Menarche and the onset of depression and anxiety in Victoria, Australia

G C Patton, M E Hibbert, J Carlin, Q Shao, M Rosier, J Caust, G Bowes

Abstract
Study objective – Psychiatric disorder often begins at adolescence. This study aimed to examine the associations between puberty and social circumstances and the adolescent rise in depression and anxiety.

Design – A two stage cluster sampling procedure was used to identify a representative group of Australian secondary school students in years 7 (age 12–13 years), 9 (14–15 years), and 11 (16–17 years) of 45 Victorian schools. The computerised clinical interview schedule (CIS) was used to evaluate psychiatric morbidity.

Main results – A total of 2525 subjects completed the survey – an overall participation rate of 83%. Levels of depression and anxiety increased with the secondary school years and girls had significantly higher rates at each school year level. For boys, the clearest independent associations with depression and anxiety were rising school year level and high parental educational achievement. For girls menarchal status emerged as the strongest predictor. Associations with age and school year level, evident on univariate analysis, did not persist when the recency of menarche was taken into account. After addition of measures of perceived social stress to a multivariate model, a significant association between depression/anxiety and parental divorce disappeared but the association with menarche persisted.

Conclusions – Menarche marks a transition in the risk of depression and anxiety in girls. The pattern of findings is consistent with a biological mediation of this association.

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There is much recent evidence that depression and anxiety become common during adolescence.12 Prospective community studies have shown a rise from low prevalence rates at the beginning of the second decade to adult-like levels and gender distribution by the age of 18 years.13 Retrospective studies of adults with psychiatric disorders have highlighted the frequency with which depression and other functional psychiatric disorders begin in the teens.14 Prospective studies of adolescents who present with psychiatric disorder have further emphasised continuity with adult disorders.9–11

Finally, family studies have shown high rates of first onset of major depression in the early teens for female subjects with a family history of depression.12

Such evidence for early adolescence as a common point of transition to psychiatric disorder has provoked speculation that the biological and social changes accompanying puberty increase the risks of developing psychiatric disorder. There are, however, few epidemiological data on the associations between adolescent psychiatric morbidity and puberty. Available data derive principally from the study of small and unrepresentative groups with relatively crude measures of psychiatric symptoms.13 In contrast, this paper reports on the relationships between puberty and social circumstances and the occurrence of depression and anxiety in a large representative group of adolescents.

Method
PROCEDURE AND SAMPLE
Data were collected from subjects in a statewide survey of adolescent health in Victoria, Australia between August and November 1992. This state has a population of 4.4 million, of whom 63% live in the capital city Melbourne.14 A two stage cluster sampling procedure was used to define the study sample. At stage one, 60 schools were chosen at random from a stratified frame of government, Catholic, and independent schools with a probability proportional to the number of year 7, 9, and 11 students in the schools in each stratum in the state (total numbers 59 746, 60 905, and 59 133 respectively). These correspond to the 10th, and 12th years of full time education respectively. Five schools declined to participate and each was replaced by a previously defined school from the equivalent stratum. At stage two, a single intact class was selected at random from each of years 7, 9, and 11 in selected schools. The sample was designed to have a standard error of a proportion of 0.02 for prevalence rates of 20% after adjustment for the effects of clustering.

The survey was presented as dealing with important health issues for adolescents and included questions on a broad range of health related issues. Active consent for participation, including written parental permission, was sought. Twenty eight lap top computers were used to administer the questionnaire to class groups.15

MEASURES
Mental health status
Mental health status was evaluated using a computerised form of the clinical interview
schedule (revised) (CIS-R),\textsuperscript{16-18} a structured psychiatric interview designed for use in non-clinical populations. The CIS has previously been used as a criterion measure for the definition of psychiatric caseness in teenage groups,\textsuperscript{19,20} and has an ease of reading consistent with its suitability for the younger group (Flesch reading ease 78.5, Flesch grade level 7.1). The CIS generates scores (1 to 4) on 14 subscales covering the common psychiatric symptoms found in non-clinical samples. These were summarised into a total score and stratified into four levels of psychiatric morbidity: level 1 (0–5), level 2 (6–11), level 3 (12–17), and level 4 (18+). The stratification incorporates a suggested threshold of 12 for "caseness", corresponding to the point at which a general practitioner might be concerned about a subject's mental health.\textsuperscript{17}

**Pubertal indices**

Girls reported the onset of menarche to the nearest month.\textsuperscript{21} In conjunction with the subject's date of birth and date of survey, the time from menarche was stratified into five levels as follows: premenarche, onset in the last 3 months, 3–12 months, 12–36 months, and greater than 36 months. In addition, pubertal status was evaluated using a pictorial display representing Tanner stages. Subjects were asked to choose from a pictorial representation of four phases of pubertal development corresponding to Tanner stages I/II, III, IV, and V.\textsuperscript{22}

**Social indices**

Social indices were based on the response to fixed format questions and covered parental marital status, birthplace of parents and languages spoken at home, and school characteristics. Parental education was classified on three levels as follows: neither parent finished secondary school, at least one parent finished secondary school or non-tertiary vocational training, and at least one parent completed a university degree. Perceived social stress was measured using a modification of the social stress and support interview,\textsuperscript{23} and covered the areas of school life, money, housing, social life, home life, and relationships with the opposite sex.

**Results**

**SAMPLE CHARACTERISTICS (TABLE 1)**

Survey time limitations forced a reduction in school numbers, particularly at year 11, so that the achieved school numbers were 46 in year 7, 45 in year 9, and 36 in year 11. Of the 46 participating schools, 26 were government, 11 Catholic, and 9 independent private schools. Stratum weights for overall estimation of state prevalence rates were less than 1.5 for all but two of the 12 geographic regions of Victoria (weights of 2.3 in metropolitan west Melbourne, 2.1 in rural north). In all, 2525 students completed the survey – 956 in year 7, 911 in year 9, and 658 in year 11. The response rates varied in relation to year levels, and were 85% for year 7, 84% for year 9, and 79% for year 11, giving an overall response rate of 83%. Reasons for not participating were as follows: failure to return the consent form, 10.2%; absence on day of survey, 3.5%; and parental refusal, 3.3%. The higher non–response rates in year 11 pupils were largely due to a higher rate (13.7%) of failure to return consent forms. The gender ratio (males year 7: 50.0%, year 9: 47.0%, and year 11: 43.8%) was similar to that in Victorian schools.\textsuperscript{27}

The internal consistency (Cronbach's $\alpha$) of response on the CIS subscales was consistent across gender and year levels (boys year 7 – 0.86, year 9 – 0.87, year 11 – 0.85; girls year 7 – 0.82, year 9 – 0.85, year 11 – 0.85). Based on the cut off point of 12 and above, the prevalence of high psychiatric morbidity rose significantly across school year levels for both boys ($\chi^2=34$, $p<0.001$) and girls ($\chi^2=50$, $p<0.001$). Controlling for year level, morbidity rates were substantially higher in girls (Mantel-Haenzel OR = 1.9 (95% CI 1.6,2.3), ($\chi^2=49$, $p<0.001$).

**MULTIVARIATE ANALYSIS OF PATTERNS OF ASSOCIATION**

Both multiple and logistic regression models were employed to examine associations between CIS scores and pubertal status and social variables. Multiple regression, using a logarithmic transformation of the CIS score to deal with the skewed distribution of responses, allowed a dimensional representation of psychiatric morbidity, whereas logistic regression, using the threshold of $\geq 12$ on the CIS, provided an analysis that was more easily interpretable in terms of clinically significant symptomatology.

A multiple regression model developed for the entire sample showed significantly higher scores in girls ($p<0.001$) and a different pattern of predictors. Models were therefore developed separately for each gender (table 2). For girls, time from menarche, treated as an ordinal variable with the lowest level corresponding to those who had not reached menarche, was the factor most strongly associated with psychiatric morbidity. Girls in the highest category ($\geq 36$ months post menarche) had a 60% increase in the CIS score. Parental divorce was associated with a 20% increase in the CIS score. There was an association with school year level but...
Menarche and depression

Table 1  Psychiatric morbidity (clinical interview schedule (CIS)), pubertal and social indices of Victorian secondary school students grouped by school year level and gender (n = 2525)

<table>
<thead>
<tr>
<th>Year 7</th>
<th>Year 9</th>
<th>Year 11</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Mean (SD) age (y)</td>
<td>12.5 (0.6)</td>
<td>12.5 (0.6)</td>
</tr>
<tr>
<td>Psychiatric morbidity (%):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIS 0-5</td>
<td>64</td>
<td>22</td>
</tr>
<tr>
<td>CIS 6-11</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>CIS 12-17</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>CIS 18+</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Pubertal indices:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tanner stage (%): Premenarchal</td>
<td>62</td>
<td>12</td>
</tr>
<tr>
<td>Onset in last 3 mth</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Onset 4-11 mth ago</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>Onset 13-35 mth ago</td>
<td>13</td>
<td>60</td>
</tr>
<tr>
<td>Onset 36 mth ago</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Social indices:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parental divorce:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parental education:</td>
<td>24</td>
<td>21</td>
</tr>
<tr>
<td>Completed secondary education</td>
<td>39</td>
<td>38</td>
</tr>
<tr>
<td>Did not complete secondary school</td>
<td>37</td>
<td>41</td>
</tr>
<tr>
<td>Residency (%):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metropolitan Melbourne</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>Rural cities &gt;10 000</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Rural cities 25 000-100 000</td>
<td>26</td>
<td>7</td>
</tr>
<tr>
<td>Rural towns 40 000-25 000</td>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>Remote rural areas &lt;4000</td>
<td>7</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 2  Multiple regression model of the relationship between depression and anxiety* (log transformation of total clinical interview schedule (CIS) score), pubertal status and social indices in a representative sample of 2525 Victorian secondary school students

<table>
<thead>
<tr>
<th>Variable</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Regression coefficients (95% CI)</td>
<td>p value</td>
</tr>
<tr>
<td>Year level</td>
<td>0.08 (0.04,0.13)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Time from menarche:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men 3 3-12 mth</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Men 4 12-36 mth</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Men 5 &gt;36 mth</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Parental divorce:</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Parental university education</td>
<td>0.18 (0.05-0.301)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Psychiatric morbidity defined as log(1 + CIS).

NS = No significant relationship (p>0.1) and therefore not included in final model.

no independent association was found with age calculated in months. For boys, year level, parental university attendance, and residence in a rural city predicted CIS scores, with a trend for those in the highest Tanner stage to have higher scores.

In the logistic regression model for girls, parental divorce was associated with an almost twofold increase in high morbidity (table 3). The strongest association was with time from menarche, with those in the highest level (≥ 36 months post menarche) carrying a greater than twofold increase in risk. For boys, parental university education, school year level and residence in a small rural city were significantly associated with high morbidity.

Two further multiple regression analyses were undertaken, adding the perceived stress variables to the model to examine their potential mediating role in the above associations. Each of the six areas of stress was significantly and independently associated with the CIS scores in both boys (family p<0.0001, accommodation p<0.05, schoolwork p<0.0001, money p<0.0001, peer relationships p<0.05, girlfriends p<0.0001) and girls (family p<0.001, accommodation p<0.05, schoolwork p<0.0001, money p<0.0001, peer relationships p<0.0001, boyfriends p<0.0001). Despite the addition of reported stress variables, the association with year level (p<0.0001), parental university education (p<0.05), and rural city residence (p<0.02) persisted for boys. For girls the associations with year level and parental
divorce disappeared but the significant association with time from menarche persisted (men 3 p<0.05, men 4 p<0.0001, men 5 p<0.00001).

### Menarche and Psychiatric Morbidity in Relation to Age (Table 4)

Two analyses of the association between depression and anxiety and menarchal status stratified by age were undertaken in girls between the ages of 12 and 16 years. In the first analysis premenarchal girls were compared to postmenarchal subjects and these postmenarchal subjects with a recent onset of periods (<12 months) were compared to those with longer postmenarchal duration (≥12 months). At each age level a trend was observed for those in the postmenarchal group to fall in the high morbidity group with an overall higher risk greater than 50%. The comparison of postmenarchal subjects to those with a more remote onset of menstruation also showed a trend at each age level to higher rates of morbidity, with an overall rise in risk of over 50% compared to subjects with more recent menarche. The homogeneity of the odds ratio across age was tested using logistic regression. There was no significant interaction between age and menarchal status for either the comparison of premenarchal and postmenarchal subjects ($\chi^2 = 1.0$, NS) or those with more or less remote (<12 months) menarche ($\chi^2 = 2.9$, NS).

In order to consider the possibility that higher psychiatric morbidity was related to the development of premenstrual dysphoria, both stratified analyses were repeated excluding subjects who reported an onset of symptoms in the previous two weeks (n = 353). In both the comparison of pre and postmenarchal subjects (Mantel-Haenzel OR 1.6; 95% CI 1.0,2.5) and those with a longer (≥12 months) compared with a shorter duration of menstruation (1.9, 95% CI 1.1,3.3) a significant association persisted.

### Discussion

This study extends understanding of the onset of depression and anxiety in young women and supports the view that menarche represents a transition point in risk. This finding derives from a large cross sectional survey of Australian teenagers in whom patterns of association with psychiatric morbidity were different in boys and girls. For boys, school year level and high parental educational achievement were linked to levels of depression and anxiety. In girls, the recency of menarche and parental divorce held the clearest associations. The association with recency of menarche became evident three months after the first onset of periods, and by three years later, rates of depression and anxiety were 60% higher after adjustment for possible confounders including age.

The observed rise in depression and anxiety across the secondary school years, with a greater increase in girls, concurs with earlier studies. The possibility that pubertal development plays a role in this rise has not previously been investigated in a large representative population based study. One large study based on a referred patient sample failed to show an association with puberty that was independent of age but the authors acknowledged that both the lack of a systematic and detailed assessment of puberty as well as selection biases arising from the use of a clinical series may have contributed to the negative finding. Previous community studies have demonstrated associations between pubertal and menarchal status and psychological attributes such as low self esteem and negative self concepts. More recently, large scale community studies have used detailed measures of psychopathology. Several smaller studies of puberty based on volunteer and selected samples have reported a modest association between pubertal development and negative affect. However, the sample sizes and lower age range in these earlier studies are likely to have reduced their capacity to observe the association between psychiatric morbidity and menarche reported in this paper.

These findings provide clarification of a previously reported association between early menarche and depressive symptoms in girls. A stratification by age showed no significant age related trend in the association between menarche and psychiatric morbidity. However, girls with an earlier menarche will have spent longer in the time period of higher risk and therefore would be expected to experience higher morbidity rates than those with later menarche.

No data were collected in this study on a subject's point in the menstrual cycle at the time of survey. The premenstrual rise in symptoms of depression and anxiety is one factor which might potentially explain the observed associations. However, the morbidity threshold was chosen to be clinically significant for a general practitioner, and, though lower than thresholds for depression or anxiety in DSM-IV or ICD-10, it thus seems unlikely that the association with menarche is due to subclinical premenstrual dysphoria in otherwise well subjects. More importantly, after exclusion of subjects with a recent onset of symptoms, the relationship with menarchal status remained strong, indicating that transient premenstrual dysphoria is an unlikely explanation.

The study population was drawn from a representative sample of secondary school in
the state of Victoria but is potentially open to three sources of selection bias. Five of the 60 schools that were originally sampled did not agree to random sampling and were replaced. Survey time constraints further reduced school numbers. Although findings of expected age and geographical distributions for participants suggest that minimal bias resulted, this cannot be totally excluded. Secondly, there is evidence that pupils who leave school early, a group not included in this study's sampling frame, have higher levels of psychiatric morbidity. In Victoria in the year of the study, 93% of pupils stayed on until year 11, and this should have minimised this bias. Nevertheless, it is possible that the observed prevalence rates of psychiatric morbidity underestimate true population rates with some potential for bias in estimating associations with the factors examined here. This may be relevant for the association between parental education and psychiatric morbidity in boys. However, the association with university education was similar in all year levels, suggesting that selective school drop-out of boys with low parental educational achievement was not responsible. The possibility that school non-participants have higher rates of psychiatric morbidity than those who attend raises a possible third source of bias. However, satisfactory response rates at all year levels, with low rates of absenteeism (<4%), should have minimised this source of non-participation bias.

Parental divorce is one of the best established risk factors for depression in adolescence and previous studies have reported a two to threefold increase in associated psychiatric symptoms. It is therefore of note that menarchal status both carried a higher degree of risk than parental divorce and was more prevalent as a risk factor. The persistence of an association with menarchal status when perceived stress was added to the multivariate model also contrasted with the disappearance of an association with parental divorce. This may therefore arise through either high levels of social stressors in children of divorced parents or their diminished capacity to deal with encountered stress.

The independent association between menarche and psychiatric morbidity implicate developmental processes in the teenage rise in depression and anxiety in girls. Changes in peer, sexual, and family relationships and consequent rise in social stress following puberty have commonly been implicated in early adolescent emotional problems. This study's findings suggest that external stressors play little role in mediating an early adolescent rise in depression and anxiety. The onset of menarche is, however, also associated with internal psychological shifts not measured in this study. These include shifts in self concept, in perceived roles, and in expectations - changes which in some instances may be negative. It remains possible that such internal psychological shifts mediate this association.

The persistence of an independent association with menarche also raises a possibility that the biological changes of late puberty, coinciding with the establishment of cyclical patterns of gonadal hormone secretion, bring an increase in the risk of depression and anxiety in girls. Both oestrogens and progestins can alter the function of serotonergic and noradrenergic hypothalamic neurones implicated in affective and anxiety disorders. Increased rates of depression and anxiety are commonly observed at other points of fluctuation in gonadal hormones, most notably in association with perimenstrual, puerperium, and menopause with underlying neuroendocrine mediation postulated in each instance. Women with a history and treatment of child psychiatric disorders have a higher prevalence of menstrual cycle changes not only in the premenstrual worsening of the symptoms of major depression and in causing late luteal phase dysphoric disorder. Suppression of these hormonal fluctuations of the ovarian cycle, either through addition of oestrogens or suppression of oestrogen secretion, is effective in the treatment of premenstrual depression. Taken with the findings of this study, these links raise a possibility that the amplification of cyclical gonadal hormonal secretion after menarche trigger mood disorders in women with an as yet ill defined underlying biological vulnerability. The observed progression in risk after menarche is consistent with models of pharmacological sensitisation or kindling previously implicated in the development and progression of affective disorders.

The study findings are in keeping with a multifactorial origin of depression and anxiety in adolescence. For young women, they nevertheless implicate menarche and the accompanying augmentation of cyclical hormonal change in gonadal hormones. As such they may offer a clue to the origins of gender differences in depression and anxiety which begin in early adolescence and persist into adult life. Further clarification of the mediation of this association with menarche has the potential to make a substantial contribution to our understanding of the aetiology, prevention, and treatment of common psychiatric disorders.

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