Lifetime incidence and healthcare disparities in alopecia areata: A UK population-based cohort study

Runing head: Incidence and healthcare disparities in alopecia areata

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Conflicts of interest disclosures

AT has no competing interest to declare. CT is a principal and (national) chief investigator on the Pfizer-funded ALLEGRO clinical trials in alopecia areata. CT provides consulting services to Pfizer; and has received speaker fees from Leo Pharma.

JN, RR and MC are employees and shareholders of Pfizer Ltd.

AM provides consultancy for Pfizer and for Manentia.

Data availability statement

Data sharing statement: The RCGP RSC dataset is held securely at Oxford University and can be accessed by bone fide researchers. Approval is on a project-by-project basis (www.rcgp.org.uk/rsc). Ethical approval by an NHS Research Ethics Committee may be needed before any data release/other appropriate approval. Researchers wishing to directly analyse the patient-level pseudonymised data will be required to complete information governance training and work on the data from university secure servers. Patient-level data cannot be taken out of the secure network.

Ethics statement

Ethics statement: "Study approval was granted by the Royal College of General Practitioners Research and Surveillance Centre research committee. The study did not meet the requirements for formal ethics board review as defined using the National Health Service Health Research Authority research decision tool (http://www.hra-decisiontools.org.uk/research).

What is already known about this topic?

- Alopecia areata is an immune mediated form of hair loss, which can occur at any age.
- Alopecia areata can be a distressing condition and is associated with a high burden of mental health comorbidity.
- Although it is known that incidence of alopecia areata peaks in young adults, how lifetime incidence and impact of alopecia areata varies by sex, ethnicity, and socio-economic status has not previously been described.

What does this study add?

- Overall lifetime incidence of alopecia areata in the UK is 2.1%, with marked variation across ethnic groups, with people of Asian ethnicity having the greatest risk (5.9%).
- Lifetime risk of alopecia areata is also higher for people from more deprived and urban areas.
- The impact of alopecia areata differs by ethnic group, with people of black ethnicity experiencing the greatest burden of anxiety and time off work.

Plain Language Summary

The risk and impact of alopecia areata varies across ethnic groups

Alopecia areata is a form of hair loss that involves the immune system. It can occur at any age but most often occurs in young adults. Alopecia areata can be an unpredictable and distressing condition. People with alopecia areata have a higher risk of mental health conditions. We wanted to investigate how the impacts of alopecia areata may vary between groups.

We used electronic medical records from general practices in the UK from 2009 to 2018. We investigated how many people developed alopecia areata and looked at what age they were when diagnosed. We compared the risk of alopecia areata between females and males. We also compared the risk between different ethnic groups, and between areas in which people lived.

We found around 2 in every 100 people will develop alopecia areata across their lifetime. The risk of alopecia was different across ethnic groups. Those from the Asian ethnic group had the greatest risk with nearly 6 cases per 100 people. This compared to less than 2 cases per 100 people for the white ethnic group. Those people living in more deprived or urban areas were also at higher risk of alopecia areata.

The impact of having alopecia areata also differed with ethnic groups. We compared people with and without alopecia areata from each ethnic group. People from the black ethnic group with alopecia areata were most likely to have anxiety. They were also most likely to have time off work certificates issued by their doctor.

Both the risk and impact of alopecia areata varies across the population of the UK. This information should help clinicians target support towards those with the greatest burden.

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Keywords: Incidence, Alopecia Areata, mental health, psychological conditions, anxiety, depression, primary care, healthcare utilisation, work, employment.

The study protocol for this retrospective observational study was registered with ClinicalTrials.gov (Identifier: NCT05727306).

This research was sponsored by Pfizer. Project management, medical writing, and statistical support was provided by Momentum Data, UK, and was funded by Pfizer. This summary is related to an approved indication of a Pfizer product and reports the results of a single study. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study.

Abstract

Background:

Alopecia areata (AA) is an immune-mediated form of hair loss that can occur at any age, often with a significant mental health burden.

Objectives:

We aimed to provide estimates of the lifetime incidence of AA, and the impacts on mental health, healthcare utilisation and work-related outcomes, assessing variation across major sociodemographic subgroups.

Methods:

AA cases were identified in primary care from the UK population-based Oxford-Royal College of General Practitioners Research and Surveillance Centre database (2009-2018). Lifetime incidence of AA was estimated at age 80 using modified time-to-event models with age as the timescale, overall and stratified by sex, ethnicity, deprivation, and geography. Mental health, healthcare utilisation and work-related outcomes were assessed in the two years after AA diagnosis compared to matched unaffected controls, and stratified by the same sociodemographic subgroups .

Results:

6,961 people developed AA during the study period. Overall lifetime incidence of AA was 2.11% (95% Confidence Interval [CI] 2.06, 2.16%). Females had a higher lifetime incidence 2.35% (95%CI 2.28, 2.43%) than males 1.88% (95%CI 1.81, 1.94%). Lifetime incidence was higher in those of Asian ethnicity 5.87% (95%CI 5.51, 6.24), other 4.47% (95%CI 3.63, 5.31), mixed 4.44% (95%CI 3.50, 5.37) and black 3.03% (95%CI 2.63, 3.42) ethnicity, compared to white ethnicity 1.74% (95%CI 1.68, 1.80). Lifetime

incidence was highest in those with the greatest deprivation; most-deprived quintile 2.92% (95%CI 2.77, 3.07%) compared to least-deprived 1.68% (95%CI 1.59, 1.78%). Across sociodemographic subgroups, people with AA of black ethnicity were most likely to have anxiety (adjusted Odds Ratio versus matched controls 2.92, 95%CI 1.71, 4.91), and had the greatest risk of time off work (adjusted Hazard Ratio versus matched controls 2.54, 95%CI 1.80, 3.56).

Conclusions:

AA affects around 1 in 50 people over their lifetime. Incidence and the impact of AA on mental health and work outcomes, is highest in ethnic groups other than white. Clinicians should be aware of the marked heterogeneity in the incidence and impact of AA, and support targeted healthcare to groups at the highest risk of alopecia and its consequences.

The study protocol for this retrospective observational study was registered with ClinicalTrials.gov (Identifier: NCT05727306).

Words: 350 (Max 350)

Introduction

Alopecia areata (AA) is a non-scarring, immune-mediated form of hair loss. AA can occur at any age, although incidence peaks in young adults.[1, 2] UK data suggests a point prevalence of 0.58% in adults, and an annual incidence of 0.26 per 1,000 person years.[1] The lifetime incidence of developing AA has been estimated at 2.1%,[3] although this was based on one relatively small (n=530) population. Variation in AA lifetime incidence by sex, ethnicity, and deprivation has not been previously described and may be important given the recently observed differences in prevalence of AA across ethnic groups.[4]

AA can be a distressing condition, especially as prognosis is unpredictable and relapse is common.[5] People with AA experience a high burden of mental health conditions,[6-10] including a 33% greater risk for new-onset anxiety and 38% greater risk for depression.[11] Furthermore, nearly 80% of people with AA report impacts on their quality of life[8] across a range of different measures,[12-15] and those with AA are 56% more likely to have time off work and 82% more likely to be unemployed.[11] Although people with AA from lower socioeconomic groups are more likely to attend primary care, they are less likely to be referred to specialist dermatology services.[1] To our knowledge no previous study has provided a comprehensive evaluation of variation in the impact of AA by age and major sociodemographic factors.

In a large-scale UK population-based study, we aimed to provide contemporary estimates of lifetime incidence of AA. We also sought to identify any sociodemographic disparities in lifetime incidence, and the wider impacts and healthcare burden of AA.

Methods

Study design

The study protocol for this retrospective observational study was registered *a priori* with ClinicalTrials.gov (Identifier: NCT05727306). Routinely collected, population-based primary care data were extracted from the UK Oxford-Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) database (registered population 2.6 million), which is representative of the national population.[16 1, 17, 18]

Study population

All adults and children registered in the Oxford-RCGP RCS between January 1, 2009 and December 31, 2018, with at least 1 day of follow-up, and without a diagnosis of AA prior to the study start date, were eligible for inclusion (excluding 1.8% who have opted out of record sharing).

Definition of sociodemographic characteristics

Sociodemographic data comprised of age, sex, ethnicity, socioeconomic status (SES), geographic area and region. Ethnicity was grouped using standard UK groups: 'white' (Irish, Gypsy or Irish Traveller, Roma, other white), 'black' (black British, black Welsh, Caribbean, African, other black), 'Asian' (Asian, Asian British, Asian Welsh, Bangladeshi, Chinese, Indian, Pakistani, other Asian), 'mixed or other' (mixed, Arab, any other ethnic group).[19] SES was derived from patient postcode and defined using Index of Multiple deprivation (IMD)[20] stratified into quintiles of deprivation. Geographic area (urban/rural) and English region (London, South East, South West, West Midlands,

North West, North East, Yorkshire and the Humber, East Midlands, and East of England) were defined from patient postcode.

AA case definition

Individuals newly diagnosed with AA (AA cases), either by a GP in primary care or by a dermatologist following referral, were defined by the presence of a first ever AA specific Read code and no diagnosis codes for an alopecia alternative condition (scarring alopecia, traction alopecia, congenital alopecia, androgenetic alopecia, telogen effluvium, tinea capitis, trichotillomania, or secondary syphilis of the scalp) in the subsequent 365 days.[17] People diagnosed with AA within 6 months of practice registration were excluded (to ensure we captured only incident AA cases). The index date of each AA case was assigned to the date of their AA diagnosis.

Definition of matched controls

A matched control population was defined to evaluate impacts of AA in those aged 12+. Each individual aged 12+ diagnosed with new onset AA during the study period was matched at their diagnosis date with up to four unaffected controls without a diagnosis of AA. Individuals without AA but with a diagnosis of a non-specific or alopecia alternative condition, or less than 12 months of follow-up available, were excluded. A rolling matched cohort design was used, defining eligible matched controls at the date of AA diagnosis for each case, and then exact matching on age category (adolescents aged 12-17, and adults aged 18-29, 30-49 and 50+), sex, ethnicity, SES, geographical area and region. To further improve matching quality, the algorithm included

additional nearest neighbour matching by age in years. After matching, the index date of each matched control was set to the index date of their matched AA case counterpart.

Study outcomes

Mental health outcomes

Three mental health condition outcomes were assessed; depressive episodes, recurrent major depressive disorder and anxiety disorders, defined by the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD10) classification, and identified using algorithms validated for use in UK primary care data[21] (Supplementary Materials Code Lists).

Healthcare utilisation outcomes

Healthcare utilisation comprised of three outcomes; primary care visits, dermatology referrals and referrals for psychological therapy (including those via Improving Access to Psychological Therapies and psychiatric reviews) (Supplementary Materials Code Lists).

Work-related outcomes

Work-related outcomes comprised time off work, identified by issued Med 3 certification from primary care for time off work, and unemployment, defined by issues of IB113 or ESA113 forms for unemployment (Supplementary Materials Code Lists).

Statistical analyses

Lifetime incidence of AA

Cumulative lifetime incidence of AA was estimated in the whole study population using adapted survival models with age as the timescale, fitted as Aalen-Johansen cumulative risk estimates using the *etm* package in R[22], and adjusted for the competing risk of death.[23, 24] Individuals were followed-up from the latest of their age at study start date or their age at their date of practice registration until the earliest of their age at an AA diagnosis (if recorded) or a censoring event (death, deregistration, date aged 95, or study end date). Lifetime incidence was calculated overall and by sociodemographic subgroups at age 80 years.

Disparities in the impact of AA

Mental health and healthcare utilisation outcomes were compared in AA cases and matched controls. Analysis of work-related outcomes was restricted to individuals aged 18-65. All outcomes were evaluated in the overall matched population, and by sociodemographic subgroups with mixed and other ethnicity groups combined into a single 'other' group.

Burden of mental health conditions

The relative burden of each mental health condition recorded prior to and in the two years post index date was estimated in AA cases versus matched controls using logistic regression. Three adjustment sets were used to assess the robustness of the estimates

by sequentially adding measured confounders: unadjusted, sex-and-age adjusted, and a set adjusted for sociodemographic, clinical characteristics and count of 0-3+ major comorbidities (Table 1). Logistic regression models were reported using adjusted odds ratios with 95% confidence intervals [CI].

Healthcare utilisation and work-related outcomes

The relative incidence of dermatology referrals, referrals for psychological therapy, time off work, and unemployment were compared in AA cases versus matched controls up to two years post index date using Cox proportional hazard regression, with visual assessment of proportional hazards-assumptions, and applying the same three covariate adjustment sets as for mental health outcomes). Negative binomial regression, accounting for overdispersion, was used to compare rates of primary care visits, also using the same covariate adjustment sets.

Sensitivity analysis

To evaluate the magnitude of potential bias from including, as matched controls, individuals who are registered with a General Practitioner but who do not attend their practice, we repeated the analysis for mental health, healthcare utilisation and work-related outcomes restricting the matched control set to individuals with at least one primary care consultation in the year preceding their index date. Furthermore, a parallel sensitivity analysis was performed to assess the impact of missing ethnicity data, by amending missing ethnicity entries to white.

All statistical analyses were performed using R version 4.2.1. The study was conducted and reported following RECORD (Reporting of studies conducted using observational routinely collected data) guidelines.[25]

Results

Cumulative lifetime incidence of AA is highest in people of Asian ethnicity, with greater deprivation, and in urban areas

6,961 of 4,052,231 individuals in the final study population (Fig S1) developed AA over the study period. The median age of those with AA was 35 years (Inter Quartile Range; 26, 47). People were commonly diagnosed in childhood (8.6% aged 12-17) and early adulthood (27.5% aged 18-29). The largest proportion of AA cases of 43.1% were aged 30-49 years, with 20.8% aged over 50 years (Table 1). Although alopecia can be diagnosed at any age and risk continued to accumulate into later life (Fig S2). This translated to a cumulative lifetime incidence of 2.11% (95%CI 2.06, 2.16, Fig 1A) by age 80. Females had a slightly higher lifetime incidence of 2.35% (95%CI 2.28, 2,43) compared to males 1.88% (95%CI 1.81, 1.94), although no difference was evident until after age 50 years (Fig 1B). Marked differences existed between ethnic groups; those of Asian ethnicity had the greatest lifetime incidence of 5.87% (95%CI 5.51, 6.24, Fig 1C). Lifetime incidence was highest in those with the greatest deprivation 2.92% (95%CI 2.77, 3.07) and lowest in those with least deprivation 1.68% (95%CI 1.59, 1.78) (Fig 1D). London had a higher lifetime incidence than any other geographical area of 3.15% (95%CI 2.98, 3.31), there was no clear variation in lifetime incidence across the remaining geographical areas (Table S1). Lifetime incidence was higher in those from urban areas 2.27% (95%CI 2.21, 2.33), compared to rural areas 1.49% (95%CI 1.39, 1.58) (Table S1).

Disparities in mental health, healthcare utilisation and work-related impacts

6,183 eligible adults and adolescents with incident AA were matched to 24,718 controls without AA (Fig S1). AA cases and controls were well matched on all sociodemographic and clinical characteristics except for smoking status (Table 1).

Burden of mental health comorbidity was highest in those of black ethnicity

AA was associated with a greater risk of depressive episodes (adjusted Odds Ratio; aOR 1.35, 95%CI 1.25, 1.46, Fig 2A, Table S2), recurrent major depressive disorder (aOR 1.45, 95%CI 1.32, 1.58. Fig 2B, Table S3) and anxiety disorders (aOR 1.40, 95%CI 1.30, 1.51. Fig 2C, Table S4). The AA associated increase in risk was consistent across age and ethnicity groups, with the exception of the black ethnicity subgroup, which had a higher rate of AA associated risk of anxiety disorders (aOR 2.92, 95%CI 1.71, 4.91. Fig 2C, Table S4). AA associated increase in risk for depressive episodes, recurrent major depressive disorder and anxiety disorders were observed in urban but not rural areas (Tables S2, S3 and S4). There were no clear trends across English geographical regions (Tables S2, S3 and S4). These associations were consistent when evaluating only new-onset mental health diagnoses in the two years post-index date with the exception of the black ethnicity subgroup (Tables S10, S11 and S12).

Healthcare utilisation was highest in men and those of Asian ethnicity

People diagnosed with AA were more likely to attend primary care compared to matched controls without AA (aIRR 1.42, 95%CI 1.37, 1.46, Fig 3A, Table S5). This association was consistent across deprivation quintiles and between urban and rural

areas. Those with AA aged over 50 years were less likely to attend primary care (aIRR 1.24, 95%CI 1.16, 1.33. Table S5). Males with AA were more likely to attend primary care (aIRR 1.54, 95%CI 1.46, 1.63) than females with AA (aIRR 1.35, 95%CI 1.30, 1.40). Those of Asian ethnicity with AA (aIRR 1.64, 95%CI 1.51, 1.78) were more likely to attend primary care than those of white ethnicity (aIRR 1.30, 95%CI 1.25, 1.36, Fig 3A, Table S5).

Dermatology referral rates were similar across all subgroups, with the exception of those aged over 50 years with AA who were less likely to be referred to dermatology than younger groups with AA (Table S6).

People with AA were more likely to be referred for psychological therapy (aHR 1.36, 95%CI 1.17, 1.57. Table S7) compared to matched controls, although higher referral rates were not observed in all subgroups. Those subgroups with higher referral rates included females, those under 18 years or over 50 years, and those of white or Asian ethnicity (Fig 3B, Table S7).

Burden of work-related impacts was highest in those of black ethnicity

People with AA were more likely to have time off work (aHR 1.49, 95%CI 1.38, 1.61. Fig 3C , Table S8) and were more likely to be unemployed (aHR 1.46, 95%CI 1.14, 1.87. Fig 3D, Table S9.) compared with matched controls. These associations were consistent across subgroups for sex, age, and deprivation, with the exception of those of black ethnicity who had a greater risk of time off work (aHR 2.54, 95%CI 1.80, 3.56) than those of white ethnicity (aHR 1.42, 95%CI 1.28, 1.58). Associations between AA and unemployment were observed in males and females, 30-49 age group, those of white

ethnicity, those with the greatest deprivation and those in urban areas. Associations between AA and unemployment were only observed in the 'South West' and 'Yorkshire and The Humber' regions (Fig 3D, Table S9).

Sensitivity analysis

Associations remained consistent when evaluating all outcomes following exclusion of matched controls without at least one recent primary care consultation in the year preceding their index date (n=9,168 matched controls excluded) (Tables S13, S14). Associations were also consistent when missing ethnicity was replaced with white ethnicity (Tables S15, S16 and S17).

Discussion

Our contemporary population-based study identified major variation in the lifetime incidence and impact of AA. Overall, AA lifetime incidence was 2.1%, but this differed markedly across ethnic groups; Asian (5.9%), other (4.5%), mixed (4.4%), black (3.0%), and white (1.7%). We identified a clear socioeconomic gradient, with a greater than 50% excess lifetime incidence in individuals from the most deprived compared to least deprived areas, and in those living in urban compared to rural locations. The impacts of AA also differed by ethnic group; people with AA of black ethnicity had the greatest burden of concomitant anxiety and were the most likely to have recorded time off work. Despite this, there were no clear differences between ethnic groups in the provision of specialist referrals to either dermatological or mental health services.

Our overall lifetime incidence estimate is concordant with, to our knowledge, the only population-based study which reported a very similar lifetime incidence of 2.1%.[3] By evaluating a greater than 10-fold number of AA cases, we are able to demonstrate this summary estimate masks considerable heterogeneity in AA risk and major differences by ethnicity.

There is a lack of research investigating rates of AA across differing ethnic groups within populations. Where research has investigated ethnic differences in AA within a population, risk of AA tends to be greater in ethnic groups other than white, although it is not always easy to draw comparisons between studies with populations of differing ethnicity profiles. A cross-sectional analysis in the US found higher odds of AA in those

425 of African-American ethnicity compared to those of white ethnicity, and conversely
426 lower odds in those of Asian ethnicity, although non-cases in this registry are non-blood
427 relatives or friends, research team members or were recruited at alopecia conferences
428 and via internet advertising, and so are potentially subject to significant selection bias.[26]
429 This lower risk of AA in those of Asian ethnicity contrasts with our findings where the
430 Asian ethnic group had the highest lifetime incidence of AA, but this may at least in part
431 be explained by differences in ethnic composition between countries. For example
432 within the UK those who identify as Indian, Pakistani or Bangladeshi make up around
433 74% of the Asian ethnic group with only 7.5% identifying as Chinese,[27] compared to the
434 US where just under 25% identify as Indian, Pakistani or Bangladeshi, and around 20%
435 identify as Chinese.[28] Cross-sectional results in nurses also found higher AA in women
436 of black ethnicity compared to white, although this was based on self-reported
437 diagnosis of AA.[29] For immune-mediated conditions analysis using US electronic
438 medical records, a higher incidence was observed in African-Americans, Asian or Pacific
439 Islanders, multiracial and Native American compared to the reference white
440 population.[30] However, this analysis is limited by the fact that it covers only people seen
441 in healthcare facilities during the study period and therefore comparisons are not made
442 against a true denominator population. Taken collectively, these prior studies suggest
443 potential important ethnicity differences, but no assessment of lifetime AA incidence
444 across ethnicity groups with a population-representative denominator has been
445 previously conducted.
446
447 Similarly, there is limited previous research investigating disparities in the impact of
448 AA. While there is a growing body of evidence investigating a strong negative overall
449 impact of AA on mental health comorbidity, in particular depression and anxiety,[8, 9, 31]

450 we are not aware of any previous studies investigating sociodemographic variation in
451 mental health outcomes. In concordance with our findings, AA has previously been
452 associated with negative impacts on self-reported work productivity,[15, 32] and with
453 increased healthcare utilisation,[33-35] with one US study suggesting AA-associated
454 healthcare utilisation is higher in females and older individuals, and varies with
455 geographical area.[36]
456
457 It is likely that AA shares features with other immune-mediated conditions, where it has
458 been highlighted that disparities between sociodemographic subgroups will comprise of
459 a combination of contributing factors. For example, there are biological factors such as
460 genes,[37] immunological mechanisms[38] and development in early life. There are also
461 environmental determinants of health, including housing and pollution,[39] as well as
462 socio-cultural factors.[40] All of these may influence not only disease course but may also
463 impact on access to healthcare.[41] It is recognised that health disparities are linked to
464 multiple disadvantages experienced by different groups of people, and further research
465 is a key part in addressing these inequalities,[42] especially in groups who are at increased
466 risk but are often less well represented in clinical and epidemiological research.
467
468 A considerable strength of our study is the use of a population-representative primary
469 care database, meaning results are likely to be generalisable to the wider UK population,
470 although generalisability may not extend to other populations especially those in
471 different sociocultural settings. Disparities do not occur in isolation and our subgroup-
472 stratified lifetime incidence estimates are unadjusted, and so reflect other disparities
473 experienced by each group (such as socioeconomic differences) meaning they should
474 not be interpreted as causal differences. However, our evaluation of the impacts of AA is

strengthened by our use of an extensive matching algorithm. It is a limitation that people with an existing condition, such as AA, may have more regular contact with healthcare providers and therefore increased chances of having other conditions or outcomes detected. We sought to minimise the risk of this detection bias by using a sensitivity analysis, repeating the same analysis but restricting matched controls to those with at least one primary care consultation in the year preceding their index date and found that associations remained consistent. In the case of the primary care visits outcome, we did not have details for the reason visit, so cannot draw conclusions as to whether the increased visits were for AA or other conditions. We did not include thyroid disorders and atopic dermatitis, both common comorbidities in people with AA,[18] in our comorbidity count when evaluating healthcare disparities, although as we show consistent effects with sex-and-age adjusted and fully adjusted models we expect this to have a minimal impact on our findings. We were also unable to investigate more detailed aspects of AA, such as the locations and extent of hair loss, or if the condition was stable or worsening, as this information is more often coded in detailed notes and is not routinely available for research. A further limitation of our analysis is the use of routine primary care data which is dependent on accurate diagnosis and coding. Within the UK most patients would initially visit their GP and typically about a quarter of AA patients are referred to secondary care within the first year.[1] Diagnoses made within secondary care are routinely transcribed into the primary care record, however the provenance of the diagnosis (primary or secondary care) is not recorded and it is possible capture may not be complete. Furthermore, events may not be repeatedly coded within primary care, so it can be harder to ascertain if a condition is ongoing or if it has resolved. To mitigate as far as possible against this, we used validated algorithms to identify outcomes and extensive code lists where no validated definition exists.

Patients were excluded if an alternative differential diagnosis was recorded. Our analysis is however likely to under capture the true burden of AA and its impacts as not all individuals will seek health care.

Given the disparities in risk of developing AA, there is a need for better targeting of support to those groups most affected, especially those from ethnic groups other than white who experience the greatest AA burden. Although our study did not identify consistent disparities in healthcare provision, we found no evidence to suggest that healthcare provision is being effectively targeted to those with greatest burden.

Conclusions

AA affects around 1 in 50 people over their lifetime. There is, however, considerable variation in lifetime incidence, which in the UK, is highest in those of Asian ethnicity, those experiencing greater socioeconomic deprivation, and those living in urban areas. The striking differences in risk of AA across ethnic groups warrants further research to identify the underlying mechanisms involved, and ultimately to develop precision treatment.

The impacts of AA also vary markedly across the population, in particular the mental health and work-related impact of AA may be highest in ethnic groups other than white. Clinicians should be aware of the marked heterogeneity in both the risk and impact of AA. There is a need for psychological assessment and targeted support to be included in the dermatology service for patients with AA. Future research is needed to understand

the experiences of minority ethnic groups living with AA and to inform strategies to optimise clinical care for those most at risk of AA and its consequences.

Declarations

Study registration:

The study protocol for this retrospective observational study was registered *a priori* with ClinicalTrials.gov (Identifier: NCT05727306).

Author contributions: The study concept and design were conceived and developed by AT, CT, JN, RR, MC, and AM. The study was performed and written under the direction of AT, CT, JN, RR, MC, and AM. All authors approved the final submitted version. AM attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Table 1. Sociodemographic and clinical characteristics of AA cases and matched controls.

	AA cases	Matched controls	SMD†
n	6,183	24,718	
Follow up duration years (median [IQR])	3.5 [1.7, 6.0]	3.1 [1.5, 5.8]	0.061
Sex			
Female	3,342 (54.1)	13,366 (54.1)	<0.001
Male	2,841 (45.9)	11,352 (45.9)	
Age years (median [IQR])	35.0 [26.0, 47.0]	35.0 [25.0, 47.0]	0.003
Age (years) group (%)			0.001
12-17	529 (8.6)	2,111 (8.5)	
18-29	1,699 (27.5)	6,792 (27.5)	
30-49	2,666 (43.1)	10,659 (43.1)	
50+	1,289 (20.8)	5,156 (20.9)	
Ethnicity (%)			0.002
White	3,205 (66.2)	12,820 (66.3)	
Black	241 (5.0)	960 (5.0)	
Asian	1,129 (23.3)	4,515 (23.3)	
Other	264 (5.5)	1,047 (5.4)	
IMD quintile (%)‡			0.001
1 (most deprived)	1,339 (22.1)	5,356 (22.1)	
2	1,277 (21.1)	5,108 (21.1)	
3	1,091 (18.0)	4,356 (18.0)	
4	1,144 (18.9)	4,573 (18.9)	
5 (least deprived)	1,205 (19.9)	4,818 (19.9)	
Geographic area (%)			<0.001
Urban	5,150 (84.9)	20,590 (84.9)	
Rural	913 (15.1)	3,648 (15.1)	
Region (%)∑			0.001
London	1,488 (24.6)	5,952 (24.6)	
East Midlands	227 (3.7)	904 (3.7)	
East of England	253 (4.2)	1,009 (4.2)	
North East	209 (3.5)	833 (3.4)	
North West	1,160 (19.2)	4,640 (19.2)	
South East	1,053 (17.4)	4,212 (17.4)	
South West	635 (10.5)	2,540 (10.5)	
West Midlands	417 (6.9)	1,665 (6.9)	
Yorkshire and The Humber	614 (10.1)	2,456 (10.1)	
BMI category (%)β			0.112
<18.5 Underweight	315 (6.0)	1,303 (6.5)	
18.5-25 Normal weight	2,277 (43.1)	8,842 (43.9)	
25-30 Overweight	1,644 (31.1)	5,901 (29.3)	

	AA cases	Matched controls	SMD†
30-35 Class I obesity	665 (12.6)	2,664 (13.2)	
35-40 Class II obesity	245 (4.6)	941 (4.7)	
40+ Class III obesity	132 (2.5)	496 (2.5)	
Smoking status (%)µ			0.222
Non-smoker	2,538 (42.8)	11,676 (50.8)	
Active smoker	1,868 (31.5)	5,561 (24.2)	
Ex-smoker	1,529 (25.8)	5,741 (25.0)	
Alcohol status (%)Ω			0.096
Non-drinker	1,272 (26.4)	4,628 (25.1)	
Safe use	2,750 (57.0)	10,927 (59.2)	
Hazardous use	686 (14.2)	2,596 (14.1)	
Alcoholism	117 (2.4)	314 (1.7)	
Comorbidities (%)			
Type 2 diabetes	173 (2.8)	822 (3.3)	0.031
Hypertension	521 (8.4)	2,098 (8.5)	0.002
Atrial Fibrillation	37 (0.6)	140 (0.6)	0.004
Angina	50 (0.8)	183 (0.7)	0.008
Myocardial infarction	32 (0.5)	143 (0.6)	0.008
Stroke	31 (0.5)	120 (0.5)	0.002
Heart failure	21 (0.3)	84 (0.3)	<0.001
Chronic liver disease	40 (0.6)	104 (0.4)	0.031
Dementia	65 (1.1)	224 (0.9)	0.015
Rheumatoid arthritis	31 (0.5)	91 (0.4)	0.020
Asthma	1,230 (19.9)	3,913 (15.8)	0.106
Chronic obstructive pulmonary disease	86 (1.4)	301 (1.2)	0.015
Malignancy	105 (1.7)	452 (1.8)	0.010
Irritable bowel disease	56 (0.9)	248 (1.0)	0.010
Chronic kidney disease	98 (1.6)	370 (1.5)	0.007

IQR=Interquartile Range.†Standard Mean Difference (SMD) total AA cases compared with matched controls. SMD> 0.1 indicates meaningful imbalance between AA cohort and matched control cohort.

‡Index of Multiple Deprivation (IMD) missing for n = 127 AA cases and n = 507 matched controls.

¶Ethnicity missing for n = 1,344 AA cases and n = 5,376 matched controls.

¥Region missing for n = 127 AA cases and n = 507 matched controls.

Σ Urban/Rural classification missing for n = 120 AA cases and n = 480 matched controls.

βBody Mass Index (BMI) category missing for n = 905 AA cases and n = 4,571 matched controls.

µSmoking status category missing for n = 248 AA cases and n = 1,740 matched controls.

ΩAlcohol status category missing for n = 1,358 AA cases and n = 6,253 matched controls.

Figure 1. The cumulative lifetime incidence of AA (95% Confidence Interval), A) overall and stratified by B) sex, C) ethnicity, and D) index of multiple deprivation quintile.

Figure 2. The adjusted odds ratios for depressive episode (A), recurrent depressive disorder (B) and anxiety disorder (C) in AA cases compared with matched controls in the overall cohort and sociodemographic subgroups.

IMD=Index of Multiple Deprivation.
Outcomes with fewer than 10 events in total were not examined as specified *a priori* due to lack of power in statistical models. Adjusted odds ratio adjusted for age (3 knot spline), sex, socioeconomic status, ethnicity, region, urban/rural classification, BMI category, smoking status, alcohol status and count of major comorbidities (0-3+); type 2 diabetes, hypertension, atrial fibrillation, angina, acute myocardial infarction, stroke, heart failure, chronic liver disease, dementia, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease, chronic kidney disease, malignancy and inflammatory bowel disease.

Figure 3. Adjusted incident rate ratios for primary care visits (A), and Adjusted hazard ratios for psychology referrals (B), time off work (C) and unemployment (D) in AA cases compared with matched controls in the overall cohort and sociodemographic subgroups.

IMD=Index of Multiple Deprivation.
Outcomes with fewer than 10 events in total were not examined as specified *a priori* due to lack of power in statistical models. Adjusted hazard ratio and adjusted incident ratio adjusted for age (3 knot spline), sex, socioeconomic status, ethnicity, region, urban/rural classification, BMI category, smoking status, alcohol status and count of major comorbidities (0-3+); type 2 diabetes, hypertension, atrial fibrillation, angina, acute myocardial infarction, stroke, heart failure, chronic liver disease, dementia, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease, chronic kidney disease, malignancy and inflammatory bowel disease.