levocetirizine for the control of nasal and eye symptoms for 2 weeks, and reported that each drug and their combination were equally effective in controlling symptom scores.

In summary, 1 DBRCT of AR patients has shown benefit with the addition of montelukast to INCS for symptom improvement, though the patient symptoms were largely allergic in nature, without a clear diagnosis of true CRS. Three other studies, also largely of AR patients, demonstrated no or very limited symptom improvement with the use of montelukast. Montelukast may provide some benefit in AR, but it is unclear whether anti-LT therapy would provide benefit in non-allergic CRSsNP.

Anti-Leukotriene Therapy for CRSsNP

Aggregate Grade of Evidence: C (Level 2: 2 studies; level 3: 2 studies; level 4: 1 study; Table IX-36).
Benefit: Improvement in symptoms for patients with comorbid AR, lack of evidence for utility in non-allergic CRSsNP.
Harm: Limited risks. Montelukast has been associated with rare neuropsychiatric events in postmarketing reports (see Table II-1).
Cost: Moderate.
Benefits-Harm Assessment: No clear benefit in undifferentiated patients with CRSsNP though there appears to be benefit in patients with comorbid allergy.
Value Judgments: Montelukast may be beneficial for allergic patients with CRSsNP who are not sufficiently responsive to INCS.
Policy Level: No recommendation for non-allergic CRSsNP; Option for CRSsNP with comorbid allergy.
Intervention: Montelukast is an option for CRSsNP patients with an allergic component to their disease, as an adjunct to INCS.

IX.D.8 | Management of CRS: Probiotics

Because of limited data, CRSsNP and CRSwNP are combined in this analysis and recommendations.

Microbial communities encode millions of genes and associated functions which act in concert with those of human cells to maintain homeostasis.[1182] Numerous studies have now established the microbiota as an important contributor to essential mammalian functions such as metabolism,[1183] biosynthesis,[1184] neurotransmission[1185,1186] and immunomodulation[1187,1188] The perturbation of the healthy microbial ecology, referred to as microbial dysbiosis, has now been linked to many chronic diseases including RS.[1183] Theoretically it is postulated that restoration of a healthy or physiological microbiome through the use of pre or probiotic therapy, may reverse the disease process and reestablish health.

As defined by the World Health Organization, probiotics are "live microorganisms, which when consumed in adequate amounts confer health and benefit to the host."[1189] Proposed mechanisms of action include maintenance of the epithelial barrier, production of anti-microbial substances, competitive inhibition of pathogenic organisms, and modulation of the immune system.[1190] Numerous studies have been performed assessing probiotics as a treatment option in allergic rhinitis with mixed outcomes,[1191] however, research in CRS treatment is limited.

Oral probiotics have been investigated in the treatment of CRS and RARS in 3 clinical studies. Two of the studies demonstrated that oral administration of *Enterococcus faecalis* in the treatment of recurrent acute and chronic RS conferred a benefit.[1192,1193] In a double-blind placebo-controlled study, Habermann et al. showed a reduction in the frequency and time to recurrence of acute exacerbations of CRS in patients who received a 6-month course of oral *Enterococcus faecalis* and that this benefit was sustained for 8 months post treatment.[1192] Kitz et al. also demonstrated a reduction in frequency and duration of RARS in children who received 8 weeks of oral probiotic *Enterococcus faecalis* in suspension post standard oral antibiotics and intranasal decongestant treatment in a non-randomized controlled study.[1193] In contrast, a randomized controlled trial in by Mukerji et al. did not identify any improvement of sinonasal QoL scores with oral *Lactobacillus rhamnosus* for 4 weeks.[1194]

There is a paucity of data regarding the use of topical probiotics in the treatment of CRS with only 1 placebo controlled trial in the literature.[1195] In this double-blind study, CRSsNP patients were randomized to receive topical nasal *Honey bee microbiome* spray or placebo sprays for 2 weeks. The authors could not identify a statistically significant change in sinonasal symptom scores, microbiologic flora, or local inflammatory markers.[1195] A recent *in vitro* study evaluating the effect of a commercially available probiotic suspension on *Pseudomonas aeruginosa* clinical isolates has also shown concerning signs with the rinse inducing the growth of a virulent isolate when co-cultured with the probiotic suspension.[1196]

Results from the studies in the current literature revealed mixed and limited success with oral probiotics in CRS treatment while topical probiotics have not yet shown clinical benefit in human studies. In summary, no