

The incidence and prevalence of manic-melancholic syndromes in North West Wales: 1875–2005

Farquhar F, Le Noury J, Tschinkel S, Harris M, Kurien R, Healy D.
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Objective: Against a background of recent interest in the concept of melancholia, we report data on the incidence and prevalence of manic, melancholic and postpartum syndromes from North West Wales.

Method: We have utilized a database of the complete records of all admission to the North Wales Asylum from 1875 to 1924, and compared the findings for mania, melancholia, and postpartum psychoses from this sample, with admissions for these disorders to the North West Wales mental health services between 1995 and 2005.

Results: The incidence of bipolar disorder, as well as melancholia with and without psychotic features appears stable from 1875 to 2005 but there has been a dramatic decline in the incidence of *de novo* onset psychoses in the postpartum period. The prevalence of admissions for bipolar disorder, and for severe depressive disorders has increased dramatically during this period.

Conclusion: There are some grounds for revisiting the concept of manic-melancholic disorder put forward by Rafaelsen. The changes in the incidence of postpartum psychoses may have a wider significance for the affective disorders in general.

**F. Farquhar¹, J. Le Noury¹,
S. Tschinkel¹, M. Harris¹,
R. Kurien¹, D. Healy²**

North Wales Department of Psychological Medicine,
Cardiff University, Hergest Unit, Bangor, UK

¹Declares no conflict of interests.

²In recent years DH has had consultancies with, been a principal investigator or clinical trialist for, been a chairman or speaker at international symposia for or been in receipt of support to attend meetings from almost all major pharmaceutical companies. In the past two years, DH has had lecture fees and support to attend meetings from Astra-Zeneca and Lundbeck. In the past two years DH has been an expert witness for the plaintiff in nine legal actions involving SSRIs and has been consulted on a number of attempted suicide, suicide and suicide-homicide cases following antidepressant medication.

Key words: mania; melancholia; bipolar disorder; psychosis; postpartum psychosis

D. Healy, North Wales Department of Psychological Medicine, Cardiff University, Hergest Unit, Bangor LL57 2PW, UK.

E-mail: healy_hergest@compuserve.com

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Introduction

While the terms 'mania' and 'melancholia' date back to the Greeks, the notion of an affective disorder only began to take shape with Esquirol in the early 19th century. Esquirol's lypomania helped transform the old underactive insanity of melancholia into something closer to the modern understanding of 'depression' (1, 2). Melancholia up to the end the 19th century, however, still theoretically involved a psychotic element. Patients with the features of what were later called the endogenous depressions but without psychotic features were in something of a limbo. Physicians outside the asylum, such as Denmark's Carl Lange, began to encounter such patients. Lange's descriptions in 1886 of periodical depression included the typical vegetative features of melancholia but without the

psychotic elements found in melancholia (3). This lack of psychotic features led him to distinguish periodical depression from melancholia, while many alienists countered that the vegetative features of melancholia could present to asylums without psychotic features (4).

Karl Kahlbaum in Germany coined the term dysthymia for a state comparable with that of Lange's periodical depression (5). Kahlbaum also described cyclothymia, and noted its occurrence in milder forms in non-asylum settings. From 1854 onwards, in fact, a number of alienists from France and Germany had described a variety of circular insanities, starting with Falret's *folie circulaire*, and Baillarger's *folie à double forme* (1).

In 1899, Kraepelin pulled these various affective disorders together into manic-depressive insanity (6). The guiding principle behind his new classifica-

tion centred on the primacy of the clinical course of the disorders being classified. The affective disorders were characterized by a remitting course, whereas in dementia praecox remissions were unlikely. There was one condition that posed Kraepelin particular problems – involuntional melancholia. This appeared to share the clinical features of other affective disorders but it seemed much less likely to remit and accordingly was not initially included in the manic-depressive concept (7).

In contrast to involuntional melancholia, in the case of the postpartum psychoses, even though he described the clinical features of these conditions as being quite distinctive, Kraepelin included them in manic-depressive illness on the basis of their remitting course. For Kraepelin, at this point in his thinking, clinical course trumped everything.

Aims of the study

Owing to a number of distinctive features of North Wales and its mental health services, we have the opportunity to provide data on the comparative incidence and admission prevalence of this group of conditions in North West Wales over the period from 1875 to 2005, and these data may be of some use in determining the best classification for the melancholias.

Material and methods

We bring four sets of data to this study. First is a data set from the old asylum in North Wales, which includes admissions for mania, melancholia and postpartum disorders. A second data set involves all recent admissions to mental health services in North West Wales for bipolar disorder. A third data set involves all recent admissions for severe depressive disorder. Finally, we have tracked down all recent cases of postpartum psychosis in North West Wales.

North West Wales historical database

The first data set consists of admissions from North West Wales to the North Wales Asylum at Denbigh in the 50 years from 1875 to 1924. This timeframe was picked for two reasons. Rates of admission to the North Wales Asylum had begun to stabilize by 1870, after the opening of the hospital 27 years earlier (8). Secondly, records from North West Wales are complete for this period. Thirdly, 1924 was the year when the hospital first began to record diagnoses of manic-depressive illness.

The population of North West Wales has remained essentially unchanged in numbers and

ethnic mix for 120 years. Thus in 1891 the population was 232 109, with 116 924 people between 15 and 55, while in 1996 it was 240 683 people with 119 323 in the 15–55 age band (9). Secondly, the region has remained undeveloped, so that patterns of service utilization can be more readily compared over time in this area than elsewhere. Thirdly, major geographical and financial constraints minimize the clinical and economic selection biases that appear to have affected other precommunity care mental illness service utilization studies. There was and is no private practice in North West Wales for the patients described here and no other point of service contact.

The procedures underpinning diagnosis have been outlined elsewhere (10). All diagnoses on both historical and contemporary samples were made according to ICD-10 criteria and had been made before this study of incidence and prevalence of admissions was undertaken. The historical records offered five sets of information relevant to diagnosis. First, all patients were compulsorily detained and their records included the medical and legal certificates outlining the circumstances that led to detention. Secondly, the records contain standard demographic data including age, sex, educational, employment and marital status, a family history of mental illness and prior mental or physical illness. Thirdly, there were standard assessments of dangerousness, suicidality, seizure-proneness, along with food refusal and a range of other clinical features. Fourthly, there was a description of the patients' mental and physical state on admission. Finally, there was a set of case notes covering the patient's stay in hospital until discharge or death. We could retrieve the records of prior admissions back to 1865 or subsequent admissions through to 1965. Modern clinicians making a diagnosis on the historical sample did so on the basis of a full set of records from all admissions for that patient rather than simply on the case record for that admission.

In the period from 1875 to 1924, 50% of admissions was diagnosed as mania and 30% as melancholia (10). These were older uses of these terms; patients with schizophrenia, agitated depression and senile disorders were typically diagnosed as having mania. Based on the information outlined above in a complete set of all case records for each patient, we have given contemporary diagnoses to all patients in the sample. For manic episodes (F30), bipolar affective disorder (F31), depressive disorder (F32), recurrent depressive disorder (F33) and postpartum disorders (F53) were relatively clearcut. A remaining sample of patients with unspecified affective disorder (F38/

39) have not been included in this study, except in the case of those patients with postpartum disorders.

In the case of postpartum psychoses, in addition to F30–39 diagnoses, ICD-10 diagnoses for schizophrenia (F20), schizoaffective disorders (F25), and acute and transient psychotic disorders (F23) were also included. If there were difficulties determining whether a psychosis was affective or non-affective, these patients were coded as unspecified non-organic psychoses (F29). The diagnoses on historical cases were made by the sector consultant as though that case had arisen from their current catchment area. The vast majority of women had psychoses with onsets within days of delivery but we included all cases up to 6 months.

A number of postpartum cases involved clear organic concomitants (F06, F09). Two-thirds of these cases were diagnosed as ‘organic’ because of marked catatonic but no schizophrenic features and ICD offers only two options – organic catatonia or catatonic schizophrenia. Of the remaining seven cases diagnosed as F09, five had physical conditions potentially consistent with a postpartum delirium, of whom one had a pre-existing mental illness and four had no prior history. One of these women died of pulmonary embolus and one from diarrhoea. Two had tuberculosis.

The diagnosis of cycloid psychosis as operationalized by Perris (11) was considered for all cases by the authors and applied where indicated. The presence of clinical features such as confusion, motility disorders, and delusions were readily determined from the notes.

In addition to diagnosing postpartum cases occurring during the period 1875–1924, we set up a control cohort of 101 women, matched for ICD-10 diagnosis and for age. There were sufficient cases within all diagnostic groups to make a one-to-one case match for all postpartum cases.

Modern first admissions for bipolar disorder and severe depressive disorder

The second and third data sets are drawn from an ongoing study of the incidence of service utilization for all psychotic disorders in North West Wales. From this we have assembled all patients with first admissions between 1995 and 2005 for manic episodes and bipolar disorders (F30–F31), and for postpartum patients from 1994 to 2005. We have also assembled all patients with severe depressive disorders without psychotic features (F322) and with psychotic features (F323), and patients with recurrent severe depressive disorders without psychotic features (F332) and with psy-

chotic features (F333) for the years from 1995 to 1999.

Patients were included in this study if they were native to North Wales or resident in North Wales following their initial episode. Patients not resident in or native to North Wales, who had an initial illness episode in North Wales, but who left the region thereafter, such as college students, are not included here.

Initial cross-sectional diagnoses of affective disorder made by sector consultant psychiatrists, have been supplemented by longitudinal clinical course data with renewed consultant and community mental health team diagnostic input. This procedure picked up patients with an initial diagnosis of depressive but later diagnoses of schizophrenia or bipolar disorder. Patients going on to a bipolar disorder are included in the bipolar sample, while those who developed schizophrenia or other disorders have been excluded.

For the modern sample the diagnoses of affective disorders were made in the following way. First, we scrutinized all discharge codes from all patients admitted between 1 January 1995 and 31 December 1999 and searched for all patients which a diagnostic coding falling between F30 and F39. This identified a number of patients with affective disorders who had been previously admitted from the North West Wales area prior to 1995. Admissions for these patients are included in figures for admission prevalence but not for incidence.

Modern first admissions for puerperal psychosis

A fourth data set is drawn from all patients with first admissions to the sole district general hospital (DGH) unit accessible from the area for the years between 1994 and 2005. We scrutinized the records of all patients diagnosed F53 (postpartum disorders) and all records of all female admissions coded as F20–F39 for possible uncoded postpartum psychoses. In addition data were obtained for all admissions to the district obstetric service and all patients coded by this service as having O990 (behavioural problems in pregnancy) and F53 were assessed. A meeting was convened with the consultants and midwives of the obstetric service to determine whether any postpartum psychoses might have happened in and been handled entirely in the obstetric unit or the community. The electronic records of all women coded O990 were scrutinized for possible contact with out-patient mental health services. Further details on this study are given in Tschinkel et al. (12).

Patients were included in this study if they were native to North Wales or resident in North

Wales prior to and following their initial episode. One patient not originally resident in or native to North Wales, with a record of prior mental illness before coming to North Wales, and who left the region shortly after her postpartum psychosis, has not been included in these figures. The DGH unit in question runs at 85% occupancy, so bed-pressure has not been a factor in determining likelihood of admissions. Again initial cross-sectional diagnoses made by sector psychiatrists were supplemented by longitudinal data with renewed consultant and community mental health team diagnostic input for all modern cases.

In the modern sample, we have categorized as patients with a previous mental illness, patients who had at least one prior admission for mental illness, along with one woman who had a clear previous history and treatment with medication but no admission. In the historical sample, two patients have case records noting a prior admission for postpartum psychosis to an asylum elsewhere or a prior postpartum psychosis without admission; these were included in the prior mental illness group. Finally, it can be noted that the results outlined below form part of a larger project to establish the incidence and prevalence of all psychotic disorders in North West Wales.

Results

In the assay system outlined here, the incidence of both schizophrenia and all non-affective psychotic disorders has remained constant in North West Wales from 1875 to 2005. The prevalence of admissions for schizophrenia and other non-affective psychotic disorders has risen greatly. A fuller communication of these results is in train, but the results outlined below are ideally viewed against a background of a stable incidence of non-affective psychotic disorders.

Bipolar disorder

In the period from 1875 to 1924, there were 343 admissions for F31 diagnoses from 127 individuals. This gives an incidence rate of 1.1/100 000 per annum and an admission prevalence of 3/100 000 per annum. There were a further 76 admissions from 67 individuals with single manic episodes that under ICD-10 could be diagnosed as manic episodes but DSM-IV would diagnose as bipolar. Adding these, gives an incidence rate of 1.7/100 000 per annum, and an admission prevalence of 3.6/100 000 per annum. A preliminary report of results from this study has been published (13).

The median age at first hospitalization for bipolar disorder was 43 years with indicators of a median age of onset of the disorder of 29 years. Many patients had clearly had episodes of illness prior to first admission. After first admission, patients had a mean of 5.7 admissions in total, with 4 being the median number of admissions.

In the period from 1994 to 2005, there have been 26 first admissions for which there is a consensus that the diagnosis is likely to be bipolar disorder. This gives an incidence rate of 1.0/100 000 per annum. There have been a further nine manic episodes in individuals that under DSM-IV criteria would lead to a diagnosis of bipolar disorder, giving an incidence of 1.4/100 000 per annum. During the period from 1995 to 2005, there have also been 630 admissions coded under F31 from 260 individuals, giving an admission prevalence of 25/100 000 per annum.

Melancholia – severe depressive disorders

In the period from 1875 to 1924, there were 658 admissions for F32–F33 diagnoses. This was 17% of all admissions. Of these 377 (57.3%) were women and 281 (42.7%) men. These admissions came from 568 individuals, of which 326 (57.4%) were women and 242 (42.6%) were men. This gives an incidence rate of 5/100 000 per annum. The admission prevalence is 5.7/100 000 per annum.

Of these, 457 (69.5%) admissions were for psychotic depression, 263 (57.5%) of which came from women and 194 (42.5%) from men (26 female admissions were postpartum). These 457 admissions came from 389 individuals, of which 222 (57.1%) were women and 167 (42.9%) were men. This gives an incidence rate of 3.4/100 000 per annum, with an admission prevalence of 4/100 000 per annum.

Of the women, 82.5% had only one admission, and only 5% of women had more than two admissions. While 83% of men had only one admission, and only 3% of men had more than two admissions. Forty per cent of women had a length of stay less than 6 months and the median length of stay for first admissions was 195 days. Forty-three per cent of men had an admission lasting less than 6 months, and the median length of stay of the male group was 160 days.

In the modern period we have restricted ourselves to admissions from 1 January 1995 to 31 December 1999. During this period, there were 95 first admissions for severe depression with or without psychotic features. There were 61 admissions for severe depression without psychotic features (F32.2 or 33.2), and 34 admissions for

depression with psychotic features (F32.3 or 33.3). The incidence of severe depression was therefore 8.2/100 000 per annum and 3.0/100 000 per annum for psychotic depression.

While the population of North West Wales has remained constant from 1880 through to now, the number of people over the age of 55 has increased substantially. Accordingly we have standardized the incidence rate for melancholia in the 1875–1924 period against the population data for North West Wales for 1991. When this is done, the incidence of admissions for F32 and F33 diagnoses in the 1875–1924 period rises to 6.1/100 000 per annum, and the incidence of psychotic depression to 4.2/100 000 per annum.

During the modern period there were 288 admissions for F32.2, 32.3, 33.2 and 33.3 diagnoses, 58 per annum, giving an admission prevalence of 25/100 000 per annum. Approximately 30% of these admissions were involuntary, and 50% of the depression with psychosis admissions were involuntary. For all F32 and F33 diagnoses, including mild to moderate depressions, there were 718 admissions from 484 individuals, giving an admission prevalence of 144 per annum or 62/100 000 per annum.

The mean age of first hospitalization for melancholia for women in the period 1875–1924 was 48.8 years and for men was 47.8 years. The mean age of first hospitalization for the modern period was 55.4 years for women and 53.5 years for men. From 1875 to 1890 males accounted for 58% of the admissions. From 1890 to 1924, they accounted for 39% of admissions for melancholia. In the modern period, men account for 46% of admissions for severe depression with or without psychotic features.

Finally, the duration of stay for, rates of recovery from and rates of readmission for melancholia in the 1875–1924 period, broken down by age at time of first admission are laid out in Table 1. This is aimed at testing where melancholia in the involutional period had a distinctively different outcome to melancholia at other stages. Length of stay for melancholic admissions remains relatively constant across the lifespan. There is a declining rate of recovery for these patients with

age, from 87% for patients admitted in their 20s to 56% for patients admitted over the age of 60. If we compare patients admitted in their 30s or 40s, with those admitted in their 50s or 60s, the odds ratio for recovery in the younger group is 1.2 times greater than in the older group (95% CI 1.06, 1.36; $P = 0.0031$). Once recovered, the norm for melancholic patients appears to have been that they remained relatively well, regardless of age.

Postpartum psychoses

In the modern period there has been a much greater rate of admissions of both women and women of childbearing age to the North West Wales DGH psychiatric unit than there was to the North Wales Asylum in the historical period (Table 2). Postpartum psychoses in the historical period for this reason formed a much greater proportion of female admissions to the asylum than they do to the DGH unit now (Table 2).

It is also clear, that there are differences between the historical period and now in the group of disorders that had their onset during the postpartum period. Patients who had a pre-existing diagnosis of schizophrenia or a related psychosis or an affective disorder occur at roughly the same rate – one every two years – in the historical period and now. In contrast, the rate of hospital service utilization for *de novo* onset postpartum psychoses is significantly different in the historical period than now.

Using birth as a denominator, the rate of puerperal psychosis of any kind in the period of 1875–1924 was 0.34/1000 births, with a rate 0.26/1000 births for *de novo* onset postpartum psychosis. Modern rates in contrast for all postpartum psychoses are 0.19/1000 births, with a rate of 0.03/1000 births for *de novo* onset postpartum psychoses. There is no significant difference between the overall postpartum mental illness rate in the historical and contemporary periods, expressed this way (relative risk 1.73; 95% CI 0.8, 3.7). But

Table 2. The incidence of postpartum psychoses in North West Wales: 1875–1924 vs. 1994–2005

	1875–1924	1994–2005
Female admissions	1946	3956
Women	1577	1827
Women of childbearing age	1100	1032
Postpartum psychotic episodes	103	7
Postpartum psychotic women	101	7
Women with postpartum onset	80	1
Women with prior illness	21	6
All postpartum cases/1000 births	0.34	0.19
Postpartum onset cases/1000 births	0.26	0.03
All postpartum cases/ 100 000 childbearing years	3.43	0.94
Postpartum onset cases/100 000 childbearing years	2.70	0.13

Table 1. Recovery rates in patients with melancholia: 1875–1924

First admissions	No. of patients	Median length of stay (days)	Discharge rate (%)	Never readmitted (%)
Aged 20–29	52	219	87	71
Aged 30–39	112	224	76	86
Aged 40–49	138	286	72	78
Aged 50–59	142	261	65	87
Aged ≥60	97	203	56	87

there is a significant difference in the rate of *de novo* onset postpartum psychoses between the historical and contemporary periods (relative risk 8.1; 95% CI 1.13, 58.2; $P = 0.013$).

Figures for the rates expressed in terms of person years are as follows. There were in the historical period a mean of 60 000 women of childbearing age per annum, and 62 000 per annum in the modern period. This gives a rate of 103 postpartum episodes in 3 000 000 childbearing years in the historical period vs. a rate of seven postpartum episodes in 744 000 childbearing years in the contemporary period. There was a 3.65 (95% CI 1.7, 7.8; $P = 0.0004$) greater relative risk of postpartum psychoses on this basis in the historical period. The relative risk of a *de novo* onset puerperal psychoses calculated on the same basis in the historical period was 20 times greater (95% CI 2.8, 144.0).

In the historical sample using the ICD-10 criteria 21 patients were diagnosed as having an organic disorder, 14 of which had a catatonic syndrome while 26 were diagnosed with schizophrenia or related psychosis and 52 with a mood disorder and along with two others also. We employed the operational diagnostic criteria for cycloid psychosis outlined by Perris (11). When these were used 32 of the historical sample had a definite cycloid psychosis with six further possible cases meeting cycloid psychosis criteria. In the contemporary sample three of seven patients met criteria for cycloid psychosis.

Discussion

This is a study of the incidence and prevalence of service utilization for psychotic disorders rather than a study of the incidence and prevalence of disease entities. It will accordingly give much lower estimates of incidence and prevalence than will community surveys. In contrast to community surveys, a study of hospital service utilization however can be complete and such a study has the merit of introducing a clear disability criterion. The true estimate for incidence and prevalence for significant disorder in any of these domains awaits a validated biological screening tool.

It appears from this study and ongoing parallel studies on non-affective psychoses that the incidence of the major psychoses, except for postpartum psychoses, has remained close to constant over 130 years. The current estimates for the incidence of non-affective psychoses and depressive psychoses in North West Wales are also very close to estimates from an ongoing epidemiological survey in Ireland (J.L. Waddington, personal communication).

There is a difference however between the incidence reported for bipolar disorders here and that reported by Scully and colleagues, with Irish estimates four times higher than those reported here (14). In terms of bipolar disorders, the historical sample leaves no room for compromise. While others might have diagnosed a handful of historical cases diagnosed currently as non-affective psychoses as bipolar disorders instead, they are not likely to be sufficient cases to make any substantial difference to the incidence estimates cited here.

In terms of the modern sample, the true incidence of bipolar disorder is likely to increase to some extent, as this is an illness that can take some time to declare itself properly, presenting first with substance misuse or recurrent depressive episodes. A major difference between Irish and Welsh samples may stem from the Irish use of DSM-IV which requires manic episodes to be diagnosed as bipolar disorder, whereas ICD permits state with psychotic and affective features to be diagnosed as either acute and transient psychoses or manic episodes. Similarly admissions for disturbances linked to social situations or personality factors that might otherwise be diagnosed as acute situational disturbances can be diagnosed as manic episodes without committing the clinician to a diagnosis of bipolar disorder.

There is a striking increase in admission prevalence in the modern period that at first sight seems inconsistent with the availability of effective treatments. However the data in terms of underlying episodes in the historical and modern period may be more comparable than appears here. Modern treatments get patients out of hospital fast, but a significant proportion of the admissions for bipolar disorders and severe depressive disorders were for individuals readmitted several weeks or months after their discharge. This did not happen 100 years ago. If we could set up operational criteria for, or had a marker for, the duration of an affective episode rather than the duration of a hospitalization, it might be possible to establish whether there has been any change in the length of episodes and how this relates to admission prevalence.

In terms of the questions posed at the start, both the alienists and Lange were correct. The alienists were correct in that up to 30% of patients admitted with a diagnosis of melancholia showed all the vegetative features of the disorder but without psychotic features. Lange was correct in that it was the norm for melancholia to present with psychotic features.

There is a good case for extending the concept of melancholia beyond depressive psychosis to include what would once have been called endog-

enous depression, excluding most of what is now diagnosed in DSM as major depressive disorder, or in ICD as mild or moderate depressions. The former depressions and the depressions of bipolar disorder might be expected to share common physiological markers, such as dexamethasone non-suppression, not found in mild to moderate depressive disorders. If so this might support a proposal first put forward by Rafaelsen (15) that we should recognize manic-melancholic disorder. Instead, in recognizing major depressive disorder, the field has all but necessitated a distinction between depression and bipolar disorder.

On the issue of involuntional melancholia, while the data here show slightly worse outcomes with age, the differences in recovery rates between older onset and earlier onset melancholia do not appear sufficiently great to warrant considering that they might represent distinctly different disorders. In Kraepelin's selected sample, he may have been faced with an unusual selection of older patients.

Some of the most interesting findings come from the postpartum group. The clinical features of the postpartum patients in the historical sample show a high rate of motility disturbances (82%) and confusion (77%) (12). This might indicate that these disorders are better classified in a cycloid psychosis group. Alternatively, motility and confusion disturbances may have been commoner in classic manic-depressive disease than is now recognized (16). Features of this type led Kraepelin to discuss the existence of mixed affective states (6; Akiskal this symposium).

This led us to assemble an age- and diagnosis-matched group of female controls. There were continuing differences and considerable overlap between the postpartum cases and the control sample, of whom 58% showed motility disturbances and 50% showed confusion. What these figures cannot convey, however, is the extent to which the cycloid cases in the postpartum group demonstrated a multiform clinical picture, swinging from excited to inhibited motoric states or confusion to lucidity or anxiety to happiness, as outlined in classic accounts of the cycloid psychoses.

The key element in the postpartum data however is the comparative disappearance of *de novo* onset postpartum psychoses in the modern period. This decline in frequency has been noted by others but attributed to a loss of psychiatric beds (17). This latter explanation cannot account for the decline demonstrated in our data set which took place against a background of available beds.

The change in frequency of *de novo* onset postpartum psychoses reported here argues for the possibility that within the group of postpartum

psychoses there may be a disorder distinct from other affective or non-affective psychotic disorders. If the disappearance of these syndromes is not regarded as a conclusive argument for differentiating postpartum psychosis from other psychoses, the issue for those who prefer to continue grouping postpartum psychoses within the affective disorders is that something appears to be happening to this affective disorder that may have implications for the management of other affective disorders. An alternate implication is that the affective disorder category is itself heterogeneous.

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