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## Variability in skin microbiota between smokers, former smokers, and nonsmokers

*To the Editor:* Smoking may induce significant changes in the skin milieu that may affect microbial communities harbored by the skin, potentially disrupting the normal functions of the skin microbiome.[1,2]

We performed a case-control study of the skin microbiota of current (n = 11), former (n = 5), and never smokers (n = 7). Current smokers included 6 heavy smokers (≥5 pack-years) and 5 light smokers (<5 pack-years). The study was approved by the Johns Hopkins School of Medicine institutional review board, and participants provided written informed consent. The bilateral cheeks and dorsal aspect of the forearms were separately swabbed with sterile foam-tipped swabs moistened with Amies medium. After DNA extraction, the V4 region of the bacterial 16S ribosomal RNA gene was amplified with polymerase chain reaction and sequenced using Illumina (San Diego, CA) MiSeq. Comparison of alpha diversity with the Shannon metric was performed by using *t* tests with Monte Carlo permutations on QIIME1 open-source software. Beta diversity, computed with UniFrac metric, was compared by using analysis of similarity. Metagenomic profiles were created with MetaStats 2.0 software.

At the phylum level, smokers were overall enriched in *Actinobacteria* species and depleted in *Fusobacteria* species compared with never smokers (Fig 1). We also detected numerous genera that were significantly enriched/depleted in smokers (Table I).

We found no significant difference in mean alpha diversity (± standard deviation) between heavy smokers (cheeks: 4.909 ± 0.654; arms: 5.563 ± 0.706), light smokers (cheeks: 5.639 ± 0.633; arms: 5.562 ± 0.514), former smokers (cheeks: 4.993 ± 0.946; arms: 5.186 ± 0.702), or never smokers (cheeks: 5.348 ± 1.243; arms: 5.793 ± 0.627). However, significant differences were observed in beta diversity between participant groups (cheeks: $R = 0.171$, $P = .001$; arms: $R = 0.182$, $P = .002$).

Although the diversity within each sample (alpha diversity) was not significantly different among participant groups, we observed significant differences among participant groups at each sampling site when examining diversity among samples (beta diversity). Therefore, although sample-to-sample differences in diversity were insignificant, significant differences existed between the overall diversity of the microbial communities.

Interestingly, our findings correlate fairly well with studies investigating the oral microbiota in smokers, suggesting that smoking has similar effects on the microbiota of the mouth and skin.[3,4] Many of the genera that were enriched/depleted in the skin microbiota of smokers have been shown to be enriched/depleted in oral microbiota as well.[4] The effect of smoking on the oral microbiome has been attributed to the direct effect of toxicants, impaired host immunity, and the depletion of oxygen, mechanisms that may also be at play in the skin.[4] Furthermore, we found that fewer bacterial taxa were significantly enriched/depleted in former smokers than in current smokers, which may suggest that some of the skin microbiota perturbations associated with smoking may be reversible.

Our study was limited by a relatively low sample size in each group. Secondhand smoke exposure was not evaluated. Additionally, participants were not directly matched by demographics to control individuals. V4 sequencing may also underestimate the relative abundance of some skin commensals.[5]

In this study, we found that smoking is associated with significant changes in microbial beta diversity and the relative abundance of many bacterial taxa on the skin. Future studies will be useful to understand the significance of these microbial disturbances and their role in the physiology of the skin.

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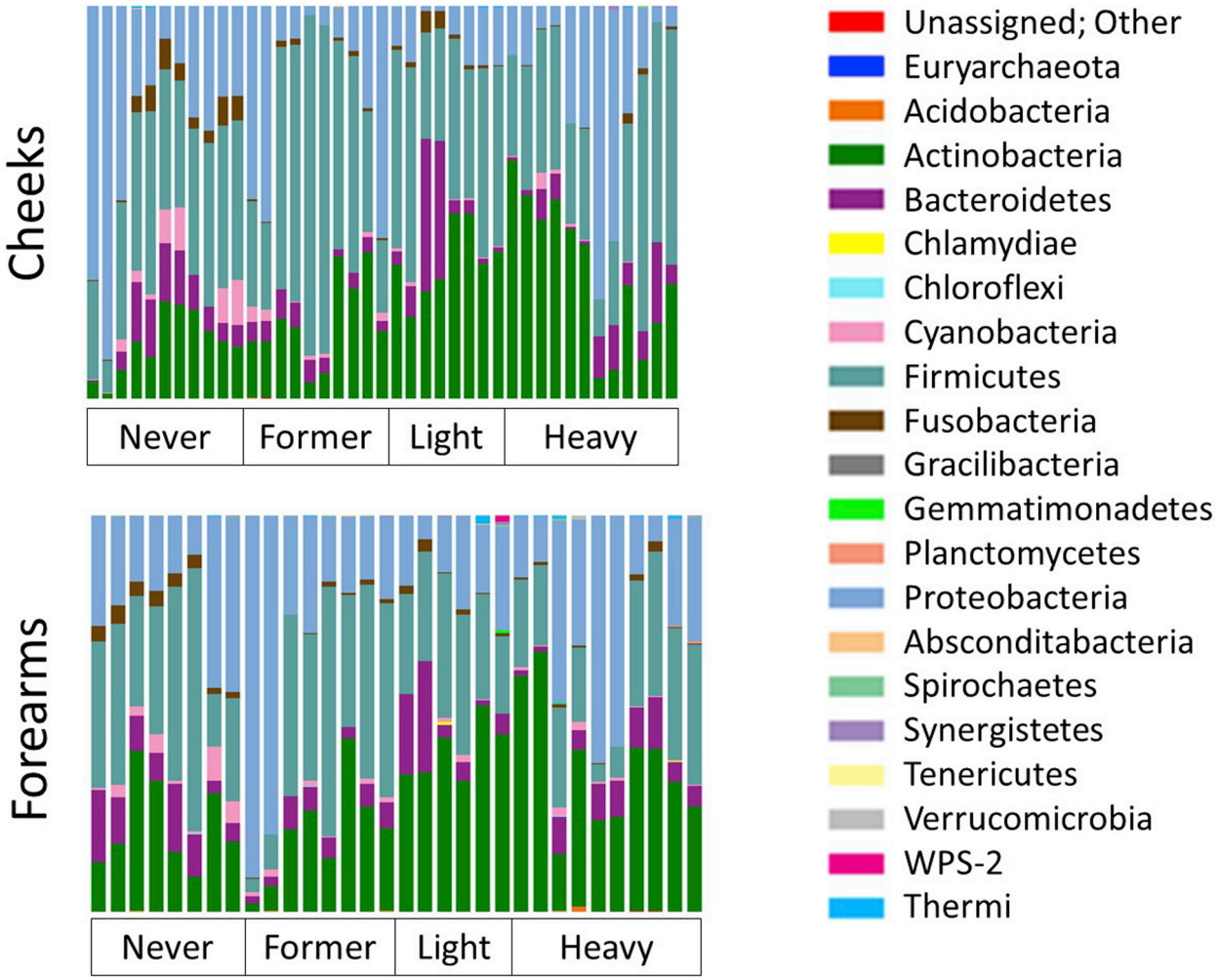


**Fig 1.** Phylum level relative abundance distribution in the microbiota of the cheeks and dorsal aspect of the forearm of heavy (≥5 pack-years), light (<5 pack-years), former, and never smokers.

**Table I.** Significantly enriched/depleted genera in microbiota of the cheeks and forearms of heavy smokers compared with never smokers*

| | Cheeks of heavy smokers (*P* value) | Arms of heavy smokers (*P* value) |
|---|---|---|
| Enriched | *Corynebacteria* (.004) | *Bifidobacterium* (.044) |
| | *Cutibacterium* (.005) | *Megasphaera* (.046) |
| Depleted | *Neisseria* (.001) | *Neisseria* (.001) |
| | *Lactobacillus* (.001)† | *Leptotrichia* (.001)† |
| | *Selenomonas* (.001)† | *Gemella* (.001) |
| | *Leptotrichia* (.001)† | *Prevotella* (.002)† |
| | *Haemophilus* (.003) | *Fusobacterium* (.003) |
| | *Aggregatibacter* (.003) | *Abiotrophia* (.008)† |
| | *Capnocytophaga* (.004) | *Lactobacillus* (.010)† |
| | *Abiotrophia* (.005) | *Haemophilus* (.011) |
| | *Fusobacterium* (.006)† | *Selenomonas* (.024) |
| | | *Streptococcus* (.030) |

*For all comparisons, $P < .05$ is considered statistically significant.
†Also significantly depleted in former smokers compared with never smokers.

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## Placebo tailoring improves patient satisfaction of treatment plans in atopic dermatitis

*To the Editor:* Atopic dermatitis (AD) treatment outcomes are often limited by poor adherence to topical treatments and behavior recommendations. Patient perception of health messages in chronic diseases such as AD can be enhanced by the use of tailoring techniques such as personalization.[1] Personalization increases a patient's attention to a message by communicating that the instruction has been designed specifically to suit them uniquely as an individual.[2,3] However, expectations of customization can also be raised without actually providing content matching with the receiver, a method termed *placebo tailoring*.[4] This study assessed the effect that placebo tailoring of a treatment plan has on AD patients' level of satisfaction and confidence with their treatment plan and provider.

After the institutional review board approved the survey-based study, 468 adults with AD from the Amazon Mechanical Turk platform, used regularly by psychologists to recruit participants for survey-based studies,[5] met screening criteria. Screening criteria included several questions and attention checks to exclude participants without AD. Patients were randomly assigned to 1 of 2 survey groups (Figs 1 and 2). Participants were provided a hypothetical scenario about their regularly scheduled AD appointment where their dermatologist has provided them with a treatment plan summary; 1 group received a generic printout, and the other group received a placebo tailored printout with circled selections alongside decoy options. Survey participants were asked about satisfaction with the treatment plan, confidence in the treatment plan, perception that the treatment plan was individualized to them, and willingness to follow the treatment plan recommendations (all assessed with a 9-point Likert-type scale). The results were analyzed using Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL), version 26.0, with Mann-Whitney test for significance and Cohen $d$ for effect size.

Patient age ranged from 18 to 78 years, with a mean of 34 years. There were 313 women and 155 men; 300 of the 468 respondents (64.1%) had at least an associate's degree. No statistically significant differences were present between the 2 groups' demographics. Participants had a median length of AD diagnosis of 9 years, ranging from 1 to 65 years. Placebo tailoring may be an effective tool to improve patient satisfaction (5.0 vs 6.0; $P < .0001$; $d = 0.47$) and confidence (5.0 vs 6.0; $P < .0001$; $d = 0.45$) in their prescribed treatment plan. This simple intervention may help patients feel that their care has been individualized (5.0 vs 6.0; $P < .0001$; $d = 0.52$). Patients are more willing to follow the prescribed treatment recommendations when they are presented in this format (5.5 vs 6.5; $P < .0001$; $d = 0.47$).

| Your Treatment Plan | |
|---|---|
| **Moisturizers** | Emollient |
| **Topical Corticosteroid** | Triamcinolone |
| **Topical Corticosteroid Frequency** | 2x/day |
| **Bath** | Diluted bleach |
| **Diet** | Anti-inflammatory |
| **Other** | Cool mist vaporizer |
| **Additional details:**<br>**Diluted bleach bath:** Combine ¼ cup household bleach (6.15% sodium hypochlorite) in a bathtub half-full of water. Soak for 5 to 10 minutes. Rinse completely with warm tap water.<br>**Anti-inflammatory diet:** Avoid foods high in saturated fats, refined grains, processed meat. Consume foods high in omega-3 fatty acids (fish), probiotics (yogurt with live active cultures), flavonoids (colorful fruits and vegetables). | |

**Fig 1.** Generic treatment plan.