



Probiotics for preventing children's antibiotic-associated diarrhoea

Further substantiation for the Ecologic[®] AAD dossier: large multicentre randomized control trial shows that our formulation significantly prevents development of diarrhoea during and after antibiotic use.

21/06/2021
JAMA Pediatrics

Antibiotic use and its side effects

To date, antibiotics have been one of the most frequently prescribed medications for children. Despite being a life-saving medication, antibiotics do have a common and unpleasant side effect, namely antibiotic-associated diarrhoea (AAD). It is estimated that up to 20% of children develop diarrhoea after antibiotic treatment. AAD is thought to result from a disturbance of the gut microbiota since antibiotics, especially broad-spectrum antibiotics, kill not only the bacterial pathogens that cause the disease but also the beneficial microbes residing in the gut. This may induce overgrowth of specific pathogens, most prominently *Clostridioides difficile*, and lead to altered microbiota function, which further leads to AAD. It is important to realise that, even if AAD does not occur, a disturbance of the microbiota is still present. In children as compared to adults, AAD usually has a faster onset, shorter mean duration [3-9 days], and more often leads to dehydration. Importantly, antibiotic use early in life has been linked to the development of chronic diseases later in life, most likely due to changes in the gut microbiota.

How was the RCT designed and performed

Probiotics, such as Ecologic® AAD, are effective in preventing AAD in adults. However, since AAD differs between adults and children, we have recently opted to assess the efficacy of a slightly modified version of our best-selling multispecies probiotic formulation, Ecologic® AAD [Ecologic® AAD 612], in terms of its efficacy in preventing AAD among a paediatric population [Figure 1]. The study was carried out between 2018 and 2021, and its outcomes are recently published at JAMA Pediatrics.

This multicentre study was performed in collaboration with two teams led by the internationally renowned researchers and paediatricians, Prof. Hania Szajewska in Warsaw, Poland and Dr. Tim de Meij in Amsterdam, the Netherlands. Dr. Hania Szajewska served as a member and secretary of ESPGHAN, the European Society for Paediatric Gastroenterology Hepatology and Nutrition, which is involved in developing medical guidelines. Furthermore she serves on the Board of Directors of the International Scientific Association for Probiotics and Prebiotics [ISAPP]. Dr. de Meij works as a Paediatric Gastroenterologist and heads a research group that focuses on the role of the gut microbiota and metabolomics on health outcomes in children.

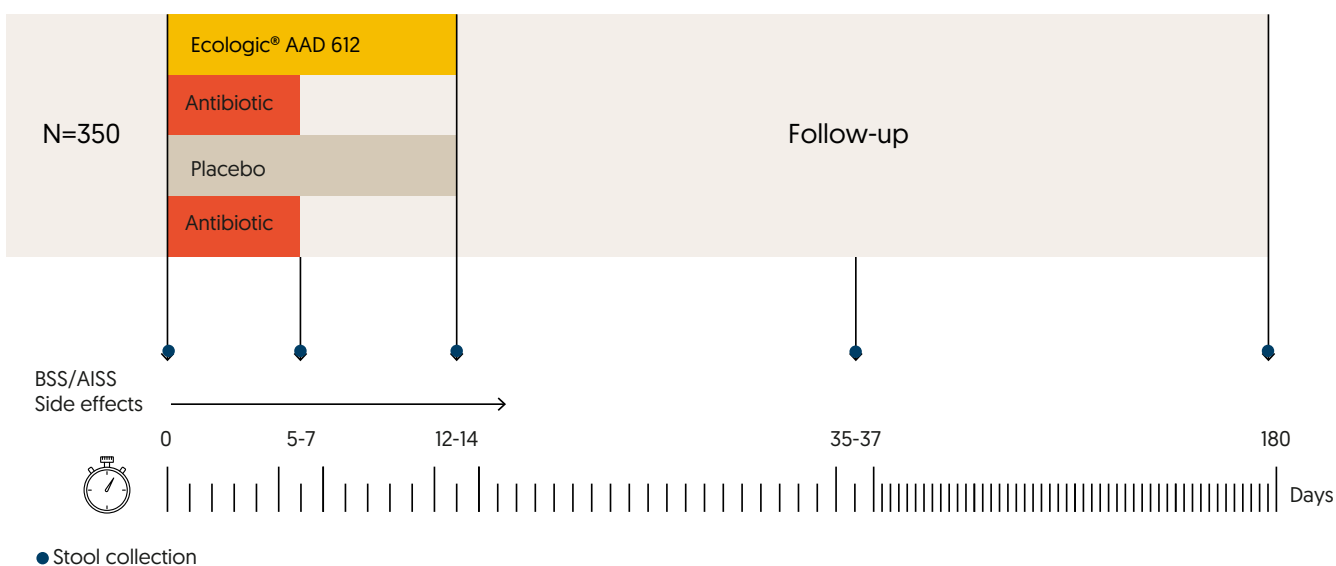


FIGURE 1: Study design.

Role of Ecologic® AAD 612 in preventing AAD in children

This randomised placebo-controlled study included 350 children (aged from 3 months to 18 years) receiving broad-spectrum antibiotics. The main indication for antibiotic treatment was a respiratory tract infection followed by urinary tract infection (Figure 2). The effect of Ecologic® AAD 612 was investigated during the antibiotic intake and one week after cessation of antibiotics (Figure 1).

This is the largest study we at Winclove Probiotics have ever performed on one of our premium quality probiotic formulations. Moreover, to the best of our knowledge, this is also the largest clinical trial investigating the effect of a probiotic containing more than three bacterial strains on the incidence of AAD in children.

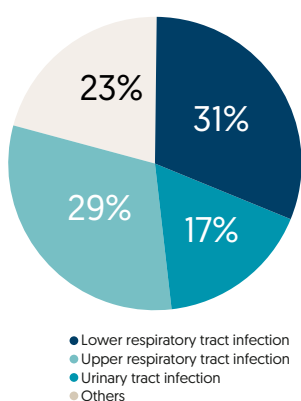


FIGURE 2: Antibiotic intake in this study cohort

In literature many different definitions of AAD and diarrhoea were used as outcome measures. In the current study we used several of these, and the study was well-powered for all of them. Compared to those in the placebo group, the children in the probiotic group had a significantly lower risk of developing diarrhoea per day for a 24-hour period regardless of aetiology - 20.1% vs. 32.3% respectively, [RR 0.65; 95% CI 0.44 to 0.94; p=0.02] (Figure 3). This is in line with other studies showing a reduction of around 35% in the development of diarrhoea during and after antibiotic use (Guo *et al*, 2019).

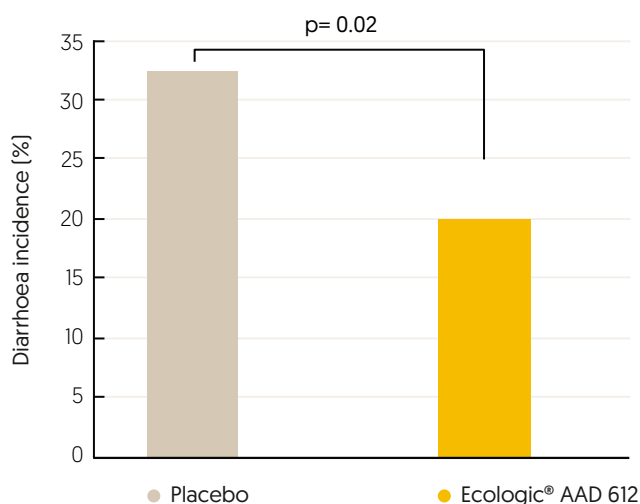


FIGURE 3: Incidence of diarrhoea regardless of aetiology.

A much more stringent definition of AAD, namely three or more loose or watery stools per day for a 24-hour period and either caused by *Clostridioides difficile* or of otherwise unexplained aetiology, was used as primary outcome. Unfortunately, compared with the placebo, the probiotic showed no significant effect on the risk of AAD. It is worth emphasizing that the literature too uses several different definitions of AAD. This raises the question of which definition is the most clinically relevant. Aetiology testing is not routinely recommended for cases of acute diarrhoea in children. More importantly, for both the patient and the physician, what caused the diarrhoea may not be relevant as long as the preventive intervention is effective. Therefore, as Ecologic®AAD 612 was shown to prevent AAD regardless of aetiology, the authors concluded that this formulation could be considered for diarrhoea prevention during antibiotic treatment in children.

New insights on the potential of Ecologic® AAD

Moreover, the study provided new insights for preventing the development of any diarrhoea, including viral diarrhoea. For example, the results showed that especially rotavirus diarrhoea was more abundant in the placebo group, suggesting that Ecologic® AAD can possibly prevent development of rotavirus diarrhoea, especially in case of antibiotic intake [Figure 4].

Diarrhoea can be a serious problem in children, especially in the very young who run a high risk of dehydration and require rehydration therapy. It seems therefore clinically very relevant that in the current study children using Ecologic® AAD 612 and suffering from AAD did not require rehydration therapy, [0% probiotics vs 3.2% placebo; $p=0.03$] [Figure 4].

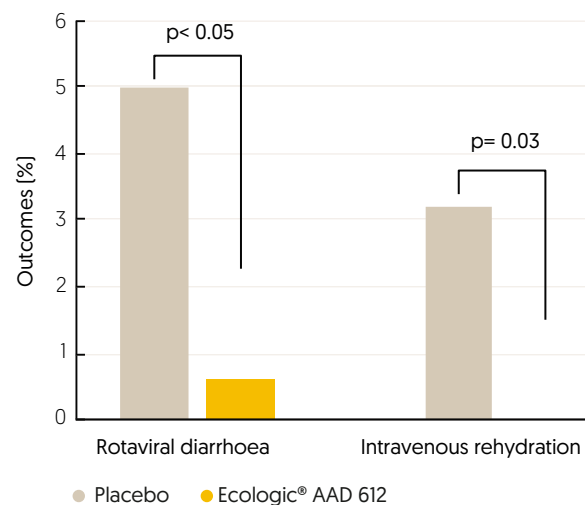


FIGURE 4: Effect of probiotics on other parameters.

Future perspective

In summary, the largest multicentre RCT ever performed by Winlove, in collaboration with leading and renowned scientists and paediatricians, provides valuable outcomes on the role of Ecologic® AAD 612 in children.

The formulation showed to be very effective in preventing diarrhoea during and after antibiotic use in children. In addition, there are good indications for the broadening of its potential, for example in preventing rotaviral diarrhoea and the consequent need for rehydration therapy.

If you have any questions or would like to know more about this study or Ecologic® AAD, do not hesitate to contact us. We would be happy to discuss the science and the market information behind Ecologic® AAD with you.

[doi:10.1001/jamapediatrics.2022.1973](https://doi.org/10.1001/jamapediatrics.2022.1973)



Winlove Probiotics
Hulstweg 11, 1032 LB
Amsterdam, The Netherlands

+31 20 435 02 35
info@winlove.com
www.winloveprobiotics.com