CLINICAL TRIALS

# Effect of Probiotic Bacteria on Oral *Candida* in Frail Elderly

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**Abstract:** *The aim of this study was to investigate the effect of a daily intake of probiotic lactobacilli on the prevalence and counts of oral* Candida *in frail elderly patients living in nursing homes. The study had a double-blind randomized placebo-controlled design with 2 parallel arms. The study group consisted of 215 older adults (range, 60 to 102 y) who were enrolled after informed consent. After baseline examination and randomization, the subjects were given 1 lozenge containing 2 strains of the probiotic bacterium* Lactobacillus reuteri *(DSM 17938 and ATCC PTA 5289) or placebo twice daily (morning and evening). The intervention period was 12 wk, and saliva and plaque samples were collected at baseline and follow-up. The primary end point was prevalence of high* Candida *counts assessed from chairside tests. Secondary end points were levels of dental plaque and gingival inflammation. The groups were balanced at baseline. The attrition rate to follow-up was 19%. There was a statistically significant reduction in the prevalence of high* Candida *counts in the probiotic group but not in the placebo group, and the difference was statistically significant in both saliva and plaque (*$P < 0.05$*). No significant differences between the groups were noted concerning the levels of supragingival plaque or bleeding on probing. Thus, daily use of probiotic lozenges may reduce the prevalence of high oral* Candida *counts in frail elderly nursing homes residents (ClinicalTrials.gov NCT02391532).*

**Key Words**: yeasts, gingivitis, lactobacilli, saliva, clinical studies/trials, geriatric dentistry.

## Introduction

Oral candidosis, or *Candida*-associated stomatitis, is a common problem in elderly patients. *Candida* species can be found as commensal microorganisms in the oral cavity in approximately 20% to 50% of the population, increasing with age (Rindum et al. 1994). The most important and frequent species is *Candida albicans*, which has the ability to shift between the blastosporic yeast form and the hyphal form. Disturbances in the oral balance can lead to *Candida* infection in carriers and are often associated with antibiotic treatment, hyposalivation due to disease or polypharmacy, impaired local or systemic immune system, neglected oral hygiene, and smoking (Shay et al. 1997; Pires et al. 2002; Torres et al. 2002; Torres et al. 2007; Anil et al. 2014). Since the condition is caused by an ecologic imbalance (dysbiosis) in the oral biofilm, a certain interest has been addressed to a bioecological approach for prevention and management instead of antifungal treatment.

Probiotics are defined as live microorganisms that confer a health benefit on the host when administrated in appropriate amounts (Sanders 2008). Previous studies have suggested that a regular intake of probiotic bacteria can affect gastrointestinal conditions and *Candida*-associated vaginitis (Falagas et al. 2006; Passariello et al. 2014). In the oral cavity, the probiotic concept has been employed primarily for oral mutans streptococci counts, caries prevention, gingivitis, and periodontal conditions (Twetman 2012). The effect of probiotic supplements on the colonization of oral *Candida* in elderly patients has been investigated with fairly consistent outcomes. Hatakka and coworkers (2007) reported a reduced prevalence of high salivary counts of yeast after intake of a multistrain probiotic cheese. This was confirmed in 2 later studies following consumption of yogurt containing lactobacilli and bifidobacteria species (Dos Santos et al. 2009; Mendonça et al. 2012). These findings were based on dietary interventions, and to our knowledge, the concept of lozenges for the local administration of probiotics has not been evaluated. The aim of this study was therefore to investigate the effect of a twice-daily intake of lozenges containing probiotic lactobacilli on the

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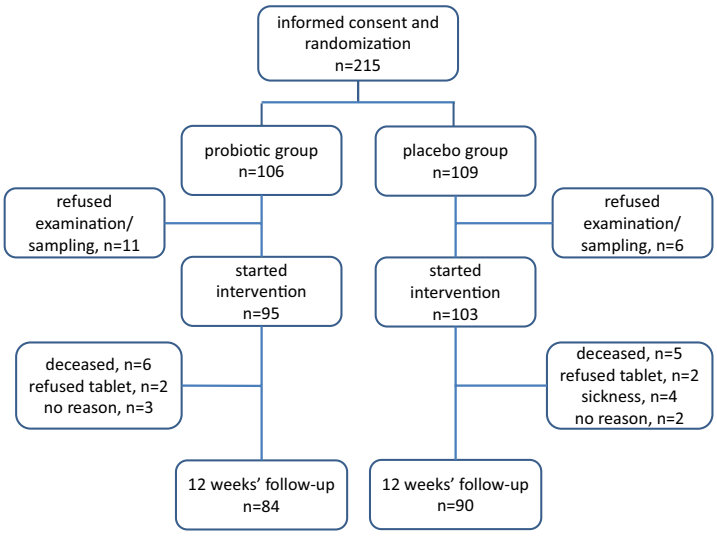
**Table 1.**
Baseline Characteristics of the Study Groups

| Variable | Probiotic (*n* = 95) | Placebo (*n* = 103) |
|---|---|---|
| Age, y, mean (SD) | 88.3 (5.7) | 87.7 (7.7) |
| Male:female, *n* | 35:60 | 42:61 |
| No. of daily prescribed drugs, % | | |
| 0 to 2 | 14 | 12 |
| 3 to 4 | 16 | 12 |
| ≥5 | 70 | 76 |
| Antibiotics within 2 mo, % | 14 | 13 |
| Dentition | | |
| Maxilla, % | | |
| >6 teeth/implants | 12 | 15 |
| ≤6 teeth/implants | 45 | 52 |
| No teeth | 43 | 33 |
| Dentures | 52 | 44 |
| Mandibula, % | | |
| >6 teeth/implants | 17 | 16 |
| ≤6 teeth/implants | 58 | 60 |
| No teeth | 25 | 24 |
| Dentures | 34 | 33 |
| Xerostomia, % | 8 | 10 |
| Daily use of fluoride toothpaste, % | 94 | 95 |
| Supplementary fluoride (rinse, tablets), % | 18 | 24 |

**Figure.**
Flowchart of the participants.




prevalence and counts of oral *Candida* in senior residents living in nursing homes. The null hypothesis was that the prevalence of oral *Candida* colonization would not differ from a group consuming placebo lozenges.

## Materials and Methods

### Study Group

The material consisted of 215 elderly persons (range, 60 to 102 y) living in 20 nursing homes in the southern parts of Sweden. Subjects were consecutively enrolled after informed consent consisting of verbal and written information directed to the individuals as well as to their relatives. Inclusion criteria were nonsmoking and ability to cooperate with a dental examination and saliva sampling. Exclusion criteria were severe chronic disease or malignancies, ongoing medication with immunosuppressive or antifungal drugs, and severe dementia or cognitive impairment. Baseline characteristics are shown in Table 1, and a flowchart of participants, with main reasons for dropping out, is presented in the Figure. The total attrition rate was 19%, and the final calculations were based on 174 subjects: 84 in the probiotic group and 90 in the placebo group.

### Study Design

Ethical approval was obtained from the Regional Ethical Committee in Lund, Sweden (Dnr. 2010/618). The study employed a double-blind randomized placebo-controlled design. After the consent form was signed, allocation to 1 of the 2 parallel groups was decided by tossing a coin (participants or staff) with a green side and a red side. Allocation concealment was secured by an independent study monitor at the University of Copenhagen. The duration of the intervention was 12 wk, and the participants were examined at baseline and at the termination of the intervention. The primary end point was prevalence and amount of *Candida* growth, and secondary outcomes were oral hygiene and gingival inflammation. Sample size estimation was based on data from a previous study (Hatakka et al. 2007). With alpha set at 0.05 and beta at 0.2, 98 participants in each study arm were needed to detect a 35% difference between groups concerning the prevalence endpoint. Because of expected attrition, the goal was to recruit

approximately 110 subjects in each arm. This trial was registered at ClinicalTrials.gov (NCT02391532).

### Intervention

Subjects in the probiotic and placebo groups were given 2 lozenges daily delivered through a prepacked pill organizer (Medi-Set, Beylikduzu, Istanbul). The distribution of the lozenges was done by the registered nursing at each nursing home on a weekly basis, and the staff kept a logbook over the daily intakes during the 12-wk period. The lozenges were taken with the other prescribed drugs in the morning and in the early evening. Subjects were instructed to let the tablet slowly melt in the mouth. The probiotic lozenges contained a minimum of $10^8$ live bacteria of each strain of the probiotic bacterium *Lactobacillus reuteri* (DSM 17938 and ATCC PTA 5289; Prodentis, Biogaia AB, Lund, Sweden). Placebo lozenges were identical to the probiotic lozenges (size, color, taste, texture) but without active bacteria. Patients and staff were both informed to immediately report any possible perceived side effects or adverse events to the research team.

### Oral Examination

All participants were interviewed and examined bedside in their private rooms at the different nursing homes by a single examiner (E.K.B.). The examiner was trained and calibrated against an experienced dental hygienist prior to the start of the project, and the first patients enrolled were scored in a peer consensus. At baseline, subjects were interviewed about their daily oral care habits, use of fluoride products and antiseptic mouth rinses, and their subjective feeling of dry mouth (xerostomia). Information on the current use of prescribed drugs was collected from the medical records. A dental mirror, periodontal probe, and portable light were used for oral examination. The number of teeth, implants, and removable dentures were recorded. Four sites of remaining teeth (or implant) were scored. The level of oral hygiene was dichotomized as "visible plaque" or "no visible plaque," and gingival inflammation was evaluated by bleeding on probing (Weinberg and Hassan 2012). Hereafter, the subjects were asked to chew on a piece of paraffin prewarmed in water, and a saliva sample was collected from the floor of the mouth (approximately 1 mL) with the aid of a plastic pipette. Supragingival plaque was collected from the upper and lower anterior teeth (approximately 30 to 40 mg) with the aid of a periodontal probe and pooled in a small plastic spoon.

### Oral *Candida* Cultivation

Growth of oral *Candida* was estimated with the selective Dentocult CA dip-slide test (Orion Diagnostica, Helsinki, Finland). The slides were covered with Nickerson's medium containing chloramphenicol and gentamicin to control bacterial overgrowth. One milliliter of saliva was applied to 1 side of the slide, and the excess was allowed to drip off. The pooled plaque sample was spread out on the other side. The slides were incubated for 4 d at 37 °C, and the number of colony-forming units (cfu) with typical morphology was counted with aid of a magnifying glass. *Candida* growth was thereafter categorized by 1 of 2 dentists into 4 scores according to Axéll and coworkers (1985): 0, no detectable growth; 1, 1 to 20 cfu (equivalent to a colony density of $10^3$ cfu/mL); 2, 21 to 50 cfu (equivalent to $10^4$ cfu/mL); 3, ≥50 cfu or confluent growth (equivalent to ≥$10^5$ cfu/mL). Intra- and interexaminer reliability was checked by a reexamination of 50 slides within a 2-wk interval.

### Statistical Methods

All data were processed by SPSS 20.0 (IBM, Chicago, IL, USA). For the statistical evaluation, the *Candida* classes were merged to "low" (score 0 or 1) and "high" (score 2 or 3) counts. Distributions of categorical data (prevalence, *Candida* growth score, plaque score, and gingival bleeding) were tested within groups before and after intervention with the McNemar's test for paired proportions. Differences in outcome between groups were subjected to Fisher's exact test. Relative risk was calculated by $z$ statistics. Intra- and interexaminer agreement was expressed with Cohen's kappa coefficient. The level of significance was set at 5% ($P < 0.05$). The blinding was not unveiled until all statistical calculations had been carried out.

## Results

The study groups were balanced at baseline with respect to age, sex, medication, chronic diseases, and dental status (Table 1). Baseline prevalence of *Candida* in saliva was 72% in the probiotic group and 66% in the placebo group. The corresponding values in plaque samples were similar, 67% and 69%, respectively. At 12-wk follow-up, the prevalence of salivary *Candida* was significantly reduced to 51% ($P < 0.05$) in the probiotic group, while it remained unchanged in the placebo group (79%). The same pattern was seen in the plaque samples with a reduction to 50% in the probiotic group ($P < 0.05$). The distribution of high and low *Candida* scores at baseline and follow-up is presented in Table 2. There was a statistically significant reduction in the proportion of high counts in saliva and plaque samples in the probiotic group but not in the placebo group ($P < 0.05$). The difference between groups at 12-wk follow-up was also statistically significant ($P < 0.05$). In the probiotic group, 65% of the subjects had the same growth score in saliva at baseline and follow-up, compared with 80% in the placebo group. The relative risk for having high *Candida* counts in saliva was 0.62 (95% confidence interval, 0.40 to 0.97; $P < 0.05$) following the intervention.

Plaque scores remained basically unchanged over the intervention period in both groups, while there was a nonsignificant tendency of reduced gingival bleeding at the follow-up in both groups compared with baseline. No significant difference was displayed between the groups. Compliance with the protocol among those that completed the study was excellent (Table 3). No major side effects were reported, but a relatively common complaint (6% of all subjects)

**Table 2.**
Percentage Distribution of the Dentocult CA Scores at Baseline and Follow-up

| Group: Time | | Dentocult CA Counts, %[a] | | |
|---|---|---|---|---|
| | *n* | Low | High | *P* Value |
| Saliva | | | | |
| Probiotic | | | | |
| Baseline | 95 | 51 | 49 | |
| Follow-up | 84 | 77 | 23 | <0.05[b] |
| Placebo | | | | |
| Baseline | 103 | 67 | 33 | |
| Follow-up | 90 | 63 | 37 | NS |
| Plaque | | | | |
| Probiotic | | | | |
| Baseline | 95 | 51 | 49 | |
| Follow-up | 84 | 71 | 29 | <0.05[b] |
| Placebo | | | | |
| Baseline | 103 | 62 | 38 | |
| Follow-up | 90 | 53 | 47 | NS |

NS, not significant.
[a]Low score (0, 1), $\leq 10^4$ colony-forming units/mL; high score (2, 3), $>10^4$ colony-forming units/mL.
[b]Significant distribution compared with baseline (McNemar's test for paired proportions).

**Table 3.**
Compliance with the Study Protocol over the 12-wk Intervention Period (90 d)

| Group | No. of Days, Mean (SD) | |
|---|---|---|
| | With No Lozenge | With 1 Lozenge |
| Probiotic | 3.1 (6.0) | 11.4 (8.6) |
| Placebo | 3.5 (7.3) | 11.6 (8.4) |

was the "strong taste" of the tablets. Five participants (2 in the probiotic group and 3 in the placebo group) reported a feeling of gastric upset and discontinued the protocol within the first weeks of the study. The interexaminer agreement concerning the *Candida* readings was very good (kappa = 0.87), and the intraexaminer correlation coefficient was 0.82.

## Discussion

This study demonstrated that locally administrated probiotic lactobacilli can reduce the prevalence of high counts of salivary yeasts in frail elderly patients. Thus, the null hypothesis was rejected, and the results confirmed findings obtained in previous investigations (Hatakka et al. 2007; Dos Santos et al. 2009; Ishijima et al. 2012; Li et al. 2014; Ishikawa et al. 2015). The absolute risk reduction in saliva was 23%, indicating a number needed to treat close to 4.5. This must be regarded as favorable since no severe adverse events were reported. In contrast to other studies (Teughels et al. 2011), we were unable to demonstrate any major clinical improvements in terms of plaque levels and gingivitis.

Our findings must be interpreted with some caution, as the possible day-to-day variation in *Candida* growth was not considered. Furthermore, this study did not provide any information on the phenotypical characteristics of the *Candida* cells or possible modes of action of the probiotic supplements. The *L. reuteri* strains used (DSM 17938 and ATCC PTA 5289) were of human origin and adapted to the oral cavity. Laboratory studies have demonstrated that growth of *Candida* strains is hampered or even inhibited in the presence of lactobacilli-derived probiotics (Hasslöf et al. 2010; Ujaoney et al. 2014). Live strains of *L. reuteri* are known to produce a hydrogen peroxide–like toxin, reuterin (Spinler et al. 2008), which may actively hamper growth of oral *Candida* through selective inhibition. There is also a possibility of systemic interference through immunomodulation via a strengthened mucosal barrier (Dicksved et al. 2012) and increased IgA production (Ericson et al. 2013). Further studies are needed to explore the antifungal mechanisms and optimize the oral dose of probiotic supplements for frail elderly patients and other vulnerable or medically compromised patients.

The participants were consecutively recruited to the study over a 12-mo period. We experienced some reluctance to enroll and presume that approximately 30% of all eligible residents did not want to participate or be examined. In addition, when doubtful autonomy was suspected, a written consent was to be collected from a near relative, a procedure that hampered the enrollment. The field character of the project meant that all clinical data were collected bedside, and the conditions were not always optimal in terms of accessibility and subject cooperation. Detailed and time-consuming registrations were simply not possible in this patient group, and that was the main reason to adopt simplified dichotomized scores for the clinical variables. The use of the simplified chairside test was chosen for practical reasons, but the method has been proven easy and reliable to use in detection of oral and vaginal candidiasis (Axéll et al. 1985; Carlson et al. 2000). The excellent compliance with the study protocol was secured through exceptional cooperation with the staff of the nursing homes who distributed the lozenges

to the participants. The relatively high attrition rate was a shortcoming but more frequently due to lack of cooperation at examination and sampling than to problems with the lozenges.

The role of the probiotic approach in oral candidosis management can be questioned, since there are effective pharmaceutic alternatives available. However, in frail elderly patients with dentures, xerostomia, and impaired ability for tooth cleaning, the condition is often more or less chronic or frequently recurrent, which may require long-term or repeated antifungal medication with a possible risk of development and iatrogenic selection of resistant strains (Pfaller 2012). Furthermore, the long-term effects of the antifungal drugs on the composition and function of the oral microbiota are unclear. An interesting observation in our study was that only 3 subjects in the probiotic group, compared with 12 persons in the placebo group, with no *Candida* growth at baseline (score 0) displayed growth at follow-up. This may indicate that intake of active lozenges can be helpful in the maintenance of homeostasis in the oral biofilm with a certain preventive effect. This study was underpowered to explore such an effect, but further research to address and elucidate this question seems warranted. Of course, beneficial clinical effects on oral health can be obtained with probiotic therapy without major changes of the composition of the oral microbiota (Toiviainen et al. 2015).

In conclusion, within the limitations of this study, the findings suggest that a daily use of probiotic lozenges could reduce the prevalence of high oral *Candida* counts in a group of frail elderly patients living in nursing homes. This indicates that probiotic supplements may be beneficial for patients at risk for oral candidosis.

## Author Contributions

E. Kraft-Bodi, contributed to conception and data analysis, critically revised the manuscript; M.R. Jørgensen, contributed to data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; M.K. Keller, C. Kragelund, contributed to design and data interpretation, critically revised the manuscript; S. Twetman, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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## References

Anil S, Vellappally S, Hashem M, Preethanath RS, Patil S, Samaranayake LP. 2014. Xerostomia in geriatric patients: a burgeoning global concern. J Investig Clin Dent [epub ahead of print 1 Sep 2014]. doi:10.1111/jicd.12120

Axéll T, Simonsson T, Birkhed D, Rosenborg J, Edwardsson S. 1985. Evaluation of a simplified diagnostic aid (Oricult-N) for detection of oral candidoses. Scand J Dent Res. 93(1):52–55.

Carlson P, Richardson M, Paavonen J. 2000. Evaluation of the Oricult-N dipslide for laboratory diagnosis of vaginal candidiasis. J Clin Microbiol. 38(3):1063–1065.

Dicksved J, Schreiber O, Willing B, Petersson J, Rang S, Phillipson M, Holm L, Roos S. 2012. *Lactobacillus reuteri* maintains a functional mucosal barrier during DSS treatment despite mucus layer dysfunction. PLoS One. 7(9):e46399.

Dos Santos AL, Jorge AO, Dos Santos SS, Silva CR, Leão MV. 2009. Influence of probiotics on *Candida* presence and IgA anti-*Candida* in the oral cavity. Braz J Microbiol. 40(4):960–964.

Ericson D, Hamberg K, Bratthall G, Sinkiewicz-Enggren G, Ljunggren L. 2013. Salivary IgA response to probiotic bacteria and mutans streptococci after the use of chewing gum containing *Lactobacillus reuteri*. Pathog Dis. 68(3):82–87.

Falagas ME, Betsi GI, Athanasiou S. 2006. Probiotics for prevention of recurrent vulvovaginal candidiasis: a review. J Antimicrob Chemother. 58(2):266–272.

Hasslöf P, Hedberg M, Twetman S, Stecksén-Blicks C. 2010. Growth inhibition of mutans streptococci and candida by commercial probiotic lactobacilli: an in vitro study. BMC Oral Health. 10:18.

Hatakka K, Ahola AJ, Yli-Knuuttila H, Richardson M, Poussa T, Meurman JH, Korpela R. 2007. Probiotics reduce the prevalence of oral *Candida* in the elderly: a randomized controlled trial. J Dent Res. 86(2):125–130.

Ishijima SA, Hayama K, Burton JP, Reid G, Okada M, Matsushita Y, Abe S. 2012. Effect of *Streptococcus salivarius* K12 on the in vitro growth of *Candida albicans* and its protective effect in an oral candidiasis model. Appl Environ Microbiol. 78(7):2190–2199.

Ishikawa KH, Mayer MP, Miyazima TY, Matsubara VH, Silva EG, Paula CR, Campos TT, Nakamae AE. 2015. A multispecies probiotic reduces oral *Candida* colonization in denture wearers. J Prosthodont. 24(3):194–199.

Li D, Li Q, Liu C, Lin M, Li X, Xiao X, Zhu Z, Gong Q, Zhou H. 2014. Efficacy and safety of probiotics in the treatment of *Candida*-associated stomatitis. Mycoses. 57(3): 141–146.

Mendonça FH, Santos SS, Faria Ida S, Gonçalves e Silva CR, Jorge AO, Leão MV. 2012. Effects of probiotic bacteria on *Candida* presence and IgA anti-*Candida* in the oral cavity of elderly. Braz Dent J. 23(5):534–538.

Passariello A, Agricole P, Malfertheiner P. 2014. A critical appraisal of probiotics (as drugs or food supplements) in gastrointestinal diseases. Curr Med Res Opin. 30(6):1055–1064.

Pfaller MA. 2012. Antifungal drug resistance: mechanisms, epidemiology, and consequences for treatment. Am J Med. 125 Supp 1:S3–S13.

Pires FR, Santos EB, Bonan PR, De Almeida OP, Lopes MA. 2002. Denture stomatitis and

salivary *Candida* in Brazilian edentulous patients. J Oral Rehabil. 29(11):1115–1119.

Rindum JL, Stenderup A, Holmstrup P. 1994. Identification of *Candida albicans* types related to healthy and pathological oral mucosa. J Oral Pathol Med. 23(9):406–412.

Sanders ME. 2008. Probiotics: definition, sources, selection, and uses. Clin Infect Dis. 46 (Suppl 2):S58–S61.

Shay K, Truhlar MR, Renner RP. 1997. Oropharyngeal candidosis in the older patient. J Am Geriatr Soc. 45(7):863–870.

Spinler JK, Taweechotipatr M, Rognerud CL, Ou CN, Tumwasorn S, Versalovic J. 2008. Human-derived probiotic *Lactobacillus reuteri* demonstrate antimicrobial activities targeting diverse enteric bacterial pathogens. Anaerobe. 14(3):166–171.

Teughels W, Loozen G, Quirynen M. 2011. Do probiotics offer opportunities to manipulate the periodontal oral microbiota? J Clin Periodontol. 38 (Suppl 11):159–177.

Toiviainen A, Jalasvuori H, Lahti E, Gursoy U, Salminen S, Fontana M, Flannagan S, Eckert G, Kokaras A, Paster B, et al. 2015. Impact of orally administered lozenges with *Lactobacillus rhamnosus* GG and *Bifidobacterium animalis* subsp. *lactis* BB-12 on the number of salivary mutans streptococci, amount of plaque, gingival inflammation and the oral microbiome in healthy adults. Clin Oral Investig. 19(1):77–83.

Torres SR, Peixoto CB, Caldas DM, Akiti T, Barreiros MG, de Uzeda M, Nucci M. 2007. A prospective randomized trial to reduce oral *Candida* spp. colonization in patients with hyposalivation. Braz Oral Res. 21(2):182–187.

Torres SR, Peixoto CB, Caldas DM, Silva EB, Akiti T, Nucci M, de Uzeda M. 2002. Relationship between salivary flow rates and *Candida* counts in subjects with xerostomia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 93(2):149–154.

Twetman S. 2012. Are we ready for caries prevention through bacteriotherapy? Braz Oral Res. 26(Suppl 1):64–70.

Ujaoney S, Chandra J, Faddoul F, Chane M, Wang J, Taifour L, Mamtani MR, Thakre TP, Kulkarni H, Mukherjee P, Ghannoum MA. 2014. In vitro effect of over-the-counter probiotics on the ability of Candida albicans to form biofilm on denture strips. J Dent Hyg. 88:183–189.

Weinberg MA, Hassan H. 2012. Bleeding on probing: what does it mean? Gen Dent. 60:271–276.