric dysbiosis, and disease. Cell Host Microbe. 2015 May 13;17(5):553-64. doi: 10.1016/j.chom.2015.04.006.

Antibiotics and inflammatory bowel disease



Martin Blaser is chair of the Department of Medicine, New York University Langone Medical Center, New York, New York 10016, USA



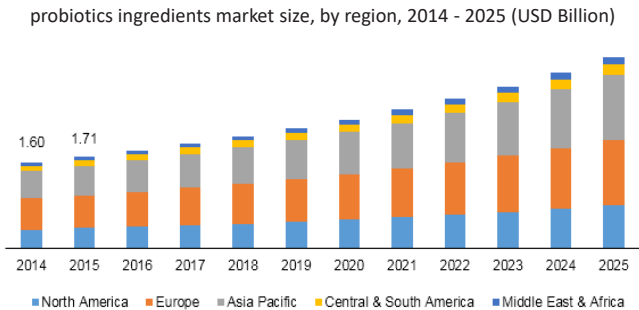
Preventing the harms of
antibiotics with probiotics?

Probiotics are...

“live microorganisms which when administered in adequate amounts confer a **health benefit on the host**”

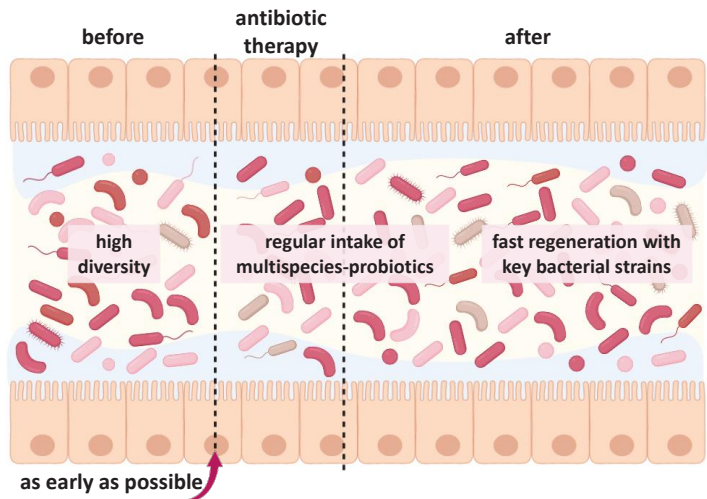
definition according to the WHO

Probiotics – nature in the fast lane



Market Research Report: Probiotics Ingredients Market Size And Forecast, By Product (Bacteria, Yeast, Spore), By Applications (Food & Beverage, Dietary Supplements), By End Use (Human, Animal) And Trend Analysis, 2015 – 2025 (Hexa Research, Sept. 2018)

Antibiotic therapy with probiotics



Steyer GE, Pfeifer J. Multispezies Probiotika und Antibiotika: Review zur klinischen Evidenz bei der Prävention Antibiotika-Assozierter Diarrhoe (AAD) und Clostridium difficile-Infektionen (CDI). OM & Ernährung. 2013;144:F34-F38.
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Prevention of *C. difficile* infecions with probiotics

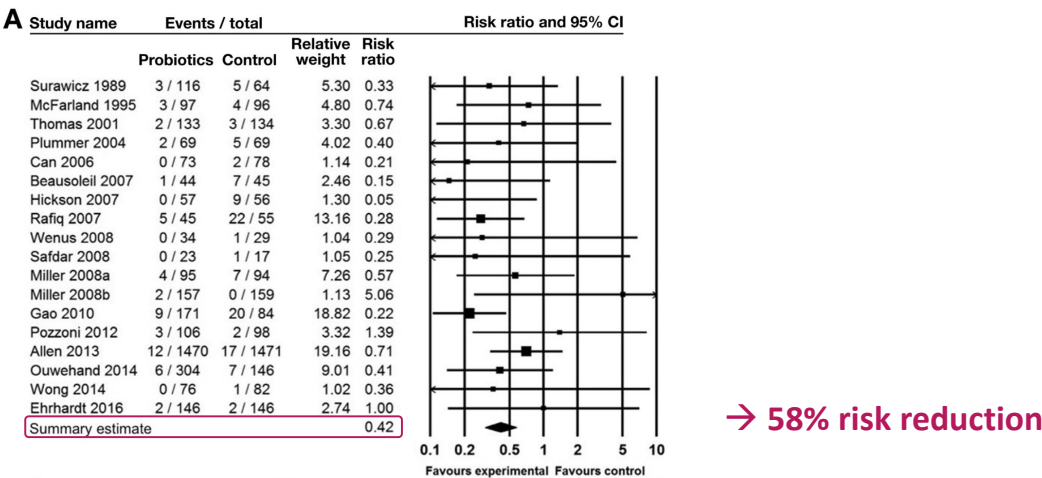
Gastroenterology 2017;152:1889–1900

Timely Use of Probiotics in Hospitalized Adults Prevents *Clostridium difficile* Infection: A Systematic Review With Meta-Regression Analysis

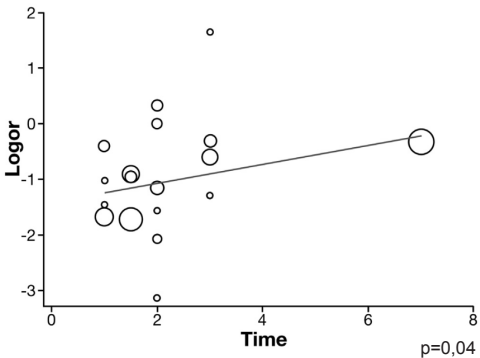
Nicole T. Shen,¹ Anna Maw,² Lyubov L. Tmanova,³ Alejandro Pino,⁴ Kayley Ancy,⁴ Carl V. Crawford,¹ Matthew S. Simon,^{5,6} and Arthur T. Evans⁵

¹Division of Gastroenterology and Hepatology, Weill Department of Medicine, Weill Cornell Medicine, New York, New York; ²Hospitalist Medicine Section, Division of General Internal Medicine, Department of Medicine, University of Colorado, Denver, Colorado; ³Samuel J. Wood Library and CV Starr Biomedical Information Center, Weill Cornell Medical College, New York, New York; ⁴NewYork-Presbyterian-Weill Cornell Medical Center, New York, New York; ⁵Section of Hospital Medicine, Division of General Internal Medicine, Weill Department of Medicine, Weill Cornell Medicine, New York, New York; and ⁶Division of Infectious Diseases, Weill Department of Medicine, Weill Cornell Medicine, New York, New York

Prevention of *C. difficile* infecions with probiotics



Timing of probiotic administration is crucial



The earlier you take probiotics, the better the effect

For each day of delay, the probability of CDI increases by 18%

Probiotics protect adults and children from *C. difficile* associated diarrhea



- *C. difficile* is found in the gut microbiome of up to **80%** of all young children
- **Timely use of probiotics reduces the proliferation of *C. difficile* and the resulting diarrhea by 60%!**

Goldenberg JZ, Ma SS, Saxton JD, et al. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children. Cochrane Database Syst Rev 2013:CD006095.



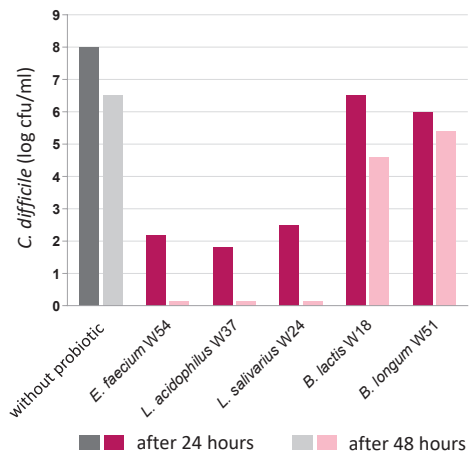
Which probiotics should be used?

Selection of probiotic strains according to scientific criteria:

- Inhibition of pathogen growth
(e.g. *C. difficile*, *Bacillus subtilis*, *E. coli*)
- Reduction of toxin A and B of *C. difficile* **to 0** within 24 h
- Stop of diarrhea within 24 - 48 h
- Strengthening of the mucosal barrier
- Decrease of intestinal pH



C. difficile – growth inhibition

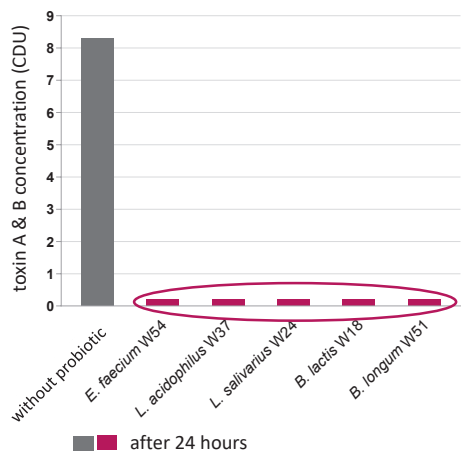


Probiotic strains inhibit the proliferation of *C. difficile*

Steyer GE, Pfeifer J. Multispezies Probiotika und Antibiotika: Review zur klinischen Evidenz bei der Prävention Antibiotika-Assoziierter Diarrhoe (AAD) und Clostridium difficile-Infektionen (CDI). OM & Ernährung. 2013;144:F34-F38.



C. difficile – reduction of toxins to 0!



Probiotic strains reduce the release of toxin A & B from *C. difficile* to **ZERO** within 24 hours

Steyer GE, Pfeifer J. Multispezies Probiotika und Antibiotika: Review zur klinischen Evidenz bei der Prävention Antibiotika-Assoziierter Diarrhoe (AAD) und Clostridium difficile-Infektionen (CDI). OM & Ernährung. 2013;144:F34-F38.



Indication specific multispecies probiotic

10 bacterial strains
at least 5 billion germs per 1 sachet (= 5 g)

- | | |
|--------------------------------------|-------------------------------------|
| <i>Lactobacillus acidophilus</i> W37 | <i>Lactobacillus salivarius</i> W24 |
| <i>Lactobacillus acidophilus</i> W55 | <i>Bifidobacterium bifidum</i> W23 |
| <i>Lactobacillus plantarum</i> W1 | <i>Lactobacillus plantarum</i> W62 |
| <i>Bifidobacterium lactis</i> W51 | <i>Lactobacillus paracasei</i> W20 |
| <i>Enterococcus faecium</i> W54 | <i>Lactobacillus rhamnosus</i> W71 |



corn starch, maltodextrin, inulin, potassium chloride, rice protein, magnesium sulfate, bacterial strains (see above), fructo-oligosaccharides (FOS), enzymes (amylases), vanilla flavoring, manganese sulfate



Positive effect of a multispecies probiotic on stool frequency during antibiotic intake

American Journal of Gastroenterology
© 2007 by Am. Coll. of Gastroenterology
Published by Blackwell Publishing

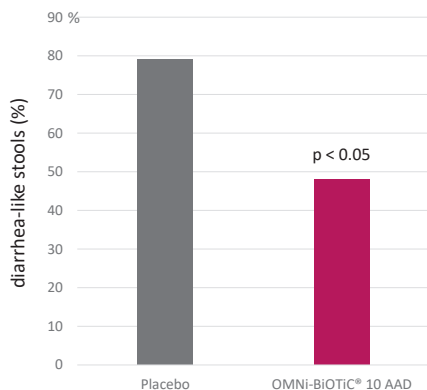
ISSN 0002-9270
doi: 10.1111/j.1572-4024.2007.01547.x

The Effect of a Multispecies Probiotic on the Intestinal Microbiota and Bowel Movements in Healthy Volunteers Taking the Antibiotic Amoxycillin

Catherina J.M. Koning, M.Sc.,¹ Daisy M.A.E. Jonkers, Ph.D.,^{1,2} Ellen E. Stobberingh, Ph.D.,² Linda Mulder, M.Sc.,³ Frans M. Rombouts, Ph.D.,⁴ and Reinhold W. Stockbrügger, M.D., Ph.D.¹
¹Division of Gastroenterology-Hepatology and ²Department of Medical Microbiology, University Hospital Maastricht, Maastricht, The Netherlands; ³Winlove Bio Industries B.V., Amsterdam, The Netherlands; and ⁴Laboratory of Food Microbiology, Department of Agrotechnology and Food Sciences, Wageningen University, Wageningen, The Netherlands



OMNi-BiOTiC® 10 AAD reduces antibiotic associated diarrhea (AAD)



significant **less diarrheal bowel movements**
due to OMNi-BiOTiC® 10 AAD

Koning CJM, et al. The effect of a multispecies probiotic on the intestinal microbiota and bowel movements in healthy volunteers taking the antibiotic amoxycillin. Am J Gastroenterol. 2008;103:178–89.



Recommendation of the World Gastroenterology Organization (WGO)

Probiotics: statements about specific complaints/diseases are usually not allowed

WGO: evaluation of existing studies regarding safety and efficacy of probiotics.

Results for OMNi-BiOTiC® 10 AAD:

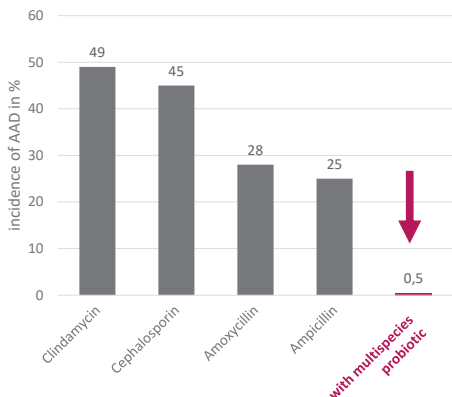
- level 2 evidence already established in 2009
- *randomized study with exceptionally good effect*



Successful use of a multispecies probiotic in clinical settings



OMNi-BiOTiC® 10 AAD reduces AAD in hospitalized patients



Incidence of AAD reduced to **only 0.5%!**

Prevention of AAD leads to*

- Shortened hospital stays
- fewer additional treatment costs
- lower risk of complications

*McFarland LV, Epidemiology, risk factors and treatments for antibiotic-associated diarrhea. Dig Dis 1998;16:292-307

Lang F. C., Erfolgreicher Einsatz von OMNI-BIOTIC® 10 AAD bei antibiotikaassoziierter Diarrhö. Journal für Gastroenterologische und Hepatologische Erkrankungen. 2009;7:38–41.

Importance of probiotic use in the elderly



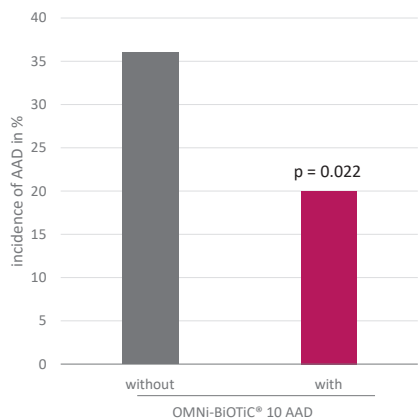
Wien klin Mag 2022 · 25:12–19
https://doi.org/10.1007/s00740-022-00435-2
Angenommen: 12. Januar 2022
Online publiziert: 26. Januar 2022
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¹ Chirurgische Ordination, Graz, Österreich
² Abteilung f. Interne Medizin, Bezirkskrankenhaus Schwaz, Schwaz, Österreich

Einsatz von Probiotika bei Antibiose

Prävention einer antibiotikaassozierten Diarrhoe bei älteren Patienten

OMNi-BiOTiC® 10 AAD prevents from AAD in nursing homes



OMNi-BiOTiC® 10 AAD significantly reduces the incidence of AAD by 45%!

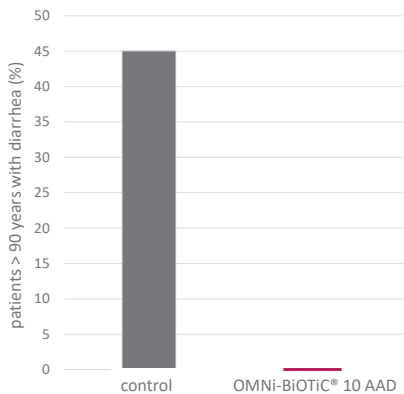
Prevention of AAD leads to

- less dehydration and malnutrition
- less hospitalization
- Cost savings

H. A. Van Wietmarschen, M. Busch, A. Van Oostveen, G. Pot, and M. C. Jong. "Probiotics use for antibiotic-associated diarrhea: A pragmatic participatory evaluation in nursing homes," *BMC Gastroenterol.*, vol. 20, no. 1, p. 151, May 2020.



Notable impact in population aged 90 and above



OMNi-BiOTiC® 10 AAD prevents diarrhea even in patients at high risk

Rabl, H., Tasser, D., Gföller, G. et al. *Einsatz von Probiotika bei Antibiose.* Wiener klinisches Magazin 25, 12–19 (2022)

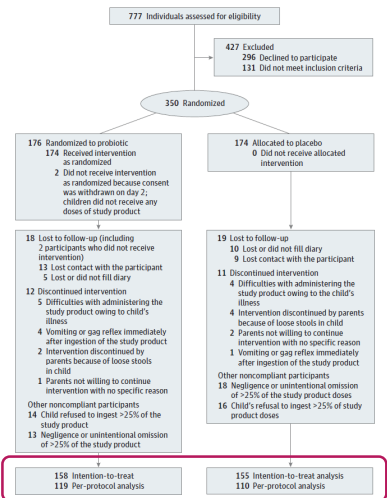


Importance of probiotic use in children

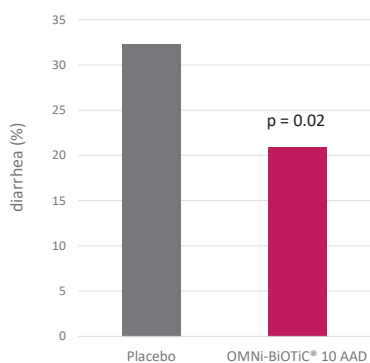
JAMA Pediatrics | Original Investigation

Multispecies Probiotic for the Prevention of Antibiotic-Associated Diarrhea in Children A Randomized Clinical Trial

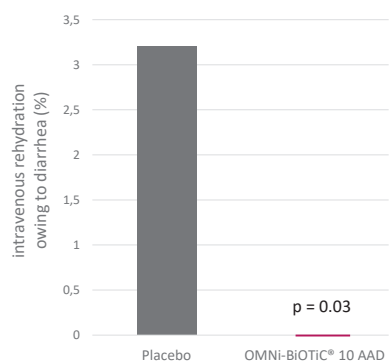
Jan Łukasik, MD; Thomas Dierikx, MD; Isolde Besseling-van der Vaart, MSc; Tim de Meij, MD, PhD; Hania Szajewska, MD, PhD; for the Multispecies Probiotic in AAD Study Group



OMNi-BiOTiC® 10 AAD reduces diarrhea in children



OMNi-BiOTiC® 10 AAD significantly reduces the risk of AAD in children



no need for intravenous rehydration due to diarrhea in the probiotic group

Lukasik J et al. Multispecies Probiotic for the Prevention of Antibiotic-Associated Diarrhea in Children: A Randomized Clinical Trial. *JAMA Pediatr.* 2022;176(9):860-866. doi:10.1001/jamapediatrics.2022.1973



Potential Additional Benefit: Reduction of antimicrobial resistance

Article

Effect of a Multispecies Probiotic on Intestinal and Skin Colonization by Multidrug-Resistant Gram-Negative Bacteria in Patients in a Long-Term Care Facility: A Pilot Study

Ines Zollner-Schwetz ^{1,*}, Monika Scarpatetti ², Gerald Pichler ², Christian Pux ², Ingeborg Klymiuk ³, Slave Trajanoski ³ and Robert Krause ¹

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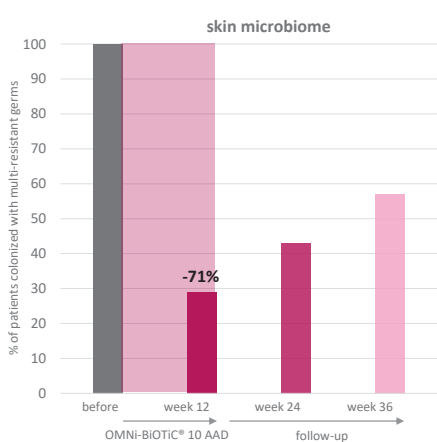
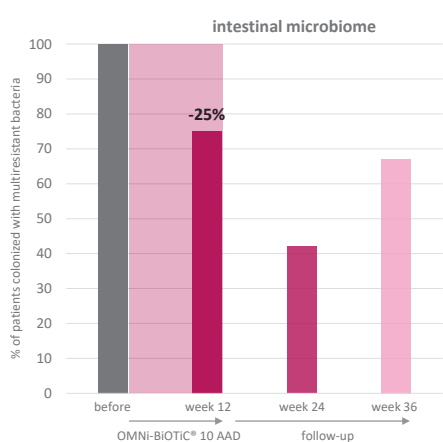
³ Core Facility Molecular Biology, Centre for Medical Research, Medical University of Graz, Stiftingtalstraße 24/1, 8010 Graz, Austria; ingeborg.klymiuk@medunigraz.at (I.K.); slave.trajanoski@medunigraz.at (S.T.)

* Correspondence: ines.schwetz@medunigraz.at

Received: 23 April 2020; Accepted: 27 May 2020; Published: 28 May 2020



OMNi-BiOTiC® 10 AAD reduces colonization with multidrug-resistant bacteria



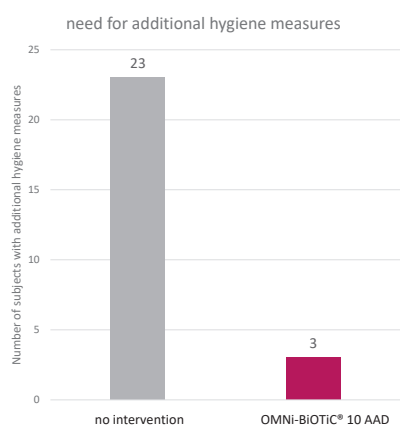
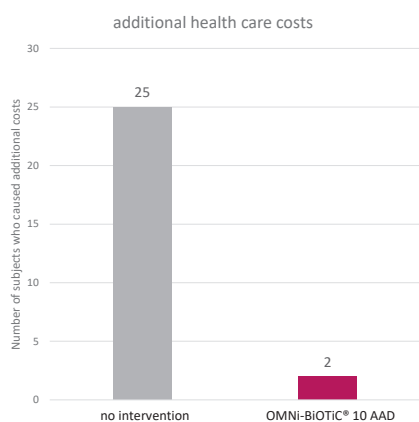
I. Zollner-Schwetz et al., "Effect of a multispecies probiotic on intestinal and skin colonization by multidrug-resistant gram-negative bacteria in patients in a long-term care facility: A pilot study," *Nutrients*, vol. 12, no. 6, Jun. 2020.



Cost reduction in the health care system



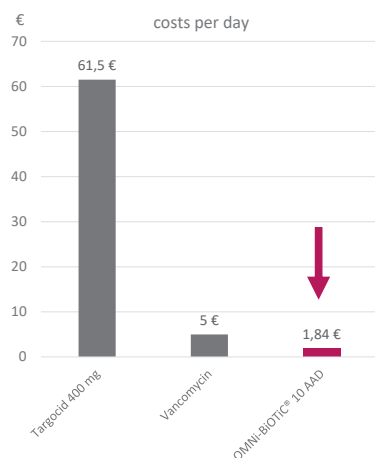
Alleviating the burden of the healthcare system via preventative use of probiotics



* e.g. extended length of hospital stay, extended hygiene measures, additional personnel costs

Rabl, H., Tasser, D., Gföller, G. et al. *Einsatz von Probiotika bei Antibiose*. Wiener klinisches Magazin 25, 12–19 (2022)

2009: Costs of AAD-medication vs. prevention with OMNi-BiOTiC® 10 AAD



treatment costs per week*

OMNi-BiOTiC® 10 AAD	12,88 €
Anaerobex (Metronidazole) 1500 mg + Claversal (Mesalazine) 500 mg	24,99 €
Vancomycin	25 €
Targocid (Teicoplanin) 400 mg	430,50 €

* as of 2009

Not taking into account:
complications, personnel costs, hygiene measures, longer hospital stay, etc.

Range of indication



during and after
antibiotic therapies



diarrhea and flatulence



infections with pathogens



chemotherapy and radiation



postinfectious IBS



diverticulitis



elderly and children



parodontitis

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Practical tip: Use the best probiotic along with every antibiotic



During the entire antibiotic therapy

- 2x daily stir 1 bag OMNI-BiOTiC® 10 AAD into a glass of water
- wait at least for 1 minute for it to activate, stir again and then drink
- take the probiotic at least 1 hour apart from the antibiotic

After antibiotic therapy

- 1x daily 1 bag for 14 days

→ for children below the age of 3 use half the dose

Important: do not heat above 40°C!

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Thank you for your attention!