

## Alopecia areata: A global perspective of a disease that extends beyond hair loss

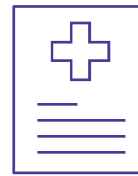
Alopecia areata (AA) is a chronic autoimmune disease that may result in hair loss, ranging from well-defined patches on the scalp to total hair loss on the scalp up to the whole body. AA affects all ages, any gender, and all skin types.<sup>1</sup> The burden of AA is multifactorial and stems from the physical and psychological impact of the disease. All aspects of life can be affected including work, leisure, family, relationships, and daily activities. In fact, **the British Association of Dermatologists outlines the substantial psychological and social disability that may be caused by AA, particularly in those patients with chronic and persistent disease.**<sup>2</sup> AA often carries a lifetime burden for patients, and when left untreated or undertreated, has a substantial cost for payers and patients.

A significant unmet need exists for patients with AA, and one way to address this need is to improve treatment strategies and the options available to people with AA. Until recently, there were no regulatory-approved treatments available for patients with AA. The management of AA relies on the off-label use of therapies that have not been well evaluated in clinical trials, making it difficult for healthcare providers to treat patients with AA effectively.

**Traditional treatment options are associated with inconsistent short-term outcomes that are accompanied by a safety profile that limits long-term use by patients; these suboptimal outcomes carry feelings of hopelessness and despair.**<sup>3</sup>

Additionally, despite advanced understanding of the autoimmune nature of the disease and the significant impairment in quality of life and the psychological burden for patients,<sup>1</sup> only limited support is provided to cover expenses such as the ones for concealment, like wigs. As a result, patients' annual and lifetime out-of-pocket costs can be significant in trying to restore their loss.

Expanding policymakers' and payers' view of AA is vital; thinking of AA as simply "hair loss" fails to acknowledge the suffering experienced by many patients and the importance of providing access for effective treatments. There are actions payers and policymakers should take to enable access to effective treatment and help manage the major life impact AA has on patients and their families.



**Alopecia areata is a chronic autoimmune disease affecting the hair follicle.**

**Thinking of AA as simply "hair loss" fails to acknowledge the suffering experienced by many patients.**

## Solutions to improve access to effective treatment:

- 01 Officially recognising AA as an autoimmune disorder like psoriasis, atopic dermatitis, or other autoimmune diseases of the skin
- 02 Capturing the medical and therapeutic advances for AA in physician-developed treatment guidelines
- 03 Ensuring appropriate and equitable access and reimbursement appraisals for treatments for AA once they become available
- 04 Recognising the nature of AA when developing access guidelines and reimbursement criteria (e.g. hair grows minimally every 2 months and the potential for relapse)
- 05 Where applicable, ensuring that cost-sharing is affordable for patients on a monthly and annual basis and comparable to other autoimmune dermatologic diseases, such as atopic dermatitis or psoriasis
- 06 Supporting people with AA in accessing healthcare, treatment, and available resources to help manage the psychological impact associated with the disease
- 07 Identifying any health disparities and promoting health equality by ensuring access to innovative treatments for patients—regardless of income or socioeconomic status



This paper demonstrates that AA is a chronic autoimmune condition that has considerable psychological, physical, and financial impact on patients.

- We begin by describing the characteristics of AA that make it a chronic and impairing autoimmune disease.
- The paper then discusses the demographics of the AA patient population and reviews the classification and evolution of AA.
- Using patients' own words, the next section explains the mental and physical impact of AA, as well as economic impacts (including out-of-pocket costs). To understand the situation patients are experiencing, current treatments and the related unmet need are depicted.
- Finally, the paper concludes by highlighting policy and payer changes that could shift the access paradigm and put the focus on the unmet need of patients with AA.

Given the burden of this illness and the need for additional treatment options, it is imperative that payers recognise and cover any regulatory-approved treatment options for AA.

# There is pattern baldness and then there is AA; The latter is an autoimmune disease

AA is an autoimmune disease affecting hair follicles.<sup>4</sup> The prevalence of patients with a diagnosis of AA reported in population-based studies ranges between 0.1% and 0.58%.<sup>5-8</sup> AA can present in mild to severe subtypes. Experts generally agree that the severity of the disease is anchored by the amount of scalp hair loss,<sup>9,10</sup> but data on the prevalence of severe AA are rare. In the United Kingdom (UK), it is estimated that 7% to 10% of AA patients have severe AA.<sup>11</sup>

AA is the second most common type of hair loss, behind pattern baldness, also called androgenetic alopecia (AGA).<sup>4</sup> However, the presentation of AA is distinctive from pattern baldness and age-related hair thinning, which have a more progressive evolution and specific hair loss distribution. Unlike AGA, which is caused by hormones, AA is an autoimmune condition that attacks the hair follicles.

A crucial feature of the hair follicle is the existence of a zone of immune privilege that, in a normal state, prevents immune attacks against the hair follicle.<sup>4</sup> According to the current body of evidence, the entry of inflammatory cells into the hair follicle's immune privilege zone is thought to result in hair loss.<sup>12</sup>

While the exact cause of AA is not known, its origin is believed to be multifactorial, which means that a variety of genetic and environmental factors contribute to the development of the disease.<sup>13</sup> In particular, the disease has a strong association with several genes related to immune functions.<sup>13</sup> AA can also be inherited, with nearly 20% of patients with AA having a family history.<sup>14</sup>

**Unsurprisingly, patients with AA also have an increased risk of presenting several atopic and autoimmune conditions.**<sup>4</sup> A systematic review of the literature, summarising the association between AA and other autoimmune disorders, found the most common concomitant autoimmune conditions to be vitiligo, thyroid disorder, psoriasis, rheumatoid arthritis, and diabetes mellitus.<sup>15</sup> **The association with other autoimmune conditions is a strong argument supporting the autoimmune nature of AA.**

AA is also associated with a variety of comorbidities, beyond autoimmune and atopic conditions.<sup>4</sup> Patients with AA often suffer from more than one comorbidity; AA patients have a 3.8-fold increased risk of 3 or more associated diseases compared with control subjects.<sup>16</sup>

The presence of comorbid conditions can be devastating for patients, often severely affecting quality of life. In addition, comorbid conditions can drive significant healthcare costs for patients, payers, and the healthcare system overall.

**AA is more common in younger adults and affects any gender equally.**

AA presents at similar rates in males and females.<sup>2,17</sup> Onset before the age of 40 occurs in the majority (70%–80%) of patients. Almost half of patients with AA show clinical signs before the age of 20.<sup>18</sup>





# The types of AA

Hair loss associated with AA most commonly involves the scalp, but sometimes also the face (including the eyelashes, eyebrows, and beard) and/or the body. The clinical spectrum of AA ranges from randomly distributed patches of hair loss to complete hair loss across the entire body.<sup>2,19,20</sup> AA is often classified into 3 broad subtypes based on the amount of hair loss: patchy alopecia areata, alopecia totalis, and alopecia universalis.<sup>4</sup>

While the disease will have impacts reaching beyond hair loss, scalp hair loss is one of the most bothersome symptoms of AA.<sup>21</sup> As such, experts are generally in agreement that the driver for the definition of AA severity is the extent of scalp hair loss.<sup>22</sup>

AA is characterised by acute onset of hair loss and an unpredictable disease course.<sup>2</sup> Spontaneous hair regrowth is frequent early in the disease course, but relapses are also frequent. Consistent with the autoimmune nature of AA, the evolution is typically relapsing and remitting, and around 85% of patients will experience multiple episodes of hair loss.<sup>23</sup> **It is estimated that between 7% and 25% of patients with patchy AA progress to alopecia totalis or alopecia universalis, at which point full recovery is rare.**<sup>11,24</sup>

The main negative prognostic factor appears to be the extent of hair loss, especially at presentation.<sup>4</sup> Other prognostic factors have been reported; for instance, development of AA at an earlier age is associated with more severe hair loss and disease progression.<sup>2,25</sup>

Individuals with AA have indicated the random distribution of visible patches—and the unpredictable and often rapidly alternating cycles of hair loss and regrowth—are particularly disturbing aspects of the disease.<sup>3</sup>

In the section on the right, information is reported for the different subtypes of AA. However, these classifications are not always used consistently. Prevalence numbers should therefore be considered with caution, as—additionally—data on the breakdown of AA severity are scarce and vary depending on the study design and the classification of AA. Depicting this variation in prevalence estimates, prevalence numbers reported for alopecia totalis vary between 0.0037% and 0.08% and for alopecia universalis between 0.0009% and 0.03%.<sup>7,26</sup>



**1+**  
patches of  
hair loss on  
the scalp

**Patchy alopecia areata** is the most common subtype of AA, characterised by 1 or more patches of hair loss on the scalp.<sup>27</sup> The patchy subtype may remit quickly but can be persistent over time or progress to more severe subtypes.<sup>27</sup> Additionally, relapse may occur at any time.<sup>28</sup>



**100%**  
or near total  
hair loss on  
the scalp

**Alopecia totalis** is characterised by total (100%) or near-total hair loss on the scalp.<sup>2,27</sup> The median time between the presentation of AA and the development of alopecia totalis is thought to be 1 year.<sup>29</sup> The totalis subtype generally has a worse prognosis than the patchy subtype. Combining studies of treated and untreated patients shows that spontaneous recovery occurs in less than 10%, and long-term complete recovery is about 9%.<sup>2,30</sup>



**100%**  
or near total  
loss of all  
scalp and  
body hair

**Alopecia universalis** is the loss of all (or near-all) scalp and body hair. The universalis subtype is also considered more severe than the patchy subtype.<sup>31</sup> Similar to alopecia totalis, it has been reported that only 9% of universalis patients (treated and untreated combined) achieve long-term complete recovery.<sup>2,30</sup>

# Beyond hair loss: Physical, mental health, and social impacts of AA

## The physical challenges associated with AA

Hair—both on the head and on the body—serves as protection from the elements.<sup>32</sup> The hair loss associated with AA leaves patients susceptible to sunburn, eye irritation, allergies, poor thermoregulation, and harmful airborne particles.<sup>33,34</sup>

In a recent study, up to three-quarters of AA patients reported complications from their loss of eyebrows or eyelashes such as sweat, water, and debris entering their eyes.<sup>35</sup> Over half of the patients reported frequently having a runny nose and sneezing due to losing nasal hair.<sup>35</sup>

Apart from the hair loss, other physical symptoms reported by patients with AA in a qualitative interview were scalp sensations (27%) and nail involvement (31%).<sup>34</sup> Patients note that these physical impacts are restrictive in their day-to-day life.<sup>34</sup> For instance, some individuals who do not have eyebrows or eyelashes avoid activities involving excessive sweating, as they cannot keep the water out of their eyes.<sup>21</sup>

## Comorbidities

Comorbid conditions in patients with AA have also been described and further affect patient wellbeing and functioning. For example, a higher prevalence of respiratory conditions such as asthma (6.5%–7.8%), allergic rhinitis (12.8%–16%), and allergic conjunctivitis (19.6%–23.5%) were found in a recent population-based study of AA patients.<sup>36</sup> These are all considered long-standing illnesses that affect quality of life and productivity and can require pharmacologic treatment.

Additionally, several dermatologic disorders are linked to AA. First, patients with AA have a significantly increased risk for atopic dermatitis (eczema), a chronic inflammatory skin disease that causes the skin to become inflamed and irritated, making it extremely itchy.<sup>36</sup> A systematic review and meta-analysis found that 9.4% of patients with AA had a previous and/or current history of atopic dermatitis compared to 1.9% of patients without AA.<sup>37</sup> Alopecia totalis or universalis patients were associated with higher odds of atopic dermatitis than those with patchy alopecia.<sup>37</sup> Psoriasis is also more likely in patients with AA and is estimated to occur in up to 6.3% of AA patients.<sup>15,18</sup> Patients with AA have a higher incidence of vitiligo, a disease that causes loss of skin colour in patches. It is estimated that up to 8% of patients with AA develop vitiligo compared to 1% of the general population in the United States (US).<sup>38</sup> Conversely, patients with vitiligo are more likely to develop extensive AA.<sup>18</sup>



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**Several dermatologic disorders are linked to AA, with up to 8% of AA patients developing vitiligo, 6.3% developing psoriasis, and around 9.4% (previously) having an history of atopic dermatitis.<sup>18,37</sup>**





## Mental health impacts of AA from a patient perspective

Human hair has important physical functions and is a component of our identity and self-image.<sup>39</sup> As a result, AA is more than “just hair loss”; it carries a significant and multifactorial burden with widespread implications for patients’ lives.

Given the unpredictable course of AA and its impact on appearance, it is not surprising that the disease carries significant emotional burden<sup>40</sup> and psychological distress.<sup>41-43</sup>

A recent study in the UK investigating the experience of living with AA reported a range of feelings associated with having the disease, including trauma, shock, and a loss of identity.<sup>3</sup> Patients with AA described feeling ashamed, humiliated, and profoundly depressed as a result of hair loss.<sup>3</sup> Women, for example, reported considering their hair as a symbol of their femininity and losing it was compared to having a mastectomy.<sup>3</sup> The patients surveyed often associated their hair loss to “bereavement” or “the loss of a limb or part of the self.”<sup>43</sup> For instance one participant said “Leaves you feeling you are not the same person. People say it’s only hair; yes, it is, but when you lose eyebrows, lashes, facial hair, and look in the mirror—not a good look. You just want to fit in like everybody else, not be stared at.”<sup>43</sup> Eyebrows carry a significant meaning for patients, going beyond the physical challenges described above. In a study investigating the significance of eyebrows to patients with AA, about 1 in 4 persons answered that they would prioritise eyebrow regrowth over scalp hair (40.6% prioritised scalp hair and 33.6% said that both were equally important).<sup>44</sup>

**The effects of AA are far-reaching, not only for the patient, but also for the patient’s family and friends.**<sup>21</sup> All aspects of life can be affected including work, leisure, family, relationships, and daily activities. In a study conducted in the US, most respondents (85%) said that coping with AA was a daily challenge.<sup>35</sup>

Patients with AA indicated in a study that the emotional effects of AA (e.g. self-consciousness and low confidence) contributed to their performance at work (or school) (40% of participants).<sup>34</sup> Other specific impacts of AA on employment mentioned by participants in this study included alteration in working hours to avoid contact with other people, losing out on jobs because interviewers assumed they must be seriously ill, or not working at all due to AA.<sup>34</sup>



**Patients with AA describe feeling ashamed, humiliated, and profoundly depressed as a result of hair loss.<sup>3</sup>**

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## Depression/anxiety/impact on overall quality of life

Substantial evidence exists demonstrating that people are at increased risk of suffering from mental health disorders when living with a chronic skin condition such as AA.<sup>45,46</sup>

The prevalence of mental health conditions such as depression, anxiety disorders, body dysmorphic disorders, social phobia, and suicidal thoughts is high among patients with AA.<sup>47</sup>

**The association between AA and the risk of anxiety and depression has been well documented.** In a literature review, generalised anxiety disorder was reported to occur in 18.2% of patients with AA compared with 2.5% in the general population.<sup>18</sup> Patients with AA often exhibit considerable anxiety from the general uncertainty surrounding disease progression, and many patients endure emotional and psychological distress on a daily basis.<sup>14,48</sup> On the other hand, the occurrence of major depression was reported in 8.8% of patients with AA compared with 1.3% to 1.5% in the general population.<sup>49</sup>

In a recent population-based study conducted in the UK primary care setting, depression (19.4% vs. 14.7%) and anxiety (16.6% vs. 12.9%) were more prevalent in people diagnosed with AA compared to controls.<sup>50</sup> AA patients were also more likely to subsequently develop new-onset depression (adjusted hazard ratio [aHR]: 1.38) and anxiety (aHR: 1.33).<sup>50</sup> Similarly, a study conducted in Korea showed that 14.3% of patients with AA had anxiety and 50.3% had depression.<sup>51</sup> In France, a study also found impaired quality of life in AA patients, particularly in the self-perception, mental health, and social life dimensions, which were at the same level as for psoriasis and atopic dermatitis patients.<sup>52</sup> The results from these studies suggest limited ethnic or cultural differences with AA psychological burden.

Of note, the impact on mental health with skin diseases including AA is so extensive that in the UK, an All-Party Parliamentary Group (APPG) on Mental Health and Skin Disease published a report in 2020 outlining the repercussions on patients and the urgent need to address the provision of services for this group.<sup>53</sup> The report was led by leading doctors in dermatology and mental health, patient organisations, the British Association of Dermatologists, and members of the UK Parliament. The urgent need to establish and commission psychodermatology clinics across UK regions for the mental health support of patients living with skin diseases, including AA, was highlighted as a priority in the report.



**Patients with AA have an increased risk of developing a major depressive disorder.<sup>46</sup>**

**Generalised anxiety disorder has been reported in 18.2% of patients with AA compared with 2.5% of the general population.<sup>49</sup>**

**Almost 80% of patients with AA reported impaired HRQoL.<sup>40</sup>**

A summary of multiple studies found that almost 80% of patients with AA reported impaired health-related quality of life (HRQoL).<sup>40</sup> Studies using non-specific HRQoL instruments reported that patients with AA tended to have lower scores in mental health, vitality, and role-emotional domains, suggesting diminished energy levels and reduced social functioning.<sup>48</sup> Studies implementing hair-specific quality of life measures indicated that HRQoL can be affected by many factors, including more severe hair loss and concomitant depression. These results illustrate that the detrimental impact of AA on individuals is significant, extending far beyond hair loss, and that the more severe AA is, the larger the negative impact tends to be.<sup>48</sup>

Additionally, a lower HRQoL was observed in the paediatric population based on the Paediatric Quality of Life Inventory. Children with AA may also have a higher incidence of anxiety and depression.<sup>40</sup> The overall HRQoL for parents of children with AA was also found to be poor.

## Risk of death associated with AA

Mortality risk associated with intentional self-harm and psychiatric diseases has been reported to be higher in patients with AA compared to individuals without AA.<sup>54</sup> **Patients in the aforementioned UK qualitative study described the connection between being depressed and having low self-esteem from AA together with suicidal thoughts.**<sup>3</sup> Similarly, a group of patients from the US commented that the depression and emotional toll of AA brought suicidal ideation, while some stated that they had already previously attempted suicide.<sup>21</sup> Furthermore, patients with alopecia totalis or alopecia universalis seem to present with an increased prevalence of thoughts related to self-harm.<sup>54,55</sup> In a study, patients with alopecia universalis were 3 times more likely to have suicidal thoughts than patients with patchy AA (60% and 18%, respectively).<sup>56</sup>

## Social stigmatisation

**Patients with AA are often misunderstood and mischaracterised. Much of the public continues to incorrectly regard AA as a cosmetic or communicable disease.** Stigmatisation and cultural perception of hair loss drive cumulative life course impairment for patients with AA.<sup>57</sup> This stigma leads to a significant reduction in patients' quality of life. The diagnosis of AA has been described as "emotionally devastating."<sup>3</sup>

In a study, participants reported social judgement from others because of their condition.<sup>34</sup> It is often assumed that hair loss is due to chemotherapy and patients are mischaracterised as sick.<sup>3,58</sup> Notably, individuals become less empathetic and adopt an attitude of "it's only hair" when they learn that the hair loss is not due to cancer. One patient even said, "When I was 12, I used to wish I had cancer so there would be a greater understanding towards my hair loss."<sup>3</sup>

The stigmatisation associated with AA often presents in the form of bullying or being misunderstood by co-workers and the public.<sup>3,21</sup> Patients with AA often describe being bullied at school, having wigs and hats snatched off, and being insulted or mocked by classmates.<sup>3,21</sup> Although wigs and makeup are commonly used to disguise hair loss, this can lead to emotions of inauthenticity, embarrassment, and anxiety.<sup>3</sup> Itching, discomfort, and the worry of it being dislodged are all negative aspects of wearing a wig, and some also express concern about how others may react to them wearing one.<sup>58</sup> For others, on the other hand, wigs were described as a survival tool because they felt more confident going out in public and it also reduced comments about their hair loss from others.<sup>58</sup> However, due to the nature of AA, in some situations like sports, patients are not able to conceal their illness even if they would prefer to.<sup>58</sup>

The fear of being stigmatised leads many AA patients to avoid social gatherings altogether and other activities, such as sports and shopping.<sup>3</sup> The negative societal views towards alopecia are also reinforced by the predominant representation in movies of bald evil characters and its association with moral decay.<sup>59</sup> Consequently, the psychological burden of AA patients is exacerbated.<sup>59</sup> In the previously mentioned British study, some individuals described themselves as monsters or aliens, as illustrated in the following statement "I get quite upset when I see myself bald. There is a reason monsters are portrayed bald. In 'Lord of the Rings,' when Gollum was a hobbit, he had hair; when he turned evil—bald. Then of course there is Nosferatu, Voldemort, trolls, and orcs."<sup>3</sup>

Patients with AA have similar stories to patients with chronic skin conditions such as psoriasis. **Like AA, psoriasis—which has seen 15+ European Medicines Agency (EMA)-approved and covered drugs become available over the last 20 years—is a highly stigmatised autoimmune dermatologic condition.** It is perceived as a contagious disease that can lead to exclusion from normal social environments, including schools and workplaces.<sup>60</sup> As a result, patients with psoriasis experience depression and lower quality of life.<sup>40,45</sup>

## Relationships

Having AA is reported as an impediment to developing new relationships. In a study, patients with AA mentioned concerns that someone would not want to have a romantic relationship with them, and they found dating difficult or avoided it entirely due to low confidence and fear of judgment or rejection.<sup>3,34</sup> They reported not knowing how to speak to new partners about AA and worried that potential partners would find them unattractive.<sup>3,34</sup> Additionally, the significance of eyebrows in interpersonal relationships is widely recognised, and studies suggest that they play a critical role in emotional expression, communication, and facial attractiveness and recognition.<sup>44</sup>

**The social impact to relationships is similar for conditions like psoriasis.** In an assessment of the psychological impact of psoriasis, acne, and vitiligo, the conditions were found to negatively affect personal relationships.<sup>61</sup> Individuals affected by AA have also reported problems within their existing romantic relationships, citing feelings of insecurity about appearance, which was often related to decreased intimacy.<sup>62</sup> As a result, 40% of women reported marital issues.<sup>58</sup> This anxiety can further increase feelings of isolation and depression.<sup>34,58</sup>



# Economic impact of AA

Beyond the physical and mental health impact of AA, there is a financial impact of AA for patients and the healthcare system. Patients with AA may face significant out-of-pocket costs. These costs are from copayments associated with medical services for AA and comorbid conditions, as well as other interventions not covered by insurance. For example, many AA patients reported use of restorative interventions such as wigs or make-up as camouflage, and/or dietary changes or supplements.<sup>3</sup>

## AA and its associated comorbidities, including mental impairment, have a large effect on patients' work performance and employment

**AA can affect patients' professional lives and income.** It is common for patients with AA to miss time from work or school due to their AA and/or their comorbid conditions.<sup>18,34,50</sup> Some patients with AA may even resign from their positions entirely or pause from seeking employment, as many experience stress from having to wear a wig at work or from unsupportive coworkers.<sup>58</sup>

In a qualitative study from North America, patients described the impacts of AA on their work performance and how their lowered self-confidence due to AA prevented them from giving their best at work.<sup>34</sup> In addition, a UK population-based study found that people with AA were more likely to be issued time-off work certificates (aHR: 1.56; 95% confidence interval [CI]: 1.43–1.71) and be recorded as unemployed (aHR: 1.82; 95% CI: 1.33–2.49) compared with matched controls.<sup>50</sup> This was accompanied with higher likelihood to subsequently develop depression and anxiety, as mentioned above.<sup>50</sup>

## AA has a high financial impact on the healthcare system and patients

As success rates of first-line AA treatment with topical steroids for hair regrowth vary broadly (18%–60%), nearly every fourth patient will be referred to a specialist dermatologist. As a reflection of this, it has been reported that **AA patients have consistently higher rates of primary care visits, with nearly double the number of visits as the general population.**<sup>8</sup> Rates of primary care visits varied depending on gender, socioeconomic gradient, and race: more frequent visits were observed among women and patients with higher socioeconomic status, whereas people of mixed race had the lowest rate of primary care visits.<sup>8</sup>

Currently, the vast majority of studies assessing healthcare costs for AA appear to have been performed in the US. Based on recently published research, the average total healthcare costs per AA patient in the 12 months after diagnosis amounted to \$11,241.21 for all causes, of which \$419.12 were specifically associated with treating AA.<sup>42</sup> **This shows that healthcare costs resulting from AA go beyond the directly attributable cost for treating AA.**<sup>42</sup> Another claims analysis from a US managed care population found that the total average 12-month all-cause costs for patients with AA were higher compared to non-AA patients (\$8,853 vs \$5,548), primarily due to higher average differences in ambulatory and pharmacy costs.<sup>63</sup> Unsurprisingly, among patients with AA, those with alopecia totalis and universalis subtypes incurred significantly higher costs.<sup>63</sup>

Besides the healthcare system, patients incur significant costs associated with AA. When looking at different categories of expenditures to manage AA, a US survey found the proportion of patients with AA spending money on concealment like wigs, eyebrows, or eyelashes to be the highest. This was followed by vitamins and supplements. The median total out-of-pocket cost was \$1,354 per person per year.<sup>64</sup> As described above, AA often occurs with other autoimmune diseases. The onset of multiple autoimmune diseases may require significant expenditures for diagnostics and treatment management on top of the expenditures for AA.



**Mitigating high out-of-pocket costs faced by patients with AA by enabling access to medical and restorative treatments is key to lessening the burden on patients with AA.**

## Concealment strategies

Society puts an inordinate amount of pressure on beauty and attractiveness. While it may be more socially acceptable for a man to be bald, as some choose to shave their head regardless of thinning or lost hair, there is limited societal acceptance of a bald woman. Patients with AA often rely on wigs and cosmetic devices to restore their hair loss.<sup>21</sup>

Even though wigs are critical to help with the emotional burden of AA, they are not fully covered by health insurance in many cases and countries.<sup>2,65</sup> Choice of wigs is limited for AA patients; most health insurance will only cover part of the costs for wigs, if any, and mostly for synthetic wigs. In some countries, wigs from human hair are only covered if an allergy to synthetic wigs can be proven.<sup>66,67</sup> Synthetic wigs will need replacing every 3 to 4 months, while wigs from human hair can last up to 1 to 2 years.<sup>2</sup> The reimbursement for wigs varies widely between countries; for instance, patients in France can be fully reimbursed, whereas in Italy, reimbursement will vary across regions, but in the majority of cases, reimbursement will be restricted to chemotherapy-induced alopecia, despite these camouflage efforts being restorative for both diseases (cancer and AA).<sup>66,67</sup> Additionally, patients in Italy receive a maximum of €200 for 1 synthetic wig per year, which is assumed to cover 80% of the cost for 1 wig.<sup>67</sup> In the UK, wigs are only reimbursed for specific subsets of patients such as children under the age of 16 or patients with state-funded income support.<sup>11</sup>

Wig prices were reported to range from £50 to £5,000 in the UK.<sup>2</sup> This can place an enormous financial strain on patients; in a UK study, it was reported that 65% of participants worried about affording new wigs.<sup>58</sup>

In addition to wigs, there are other concealment methods patients may apply (e.g. pigmented concealment powders, eyelashes, eyebrows), none of which are covered.<sup>21</sup> This added financial burden is another source of stress for patients with AA.

## Mental health treatment

Patients with AA may utilise mental health treatments in the management of the psychological impact of their disease.<sup>2,58</sup> **Guidelines on AA recommend counselling for patients and label it as "essential."**<sup>2,19</sup> Especially in cases of long-standing and extensive AA, patients require help to establish coping strategies and gain self-acceptance.<sup>2</sup>

As previously described, **the prevalence of mental health conditions such as depression, anxiety disorder, body dysmorphic disorders, social phobia, and suicidal thoughts is high among patients with AA.**<sup>47</sup>

While the approach to inpatient and outpatient care for mental health may vary from one country to another, the average length of primary hospitalisation for a mental health disorder in patients with AA was 6 days in the US.<sup>68</sup>

Despite the high demand for mental health treatment, barriers to mental health access still exist. No guidance is provided on what forms of psychological support is available, and services specialising in dermatology are rare.<sup>3</sup> Additionally, long waiting lists with mental health specialists discourage patients who are trying to get an appointment and leave patients untreated.



**Patients often rely on wigs and cosmetic devices that are often uncomfortable and expensive.**

**Wigs are often only partly reimbursed, if at all, adding to the patient burden.**

**The added financial burden associated with hair concealment options constitutes another source of stress for patients with AA.**

# Traditional treatments of AA fail to address the needs of patients

A significant unmet need exists for patients with AA, particularly for patients with severe AA, and one way to address this need is to ensure access to innovative treatment options available for the management of the disease.

## Lack of evidence-based, effective, and well-tolerated treatment options...

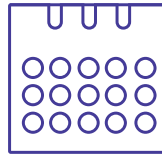
**Until recently, there were no regulatory-approved treatments available for patients with AA. Physicians could only rely on the use of off-label therapies to manage the condition, often sub-optimally.** These therapies have not been well evaluated in clinical trials, so it is unclear if therapies used off-label provide any clinically meaningful hair regrowth. As a result, most of the existing guidance for managing patients with AA derives from clinical and patient experiences.<sup>2,11,25</sup>

Therapies traditionally used for managing AA include topical, intralesional, and systemic glucocorticoids, conventional immunosuppressants, phototherapy, contact immunotherapy, and minoxidil. To date, the first-line and most common treatment for AA is topical corticosteroids.<sup>2,4,19</sup> Conventional immunosuppressants are used after failure of corticosteroids. Topical immunotherapy is not widely available, which limits its role in AA management. No consensus has been reached on the efficacy of phototherapy in AA, and prolonged and repeated courses are associated with potential serious side effects.<sup>2</sup> The overall efficacy of these therapies seems particularly low for severe AA. Moreover, treatment can be uncomfortable for the patient, time consuming, and associated with unpleasant side effects that limit their long-term use.<sup>3,4</sup>

However, new treatments are being developed. These potential additional options are needed to address the unmet need.

## ...and lack of reimbursement

**The limited reimbursement of treatment and camouflage options for AA adds up to the burden of the disease, making AA a daily challenge difficult to cope with.** As described above, many patients are forced to pay out-of-pocket for unsatisfactory therapies and camouflage options, such as wigs or microblading, often with limited to no health insurance coverage depending on the country they live in.



**Coping with AA is a daily challenge, with limited treatment and camouflage options being reimbursed.**

## Coverage of future AA treatments needs to be equal to other autoimmune diseases

AA is an autoimmune condition with a high burden, and treatments to manage the disease therefore should be reimbursed similarly to treatments for autoimmune diseases associated with AA, such as psoriasis or atopic dermatitis.

With several shared characteristics between AA and covered dermatologic autoimmune conditions, there is no question that treatments for AA approved by the EMA and other regulatory agencies should be covered by national health systems. Ultimately, it is about enabling equity in access to treatment for patients with AA. Supporting emerging treatments can be the catalyser needed to bring effective treatments to market, as seen by the considerable improvement in treatment for patients with psoriasis over the last years.<sup>69</sup> Equitable access for AA treatments will enable improvement in patients' general health state and quality of life in this debilitating condition.

**Given the high burden of illness for patients with AA, long-term access and coverage of regulatory-approved treatments for AA is critical.** Innovative treatments for AA approved by regulatory authorities should be covered by healthcare systems and deemed "medically necessary" by payers, as they are needed to treat patients and can meet the high unmet need associated with AA.



# Alleviating the burden of AA on patients

There is a clear need to rethink how AA is framed among payers and policymakers, given the burden of the illness, unmet needs, and limited recognition of the importance of treating the condition. The following measures outline the framework to support patients affected by this debilitating autoimmune skin condition to address their unmet needs:

- 1 Officially recognising AA as an autoimmune disorder like psoriasis, atopic dermatitis, or other autoimmune diseases of the skin.** AA is an autoimmune condition with a similar disease burden and comparable impact on physical and mental health as other autoimmune conditions such as atopic dermatitis and psoriasis.<sup>18</sup> The importance of treating patients with AA should therefore be placed on a par with other autoimmune conditions. Payers should recognise the physical and psychological burden of the disease and the value that new efficacious treatment will bring to patients' lives in the near future. Furthermore, officially recognising the unmet need of patients with AA can help facilitate innovation and generate research possibilities, as seen in comparable conditions like psoriasis.<sup>69</sup>
- 2 Capturing the medical and therapeutic advances for AA in physician-developed treatment guidelines.** Guidelines need to be updated in a timely manner to ensure that clinical practice adopts new treatments and helps high-need patients.
- 3 Ensuring appropriate and equitable access and reimbursement appraisals for treatments for AA once they become available.** The need for effective long-term treatments is made clear by a willingness shown by AA patients to endure high personal costs for currently ineffective therapies, wigs, and concealment strategies.<sup>64</sup> Moreover, the considerable physical, social, and psychological impact on patients and the detrimental ramifications on mental wellbeing and quality of life substantiate the urgent and pronounced unmet need for payers to allow access to new AA treatments and to ensure this patient group is treated with equal consideration compared to those with other autoimmune conditions. In preparation of new medicines being approved by the EMA and other regulatory authorities, health technology assessment (HTA) bodies and payers should be educated on the substantial burden of AA for patients and the unmet need that currently exists.
- 4 Recognising the nature of AA when developing access guidelines and reimbursement criteria (e.g. hair grows minimally every 2 months and the potential for relapse).** Treatment paradigms within the pathways and guidelines of reimbursement bodies should account for the nature of the condition and accommodate alternative and consecutive options in the pathway of care. It is imperative to recognise the mental, physical, and social ramifications of suffering from AA as well as the nature of hair growth (e.g. hair grows slowly). Additionally, the devastating impact of regrowing hair and losing it again due to limited long-term therapy access on patients needs to be considered. By providing patient access to licensed treatments, healthcare professionals and dermatologists can treat patients with AA with the most effective treatment option.
- 5 Ensuring that cost-sharing is affordable for patients on a monthly and annual basis and comparable to other autoimmune dermatologic diseases, such as atopic dermatitis or psoriasis.** Patients with AA are already significantly burdened, and access to treatment should not add to the burden. Currently, many patients pay out-of-pocket for treatment, in addition to paying for restorative or cosmetic procedures, as both are often not covered. The cost of treatment and/or concealment can lead to considerable financial burden for patients and consequently increased emotional distress, resulting in the deterioration of mental, social, and physical wellbeing in a group of vulnerable people already suffering from significant psychological stress.<sup>49</sup> Similarly to other autoimmune diseases such as psoriasis, policies should be revised to make approved treatment options, as well as restorative interventions available to patients without adding to their financial burden.
- 6 Supporting people with AA in accessing healthcare, treatment, and available resources to help manage the psychological impact associated with the disease.** Mental and physical health are intrinsically linked. Substantial evidence exists to demonstrate that people are at increased risk of suffering from poor mental health when living with a chronic skin condition such as AA, and the heightened need for resources with support has also been emphasised.<sup>46,49,53</sup> A significantly greater likelihood of anxiety exists for patients with AA, and the incidence of depression is also greater in patients with AA compared to the general population.<sup>49</sup>
- 7 Identifying any health disparities and promoting health equality by ensuring access to innovative treatments for patients—regardless of income or socioeconomic status.** Most patients with AA struggle to gain access to treatment and support for their condition. In the hope and desperation to find a cure, those who have the means may resort to experimental treatments that may not be covered by health insurances or other costly restorative options. Patients who do not have the means to finance treatment may forgo other essential commodities to be able to self-fund treatment or otherwise continue to suffer with the condition with minimal means of support.

Socially deprived populations are less likely to receive specialist care.<sup>8</sup> The emergence of new medicines should not displace these patients compared to higher social classes or limit their access to care, and it is imperative that all patients, regardless of background, gain equal access to treatment and care. The UK HTA authority has explicitly emphasised the fact that new AA treatments should be made available to all patient populations, including those with disabilities and from deprived backgrounds, and no group should be discriminated against.<sup>17</sup> This is an important approach from a nationally and globally recognised HTA authority in endorsing absolute equity across all populations for access to new and innovative treatments and egalitarian care.

# Conclusion

AA is an autoimmune disease with a significant burden of illness that affects patients' quality of life, can cause mental and physical distress, and result in loss of productivity and impacts in various spheres of a patient's life.

A strong unmet need exists for efficacious long-term therapies that treats the underlying cause of the condition and improves the prognosis of the disease. The approved licensing and reimbursement of new treatments will bring much-needed stability and improved quality of life into patients' lives.

Payers and policymakers across the world need to develop access policies for treatments approved by regulatory authorities, particularly treatments that will reach the market soon, to ensure access and affordability for innovative therapies to become readily available. Market access and reimbursement policies for new treatments should acknowledge the physical and psychological burden faced by patients with AA, like patients with other chronic autoimmune skin conditions. These policies will play a pivotal role to help patients with AA avoid the long-term suffering and overwhelming burdens associated with this disease.

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