ORIGINAL REPORT

Global, Regional, and National Burden of Alopecia Areata and its Associated Comorbidities, 1990–2021, and Projections to 2050: An Analysis of the Global Burden of Disease Study 2021

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There are no updated epidemiological data on alopecia areata up to 2021. The objective of this study was to emphasize the urgency of addressing the evolving public health challenges of alopecia areata. The annual point prevalence, incidence, and years lived with disability of alopecia areata from 204 countries and regions from 1990–2021 were extracted. Subgroup analyses based on gender, age, global, national, regional, sociodemographic index, and World Bank income were conducted. From 1990–2021, age-standardized prevalence, incidence, and years lived with disability of alopecia areata globally show a decreasing trend, with females dominating. There was a reduction in the disease burden in high sociodemographic index regions, but alopecia areata in general did not reflect a concentration in certain regions and was more equally distributed. Decomposition analysis revealed that population growth was the major contributor to the burden of alopecia areata, followed by population ageing. Patients with alopecia areata before the age of 14 were associated with anxiety disorders and other psychological disorders, but patients after the age of 14 were not associated with the onset of these disorders. Also, atopic dermatitis has been associated with alopecia areata. The epidemiological differences in psychological disorders between children and adolescents/adults with alopecia areata further demonstrate the importance of differentiated recognition at different ages.

Key words: alopecia areata; epidemiology; GBD 2021; anxiety disorder; COVID-19; prediction.

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SIGNIFICANCE

- We found that the disease burden of alopecia areata decreased from 1990 to 2021, but it is still predicted to increase by 2050, and alopecia areata patients in different age groups show different trends in the occurrence of psychological disorders.
- This study is the first to assess the global, national, and regional disease burden of alopecia areata up to 2021, and we are also the first to present epidemiological data on the differences in comorbidities between children and adolescents/adults with alopecia areata and to identify the connection between the onset of psychological disorders, atopic dermatitis, and alopecia areata in different ages.

Alopecia areata (AA) is a common chronic autoimmune disease, usually characterized by patchy loss of hair on the skin, with a global prevalence of about 2% (1). Currently, the treatment effect for some patients is still unsatisfactory and has high recurrence rates, which has a definite impact on the patients' economy and life. Moreover, 70% of AA patients suffer from different degrees of psychological diseases, and their psychological and social pressures have not been effectively emphasized (2), which not only further aggravates their diseases, but also affects their psychosocial and disease burdens.

The Global Burden of Disease (GBD) has data on diseases from more than 200 countries and regions, offering a powerful tool for assessing global health risks (3). However, previous epidemiological studies of AA have only assessed the burden and projected trend to 2019, and it is important to note that global healthcare and economic development have suffered a major blow due to COVID-19 since 2019, and that screening and diagnosis of some patients with AA cannot be sustained as a result. A recent study has shown that people infected with COVID-19 are at a higher risk of autoimmune diseases compared with those who are uninfected (4). Additionally, the recurrence rate of children with AA is high and difficult to treat, and there is less epidemiology on children with AA, but some differences in treatment options between children and adolescents/adults are indeed seen in the expert consensus (5), which suggests that previous data do not provide a good description of the disease burden and trends in AA at this stage.

This study aims to analyse the GBD data from 1990–2021 to understand the trends in AA incidence, prevalence, and years lived with disability (YLDs) globally. We also focused on understanding the relationship between AA and its comorbidities before and after the age of 14, as a way to help guide the diagnosis and treatment of children and adolescents/adults with AA,

and to improve the understanding of AA at different ages. Furthermore, we also prospectively projected the disease burden of AA in 2050. By interpreting both the current and future aspects, we hope to provide guidance on the gender- and region-specific impacts of AA and its associated burden, as well as on public health measures.

METHODS

The prevalence of the disease is estimated using the methodology of GBD study as the annual point prevalence, which is the proportion of individuals living with AA on a given day in each calendar year. GBD uses age 14 as the cutoff between children and adolescents/adults, aligning with the World Health Organization official definitions and with the GBD's 5-year age grouping format, thereby ensuring comparability across countries and over time, as well as statistical precision (6, 7). This study has all the methods detailed in Appendix S1.

RESULTS

Global alopecia areata burden

Until 2021, the global age-standardized prevalence and incidence rates had changed by –2.12% (–2.36 to –1.86) and –3.78% (–4.82 to –2.72). The age-standardized YLD rates had also changed by –2.67% (–5.02 to –0.95) (**Fig. 1, Table I**).

Both age-standardized incidence and prevalence of AA observed an increasing trend during 1990–1993 (APC = 0.17); the rest showed decreasing trends (**Fig. 2**A, 2B). For the global age-standardized YLD rate there is an overall decreasing trend between 1990 and 2021 (AAPC = –0.12) **(**Fig. 2C).

Meanwhile, the prevalence, incidence, and the increase in AA were shown to be higher in females than in males (Table SI). Age-standardized prevalence and incidence rates for both females and males showed a decreasing trend in the AAPC over the period 1990–2021, which is broadly in line with the general trend (Fig. S1). In 2021, the highest AA incidence and YLD rate were in the 30–34 year age range, and with higher rates and numbers for females than for males in all age ranges (Fig. S2).

Considering the impact of COVID-19, the percentage change in age-standardized incidence was –1.54% (–2.02 to –1.04). In contrast, the percentage change in the age-standardized incidence was –6.74% (–7.23 to –6.31) during 2019–2021 (Table SII).

National and regional alopecia areata burden

By analysing the 2021 AA data for 204 countries (Table SIII), high SDI had the highest age-standardized prevalence rate of 247.25 (238.95–255.64). The quantitative change in age-standardized incidence rate (3.27%, 1.48–5.09) was most pronounced in the low–middle SDI region. With the World Bank income level classification, the prevalence, incidence as well as age-standardized prevalence and incidence rate for high income are the only group that showed a decrease compared with the 1990 data (see Table I). In terms of gender and SDI regions, as well as in terms of gender and World Bank income classifications, trends in incidence, prevalence, and YLD rate for males and females were generally consistent with global changes, and the rate of change was dominated by females (see Table SI, Fig. 3, Fig. S3).

From the perspective of COVID-19, only the changes in age-standardized incidence for high SDI (–2.22%, –2.78 to –1.67) and middle SDI (–0.49%, –1.08 to 0.11) were decreasing over the period 1990–2019. However, during 2019–2021, the change in age-standardized incidence decreased in all SDI regions and the most significant decrease was observed in low SDI (–8.11%, –8.92 to –7.27) (see Table SII).

Decomposition analysis of change in the alopecia areata burden worldwide between 1990 and 2021

We used case-number decomposition analysis to explore the impact of population growth, population ageing, and epidemiological change on the burden of disease in AA (Table SIV). The contributions of population growth and population ageing both increased. Among them, population growth contributed most to the prevalence (126.55%), incidence (128.95%), and YLDs (133.29%) of high SDI. For epidemiological change there was only a slight upward trend in low–middle SDI and low SDI, and the rest declined. Notably, the contribution of epidemiological change decreased in incidence, prevalence, and YLDs in males, whereas it was the opposite in females and globally (**Fig. 4**).

Cross-country inequality analysis

In 1990, the slope index of inequality for incidence, prevalence, and YLDs was 161, 93, and 3, and in 2021, these values were 133, 79, and 2 (**Fig. 5**). Similarly, the concentration indexes for incidence, prevalence, and YLDs were all lower in 2021 (0.09) compared with the concentration index in 1990 (0.11) (**Fig. 5,** Table SV). Our findings also do not show that AA is mainly concentrated in certain areas, and the distribution is generally more homogeneous.

Alopecia areata and related comorbidities show that children's alopecia areata is associated with anxiety, whereas adults' alopecia areata has little to do with anxiety

We analysed the association of AA with the age-standardized incidence of 21 comorbidities of AA according to age and sex, and focused on the Pearson correlation coefficients for males, females, and various comorbidities

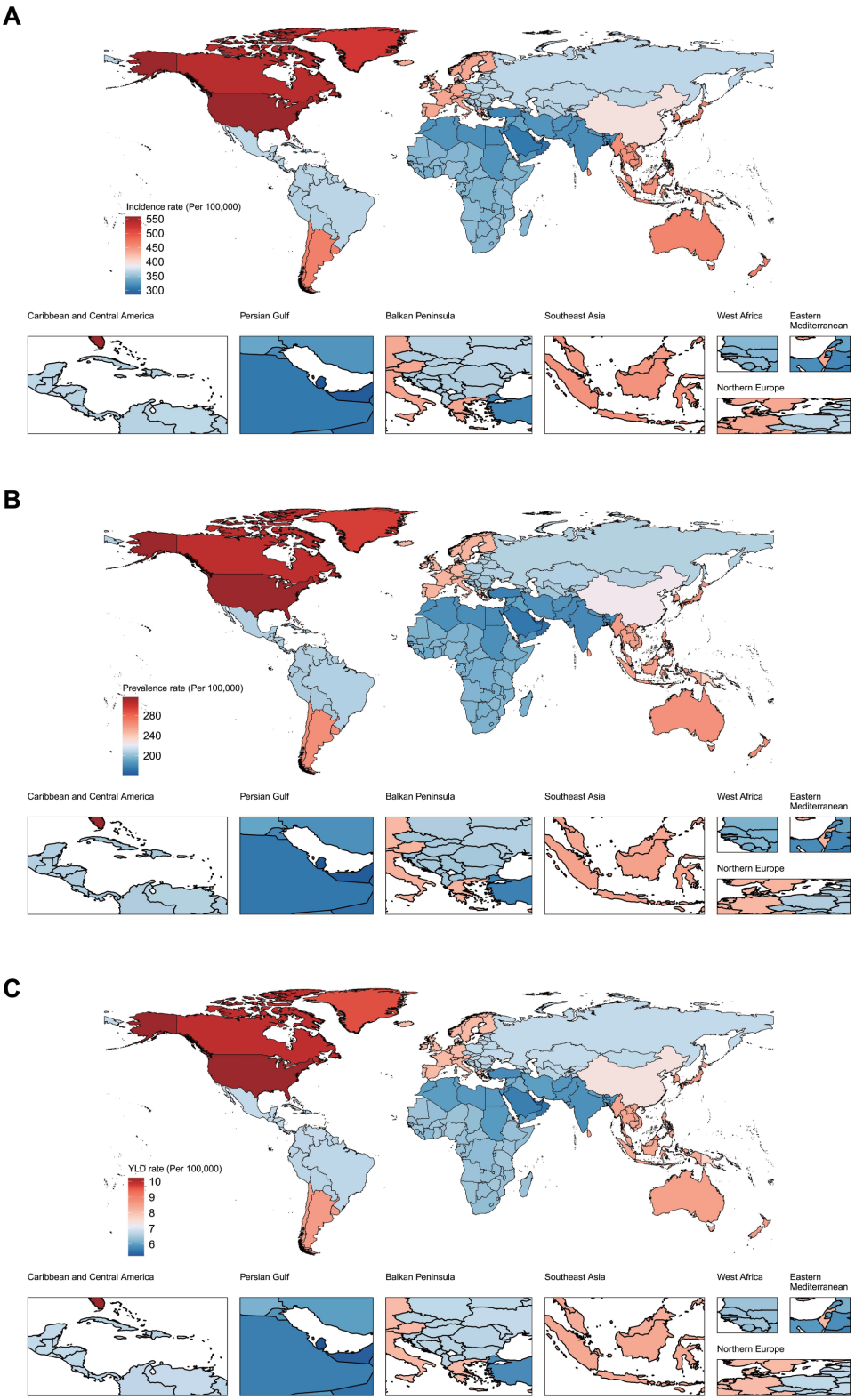

Fig. 1. Age-standardized (A) incidence, (B) prevalence, and (C) YLD rate (per 100,000) of alopecia areata by location for male and female sexes combined, 2021. YLD: years lived with disability.

before and after the age of 14 (**Fig. 6**). Notably, we found a strong association between children with AA and the onset of anxiety disorders ($r=0.9001$, $p<0.05$), conduct disorders ($r=0.9863$, $p<0.01$), and depressive disorders ($r=0.9001$, $p<0.001$), whereas adolescents/adults with AA showed no correlation among these diseases, with Pearson correlation coefficients of –0.9037, –0.3048, and –0.8705. All 3 diseases were closely related to psycholo-

Table I. Prevalence, incidence, YLDs, age-standardized rates of prevalence, incidence, and YLDs (per 100,000) in 2021, and percentage change between 1990 and 2021 for alopecia areata, by countries and territories

Item	Episode counts (95% UI), 2021	Percentage change in counts (95% UI), 1990–2021	Age-standardized rate per 100,000 (95% UI), 2021	Percentage change in age-standardized rate per 100,000 (95% UI), 1990–2021
Prevalence				
Global	17525630.07 (16977877.60 to 18072092.09)	3.61 (2.91 to 4.3)	256.15 (247.53 to 265.10)	−2.12 (−2.36 to −1.86)
Low SDI	1910521.60 (1843545.76 to 1976156.43)	8.17 (7.85 to 8.53)	203.93 (197.59 to 211.51)	1.79 (1.60 to 1.98)
Low–middle SDI	3718599.94 (3591040.48 to 3839574.15)	14.07 (13.43 to 14.68)	203.06 (196.74 to 210.58)	2.18 (1.94 to 2.45)
Middle SDI	5575450.97 (5397028.05 to 5754508.72)	9.36 (8.13 to 10.54)	190.35 (183.32 to 196.33)	0.93 (0.59 to 1.31)
High–middle SDI	3157763.39 (3062193.40 to 3262622.26)	5.33 (4.13 to 6.51)	205 (198.59 to 212.65)	2.02 (1.65 to 2.41)
High SDI	3149347.42 (3057067.31 to 3240463.36)	−3.84 (−4.57 to −3.11)	247.25 (238.95 to 255.64)	−3.55 (−3.84 to −3.24)
World Bank Lower Middle Income	6850288.61 (6612024.71 to 7076392.44)	12.6 (11.93 to 13.25)	261.01 (252.78 to 269.41)	1.51 (1.29 to 1.73)
World Bank Low Income	1190823.65 (1150404.07 to 1232096.85)	6.24 (5.96 to 6.54)	198.08 (191.49 to 205)	0.10 (−0.05 to 0.27)
World Bank High Income	3501450.20 (3397194.76 to 3601763.16)	−3.01 (−3.75 to −2.30)	196.84 (190.32 to 203.69)	−2.60 (−2.85 to −2.30)
World Bank Upper Middle Income	5969069.70 (5783110.56 to 6166606.08)	7.46 (5.98 to 8.84)	217.80 (210.75 to 224.99)	2.19 (1.81 to 2.63)
Incidence				
Global	30893047.02 (29948975.05 to 31819276.70)	5.25 (3.43 to 7.13)	379.54 (368.00 to 391.05)	−3.78 (−4.82 to −2.72)
Low SDI	6586006.87 (6366705.95 to 6796467.56)	16.21 (13.90 to 18.61)	337.67 (327.12 to 348.30)	2.64 (0.94 to 4.17)
Low–middle SDI	3402714.95 (3283984.78 to 3516968.15)	21.27 (18.21 to 24.26)	340.76 (329.97 to 351.38)	3.27 (1.48 to 5.09)
Middle SDI	5538253.69 (5364897.64 to 5715418.87)	11.95 (9.39 to 14.92)	378.55 (366.49 to 390.7)	−0.89 (−1.96 to 0.23)
High–middle SDI	9819522.24 (9505583.09 to 10126013.42)	5.66 (3.25 to 7.93)	390.00 (377.16 to 403.04)	−0.83 (−1.64 to 0.21)
High SDI	5521975.86 (5363379.31 to 5679291.70)	−0.93 (−2.68 to 0.94)	464.92 (450.92 to 479.00)	−3.61 (−4.31 to −2.91)
World Bank Lower Middle Income	12124176.37 (11734000.33 to 12511024.53)	17.91 (15.22 to 20.65)	349.69 (338.65 to 360.48)	1.39 (−0.20 to 2.91)
World Bank Low Income	2121209.98 (2046321.12 to 2191856.08)	13.03 (10.92 to 15.35)	344.51 (333.24 to 354.89)	−0.25 (−1.71 to 1.34)
World Bank High Income	6139073.17 (5962927.13 to 6315926.23)	−1.40 (−3.11 to 0.41)	461.12 (446.89 to 475.04)	−3.56 (−4.16 to −2.87)
World Bank Upper Middle Income	10483923.92 (10150666.66 to 10819160.56)	10.97 (8.33 to 13.86)	384.60 (371.82 to 397.75)	1.31 (0.40 to 2.33)
YLDs				
Global	571860.27 (371725.08 to 808502.09)	−9.55 (−11.73 to −7.67)	..	−2.67 (−5.02 to −0.95)
Low SDI	62582.88 (40359.74 to 88859.20)	15.63 (10.50 to 19.90)	..	8.58 (4.20 to 12.12)
Low–middle SDI	121492.57 (78844.08 to 172775.43)	5.42 (1.07 to 9.07)	..	5.21 (1.68 to 8.29)
Middle SDI	182391.52 (118681.10 to 257496.83)	−12.35 (−14.76 to −10.12)	..	−0.75 (−3.30 to 1.37)
High–middle SDI	103101.29 (67638.23 to 144907.46)	−12.40 (−14.73 to −10.35)	..	2.81 (0.01 to 5.10)
High SDI	101836.97 (66507.67 to 144884.30)	−20.76 (−22.58 to −18.98)	..	−9.36 (−11.31 to −7.47)
World Bank Lower Middle Income	223998.45 (145000.5 to 317794.08)	3.92 (0.18 to 70.00)	..	4.47 (1.31 to 7.03)
World Bank Low Income	39054.89 (25244.40 to 55408.92)	11.53 (7.07 to 15.45)	..	4.63 (0.98 to 7.92)
World Bank High Income	113211.83 (74064.41 to 161151.33)	−19.62 (−21.47 to −17.85)	..	−8.16 (−10.13 to −6.27)
World Bank Upper Middle Income	195138.41 (127869.38 to 274063.78)	−15.31 (−17.47 to −13.17)	..	1.10 (−1.58 to 3.02)

Data in parentheses are 95% uncertainty intervals. YLDs: years lived with disability.

gical disorders and did not show significant differences between males and females in these diseases.

In addition, atopic dermatitis tended to be strongly negatively correlated before the age of 14 ($r=-0.9759$, $p<0.05$) and strongly positively correlated after the age of 14 ($r=0.9986$, $p<0.001$). Furthermore, the 3 infection-related skin diseases showed different trends in AA patients before and after 14 years.

Projected global burden of alopecia areata

We projected that age-standardized incidence, prevalence, and YLD rate would continue to decline to a certain point before increasing from 2021 to 2050, and could ultimately increase to equal or even higher than the 1990 rate. The trends in the change curves for females and the global are essentially the same, while the male curves all change more gently, without large increases or decreases (Fig. S4).

Looking at the results for each age group, the incidence, prevalence, and YLD rate in the pre-34 age group all increase significantly between 2021 and 2050 and exceed the 1990 values, with the projected curves for females more reflective of this change, and males generally smoother (**Fig. 7**). Similarly, changes are more pronounced and significant for females at all ages.

DISCUSSION

This study provides a comprehensive picture of AA disease burden and trends based on gender and age by analysing GBD data from 204 countries and regions from 1990–2021. We also investigated the epidemiological differences in AA patients before and after the age of 14 in the hope of providing a basis for the diagnosis and treatment of children with AA.

As the quality of life and the importance of appearance increased, the health awareness of AA gradually rose, and screening and treatment of AA were enhanced, the high SDI group showed a significant decrease in age-standardized prevalence and incidence. Similarly, the percentage of age-standardized YLDs observed in high SDI and middle SDI represents a reduction in the burden of workforce loss due to AA, possibly due to factors such as economic development, technological advances, and improved healthcare resources. Moreover, international attention to AA is increasing year by year, and the esta-

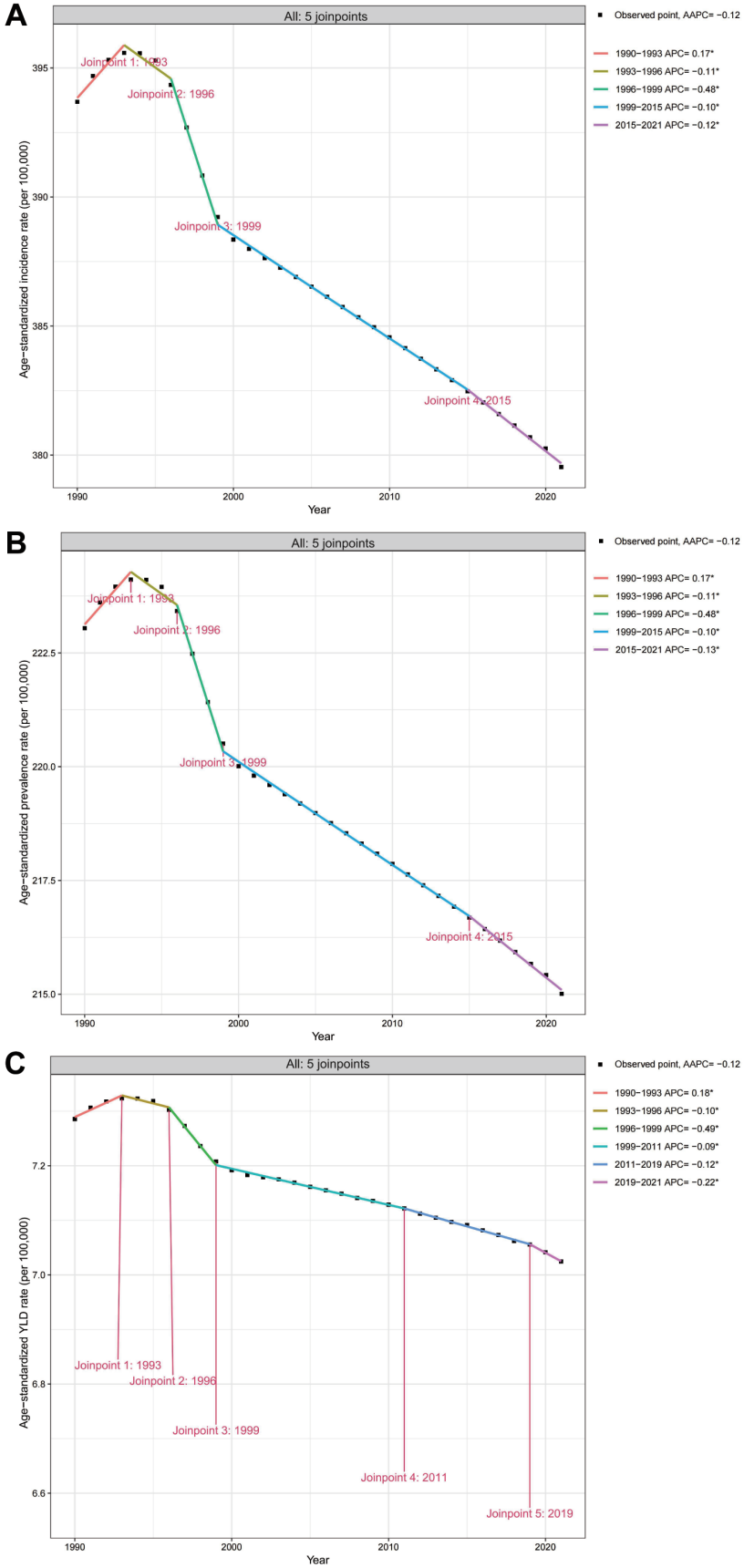

Fig. 2. Global trends for age-standardized rates (per 100,000 population) of alopecia areata from 1990 to 2021. (A) age-standardized incidence rate; (B) age-standardized prevalence rate; (C) age-standardized YLD rate. YLD: years lived with disability.

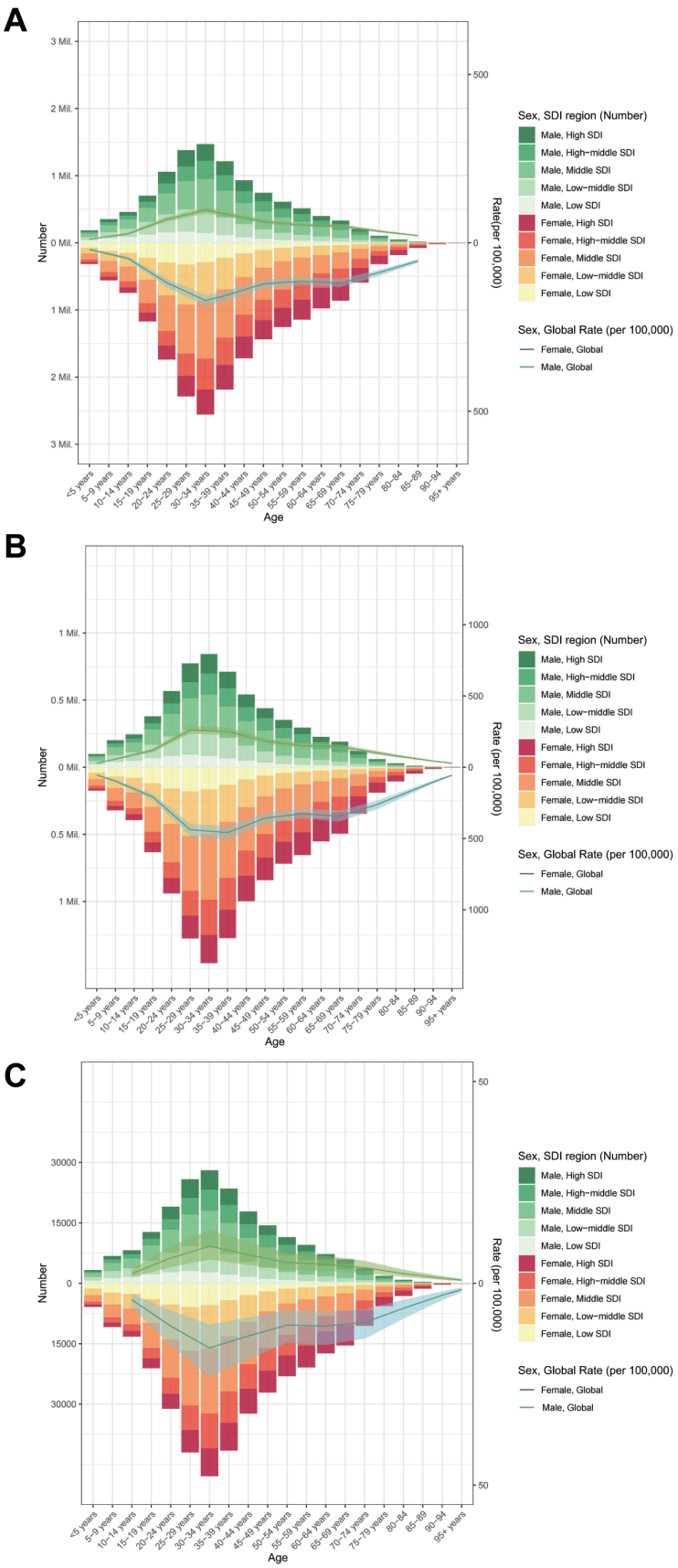

Fig. 3. Global alopecia areata number and rate (per 100,000 population) of (A) incidence, (B) prevalence and (C) YLD by age-specific, sex, and SDI region in 2021. The shaded area represents 95% uncertainty intervals, including overlap between male and female. YLD, years lived with disability.

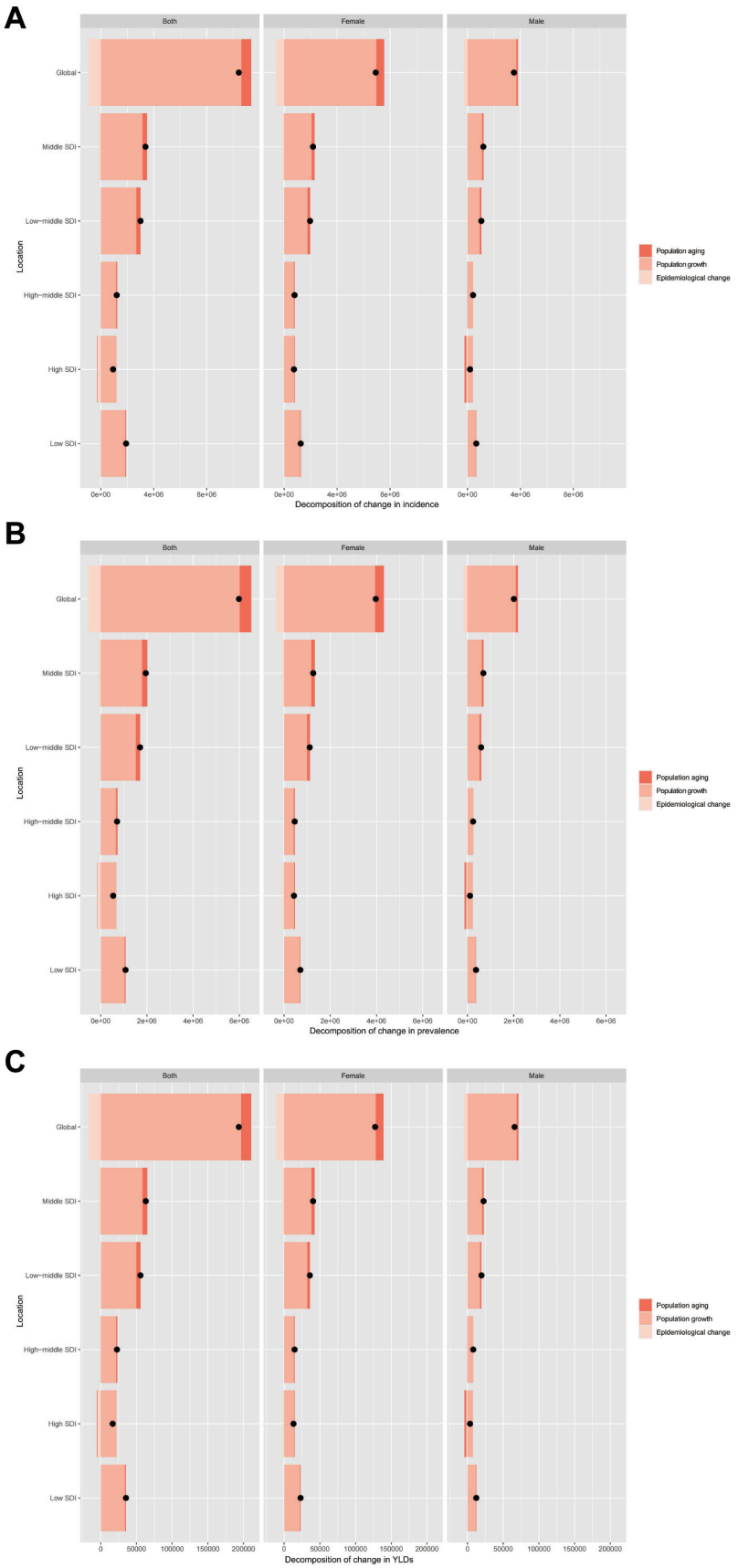

Fig. 4. Decomposition of changes in the number of (A) incidence, (B) prevalence, and (C) YLDs of alopecia areata attributable to population growth, population ageing, and epidemiological change by global and SDI region, 1990 and 2021. The decomposition was conducted using the incidence, prevalence, and number of YLDs in 1990 as the reference.

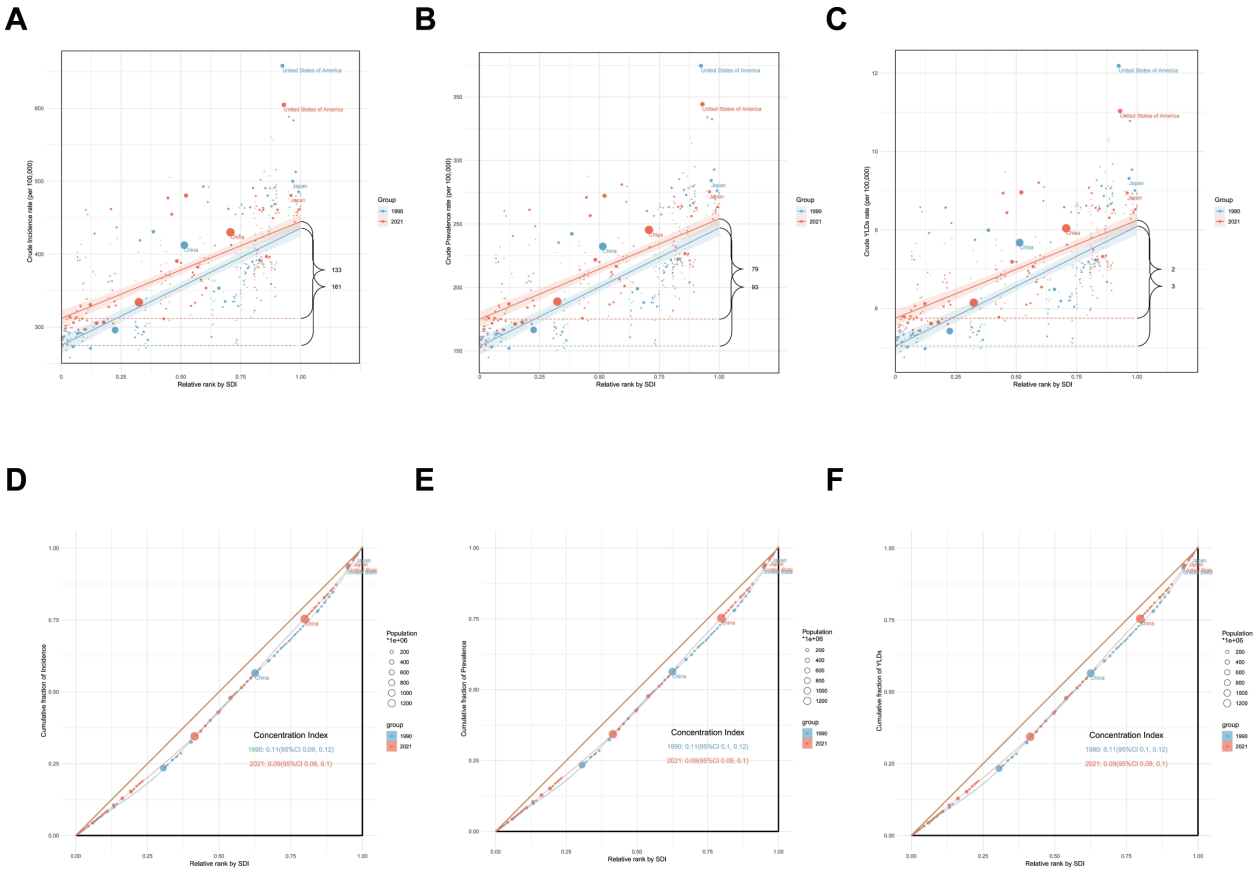

Fig. 5. Health inequality regression curves and concentration curves for the (A, D) incidence, (B, E) prevalence, (C, F) YLDs of alopecia areata worldwide, 1990 and 2021.

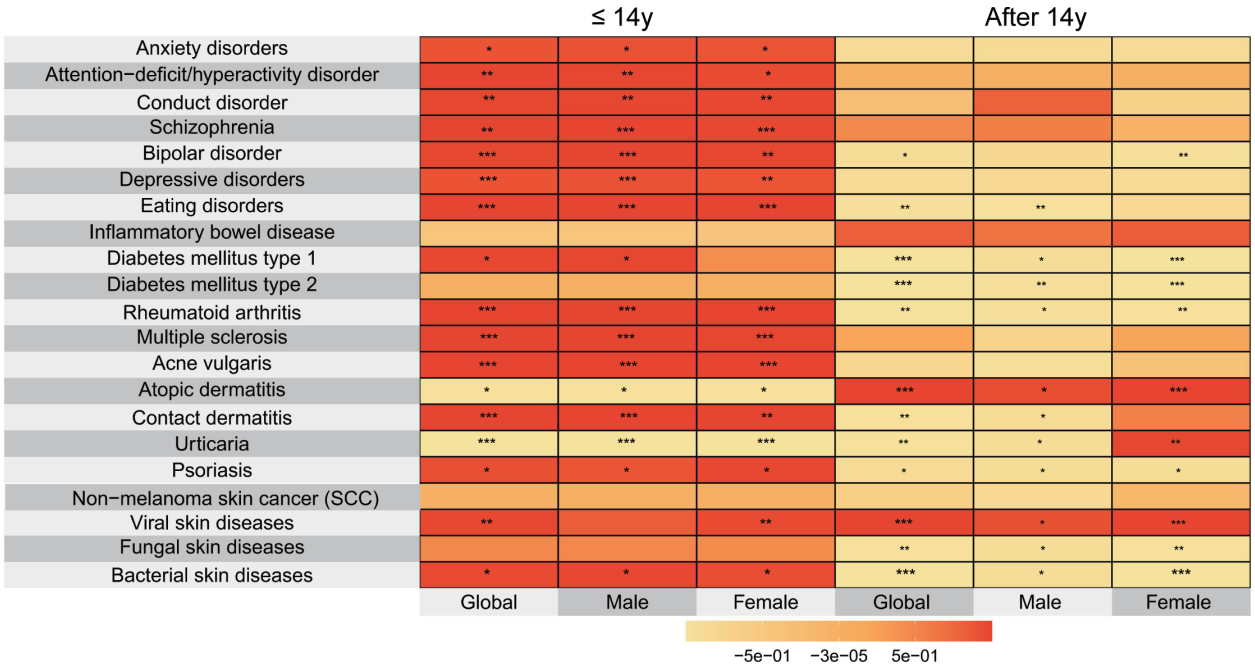

Fig. 6. Pearson correlation coefficient of age-standardized incidence rate (per 100,000) between AA and comorbidities of AA by sex and age. Statistical significance was presented as follows: *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$. SCC: squamous-cell carcinoma.

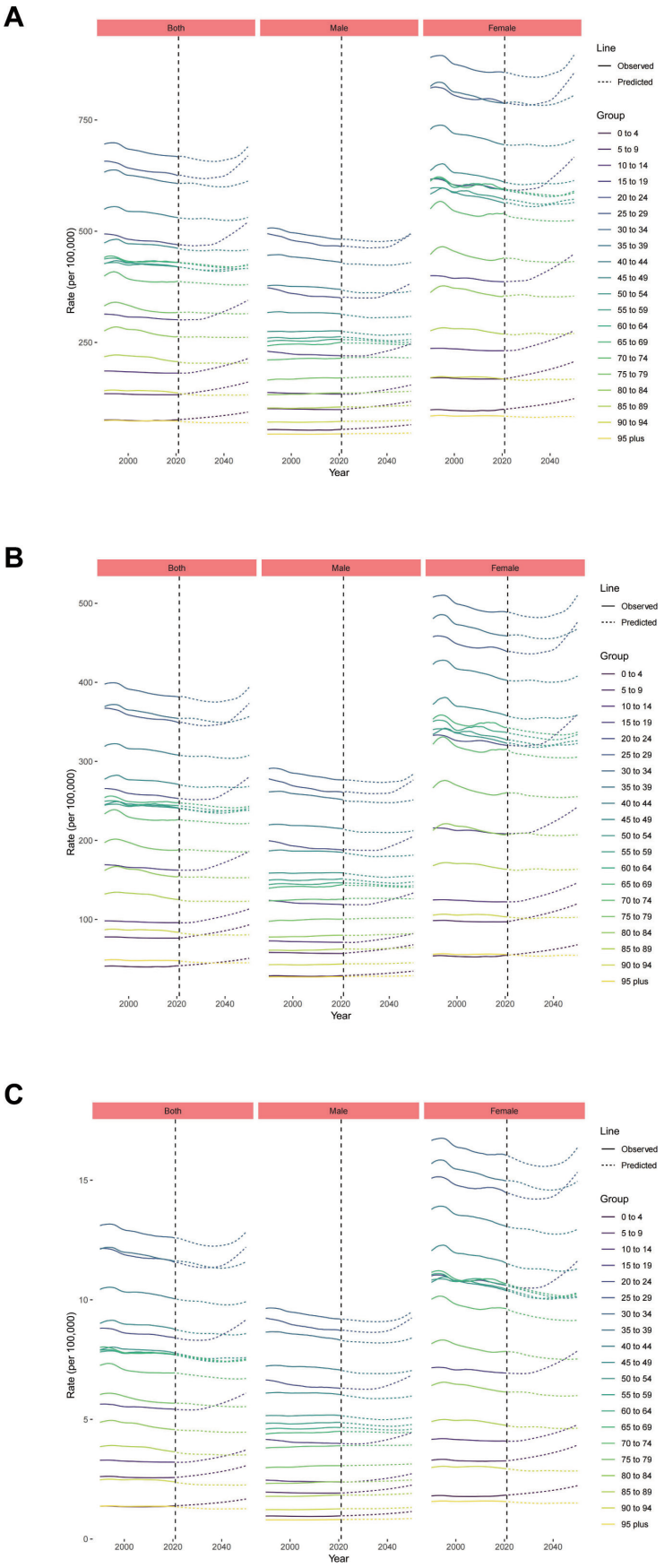

Fig. 7. Estimated trends in the global age-standardized alopecia areata (A) incidence, (B) prevalence, and (C) YLD rate by different age groups.

blishment of the National Alopecia Areata Foundation (NAAF) and the emergence of different rating scales and guidelines for assessing the extent of the condition (e.g., the SALT score) (8) have provided favourable conditions for standardizing the diagnosis and treatment of AA. Besides this, the reduction in age-standardized YLDs is likewise attributed to diverse and novel therapeutic approaches. In addition to traditional minoxidil and corticosteroids (9), the utilization of novel JAK inhibitors has dramatically improved clinical symptoms and reduced relapses, posing new challenges in terms of safety, cost-effectiveness, and economic burden (10).

Interestingly, our results show a decrease in the global age-standardized prevalence of AA in 2021 (see Table I), which is broadly consistent with the conclusions of a study looking at GBD data from 2019 (11); however, there are other findings that suggest an increase in AA prevalence over time (12), and describe a continued increase in AA prevalence from 2016 to 2019 (13). Regarding the discrepancy in these results, the increase in AA prevalence over time shown by Lee et al. (12) may be due to the fact that their study took a meta-analysis, which may be subject to detection bias, which is due to increased awareness of the disease and improved research methodology associated with the increase in time, and likewise to the effects of multiple environmental factors (e.g., micronutrient deficiencies). Similarly, we consider it is possible that the study by Mostaghimi et al. was limited to the US population actively utilizing medical resources for healthcare, and although they weighted their sample sizes (13) they were still unable to avoid the problems of data omission and inaccuracy of generalizability. In addition to this, the significantly higher AA prevalence based on clinical studies rather than population-based studies may also be due to selection bias, with more patients with AA likely to be present in dermatological consultations. Also, due to the increased disease awareness of AA, people are more concerned about their health and appearance, as well as the approval of new drugs to treat AA, which have shown their effectiveness and safety (14). All of these have greatly increased the motivation of people, and this has led to an increase in AA prevalence from the clinical point of view.

At the global level, age-standardized prevalence, incidence, and YLD showed an overall increase from 1990–1993 and a decrease thereafter, with the overall increase probably due to the fact that the GBD database was first used in 1990, and with the annual updating of data and the increasing number of regions (15), which led to a short period of increase in the rates. All 3 rates had a turning point in 1999, which may be due to the fact that NAAF released the first version of "Alopecia areata investigational assessment guidelines" in 1999, which standardized and improved the estimation of hair loss area and assessment of hair loss severity, as well as establishing a registration system for American patients with AA (16).

Although some studies have concluded that AA is not gender-biased (17), in our results, age-standardized incidence and prevalence rates are significantly higher in women than in men, and the rates for women are dominant. Based on the previous data, we observe that the finding that the burden is significantly higher in females than in males is evident in all age groups, countries, and regions. This reason may be related to the pathogenesis of AA, which is an autoimmune disease associated with T-cell activation (1). However. women typically exhibit a higher prevalence of autoimmune diseases than men, such as rheumatoid arthritis (18), inflammatory bowel disease (19), atopic dermatitis (20), and multiple sclerosis (21). This may be due to the fact that women undergo a number of comprehensive endocrine changes throughout their lives, such as puberty, menopause, pregnancy etc. These changes in the endocrine environment affect pro-inflammatory and anti-inflammatory cytokines to a certain extent (22), and influence T-cell activity (23), which in turn affects the autoimmune system and thus contributes to a woman's susceptibility to autoimmune diseases.

Yet our data showed a significant reduction in age-standardized incidence rates between 2019 and 2021. We analysed that this could be due to the COVID-19 pandemic, which dealt a heavy blow to global healthcare, and because the outbreak also caused many deaths, as well as delayed screening and diagnosis of many diseases, which could also include AA. According to joinpoint analysis, the age-standardized YLD rate had a turning point in 2019, which is closely related to the reduction in global incidence after 2019.

The GBD due to AA increased rapidly over the 1990–2021 period and population growth was the major contributor to the increase in disease burden; however, the current epidemiological change (standardized diagnosis, treatment of AA, and thus reduction of potential incidence) does not fully offset the contribution of population growth and ageing to the increased disease burden of AA. Population growth inevitably drives the increase in AA and dominates this contribution, whereas the contribution of ageing is slight. This may be due to the fact that 66% of people with AA have a first onset of disease at younger than 30 years old (17), and the median age of onset of AA is 30 years old in men and 31 years old in women (24). At the same time, this is consistent with our finding that the highest incidence and prevalence rates at the global level are found in the 30–34 age group.

Comorbidities

Our study is the first to discuss the differences in associations between AA and its comorbidities before and after the age of 14, and we have identified a possible important relationship between AA and altered psychological status. Children with AA were strongly associated with psychological disorders (including anxiety disor-

ders, behavioural disorders, and depressive disorders), whereas in adolescents/adults with AA, these disorders were not associated. Some studies have shown that AA is associated with a severe mental health burden, with 30–68% of patients experiencing varying degrees of mental health symptoms (25), and that anxiety disorders affect 15–20% of children and may even lead to self-harm and suicidal tendencies (26). When we consider the differences between children and adolescents/adults with AA in terms of these disorders, it is possible that some childhood-onset anxiety disorders get better or resolve on their own because of milder symptoms, due to the fact that children grow and develop psychologically and intellectually when they grow older. As well, female AA incidence is significantly higher than that for male AA patients regarding the above-mentioned psychological comorbidities, which may be related to the fact that women have a poorer quality of life (27), and that the poorer quality of life also has a serious impact on the mental health of female patients.

Additionally, there is a general consensus among scholars that AA is associated with the onset of atopic dermatitis (2), and the same conclusion was reached in our results. The onset of atopic dermatitis is perhaps more closely related to adolescents/adults with AA. This result may be because AA has similar aetiological factors to atopic dermatitis. Similarly, our results showed an association between infection-related diseases and AA at different ages. This is probably because, although AA is an autoimmune disease, it can be secondary to a range of infections or inflammatory conditions (28).

Limitations

Our data analysis may be lower than the true disease burden of AA, the actual prevalence may be underestimated, and in some low healthcare countries and regions the attention to AA lags far behind that of most countries. They may also lack some methods that can be helpful in the diagnosis and treatment of AA, which results in their AA consultation rate not being high. In addition, some mild AA is self-limiting, healed before consultation, or undetected by patients because of its small size, which cannot be avoided by GBD, thus leading to inaccurate GBD data. Moreover, as the diagnostic criteria for AA and the methods and tools used to collect data may vary between countries and regions, this may also have an impact. Unfortunately, AA is usually diagnosed with scoring modalities such as SALT scores, but this aspect cannot be captured in the data of this study.

Clinical and practical implications

Despite these limitations, our article is the first to critically analyse the epidemiological differences between children and adolescents/adults with AA, filling a gap in the data on this. These findings also provide valuable epidemiological information for the diagnosis and innovative treatment of patients with AA in different age groups, thereby increasing awareness of how to diagnose and treat AA in different age groups. These results also emphasize the need to continuously update and improve policies for the diagnosis, treatment, and management of AA, and are important for improving our understanding of the rational allocation of healthcare resources and the formulation of related health policies.

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The authors have no conflicts of interest to declare.

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