BJD
British Journal of Dermatology

The associated burden of mental health conditions in alopecia areata: a population-based study in UK primary care*

Abby E. Macbeth,[1] Susan Holmes,[2] Matthew Harries,[3,4] Wing Sin Chiu,[5] Christos Tziotzios,[6,7] Simon de Lusignan,[8,9] Andrew G. Messenger[10] and Andrew R. Thompson[11]

[1]Department of Dermatology, Norfolk & Norwich University Hospitals NHS Foundation Trust, Norwich, UK
[2]Alan Lyell Centre for Dermatology, Queen Elizabeth University Hospital, Glasgow, UK
[3]The Dermatology Centre, Salford Royal NHS Foundation Trust, Salford, UK
[4]Centre for Dermatology Research, University of Manchester, MAHSC and NIHR Manchester Biomedical Research Centre, Manchester, UK
[5]Pfizer Ltd, Walton Oaks, Walton on the Hill, Tadworth, KT20 7NS, UK
[6]St John's Institute of Dermatology, King's College London, London, UK
[7]Guy's and St Thomas' NHS Foundation Trust, London, SE1 9RT, UK
[8]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK
[9]Royal College of General Practitioners, Research and Surveillance Centre, London, UK
[10]Department of Dermatology, Royal Hallamshire Hospital, Sheffield, S10 2JF, UK
[11]South Wales Clinical Psychology Training Programme, Department of Psychology, Cardiff University, 11th Floor, Tower Building, 70 Park Place, Cardiff, CF10 3AT, UK

Linked Comment: N. Hunt. Br J Dermatol 2022; **187**:9–10.

Correspondence
Andrew R. Thompson.
Email: thompsona18@cardiff.ac.uk

Accepted for publication
8 February 2022

Funding sources
This research was sponsored by Pfizer. Project management, medical writing and statistical support were provided by Momentum Data, UK, and were funded by Pfizer UK. M.H. is supported by the Manchester NIHR Biomedical Research Centre.

Conflicts of interest
S.deL. is director of the Royal College of General Practitioners Research and Surveillance Centre and has received funding for projects from AstraZeneca, Eli Lilly, GSK, MSD, Sanofi, Novo Nordisk, Sequirus and Takeda – all through his universities and none related to this study. W.S.C. is an employee of Pfizer Ltd. S.H. is principal investigator and C.T. is principal and (national) chief investigator on the Pfizer-funded ALLEGRO clinical trial in alopecia areata. M.H., A.E.M., S.H. and A.G.M. are members of the British Association of Dermatologists guidelines group for alopecia areata.

Data availability

Abstract

Background Alopecia areata (AA) is a common cause of nonscarring hair loss that can have a profound psychological impact.
Objectives To assess the co-occurrence of depression and anxiety in adults with AA compared with the general population, and to evaluate the mental health treatment burden and impact on time off work and unemployment.
Methods In total, 5435 people with newly diagnosed AA in UK primary care were identified from the Oxford Royal College of General Practitioners Research and Surveillance Centre network database, and matched to 21 740 controls. In cases and controls, we compared the prevalence and incidence of depressive episodes, recurrent depressive disorder and anxiety disorder, rates of time off work and unemployment, and, in those with pre-existing mental health conditions, rates of mental health-related prescribing and referral rates. This observational was registered with ClinicalTrials.gov (NCT04239521).
Results Depression and anxiety were more prevalent in people diagnosed with AA than in controls ($P < 0{\cdot}001$). People with AA were also more likely to subsequently develop new-onset depression and anxiety: adjusted hazard ratio (aHR) for recurrent depressive disorder 1·38 [95% confidence interval (CI) 1·13–1·69], depressive episodes aHR 1·30 (95% CI 1·04–1·62) and anxiety disorder aHR 1·33 (95% CI 1·09–1·63); to be issued time off work certificates (aHR 1·56, 95% CI 1·43–1·71); and to be recorded as unemployed (aHR 1·82, 95% CI 1·33–2·49). Higher rates of antidepressant prescribing were also seen in people with AA.
Conclusions People with AA have higher rates of depression and anxiety than those without AA. This impacts deleteriously on mental health treatment burden, time off work and unemployment. Evidence-based mental health treatment programmes are needed for people with AA.

The Royal College of General Practitioners Research and Surveillance Centre 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 a National Health Service research ethics committee may be needed before any data release or other appropriate approval. Researchers wishing to directly analyse the patient-level pseudonymized 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

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).

*Plain language summary available online

DOI 10.1111/bjd.21055

What is already known about this topic?

- Alopecia areata is a common cause of nonscarring hair loss.
- Psychological comorbidity is common in people with alopecia areata, but limited information is available on the co-occurrence and impact of depression and anxiety in this group.

What does this study add?

- Adults newly diagnosed with alopecia areata (5435 in UK primary care) have a higher background prevalence of depression and anxiety than population controls, and are also at 30–38% higher risk of being subsequently diagnosed with new-onset depression and anxiety.
- After alopecia areata diagnosis, people with the condition are more likely to be issued time off work certificates (56% higher) and to be recorded as unemployed (82% higher risk) than population controls.

Alopecia areata (AA) is a chronic inflammatory disease of the hair follicle with a peak incidence in early adulthood.[1] AA results in nonscarring hair loss, and in its more severe forms it can cause total loss of scalp hair (alopecia totalis) or both scalp and body hair (alopecia universalis).[2] It is well recognized that AA can have a profound psychological impact on patients.[3–5] Indeed, the British Association of Dermatologists' guidelines for AA highlight psychosocial impact as a possible complication of the disease, encompassing altered body image, as well as social, work-related and personal problems.[6] This is not surprising when considering the often highly visible manifestations of the disease, the lack of effective long-term treatments,[7] the high rate of relapse,[8] and the fact that for many people, their hair forms an important part of their identity and is intrinsically linked with self-image, self-esteem and social perceptions.[3,4,9]

While it has been established that anxiety and depression are common in people with AA,[10,11] few large cohort studies have evaluated the co-occurrence and impact of these common mental health conditions. A case–control analysis from Taiwan supports a higher prevalence of anxiety and depression in people with AA than in matched population controls,[12] but similar evidence is not available for white populations. A recent UK population-based study identified a bidirectional positive association between major depressive disorder and AA, with depression risk increased in people with AA and AA risk increased in those with depression, but did not evaluate other mental health disorders.[13] Information on mental health-related healthcare utilization in people with AA is lacking, as well as impacts on time off work and unemployment.

We therefore examined whether adults with AA are more likely to present to primary care with anxiety and depression than people without AA. We also investigated the impact of an AA diagnosis by assessing subsequent time off work, unemployment, and mental health prescribing and management.

Patients and methods

Study design and setting

The study protocol was prespecified as part of an AA observational study series,[14] and was registered with ClinicalTrials.gov (NCT04239521). The protocol includes detailed definitions and code lists for all study exposures and outcomes.[14] Clinical information was extracted from the Oxford Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) primary care database. The RCGP RSC cohort is drawn from a large network of general practitioner (GP) practices (293 at the time of the study). While the network of practices currently only covers England, the cohort provides a broadly representative sample of the UK population.[15]

Study population

The study population consisted of all adults aged ≥18 years actively registered with RCGP RCS GP practices between 1 January 2009 and 31 December 2018.

Definition of people with new-onset alopecia areata

AA was defined by the presence of an AA-specific Read code, and no Read codes for an alternative diagnosis (any form of scarring alopecia,[16] traction alopecia, congenital alopecia, androgenetic alopecia, telogen effluvium, tinea capitis, trichotillomania or secondary syphilis of the scalp) in the subsequent 365 days.[14] People with these alternative diagnostic codes were excluded, as were people with a diagnosis of AA prior to the study period.

Definition of matched controls without alopecia areata

Each person with AA was matched at their date of diagnosis (index date) with four controls, by current age, sex and time since practice registration at the GP practice level, using nearest neighbour matching with replacement.[17] Eligible controls comprised actively registered patients without a history of AA and a minimum 1-year registration with their GP practice (to minimize the risk they had a nonrecorded AA diagnosis). After matching, the index date for each control was set to the index date of their matched counterpart.

Mental health outcomes

Three primary common mental health outcomes were evaluated: depressive episodes (DE), recurrent depressive disorder (RDD) and nonphobia-related anxiety disorder (AD). They were identified using validated algorithms,[18] and were chosen as they represent the most common mental health conditions presenting to primary care.[19] We also identified less common mental health conditions: adjustment disorder, agoraphobia, self-harm and suicide attempt/parasuicide.[14]

Healthcare utilization outcomes

Healthcare utilization outcomes comprised mental health prescriptions, mental health management, time off work and unemployment. The following prescriptions were evaluated: selective serotonin reuptake inhibitors (SSRIs) and related medications (serotonin and norepinephrine reuptake inhibitors, and noradrenergic and specific serotonergic antidepressants), tricyclic antidepressants (TCAs) and anxiolytics. Monoamine oxidase inhibitors were not evaluated due to low numbers of patients. Five management outcomes were defined, individually and as a composite, as referrals for cognitive behavioural therapy: counselling, psychotherapy, psychiatry and other psychological interventions through either direct referral or the Improving Access to Psychological Therapies (IAPT) services programme,[20] which forms one of the first-line treatment recommendations for depression. Time off work was defined by the issue of Med 3 certificates of fitness for work,[21] which are issued to provide evidence of a patient being medically unable to perform usual work activities, and thus indicate absenteeism. Unemployment was defined by the presence of a coded unemployment record or issue of forms indicating incapacity from work: IB113 (incapacity benefit) or ESA113 (Employment Support Allowance, which replaced IB113 from January 2011).[14]

Recorded sociodemographic characteristics and clinical features

The burden of common mental health conditions was examined across sociodemographic groups defined by age category, sex, socioeconomic status (SES) and ethnicity. SES was defined using index of multiple deprivation, the national deprivation measure.[22] Ethnicity was categorized as white, black, Asian, mixed or other.[23,24] Other clinical features comprised body mass index, smoking status, alcohol use and common comorbidities: 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.

Statistical analyses

Prevalence of mental health conditions

The prevalences of RDD, DE and AD in cases of AA were compared with those of matched controls, overall and by sociodemographic subgroups defined by age, sex, SES and ethnicity. The prevalences of adjustment disorder, agoraphobia, self-harm and suicide attempt/parasuicide were examined overall in cases of AA and controls; evaluation across subgroups was not conducted due to low numbers.

Incidence of new-onset mental health conditions

Incidence of new-onset mental health conditions was assessed prospectively in cases of AA and matched controls from the index date. To examine only new-onset mental health conditions, only cases of AA without the relevant mental health condition at the index date were included, and we included their matched controls only if they also did not have the relevant mental health condition at the index date. The unadjusted incidence of each common mental health condition was estimated within 2 years of the index date both for cases of AA and for controls, overall by sociodemographic subgroups defined by age, sex, SES and ethnicity. The end of follow-up was defined as the earliest of the study end date (1 January 2018), the date of patient deregistration, the date of death, the date an individual first developed a mental health condition of interest, or 2 years after the index date. The risk of developing each mental health condition was then compared in cases of AA and controls using unadjusted and adjusted (controlling for baseline sociodemographic and clinical features as defined above) Cox proportional hazards models, stratified by matched set (cases of AA vs. matched controls).

Time off work and unemployment

Differences between cases of AA and controls in issue of time off work certificates or records of unemployment in the 1 year following the index date were examined in people of normal working age (18–65 years). The incidence was estimated using the Kaplan–Meier method, and adjusted Cox models to compare cases and controls.

Healthcare utilization: mental health treatment and management outcomes

We examined subsequent mental health treatment and management patterns in the subset of cases of AA and matched controls with a prevalent common mental health condition at their index date. We estimated the proportion of these people who, within 1 year of their index date, were prescribed a mental health medication (treatment outcomes) or were referred for mental health specialist care (management outcomes), using the Kaplan–Meier method.

Sensitivity analysis

To evaluate the magnitude of potential bias from including, as matched controls, people who are registered with GP practices but who do not attend their practice, we repeated the analysis including only controls with a least one primary care consultation in the year preceding their index date. To evaluate the sensitivity of results to the case definition used for AA, we repeated estimation of the prevalence and incidence of common mental health conditions defining cases as people with coded nonspecific alopecia.

All statistical analyses were performed using R v3.4.1 (R Foundation, Vienna, Austria). The study followed the RECORD reporting guidelines.[25]

Results

In total, 5435 adults were diagnosed with AA over the study period and were matched to 21 740 controls (Figure S1; see Supporting Information). Their baseline characteristics and those of their matched counterparts are shown in Table 1. Age (mean 39 years), sex (54% female) and SES were similar in cases of AA and matched controls. Cases of AA were more commonly of Asian, mixed and other ethnicities. Additional clinical characteristics are reported in Table S1 (see Supporting Information).

Table 1 Demographic and clinical characteristics of people newly diagnosed with alopecia areata (AA) and matched controls without AA. Additional baseline clinical characteristics are provided in Table S1 (see Supporting Information)

	Cases of AA	Matched controls
Total number	5435	21 740
Age (years), mean (SD)	38·9 (14·4)	39·1 (15·4)
Age group (years), n (%)		
18–29	1671 (30·7)	7164 (33·0)
30–39	1503 (27·7)	5857 (26·9)
40–49	1063 (19·6)	3887 (17·9)
50–59	631 (11·6)	2134 (9·8)
60–69	374 (6·9)	1513 (7·0)
70–79	149 (2·7)	778 (3·6)
≥ 80	44 (0·8)	407 (1·9)
Sex, n (%)		
Female	2942 (54·1)	11 746 (54·0)
Male	2493 (45·9)	9994 (46·0)
Deprivation quintile, n (%)		
1 (most deprived)	1194 (22·4)	4546 (21·3)
2	1126 (21·1)	4365 (20·4)
3	962 (18·1)	3882 (18·2)
4	995 (18·7)	4122 (19·3)
5 (least deprived)	1047 (19·7)	4443 (20·8)
Ethnicity, n (%)		
White	2920 (67·0)	13 222 (77·4)
Asian	1005 (23·1)	2482 (14·5)
Black	196 (4·5)	831 (4·9)
Mixed	107 (2·5)	282 (1·7)
Other	132 (3·0)	264 (1·5)

Deprivation quintile was missing for 111 cases of AA and 382 matched controls. Ethnicity was missing for 1075 cases of AA and 4659 matched controls.

Common mental health conditions are more prevalent in people diagnosed with alopecia areata than in matched controls

All common mental health conditions were more prevalent in people with AA (RDD 12·3%, DE 19·4%, AD 16·6%) than in matched controls (RDD 8·6%, DE 14·7%, AD 12·9%) (Figure 1). This pattern was consistent across sociodemographic subgroups (Figure 1; and Table S2; see Supporting Information). A higher proportion of people with AA had both depression and anxiety compared with matched controls – RDD and AD: cases of AA n = 379 (7·0%) vs. matched controls n = 1024 (4·8%); DE and AD: cases of AA n = 553 (10·2%) vs. matched controls n = 1573 (7·3%). There was no evidence of a difference in the prevalence of less common mental health conditions between cases of AA and matched controls: prevalence in cases of AA 1·7% for adjustment disorder, 0·3% for agoraphobia, 1·0% for self-harm and 1·0% for suicide attempt/parasuicide; all $P > 0·05$ for a difference in prevalence compared with controls (Table S3; see Supporting Information).

People diagnosed with alopecia areata are also at increased risk of new-onset mental health conditions

In the 2 years after AA diagnosis, 3·5% [95% confidence interval (CI) 3·0–4·1] of cases of AA were diagnosed with new-onset RDD, 3·1% (95% CI 2·5–3·6) with DE and 3·6% (95% CI 3·0–4·2) with AD (Figure 2). In adjusted analysis, there was evidence of a similarly increased risk of all three common mental health conditions in people diagnosed with AA compared with controls: adjusted hazard ratio (aHR) range 1·30–1·38, all $P < 0·05$

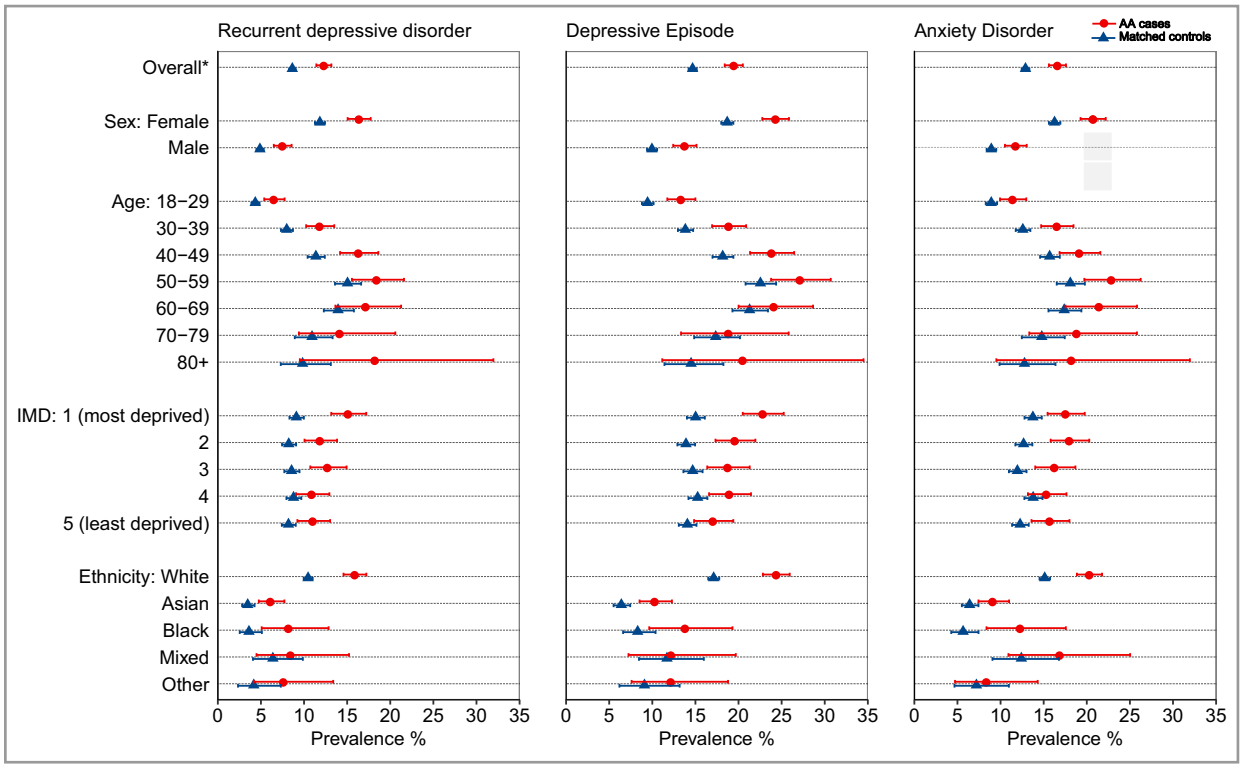

Figure 1 Prevalence of common mental health conditions in cases of alopecia areata (AA) and matched controls without AA. Point estimates represent the proportion with each mental health condition in each subgroup. Bars represent 95% confidence intervals. The data underlying the plot are reported in Table S2 (see Supporting Information). Overall P-values for difference in populations: recurrent depressive disorder $P < 0{\cdot}001$, depressive episodes $P < 0{\cdot}001$, anxiety disorder $P < 0{\cdot}001$. IMD, index of multiple deprivation.

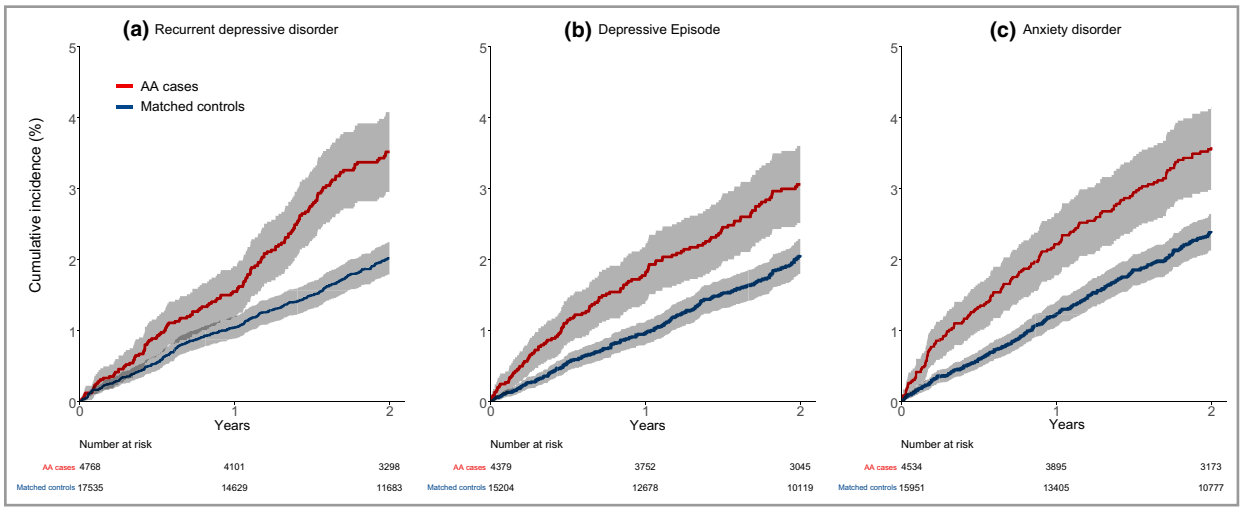

Figure 2 Kaplan–Meier plots for the cumulative incidence of new-onset common mental health conditions in newly diagnosed cases of alopecia areata (AA) and matched controls. People with a pre-existing record of each mental health condition (prevalent people) are excluded from the analysis of that condition. Grey shading represents 95% confidence intervals.

(Table 2). Overall, 1·1% of cases of AA developed both anxiety and depression (either RDD or DE) within 2 years, compared with 0·6% of controls (aHR 1·46, 95% CI 1·00–2·12; $P = 0{\cdot}051$). Across sociodemographic subgroups, differences in incidence had a similar pattern to differences in prevalence, except that there was no evidence of an increased incidence of presentation of any common mental health condition in people with AA of Asian ethnicity (Figure S2 and Table S4; see Supporting Information).

Table 2 Associations between alopecia areata (AA) and risk of new-onset common mental health conditions

	Number of patients	Person-years at risk	Events	Unadjusted	Sex and age adjusted	Adjusted[a]
Recurrent depressive disorder						
Matched controls	17 535	29 308	302	1·00 (ref)	1·00 (ref)	1·00 (ref)
Cases of AA	4768	8188	147	1·74 (1·43–2·12)***	1·72 (1·42–2·10)***	1·38 (1·13–1·69)**
Depressive episodes						
Matched controls	15 204	25 399	264	1·00 (ref)	1·00 (ref)	1·00 (ref)
Cases of AA	4379	7519	120	1·54 (1·24–1·91)***	1·53 (1·23–1·90)***	1·30 (1·04–1·62)*
Anxiety disorder						
Matched controls	15 951	26 845	328	1·00 (ref)	1·00 (ref)	1·00 (ref)
Cases of AA	4534	7804	147	1·54 (1·27–1·88)***	1·53 (1·26–1·86)***	1·33 (1·09–1·63)**

[a]Adjusted for age, sex, index of multiple deprivation quintile, ethnicity, body mass index category, smoking status, alcohol use category, number of visits in year prior to diagnosis, 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 stage 3–5, malignancy and inflammatory bowel disease. ***$P < 0·001$, **$P < 0·01$, *$P < 0·05$. There was no significant improvement in the overall model fit when fitting age with a restricted cubic spline (three knots) instead of as linear ($P = 0·20$).

Time off work and unemployment are more common in people with alopecia areata than in matched controls

Time off work certificates were more frequently issued to people with AA (13·0% within a year of diagnosis) than matched controls (7·9%) (aHR 1·56, 95% CI 1·43–1·71; $P < 0·001$). Similarly, people with AA were more likely to have a record of unemployment in the year after diagnosis (1·3% of cases of AA, 0·6% of matched controls; aHR 1·82, 95% CI 1·33–2·49).

Alopecia areata is associated with increased prescribing of antidepressants in people with mental health conditions

Comparing cases of AA and controls with prevalent RDD, DE or AD, prescribing of SSRI and related antidepressants and TCA treatments was more common in people with AA than in controls (Table 3). Prescribing of anxiolytics was similar in both groups. Less than 10% of either cases of AA or controls with a recorded mental health condition were referred for nonpharmacological management; overall referral rates were slightly higher in people with AA (Table 3).

Sensitivity analysis

When controls with no consultation in the year prior to their index date were excluded (approximately 33%), a positive association remained between AA and RDD (aHR 1·30, 95% CI 1·05–1·60) (Table S5; see Supporting Information). Associations for DE and AD were consistent with the primary analysis but did not reach statistical significance: aHR 1·17 (95% CI 0·93–1·47) and 1·18 (95% CI 0·96–1·45), respectively. Differences in the prevalence and incidence of common mental health conditions were similar when the analysis was repeated including only people with nonspecific alopecia as cases (Tables S6–8; see Supporting Information).

Discussion

This study of 5435 adults with AA, compared with age-and-sex-matched population controls, demonstrates that people diagnosed with AA are more likely to have a pre-existing diagnosis of depression and anxiety, and are also at 30–38% higher risk of being subsequently diagnosed with new-onset depression or anxiety. We also show that people with AA have higher rates of time off work and are more likely to be recorded as unemployed, and, if they have anxiety or depression, are more likely to be prescribed SSRIs and related antidepressants or TCA treatment.

Our analysis provides the first evaluation of common mental health conditions in people with AA in a predominantly white population. Our finding that people with AA have a higher prevalence and incidence of common mental health conditions corroborates and extends the findings of previous smaller studies from both primary and secondary care settings.[11,12,26–28] A recent systematic review concluded that patients with AA are likely to experience anxiety and depression at a rate higher than controls, and at rates similar to those seen in other chronic skin conditions including psoriasis and atopic dermatitis, although the review included only one large ($n > 400$) cohort analysis (from Taiwan)[12] in the 28 studies evaluated.[10]

The question of 'which comes first?' has been much discussed when considering AA and mental health conditions. We found that anxiety and depression are more prevalent at AA diagnosis, and that people diagnosed with AA are more likely to be diagnosed with new-onset anxiety and depression. While our study was not designed to ask this 'which comes first' question, our results support a recent primary care-based UK cohort study suggesting a bidirectional association between major depressive disorder and AA: patients with AA had a 34% increased risk of developing major depressive disorder, while patients with major depressive disorder were at 90% increased risk of developing AA.[13] Similarly to our study, the earlier

Table 3 Healthcare utilization in cases of alopecia areata (AA) and matched controls with a prevalent common mental health condition. This analysis includes only the subset of cases of AA and controls with a prevalent common health condition at their index date (the date of diagnosis for cases of AA, the date of diagnosis of their matched counterparts for matched controls). The data represent the proportion of people within each group with the outcome of interest within 1 year of the index date, expressed as percentages with 95% confidence intervals

	Recurrent depressive disorder		Depressive episodes		Anxiety disorder	
	Matched controls	Cases of AA	Matched controls	Cases of AA	Matched controls	Cases of AA
Number of patients	1878	667	3190	1056	2802	901
Medications						
SSRIs[a]	46·4 (44·0–48·6)	51·0 (47·0–54·7)	33·7 (32·0–35·4)	40·7 (37·6–43·6)	29·9 (28·2–31·6)	34·8 (31·5–37·8)
Tricyclic antidepressants	15·3 (13·7–17·0)	17·4 (14·4–20·3)	10·8 (9·7–11·9)	12·6 (10·6–14·6)	9·7 (8·5–10·8)	11·9 (9·7–14·0)
Anxiolytics	9·0 (7·6–10·3)	9·0 (6·7–11·1)	6·4 (5·6–7·3)	7·1 (5·5–8·7)	7·6 (6·6–8·6)	9·0 (7·1–10·9)
Nonpharmacological management						
Any nonpharmacological management	7·16 (5·96–8·35)	8·35 (6·19–10·5)	5·71 (4·88–6·53)	7·00 (5·42–8·54)	5·04 (4·20–5·88)	7·06 (5·33–8·76)
Cognitive behavioural therapy	0·17 (0·00–0·36)	0·15 (0·00–0·44)	0·26 (0·08–0·45)	0·19 (0·00–0·45)	0·22 (0·04–0·40)	0·46 (0·01–0·91)
Counselling	0·52 (0·18–0·86)	0·76 (0·09–1·43)	0·53 (0·27–0·79)	0·67 (0·17–1·17)	0·41 (0·17–0·65)	0·68 (0·14–1·22)
Psychotherapy	0·11 (0·00–0·26)	0·00 (0·00–0·00)	0·17 (0·02–0·31)	0·20 (0·00–0·47)	0·12 (0·00–0·25)	0·23 (0·00–0·55)
Psychiatric review	6·31 (5·17–7·43)	7·44 (5·39–9·44)	4·81 (4·05–5·57)	5·95 (4·49–7·39)	4·33 (3·55–5·11)	5·83 (4·25–7·39)
Other psychological therapy or IAPT	0·45 (0·14–0·76)	0·00 (0·00–0·00)	0·33 (0·13–0·54)	0·19 (0·00–0·45)	0·19 (0·02–0·35)	0·22 (0·00–0·53)

IAPT, Improving Access to Psychological Therapies. [a]Selective serotonin reuptake inhibitors (SSRIs) also included related antidepressants: serotonin and norepinephrine reuptake inhibitors, and noradrenergic and specific serotonergic antidepressants.

case–control analysis in Taiwan found that 50% of psychological presentations or disorders preceded the diagnosis of AA, while the other 50% developed after the diagnosis.[12]

Among cases of AA, we observed that all common mental health conditions were more prevalent in older adults and women. This is concordant with the previous Taiwanese analysis, which found that the highest risks for anxiety were observed in patients diagnosed with AA over the age of 40 years.[12] The higher presentation of mental health conditions in people of white ethnicity compared with those in other ethnic groups is concordant with previous general population studies and studies of other diseases.[29,30] Further qualitative studies are needed to understand the sociodemographic differences observed.

Strengths of our study include the large population-representative sample, and the validated approach to identify common mental health conditions. A limitation of our study is that it is possible that people with AA may have higher contact with primary care providers (to seek treatment for their AA or because of increased susceptibility to mental health conditions), which may result in data capture biases leading to overestimation of the association between AA and mental health conditions. Another limitation, as with all studies using routine clinical data, is the possibility of incomplete coding. Some mental health referrals will have been coded as unspecified without mention of clinical specialty and would therefore not have been included in our estimates. As well as incomplete coding, low rates of psychological and IAPT referrals may relate to lack of dermatology specialization within IAPT and other psychological services, which means that GPs and patients may not be aware that the service might be relevant.

Our analysis is not able to determine whether the identified effects are causal. Any study of this nature is potentially subject to confounding associated with variables that have not been measured. While we have adjusted for a wide variety of common comorbidities in our analysis, it has not been possible to adjust for all possible comorbid conditions and therefore it is possible that some of the observed associations may be attributable in part to a third as yet unidentified factor, such as a specific immune reaction or type of coping style.

We were not able to see the reason why prescriptions were issued, therefore we cannot be sure that they were for anxiety or depression (SSRIs and TCAs are also licensed for other indications). The use of Read codes to identify unemployment is likely to underestimate unemployment prevalence but is suitable for providing a comparison with controls. We also lacked information on the indication for and duration of time off work, or the reason for unemployment, meaning that, despite adjustment for a wide range of sociodemographic factors and comorbidities, we cannot be certain whether the increased burden in people with AA relates to comorbid mental health conditions or AA itself.

Our sensitivity analysis in people with nonspecific alopecia suggested that the associations between AA and mental health conditions are not limited to AA but may also occur in all forms of hair loss. However, as the type or cause of alopecia was not recorded in these patients, we were unable to explore this further, and this warrants further investigation in future studies. We also found that the coding of the distribution and extent of AA was poorly recorded in the primary care record and therefore was not available for subgroup analysis in our study. For example, we were unable to determine whether

there are differences in mental health impact in patients with patchy AA, alopecia totalis or alopecia universalis. Finally, we included only adults with AA, meaning the impact of AA on mental health in children and adolescents cannot be concluded from our study.

The common co-occurrence of mental health conditions in people with AA in our study suggests that evidence-based mental health treatment programmes are urgently needed to identify those who do experience psychological distress and to provide appropriate support. Further research is needed to find out whether treatments for the alopecia itself (both medical interventions and treatments that involve changing one's appearance through, for example, wigs and tattoos) reduce the psychological burden associated with the condition. In addition, further studies are needed to develop and test psychological therapies and interventions for use with AA. Consideration is also needed as to where to locate these treatments (e.g. within psychological services) and whether they would be better placed within specific psychodermatology services. The possible bidirectional nature of the association between AA and common mental health disorders suggests that further research is warranted to determine whether active treatment of AA may improve long-term mental health outcomes.

In conclusion, our study highlights the increased burden of comorbid mental health conditions in patients with AA in primary care. This identifies a need for GPs and dermatologists to routinely screen for psychological distress when reviewing patients with AA and to consider treatment for mental health conditions alongside the physical aspects of the disease. Further research is needed to examine the pathophysiological basis for the possible bidirectional causal association between AA and common mental health disorders, as well as the impact of AA treatments on patients' psychological outcomes.

Acknowledgments

We thank the patients and practices who are members of the Oxford RCGP RSC network, who allow their data to be shared for surveillance, research, quality improvement and education. We acknowledge the collaboration of the primary care computerized medical record system providers EMIS, TPP, InPractice Systems, Microtest and Apollo Medical in facilitating the RCGP RSC data; data access support from the RCGP RSC team of the University of Oxford and University of Surrey; and project management, medical writing and statistical input from Anita Lynam, Louise Jordan and Anna-Louise Dennis of Momentum Data, and project management support from Filipa Ferreira of the University of Oxford and University of Surrey.

References

1 Harries M, Macbeth AE, Holmes S *et al.* The epidemiology of alopecia areata: a population-based cohort study in UK primary care. *Br J Dermatol* 2022; **186**:257–65.
2 Gilhar A, Etzioni A, Paus R. Alopecia areata. *N Engl J Med* 2012; **366**:1515–25.
3 Hunt N, McHale S. The psychological impact of alopecia. *BMJ* 2005; **331**:951–3.
4 Alfonso M, Richter-Appelt H, Tosti A *et al.* The psychosocial impact of hair loss among men: a multinational European study. *Curr Med Res Opin* 2005; **21**:1829–36.
5 Titeca G, Goudetsidis L, Francq B *et al.* 'The psychosocial burden of alopecia areata and androgenetica': a cross-sectional multicentre study among dermatological out-patients in 13 European countries. *J Eur Acad Dermatol Venereol* 2020; **34**:406–11.
6 Messenger AG, McKillop J, Farrant P *et al.* British Association of Dermatologists' guidelines for the management of alopecia areata 2012. *Br J Dermatol* 2012; **166**:916–26.
7 Baran R, Dawber RP, Haneke E. Hair and nail relationship. *Skinmed* 2005; **4**:18–23.
8 Harries MJ, Sun J, Paus R, King LE. Management of alopecia areata. *BMJ* 2010; **341**:c3671.
9 Montgomery K, White C, Thompson A. A mixed methods survey of social anxiety, anxiety, depression and wig use in alopecia. *BMJ Open* 2017; **7**:e015468.
10 Toussi A, Barton VR, Le ST *et al.* Psychosocial and psychiatric comorbidities and health-related quality of life in alopecia areata: a systematic review. *J Am Acad Dermatol* 2021; **85**:162–75.
11 Singam V, Patel KR, Lee HH *et al.* Association of alopecia areata with hospitalization for mental health disorders in US adults. *J Am Acad Dermatol* 2019; **80**:792–4.
12 Chu SY, Chen YJ, Tseng WC *et al.* Psychiatric comorbidities in patients with alopecia areata in Taiwan: a case–control study. *Br J Dermatol* 2012; **166**:525–31.
13 Vallerand IA, Lewinson RT, Parsons LM *et al.* Assessment of a bidirectional association between major depressive disorder and alopecia areata. *JAMA Dermatol* 2019; **155**:475–9.
14 Harries M, Macbeth A, Holmes S *et al.* Epidemiology, management, and the associated burden of mental health illness, atopic and autoimmune conditions, and common infections in alopecia areata: protocol for an observational study series. *BMJ Open* 2021; **11**:e045718.
15 Correa A, Hinton W, McGovern A *et al.* Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) sentinel network: a cohort profile. *BMJ Open* 2016; **6**:e011092.
16 Olsen EA, Bergfeld WF, Cotsarelis G *et al.* Summary of North American Hair Research Society (NAHRS)-sponsored Workshop on Cicatricial Alopecia, Duke University Medical Center, February 10 and 11, 2001. *J Am Acad Dermatol* 2003; **48**:103–10.
17 Ho D, Imai K, King G, Stuart E. MatchIt: nonparametric preprocessing for parametric causal inference. *J Stat Softw* 2011; **42**(8):1–28.
18 John A, McGregor J, Fone D *et al.* Case-finding for common mental disorders of anxiety and depression in primary care: an external validation of routinely collected data. *BMC Med Inform Decis Mak* 2016; **16**:35.
19 Kessler RC, Chiu WT, Demler O *et al.* Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005; **62**:617–27.
20 Thornicroft G. Improving access to psychological therapies in England. *Lancet* 2018; **391**:636–7.
21 Chan T, Cohen A, de Lusignan S. Using routine data to conduct small area health needs assessment through observing trends in demographics, recording of common mental health problems (CMHPs) and sickness certificates: longitudinal analysis of a northern and London locality. *Inform Prim Care* 2010; **18**:273–82.

22 Department for Communities and Local Government. English indices of deprivation 2015. Available at: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015 (last accessed 21 March 2022).
23 Office for National Statistics. Ethnicity. Available at: https://www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/ethnicity (last accessed 21 March 2022).
24 Tippu Z, Correa A, Liyanage H *et al*. Ethnicity recording in primary care computerized medical record systems: an ontological approach. *J Innov Health Inform* 2017; **23**:920.
25 Benchimol EI, Smeeth L, Guttmann A *et al*. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLOS Med* 2015; **12**:e1001885.
26 Sellami R, Masmoudi J, Ouali U *et al*. The relationship between alopecia areata and alexithymia, anxiety and depression: a case–control study. *Indian J Dermatol* 2014; **59**:421.
27 Ruiz-Doblado S, Carrizosa A, García-Hernández MJ. Alopecia areata: psychiatric comorbidity and adjustment to illness. *Int J Dermatol* 2003; **42**:434–7.
28 Baghestani S, Zare S, Seddigh SH. Severity of depression and anxiety in patients with alopecia areata in Bandar Abbas, Iran. *Dermatol Reports* 2015; **7**:6063.
29 Kuan V, Denaxas S, Gonzalez-Izquierdo A *et al*. A chronological map of 308 physical and mental health conditions from 4 million individuals in the English National Health Service. *Lancet Digit Health* 2019; **1**:e63–77.
30 Ali S, Davies MJ, Taub NA *et al*. Prevalence of diagnosed depression in South Asian and white European people with type 1 and type 2 diabetes mellitus in a UK secondary care population. *Postgrad Med J* 2009; **85**:238–43.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Figure S1 Flow diagram showing the eligibility and final study population.

Figure S2 Incidence of new-onset common mental health conditions in cases of alopecia areata and matched controls.

Table S1 Additional clinical characteristics of people newly diagnosed with alopecia areata and matched controls.

Table S2 Prevalence of common mental health conditions in cases of alopecia areata and matched controls.

Table S3 Prevalence of additional mental health conditions in cases of alopecia areata and matched controls.

Table S4 Incidence of new-onset common mental health conditions in cases of alopecia areata and matched controls.

Table S5 Associations between alopecia areata and incident mental health conditions, excluding matched controls with no consultation in the year prior to diagnosis.

Table S6 Prevalence of common mental health conditions, with cases of alopecia areata defined as people newly diagnosed with nonspecific alopecia, matched to controls without nonspecific alopecia.

Table S7 Incidence of new-onset common mental health conditions in cases of nonspecific alopecia and matched controls.

Table S8 Associations between nonspecific alopecia and risk of new-onset common mental health conditions.

Video S1 Author video.