Adult mental health disorders and their age at onset

P. B. Jones

Summary
The study of age at onset of mental health disorders is technically and conceptually difficult. It is important to consider these age distributions in order to understand causes and mechanisms of illness and to intervene at an appropriate juncture for primary and secondary prevention. This article reviews some of the approaches to studying age at onset, sets out the evidence to support the assertion that adult mental disorders begin in adolescence, and finds that perhaps half of all adult mental health disorders have begun by the teenage years. The paper then discusses whether this fits what is known about the developmental neurobiology of the brain and introduces the implications for mental health services.

Declaration of interest
P.B.J. nominated his department to receive a fee for providing scientific advice to Roche. He receives honoraria for contributing to the biannual British Association of Psychopharmacology schizophrenia master class series.

Adult mental health disorders begin by adolescence. This seems a simple enough statement that suggests we cannot understand mental illness affecting adults unless we appreciate what goes on during the preceding period of life. If true, childhood and adolescence, divided by the biological gateway of puberty, would be crucial epochs in terms of understanding causes and mechanisms of adult illness. This would frame attempts at early intervention and both primary and secondary prevention. Following the theme of this supplement, this paper focuses on the continuities between the adolescent and early adult stages of the life course, arguing that these are better seen as a single developmental epoch. However, the seeds of many conditions manifest in this period are sown in even earlier life, such that some reference is also made to childhood.

In some conditions such as psychotic illness, intervention during incipient illness or its early stages may prevent a lifetime of disability for a proportion of those affected.1 Onset of the full syndrome at a very young age is often associated with a severe course,2 but – intriguingly – a good response to treatment.3 In other conditions such as dementia, very early onset may suggest a different disease entity and so direct management accordingly. From the perspectives of surveys, epidemiological research and health service planning, it is also essential to understand the distribution of different disorders over the life course. This underpins precise estimates of projected morbidity and appropriate policy development. For example, most people with chronic psychotic disorders in a mental health service are middle-aged, but our understanding of the onset distribution of these conditions means preventive and early intervention services must target a much earlier age group, as described below.

Defining and measuring age at onset

This life-course view means that identifying the age at onset of mental disorders is important, but it is difficult.4 The classic psychiatric disorders of adult life often begin with non-specific symptoms. As studies of the evolution of symptoms become more detailed, it is clear that early psychopathologic changes can be transient and dynamic before crystallising into a syndrome fitting some operational category such as the American Psychiatric Association's DSM. Only in retrospect can a decision be taken as to whether the early features were in fact part of the eventual picture. In epidemiological terms this leads to enormous scope for error or bias in the recall or memory of events;5 some elements may be misattributed to illness and others simply forgotten. From a clinical point of view it is well known that the better the history, the earlier the age at onset can be dated. Furthermore, just as periods of low mood and occasional elation are part of normal life, it seems likely that some psychological experiences such as voice hallucination, hitherto considered psychopathological, are relatively common during certain developmental periods; it is their persistence or coexistence with other features that marks them as significant. This is leading to conceptual difficulties with clinical concepts such as the prodrome that are at best meaningless or confusing when used at the population level, and may be damaging if they lead to interventions that have adverse benefit-to-harm profiles quite different from the clinical situation.

Retrospective accounts of age at onset for some disorders are more useful than others, and perfect for none. Despite the problems alluded to above, it is a reasonable (and useful) assumption that a large proportion of people with psychotic illness eventually receive treatment, especially given that in the definitions of some types of psychosis such as schizophrenia, disability and loss of function are included in their definition. Thus, a survey using retrospective accounts of age at onset for schizophrenia or a broader group of non-affective psychosis yields useful information. It also avoids contamination by the data for the vast majority of young people who may experience psychotic phenomena without ever being ill. However, this is at the cost of excluding the few people with incipient illness but not yet in contact with services and, for many years, of masking researchers to the extent of psychotic phenomena as part of normal experience; for many decades epidemiologists regarded such phenomena simply as false positives. The retrospective approach is also hampered by the long duration of untreated psychosis in many with non-affective psychosis who eventually make service contact, but the alternative approach – using a community survey for incident illness – would be hugely inefficient given the relative rarity of cases and the fact that the illness itself means that affected people would be less likely to take part.6 It is important to recognise that the retrospective approach in clinical samples yields a self-fulfilling estimate of the age at onset of psychotic disorders.
that are seen and treated in clinical services, not a broader phenotype that does not meet this threshold. That said, the method – especially when combined with population registers of treated mental disorder – can lead to definitive results.6

Using retrospective accounts of age at onset from cohorts of treated individuals is not useful for less disabling mental disorders because most are never treated. In some areas such as cardiovascular disease and cancer it is effective to follow up large cohorts of individuals and track these outcomes which are relatively easy to measure.7 This is much more difficult for common mental disorders where the true incidence and age at onset need intensive study, but has been achieved for psychotic illness using population-based birth cohort studies where follow-up is achieved either through regular interviews and surveys,8 or through population registers.9 Such studies are rare and usually problematic in some way as they were initiated for reasons other than mental health disorders. For these reasons, retrospective reports from carefully designed cross-sectional community surveys provide most evidence on age at onset for most mental health disorders.

Examples of each of these methodological approaches to age at onset are outlined below, taking different exemplar disorders. This is followed by a discussion as to whether the findings on age at onset need intensive study, but has been achieved for psychotic illness using population-based birth cohort studies where follow-up is achieved either through regular interviews and surveys,8 or through population registers.9 Such studies are rare and usually problematic in some way as they were initiated for reasons other than mental health disorders. For these reasons, retrospective reports from carefully designed cross-sectional community surveys provide most evidence on age at onset for most mental health disorders.

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**Clinical studies and clinical epidemiology**

Schizophrenia

Schizophrenia is an archetype among the psychotic disorders for which retrospective accounts reconstructing the evolution of illness in treated clinical samples yield strong results; it is also a disorder with a developmental component. The same arguments also pertain to a broader spectrum of these illnesses seen in clinical practice.11 The idea that schizophrenia might be developmental in origin is not new.12 It was evident in early clinical descriptions of the syndrome (broad definition, ICD-9 codes 295, 297, 298.3, 298.4). (a) Males: earliest sign of mental disturbance, n = 117 (dotted line); first psychotic symptom, n = 125 (dashed line); index admission, n = 133 (solid line). (b) Females: earliest sign of mental disturbance, n = 131 (dotted line); first psychotic symptom, n = 139 (dashed line); index admission, n = 143 (solid line).

Depression and anxiety

Depression and anxiety, unlike schizophrenia, are well-known entities before puberty.18 Follow-up studies of these disorders in children and adolescents in clinical settings indicate a high degree of homotypic continuity into adult life, meaning that the same clinical syndrome is found in both earlier and later life,18–22 this being the case also for conduct disorders, which in addition showed a broader range of adverse outcomes (i.e. heterotypic
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experiences and masked to their outcomes; these individuals
continue to be followed as many contemplate the milestone of
retirement and all that is brought by later middle age. Colman et al
used ratings made by teachers when the survey members were
aged 13 and 15 years (in 1959 and 1962 respectively) that included
items akin to those seen in internalising disorders such as
depression and anxiety.27 Survey participants scoring in the top
6% of the population distribution were defined as cases of
‘common mental disorder’ (CMD); 277 were in this group at
either age, whereas 46 met case definition at both 13 years and
15 years of age and were defined as ‘persistent CMD’ cases;
interestingly, these observations were made before it was believed
that these disorders occurred in children and well before current
classifications of mental illness such as DSM and the World Health
Organization’s (WHO’s) ICD. The remaining survey members
(n = 3002) were classified as healthy, falling into neither group.

The presence of common mental disorder in the teenage years had
a profound association with mental health in subsequent surveys of
this cohort stretching out into middle life when assessments were
made at ages 36, 43 and 53 years. Those in the CMD group were over
two-and-a-half times more likely to be rated as having common
mental disorder at age 36 years compared with the mentally healthy
teenagers, and one-and-a-half times more likely to be ill at age 43
years; the effect was no longer present at age 53 years. For those with
persistent CMD as teenagers the outlook was bleaker: they were over
six times more likely to be ill with a common mental disorder at ages
36 and 43 years, with the effect persisting at age 53 years, when they
were at fourfold risk. The ripples of episodic common mental disorder
had faded by middle age but persisted after the age of 50 years for
those who had experienced persistent depression and anxiety in their
early teenage years; their poor mental health could be traced back to
adolescence, perhaps even earlier.

The Dunedin Longitudinal study
Another example of the birth cohort approach comes from
New Zealand and the Dunedin Multidisciplinary Health and
Development Study.28 This is based on a sample of 1037 children
born between April 1972 and March 1973 in Dunedin and first
assessed at age 3 years. Now in the era of operational criteria
and standardised diagnostic measures, the participants were
assessed at ages 11, 13 and 15 years with the Diagnostic
Interview Schedule for Children, and then at ages 18, 21 and 26
years with the Diagnostic Interview Schedule;29 these measures
allowed DSM-IV diagnoses to be generated.30 Cohort members
receiving treatment and those using intensive mental healthcare
were also identified.

The prevalence in the past year of any mental disorder at
age 26 years was high at 48%, with men and women being equally
affected. Over 80% of those with a mental health disorder at this
age also had a prior diagnosis of any mental illness since the age of
11 years; overall, 74% had received a diagnosis before 18 years of
age and 50% before 15 years of age. The percentage of prior
diagnoses increased according to the severity of disorder by age 26
years in terms of treatment received. Of those with a disorder
seeking treatment, 77% were categorised as meeting diagnostic
criteria before 18 years of age and 58% before age 15 years. For those
using intensive mental health services, 80% received a diagnosis
before 18 years of age and 60% before age 15 years. There was a
pattern of homotypic continuity, especially for conduct disorder
and adult antisocial personality disorder, but there were also hetero-
typic associations; adult anxiety and schizophreniform disorders
were preceded by a wide range of adolescent diagnoses. For all adult
disorders, 25–60% of cases had a history of conduct and/or
oppositional defiant disorder. The authors concluded that the
majority of mental health disorders manifest at age 26 years should
be considered as extensions of adolescent disorders, just as suggested
by Colman et al for common mental disorders in the British
1946 birth cohort.27 The eradication of adolescent disorders,
particularly conduct disorders, would have a profound effect on
reducing subsequent morbidity.

Cross-sectional surveys
These two birth cohorts give clear evidence that a considerable
proportion of mental health disorders are already manifest in
adolescence; these studies have many methodological advantages
in their prospective approach but are limited by their periodic
assessments during the life course, and the relatively small
proportion of whole life that they have yet covered. A major
advance in our understanding of age at onset distributions has
come with developments in the methodology that can be used
with cross-sectional mental health surveys. The National
Comorbidity Survey Replication (NCS-R) built on a succession
of major epidemiological surveys in the USA, particularly the
Epidemiological Catchment Area study and the National
Comorbidity Survey, and was a major part of a global initiative,
the WHO World Mental Health Survey Initiative.29,31–34

The NCS-R used the WHO Composite International Diagnostic
Interview (WHO-CIDI),35 a fully structured lay-administered
interview, to generate DSM-IV diagnoses from data collected
in a household survey of 9282 respondents (70.9% response
rate). Relative to prior studies, methodological innovations
included an expanded set of diagnoses; in-depth clinical validation
of field research diagnoses based on clinician-administered
Structured Clinical Interview for DSM-IV re-interviews,36
dimensional self-ratings on clinically anchored scales,37,38
inclusion of subthreshold diagnostic syndromes; assessment of
disability and impairment; the use of disease burden metrics

Population-based approaches
Children who present to clinical services with psychiatric illness
may not be at all typical of those in the general population, where
even specific operational diagnoses are common at around one in
ten of the population under 16 years old; few of these ever cross
the threshold into clinical care. For instance, the British Child
and Adolescent Mental Health Survey of 1999 surveyed 10 438
children, triangulating information from the children themselves
and from their parents and teachers; around 9.5% had at least
one current DSM-IV diagnosis.24 Following such large samples
into adult life is a considerable undertaking but has been done
on several occasions in the context of birth cohorts. In these
studies large samples of people defined by geography and birth
date or period are followed, often for many years, simply because
they represent the general population. Several birth cohorts
have contributed a great deal to our knowledge about risk
factors and long-term outcomes of psychiatric illness.25 Here,
we look in more detail at two studies: one from Britain and one from
New Zealand. Both studies have been influential in elucidating the
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continuity) in addition to homotypic adult antisocial personality
traits.23 Thus, for the proportion of children and adults who went
on to develop the adult syndrome, their adult mental health
disorders can be said to have begun in childhood and adolescence.
linked to marker physical disorders; and assessments of service use, treatment barriers and adequacy of treatment. The study was not designed for rare disorders such as schizophrenia and autism which lead to considerable non-response, but generated remarkable information on the lifetime prevalence of many conditions.

A number of methodological enhancements allowed this survey to obtain helpful estimates of age at onset, despite its retrospective method which is often associated with error. Questions were designed to avoid implausible responses by using a time-line approach, and by breaking the life course into blocks such as pre-school, high school, university and employment, so that respondents could date both important symptoms (e.g. first panic attack) and full syndromes at least to a certain epoch of their lives. The ages by which 25%, 50% and 75% of respondents first became affected are shown for a number of syndrome groups in Table 1 together with their overall lifetime prevalence, standardised to age 75 years.

Overall, there are four headlines from the NCS-R relevant to this review. First, half (51%) of Americans will experience a DSM-IV mental health disorder during their lifetime, with some evidence that this proportion may be increasing with younger cohorts. Second, half of these disorders (as shown by the 50th percentile or median) were incident by age 14 years. The median onset tended to be earlier for anxiety disorders (age 11 years), some of which begin and end in childhood, and for impulse control disorders (age 11 years) than for substance use disorders (age 20 years) and mood disorders (age 30 years). Third, age at onset was concentrated in a narrow age range for most disorders: interquartile ranges (the number of years of age between the 25th and 75th percentiles of the age-at-onset distributions) were only 8 years (age 7–15 years) for impulse control disorders, 9 years (age 18–27 years) for substance use disorders, and 15 years (age 6–21 years) for anxiety disorders, compared with 25 years (age 18–43 years) for mood disorders. Half of all mental health disorders over the life course occurred first between the ages of 7 years and 24 years.

Analysis of service contact data from the NCS-R leads to the fourth major finding and presents a dismal tale of failure, delay and lost opportunity. The vast majority of people with lifetime fourth major finding and presents a dismal tale of failure, delay and lost opportunity. The vast majority of people with lifetime

### From neurobiology to service provision

One further question is whether what is happening to the brain during the adolescent period mirrors this tide of incident mental health disorder where, excluding the neurodegenerative disorders of later life, half of all onsets have occurred by the mid-teens.

The brain is constantly changing throughout life; even reading this article may consolidate some aspect of neural circuitry and leave a memory trace. That said, there are several epochs over the life course where there is radical transformation of neural architecture and function. One of these epochs spans the traditional legal, educational and service boundary of 17–18 years of age. In fact, this artificial transition falls right in the middle of a crucial phase of brain development that begins shortly before puberty and ends during the third decade of life. This questions the whole concept of adolescence (based on sexual maturity) being distinct from adulthood (based on a concept of attainment of mental and physical capacity).

Development of the neonatal brain from its ectodermal origins is a dramatic achievement of nature. Its complex and depending on a variety of processes such as the establishment of connectivity and programmed cell death, followed by a rapid development of basic cabling through myelination in the first year, this epoch ushers in some classical neurodevelopmental disorders and learning delays; but this is only part of the story. It takes three decades to grow a mature human brain, during which time there is much further development. The period from mid-childhood through puberty to the mid-20s is another phase of profound change, particularly in the balance of connectivity between brain areas. It is during this period that the risk of adult mental health disorders becomes apparent; it may be the characteristics of normal development that lead to this risk, rather than any particular abnormality in this process. Indeed, aspects of syndromes such as impulse control disorders are so common during adolescence that it is questionable as to whether they should be considered abnormal. This second, more leisurely phase of development has only recently begun to be understood. It is probably heralded by prepubertal maturational events in the adrenal glands known as adrenarche that take place around 6–8 years of age. Adrenarche involves the production of two steroid compounds, dehydroepiandrosterone (DHEA) and its metabolite dehydroepiandrosterone sulfate (DHEAS), which are abundant within the brain. Longitudinal studies of brain structure using repeated magnetic resonance imaging scans in healthy children have demonstrated considerable pre-adolescent increases in cortical grey matter, peaking some 2–3 years after adrenarche and then declining in an inverted U-shaped manner. Increases

<table>
<thead>
<tr>
<th>Table 1 A Ages at onset for five categories of mental health disorder</th>
<th>Age at which % of projected lifetime risk attained, years&lt;sup&gt;b&lt;/sup&gt;</th>
<th>25%</th>
<th>50% (median)</th>
<th>75%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Projected lifetime risk, % (s.e.)</td>
<td>31.5 (1.1)</td>
<td>6</td>
<td>11</td>
<td>21</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>26.0 (0.8)</td>
<td>18</td>
<td>30</td>
<td>43</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>25.4 (1.1)</td>
<td>7</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Impulse control disorders</td>
<td>16.3 (0.6)</td>
<td>18</td>
<td>20</td>
<td>27</td>
</tr>
<tr>
<td>Substance use disorders</td>
<td>50.8 (1.2)</td>
<td>7</td>
<td>14</td>
<td>24</td>
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<sup>a</sup> Proportion of whole population that will have experienced disorder by age 75 years.

<sup>b</sup> Data for standardised age-at-onset distributions of DSM-IV diagnoses derived from the World Health Organization Composite International Diagnostic Interview with projected lifetime risk at age 75 years; adapted from Kessler et al where data on specific diagnoses and details of the sample are available.
in white matter occur over a longer period into the third decade. There is a general pattern of childhood peaks of grey matter followed by adolescent declines, functional and structural increases in connectivity and integrative processing:46 the balance between limbic and subcortical and frontal lobe functions extends well into young adulthood.46 The higher-order association cortices mature after lower-order somatosensory and visual cortices, and phylogenetically older brain areas mature earlier than those more recently evolved such as the frontal cortex. The control of these changes, particularly the initial childhood growth in grey matter, is likely to be dependent on androgens, with regional differences and contrasts between girls and boys being mediated by differences in androgen receptor density and function.47 Cortical developments are more dependent on environmental influences and transactions. Although the brains of children and young adults may have similar ‘small world’ organisation at the global level, they differ significantly in hierarchical organisation and interregional connectivity. These large-scale changes underpin the transition from dependent child to independent adult able to draw on sophisticated learning from reward and punishment, and effective executive and emotional control.48–50

Casey et al provide a model of these key brain structural and neurocognitive phenotypes developing at different rates.42 They highlight the relevance of normal development in understanding emergence of psychopathology in the developmental epoch from puberty to the late 20s.43 A ‘neural maturation gap’ during adolescence exists between earlier maturation of limbic and subcortical reward processing networks dependent on the neurosteroid growth spurt, and later consolidation of neocortical cognitive and emotional control networks dependent on environmental experience. This maturation gap may present a window of vulnerability during which these two different systems are not yet fully coordinated.

Health service implications

It seems that from the perspective of brain development it should come as no surprise that most adult mental health disorders have their roots in adolescence. We may ask why they persist thereafter, and what can be done about them. Mechanisms of persistence are beyond the scope of this article but the robust findings from modern epidemiology and their consilience with the emerging neurobiology of adolescence should be a clarion call for intervention involving both primary and secondary prevention.50 Many incident disorders will resolve but it is clear that many do persist, and result in lifelong disability and cost to society and the individual. Not every anxiety disorder or depression in childhood or teenage years will lead to adult disorder. However, the findings suggest that appropriate interventions should be widely available to speed initial treatment contact and reduce the burdens and hazards of untreated mental disorder.60 It is straightforward to propose that early signs of recurrence or persistence of adolescent mental health disorder should lead to a concerted therapeutic effort, probably coordinated by primary care, and there is evidence to suggest that – in psychiatric disorders at least – such early specialist intervention is cost-effective.51 However, the appropriate response to the earliest signs of disorder in large numbers of young people is less clear, and the risk to benefit ratio of specialist care will be totally different in the wider subclinical or primary care population from that in the services in which many interventions are developed. Traditional mental health services have evolved without the knowledge that psychopathology observes no transition between adolescence and early adulthood. From the perspective of brain development, services may require re-engineering to provide an appropriately seamless and developmentally sensitive approach to individuals on the two-decade journey from puberty to adulthood. These questions are explored elsewhere in this supplement and require considerable and sophisticated research in order to guide appropriate care at the clinical and public health levels.

Establishing age at onset of mental health disorders is methodologically difficult. A range of epidemiological approaches provide convergent evidence not only that adult mental health disorders are common in the population, but that most of them have their onset by adolescence. This period of life after puberty also sees a range of important organisational developments in the brain that last until the late 20s and usher in adulthood as might be defined from a developmental rather than a social or legal point of view. These biological changes are characterised by a temporary uncoupling of higher-order, more recently evolved cortical functions from the limbic and subcortical systems that mature earlier. This maturational gap is normal, but appears to leave the adolescent vulnerable to a range of experiences and responses, some of which form the components of mental disorders and may persist as such. These findings provide a persuasive argument to reappraise our formulations of mental health disorder into a new developmental psychiatry embracing a modern life-course approach that focuses on the second and third decades of life. Such a view also triggers the need for a new research agenda to guide these new ventures, the therapeutic interventions they may wield and the service structures through which these are delivered to young people.

Funding

P.B.J. acknowledges research support from the Wellcome Trust and the National Institute for Health Research (NIHR; programme grant RP-PG-0606-1335). The work forms part of the NIHR Collaboration for Leadership in Applied Health Research and Care for Cambridge & Peterborough.

Acknowledgements

The author thanks Mrs Anne Robinson and Dr Golam Khandaker for their help with referencing.

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BJP 2013, 202:s5-s10.
Access the most recent version at DOI: 10.1192/bjp.bp.112.119164

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