



HOWARU® PROTECT PRENATAL+

Delivering immune, mood and vaginal benefits for women during pregnancy

Your daily challenge

Helping to keep women healthy during pregnancy

Supporting immune health of mother and baby

Promoting mother's happiness and calmness

Helping to maintain healthy vaginal microbiota and pH

Proven safe, well tolerated, clinically-documented probiotics

Clinically-documented targeted probiotics for prenatal health and beyond

Diet and lifestyle are key to a healthy pregnancy and healthy maternal nutrition has a profound influence on the development of the immune system during fetal and postnatal periods. Keeping mothers healthy during pregnancy is vital to the healthy development of the infant and child.

Microbial colonization of the digestive tract of the infant begins at birth where the mother becomes the primary source of bacterial species. Clearly, the mother's health plays a critical role at this stage and disruption of the development of the microbiota and immunity of the infant during this period has been linked to the development of allergies and eczema.

It has been shown in human clinical studies that both mothers and their babies benefit from probiotic dietary supplementation during pregnancy, birth and beyond.



The Probiotics in Pregnancy Study - HOWARU® Protect Prenatal+

The primary aim of this human clinical study was to evaluate whether probiotic supplementation in pregnant mothers with *Lactobacillus rhamnosus* HN001™ and during breastfeeding can reduce the rates of infant eczema and allergy. But important secondary aims of the study considered the effects on postnatal depression and anxiety and the risk of gestational diabetes mellitus (GDM) in the mother. (1)

Pregnant women received daily probiotic supplements of *Lactobacillus rhamnosus* HN001™ (6 x 10⁹ CFU) from 5 weeks pre-term to 6 months post-term if breastfeeding. The probiotic was administered in capsules to mothers and as a powder diluted in milk or sprinkled on top of the infant food until 2 years of age.

Immune Benefits for the Pregnant Mother and Fetus

The Probiotics in Pregnancy Study has shown that *Lactobacillus rhamnosus* HN001™ supports the development of immune health of infants and children by significantly reducing the prevalence of eczema and allergic sensitization compared to the placebo after 2, 4, and 6 year follow-up. (2) For further information see HOWARU® Protect Earlylife.

Postnatal Depression and Anxiety

10-15% of all women in the western world suffer from postnatal depression (PND) which affects the mother's ability to care for her new infant and her quality of life. PND can be associated with persistent depression and, in a few cases each year, death from suicide. Mothers in The Probiotics in Pregnancy Study were invited to fill out a questionnaire that considered their psychological well-being at 1-2 months after birth. (3) A summary of the results is given in table 1. Mothers in the probiotic treatment group reported significantly lower depression and anxiety scores than those in the placebo group (univariable effect*). Further statistical analysis shows that when more than one effect was considered (including infant colic and time since birth that questionnaires were completed) probiotic scores still remained significantly associated with reduced depression and anxiety (multivariable effect**).

Depression score	Mean score	Standard deviation	Univariable effect size (95%CI) p-value	Multivariable effect size (95%CI) p-value
HN001™	7.7	5.4	-1.2(-2.4,-0.1) p=0.035*	-1.2(-2.3,-0.1) p=0.037**
Placebo	9.0	6.0		
Anxiety score	Mean score	Standard deviation	Univariable effect size (95%CI) p-value	Multivariable effect size (95%CI) p-value
HN001™	12.0	4.0	-1.1(-1.9,-0.2) p=0.014*	-1.0 (-1.9,-0.2) p=0.014**
Placebo	13.0	4.3		

Table 1. Depression and anxiety scores in the probiotic treatment (HN001™) and placebo groups. Adapted from Slykerman et al., 2017.

Gestational Diabetes Mellitus

Dietary changes with economic development have led to increasing problems of obesity and associated diseases including gestational diabetes mellitus (GDM). Mothers from The Probiotics in Pregnancy Study were evaluated for GDM using both the International Association of Diabetes and Pregnancy Study Group (IADPSG) and New Zealand (NZ) guideline definitions for glucose tolerance tests (GTT). The tests were given at 24- 30 weeks gestation following a 12 hour overnight fast. (4) The results indicate that there were significant differences between the *Lactobacillus rhamnosus* HN001™ group and placebo group - see table 2. Daily consumption of probiotics is associated with a lower prevalence of GDM. Subpopulation analysis revealed that HN001™ supplementation may especially benefit those with higher risk of developing GDM during pregnancy due to higher maternal age (>35 y) at conception or previous GDM diagnosis.

Balanced Vaginal Microbiota

Bacterial vaginosis (BV) is the most common infection in women of reproductive age and is characterized as an imbalance of the vaginal microbiota caused by an overgrowth of atypical bacteria. Typically between 10-30% of women experience BV during pregnancy. The healthy human vagina is colonized predominately by *Lactobacillus* and any reduction in the proportion of lactobacilli in the vaginal microbiota is associated with disease or increased disease risk.

	HN001™		Placebo		RR	95%CI	P	P Multiple imputation
	Prevalence (%)	95%CI (%)	Prevalence (%)	95%CI (%)				
IADPSG*	8.2	4.6,13.1	13.8	9.2,19.5	0.59	0.32,1.08	0.08	0.12
NZ**	2.1	0.6,5.2	6.5	3.5,10.9	0.32	0.11,0.96	0.03	0.07

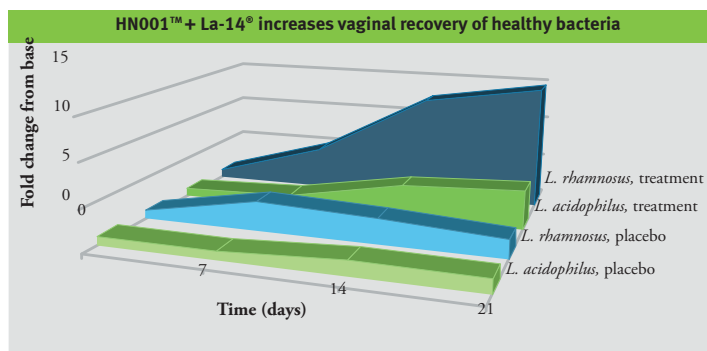
Table 2. Treatment effects on the prevalence of GDM defined according to International Association of Diabetes and Pregnancy Study Groups (*IADPSG) and New Zealand definitions (**NZ). Adapted from Wickens et al., 2017.

*IADPSG GTT definitions - Fasting ≥5.1mmol/l, 1h ≥10mmol/l, 2h ≥8.5mmol/l.

**NZ GTT definitions - Fasting ≥5.5mmol/l, 2h ≥9mmol/l.

It has been shown that after a 14-day dietary supplementation with HOWARU® Protect Prenatal+ containing *Lactobacillus rhamnosus* HN001™ and *Lactobacillus acidophilus* La-14® plus lactoferrin, that there is colonization of the vagina of healthy women with these microbes and that the colonization persists at least one week after intervention compared to the placebo. (5) Vaginal pH remained in the healthy range throughout the study. The probiotics (5 x 10⁹ CFU) were taken twice daily.

In a similar, human clinical study HOWARU® Protect Prenatal+ containing *Lactobacillus rhamnosus* HN001™ and *Lactobacillus acidophilus* La-14® plus lactoferrin, (5 x 10⁹ CFU, twice/day) was also shown to support healthy vaginal microbiota in women with intermediate vaginal microbiota and symptoms of vaginitis or vaginosis. Significant improvement in vaginal symptoms were also experienced in the probiotic group compared to the placebo. (6)



Adapted from Arch Gynecol Obstet (2015) 292:861-867 DOI 10.1007/s00404-015-3711-4.

Why Choose HOWARU® Protect Prenatal+?

Daily consumption of oral probiotic benefits women through pregnancy and beyond

- Supports the immune health of expectant mothers and infants
- Promotes mother's happiness and calmness
- Helps maintain a healthy vaginal microbiota and pH
- Increases the number of beneficial bacteria
- Proven safe and well tolerated

Why Choose DuPont?

- Leader in probiotic science
- Broadest range of clinically-documented probiotics
- Unrivalled dietary supplement formulation expertise
- Robust regulatory support
- Marketing support and industry insights to help you successfully position your products

References

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4. Wickens KL et al (2017) *British Journal of Clinical Nutrition* 17:804-813
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6. Russo R et al., (2018) *Arch Gynecol Obstet* 298 (1):138-145

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