A Population-Based Cohort Study Examining the Incidence and Impact of Psychotic Experiences From Childhood to Adulthood, and Prediction of Psychotic Disorder

Sarah A. Sullivan, Ph.D., Daphne Kounali, Ph.D., Mary Cannon, Ph.D., Anthony S. David, M.D., Paul C. Fletcher, Ph.D., Peter Holmans, Ph.D., Hannah Jones, Ph.D., Peter B. Jones, Ph.D., David E.J. Linden, Ph.D., Glyn Lewis, Ph.D., Michael J. Owen, Ph.D., Michael O'Donovan, Ph.D., Alexandros Rammos, Ph.D., Andrew Thompson, M.D., Dieter Wolke, Ph.D., Jon Heron, Ph.D., Stanley Zammit, Ph.D.

Objective: The authors investigated the incidence, course, and outcome of psychotic experiences from childhood through early adulthood in the general population and examined prediction of psychotic disorder.

Methods: This was a population-based cohort study using the semistructured Psychosis-Like Symptoms Interview at ages 12, 18, and 24 (N=7,900 with any data). Incidence rates were estimated using flexible parametric modeling, and positive predictive values (PPVs), sensitivity, specificity, and area under the curve were estimated for prediction.

Results: The incidence rate of psychotic experiences increased between ages 13 and 24, peaking during late adolescence. Of 3,866 participants interviewed at age 24, 313 (8.1%, 95% CI=7.2, 9.0) had a definite psychotic experience since age 12. A total of 109 individuals (2.8%) met criteria for a psychotic disorder up to age 24, of whom 70% had sought professional help. Prediction of current psychotic

disorder at age 24 (N=47, 1.2%), by both self-report and interviewer-rated measures of psychotic experiences at age 18 (PPVs, 2.9% and 10.0%, respectively), was improved by incorporating information on frequency and distress (PPVs, 13.3% and 20.0%, respectively), although sensitivities were low. The PPV of an at-risk mental state at age 18 predicting incident disorder at ages 18–24 was 21.1% (95% CI=6.1, 45.6) (sensitivity, 14.3%, 95% CI=4.0, 32.7).

Conclusions: The study results show a peak in incidence of psychotic experiences during late adolescence as well as an unmet need for care in young people with psychotic disorders. Because of the low sensitivity, targeting individuals in non-help-seeking samples based only on more severe symptom cutoff thresholds will likely have little impact on population levels of first-episode psychosis.

Am J Psychiatry 2020; 177:308-317; doi: 10.1176/appi.ajp.2019.19060654

Psychotic disorders have a lifetime prevalence of approximately 3% (1) and have a substantial impact on individuals, their families, and society. While psychotic disorders are defined in part by the presence of psychotic experiences, psychotic experiences commonly occur outside the context of a full psychotic disorder (2). Studies using semistructured interviews, which are similar to the cross-questioning style of clinical practice, report 6-month prevalence estimates of approximately 5% in late childhood or adolescence (3–5), although estimates from fully structured interviews and questionnaires are generally higher (2).

In the general population, the vast majority of people with psychotic experiences do not present to clinical services,

See related features: CME course (p. 361) and AJP Audio (online)

let alone with a psychotic disorder (4, 6–8). While psychotic experiences are usually transient (7, 9–14), they are nevertheless often distressing and associated with impaired social and occupational function, both concurrently and longitudinally (4, 15, 16), and with suicidality (17–21); thus, psychotic experiences may index a common, and underrecognized, public health burden (4, 22). Given the global burden of disease of psychotic disorders and the promise of benefit from early intervention in improving clinical outcomes, there is an imperative to understand the developmental trajectories from onset of psychotic experiences to clinical disorder and to improve identification of individuals at greatest risk of requiring intervention. A number of studies suggest that psychotic experiences are more common in children and young adolescents compared with adults (2, 23, 24), but few longitudinal studies have assessed psychotic phenomena at multiple time points using semistructured interviews, and none have assessed such experiences sequentially from childhood through adolescence and early adulthood.

The aims of this study were 1) to describe the change in incidence of psychotic experiences in the general population from ages 12 through 24; 2) to describe the prevalence of at-risk mental states for psychosis and psychotic disorder at age 24 and to quantify the likely burden of unmet clinical need among young adults in the general population; and 3) to examine the predictive ability of both self-reported and interviewer-rated measures of psychotic experiences during childhood and adolescence in identifying psychotic disorder by age 24.

METHODS

Sample

Pregnant women residing in Avon, U.K., with expected dates of delivery between April 1, 1991, and December 31, 1992 (enrolled, N=14,541; live births alive at 1 year, N=13,988) were invited to take part in the Avon Longitudinal Study of Parents and Children (ALSPAC) (25; http://www.bris.ac.uk/ alspac/researchers/data-access/data-dictionary/). To estimate incidence rates, we examined data from 7,919 individuals who were assessed at age 12, 18, or 24 years. The focus of the rest of the study were the 3,866 young adults (9,958 invited; response rate, 39%) who participated at age 24 (mean age, 24.04 years, SD=0.85). All participants provided written consent. Ethical approval was obtained from the ALSPAC Law and Ethics Committee and the local research ethics committees.

Measures

Psychotic experiences. The semistructured Psychosis-Like Symptoms Interview (4, 5) includes 12 core questions eliciting key psychotic experiences: hallucinations (visual and auditory), delusions (spied on, persecution, thoughts read, reference, control, grandiosity, and other), and experiences of thought interference (broadcasting, insertion, and withdrawal). Questions about each experience started with a structured stem question asking if the participant had ever had that experience since age 12. Participants endorsing "yes" or "maybe" responses (henceforth referred to as "selfreported experiences") were then cross-questioned to establish whether the experience was psychotic (henceforth referred to as "interview-rated experiences"). Coding of psychotic experiences followed glossary definitions and rating rules for the Schedules for Clinical Assessment in Neuropsychiatry (26). Interviewers rated psychotic experiences as not present, suspected, or definitely present. Unclear responses after probing were "rated down," and items were rated as definite only when an example that clearly met the rating rules for the Schedules for Clinical Assessment in Neuropsychiatry was provided (see the online supplement).

current (past 6 months) self-reported and interviewer-rated psychotic experiences, and of the age-18 interview (4), which assesses ever (since age 12) self-reported and interviewerrated psychotic experiences and current (past 6 months) interviewer-rated psychotic experiences. At age 18, information on current (past 6 months) self-reported experiences was available only for auditory hallucinations and delusions of being spied on. In this study, we report data from the age-24 Psychosis-Like Symptoms Interview, which we also compare with data from the previous interviews. Reliability of the age-24 Psychosis-Like Symptoms Interview was good (interrater reliability, intraclass correlation coefficient=0.81, 95% CI=0.68, 0.89; test-retest reliability: intraclass correlation coefficient=0.9, 95% CI=0.83, 0.95), and it was comparable to the Psychosis-Like Symptoms Interview at ages 12 (5) and 18 (4).

We have previously published studies of the age-12

Psychosis-Like Symptoms Interview (5), which assesses

At-risk mental state for psychosis. Individuals with a current at-risk mental state for psychosis were identified by relating the Psychosis-Like Symptoms Interview data to the Structured Interview for Prodromal Symptoms (SIPS) (27, 28) definitions of prodromal symptoms at age 18 (4), and to both SIPS and Comprehensive Assessment of At-Risk Mental State (CAARMS) (29) criteria at age 24 (see the online supplement for criteria).

Psychotic disorder. We classified individuals as having a psychotic disorder if 1) they were rated as having had a definite psychotic experience not attributable to the effects of sleep or fever; 2) this had recurred regularly (at least once per month) over the previous 6 months; and 3) they reported this as either very distressing or having a very negative impact on their social or occupational functioning or led them to seek help from a professional source. Psychotic disorder was assessed at age 18 (4) (current) and at age 24 (current and lifetime since age 12).

Sociodemographic characteristics. Data on sex, parental social class, maternal marital status, financial difficulty, housing type, and parental education were collected from birth records and parental questionnaires (see the online supplement).

Statistical Analysis

We used data from the Psychosis-Like Symptoms Interview conducted at ages 12, 18, and 24 to identify the first reported psychotic experience and the age at which it first occurred. To estimate the change in incidence with age, we used the Royston-Parmar flexible parametric modeling approach allowing for interval-censored data and employing splines for modeling the log-cumulative hazard as a function of time (30, 31), excluding 928 participants with an event rated at the age-12 visit, as there was no information on age at onset at that assessment. As a sensitivity analysis, we also estimated

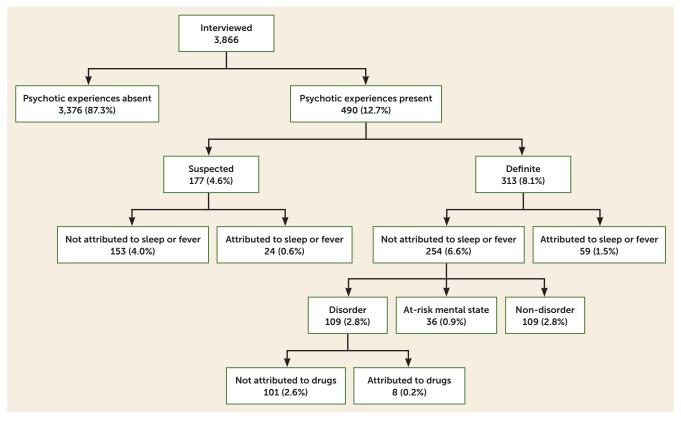


FIGURE 1. Flow chart of psychotic experiences rated at age 24 as having ever occurred since age 12

incidence rates including these 928 individuals, making the assumptions that age of risk for psychotic experiences starts at age 6 and that the hazard is constant from ages 6 to 12 (see Figure S2 in the online supplement). For estimating sexspecific incidence rates, probability weights were used based on modeling age at dropout. Logistic regression was used to calculate odds ratios and 95% confidence intervals for psychotic disorder occurring at age 24 in relation to psychotic experiences reported at ages 12 and 18. These computations as well as positive predictive values (PPVs), sensitivity and specificity estimates, and the area under the curve (AUC) for receiver operator characteristic graphs were estimated using Stata, version 15.

Individuals were more likely to be missing age-24 data if they were male, came from more socioeconomically disadvantaged backgrounds, or had more severe psychotic experiences at age 18 (see Table S1 in the online supplement). To address potential attrition bias, we undertook multiple imputation of missing data (imputed up to N=7,919; see the sample description) using flexible additive imputation models as implemented in the aregImpute function (32) in the R statistical package, with estimates averaged over 100 imputed data sets using Rubin's rules (33). We included auxiliary variables that could inform psychotic experience or missingness status to make the missingness-at-random assumption more plausible. Analyses using imputed data (see Table S6 in the online supplement) showed that estimates were similar to those presented below from complete-case data.

RESULTS

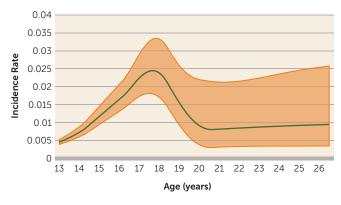
Frequency of Psychotic Experiences at Age 24

Of 3,866 individuals interviewed at age 24, 490 (12.7%, 95% CI=11.6, 13.8) were rated as having ever experienced a suspected (N=177, 4.6%) or definite (N=313, 8.1%) psychotic experience since age 12 (see Figure 1 and Table S2 in the online supplement for individual items). Of those with a definite psychotic experience, 268 (6.9% of the sample) had experienced a hallucination and 91 (2.4%) a delusion, and 46 individuals (1.2%) had experienced both.

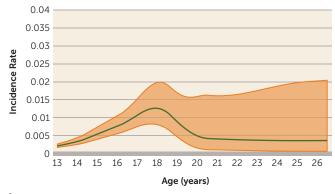
Of those who were rated as having a psychotic experience, 43.7% described their experience as quite or very distressing. A higher proportion of those with a definite psychotic experience rated the experience as quite or very distressing (54.0%) compared with those with a suspected psychotic experience (25.4%; $p \le 0.001$). Similarly, those with a definite psychotic experience were more likely than those with a suspected psychotic experience to describe any impaired social (27.5% compared with 10.9%, $p \le 0.001$) or occupational (27.1% compared with 7.2%; $p \le 0.001$) functioning and to report help-seeking from a professional source (29.4% compared with 6.2%; $p \le 0.001$).

FIGURE 2. Incidence rates of psychotic experiences from ages 13 to 24^a

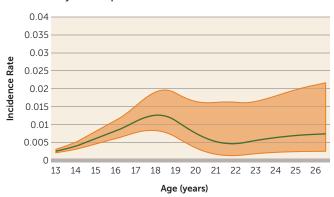
A. Suspected or Definite Psychotic Experiences



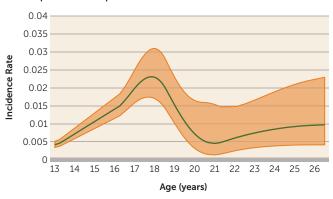
C. Suspected or Definite Psychotic Experiences Occuring at Least Monthly



B. Definite Psychotic Experiences







^a Shaded area indicates 95% confidence interval.

The prevalence of current (past 6 months) definite psychotic experiences at age 24 was 3.5% (95% CI=3.0, 4.2). This was similar to the prevalence of current definite psychotic experiences at age 18 (3.2%) but substantially less than the prevalence at age 12 (5.6%).

The risk of ever having a definite psychotic experience between ages 12 and 24, as estimated using only data from the interview at age 24 (8.1%), increased when we supplemented this information with data from the age-18 interview (9.6%), and substantially so when we further included information from the age-12 interview (13.4%). This was due, at least in part, to measurement error from inconsistent responses across time points (see Table S3 in the online supplement).

Incidence Rates

The incidence rate of the repeatedly assessed 12 psychotic experience items increased overall from early adolescence to early adulthood, with a peak around ages 17–19 (Figure 2 and Tables S4 and S5 in the online supplement). This pattern was similar when we restricted the analyses to definite psychotic experiences, to psychotic experiences that recurred at least monthly over a 6-month period, or to individuals with completely observed data. There was no evidence of a difference in incidence rates between males and females (see Figure S1 in the online supplement). The overall incidence

rate in our study was approximately 1.0 per 100 person-years for suspected or definite psychotic experiences and 0.6 per 100 person-years for definite psychotic experiences.

In a sensitivity analysis that included experiences rated at the age-12 interview, where age at onset was unmeasured, the pattern of rates for definite psychotic experiences remained similar, whereas that for suspected experiences was higher in childhood (see Figure S2 in the online supplement).

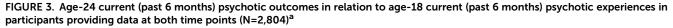
At-Risk Mental States for Psychosis and Psychotic Disorder

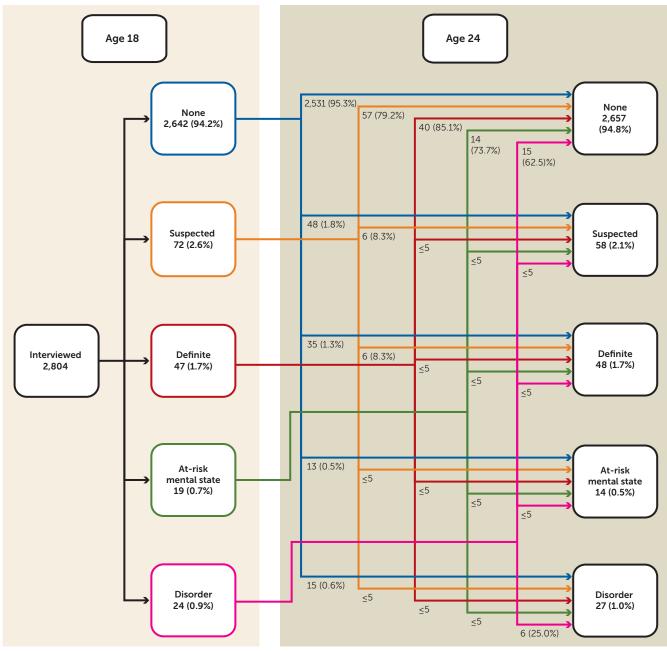
In total, 36 individuals (0.9% of the sample, 95% CI=0.7, 1.3) met either SIPS or CAARMS criteria for a current at-risk mental state at age 24. Forty-seven individuals (1.2%, 95% CI=0.9, 1.6) met our criteria for a current psychotic disorder at this age.

At the age-24 assessment, 109 individuals (2.8%) met criteria for ever having had a psychotic disorder since age 12. Of these, 38 (34.9%) had received medication prescriptions for their symptoms, and 76 (69.7%; 95% CI=60.2, 78.2) had sought professional help for their symptoms.

Continuity of Psychotic Experiences

A total of 2,804 individuals participated in the interviews at ages 18 and 24 (Figure 3). Of 84 individuals with definite





^a The Avon Longitudinal Study of Parents and Children confidentiality regulations prevent us from providing exact numbers for events where five or fewer people are affected.

psychotic experiences present at age 18, 16 (19.1%) had current definite psychotic experiences at age 24 (i.e., had recurrent definite psychotic experiences over a period of approximately 6 years), and 68 (80.9%) no longer had current definite psychotic experiences at age 24 (i.e., had transient psychotic experiences over this period).

Prediction

We examined the utility of both the self-reported stem questions and the interview-rated measures of psychotic experiences at ages 12 and 18 in predicting the presence of current psychotic disorder at age 24.

As can be seen in Tables 1 and 2, the PPV of experiences at ages 12 and 18 increased as the experiences were more stringently defined, with the poorest predictor being selfreported psychotic experiences that were not endorsed by the interviewer as being psychotic. Approximately 60% of those who met criteria for a psychotic disorder at age 24 had endorsed a "yes" or "maybe" response to the stem questions at age 12. However, only 4.8% of those rated by the TABLE 1. Prediction of current psychotic disorder at age 24 in relation to (non-mutually exclusive) ratings at age 12 (N=3,148) and age 18 (N=2,804)^a

Age (years) and Predictor	Psychotic Disorder at Age 24						
	PPV (%)	95% CI	Sensitivity	95% CI	Specificity	95% Cl	
Age 12							
Interviewer rating							
Stem (yes/maybe)	1.6	0.9, 2.4	57.6	39.2, 74.5	61.3	59.6, 63.1	
Suspected/definite psychotic experience	3.1	1.7, 5.3	39.4	22.9, 57.9	87.1	85.9, 88.3	
Suspected/definite psychotic experience (not attributed)	3.7	2.0, 6.2	39.4	22.9, 57.9	89.1	87.9, 90.1	
Definite psychotic experience (not attributed) ROC area under the curve=0.65	4.8	1.9, 9.6	21.2	9.0, 38.9	95.5	94.7, 96.2	
Age 18							
Interviewer rating							
Stem (yes/maybe)	2.7	1.7, 4.0	75.0	55.1, 89.3	72.3	70.6, 74.0	
Suspected/definite psychotic experience	6.5	3.8, 10.4	57.1	37.2, 75.5	91.8	90.7, 92.7	
Suspected/definite psychotic experience (not attributed)	7.1	4.0, 11.4	53.6	33.9, 72.5	92.9	91.9, 93.8	
Definite psychotic experience (not attributed) ROC area under the curve=0.79	10.0	5.1, 17.2	39.3	21.5, 59.4	96.4	95.7, 97.1	
Stem (self-reported) items ^b							
Yes or maybe	2.9	1.7, 4.8	53.6	33.9, 72.5	82.1	80.6, 83.5	
Yes	3.3	1.9, 5.4	53.6	33.9, 72.5	84.2	82.8, 85.5	
Yes and distressing or frequent	6.2	3.1, 10.8	39.3	21.5, 59.4	94.0	93.0, 94.8	
Yes and distressing and frequent ROC area under the curve=0.70	13.3	3.8, 30.7	14.3	4.0, 32.7	99.1	98.6, 99.4	
Interviewer rating ^c							
Yes or maybe	2.9	1.6, 4.8	53.6	33.9, 72.5	82.1	80.6, 83.5	
Suspected/definite	6.1	3.0, 10.9	35.7	18.6, 55.9	94.5	93.5, 95.3	
Definite	10.0	4.7, 18.1	32.1	15.9, 52.4	97.1	96.4, 97.7	
Definite and distressing or frequent	12.8	4.8, 25.7	21.4	8.3, 41.0	98.5	98.0, 98.9	
Definite and distressing and frequent ROC area under the curve=0.70	20.0	2.5, 55.6	7.1	0.9, 23.5	99.7	99.4, 99.9	

^a PPV=positive predictive value; ROC=receiver operating characteristic.

^b Questions on auditory hallucination and delusions of being spied on only, as data on frequency/distress were not available for other items; area under the curve (AUC)=0.68 for auditory hallucination and delusions of being spied on excluding information on frequency/distress; AUC=0.74 for all self-report items excluding information on frequency/distress.

^c Using questions on auditory hallucination and delusions of being spied on only, to make results comparable to those for the stem (self-report) measure; AUC=0.70 for auditory hallucination and delusions of being spied on excluding information on frequency/distress; AUC=0.78 for all items with information on frequency/ distress.

interviewer as having definite, nonattributed psychotic experiences at this age met criteria for a psychotic disorder 12 years later.

The PPV for predicting psychotic disorder at age 24 was greater for interviewer ratings from the age-18 assessment compared with the age-12 assessment, with 10.0% of those rated as having nonattributed definite psychotic experiences at age 18 meeting criteria for a current psychotic disorder at age 24.

While simple "yes or maybe" responses to the stem (selfreported) items at age 18 performed more poorly than interviewer ratings for predicting psychotic disorder, their PPV was improved by addition of information on frequency and distress (Table 1). Approximately 6% of participants who selfreported frequent or distressing experiences of hearing voices or believing they were being spied on met criteria for a psychotic disorder at age 24, and this rose to 13% for those reporting experiences that were both frequent and distressing. The corresponding estimates for interview-rated definite auditory hallucinations or delusions of being spied on were 13% and 20%, respectively.

As a result of the trade-off between sensitivity and specificity, evidence of a difference in discriminative ability between interview ratings and self-report measures at age 18 for predicting psychotic disorder at age 24 (all psychotic experiences items: AUC=0.79 compared with AUC=0.75; p<0.001; auditory hallucinations and delusions of being spied on only: AUC=0.70 compared with AUC=0.68; p=0.038) was lost once information on frequency and distress was included (auditory hallucinations and delusions of being spied on: AUC=0.70 compared with AUC=0.70; p=0.868) (Table 1).

Of 19 individuals who met criteria for an at-risk mental state at age 18, four (21.1%, 95% CI=6.1, 45.6) developed an incident psychotic disorder between ages 18 and 24, and the sensitivity was 14.3% (95% CI=4.0, 32.7).

	Psychotic Disorder at Age 24						
Predictor	PPV (%)	Odds Ratio	95% CI	р			
Interviewer rating at age 12							
No to all stems	0.7		Reference				
Stem (yes/maybe) but not rated	0.7	1.02	0.4, 2.7	0.966			
Suspected/definite psychotic experience (attributed)	_	-	—	_			
Suspected psychotic experience (not attributed)	2.9	4.1	1.5, 10.7	0.004			
Definite psychotic experience (not attributed)	4.8	6.8	2.7, 17.2	<0.001			
Interviewer rating at age 18							
No to all stems	0.4		Reference				
Stem (yes/maybe) but not rated	0.9	2.7	0.8, 8.4	0.097			
Suspected/definite psychotic experience (attributed)	3.0	9.0	1.1, 75.0	0.043			
Suspected psychotic experience (not attributed)	3.9	11.7	3.4, 40.7	<0.001			
Definite psychotic experience (not attributed)	10.0	31.9	12.1, 83.9	<0.001			

TABLE 2. Odds of current psychotic disorder at age 24 in relation to (mutually exclusive) ratings at age 12 (N=3,169) and age 18 $(N=2,824)^a$

^a PPV=positive predictive value.

DISCUSSION

In this study, we conducted semistructured interviews, for the third time over a 12-year period, to assess the presence of psychotic experiences occurring from late childhood through early adulthood in a population-based birth cohort sample. While the presence of current definite psychotic experiences has remained relatively stable since late adolescence, the incidence rate of such experiences increased slightly from ages 13 to 24, with a substantial peak during late adolescence, occurring a few years earlier than the sharp rise in incidence of schizophrenia in early adulthood (34).

The estimate of cumulative risk of psychotic experiences up to age 24 using data from multiple assessments indicates a higher occurrence of psychotic experiences than the estimate we obtained when using only the age-24 measure, and it demonstrates the importance of a repeated-measures design. Reasons for this measurement error include forgetfulness, changes in interpretation of questions with maturity, changes in valuation of social norms, and a learning bias to avoid longer assessments. Indeed, underestimates in single-timepoint recall of a measure compared with multiple-time-point assessments is common (35–37). Such measurement error, and error in recalling age at onset of experiences, may have affected the patterns of incidence observed, although our use of repeat measures with relatively short time intervals between them will have helped minimize this error.

The transitory nature of most psychotic experiences recorded in general population samples has been well documented (7, 9–14), and our findings here are consistent with the literature. Nevertheless, it is germane that almost a third of individuals rated as having had definite psychotic experiences had sought professional help for them or reported impaired function because of their occurrence, indicating that as well as indexing a heightened risk of developing a psychotic disorder in the future (4, 8, 19, 38), these experiences in themselves are often of current clinical relevance (39, 40).

Furthermore, 30% of participants who met our criteria for a psychotic disorder had not sought professional help for their experiences, indicating a significant and important unmet public health need in adolescents and young adults in the general population.

The use of individual-level interventions to reduce the individual and population health burden of psychotic illnesses requires identification of individuals at high risk. Our study demonstrates that approximately 60% of those who met criteria for a psychotic disorder at age 24 had a self-reported psychotic experience at age 12, indicating that onset of odd or unusual experiences, even if they do not meet interviewer-rated criteria for being psychotic, are present from childhood in the majority of

people who develop a psychotic disorder by their mid-20s. While the positive predictive value of such self-rated experiences was poor, it was improved by the addition of information on frequency and distress, although sensitivity was reduced. The predictive ability of these measures may well be improved by utilizing additional information on functional decline, cognitive ability, and other biomarkers of early transitioning to psychosis (41, 42).

Structured interviews and questionnaires overestimate psychopathology compared with semistructured approaches, especially in general-population samples (43, 44), and indeed, in our study, interviewer ratings of psychotic experiences performed better than self-report measures of psychotic experiences in predicting psychotic disorder. However, this distinction was less clear after we included measures of frequency and distress. Further studies, particularly ones that can utilize linkage to clinical health records, are required to examine whether self-report measures supplemented with information on frequency and distress are more efficient than semistructured interviews for prediction of psychotic disorder in general-population samples.

Approximately 1% of our general-population sample met criteria for an at-risk mental state for psychosis at age 24, as defined using CAARMS or SIPS criteria, compared with 0.6% at age 18 (4). Our finding that approximately 21% of those with an at-risk mental state at age 18 transitioned to a new-onset psychotic disorder by age 24 is compatible with the estimates of transition in clinical services (45, 46), and it is substantially greater than the transition risk of 0.9% in those not meeting at-risk criteria at age 18. Nevertheless, this means that nearly 80% of those meeting at-risk criteria did not transition over this 6-year period. It is not known to what extent cases of first-episode psychosis can be prevented by identifying a larger pool of people with an at-risk mental state in the general population. In our population-based study, which was not sampled on help-seeking behavior, approximately 85% of participants with new-onset psychotic disorder between ages 18 and 24 did not meet criteria for an at-risk mental state at age 18.

These findings appear consistent with the observation within a clinical service in the United Kingdom that 4% of people with a first-episode psychosis in a service in South London came through the at-risk mental state route (47). Sensitivity was similarly very low for the cutoff thresholds of frequent and/or distressing experiences for both selfreported and interviewer-rated measures at age 18. Further studies examining the trajectory of symptoms and referral pathways of people with first-episode psychosis into services are required. However, our findings suggest that targeting individuals in the general population solely on the basis of severity characteristics of psychotic or psychoticlike experiences, or on at-risk mental state criteria, while beneficial at an individual-patient level, may have little impact on rates of first-episode psychosis at the population level (46).

Our study has a number of strengths, including use of a large and well-characterized birth cohort, semistructured interviews to assess psychotic experiences, and measures repeated at three time points from childhood through early adulthood to allow us to estimate patterns of incidence over this age period. However, the study also has some important limitations. First, while our sample is probably the largest cohort study available worldwide with this level of detailed information (with over 7,000 individuals interviewed on at least one of the three assessments), it is nevertheless relatively small for examining uncommon outcomes such as psychotic disorder. Our results therefore are often imprecisely estimated.

Second, there has been substantial attrition over time, as is common with long follow-ups. However, our estimates using multiple imputation were very similar to those from observed data, suggesting that they are unlikely to be substantially affected by selection bias, although this remains possible.

Third, while the incidence rate for psychotic experiences from age 13 onward increased overall through adolescence and early adulthood, most psychotic experiences that occurred in this cohort (928 of 1,547; 60%) were rated at the age-12 interview. Because age at first onset was not measured at this interview, our primary analysis did not model incidence rates prior to age 13. However, under specific assumptions, as shown in the online supplement, we can see that the incidence of suspected experiences may be higher before age 13, whereas the incidence of definite experiences is consistent with our primary analysis, rising from midchildhood onward and peaking in late adolescence or early adulthood.

Finally, there may be some misclassification of at-risk mental states, as the Psychosis-Like Symptoms Interview is not wholly comparable to the SIPS or the CAARMS, and it is also possible that our definition of psychotic disorder is too broad and includes individuals who would not be classified as having a disorder in a clinical setting. However, our requirement that psychotic experiences be recurring and cause either severe distress, very impaired function, or helpseeking from a professional suggests that these individuals have a need for clinical care. Furthermore, applying more stringent criteria so that experiences need to be recurring on a weekly rather than a monthly basis, which might be more akin to the frequency level that would be seen in clinical practice, only changes our estimate of psychotic disorder at age 24 from 1.2% to 1.0%.

Although our findings must be interpreted within the context of these limitations, our study shows a peak in incidence of psychotic experiences during late adolescence, and our findings highlight an important unmet need for care in the general population of young people with a psychotic disorder. Furthermore, we demonstrate the potential utility of both self-report and semistructured assessments of psychotic experiences for prediction of psychotic disorders in the general population, but because of the low sensitivity, targeting individuals only on the basis of more severe symptom characteristics will likely have little impact on population levels of first-episode psychosis.

AUTHOR AND ARTICLE INFORMATION

Centre for Academic Mental Health, Bristol Medical School, University of Bristol, Bristol, U.K. (Sullivan, Kounali, H. Jones, Heron, Zammit); Department of Psychiatry, Royal College of Surgeons in Ireland, Dublin (Cannon); Institute of Mental Health, University College London (David, Lewis); Department of Psychiatry, Addenbrooke's Hospital, University of Cambridge, Cambridge (Fletcher, P.B. Jones); MRC Centre for Neuropsychiatric Genetics and Genomics, School of Medicine, Cardiff University, Cardiff, U.K. (Holmans, Linden, Owen, O'Donovan, Rammos, Zammit); Division of Psychiatry, Warwick Medical School, Warwick, Coventry, U.K. (Thompson); Orygen, Centre of Excellence in Youth Mental Health, Melbourne, Australia (Thompson); and Department of Psychology, Division of Mental Health and Wellbeing, University of Warwick, Coventry, U.K. (Wolke).

Send correspondence to Dr. Sullivan (sarah.sullivan@bristol.ac.uk).

Drs. Sullivan and Kounali share first authorship.

The U.K. Medical Research Council and Wellcome (grant ref. 102215/2/13/ 2) and the University of Bristol provide core support for the Avon Longitudinal Study of Parents and Children. The study was funded by Medical Research Council grant MR/M006727/1.

Dr. Zammit acknowledges support from the NIHR Biomedical Research Centre (BRC) at University Hospitals Bristol NHS Foundation Trust and the University of Bristol; Dr. David and Dr. Lewis from the NIHR BRC at University College London Hospital; Dr. P.B. Jones from the NIHR CLAHRC East of England, NIHR PGfAR RP-PG-0616-20003 (TYPPEX) and the Wellcome Trust Neuroscience in Psychiatry Network (095844/Z/11/ Z); Dr. Fletcher from the Wellcome Trust (206368/Z/17/Z) and the Bernard Wolfe Health Neuroscience Fund; and Dr. Cannon from a European Research Council Consolidator Award (iHEAR 724809).

The authors are grateful to all the families who took part in the study, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, and nurses.

The views expressed in this article are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, or the Department of Health and Social Care.

Dr. Fletcher serves as a consultant for Ninja Theory Ltd., a video game design studio. Dr. Linden has received royalties from Oxford University Press and Springer Nature and editorial fees from Elsevier. Dr. Owen and Dr. O'Donovan receive support from a research grant from Takeda. The other authors report no financial relationships with commercial interests.

Received June 24, 2019; revision received September 9, 2019; accepted October 10, 2019; published online Jan. 7, 2020.

REFERENCES

- 1. Perälä J, Suvisaari J, Saarni SI, et al: Lifetime prevalence of psychotic and bipolar I disorders in a general population. Arch Gen Psychiatry 2007; 64:19–28
- 2. van Os J, Linscott RJ, Myin-Germeys I, et al: A systematic review and meta-analysis of the psychosis continuum: evidence for a psychosis proneness-persistence-impairment model of psychotic disorder. Psychol Med 2009; 39:179–195
- 3. Polanczyk G, Moffitt TE, Arseneault L, et al: Etiological and clinical features of childhood psychotic symptoms: results from a birth cohort. Arch Gen Psychiatry 2010; 67:328–338
- Zammit S, Kounali D, Cannon M, et al: Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study. Am J Psychiatry 2013; 170:742–750
- 5. Horwood J, Salvi G, Thomas K, et al: IQ and non-clinical psychotic symptoms in 12-year-olds: results from the ALSPAC birth cohort. Br J Psychiatry 2008; 193:185–191
- Poulton R, Caspi A, Moffitt TE, et al: Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. Arch Gen Psychiatry 2000; 57:1053–1058
- 7. Dominguez MDG, Wichers M, Lieb R, et al: Evidence that onset of clinical psychosis is an outcome of progressively more persistent subclinical psychotic experiences: an 8-year cohort study. Schizophr Bull 2011; 37:84–93
- Kaymaz N, Drukker M, Lieb R, et al: Do subthreshold psychotic experiences predict clinical outcomes in unselected non-help-seeking population-based samples? A systematic review and meta-analysis, enriched with new results. Psychol Med 2012; 42:2239–2253
- Hanssen M, Bak M, Bijl R, et al: The incidence and outcome of subclinical psychotic experiences in the general population. Br J Clin Psychol 2005; 44:181–191
- Papmeyer M, Würsch I, Studerus E, et al: The role of vulnerability factors in individuals with an at-risk mental state of psychosis. Neuropsychiatr 2016; 30:18–26
- Bartels-Velthuis AA, van de Willige G, Jenner JA, et al: Course of auditory vocal hallucinations in childhood: 5-year follow-up study. Br J Psychiatry 2011; 199:296–302
- Bartels-Velthuis AA, Wigman JTW, Jenner JA, et al: Course of auditory vocal hallucinations in childhood: 11-year follow-up study. Acta Psychiatr Scand 2016; 134:6–15
- 13. Hengartner MP, Heekeren K, Dvorsky D, et al: Course of psychotic symptoms, depression, and global functioning in persons at clinical high risk of psychosis: results of a longitudinal observation study over three years focusing on both converters and non-converters. Schizophr Res 2017; 189:19–26
- Werbeloff N, Drukker M, Dohrenwend BP, et al: Self-reported attenuated psychotic symptoms as forerunners of severe mental disorders later in life. Arch Gen Psychiatry 2012; 69:467–475
- Davies J, Sullivan S, Zammit S: Adverse life outcomes associated with adolescent psychotic experiences and depressive symptoms. Soc Psychiatry Psychiatr Epidemiol 2018; 53:497–507
- Asher L, Zammit S, Sullivan S, et al: The relationship between psychotic symptoms and social functioning in a non-clinical population of 12 year olds. Schizophr Res 2013; 150:404–409

- Kelleher I, Ramsay H, DeVylder J: Psychotic experiences and suicide attempt risk in common mental disorders and borderline personality disorder. Acta Psychiatr Scand 2017; 135:212–218
- Sullivan SA, Lewis G, Gunnell D, et al: The longitudinal association between psychotic experiences, depression, and suicidal behaviour in a population sample of adolescents. Soc Psychiatry Psychiatr Epidemiol 2015; 50:1809–1817
- Fisher HL, Caspi A, Poulton R, et al: Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: a birth cohort study. Psychol Med 2013; 43:2077–2086
- Sharifi V, Eaton WW, Wu LT, et al: Psychotic experiences and risk of death in the general population: 24-27 year follow-up of the Epidemiologic Catchment Area study. Br J Psychiatry 2015; 207:30–36
- 21. Cederlöf M, Pettersson E, Sariaslan A, et al: The association between childhood autistic traits and adolescent psychotic experiences is explained by general neuropsychiatric problems. Am J Med Genet B Neuropsychiatr Genet 2016; 171B:153–159
- Murphy J, Shevlin M, Houston J, et al: A population based analysis of subclinical psychosis and help-seeking behavior. Schizophr Bull 2012; 38:360–367
- 23. Kelleher I, Connor D, Clarke MC, et al: Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. Psychol Med 2012; 42: 1857–1863
- 24. Gerstenberg M, Theodoridou A, Traber-Walker N, et al: Adolescents and adults at clinical high-risk for psychosis: age-related differences in attenuated positive symptoms syndrome prevalence and entanglement with basic symptoms. Psychol Med 2016; 46: 1069–1078
- 25. Northstone K, Lewcock M, Groom A, et al: The Avon Longitudinal Study of Parents and Children (ALSPAC): an update on the enrolled sample of index children in 2019. Wellcome Open Res 2019; 4:51
- World Health Organization (WHO), Division of Mental Health: Schedules for Clinical Assessment in Neuropsychiatry. Washington, DC, American Psychiatric Press (on behalf of WHO), 1994
- 27. McGlashan TH, Miller TJ, Woods SW, et al: Structured Interview for Prodromal Syndromes, version 4. New Haven, Conn, PRIME Research Clinic, Yale School of Medicine, 2003
- Addington J, Cadenhead KS, Cannon TD, et al: North American Prodrome Longitudinal Study: a collaborative multisite approach to prodromal schizophrenia research. Schizophr Bull 2007; 33:665–672
- 29. Yung AR, Yuen HP, McGorry PD, et al: Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. Aust N Z J Psychiatry 2005; 39:964–971
- 30. Royston P, Lambert P: Flexible Parametric Survival Analysis Using Stata: Beyond the Cox Model. College Station, Tex, Stata Press, 2011
- 31. Royston P, Parmar MK: Flexible parametric proportional-hazards and proportional-odds models for censored survival data, with application to prognostic modelling and estimation of treatment effects. Stat Med 2002; 21:2175–2197
- 32. Little R: Statistical Analysis With Missing Data. New York, Wiley, 2002
- Harell FE: Regression Modelling Strategies: With Applications to Linear Models, Logistic Regression and Survival Analysis. New York, Springer, 2001
- 34. Kirkbride JB, Errazuriz A, Croudace TJ, et al: Incidence of schizophrenia and other psychoses in England, 1950–2009: a systematic review and meta-analyses. PLoS One 2012; 7:e31660
- 35. Giuffra LA, Risch N: Diminished recall and the cohort effect of major depression: a simulation study. Psychol Med 1994; 24:375–383
- 36. Ottman R, Lee JH, Hauser WA, et al: Birth cohort and familial risk of epilepsy: the effect of diminished recall in studies of lifetime prevalence. Am J Epidemiol 1995; 141:235–241
- 37. Streiner DL, Patten SB, Anthony JC, et al: Has "lifetime prevalence" reached the end of its life? An examination of the concept. Int J Methods Psychiatr Res 2009; 18:221–228

- Healy C, Brannigan R, Dooley N, et al: Childhood and adolescent psychotic experiences and risk of mental disorder: a systematic review and meta-analysis. Psychol Med 2019; 49:1589–1599
- Bak M, Myin-Germeys I, Delespaul P, et al: Do different psychotic experiences differentially predict need for care in the general population? Compr Psychiatry 2005; 46:192–199
- 40. Kelleher I, Wigman JT, Harley M, et al: Psychotic experiences in the population: association with functioning and mental distress. Schizophr Res 2015; 165:9–14
- Cannon TD, Yu C, Addington J, et al: An individualized risk calculator for research in prodromal psychosis. Am J Psychiatry 2016; 173:980–988
- 42. Schubert KO, Clark SR, Baune BT: The use of clinical and biological characteristics to predict outcome following first episode psychosis. Aust N Z J Psychiatry 2015; 49:24–35
- 43. Brugha TS, Bebbington PE, Jenkins R: A difference that matters: comparisons of structured and semi-structured psychiatric

diagnostic interviews in the general population. Psychol Med 1999; 29:1013–1020

- 44. Levis B, Benedetti A, Riehm KE, et al: Probability of major depression diagnostic classification using semi-structured versus fully structured diagnostic interviews. Br J Psychiatry 2018; 212: 377–385
- 45. Fusar-Poli P, Bonoldi I, Yung AR, et al: Predicting psychosis: metaanalysis of transition outcomes in individuals at high clinical risk. Arch Gen Psychiatry 2012; 69:220–229
- 46. Ajnakina O, David AS, Murray RM: "At risk mental state" clinics for psychosis: an idea whose time has come—and gone! Psychol Med (Epub ahead of print, December 26, 2018)
- 47. Ajnakina O, Morgan C, Gayer-Anderson C, et al: Only a small proportion of patients with first episode psychosis come via prodromal services: a retrospective survey of a large UK mental health programme. BMC Psychiatry 2017; 17:308