**Table S1: Summary of vaginal probiotic strain detection results**.

*BV* bacterial vaginosis, *PY* person-years at risk, *RCT* randomised controlled trial, *spp* species, *VMB* vaginal microbiota.

Main results of studies reporting vaginal detection of probiotic strains as endpoints: 14 studies reporting 15 results.

| **Reference** | **Probiotic** | **Methods** | **Vaginal detection results** | **Other results of interest** |
| --- | --- | --- | --- | --- |
| Gardiner1 | RC-14/GR-1 *(L. fermentum* RC-14 + *L. rhamnosus* GR-1) and *L. rhamnosus* GG; vaginal detection in healthy women only. | RAPD of vaginal culture isolates; PFGE on selected samples to distinguish *L. rhamnosus* GR-1 from *L. rhamnosus* GG. | 5/5 users had at least one strain detected directly after the 3-day use period. Decreased to 1-2/10 users per strain at 18 days after use. | None |
| Antonio2 | *L. crispatus* CTV-05 (not Lactin-V); vaginal detection in healthy women only. | DNA hybridization with whole-chromosome probes to identify *Lactobacillus* spp.; rep-PCR to identify CTV-05. | CTV-05 detected in 5/9 users directly after the 3-day use period. This increased to 6/9 users at 6-8 days after use. | CTV-05 detected in 5/5 users without native *L. crispatus* at baseline and in 0/4 without. |
| Burton3 | RC-14/GR-1 *(L. fermentum* RC-14 + *L. rhamnosus* GR-1); vaginal detection in healthy women only. | RAPD DNA fingerprinting of culture isolates. VMB changes after RC-14/GR-1 use determined by DGGE analysis and Sanger sequencing of excised gel bands. | 10/10 users had at least one strain detected directly after the 3-day use period. Decreased to 0-2/10 users per strain at 18 days after use. | None |
| Czaja4 | *L. crispatus* CTV-05 (not Lactin-V) as maintenance tx to prevent UTI. | Rep-PCR for *L. crispatus* CTV-05, on culture isolates. Rep-PCR to identify *Lactobacillus* spp. | CTV-05 detected in 4/15 users during FU (one or two days after 5 days of use and at 4 weeks). | None |
| Antonio5 | *L. crispatus* CTV-05 (not Lactin-V) vaginal detection in healthy women. | Rep-PCR for *L. crispatus* CTV-05, on culture isolates. Rep-PCR to identify *Lactobacillus* spp. | After 3 days of use, CTV-05 detected in 69% of 45 women at one or more D7 or D21 visits, and 59% at the D28 visit. | 90% without native *L. crispatus* had CTV-05 detected, and 51% with (p<0.001). Lack of CTV-05 detection associated with sexual intercourse with or without condoms and with having native *L. crispatus* at baselines. |
| Ehrström6 | Ellen capsules (*L. gasseri* LN40 + *L. fermentum* LN99 + *L. casei* subsp*. rhamnosus* LN113 + *P. acidilactici* LN23) as maintenance tx after clotrimazole. | qPCR to identify *Lactobacillus* and *Pediococcus* culture isolates. Strain identification of vaginal culture isolates using RAPD. | At least one probiotic strain detected in 47/53 users directly after the 5-day use period; 27/51 after first menses; 3/50 at 6 months. | None |
| Hemmer-ling7 and Ngugi8 | L. crispatus CTV-05 (Lactin-V) as maintenance tx after vaginal metronidazole. | Rep-PCR to identify CTV-05 strains, 16S qPCR of specific vaginal bacteria. | CTV-05 detected in 11/18 users during and/or up to 7 days after the 19 day use period; this was 7/9 in women who had used all seven applicators. | Lack of CTV-05 detection associated with sexual intercourse with or without condoms and with having native *L. crispatus* at baseline; no association with baseline presence of anaerobes. |
| Bisanz9 | RC-14/GR-1 (*L. reuteri* RC-14 + *L. rhamnosus* GR-1) as main tx for NS 4-6. | 16S rRNA gene V6 sequencing | At least on probiotic strain detected in 7/12 users directly after the 3-day use period, but only in one user within the 17 days after cessation. | GR-1 was usually far more abundant than RC-14, but never dominated the VMB. |
| Pendharkar – Trial I10 | EcoVag (*L. gasseri* DSM 14869 + *L. rhamnosus* DSM 14870) as adjuvant/maintenance tx to prevent BV recurrence. | Gram-positive bacilli on culture used for rep-PCR, DNA profiles were compared with those of EcoVag strains. Identification was confirmed by using RAPD with primers for both EcoVag spp. | At least one probiotic strain detected in 9/10 users during use, which persisted for two weeks after cessation in 8/10, two months in 3/9, and three months in 2/9. | The proportion of women with EcoVag strains detected was non-significantly higher in those cured for BV compared to those experiencing a relapse (Fisher's exact p=0.16). |
| Pendharkar – Trial II10 | EcoVag *(L. gasseri* DSM 14869 + *L. rhamnosus* DSM 14870) as adjuvant/ maintenance tx to prevent BV and VVC recurrence (different pt groups). | Gram-positive bacilli on culture used for rep-PCR, DNA profiles were compared with those of EcoVag strains. Identification was confirmed by using RAPD with primers for both the EcoVag spp. | Probiotic strains detected in 5/7 adherent women using EcoVag+antibiotics, and 8/9 using EcoVag+antifungals, during the 6-month intervention period. Detection decreased from two weeks after tx cessation onwards (data not reported). | Natural lactobacilli more common than probiotic strains in 73% of the samples. EcoVag strains detected more often among women who did not have natural lactobacilli at baseline. |
| Tomusiak11 | InVag (*L. fermentum* 57A + *L. plantarum* 57B + *L. gasseri* 57C) as main tx for NS 4-6 or "low lacto count". | PCR for spp. identification, PFGE/multilocus sequence-typing to confirm InVag spp. presence. | At least one probiotic strain detected in 82% of 86 users directly after use, and in 47.5% 14 days after cessation. | None |
| Verdenelli12 | SYNBIO Gin (*L. rhamnosus* IMC 501 + *L. paracasei* IMC 502) as maintenance tx to prevent BV and VVC. | Real-time qPCR for total lactobacilli and SYNBIO strains using specific primers, and RAPD on culture isolates for SYNBIO strains presence. | At least one probiotic strain detected in 35/35 users directly after 7 days of use. Decreased to 21/35 users 21 days after use. | Proportion of total lactobacilli: 22.9% for IMC501 and 23.8% for IMC502 directly after use. Decreased to 14.3% and 9.4% 21 days after use. Significant increase in total *Lactobacillus* after SYNBIO use. |
| Dausset13 | Gynophilus (*L. rhamnosus* Lcr35 regenerans) in two formulations: immediate release (IR) and slow-release (SR). Vaginal detection in healthy women only. | Lcr35 by qPCR. | Data are presented as daily mean concentrations per regimen (a total of 35 women used the probiotic for 21 days every 3, 4 or 5 days, and sampled daily) but the means suggest that all women at all visits had Lcr35 detected. | Proportion of total lactobacilli: 22.9% for IMC501 and 23.8% for IMC502 directly after use. Decreased to 14.3% and 9.4% 21 days after use. One woman's VMB was dominated by Lcr35. |
| van de Wijgert14 | Ecologic Femi+ *(B. bifidum* W28 + *L. acidophilus* W70 + *L. helveticus* W74 + *L. brevis* W63 + *L. plantarum* W21 + *L. salivarius* W24) as maintenance tx to prevent BV recurrence. | 16S rRNA gene V3V4 sequencing, total 16S rRNA copies concentration by BactQuant, and estimated concentrations per taxon using both. | At least one probiotic strain detected in 39.3% of samples during the 2-month intermittent use period. No longer detected 4 months after cessation of use. | Mean concentration of 0.48-1.92 log10 cells/μl per FU visit during the 2-month intervention period. Mean relative abundance of 3% (7.7% if any strains detected). Concentrations were much higher (up to 4 log10 cells/μl) in women with any probiotic strain detected. There was no clear association with self-reported adherence. |
| van de Wijgert14 | Gynophilus LP (*L. rhamnosus* Lcr35 regenerans) as maintenance tx to prevent BV recurrence. | 16S rRNA gene V3V4 sequencing, total 16S rRNA copies concentration by BactQuant, and estimated concentrations per taxon using both. | The probiotic strain detected in 19.8% of samples during the 2-month intermittent use period. No longer detected 4 months after cessation of use. | Mean concentration of 0.25-1.05 log10 cells/μl per FU visit during the 2-month intervention period. Mean relative abundance of 3% (15.1% if any strain detected). Concentrations were much higher (up to 4 log10 cells/μl) in women with any probiotic strain detected. There was no clear association with self-reported adherence. |

**Table S2: Vaginal probiotic characteristics**.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Brand name** | **Probiotic strains** | **Other active ingredients** | **Current company** | **# Studies (references)** | **# Users in studies** | **Evidence in Table(s):** |
| Gynoflor | *Lactobacillus acidophilus* KS400 | 30 μg oestriol | Medinova AG, Zurich, Switzerland | 3 studies15–18 | 359 | 1, 2 |
| Lactagyn | *L. acidophilus,* *L. rhamnosus,* *Streptococcus thermophilus,* *L. delbrueckii* subsp. *bulgaricus* | None | PalCare Enterprises Inc, Victoria, BC, Canada | 1 study19 | 209 | 2 |
| Estromineral Probiogel | *L. fermentum* LF10, *L. plantarum* LP02 | None | Meda Pharma - Mylan Group, Monza, Italy | 1 study20 | 209 | 2 |
| Gynophilus (different formulations) | *L. rhamnosus* Lcr35 | None | Biose, Aurillac, France | 3 studies13,14,21 | 145 | 2, S1 |
| Femilac | *L. rhamnosus*, *L. delbrueckii, L. acidophilus, S. thermophilus* | None | Donated by Institut Rosell (now Lallemand Inc, Montreal, Canada), but this product is no longer listed on their website. | 1 study22 | 137 | 2 |
| Lactin-V (with or without applicator) | *L. crispatus* CTV-05 | None | Osel Inc, Mountainview, CA, USA | 4 studies2,4,5,7,8 | 132 | 1, 2, S1 |
| Unnamed impregnated tampons | *L. gasseri, L. rhamnosus Lcr35, L. fermentum* | None | Euroform Medipharm AB, Chr Hansen Holding A/S, Motala, Sweden | 1 study23 | 127 | 1 |
| Unnamed tablet | *L. acidophilus* LA14 | Lactic acid | Unnamed | 1 study24 | 106 | 2 |
| Kramegin | *L. acidophilus* | Plant extract *Krameria tiandra*, 15 mg lactic acid | PharmExtracta, Pontenure, Italy | 1 study25 | 105 | 2 |
| Florisia | *L. brevis* CD2, *L. salivarius* subsp. *salicinius* FV2, *L. plantarum* FV9 | pH-lowering excipients (ascorbic acid, adipic acid, stearic acid) | VSL3 Pharmaceuticals, Rome, Italy | 2 studies26,27 | 102 | 1 |
| Ellen capsules | *L. gasseri* LN40, *L. fermentum* LN99, *L. rhamnosus* LN113, *P. acidilactici* LN23 | None | Ellen AB, Stockholm, Sweden. These capsules not listed on their website but similar probiotic tampons and creams are. | 1 study6 | 95 | S1 |
| inVag | *L. fermentum* 57A, *L. plantarum* 57B, *L. gasseri* 57C | None | IBBS BioMed, Krakow, Poland | 1 study11 | 86 | S1 |
| EcoVag | *L. gasseri* Lba EB01-DSM 14869, *L. rhamnosus* Lbp PB01-DSM 14870 | None | Bifodan A/S, Hundested, Denmark | 3 studies10,28 | 80 | 1, 2, S1 |
| Unnamed suppository | *L. delbrueckii* subsp. *lactis* DM8909 | None | Unnamed Chinese company | 1 study29 | 53 | 1 |
| Physioflor | *L. crispatus* IP 174178 | None | IPRAD Pharma, Paris, France | 1 study30 | 52 | 1 |
| Unnamed | L. *gasseri* |  | Gebro Pharma, Fieberbrunn, Austria. No vaginal probiotics on their website. | 1 study31 | 50 | 2 |
| Unnamed capsules | *L. reuteri* RC-14 (formerly *L. fermentum* RC-14), *L. rhamnosus* GR-1 | None | Chr. Hanssen A/S, Hoersholm, Denmark. Have not yet marketed vaginal application of these strains. | 4 studies1,3,9,32 | 47 | 1, S1 |
| Gyno-Canesflor | *L. plantarum* P17630 | None | Bayer Canesten, Leverkussen, Germany | 1 study33 | 45 | 2 |
| SYNBIO gin | *L. rhamnosus* IMC 501, *L. paracasei* IMC 502 | None | Synbiotec, Camerino, Italy | 1 study12 | 35 | 1, S1 |
| ActiCand 30 | *L. fermentum* LF10, *L. acidophilus* LA02 | Citric acid | ItalFarmaco, Milan, Italy | 1 study34 | 30 | 2 |
| Ecologic Femi+ | *B. bifidum* W28, *L. acidophilus* W70, *L. helve-ticus* W74, *L. brevis* W63, *L. plantarum* W21, *L. salivarius* W24 | None | Winclove Probiotics, Amsterdam, Netherlands | 1 study14 | 17 | S2, S4 |
| Unnamed capsules | *L. rhamnosus* GG | None | ConAgra Foods, Chicago, IL, USA | 1 study1 | 5 | S4 |

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