

November 3, 2017



Anna K. Abram,  
Deputy Commissioner for Policy, Planning, Legislation, and Analysis  
Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

**RE: Docket No. FDA-2017-N-3067 for Patient-Focused Drug Development for Alopecia Areata**

Dear Deputy Commissioner Abram,

On behalf of the 6.8 million Americans affected by alopecia areata, the National Alopecia Areata Foundation (NAAF) appreciates the opportunity to offer input during the Food and Drug Administration (FDA) Public Meeting on Patient-Focused Drug Development for Alopecia Areata (FDA-2017-N-3067) held on September 11, 2017. We again wish to thank the FDA for selecting alopecia areata, one of the most common autoimmune diseases in the United States, for a public meeting in Fiscal Year 2016-2017 through the Patient-Focused Drug Development Initiative following our nomination of the disease in 2015. NAAF shares the FDA's interest in improving treatment options by incorporating the patient perspective into therapy evaluation to more appropriately inform critical benefit-risk decision making. It has been our pleasure to engage with the agency over the last several months to support your commitment to obtain diverse stakeholder perspectives on disease severity and unmet medical needs from the alopecia areata community. We are humbled by the hundreds of individuals living with alopecia areata who have bravely shared their personal experiences with the FDA already, and we offer the following comments to supplement those you have already gathered from the September 11<sup>th</sup> meeting, webcast and the comment process.

**The challenges of alopecia areata**

Alopecia areata is a disfiguring autoimmune disease associated with a number of serious comorbidities that are debilitating for patients and contribute to a significant healthcare burden.<sup>i</sup> Alopecia areata affects as many as 6.8 million people in the U.S. with a cumulative lifetime incidence of 2.1% and there is a large unmet medical need for treatment options for both adult and children.<sup>ii</sup> As the FDA is aware, alopecia areata is a noncontagious, chronic, inflammatory, disfiguring, and disabling disease for which there is no cure or FDA-approved therapies. It appears on the skin, most often as one or more small, round, smooth patches of hair loss on the scalp and can progress to total scalp hair loss (alopecia totalis) or complete body hair loss (alopecia universalis). The disease onset often occurs at an early age and alopecia areata affects as many as 1.2 million children under the age of 12 in the U.S.<sup>iii</sup>

Founded in 1981, NAAF serves the community of people affected by alopecia areata through three primary program areas of support and education, awareness and advocacy, and research. Our work with and for the community of people affected by alopecia areata—including family, friends, medical professionals, research scientists, biopharmaceutical developers and government representatives—exists to drive efforts toward finding safe, effective treatments and a cure for all those affected by the disease.

Alopecia areata is known to have a profound impact on patients' quality of life.<sup>iv</sup> The sudden onset, recurrent episodes, and unpredictable course of hair loss can lead to difficulties at work, at school and in relationships. Alopecia areata patients experience higher rates of depression, anxiety and suicidal ideation, especially in children and adolescents.<sup>v</sup> The knowledge that medical interventions are extremely limited and of minor effectiveness further exacerbates the emotional stresses patients' experience. In recent years, scientific advancements have been made but there is no cure or indicated treatments for this life-altering disease. The standard of care for alopecia areata is grossly inadequate. There is no universally proven therapy that induces

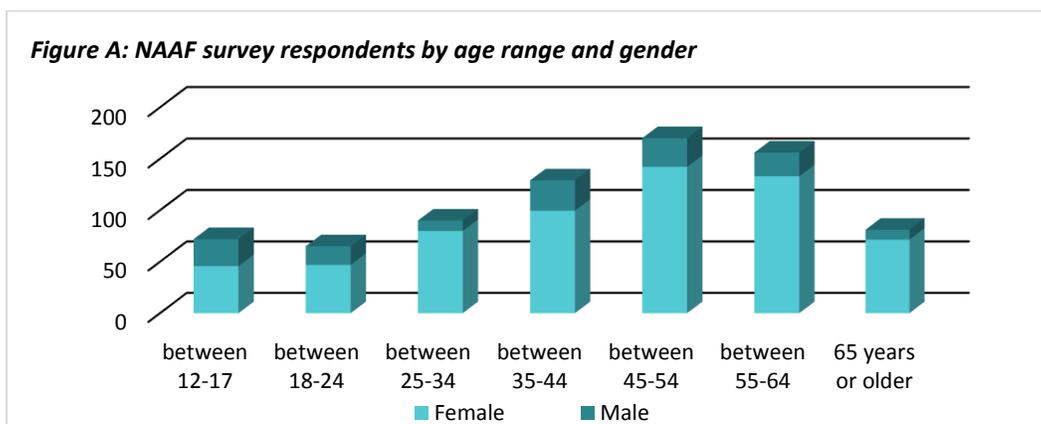
and sustains remission and available treatment options are of limited effectiveness, especially in more extensive forms of the disease. The most commonly used off-label treatments such as intralesional corticosteroid injections and topical immunotherapies are painful, require continuous administration, and can have prohibitive irritant and allergic side effects.

Patients are desperate to have treatments approved that are safe and efficacious for alopecia areata. As you heard from multiple September 11, 2017 PFDD meeting participants, many in our community are frustrated by the lack of effective therapeutic options for all age groups with the disease. While re-growing hair or preventing hair loss may serve as important endpoints for treatment development, the reduction in quality of life that alopecia areata patients endure should be taken into account when establishing an appropriate benefit-risk profile for potential treatments. Alopecia areata should no longer be considered a cosmetic disorder, but a disfiguring, psychologically devastating disease of the skin that requires medical treatment, supported by the article recently accepted by the Journal of the Academy of Dermatology for publication, *Alopecia Areata is a Medical Disease*.

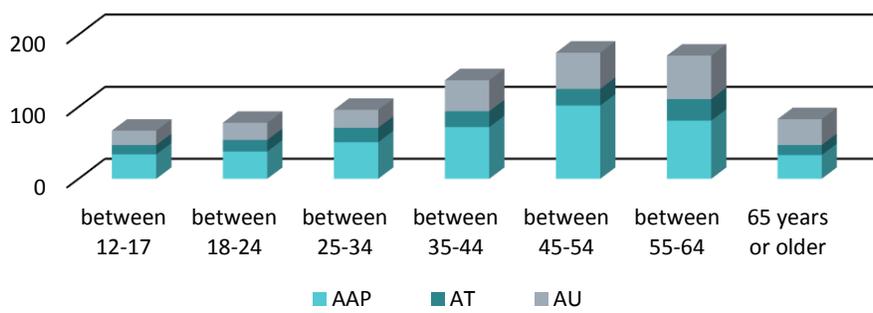
**Gathering patient perspectives: Health effects, daily impacts and treatment approaches**

NAAF is widely regarded as the largest, most influential, and most representative foundation associated with alopecia areata. NAAF is connected to patients through local support groups and also has an important, well-attended annual conference each year that reaches many children and families. NAAF has a database of a committed and engaged cadre of more than 80,000 patients and stakeholders allowing us to easily promote patient involvement in clinical research, vital to bringing safe and effective treatments to market. In addition, the Alopecia Areata Registry and Biobank, with over 10,000 participants, provides an instant network of trial-ready sites to alert and recruit patients for studies. These programs complement the self-reported patient data gathered by NAAF.

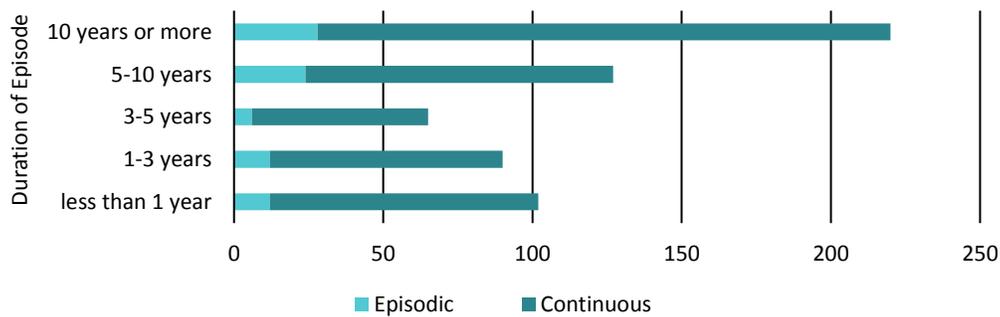
To further enhance the FDA’s understanding of alopecia areata stakeholder perspectives, NAAF has pulled self-reported patient data from surveys of our community conducted in 2015 and 2017 on the quality of life impacts of alopecia areata and current treatment and management approaches (manuscript in preparation). Figure A contains a breakdown of NAAF survey responders by age group and gender. Figure B contains a breakdown of NAAF survey responders by age group and diagnosis, alopecia areata patchy (AAP), alopecia totalis (AT) and alopecia universalis (AU). Figure C contains a breakdown of NAAF survey respondents by duration of and type of current hair loss episode. We have also gathered relevant non-NAAF data cited in recently published professional papers.



**Figure B: NAAF survey respondents by age range and diagnosis**



**Figure C: NAAF survey respondents by duration and type of episode**

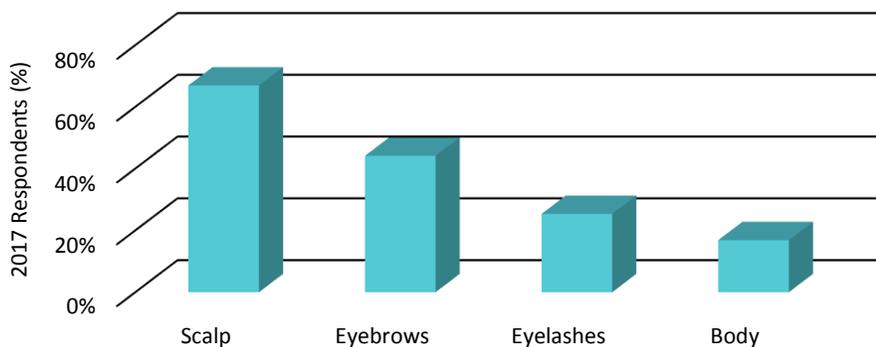


**Topic 1: Disease Symptoms and Daily Impacts That Matter Most to Patients**

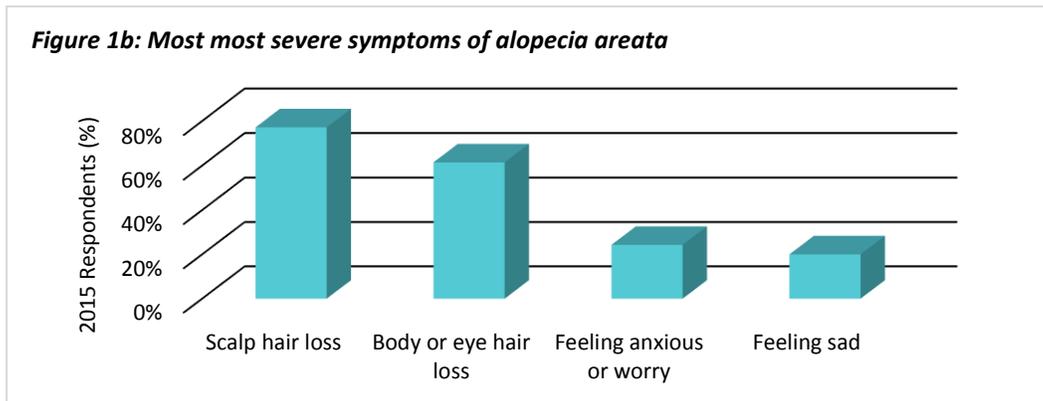
1. *Of all the symptoms or disease manifestations that you experience because of your condition, which 1 to 3 symptoms or manifestations have the most significant impact on your life? (Examples may include location or type of hair loss, nail changes, hair quality upon regrowth)*

This question of which symptom or symptoms have the most significant impact on quality of life for individuals living with alopecia areata was directly addressed in a 2017 NAAF survey of 671 patients on their perceptions of living with alopecia areata. Symptom manifestations were quantified based on the frequency of specific keywords from open-ended responses. According to the results, 67% of patients surveyed indicated loss of hair on the scalp as the most bothersome symptom, followed by loss of eyebrows (44%), eyelashes (25%) and body hair (17%) (Figure 1a).

**Figure 1a: Most bothersome hair loss location**

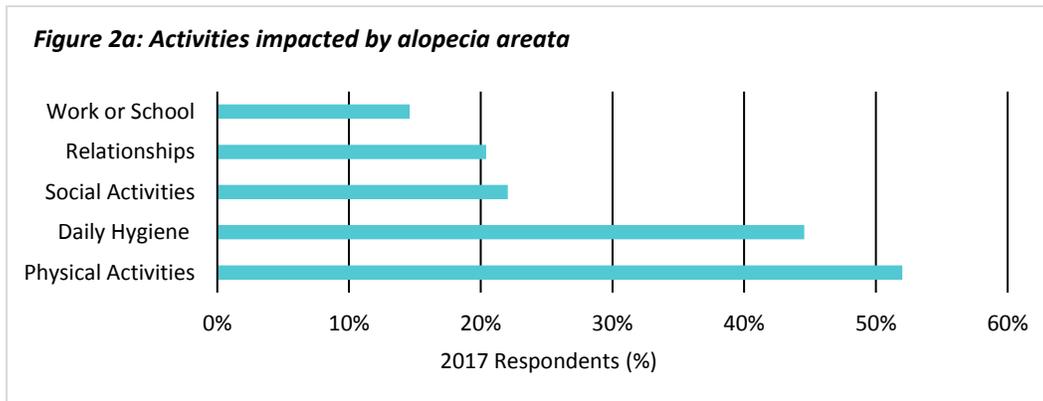


Similarly, in a 2015 NAAF survey of 101 patients living with alopecia areata rated scalp hair loss (77%), body or eye hair loss (61%), feeling anxious or worry (24%) and feeling sad as the most severe symptoms of the disease (Figure 1b).

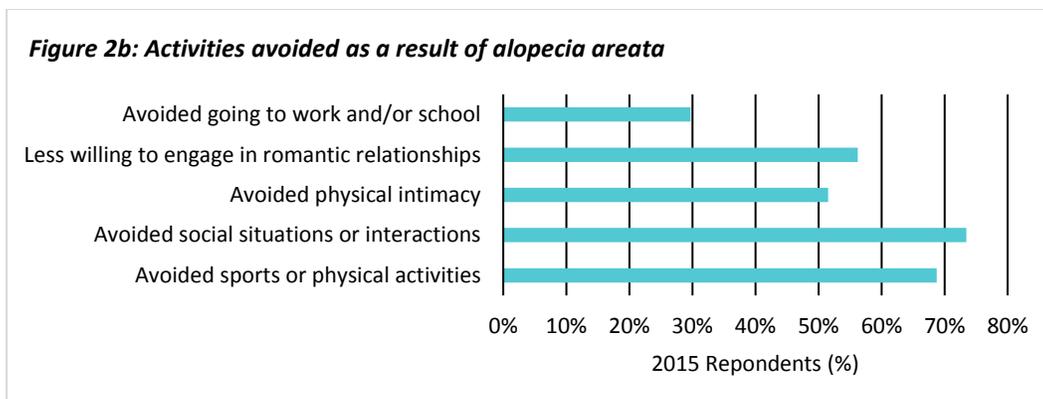


2. *Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your condition? Examples of activities may include daily hygiene, engagement in personal relationships, participation in sports or social activities, completion of school or work activities, etc.*

Results from this open-ended question asked directly in the 2017 NAAF survey were quantified based on the frequency of specific key-words. Respondents indicated that their alopecia areata impacts physical activities (52%), daily hygiene (45%), social activities (22%), relationships (20%), and work or school (15%) (Figure 2a).

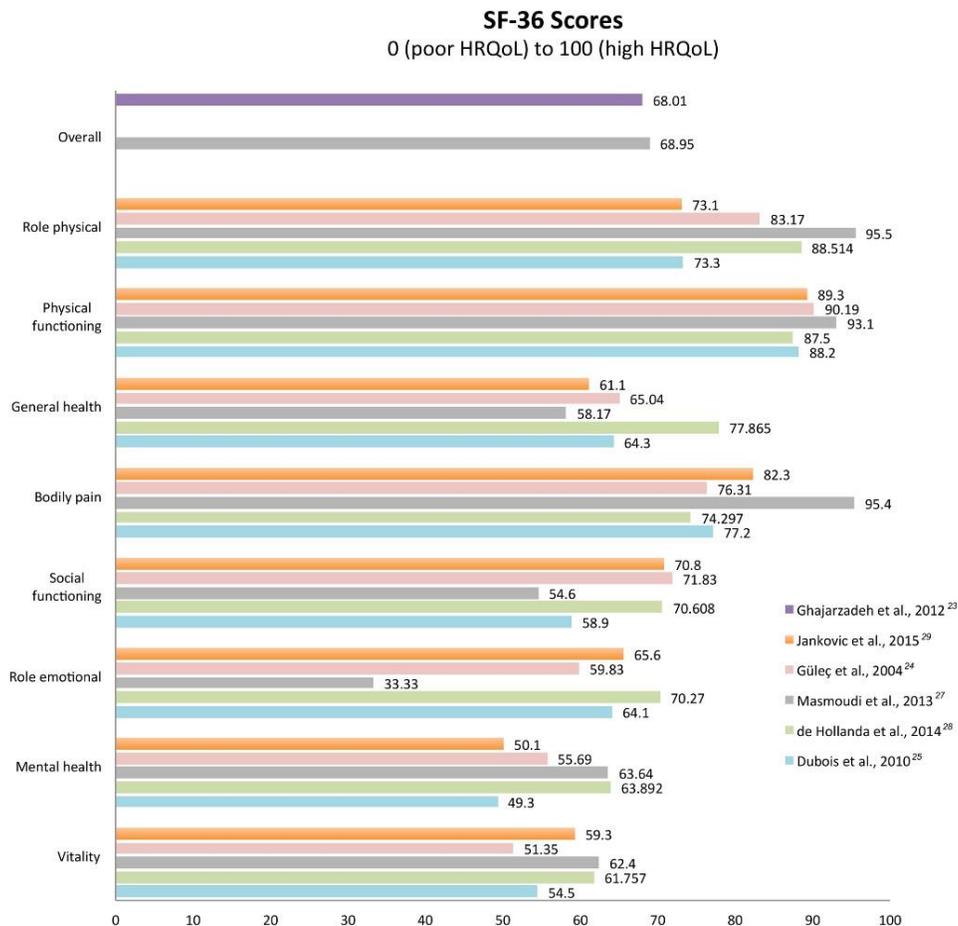


Results from the 2015 NAAF survey found that substantial proportions of respondents avoided sports or physical activities (69%), social situations or interactions (73%), physical intimacy (52%), going to work or school (30%) and that they were less willing to engage in romantic relationships (56%) as a result of their alopecia areata (Figure 2b).



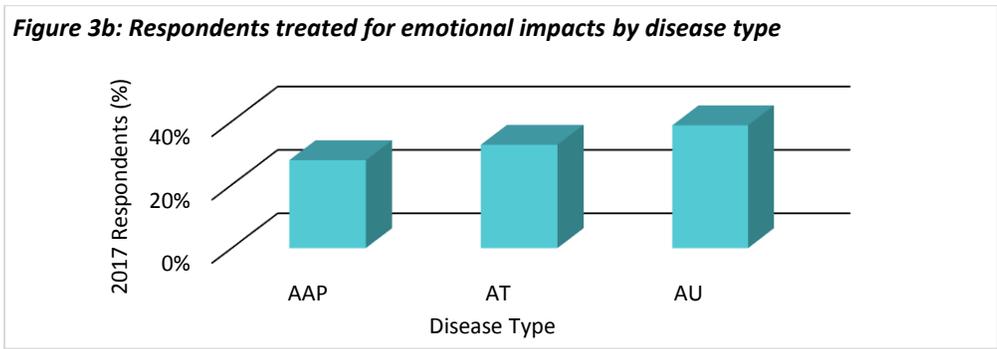
These findings are consistent with a systematic review of 11 published studies of health-related quality of life (HRQoL) measures including the Dermatology Life Quality Index (DLQI), Skindex-16, and Short Form Health Survey (SF-36), and other indices incorporating data from 1,986 patients with alopecia areata.<sup>iv</sup> Patients with alopecia areata had poorer HRQoL in role emotional, mental health, and vitality aspects of SF-36 compared with control groups, indicating poor social functioning, higher psychological distress, and diminished energy levels as a result of disease. (See Figure 2c copied from the original paper *Health-related quality of life (HRQoL) among patients with alopecia areata (AA): A systematic review*, Figure 1).

**Figure 2c: Mean Short Form Health Survey (SF-36) scores, overall and for each domain, for patients with alopecia areata.<sup>iv</sup>**



### 3. How do your symptoms and their negative impacts affect your daily life?

Data from a 2015 NAAF Survey found that respondents experienced anxiety or worry (91%), sadness or depression (84%), embarrassment (76%), and frustration (90%) as well as negative impacts on self-esteem (75%), academic performance (20%) and career opportunities (33%) as a result of living with alopecia areata (Figure 3a). In addition, 28% of responding patients had been treated by a physician for anxiety related to their alopecia areata, and 20% of responding patients had been treated by a physician for depression related to their alopecia areata.



Data from the 2017 NAAF Survey found that 28% of respondents with alopecia areata patchy (AAP), 33% of respondents with alopecia totalis (AT) and 39% of respondents with alopecia universalis (AU) have received treatment for the emotional impacts of the disease (Figure 3b). Six respondents specifically mentioned suicide as something they have struggled with or attempted as a result of their alopecia areata. When we consulted with Children’s Alopecia Project about what they would want the FDA to know about impacts of alopecia areata in children based on what they hear at their summer camps, they mentioned suicide attempts and thoughts, self-mutilation (cutting), leaving school to be home schooled, and bullying.

4. *How have your condition and its symptoms changed over time? Would you define your condition today as being well-managed?*

In the 2017 NAAF survey, responses describe their disease as either appearing as a cyclic phenomenon or becoming progressively worse over time. All answers related to management of disease were quantified towards negative (no/not) responses and positive (yes) responses. More than 3 times as many patients report their condition as not being well-managed with 65% of responses being negative versus 18% positive.

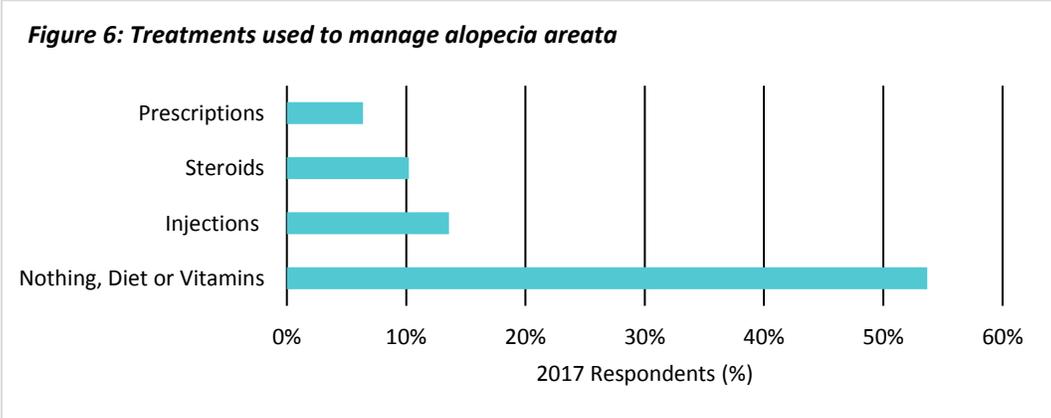
5. *What worries you most about your condition?*

Based on topic modeling of open-ended answers to this 2017 NAAF survey question, we can define important topics that concern respondents, including fears of future response (or non-response) to treatment, development of other autoimmune diseases and familial concerns – including the hereditary pre-disposition to the disease and a desire to not “pass on” alopecia areata to future generations.

**Topic 2: Patient Perspectives on Current Treatment Approaches**

6. *What are you currently doing to help treat your condition or its symptoms? How has your treatment regimen changed over time, and why?*

According to the top words used in response to this 2017 NAAF Survey question, alopecia areata patients are currently using nothing, diet or vitamins (54%), injections (14%), steroids (10%), and prescriptions (6%) to manage their disease (Figure 6).



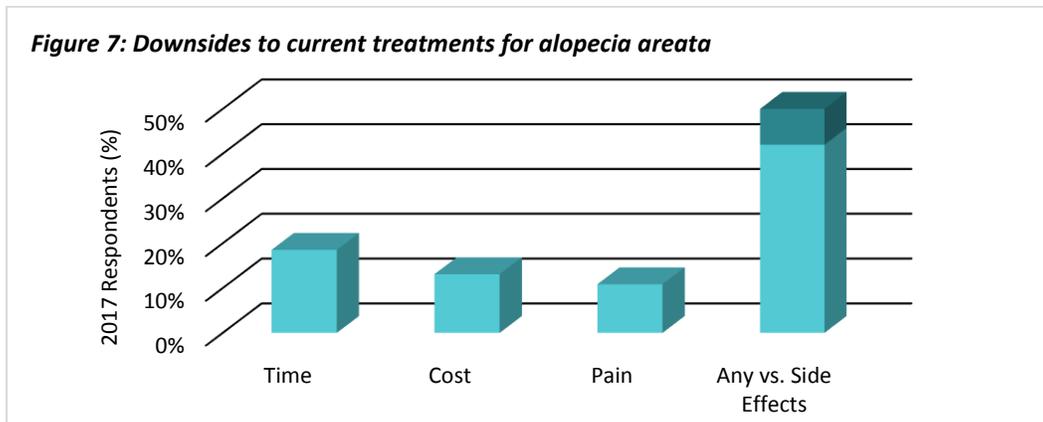
In addition, 30% of respondents report no changes in their treatment regimen over time, and 11% report that they have stopped treatment.

7. *How well does your current treatment regimen control your condition? How well have these treatments worked for you as your condition has changed over time?*

According to the 2017 NAAF Survey respondents, a total of 34% report that their current treatment (or lack of treatment) does nothing to control the disease. And a third of the respondents indicate that there has been no change in success of treatment over time, indicating that unsuccessful treatment is a mainstay.

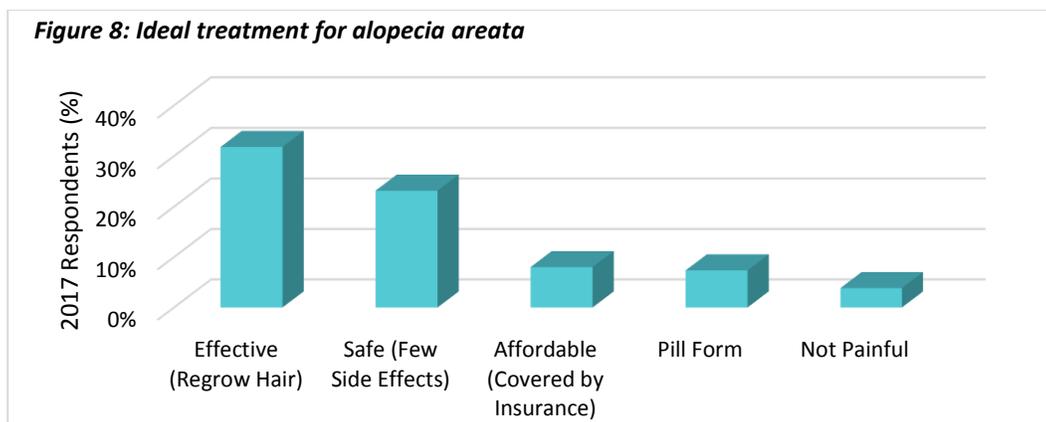
8. *What are the most significant downsides to your current treatments, and how do they affect your daily life? (Examples of downsides may include going to the clinic for treatment, time devoted to treatment, side effects of treatment, route of administration, etc.)*

For 2017 NAAF survey respondents receiving treatment, major downsides are time (19%), cost (13%), and pain (11%). In addition, only 8% of respondents mention side effects as a barrier to treatment versus 42% indicating time, cost and/or pain (Figure 7).



9. *Since there is no cure or FDA approved treatment for alopecia areata: What specific things would you look for in an ideal treatment for your condition? What would you consider to be a meaningful improvement in your condition that a treatment could provide?*

Patients in the 2017 NAAF survey described an ideal treatment as effective/regrows hair (32%), safe/few side effects (23%), affordable/covered by insurance (8%), administered in pill form (7%), and not painful (4%) (Figure 8). Regarding meaningful improvement, 54% of respondents mentioned hair regrowth as a meaningful improvement, showing that the visible symptom is the most significant hallmark of the disease.



10. *What factors do you take into account when making decisions about selecting a course of treatment?*

For patients in the 2017 NAAF survey, factors taken account when selecting a course of treatment include side effects (47%), cost (22%), effectiveness (21%) and pain (5%).

**Understanding and incorporating the patient perspective**

As the above perspectives illustrate, alopecia areata is a disfiguring disease with devastating effects on patient’s quality of life and substantial healthcare burdens that requires medical treatment. Although alopecia areata takes a tremendous physical, emotional, and social toll on affected individuals, there are currently no FDA approved treatments and no standardized and generally accepted patient-centered and patient-reported outcome instruments to measure alopecia areata’s effect on the health-related quality of life (HRQoL) for use in clinical trials and/or patient care. Research is accelerating in alopecia areata and patient-reported outcomes are critical to inform the development of treatments relevant to patients. Current instruments used were developed prior to FDA’s 2009 PRO Guidance release and lack inclusion of concepts deemed important by patients with alopecia areata.

NAAF is in agreement with statements in the public comment submission of the Pediatric Dermatology Research Alliance (PeDRA) that the impacts of this disease can be particularly devastating when diagnosed in childhood and we echo the request that the FDA work to close the research gap for children with alopecia areata as opportunities to approve worthy pediatric clinical trials arise.

**Outcomes measures and labeling**

While re-growing hair or preventing hair loss may serve as important endpoints for treatment development, the reduction in quality of life that alopecia areata patients endure should be taken into account when establishing an appropriate benefit-risk profile for potential treatments. There are no standardized or generally accepted patient-centered and patient-reported outcome (PRO) instruments to measure alopecia areata’s effect on the health-related quality of life (HRQoL). NAAF, in collaboration with a number of pharmaceutical companies, is facilitating the development of a single, evidence-based PRO instrument that will support the evaluation of treatment benefit in terms of HRQoL in medical product clinical trials for patients with alopecia areata, with the intention to support product approval and labeling, health technology assessment, reimbursement, and patient care.

**Conclusion**

NAAF once more applauds the FDA for undertaking the Patient-Focused Drug Development Initiative and providing an opportunity for our community to explore the impacts of living with alopecia areata with the agency in the PFDD meeting. We expect that the perspectives offered through this meeting and docket have highlighted issues to better inform review and facilitate approval of innovative therapies indicated to treat alopecia areata. We thank you for your thoughtful consideration of the issues discussed.

If you have any questions about these comments, please contact Dory Kranz, President & Chief Executive Officer at 415-472-3780 or [info@naaf.org](mailto:info@naaf.org).

Sincerely,



Dory Kranz  
President & Chief Executive Officer



Natasha A. Mesinkovska, MD, PhD  
Chief Scientific Officer

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- <sup>i</sup> Chu SY, Chen YJ, Tseng WC, et al. Comorbidity profiles among patients with alopecia areata: the importance of onset age, a nationwide population-based study. *J Am Acad Dermatol*. 2011 Nov;65(5):949-56.
- <sup>ii</sup> Mirzoyev SA, Schrum AG, Davis MDP, et al. Lifetime incidence risk of Alopecia Areata estimated at 2.1 percent by Rochester Epidemiology Project, 1990–2009. *J Invest Dermatol*. 2014 Apr;134(4):1141-1142.
- <sup>iii</sup> Alkhalifah A, Alsantali A, Wang E, et al. Alopecia areata update: part I. Clinical picture, histopathology, and pathogenesis. *J Am Acad Dermatol*. 2010 Feb;62(2):177-88.
- <sup>iv</sup> Liu, LY, King BA, Craiglow BG. Health-related quality of life (HRQoL) among patients with alopecia areata (AA): A systematic review. *J Am Acad Dermatol*, 2016 Oct; 75(4):806-12.
- <sup>v</sup> Koo JY, Shellow WV, Hallman CP, et al. Alopecia areata and increased prevalence of psychiatric disorders. *Int J Dermatol*. 1994 Dec;33(12):849-50.