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Comorbidity of rosacea and depression: an analysis of the National Ambulatory Medical Care Survey and National Hospital Ambulatory Care Survey—Outpatient Department data collected by the U.S. National Center for Health Statistics from 1995 to 2002

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Summary

Background Psychogenic factors have been considered to be important in the exacerbation and possibly the onset of rosacea. However, there are very few studies that have reported conclusive findings.
Objectives To examine the association between rosacea and major depressive disease, a common and usually treatable psychiatric disorder.
Methods Data from 1995 to 2002, collected by the National Ambulatory Medical Care Survey and the outpatient component of the National Hospital Ambulatory Care Survey, which are both nationally representative surveys of healthcare visits in the U.S.A., were studied. The basic sampling unit in both surveys is the patient visit or encounter. A 'Rosacea' variable was created by grouping all rosacea (ICD-9-CM code 695.3) visits and a 'Depression' variable was created by grouping the patient visits related to major depressive disorder (ICD-9-CM codes 296.2, 296.3 and 311). As alcohol abuse has been implicated in rosacea, and alcohol can confound symptoms of depression, an 'Alcohol' variable was created by grouping all ICD-9-CM codes related to alcohol dependence and abuse (codes 303, 303.0, 303.9 and 305.0). All analyses were conducted using the Complex Samples module of SPSS version 13, to account for the multistage probability sampling design used to collect the data.
Results The weighted data were representative of over 608 million dermatology visits between 1995 and 2002. Logistic regression analysis using 'Rosacea' as the dependent variable and age, sex, 'Alcohol' and 'Depression' as independent variables revealed that the odds ratio for depressive disease in the rosacea group was 4·81 (95% confidence interval 1·39–16·62). The association between 'Alcohol' and 'Rosacea' was not significant.
Conclusions The comorbidity between major depressive disease and rosacea may have important clinical implications. Alcohol abuse does not appear to play a significant role in this association.

Psychogenic factors have been considered to be important in the exacerbation and possibly the onset of rosacea.[1,2] Factors such as major stressful life events, an anxious and immature personality with excessive feelings of guilt and shame, and social anxiety secondary to easy blushing have all been implicated; however, studies[1–12] have reported inconclusive findings. One controlled study[5] involving 70 patients reported higher depression scores among patients with rosacea, and the depression was attributed to the cosmetic impact of rosacea. More conclusive findings involve the reaction of patients to the cosmetic impact of rosacea, wherein 75% of patients with rosacea reported low self-esteem and about 70% reported feeling embarrassed and frustrated;[8,9,13] treatment of the rosacea improved these symptoms. A more recent case study[14] has

discussed a patient with rosacea whose concerns about the cosmetic disfigurement reached delusional proportions. Alcohol abuse has been implicated to be a factor in rosacea; however, this potentially stigmatizing association has not been proven by controlled studies.[15,16] In order to evaluate further the role of psychopathological factors in rosacea, we examined the relation between rosacea and depressive disease, a common and treatable psychiatric disorder.

Materials and methods

Data collected between 1995 and 2002 by the National Ambulatory Medical Care Survey (NAMCS)[17–25] and the National Hospital Ambulatory Care Survey (NHAMCS),[17,26–33] which are both nationally representative samples of healthcare visits in the U.S.A., were studied. The U.S. Bureau of the Census acts as the field data collection agent for the NAMCS and NHAMCS. NAMCS and NHAMCS are both national surveys conducted by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC).[17]

The NAMCS[17] collects information on care provided by office-based physicians and the actual data collection is carried out by the physician aided by his or her office staff when possible. The basic sampling unit for the NAMCS is the physician–patient encounter or visit. Only visits to the offices of nonfederally employed physicians classified by the American Medical Association or the American Osteopathic Association as 'office-based, patient-care' are included, except for physicians in the specialties of anaesthesiology, radiology and pathology. Sampling for the NAMCS proceeds according to a three-stage probability design that involves probability samples of primary sampling units (PSUs), physician practices within PSUs, and patient visits within practices. The first-stage sample includes 112 PSUs. PSUs are geographical segments composed of counties, groups of counties, county equivalents such as parishes or independent cities or towns and townships within the 50 states of the U.S.A. and the District of Columbia. The second stage consists of a probability sample of practising physicians selected from the master files of the American Medical Association and the American Osteopathic Association. Within each PSU all eligible physicians are stratified by 15 groups including dermatology, psychiatry, general and family practice, osteopathy, internal medicine, paediatrics, general surgery, obstetrics and gynaecology, orthopaedic surgery, cardiovascular diseases, urology, neurology, ophthalmology, otolaryngology and a residual category of all other specialties. The third and final stage involves the random selection of patient visits by the physician during a 1-week period. The sampling rate varies for this final step from 100% of the sample for 'very small' practices to a 20% sample for 'very large' practices as determined in a presurvey interview. Physicians record information on visits and record up to three diagnoses for each visit, over the randomly selected 1-week period. The visits include both scheduled and unscheduled patients but not cancellations or missed visits. The sampling procedure for the NAMCS is designed so that about 30 patient record forms are completed during the assigned reporting week.

The NHAMCS[17] uses similar methods to obtain a national probability sample of visits to hospital outpatient departments of general, short stay, nonfederal and noninstitutional hospitals in the 50 states of the U.S.A. and the District of Columbia. The basic sampling unit for the NHAMCS is the patient visit or encounter. The actual visit sampling and data collection for the NHAMCS are primarily the responsibility of the hospital staff. The NHAMCS includes data from both the Outpatient Department (OPD) and the Emergency Department; for our study of patients with rosacea, only data from the OPD were analysed. The NHAMCS-OPD uses a four-stage probability design with samples of PSUs (described above), hospitals within PSUs, clinics within hospitals, and patient visits within clinics. Within each hospital, either all outpatient clinics or a sample of such units are selected. If a hospital has more than five clinic sampling units then five are randomly selected, otherwise all clinics are sampled. Clinics are considered to be eligible for the survey if ambulatory medical care is provided under the supervision of a physician and under the auspices of the hospital. A visit is defined as a direct personal exchange between a patient and a physician, or a staff member operating under a physician's direction, for the purpose of seeking care and rendering health services. Patient visits are selected over a randomly assigned 4-week reporting period, and up to three diagnoses are recorded for each visit. The target number of patient record forms to be completed for OPDs in each hospital was around 200.

To preserve the confidentiality of participating patients and physicians, all survey data in the databases are masked through the inclusion of weighting variables for stratification, sampling unit or PSU, and patient visits.[17] Using these masked weighting variables provided by the NCHS, the two databases analysed in this report represent a weighted estimate of over 608 million dermatology patient visits to private office-based physicians and hospital outpatient clinics between 1995 and 2002.

Variables studied

Demographic factors such as sex, age and race were examined and controlled for in our analyses, as they may confound the prevalence of both rosacea and depression.

Regarding the ICD-9-CM (*International Classification of Diseases, 9th Revision, Clinical Modification*)[34] Dermatology codes used to classify dermatology visits: the physicians coded up to three diagnoses for each visit, and a patient who received one or more dermatological diagnoses was categorized in the 'dermatology visits' group. The diagnostic codes of the ICD-9-CM that were used to diagnose dermatological disorders included the following: all codes under 'Diseases of the Skin and Subcutaneous Tissue', i.e. all codes between 680 and 709; several codes under 'Infectious and Parasitic Diseases' that relate to the skin; several codes under 'Neoplasms' that relate to the skin; several codes under 'Nervous System and Sense Organs'

relating to the eyelids and periocular skin; and 'hyperhidrosis' under 'Symptoms, Signs and Ill-defined Conditions'.

The 'dermatology visits' group was then categorized into those who were diagnosed with 'Rosacea' (ICD-9-CM code 695.3) for any one of their three diagnoses during their visit to the physician's office or outpatient clinic ('Rosacea' group), and the rest of the dermatology group ('No Rosacea' group). The ICD-9-CM code 695.3 includes 'acne erythematosa', 'acne rosacea', 'perioral dermatitis' and 'rhinophyma', and defines rosacea as a 'chronic skin disease, usually of the face, characterized by persistent erythema and sometimes by telangiectasia with acute episodes of oedema, engorgement papules, and pustules'.[34]

Regarding the ICD-9-CM Psychiatry codes used to classify psychiatry visits: patients who received one or more psychiatric diagnoses were classified under the 'psychiatry visits' group. The psychiatric diagnostic codes included all ICD-9-CM codes between 290 and 319 under 'Mental Disorders'.[34]

The depression diagnostic codes in the ICD-9-CM that included major depressive disease were grouped into the 'Depression' variable, and the remaining psychiatric codes were categorized as the 'No Depression' group. The ICD-9-CM psychiatric diagnostic groups and codes used for the 'Depression' variable were as follows: 'Major Depressive Disorder, Single Episode', 'Major Depressive Disorder, Recurrent Episode' and 'Depressive Disorder, Not Elsewhere Classified', a category which represents several features of major depressive disorders that do not meet all the diagnostic criteria for major depressive disorder (ICD-9-CM codes 296.2, 296.3 and 311).

As alcohol abuse has been implicated in rosacea, and alcoholism may be a confounding factor in depressive disease, the association between alcohol and rosacea was also studied. The following ICD-9-CM diagnostic codes[34] for both alcohol dependence and alcohol abuse were included in the 'Alcohol' variable: 'Alcohol dependence syndrome', 'Acute alcohol intoxication' and 'Other and unspecified alcohol dependence' which includes 'Chronic alcoholism and dipsomania' and 'Alcohol abuse' (codes 303, 303.0, 303.9 and 305.0).

Statistical analysis

All analyses were conducted using the Complex Samples module of SPSS version 13 in order to account for the multistage probability sampling design used by the NAMCS and the NHAMCS.[35] The data from both the NAMCS and the NHAMCS were merged into one dataset. Standard errors for all estimates were computed using the Complex Samples module.[35] To provide national estimates for the U.S.A., all analyses incorporated the masked sampling weights (described above) which address the strata, PSUs and patient visits and account for the differential probability of selection and nonresponse. The weighting variables, which were provided in the dataset, are purposely masked to ensure patient confidentiality. All statistical analyses were carried out using the Complex Samples module of SPSS version 13. Most traditional statistical packages assume that the data represent a simple random sample from the study population. Unlike a simple random sample, a complex sample, such as our data, can have features such as stratification which involves the selection of samples within nonoverlapping subgroups of the population, and clustering which involves the selection of groups of sampling units (e.g. patient visits) or clusters (e.g. hospitals). The Complex Samples module accounts for the increase in variance as a result of this multistage sampling process. Descriptive statistics were examined (Table 1) using the Complex Samples module, to obtain estimates that were more representative of the population at large. As both rosacea and depression may be confounded by demographic factors such as age, sex and race, a logistic regression analysis (Table 2) was used, using 'Rosacea' as the dependent variable, and age, sex, 'Depression' and 'Alcohol' as independent variables. Race was not used in the regression model as over 95% of the patients with rosacea

Table 1 Age, sex and race of the groups with rosacea and depression

Group	Age (years), mean ± SEM; Age (years), mean ± SEM by sex	Sex, mean ± SEM	Race, mean ± SEM
Rosacea	50·83 ± 0·82 Males: 56·11 ± 1·39 Females: 48·55 ± 1·01 ($P < 0·01$)	Female 69·8 ± 1·9% Male 30·2 ± 1·9%	'White' 95·8 ± 0·9% 'Black/African American' 2·4 ± 0·8% 'Asian or Native Hawaiian/Other Pacific Islander' 1·3 ± 0·4%' American Indian/Alaska Native' 0·2 ± 0·2% 'More than 1 race reported/Other' 0·3 ± 0·3%
Depression	46·40 ± 0·37 Males: 45·34 ± 0·54 Females: 46·90 ± 0·39 ($P < 0·01$)	Female 67·8 ± 0·7% Male 32·2 ± 0·7%	'White' 90·3 ± 0·8% 'Black/African American' 7·4 ± 0·7% 'Asian or Native Hawaiian/Other Pacific Islander' 1·8 ± 0·4% 'American Indian/Alaska Native' 0·4 ± 0·1% 'More than 1 race reported/Other' 0·2 ± 0·2%

Results represent population estimates with SEM, derived after using weights provided for the multistage sampling used by the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Care Survey, respectively. The Complex Samples module of SPSS version 13 was used for the analysis.

Table 2 Results of logistic regression analysis using dichotomous 'Rosacea' variable as dependent measure

Independent variable	Wald statistic (Wald F)	Significance level (Bonferroni correction)	Odds ratio with 95% confidence interval
Depression	6·23	0·013	4·81 (1·39–16·62)
Alcohol	2·89	0·091	10·64 (0·68–165·41)
Age (age 40–70 years or 'middle age' vs. the rest)	18·20	< 0·0001	92·83 (11·44–753·47)
Sex (female vs. male)	0·33	0·57	1·63 (0·30–8·73)

Corrected model significant at $P < 0{\cdot}0001$, with pseudo R^2 (Nagelkerke's) = 0·242; logistic regression carried out with Complex Samples module of SPSS version 13.

were classified as 'White'. An odds ratio (OR) was calculated for all independent variables in the logistic regression equation.[36] The age variable was dichotomized into the 'middle aged' (age ≥ 40 years and ≤ 70 years) vs. all other ages, in order to obtain an OR. The decision to use these cut-offs was based upon the age distribution (Fig. 1) of the Rosacea and Depression groups, among both of which the largest numbers of patient visits were between ages 40 and 70 years.

Results

Analysis of the NAMCS and the NHAMCS-OPD data revealed that there were 13 978 704 visits for rosacea (ICD-9-CM code 695.3) among the 608 744 725 dermatology private office and hospital outpatient visits between 1995 and 2002. Therefore, 2·3% of all dermatology visits were associated with a diagnosis of rosacea. The overall number of office and outpatient visits for depression between 1995 and 2002, as measured by the 'Depression' variable, was 186 771 685, which represented 29·9% of all psychiatry visits. Some of the demographic characteristics of the Rosacea and Depression groups are summarized in Table 1. The histograms showing the age distributions of the Rosacea and Depression groups are shown in Figure 1.

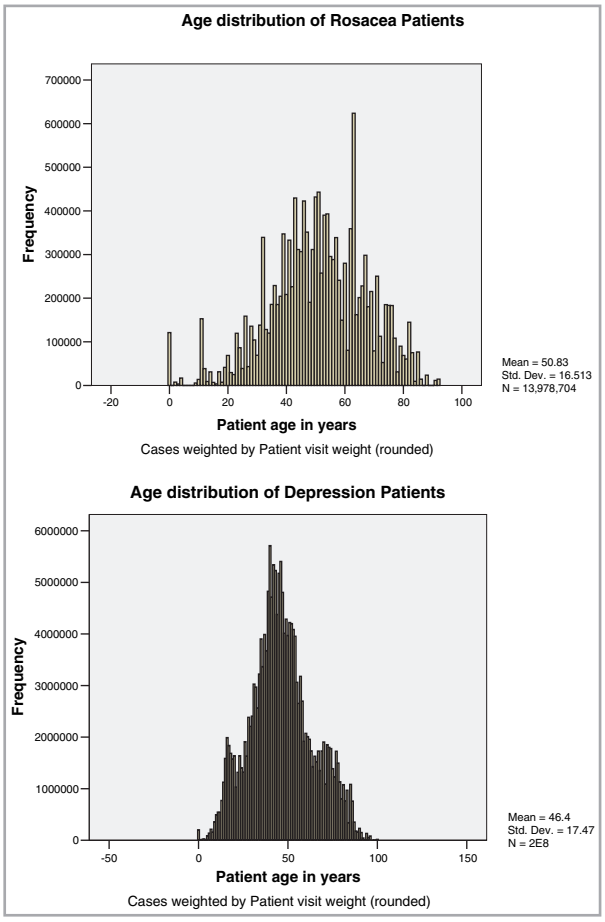

Fig 1. Age distributions of the Rosacea and Depression Groups.

Among the patients with rosacea, 145 107 (1·04%) had a comorbid psychiatric diagnosis, and of these patients 94 521 (i.e. 0·68% of all patients with rosacea and 65·1% of rosacea patients with a comorbid psychiatric diagnosis) also had a diagnosis of depression as defined by the 'Depression' variable above. This is much higher than the 29·9% prevalence of depression among all psychiatric patient visits.

The results of the logistic regression analysis are summarized in Table 2. The OR of having depressive disease ('Depression' variable) from the logistic regression model (Table 2) was 4·81 [95% confidence interval (CI) 1·39–16·62]. The OR for alcohol abuse was 10·64 (95% CI 0·68–165·41) and was not significant. The OR for age was significant at 92·83 (95% CI 11·44–753·47) when the 'middle age' group between ages 40 and 70 years was contrasted with 'all other ages'.

Discussion

We examined the comorbidity between rosacea and depressive illness among over 13·9 million patient visits to physicians' private offices and hospital outpatient clinics between 1995 and 2002, for rosacea as diagnosed by the ICD-9-CM[34] diagnostic code 695.3. The data were obtained from the NAMCS and NHAMCS, which are a nationally representative sample of healthcare visits in the U.S.A., carried out by the NCHS at the CDC.[17] The demographics of rosacea among our sample, i.e. around 2% of all dermatology visits with a preponderance among 'Whites' and females, and highest prevalence in the 40–70-year age group (Fig. 1, Table 1), are all consistent with the clinical norms[13,37] and this further supports the representativeness of the sample.

Of 13 978 704 patient visits for rosacea, 94 521 (0·68%) also led to a diagnosis for depressive disease. As 1·04% of the patients with rosacea had a comorbid psychiatric diagnosis,

therefore about 70% (0·68 × 1·04%) of the psychiatric comorbidity among the patients with rosacea was depressive disease. This is much higher than the 29·9% prevalence of visits with a diagnosis for major depression among the psychiatric sample as a whole. The 29·9% figure is consistent with the epidemiology of major depressive disorder (DSM IV-TR),[38] as the lifetime prevalence for major depressive disease among community samples has varied from 10% to 25% for women and from 5% to 12% for men. The higher prevalence of 29·9% of major depression among the dataset in this study, which was collected over an 8-year period from visits to clinics and hospitals, is consistent with the demographics of major depression (DSM-IV-TR)[38] and further supports the representativeness of our study sample. In our analysis depressive disease included only the diagnostic codes for variants of major depressive disorder, and therefore represents clinical depression. The depression variable did not include the 'minor' forms of depression such as adjustment reaction with depressive symptoms, neurotic depression and personality disorder with depression such as affective personality disorder.[34] The OR of having depressive disease in the rosacea group from the logistic regression model (Table 2) was high at 4·81 (95% CI 1·39–16·62). In our sample the relation between alcohol abuse and rosacea was not significant at $P < 0·05$, as the lower limit of the 95% CI is less than 1. Alcohol abuse did not have a significant confounding effect on the results, a finding that is consistent with some of the previous research on alcohol and rosacea.[15,16] It is interesting to note the high OR of 92·83 (95% CI 11·44–753·47) for the age group of 40–70 years, which is consistent with the clinical observation that rosacea tends to be most prevalent in this age group. All the significant ORs should be interpreted with caution, however, as the range of the 95% CI is wide, which indicates a high degree of variance in the data.

One weakness of this database is the fact that most of the ICD-9-CM diagnostic codes do not provide an index of severity of the symptoms or the therapies that were being used specifically for the rosacea. For example, milder forms of rosacea are not distinguished from the more severe forms. The overall relatively small percentage of depressive illness among patients with rosacea probably represents an underestimation of the prevalence of depressive disease in rosacea. The NAMCS and NHAMCS represent naturalistic data which are representative of the actual practice situation, and most busy physicians in a private office or outpatient clinic are not likely to make a psychiatric diagnosis during a visit for a dermatological complaint unless the psychiatric comorbidity is very significant or requires urgent attention. Our findings are especially relevant as the study sample is representative of the U.S. population at large and standard ICD-9-CM criteria were used to make all diagnoses. We have observed a significant association between the 'Rosacea' and 'Depression' variables in this case–control type study; this association has to be examined further using a prospective study design, to evaluate the nature of this association.

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