Think Outside the Gut: Modulating the Oral Microbiome for Systemic Health

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Adhesion of Bifidobacterium lactis HN019 to human intestinal epithelial cells (Caco-2)
Attachment of Streptococcus salivarius ENT-12™ to HEp-2 cells
Disclosure and Disclaimers

• Dr. Evans was a former employee of Novus International (parent company of Stratum Nutrition, Saint Charles, MO USA), a company that distributes (sells) 2 probiotic strains discussed in this presentation; Dr. Evans has no affiliation with any clinical laboratory

• The content of this presentation has been approved by the American College of Nutrition for Continuing Medical Education credits

• The information, comments, and opinions expressed in this presentation are those of Dr. Evans, based on his own interpretation of the peer-reviewed scientific literature along with his close collaborations with clinical experts

• Clinical practitioners should evaluate and judge all information, comments, and opinions using their own expertise and experience, coupled with the personalized assessment of each patient

• All content is for educational purposes only
Oral Health is Linked to Systemic Health and Disease

Source: https://www.youtube.com/watch?v=m-BGfwCoJJA
An adult human is estimated to have around 30-50 trillion cells*

Gut Microbiome
Selected Modulators of Gut Bacteria Composition and Physiological Effects of Gut Bacteria

**OTHER V THE BODY’S MICROBIOMES**

Genomic surveys of the body’s bacterial, fungal, and viral inhabitants are revealing diverse microbial communities that likely play key roles in human health and disease.

**MOUTH**
Diverse microbial communities are found on the tongue, the roof of the mouth, the teeth, and the gums, with some 700 species identified so far. In addition to affecting the health of the mouth itself, oral bacteria have been implicated in cardiovascular disease, cancer, rheumatoid arthritis, and more. The oral microbiome is also suspected of seeding the microbial communities in other body sites, including the gastrointestinal tract, the lungs, and the placenta.

**LUNGS**
With a microbiome about 1,000 times less dense than the oral microbiome that feeds it, and some 1 million to 1 billion times less dense than the gut, the microbes of the lung are nevertheless being recognized for their role in health and disease. Healthy lungs are typically home to Streptococcus, Prevotella, and Veillonella species, and shifts in the microbial community have been linked to chronic diseases, including cystic fibrosis, chronic obstructive pulmonary disease, asthma, and HIV.

**VAGINA**
While the microbial communities of most women’s vaginas are dominated by Lactobacillus bacteria—which ferment carbohydrates to lactic acid, yielding a low pH that is toxic to many pathogenic microbes—about 25 percent of women have fewer lactobacilli and greater numbers of other lactic acid-producing anaerobes. The composition of the vagina’s microbial community varies by race, among other things, and an individual’s vaginal microbiome can change dramatically over time.

**MOTHER AND CHILD**
Newborn babies are already populated with diverse bacteria, including Actinobacteria, Proteobacteria, and Bacteroides species. Analysis of the placental tissue suggests that bacteria may be seeded from the mother’s mouth microbiome. After birth, babies are exposed to the mother’s breast milk microbiome, which is home to diverse populations of Streptococcus, Staphylococcus, Serretia, and Corynebacterium.

**SKIN**
With a range of habitats, including invaginations, appendages, and various glands and follicles, the skin is home to some of the most diverse microbial communities on the human body. The oily, or sebaceous, sites of the head, neck, and trunk are dominated by Propionibacterium, including P. acnes; moist sites such as the crease of the elbow, below a woman’s breasts, or between the toes are frequented by Corynebacterium; and the dry sites of the body, such as the forearm or leg, are most commonly home to Staphylococcus species, in particular, S. epidermidis. The skin microbiome is now being appreciated for its direct and indirect roles in immunity, secreting antimicrobial substances, that help fight pathogenic invaders and interacting with human immune cells to influence their behavior.

**PENIS**
The male reproductive organ harbors diverse bacteria. The urethras of some men are home to lactobacilli and streptococci species, while others have more anaerobes, such as Prevotella and Fusobacterium. The overall density of the organ’s exterior microbiome appears to be lower when the penis is circumcised.

Source: http://www.the-scientist.com/August2014/TBM2.pdf
The Oral Microbiome

• Over 700 species of bacteria inhabit oral cavity, in populations of 1-10 billion CFUs at any given time

• Healthy oral bacteria provide first line of defense against harmful microorganisms entering the body, thereby supporting the health of the rest of the body

• Composition of each person’s oral bacteria is unique, some people have healthier bacterial environment than others

• Stress, disease, aging and medications or other ingested substances can all negatively effect oral bacterial balance

Oral Health is Linked to Systemic Health and Disease

STUDY: GUM DISEASE MAY INCREASE LUNG CANCER RISK

An analysis of existing research reveals possible link between periodontal disease and the leading cause of cancer death.

Chicago (June 23, 2016)—Chinese researchers have found that individuals with periodontal disease—also known as gum disease—might be at an increased risk of developing lung cancer. The report, published ahead-of-print in the Journal of Periodontology, found that individuals with periodontal disease have a 1.24-fold increased risk of developing lung cancer.

In the report, titled “Periodontal Disease and Incident Lung Cancer Risk: A Meta-Analysis of Cohort Studies,” the authors assess the findings of five cohort studies that evaluated 321,420 participants. The analysis notes an increased risk even after adjusting for participants’ alcohol consumption and smoking habits, both of which are common risk factors for periodontal disease. Study participants who were drinkers, smokers, and had been diagnosed with diabetes—which is an independent risk factor for both lung cancer and periodontal disease—demonstrated a 1.36-fold increase in lung cancer risk.

Proposed Pathogenic Mechanisms: How Periodontitis Contributes to Systemic Disease

- **Direct**: pathogenic bacteria enter systemic circulation and exert direct effect of target organs.
- **Indirect**: Host inflammatory response to chronic presence of periodontal bacteria may produce state of chronic inflammation contributing to pathogenesis of chronic inflammatory-based diseases.

Source: Winning et al. (2015) BDJ Team 2 Article 15163; doi:10.1038/bdjteam.2015.163
Proposed Mechanistic Link between Periodontitis and Alzheimer’s Disease

By age of normal retirement, 95% of us will have had some sort of dental repair.

<table>
<thead>
<tr>
<th>Age</th>
<th>Percent with caries, missing, or filled permanent teeth</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 to 34 years</td>
<td>85.6%</td>
</tr>
<tr>
<td>35 to 49 years</td>
<td>94.3%</td>
</tr>
<tr>
<td>50 to 64 years</td>
<td>95.6%</td>
</tr>
</tbody>
</table>

Source: CDC
Over half of us over 20 years of age have less than optimal gum health

Incidence estimates of gingivitis, periodontal disease and severe periodontal disease in US adults 20 years and older (Source: CDC)

<table>
<thead>
<tr>
<th>Item</th>
<th>%</th>
<th>Number estimate (~227M – 2010 census)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gingivitis</td>
<td>52</td>
<td>118,000,000</td>
</tr>
<tr>
<td>Destructive periodontal disease</td>
<td>26</td>
<td>59,000,000</td>
</tr>
<tr>
<td>Severe DPD</td>
<td>5.6</td>
<td>12,700,000</td>
</tr>
</tbody>
</table>
Scaling and Root Planing

- A careful cleaning of the root surfaces to remove plaque and calculus [tartar] from deep periodontal pockets and to smooth the tooth root to remove bacterial toxins.
- Sometimes followed by adjunctive therapy such as local delivery antimicrobials, systemic antibiotics, and host modulation, as needed on a case-by-case basis.
- Most periodontists would agree that after scaling and root planing, many patients do not require any further active treatment.
- However, the majority of patients will require ongoing maintenance therapy to sustain health.
- Expensive and not well covered by many dental insurance plans.

Source: https://www.perio.org/consumer/non-surgical
Confront your periodontal (gum) disease

Gum disease is caused by bacteria above and below the gumline

And it's the #1 cause of adult tooth loss in the United States.

Even so, many people are tempted to ignore their dental professional's advice to treat gum disease in its early stages.

You have a choice. Do more now, or risk further disease progression. Left untreated, gum disease may lead to more serious problems that may require painful and expensive surgery.

In combination with scaling and root planing (SRP), your dentist can apply ARESTIN® (minocycline HCl) Microspheres, 1 mg to help treat your gum disease.

Source: http://www.arestin.com/periodontal-gum-disease/
How Can I Protect My Oral Health?

- Avoid tobacco use and minimize alcohol intake
- Brush teeth at least twice a day with fluoride toothpaste (baking soda/peroxide) and floss daily
- Schedule regular dental checkups and cleanings 1-3 times per year, depending on age, health, and risk factors
- Eat a pro-oral health diet; limit between-meal snacks
- Regular exercise to maintain healthy body weight, reduce inflammation, reduce blood and salivary glucose levels, reduce carbohydrate cravings

- Based on new science, consider the use of probiotics targeting oral and immune (ENT) health
  - Reduce plaque and gingival indices
  - Reduce pathogens responsible for strep throat and other ear, nose throat conditions

Nutritional Objectives to Promote / Maintain Oral Health

Consume foods that

- Increase salivary flow (foods that require chewing)
- Are low in acid and sugars
- High in fluoride, calcium, phosphorous, magnesium
- High in Vitamins A, C, D, K2, folic acid, CoQ$_{10}$, other antioxidants
- Contain casein (may help in releasing calcium)
Examples of Foods and Beverages Beneficial for Oral Health

- **Calcium-fortified juices, milk** and other **dairy products** are rich in **calcium** and **vitamin D** and help promote healthy teeth and bones, reducing the risk for tooth loss. Adding powdered milk to cooked dishes helps those who don’t like milk or cheese to get some of the calcium needed to protect teeth and jawbones.

- **Cheese** unleashes a burst of calcium that mixes with plaque and sticks to the teeth, protecting them from the acid that causes decay and helping to rebuild tooth enamel on the spot.

- **Greek yogurt** for calcium, phosphorous, casein

- **High-fiber foods for increased salivary flow**

- **Crisp fruits and raw vegetables, like pears, apples, carrots and celery**, help clean plaque from teeth and freshen breath.

- Antioxidant vitamins, such as **vitamin C, Kiwifruit** and other nutrients from **fruits** and **vegetables** help protect gums and other tissues from cell damage and bacterial infection.

- Recent studies indicate that **fresh cranberries** interrupt the bonding of oral bacteria before they can form damaging plaque.

- **Tap water as a source of fluoride; green tea, black tea as sources of polyphenolic compounds that have mild antibiotic effects**

- **Nuts (sources of vitamins minerals)**

- **Xylitol (present in many sugarless chewing gum products): antimicrobial and stimulates salivary flow**
Food and Beverages Detrimental to Oral Health

• Carbonated sugary soft drinks
• Sport and energy drinks
• Sticky sweets (caramels, gummies)
• Dried fruits
• White starches (ie refined, processed carbs)
• Drinks and foods high in acid
• Frequency of consumption might be more detrimental than total amount
‘Probiotics’

• Term used for a product containing microorganisms which (after ingestion) have a beneficial effect on the health of the host

• Maintaining the balance of intestinal microbiota in the context of decreasing (potentially) pathogenic (gastro-)intestinal (micro)organisms

• Changes/improvements in bowel function/regularity (provided they do not result in diarrhea)

• Maintaining normal bowel function – with reduced (or maintained normal) intestinal transit, and increased bowel movements’ frequency (within a normal range)

• Normal blood concentrations of triglycerides

• Reduction of post-prandial glycemic responses

• An increase in magnesium and/or calcium absorption, with consequent improved calcium/magnesium retention

• Reducing levels of markers of inflammation (under certain circumstances)

• Increase in satiety leading to a reduction in energy intake (if sustained)

• Maintaining individual intestinal microbiota in subjects receiving antibiotic treatment

• Improvement of iron absorption

• Improving of oral health by reducing the number of *Streptococcus mutans* and by reducing the gingival and plaque indices

• Reducing tooth demineralization in the context of reducing the risk of caries

*EFSA: European Food Safety Authority*
Relationship Advice, circa 1951

Source: https://www.youtube.com/watch?v=_39gkDAbMaI
A variety of strains of *Streptococcus salivarius* are common bacteria found in the human mouth

- Comprise about 10-40% of bacteria in oral microbiome
- Provide a variety of beneficial characteristics
- Several strains produce Bacteriocin-Like Inhibitory Substances (BLIS) that play integral role in the body’s immune defenses
S. salivarius K12 Overview

- **S. salivarius K12:** Probiotic that targets the oral cavity
  - A unique strain of *Streptococcus salivarius*
    - *S. salivarius* is primary bacteria found in mouth
  - Natural occurrence in humans is very low (< 2%)
  - Discovered in University of Otago laboratory (Dunedin, New Zealand) by internationally renowned microbiologist, Professor John Tagg and Team
  - K12 strain was originally isolated from mouth of child who was NOT susceptible to throat and upper respiratory infections
  - Demonstrated ability to colonize oral cavity
  - Produces specific inhibitory peptides (salivaricins) that contribute to their demonstrated efficacy: Salivaricins A2 and B
  - BLIS = Bacteriocin-Like Inhibitory Substances

- Reduces production of volatile sulphur compounds that cause halitosis
- Supports oral and upper respiratory track health
Mode of Action: *S. salivarius* K12

- Produces two unique BLIS molecules
  - Salivaricin A2
  - Salivaricin B
- No broad-spectrum inhibition; target related species

*Salivaricins puncture cell walls of pathogens, forming pores, that result in leaking of cell metabolites and inhibition*
Good Strep vs Bad Strep

- Analogous to yeast
  - Some are good (eg *Saccharomyces boulardii*)
  - Some are not good (eg *Candida albicans*)

- Good Strep
  - *Streptococcus salivarius*
    - Principle commensal bacterium in the human oral cavity

- Bad Strep
  - *S. mutans* (*dental caries*)
  - *S. constellatus* (*periodontitis*)
  - *S. intermedius* (*periodontitis*)
  - *S. pyogenes* (*strep throat*)
**S. salivarius K12 and halitosis**

- *In vitro* data indicate antibacterial effects against multiple volatile sulfur-producing species\(^1\)

**S. salivarius K12 and halitosis**

- In humans, reduced halitosis, salivary odor, and VSCs in 7 days\(^2\)

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S. salivarius M18 Overview

- *S. salivarius* M18: Probiotic that targets the oral cavity
  - A unique strain of *Streptococcus salivarius*
  - Natural occurrence in humans is very low (< 2%)
  - M18 strain was originally isolated from mouth of a healthy young adult
  - Demonstrated ability to colonize oral cavity
  - Produces specific inhibitory peptides (salivaricins) that contribute to their demonstrated efficacy: Salivaricins A, M, and 9
    - BLIS = Bacteriocin-Like Inhibitory Substances

- *S. salivarius* M18 produces enzymes
  - Urease: converts urea into ammonium carbonate (promotes higher pH)
  - Dextranase: hydrolyzes dextran (critical for bacterial adhesion) to break down plaque biofilms

➢ *Supports dental and periodontal health*
Mode of Actions: *S. salivarius* M18

- Produces three unique BLIS molecules
  - Salivaricins A, M, and 9
- No broad-spectrum inhibition; target related species

*Salivaricins puncture cell walls of pathogens, forming pores, that result in leaking of cell metabolites and inhibition*
Dental and Periodontal Health Effects

• Multiple studies have shown *S. salivarius* M18 to significantly improve indices of dental and periodontal health (children and adults):

  o Reduced plaque index in children at Day 90 days vs placebo (P<0.02; n= ~40/group)¹
  o Reduced plaque index in adults at Day 30 vs untreated controls (P<0.01; n=14/group)²
  o Reduced gingival index, bleeding, pocket depth in adults at Day 30 vs untreated controls (P<0.01; n=14/group)²
  o Following the cessation of the M18 lozenges, the significant improvements persisted at Days 45 and 60 compared to the control (P<0.05; n=14/group)²
  o Reduced risk of developing dental caries in children at Day 90³
  o Reduced production of 2 inflammatory cytokines (IL-6, IL-8) in vitro⁴
  o Safe and well tolerated¹-³

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S. salivarius M18 Reduces Periodontal Pathogen-Induced IL-8 Production

- Human gingival cells cultured with periodontal pathogens
  - *Porphyromonas gingivalis* (PG)
  - *Aggregatibacter actinomycetemcomitans* (AA)
  - *Fusobacterium nucleatum* (FN)

- Pathogen bacteria increase IL-8
  - IL-8 is the major driver of gingivitis inflammation

- M18 ↓ pathogen-induced IL-8 production by 85-90%

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**Efficacy of S. salivarius M18 on Indices of Dental Health in Adults**

- 30 days of *Streptococcus salivarius* M18 consumption; 60 day study duration
- Subjects in M18 group: after initial scaling and root planning, were instructed to consume 2 lozenges containing M18 every day for the next 30 days only
  - Directed to place one lozenge in their mouth for few minutes after brushing their teeth; once in the morning and in the evening, allowing the lozenge to dissolve.
  - Lozenges containing not less than 100 million colony forming units BLIS M18 (per lozenge) were provided by BLIS Technologies (Dunedin, New Zealand)
- Subjects in Control group (untreated) underwent scaling and root planning but did consume M18 lozenges
- Clinical parameters were obtained for all the subjects at Baseline and on Days 15, 30 (end of active treatment), 45, and 60
Inclusion Criteria

• 28 adults enrolled (all finished and analyzed)
  • M18 group: Seven males and seven females
  • Control group (untreated): Seven males and seven females
• Good general health and age ranges between 20 to 60 years
• Individuals with moderate and severe gingivitis, and moderate periodontitis
• Gingival index scores 2 or 3, with periodontal pocket depths less than 6 mm
• Not participated in any clinical trial during the previous 4 weeks
• No ongoing antibiotic treatment

**S. salivarius M18 Reduces Plaque Index**

### Plaque index comparison between test and control group

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Day 15</th>
<th>Day 30</th>
<th>Day 45</th>
<th>Day 60</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control</strong></td>
<td>2.56</td>
<td>0.86</td>
<td>1.20</td>
<td>1.42</td>
<td>1.67</td>
</tr>
<tr>
<td><strong>M18</strong></td>
<td>2.74</td>
<td>0.95</td>
<td>0.67</td>
<td>0.89</td>
<td>1.05</td>
</tr>
</tbody>
</table>

- No statistically significant difference between the two groups at baseline or at Day 15
- Plaque index (PI) in the M18 group was significantly reduced at Day 30 (* P<0.001)
- After stopping lozenge consumption, the PI in the M18 group remained significantly lower at Days 45 and 60 (**) P<0.001)

S. salivarius M18 Reduces Gingival Index

Gingival index comparison between test and control group


- No statistically significant difference between the two groups at baseline or at day 15
- Gingival index (GI) in the M18 group was significantly reduced at Day 30 (** P<0.001)
- After stopping lozenge consumption, the GI in the M18 group remained significantly lower at Days 45 and 60 (** P<0.001)
S. salivarius M18 Reduces Sulcular Bleeding

- No statistically significant difference between the two groups at baseline or Day 15
- Sulcular bleeding index (SBI) in the M18 group was significantly reduced at Day 30 (** P<0.001)
- After stopping lozenge consumption, the SBI in the M18 group remained significantly lower at Days 45 and 60 (** P<0.001)

S. salivarius M18 Reduces Pocket Depth

Probing pocket depth comparison between test and control group

• No statistically significant difference between the two groups at baseline or at Day 15
• Pocket depth in the M18 group was significantly reduced at Day 30 (* P<0.05)
• After stopping lozenge consumption, the pocket depth in the M18 group remained significantly lower at Days 45 and 60 (* P<0.05)

Conclusions

• In the context of professional cleaning, the reduction in each of the four indices of dental health in otherwise health adults was significantly improved in the *S. salivarius* M18 group compared to the control group.

• In the *S. salivarius* M18 group, the improvements were observed at soon as Day 30.

• Even following the cessation of the *S. salivarius* M18 lozenges, the significant improvements persisted at Days 45 and 60 compared to the control.

• It is likely that the ability of *S. salivarius* M18 to reduce the amount of overall plaque contributes to (perhaps causes) the improvement in gingival index, bleeding, and pocket depth.

• Efficacy previously reported in children now extended to adults.

Typical Use for Dental and Periodontal Health

• *S. salivarius* M18 (1 lozenge per day)
  – Typically taken at night after brushing / oral hygiene regimen
  – Let dissolve in mouth rather than chewing / swallowing

Optional Supplementation

• CoQ<sub>10</sub>: 50-100 mg – daily dose to support gum health
• Vitamin C: 250 mg – daily dose to support gum health
• Alpha-Lipoic acid 600 mg – daily dose to support gum health due to its anti-inflammatory activity

*Not Recommended:* Non-specific bactericidal mouth rinses, as they could interfere with the ability of *S. salivarius* M18 to colonize
Kids under the age of 10 have high incidence of ear, nose, and throat conditions

- **Tonsillitis and bacterial infections** (e.g., ‘strep throat’)
- **Ear infections** are most common cause for doctor’s visits for children under 6
- **Pharyngitis** more common in children ages 5-17 and some adults
- **Otitis media** (<10 years of age)

Tonsillitis/Otitis media causal organisms:

| M. catarrhalis | S. pneumoniae | S. pyogenes |
• AOM is defined as an infection of the middle-ear space with rapid onset of signs and symptoms (<48 hours) of inflammation, such as otalgia, fever, irritability, anorexia, vomiting, and otorrhea

• Otoscopic findings include a yellow-red exudate behind the tympanic membrane (TM)
  – TM is often bulging, with loss of ossicular landmarks and decreased mobility of the TM

• Complications of OM and associated illnesses include otorrhea, hearing loss (and potential consequent language and developmental delay in children), tympanic membrane perforation, chronic suppurative OM and mastoiditis. Some complications, such as brain abscess and meningitis, are potentially fatal

• Bacterial pathogens can be isolated in about 80% of acute otitis media middle ear aspirates.

• Increased use of antibiotics to treat AOM is a major driver contributing to the worldwide use of antibiotics along with problem of antibiotic resistance
AOM: Major Public Health Burden

• Acute Otitis media (AOM) is a major public health concern
• Most frequent disease of childhood, affecting millions of young children worldwide every year
• Most common cause for childhood visits to a doctor’s office
• Most common infection diagnosed in the outpatient setting
• Annually, an estimated 16 million office visits (in US) are attributed to OM
  – Does not include visits to the hospital emergency room
• The global incidence rate (new episodes per hundred people per year) for acute otitis media is 10.85%, i.e. 709 million cases each year
• Annual cost for otitis media alone in the US is estimated to be US$ 3 to US$ 5 billion

Upper respiratory ENT effects

- Multiple studies have shown *S. salivarius* K12 to significantly reduce incidence of:
  - Strep-mediated pharyngitis in children (3-12 years) by 92% vs prior year (P<0.01; n=41)
  - Acute otitis media in children by 40% vs prior year (P<0.01 ; n=41)
  - Strep-mediated pharyngotonsillitis in children by 97% vs prior year (P<0.001; n=30)
  - Viral-mediated pharyngotonsillitis in children by 80% vs prior year (P<0.01; n=10)
  - Strep-mediated pharyngitis in adults by 84% vs prior year (P<0.01; n=20)

- Reduced the use of antibiotics and antipyretics
- Reduced total # of days lost from school and work due to seasonal pharyngeal infections
- Safe and well tolerated in children and adults

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61 Children enrolled with recurrent upper respiratory track infections symptoms
  • 31 treated with *S. salivarius K12* (> 1 billion CFUs/lozenge per day)
  • 30 served as an untreated control group

20 children (ten per group) also assessed for viral infections

Secondary endpoints including number of days under antibiotic and/or antipyretic therapy as well as days off from school and work (for caregiver) were also documented

**S. Salivarius K12 Reduces Episodes of Bacterial and Viral-Mediated Tonsillitis**

**S. pyogenes-mediated Tonsillitis**

<table>
<thead>
<tr>
<th>Year</th>
<th>Untreated</th>
<th>K12-Supplemented</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>3.1*</td>
<td>0.1*</td>
<td>-97%</td>
</tr>
<tr>
<td>2013</td>
<td>3*</td>
<td>2.8*</td>
<td>-7%</td>
</tr>
</tbody>
</table>

**Viral-mediated Tonsillitis**

<table>
<thead>
<tr>
<th>Year</th>
<th>Untreated</th>
<th>K12-Supplemented</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>2.5*</td>
<td>0.5*</td>
<td>-80%</td>
</tr>
<tr>
<td>2013</td>
<td>2.8*</td>
<td>2.4*</td>
<td>-14%</td>
</tr>
</tbody>
</table>

S. salivarius K12 Reduces Days Missed from School/Work, Antipyretic Use, and Antibiotic Use

Two additional clinical studies evaluating *S. salivarius* K12 in children have been published in 2015\(^1\) and 2016\(^2\)

- DiPierro et al (2015)\(^1\)
- Reduced the incidence of AOM
- Improved hearing ability (judged by tone audiometry)
- Improved tympanic membrane scores (judged by otoscopy)
- Reduced % obstruction of nasal sinuses (judged by endonasal endoscopy)
- Reduced tonsil volume (judged by tonsillar examination)
- Was safe and well tolerated

- Gregori et al (2016)\(^2\)
- Reduced pharyngo-tonsillar infections during 3-month intervention
- Reduced infections persisted for 9 months following cessation of 3-month intervention
- Was safe and well tolerated

\(AOM = \text{acute otitis media}\)

Typical Use for Halitosis or Oral/Throat Support

• *S. salivarius* K12 (1 lozenge per day)
  – Typically taken at night after brushing / oral hygiene regimen
  – Let dissolve in mouth rather than chewing / swallowing

Additional suggestions for oral /throat support:
• Change tooth brush every few days
• Drink warm liquids, such as lemon tea or tea with honey
• A cool-mist vaporizer or humidifier can moisten and soothe a dry and painful throat
• Stay home from daycare, school, or work until patient has been on probiotic for several days

*Not Recommended: Non-specific bactericidal mouth rinses, as they will interfere with the ability of BLIS K12 to colonize*
Clinical Laboratories for Personalized Oral / Periodontal Health Assessment

• **uBiome (San Francisco, CA USA)**
  – Offers personalized gut (fecal sample) and oral microbiome (swab sample) profiling services

• **OralDNA Labs (Eden Prairie, MN USA)**
  – Offers personalized salivary DNA testing services to assess risk for periodontal disease, Candida infection, others

• **Oral Microbiology Testing Service (OMTS) Laboratory (Temple University, Kornberg School of Dentistry, Philadelphia, PA USA)**
  – Offers personalized dental plaque commercial testing services
  – Quantitatively cultures major putative periodontal and peri-implant bacterial pathogens from submitted clinical dental plaque specimens

• **Rapid Strep Test**
  – Contact individual company to discuss best option for in office test
  – Beware of false negatives; requires throat culture if strep throat is suspected
  – [https://www.quidel.com/immunoassays/rapid-strep-tests](https://www.quidel.com/immunoassays/rapid-strep-tests)

Note: Links accessed 7/18/2016 and were active
### Bacteria Name

<table>
<thead>
<tr>
<th>Bacteria Name</th>
<th>You</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Firmicutes</td>
<td>50.6%</td>
<td>61.1%</td>
</tr>
<tr>
<td>Bacteroidetes</td>
<td>26.5%</td>
<td>21.0%</td>
</tr>
<tr>
<td>Proteobacteria</td>
<td>9.92%</td>
<td>3.12%</td>
</tr>
<tr>
<td>Actinobacteria</td>
<td>4.49%</td>
<td>2.66%</td>
</tr>
<tr>
<td>Cyanobacteria</td>
<td>3.32%</td>
<td>0.180%</td>
</tr>
</tbody>
</table>

Showing bacteria at phylum-level

Source: http://www.ubiomeblog.com/ubiome-sample-results/
Sample uBiome Laboratory Report

Firmicutes
Firmicutes help us to digest fat that our bodies need for energy and are among the most common microbes in our gut.

Average (45.2% - 74.3%)
You — 81.7%
Average — 59.8%

Bacteroidetes

Actinobacteria

Source: http://www.ubiomeblog.com/ubiome-sample-results/
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• DNA (bacterial)
  – **MyPerioPath®** establishes bacterial risk and can help guide therapy based on causation
    - Non-invasive ‘swish’ saliva sample facilitates patient acceptance
    - Report measures specific bacteria associated with periodontitis

• DNA (genetic)
  – **MyPerioID® and Celsus One™** establishes genetic risk and can help guide therapy based on genetics
  – **DNA DrugMap®** allows for personalizing prescription and dosing choices

• DNA (viral)
  – **OraRisk® HPV** identifies HPV status (separate risk factor for oral cancers)
  – **OraRisk® HSV** identification of Herpes Simplex Virus 1 & 2
  – **OraRisk® Candida** identifies oral yeast infections

Source: http://www.oraldna.com/
Sample OralDna MyPerioPath® Laboratory Report

Result: **POSITIVE - 5 PATHOGENIC BACTERIA REPORTED ABOVE THRESHOLD**

**Bacterial Risk: HIGH - Very strong evidence of increased risk for attachment loss**

**Legend**
- **Pathogen Load Threshold**: A horizontal line representing the threshold.
- **Detection Limit (DL)**: A horizontal line indicating the detection limit.

**Result Interpretation:** Periodontal disease is caused by specific, or groups of specific bacteria. Threshold levels represent the concentration above which patients are generally at increased risk for attachment loss. Bacterial levels should be considered collectively and in context with clinical signs and other risk factors.

### High Risk Pathogens

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Result</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aa</strong> Aggregatibacter actinomycetemcomitans</td>
<td>High</td>
<td>Very strong association with PD: Transmittable, tissue invasive, and pathogenic at relatively low bacterial counts. Associated with aggressive forms of disease.</td>
</tr>
<tr>
<td><strong>Pg</strong> Porphyromonas gingivalis</td>
<td>High</td>
<td>Very strong association with PD: Transmittable, tissue invasive, and pathogenic at relatively low bacterial counts. Associated with aggressive forms of disease.</td>
</tr>
<tr>
<td><strong>Fn</strong> Fusobacterium nucleatum/periodonticum</td>
<td>High</td>
<td>Strong association with PD: adherence properties to several oral pathogens; often seen in refractory disease.</td>
</tr>
<tr>
<td><strong>Pi</strong> Prevotella intermedia</td>
<td>High</td>
<td>Strong association with PD: virulent properties similar to Pg; often seen in refractory disease.</td>
</tr>
</tbody>
</table>

**Moderate Risk Pathogens**

- **En**, **Fn**, **Pi**, **Cr**, **Pm**, **Ec**

**Low Risk Pathogens**

- **Cs**

Culture and enumeration of major putative periodontal and peri-implant bacterial pathogens from clinical dental plaque specimens

- Aggregatibacter (Actinobacillus) actinomycetemcomitans
- Porphyromonas gingivalis
- Tannerella forsythia
- Prevotella intermedia group species
- Fusobacterium nucleatum
- Campylobacter rectus
- Parvimonas micra (Peptostreptococcus micros)
- Streptococcus constellatus
- Streptococcus intermedius
- Enterococcus faecalis
- gram-negative enteric rods/pseudomonads
- Staphylococcus aureus and other staphylococci
- Candida species (yeasts)

Source: http://dentistry.temple.edu/laboratories-centers/oral-microbiology-testing-service-laboratory
Future Challenges for Probiotics for Oral Health

- No safety concerns
- Possess ability to colonize on one or more surfaces in the oral cavity
- Sufficient stability over time
- Adequate practitioner and consumer education regarding the need and benefits of orally-targeted probiotics
- Compatibility with multiple delivery formats
- Increased regulatory scrutiny
• Oral health is contingent on the diverse composition of the oral microbiome
• Oral health is linked to systemic health and disease
• Oral health can be supported by appropriate nutrition
• Oral health can be adversely affected by poor nutrition
• Based on emerging science, oral health can be supported through the use of probiotics that target the oral cavity
• Several commercial laboratories provide personalized assessments of the oral microbiome and risk for dental and periodontal disease
**Think Outside the Gut:**
**Modulating the Oral Microbiome for Systemic Health**

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Adhesion of *Bifidobacterium lactis* HN019 to human intestinal epithelial cells (Caco-2)

Attachment of *Streptococcus salivarius* ENT-12™ to HEP-2 cells