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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:	
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.	
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.

Your Treatment Plan			
Moisturizer	Emollient	Humectant	Occlusive
Topical Corticosteroid	Hydrocortisone	Betamethasone	Triamcinolone
Topical Corticosteroid Frequency	2x/day	4x/day	6x/day
Bath	Oatmeal	Diluted bleach	Regular lukewarm
Diet	Dairy-free	Gluten-free	Anti-inflammatory
Other	Cool mist vaporizer		
Additional details:			
Oatmeal bath: Combine 2-3 cups colloidal oatmeal (oats ground into a fine powder) in a bathtub full of water. Soak for 10 minutes. Rinse completely with warm tap water.			
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.			
Dairy-free diet: Avoid ingredients such as lactose, whey, casein, cheese powder, lactalbumin.			
Gluten-free diet: Avoid ingredients such as wheat, barley, rye, oats, bulgur.			
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 2. Placebo tailored (individualized) treatment plan.

Currently, there is limited evidence of the effect of placebo tailoring in message satisfaction and subsequent behavioral changes.⁴ Furthermore, few studies have compared placebo-personalized materials with nonpersonalized materials.⁴ In this study, placebo tailoring improved patient satisfaction and confidence in the treatment plan, perception of individualization, and willingness to follow treatment plans.

Unfortunately, this randomized survey study does not capture all factors involved in satisfaction of a patient treatment plan or provider. Although a 1-point difference may not necessarily indicate a clinically significant result on this unvalidated scale, this exploratory result does show the direction of the differences between 2 items and that this small change in provider behavior has the potential to improve patient adherence and outcomes. Additionally, use of tools such as the Amazon Mechanical Turk may introduce selection biases. In this study, participants were skewed toward a slightly more educated and female group compared to the US adult AD patient population.

Based on our preliminary data, incorporating placebo tailoring techniques into AD treatment plans may be a potential method of improving patient satisfaction with and willingness to adhere to their treatment plan.

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Contact allergy to hydroperoxides of limonene and linalool in a pediatric population



To the Editor: Allergic contact dermatitis (ACD) is recognized to contribute to 20% of pediatric atopic dermatitis cases. Fragrances are the most common allergens for children with and without atopic dermatitis.¹ Limonene and linalool are 2 common fragrances found in hair and skin products, detergents, perfumes, and 90% to 97% of essential oils.^{2,3} Both limonene and linalool rapidly oxidize upon contact with air to become the hydroperoxides of limonene and linalool, which are significantly more allergenic than the reduced forms. Previous studies have determined the optimal concentration for testing to hydroperoxides of limonene and linalool to be 0.3% and 1.0%, respectively.^{2,3}

Approximately 60% to 70% of sensitizations to limonene and linalool are undetected by fragrance testing alone (testing to fragrance mixes [FMs] 1 and 2, and Balsam of Peru [BoP]).^{2,3} Despite their ubiquity and high allergenicity rates in adults, to our knowledge, no study has evaluated the rates of contact allergy to hydroperoxides of limonene and linalool in pediatric patients.

This retrospective medical record review was approved by the Partners Healthcare institutional review board and included patients younger than 18 years who had patch testing at Massachusetts General Hospital and Brigham and Women's Hospital between January 1, 2007, and March 20, 2019.

Of the 124 children, 54 (43.5%) were tested with hydroperoxides of limonene and 28 (22.6%) with hydroperoxides of limonene and linalool (Table I). In patients tested with hydroperoxides of limonene, positive reactions were observed in 7 (13.0%; 95% confidence interval, 5.4-24.9). Positive reactions to hydroperoxides of linalool were observed in 5 of 28 patients tested (17.9%; 95% confidence interval, 6.1-36.9) (Table II).

Table I. Pediatric patients undergoing patch testing (N = 124)

Characteristics	Value
Total patients identified with any patch testing	N = 124
Sex, n (%)	
Female	74 (59.7)
Male	50 (40.3)
Race, n (%)	
White	87 (70.2)
Asian	10 (8.1)
Hispanic	7 (5.6)
Black	7 (5.6)
Other or not recorded	13 (10.5)
Age at patch test, y, mean ± SD	11.0 ± 4.5
Age at patch test, range	10 months to 17 years
Type of patch testing, n (%)	
Tested to hydroperoxides of limonene and linalool	28 (22.6)
Modified ACDS Core Series	14 (11.3)
Pediatric Core Series	6 (4.8)
Fragrance Series	6 (4.8)
North American Standard Series	2 (1.6)
Tested to hydroperoxides of limonene, not of linalool	26 (21.0)
Modified ACDS Core Series	16 (12.9)
Bakery Series	10 (8.1)
Tested to hydroperoxides of linalool, not of limonene	0 (0)
Tested to neither hydroperoxides of limonene nor linalool	70 (56.5)
Thin-Layer Rapid Use Epicutaneous (TRUE) Patch Test*	25 (20.2)
North American Series	21 (16.9)
North American Comprehensive Series†	7 (5.6)
Modified American Contact Dermatitis Society Core Series	7 (5.6)
Metal Series†	4 (3.2)
Custom selected antigens	4 (3.2)
North American Photopatch Series†	2 (1.6)

*SmartPractice, Phoenix, AZ.

†Chemotechnique Diagnostics, Vellinge, Sweden.

Nine patients tested positive to 1 or both hydroperoxides. Of these 9, 5 (55.6%) did not respond to other fragrance allergens (FM1, FM2, BoP). All 9 (100%) patients had a history of atopy, and 5 (55.6%) had a history of AD.

A minority of pediatric patients in this cohort were tested to hydroperoxides of limonene or linalool (43.5% and 22.6%, respectively). Of the children tested to 1 or both hydroperoxides, 13.0% and 17.9% of patients had positive results for hydroperoxides of limonene and linalool, respectively. Although true