Age of onset of mental disorders: A review of recent literature

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Abstract

Purpose of the review—To review recent epidemiological research on age-of-onset (AOO) of mental disorders, focusing on the WHO World Mental Health (WMH) surveys.

Recent findings—Median and inter-quartile range (IQR; 25^{th}–75^{th} percentiles) of AOO is much earlier for phobias (7–14, IQR: 4–20) and impulse-control disorders (7–15, IQR: 4–35) than other anxiety disorders (25–53, IQR: 15–75), mood disorders (25–45, IQR: 17–65), and substance disorders (18–29, IQR: 16–43). Although less data exist for non-affective psychosis, available evidence suggests that median AOO is in the range late teens through early 20s. Roughly half of all lifetime mental disorders in most studies start by the mid-teens and three-fourths by the mid-20s. Later onsets are mostly secondary conditions. Severe disorders are typically preceded by less severe disorders that seldom are brought to clinical attention.

Summary—First onset of mental disorders usually occurs in childhood or adolescence, although treatment typically does not occur until a number of years later. Although interventions with early incipient disorders might help reduce severity-persistence of primary disorders and prevent secondary disorders, additional research is needed on appropriate treatments for early incipient cases and on long-term evaluation of the effects of early intervention on secondary prevention.

Keywords

Age of onset; prevention; early intervention; mental disorders; WHO World Mental Health (WMH) Survey Initiative

Introduction

The purpose of this paper is to review recent evidence from epidemiological surveys on the age of onset (AOO) distributions of commonly occurring mental disorders. Although AOO is one of the least commonly studied aspects of descriptive epidemiology, it is important for reasons described below. The recent publication of comprehensive AOO results from the World Health Organization's World Mental Health (WMH) Surveys provides unprecedented data on the AOO distributions of many commonly occurring mental disorders. These data have

several important implications for clinical practice and research that are discussed in the second half of the review.

Practical difficulties in studying age of onset

The dearth of information on AOO of mental disorders is presumably due to reluctance on the part of epidemiologists to rely on the retrospective reports obtained in general population surveys that, as a practical matter, must be used to generate the survival distributions needed to study AOO. Two theoretical alternatives exist to relying on these retrospective reports, although neither of the two is broadly feasible. The first applies largely to psychosis: to use information obtained about total-population incidence of *treated* disorder from studies of psychotic disorders in catchment areas that monitor all points of contact with the treatment system (e.g., [1,2]). The implicit assumption in this approach, that the vast majority of psychotics eventually come to clinical attention, is likely to be true, making this approach useful for studying AOO of non-affective psychosis. The same approach would not be nearly as useful, though, for less severely impairing disorders, as many people with such disorders never come to clinical attention. Even for non-affective psychosis, epidemiological surveys show that the time between onset of the first episode and first contact with the treatment system is sometimes quite long [3], although analysis of incident treated cases is still the best available approach due to the substantial under-representation of psychosis in community epidemiological surveys [4*].

The second theoretical alternative to relying on retrospective AOO reports is to carry out large long-term prospective surveys to estimate incidence directly. Numerous studies of this sort exist in such well-funded fields of cancer epidemiology (e.g., [5]) and cardiovascular epidemiology (e.g., [6]). Comparable studies of mental disorders do not exist. Although some large long-term community epidemiological studies have included some information on mental disorders (e.g., www.nshd.mrc.ac.uk), the data collection waves are not sufficient frequent and the assessment mental disorder interval incidence not sufficiently central to generate accurate prospective estimates of incidence. Prospective birth cohort studies in schizophrenia that cover the whole age range of risk for the onset of the disorder are sparse (e.g., [7,8]). As a result, we have to rely largely on retrospective reports in cross-sectional community surveys to estimate AOO distributions of commonly occurring mental disorders.

Why study age of onset?

An examination of AOO distributions is important for at least two reasons. One is that information on AOO allows us to distinguish between lifetime prevalence (the proportion of the population who had a disorder at some time in their life up to their age at interview) and projected lifetime risk (the estimated proportion of the population who will have the disorder by the end of their life). Lifetime risk cannot be estimated directly from community surveys because respondents differ in age and, therefore, number of years at risk. Projections of estimated future risk can be made from AOO distributions, though, using either the Kaplan-Meier [9] method or the slightly more precise actuarial method [10] to estimate survival distributions. Second, an understanding of AOO is important for targeting research on prevention of mental disorders [11**], early intervention with prodromal or incipient mental disorders [12], and primary prevention of secondary disorders [13]. In the absence of AOO information, we would have no way to know the appropriate age range to target preventive interventions. A related issue is that early AOO is often found to be associated with greater disorder severity [14], persistence [15], and lack of treatment response [16]. Based on these associations, AOO information can be useful in making projections of aggregate illness course associated with primary and secondary disorders.

WMH Survey Methods

As the main focus of the following review is on the WMH surveys, we present a brief overview of WMH methods. The WMH Survey Initiative consists of coordinated population surveys in 28 countries [17]. The main aim is to provide estimate of the prevalence, distribution, societal burden, and patterns of treatment of mental disorders to health policy makers for planning purposes. The WMH interview schedule and all other study materials were translated using standardized WHO protocols. Consistent interviewer training and quality control procedures were used in all surveys. The informed consent was obtained in each country using procedures approved by the Institutional Review Boards of the organizations coordinating the survey in the country.

The WHO regions and 16 countries that have completed and published WMH results up to now are Africa (Nigeria; South Africa), the Americas (Colombia; Mexico; United States), Asia and the Pacific (Japan; New Zealand; Beijing and Shanghai in the People's Republic of China - henceforth referred to as Metropolitan PRC), Europe (Belgium; France; Germany; Italy; the Netherlands; Spain; Ukraine); and the Middle East (Israel; Lebanon). The surveys in most of these countries were nationally representative (the exceptions being China, Japan, and Nigeria, which were regionally representative). Seven of the countries are classified by the World Bank as less developed (China, Colombia, Lebanon, Mexico, Nigeria, South Africa, Ukraine), while the others are classified as developed [18]. All surveys were conducted face-to-face by trained lay interviewers in multi-stage household probability samples. A total of 85,052 interviews were completed in these 16 countries, with samples ranging from 2372 in the Netherlands to 12,992 in New Zealand. The weighted average response rate was 71.1%. More details on WMH samples, designs, and field procedures are presented at www.hcp.med.harvard.edu/WMH.

The WMH diagnostic interview was the WHO Composite Diagnostic Interview (CIDI) Version 3.0 [19], a fully-structured lay-administered interview that generates both ICD-10 and DSM-IV diagnoses. DSM-IV diagnoses were used in the analyses reviewed here. Included were anxiety disorders (panic disorder, agoraphobia without panic disorder, specific phobia, social phobia, generalized anxiety disorder, post-traumatic stress disorder, separation anxiety disorder), mood disorders (major depressive disorder, dysthymic disorder, bipolar disorder I and II, sub-threshold bipolar disorder), impulse-control disorders (intermittent explosive disorder, oppositional-defiant disorder, attention-deficit/hyperactivity disorder, conduct disorder), and substance use disorders (alcohol and drug abuse with or without dependence). Not all disorders were assessed in all countries. Non-affective psychosis (NAP) was not assessed because the CIDI assessment of NAP was not sufficiently reliable and valid [20]. Clinical calibration studies [21] found that the CIDI assessed other disorders with good concordance to blinded clinical reappraisal interviews using the Structured Clinical Interview for DSM-IV (SCID) [22].

Research carried out in conjunction with the landmark Epidemiological Catchment Area (ECA) [23]. Study found that retrospective AOO reports often generate implausible response patterns, indicating the existence of retrospective recall bias [24]. Special procedures developed by survey methodologists to minimize this bias were used in the WMH surveys both to decrease recall failure involving the lifetime occurrence of disorders [19] and to decrease imprecision in dating the AOO of reported disorders [25]. Experimental research has shown that this question sequence yields responses with a much more plausible AOO distribution than standard AOO questions [25].

Age of onset distributions of commonly occurring disorders

Disorder-specific estimates of AOO distributions have either been published for WMH surveys in Italy [26], Metropolitan China [27], Mexico [28], New Zealand [29], Nigeria [30], Spain [31], Ukraine [32], and the USA [33]. In addition, a comparative analysis of these distributions across 16 WMH countries has been completed [34**]. Systematic comparison of these results documents a number of clear cross-national consistencies both within and between disorders.

The impulse-control disorders have the earliest AOO distributions, with median AOO across countries of 7–9 years for attention-deficit/hyperactivity disorder (ADHD), 7–15 for oppositional-defiant disorder (ODD), 9–14 for conduct disorder (CD), and 13–21 for intermittent explosive disorder (IED). Impulse-control disorders also have an extremely narrow age range of onset risk. For example, 80% of all lifetime ADHD begins in the age range 4–11, while the vast majority of ODD and CD begins between ages 5 and 15. Fully half of all lifetime IED begins in childhood or adolescence.

Some anxiety disorders — the phobias and separation anxiety disorder (SAD) — also have very early AOO distributions, with median AOO in the range 7–14 and inter-quartile range (IQR; 25^{th}–75^{th} percentiles of the AOO distributions) of 4–20. The other anxiety disorders (panic disorder, generalized anxiety disorder, and post-traumatic stress disorder), in comparison, have considerably later AOO distributions, although the cross-national variation in both median AOO (25–53) and in IQR AOO (15–75) is considerably wider than for the impulse-control disorders or the phobias or SAD.

The mood disorder AOO distributions in the WMH surveys are quite similar to those for the later-onset anxiety disorders. Mood disorder AOO curves show consistently low prevalence until the early teens followed by a roughly linear increase through late middle age and a declining increase thereafter. The median AOO of mood disorders has a very wide range across countries (25–45) and an even wider IQR (17–65).

The AOO distributions of substance use disorders, finally, are quite consistent across the WMH countries in that few onsets occur prior to the mid teens and cumulative increase in onset is rapid in adolescence and early adulthood. Considerable cross-national variation exists, though, in the sharpness of the change in the slope as well as in the age range of this change. This cross-national variation leads to wider cross-national variation in both the median (18–29) and the inter-quartile range (16–43) of the AOO distributions than for impulse-control disorders or phobias or SAD, but lower variation than for mood disorders or other anxiety disorders.

No strong consistency in between-country differences in AOO distributions were detected across disorders. Furthermore, between-country differences in these distributions were found to be unrelated to economic development, to region of the world, or to other structural correlates.

The age of onset distribution of treated psychosis

Psychotic disorders rarely occur before age 14, but show a marked increase in prevalence between at ages 15–17 [35]. Schizophrenia spectrum diagnoses (SSD) account for approximately two-thirds of all psychotic disorders. Schizophrenia usually bens in the age range 15–35. Disorder-specific estimates of AOO distributions for non-affective and affective psychotic disorders have not been separately reported in any of the WMH surveys due to the under-representation of these cases in surveys.

As noted above, studies that either establish the treated incidence of psychosis in a well defined catchment area or that observe onsets in long-term prospective general population cohorts are

preferred. An integrated community-based treatment system is needed to obtain accurate data on treated incidence. A good example of such a system can be found at the Early Psychosis Prevention and Intervention Centre (EPPIC) in Melbourne, Australia. This is a community-based specialized service mandated to treat all people between 15 and 29 years who present with a first psychotic episode to public mental health services in a geographically defined catchment area. Between 1997 and 2000, 1019 individuals were registered at EPPIC with a first episode of psychosis. The median age of initial presentation in this cohort was 22 with an IQR of 19–25. The same median and IQR existed for patients with SSD (69%) and those with non-SSD (31%).

Similar results were found in the 1966 North Finland Birth Cohort, where median AOO and IQR for schizophrenia were 23 and 19–27 [8], and in the 1946 British 1946 birth cohort (median AOO for schizophrenia 22) [7]. The majority of psychoses manifest in the third life decade with a median in the early twenties and a narrow inter-quartile range more similar to impulse-control disorders and some anxiety disorders than mood disorders.

Projected lifetime risk in comparison to lifetime-prevalence-to-date

As noted in the introduction, one important reason for estimating AOO distributions is to obtain data on projected lifetime risk. It is noteworthy that the estimates of projected lifetime risk of any DSM-IV disorder in the WMH surveys was roughly one-third higher (IQR 28–44%) than estimated lifetime prevalence-to-date. This means that 3–4 people in the populations of these countries are likely to develop a first mental disorder at some time in the future for every ten people who already had a disorder. The highest risk-to-prevalence ratios (57–69%) were found in countries exposed to sectarian violence (Israel, Nigeria, South Africa). Excluding these three, no strong difference in risk-to-prevalence ratios were found of less developed countries (28–41%) versus developed countries (17–49%).

Not surprisingly, the highest class-specific proportional increase in projected lifetime risk versus prevalence was associated with mood disorders (IQR 61–98%) and the lowest with impulse-control disorders (IQR 0–2%). These differences reflect the fact that many mood disorders begin in middle age or old age, while the vast majority of impulse-control disorders begin in childhood or adolescence.

The high comorbidity known to exist among mental disorders [36–38] would be expected to result in many WMH respondents who developed impulse-control disorders or early-onset anxiety disorders subsequently developing substance, mood, or later-onset anxiety disorders. This possibility was investigated by comparing the risk-to-prevalence ratios of *any* disorder versus *individual* disorders. This showed that the vast majority of projected new onsets of individual disorders would be secondary disorders, as indicated by the fact that the risk-to-prevalence ratio for *any* disorder is close to 1.0 in most countries.

Limitations

The WMH results are limited by the possibility that people with a history of mental illness might be less likely than others to participate in community surveys or might under-report their disorders. Although innovative strategies were used to minimize the latter problem [19], it is unlikely that they were completely successful. AOO might have been recalled incorrectly as well [24] despite the WMH surveys using a novel probing strategy to reduce bias in AOO reports. Estimates of psychosis AOO were limited by their being based on incident *treatment*. The AOO results are further limited by focusing on *syndrome* onset, ignoring any prodrome at an earlier age. A number of at-risk mental states are known to occur prior to the onset of many cases of NAP [39*] and bipolar disorder [40]. A number of problem behaviors indicative of impulsivity are known to occur prior to the onset of many cases of impulse-control

disorders [41]. Childhood behavioral inhibition is known to occur prior to the onset of many cases of panic disorder and depression [42]. Epidemiological analysis of these early indicators of incipient disorder would almost certainly lead to much earlier estimates of AOO than those reported here.

Implications

Within the context of these limitations, the AOO distributions reported here are consistent with those in previous epidemiological surveys [43,44]. We know of no research prior to the WMH surveys that examined AOO distributions of PTSD, but one would expect these to be quite variable due to trauma exposure occurring throughout the life course. Nor are we aware of previous research on the AOO distributions of impulse-control disorders, although the lifetime prevalence estimates of these disorders in the WMH surveys [29,33] are in the range reported in previous surveys of adolescents [45,46]. No previous research has examined the temporal concentration of AOO or highlighted the concentration of onset ages for most disorders in a very narrow time span. It is striking in this regard that the upper bounds of the AOO IQR's for disorders with narrow ranges are all quite early: the mid teens for impulse-control disorders and anxiety disorders with narrow IQR's and the late 20s for substance use disorders. These are opposite the patterns found for chronic physical disorders, where conditional risk increases with age and the upper bound of the IQR is in late middle age or old age [47].

Investigations of initial contact with the treatment system based on data collected in a number of community epidemiological surveys [48] have consistently found that many people wait more than a decade after first onset of a mental disorder before seeking treatment. These people often present with highly comorbid conditions that might have been easier to treat if they had sought treatment earlier in the course of illness. Early treatment of first-onset disorders would often mean childhood-adolescent treatment. Unfortunately, we know little about treatment of mild child-adolescent cases and even less about treatment of incipient child-adolescent cases. A complicating factor is that the effects of psychotropic medications can be quite different on children-adolescents than adults [49]. The most active research of this sort deals with treating incipient psychosis [11**] and early stages of adolescent substance use disorder [50], although much remains to be learned about the best ways to treat of these early cases.

Conclusion

The results reported here show clearly that first onset of mental disorders usually occurs in childhood or adolescence. Although it is thought that timely interventions with early-onset cases might help reduce severity-persistence of primary disorders, prevent or delay onset of secondary disorders, or reduce persistence-severity of secondary disorders, much preclinical and clinical research is needed on treatments of early cases to determine whether this is true. Epidemiological research is also needed on the long-term consequences of early interventions for long-term secondary prevention.

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References

1. Amminger GP, Harris MG, Conus P, Lambert M, Elkins KS, Yuen HP, et al. Treated incidence of first-episode psychosis in the catchment area of EPPIC between 1997 and 2000. Acta Psychiatr Scand 2006;114:337–345. [PubMed: 17022793]
2. Bromet EJ, Fennig S. Epidemiology and natural history of schizophrenia. Biol Psychiatry 1999;46:871–881. [PubMed: 10509170]
3. Norman RM, Malla AK. Duration of untreated psychosis: a critical examination of the concept and its importance. Psychol Med 2001;31:381–400. [PubMed: 11305847]

*4. Perala J, Suvisaari J, Saarni SI, Kuoppasalmi K, Isometsa E, Pirkola S, et al. Lifetime prevalence of psychotic and bipolar I disorders in a general population. Arch Gen Psychiatry 2007;64:19–28. [PubMed: 17199051]The limitations of screening for psychosis in population surveys were highlighted by comparing clinician-based assessments of psychosis based on CIDI screens with data from a population registry and documenting substantial under-representation in the survey.

5. Jenab M, Riboli E, Ferrari P, Friesen M, Sabate J, Norat T, et al. Plasma and dietary carotenoid, retinol and tocopherol levels and the risk of gastric adenocarcinomas in the European prospective investigation into cancer and nutrition. Br J Cancer 2006;95:406–415. [PubMed: 16832408]
6. Yan LL, Liu K, Daviglus ML, Colangelo LA, Kiefe CI, Sidney S, et al. Education, 15-year risk factor progression, and coronary artery calcium in young adulthood and early middle age: the Coronary Artery Risk Development in Young Adults study. JAMA 2006;295:1793–1800. [PubMed: 16622141]
7. Jones P, Rodgers B, Murray R, Marmot M. Child development risk factors for adult schizophrenia in the British 1946 birth cohort. Lancet 1994;344:1398–1402. [PubMed: 7968076]
8. Lauronen E, Miettunen J, Veijola J, Karhu M, Jones PB, Isohanni M. Outcome and its predictors in schizophrenia within the Northern Finland 1966 Birth Cohort. Eur Psychiatry 2007;22:129–136. [PubMed: 17129711]
9. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–481.
10. Halli, SS.; Rao, KV.; Halli, SS. Advanced Techniques of Population Analysis. NY: Plenum; 1992.

**11. Amminger GP, Leicester S, Yung AR, Phillips LJ, Berger GE, Francey SM, et al. Early-onset of symptoms predicts conversion to non-affective psychosis in ultra-high risk individuals. Schizophr Res 2006;84:67–76. [PubMed: 16677803]The paper examined AOO of psychiatric symptoms as predictors of conversion to non-affective and affective psychosis in help-seeking individuals at ultra-high risk for schizophrenia. Early-onset of psychiatric symptoms were found to be specifically associated with conversion to non-affective psychosis but not affective psychosis. This finding suggests that early AOO of certain psychiatric symptoms is an independent factor relevant for defining samples specifically at risk for schizophrenia.

12. Klosterkotter J, Ruhrmann S, Schultze-Lutter F, Salokangas RK, Linszen D, Birchwood M, et al. The European Prediction of Psychosis Study (EPOS): integrating early recognition and intervention in Europe. World Psychiatry 2005;4:161–167. [PubMed: 16633542]
13. Kendall PC, Kessler RC. The impact of childhood psychopathology interventions on subsequent substance abuse: policy implications, comments, and recommendations. J Consult Clin Psychol 2002;70:1303–1306. [PubMed: 12472302]
14. Kessler RC, Keller MB, Wittchen HU. The epidemiology of generalized anxiety disorder. Psychiatr Clin North Am 2001;24:19–39. [PubMed: 11225507]
15. Clark DB, Jones BL, Wood DS, Cornelius JR. Substance use disorder trajectory classes: diachronic integration of onset age, severity, and course. Addict Behav 2006;31:995–1009. [PubMed: 16675151]
16. Nierenberg AA, Quitkin FM, Kremer MB, Keller MB, Thase ME. Placebo-controlled continuation treatment with mirtazapine: acute pattern of response predicts relapse. Neuropsychopharmacology 2004;29:1012–1018. [PubMed: 14997172]
17. Kessler RC, Haro JM, Heeringa SG, Pennell BE, Ustun TB. The World Health Organization World Mental Health Survey Initiative. Epidemiol Psichiatr Soc 2006;15:161–166. [PubMed: 17128617]

18. Kessler RC, Andrews G, Mroczek D, Ustun B, Wittchen H-U. The World Health Organization Composite International Diagnostic Interview Short Form (CIDI-SF). Int J Methods Psyciatr Res 1998;7:171–185.

19. Kessler RC, Ustun TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res 2004;13:93–121. [PubMed: 15297906]

20. Kessler RC, Birnbaum H, Demler O, Falloon IR, Gagnon E, Guyer M, et al. The prevalence and correlates of nonaffective psychosis in the National Comorbidity Survey Replication (NCSR). Biol Psychiatry 2005;58:668–676. [PubMed: 16023620]

21. Haro JM, Arbabzadeh-Bouchez S, Brugha TS, de Girolamo G, Guyer ME, Jin R, et al. Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health surveys. Int J Methods Psychiatr Res 2006;15:167–180. [PubMed: 17266013]

22. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured Clinical Interview for DSM-IV axis I disorders, research version, non-patient edition (SCID-I/NP). New York: Biometrics Research, New York State Psychiatric Institute; 2002.

23. Robins, LN.; Regier, DA., editors. Psychiatric Disorders in America: The Epidemiologic Catchment Area Study. New York: The Free Press; 1991.

24. Simon GE, VonKorff M. Recall of psychiatric history in cross-sectional surveys: implications for epidemiologic research. Epidemiol Rev 1995;17:221–227. [PubMed: 8521941]

25. Knauper B, Cannell CF, Schwarz N, Bruce BL, Kessler RC. Improving the accuracy of major depression age of onset reports in the US National Comorbidity Survey. Int J Methods Psyciatr Res 1999;8:39–48.

26. de Girolamo G, Polidori G, Morosini PL, Scarpino V, Reda V, Serra G, et al. Prevalence of common mental disorders in Italy. Results from the European Study of the Epidemiology of Mental Disorders (ESEMeD). Soc Psychiatry Psychiatr Epidemiol 2006;41:853–861. [PubMed: 16915360]

27. Lee S, Tsang A, Zhang MY, Huang YQ, He YL, Liu ZR, et al. Lifetime prevalence and inter-cohort variation in DSM-IV disorders in metropolitan China. Psychol Med 2007;37:61–71. [PubMed: 17038208]

28. Medina-Mora M-E, Borges G, Lara C, Benjet C, Blanco J, Fleiz C, et al. Prevalence, age of onset, and demographic correlates of DSM-IV psychiatric disorders in Mexico: Results from the Mexican Psychiatric Survey. Psychol Med. in press

29. Oakley Browne MA, Wells JE, Scott KM, McGee MA. Lifetime prevalence and projected lifetime risk of DSM-IV disorders in Te Rau Hinengaro: the New Zealand Mental Health Survey. Aust N Z J Psychiatry 2006;40:865–874. [PubMed: 16959012]

30. Gureje O, Lasebikan VO, Kola L, Makanjuola VA. Lifetime and 12-month prevalence of mental disorders in the Nigerian Survey of Mental Health and Well-Being. Br J Psychiatry 2006;188:465–471. [PubMed: 16648534]

31. Haro JM, Palacin C, Vilagut G, Martinez M, Bernal M, Luque I, et al. [Prevalence of mental disorders and associated factors: results from the ESEMeD-Spain study]. Med Clin (Barc) 2006;126:445–451. [PubMed: 16620730]

32. Bromet EJ, Gluzman SF, Paniotto VI, Webb CP, Tintle NL, Zakhozha V, et al. Epidemiology of psychiatric and alcohol disorders in Ukraine: findings from the Ukraine World Mental Health survey. Soc Psychiatry Psychiatr Epidemiol 2005;40:681–690. [PubMed: 16160752]

33. Kessler RC, Berglund P, Demler O, Jin R, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:593–602. [PubMed: 15939837]

**34. The WHO World Mental Health Survey ConsortiumLifetime prevalence and age-of-onset distributions of mental disorders in the WHO World Mental Health (WMH) Surveys. Bull World Health Organ in press. This paper presents a detailed synthetic comparison of AOO information for a wide range of mental disorders from community surveys carried out in 16 different countries.

35. Thomsen PH. Schizophrenia with childhood and adolescent onset--a nationwide register-based study. Acta Psychiatr Scand 1996;94:187–193. [PubMed: 8891086]

36. Jacobi F, Wittchen HU, Holting C, Hofler M, Pfister H, Muller N, et al. Prevalence, comorbidity and correlates of mental disorders in the general population: results from the German Health Interview and Examination Survey (GHS). Psychol Med 2004;34:597–611. [PubMed: 15099415]

37. Kessler, RC. The prevalence of psychiatric comorbidity. In: Wetzler, S.; Sanderson, WC., editors. Treatment Strategies for Patients with Psychiatric Comorbidity. New York, NY: John Wiley & Sons; 1997. p. 23-48.

38. Krueger RF, Chentsova-Dutton YE, Markon KE, Goldberg D, Ormel J. A cross-cultural study of the structure of comorbidity among common psychopathological syndromes in the general health care setting. J Abnorm Psychol 2003;112:437–447. [PubMed: 12943022]

*39. Yung AR, Yuen HP, McGorry PD, Phillips LJ, Kelly D, Dell'Olio M, et al. Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. Aust N Z J Psychiatry 2005;39:964–971. [PubMed: 16343296]The paper describes the Comprehensive Assessment of At-Risk Mental States (CAARMS), an instrument which has been designed for monitoring subthreshold psychotic symptoms for worsening into full-threshold psychotic disorder. It has two functions: (i) to assess psychopathology thought to indicate imminent development of a first-episode psychotic disorder; and (ii) to determine if an individual meets criteria for being at ultra high risk for onset of first psychotic disorder.

40. Thompson KN, Conus PO, Ward JL, Phillips LJ, Koutsogiannis J, Leicester S, et al. The initial prodrome to bipolar affective disorder: prospective case studies. J Affect Disord 2003;77:79–85. [PubMed: 14550938]

41. McGue M, Iacono WG. The association of early adolescent problem behavior with adult psychopathology. Am J Psychiatry 2005;162:1118–1124. [PubMed: 15930060]

42. Rosenbaum JF, Biederman J, Hirshfeld-Becker DR, Kagan J, Snidman N, Friedman D, et al. A controlled study of behavioral inhibition in children of parents with panic disorder and depression. Am J Psychiatry 2000;157:2002–2010. [PubMed: 11097967]

43. Christie KA, Burke JDJ, Regier DA, Rae DS, Boyd JH, Locke BZ. Epidemiologic evidence for early onset of mental disorders and higher risk of drug-abuse in young-adults. Am J Psychiatry 1988;145:971–975. [PubMed: 3394882]

44. WHO International Consortium in Psychiatric Epidemiology. Cross-national comparisons of the prevalences and correlates of mental disorders. 78. Bull World Health Organ; 2000. p. 413-426.

45. Loeber R, Burke JD, Lahey BB, Winters A, Zera M. Oppositional defiant and conduct disorder: a review of the past 10 years, part I. J Am Acad Child Adolesc Psychiatry 2000;39:1468–1484. [PubMed: 11128323]

46. Scahill L, Schwab-Stone M. Epidemiology of ADHD in school-age children. Child Adolesc Psychiatr Clin N Am 2000;9:541–555. [PubMed: 10944656]vii

47. Murray, CJL.; Lopez, AD. Global Health Statistics. Cambridge: Harvard University Press; 1996.

48. Christiana JM, Gilman SE, Guardino M, Kessler RC, Mickelson K, Morselli PL, et al. Duration between onset and time of obtaining initial treatment among people with anxiety and mood disorders: an international survey of members of mental health patient advocate groups. Psychol Med 2000;30:693–703. [PubMed: 10883723]

49. Murrin LC, Sanders JD, Bylund DB. Comparison of the maturation of the adrenergic and serotonergic neurotransmitter systems in the brain: Implications for differential drug effects on juveniles and adults. Biochem Pharmacol. 2007epub ahead of print

50. White HR, Morgan TJ, Pugh LA, Celinska K, Labouvie EW, Pandina RJ. Evaluating two brief substance-use interventions for mandated college students. J Stud Alcohol 2006;67:309–317. [PubMed: 16562414]