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Examining psychotic experiences in two generations – findings from a rural household-based cohort study; the Lolland-Falster Health Study

Martin Køster Rimvall[1,2], Erik Simonsen[3,4], Jiawei Zhang[5], Zorana Jovanovic Andersen[5], Lene Halling Hastrup[4,6], Pia Jeppesen[1,2,3], Stephen F. Austin[4,7] and Susanne Vinkel Koch[1,3]

[1]Department of Child and Adolescent Psychiatry, Copenhagen University Hospital – Psychiatry Region Zealand, Roskilde, Denmark; [2]Child and Adolescent Mental Health Center, Mental Health Services – Capital Region of Denmark, Copenhagen, Denmark; [3]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; [4]Mental Health Services East, Copenhagen University Hospital - Psychiatry Region Zealand, Roskilde, Denmark; [5]Section of Environmental Health, Department of Public Health, University of Copenhagen, Copenhagen, Denmark; [6]Danish Centre for Health Economics, DaCHE, University of Southern Denmark, Odense, Denmark and [7]Institute of Psychology, University of Southern Denmark, Odense, Denmark

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Corresponding author:
Martin Køster Rimvall;
Email: martin.rimvall@regionh.dk

Abstract

Background. Psychotic disorders are highly heritable, yet the evidence is less clear for subclinical psychosis expression, such as psychotic experiences (PEs). We examined if PEs in parents were associated with PEs in offspring.

Methods. As part of the Danish general population Lolland-Falster Health Study, families with youths aged 11–17 years were included. Both children and parents reported PEs according to the Psychotic Like Experiences Questionnaire, counting only 'definite' PEs. Parents additionally reported depressive symptoms, anxiety, and mental wellbeing. The associations between parental and child PEs were estimated using generalized estimating equations with an exchangeable correlation structure to account for the clustering of observations within families, adjusting for sociodemographic characteristics.

Results. Altogether, 984 youths (mean age 14.3 years [s.d. 2.0]), 700 mothers, and 496 fathers from 766 households completed PEs-questionnaires. Offspring of parents with PEs were at an increased risk of reporting PEs themselves (mothers: adjusted risk ratio (aRR) 2.42, 95% CI 1.73–3.38; fathers: aRR 2.25, 95% CI 1.42–3.59). Other maternal problems (depression, anxiety, and poor mental well-being), but not paternal problems, were also associated with offspring PEs. In multivariate models adjusting for parental problems, PEs, but not other parental problems, were robustly associated with offspring PEs (mothers: aRR 2.25, 95% CI 1.60–3.19; fathers: aRR 2.44, 95% CI 1.50–3.96).

Conclusions. The current findings add novel evidence suggesting that specific psychosis vulnerability in families is expressed at the lower end of the psychosis continuum, underlining the importance of assessing youths' needs based on psychosis vulnerability broadly within the family systems.

Background

The etiology behind psychotic disorders is multifactorial, yet there is strong evidence that psychotic disorders are highly heritable given that a family history of psychosis diagnosis substantially increases the risk of being diagnosed with psychotic disorders in offspring (Sullivan, Kendler, & Neale, 2003). However, when considering psychosis as a broader transdiagnostic continuous phenotype (Linscott & van Os, 2013; van Os & Reininghaus, 2016), the evidence base regarding the heritability of subclinical psychosis expression is smaller and less clear.

In youths, psychotic experiences, i.e. subclinical hallucinations, delusions, and subjective thought disturbances, are often associated with severity of non-psychotic psychopathology (Jeppesen et al., 2015a; Kelleher et al., 2012), suicidality (Honings, Drukker, Groen, & van Os, 2016; Yates et al., 2019), poorer functioning (Calkins et al., 2017; Healy et al., 2018), decreased quality of life (Alonso et al., 2018; Rimvall et al., 2021), as well as help-seeking behaviors and an increased risk of being diagnosed with non-psychotic and psychotic disorders later in life (Healy et al., 2019; Rimvall et al., 2020b).

Numerous studies have examined parental diagnosis of psychosis as a potential risk factor of psychotic experiences in offspring. In the Copenhagen Child Cohort 2000 study, using

independent register-based data to assess parental mental illness, parental psychotic disorders were associated with psychotic experiences in preadolescents, whereas non-psychotic disorders were not (Jeppesen et al., 2015b). Data from the Danish High-Risk and Resilience Study found that children of parents with schizophrenia, but not bipolar disorder, had more psychotic experiences than children of non-affected parents (Gregersen et al., 2022), fueling a notion that there might be a specific link between primary psychotic disorder and subclinical psychosis expression in offspring. Findings from the E-risk longitudinal Twin Study found that maternal psychosis diagnosis, but also maternal admissions and suicidality broadly, predicted psychotic experiences in offspring (Polanczyk et al., 2010), and in the Families Overcoming Risks and Building Opportunities for Wellbeing (FORBOW) high-risk cohort, offspring of parents with major depression, bipolar, and schizophrenia reported similar rates of psychotic experiences across parental diagnoses (MacKenzie et al., 2016). Data from the recent ABCD study found an association between parent self-reported psychosis and psychotic experiences in children aged 10 years in a subsample of about 4000 children (Karcher et al., 2018), yet these findings were not replicated in the full sample of 11 000 children after adjusting for key sociodemographic factors (Karcher et al., 2020). Conversely, findings from the Avon Longitudinal Study of Parents and Children cohort (Zammit et al., 2008) and the TRacking Adolescents' Individual Lives Survey (Wigman et al., 2012) found little to no evidence of parental psychotic disorders as risk factors of psychotic experiences in offspring. Finally, only one study, to our knowledge, examined subclinical psychosis across two generations in adults, finding that a broader psychosis phenotype clustered in families in a Dutch general population sample of adults (Hanssen, Krabbendam, Vollema, Delespaul, & Van Os, 2006). Further studies of the continuity of familial risk along the psychosis continuum are key to expanding our understanding of the etiology of psychosis. Hence the current study aimed to study psychotic experiences across two generations in parents and their adolescent offspring.

In a cross-sectional cohort study, we examined if parental psychotic experiences indicated an increased risk of youth psychotic experiences in their offspring. Second, we examined if other parental mental health problems were associated with offspring psychotic experiences. We hypothesized that psychotic experiences in parents were associated with psychotic experiences in their offspring, and that this potential association would be present over and above the effects of other types of parental mental health problems and family sociodemographic adversities.

Table 1. Sociodemographic characteristics and frequency of reporting of psychotic experiences

	Children (*N* = 984)	Mothers (*N* = 700)	Fathers (*N* = 496)
Age, mean (standard deviation)	14.3 (2.0)	44.8 (5.1)	47.6 (6.1)
Sex (female), n (%)	502 (51.0%)	NA	NA
Higher education, n (%)	NA	371 (53.0%)	208 (41.9%)
Occupation (Employed), n (%)	NA	616 (88.0%)	472 (95.2%)
Presence of psychotic experiences			
• 0 psychotic experiences, n (%)	808 (82.1%)	650 (92.9%)	467 (94.2%)
– 1 psychotic experiences, n (%)	101 (10.3%)	39 (5.6%)	25 (5.0%)
– 2 psychotic experiences, n (%)	45 (4.6%)	8 (1.1%)	4 (0.8%)
– ⩾3 psychotic experiences, n (%)	30 (3.0%)	3 (0.4%)	0

Only psychotic experiences reported as 'definitely present' were included.

Methods

Study population

The current study utilized data from a general population cohort, the Lolland-Falster Health Study (LOFUS) (Jepsen et al., 2020a). LOFUS was set up in order to further knowledge on broad determinants of health among inhabitants from a rural-provincial area in an socioeconomically deprived geographical area, with documented disadvantages regarding educational attainment level, employment rates, and mental disorders compared to the Danish average (Egholm et al., 2020). Participants were asked to participate in both questionnaires (e.g. questionnaires on mental health, diet, pain, etc.), health examinations (blood pressure, lung function, etc.), and to deliver biological materials (blood, urine, saliva, and fecal samples), as summarized in more detail elsewhere (Jepsen et al., 2020a).

Using the civil registration number (unique for all citizens in Denmark), each participating individual, family, and household were linked (Pedersen, 2011). In total, 18 949 individuals aged 0 to 99 years from the Danish municipalities of Lolland and Guldborgsund between February 8th 2016 and February 13th 2020 (Petersen, Brønd, Benfeldt, & Jepsen, 2022). Compared to non-participants, participants were characterized by higher-socioeconomic status (Jepsen et al., 2020b). Regarding mental health problems, the 11–17-year-old participants in LOFUS exhibited lower levels of mental health problems according to the Strengths and Difficulties Questionnaire (SDQ) as compared to Danish general population norm data (mean SDQ total score [S.D.]: 8.81 [S.D. 4.49]) (Koch, Zhang, Aggernaes, Andersen, & Simonsen, et al., in preparation).

Ethical considerations

The child and adolescent sub-study of LOFUS was approved by the Danish Data Protection Agency (REG 060 + -2018). The

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authors assert that all procedures contributing to LOFUS comply with the ethical standards of the relevant national and institutional committees on human experimentation (Region Zealand's Ethical Committee on Health Research [SJ-421] and the Danish Data Protection Agency [REG-024-2015]) and with the Helsinki Declaration of 1975, as revised in 2008. Custodians gave written consent for children aged <15 years, while all individuals aged ⩾15 years provided written consent for themselves (Jepsen et al., 2020a). LOFUS is registered in Clinicaltrials.gov (NCT 02 482 896).

Measures

Psychotic experiences

Questions on hallucinations, delusions and subjective thought disturbances from the Psychotic Like Experiences Questionnaire (PLIKSq), a self-report adaptation of the PLIKS-interview developed for the ALSPAC cohort (Horwood et al., 2008; Thapar et al., 2012), were applied to assess self-reported psychotic experiences in both parents and youths. Due to the extensive test-battery of LOFUS (Egholm et al., 2020), the mental health survey was small, and the PLIKSq was shortened (Austin, Hastrup, van Os, & Simonsen, 2023), see online appendix 1 for the wording of the included questions. The current version enquired about 8 instead of 10 different psychotic experiences, and the participants were asked two questions on context (if psychotic experiences had ever occurred in relation to drugs or sleep), and one impact question enquiring about whether psychotic experiences had any effects on the responder or their family. Psychotic experiences were considered as present when the participants gave at least one 'definite' positive response to any psychotic experience. Psychotic experiences in offspring were considered first as a dichotomous variable (0 v. ⩾1) and second as count variable (0-1-2-⩾3 psychotic experiences). Given that few youths reported more than three psychotic experiences (Table 1), individuals reporting ⩾3 psychotic experiences were grouped together, in keeping with prior work utilizing PLIKSq in youths (Rimvall et al., 2020a).

Parental depressive symptoms

The Major Depression Inventory is widely used in general practice in Denmark (Bech, Rasmussen, Olsen, Noerholm, & Abildgaard, 2001; Christensen, Packness, Simonsen, & Brodersen, 2023), consisting of 12 items covering the 10 symptoms of depression in ICD-10, rated on a six-point Likert-Scale ranging from 'at no time' (coded as 0) to 'all the time' (coded as 5). A continuous total score (range 0–60) measure of depressive symptoms was utilized for the main analyses, and a dichotomous score (⩾25 v. <25), was applied in sensitivity analyses. The cut-off is consistent with the likely moderate to severe depression definition used in the Major Depression Inventory manual and validation in Denmark (Nielsen, Ørnbøl, Bech, Vestergaard, & Christensen, 2017).

Parental anxiety symptoms

The Anxiety Symptom Scale is widely used in primary care settings in Denmark (Danish College of General Practitioners, 2010), consisting of 10 self-reported items on perceived anxiety symptoms. A structural validation study was recently published using data from the LOFUS study (Christensen, Packness, Pedersen, & Simonsen, 2022). The response categories are similar to the Major Depression Inventory, applying a six-point Likert-scale ranging from 'at no time' (coded as 0) to 'all the time' (coded as 5). A continuous total score (range 0–15) measure of generalized anxiety symptoms was utilized for the main analyses. For sensitivity analyses, a dichotomous score was defined as when anxiety symptoms were present more than half of the time (⩾3 on question 10 regarding everyday impact of symptoms combined with a score > 0 on general anxiety disorders [items 1–3 that were also utilized for the continuous anxiety measure]), indicative of impairing anxiety and probable disorder (Packness, Sparle Christensen, & Simonsen, 2023).

Parental mental well-being

The World Health Organization- Five Well-Being Index contains 5 short questions on current mental well-being (Topp, Østergaard, Søndergaard, & Bech, 2015). Like the questionnaires on depression and anxiety, questions are rated on a six-point Likert-scale ranging from 'at no time' (coded as 0) to 'all the time' (coded as 5). A continuous measure of mental well-being was utilized for the main analyses and for sensitivity analyses, a dichotomous score was defined as a score of <12.5, which is a recommended score when screening for depression indicated poor well-being (Topp et al., 2015).

Covariates

We included sex and age of the youths as covariates along with parental highest education (college degree or equivalent *v.* shorter education) and employment status (any type of employment *v.* no employment) attained by self-reports, due to potential differences in expression of psychotic experiences and other mental health problems in relation to these factors.

For post-hoc sensitivity analyses, we included information on youth general mental health problems using the youth reported SDQ total score (Goodman, 1997). The SDQ total score is scored 0–40 based on four subscales inquiring about hyperactivity/inattention, conduct problems, emotional problems and peer relationships.

Statistical analyses

We used generalized estimating equations (GEE) to estimate the associations between parental and offspring psychotic experiences. To account for the clustering of observations within families, i.e. siblingship and shared exposure, we adopted an exchangeable correlation structure. Intra-household dependencies can compromise the independence assumption inherent to ordinary least squares regression, leading to biased estimates and overly narrow standard errors. By utilizing a working correlation matrix and adopting cluster-robust standard errors, the GEE method effectively addresses these concerns. Its flexibility in model specification and robustness to various correlation structures make GEE particularly suited for both longitudinal and cross-sectional analyses (Huang, 2022; McNeish, 2019; McNeish, Stapleton, & Silverman, 2017).

We modeled the binary outcome (psychotic experiences present *v.* no psychotic experiences in offspring) as Poisson distribution to estimate the risk ratios (RR). For the number of offspring psychotic experiences (0-1-2-⩾3 psychotic experiences), we applied Poisson distribution to estimate the relative difference (RD) for the number of offspring psychotic experiences, illustrating an increase of events in percentage (%). All the analyses were conducted separately for mothers and fathers.

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We first conducted univariate analyses, by estimating the effects of maternal and paternal psychotic experiences, depressive symptoms, anxiety symptoms, and mental well-being respectively on offspring psychotic experiences. We reported results from both crude models (four for each parent) and repeated the models adjusted for sociodemographic covariates. This was done for outcomes of psychotic experiences in youths as both dichotomous and count-variables.

We subsequently fitted a total of four multivariate models including all parental exposure variables (psychotic experiences, depressive symptoms, anxiety symptoms, and mental well-being), for mothers and fathers respectively, adjusted for parental sociodemographic covariates on both outcomes of dichotomous and count-variable psychotic experiences in youths. We did this to assess whether the observed associations between psychotic experiences in parents and their offspring were explained by non-psychotic parental mental health problems or specifically relating to psychosis expression.

To validate the robustness of the findings, we further repeated the multivariate models in sensitivity analyses by exploring depression, anxiety, and mental well-being as dichotomous variables (using cut-offs as described in the methods section) where considering the clinically significant levels (yes/no) of non-psychotic mental health problems in the parents. In further sensitivity analyses, we adjusted for youth reported general mental health problems using the SDQ total score, to assess the potential specificity of psychosis expression.

Finally, we assessed the potential dose-response effect of having one parent or two parents with psychotic experiences among participating families with data from both parents, using parents without psychotic experiences as the reference group in univariate analyses, adjusting for sociodemographic factors. Post hoc, we used the working matrix of the GEE models to estimate the correlation of psychotic experiences between siblings.

All statistical tests were performed in R version 4.1.2 with a two-sided significance level of 5%. In case of missing data on any variable in the individual analyses, the participant was excluded.

Results

Data on psychotic experiences were available for 984 youths (51.2% female, mean age 14.3 years [S.D. 2.0]), of whom 155 (17.2%) reported at least one definite psychotic experience. As for parents, among 700 mothers, 50 (7.1%), and among 496 fathers, 29 (5.8%) reported at least one psychotic experience. See Table 1 for basic characteristics of the study sample. For detailed information on the frequencies of responses to the different types of psychotic experiences for parents and youths, see online appendix 1. Regarding the covariates (age, sex, parental education, and employment), parental higher education (both mothers' and fathers') and employment (only mothers') were associated with less PEs in youths, see online appendix 2a for details.

In the univariate analyses (Table 2), parental psychotic experiences were associated with a dichotomous measure of psychotic experiences in their offspring: maternal RR 2.57 (95% CI 1.84–3.58) and paternal RR 2.25 (95% CI 1.42–3.59). After adjustment for sociodemographic factors, the estimates remained similar (maternal adjusted RR [aRR] 2.42, 95% CI 1.73–3.38, paternal aRR 2.30, 95% CI 1.46–3.62). Maternal depressive and anxiety symptoms were associated with psychotic experiences in offspring and higher ratings of maternal mental well-being were associated with a decreased likelihood of psychotic experiences in offspring, whereas neither of the three factors in fathers were significantly associated with offspring psychotic experiences. When viewing psychotic experiences as a count-variable in offspring (0-1-2-⩾3 psychotic experiences) the same overall patterns were found (Table 2). Between siblings, PEs were only weakly correlated (Pearson's correlation in the working matrix of the GEE models ranged from 0.028∼0.090 across the analyses).

Table 3 shows the multivariate analyses mutually adjusted for all four parental variables from the univariate analyses, i.e. psychotic experiences, depressive symptoms, anxiety symptoms, and mental well-being, and including sociodemographic factors. Psychotic experiences in each parent remained robustly associated with psychotic experiences in offspring: maternal aRR 2.25 (95% CI 1.60–3.19), paternal aRR 2.44 (1.50–3.96). However, depressive symptoms, anxiety symptoms and mental well-being in mothers as well as in fathers were not significantly associated with offspring psychotic experiences in the multivariate analyses. When we included depression, anxiety, and mental well-being as dichotomous variables instead of continuous variables in sensitivity analyses, the estimated associations between parental and offspring psychotic experiences remained largely unchanged, see online appendix 2b. When further adjusting child general mental health problems in sensitivity analyses, the estimated associations between parental and offspring psychotic experiences were somewhat attenuated, see online appendix 2c.

Finally, to examine a potential dose-response effect of having one *v.* two parents with psychotic experiences, we analyzed a subsample of families with data on both parents, including 430 parent couples with 569 youths. With no parents with psychotic experiences as reference, offspring with two parents reporting psychotic experiences were at increased odds of reporting one or more psychotic experiences (offspring psychotic experiences dichotomous aRR 3.70, 95% CI 1.77–7.74, offspring psychotic experiences count adjusted RD (aRD) 3.11, 95% CI 1.36–7.12) compared to only one parent reporting psychotic experiences (offspring psychotic experiences dichotomous aRR 1.88, 95% CI 1.14–3.10, offspring psychotic experiences count aRD 1.85, 95% CI 0.99–3.47), however with overlapping confidence intervals.

Discussion

Main findings

In a rural-provincial, general population cohort, parental psychotic experiences were associated with an approximately 2-fold risk of psychotic experiences in offspring, showing similar effects of paternal and maternal psychotic experiences. The findings were robust in multivariate models, also when including general mental health problems of the youths. While maternal, but not paternal, depression, anxiety, and poor mental well-being were associated with psychotic experiences in offspring, parental psychotic experiences remained the only factor significantly associated with offspring psychotic experiences in the multivariate models, suggesting some specificity of subclinical psychosis expression. Finally, there was evidence of dose-response, as having two parents (rather than just one) with psychotic experiences was more strongly associated with a 3-4-fold risk of psychotic experiences in offspring.

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Table 2. Univariate models: Associations between parental factors and offspring psychotic experiences for mothers and fathers separately

	One or more psychotic experiences in offspring		Number of psychotic experiences in offspring (0,1,2, ⩾3)	
	Crude model RR (95% CI)	Adjusted model RR (95% CI)	Crude model Relative difference (95% CI)	Adjusted model Relative difference (95% CI)
Maternal analyses (including 700 mothers and 901 offspring)				
Psychotic experiences	2.57 (1.84, 3.58)	2.42 (1.73, 3.38)	2.52 (1.70, 3.72)	2.34 (1.56, 3.52)
Depression symptoms	1.08 (1.03, 1.13)	1.06 (1.01, 1.12)	1.07 (1.02, 1.13)	1.05 (1.00, 1.11)
Anxiety symptoms	1.03 (1.01, 1.04)	1.02 (1.01, 1.04)	1.03 (1.01, 1.05)	1.02 (1.00, 1.04)
Mental well-being	0.95 (0.92, 0.98)	0.96 (0.93, 0.99)	0.95 (0.92, 0.98)	0.96 (0.92, 0.99)
Paternal analyses (including 496 father and 652 offspring)				
Psychotic experiences	2.25 (1.42, 3.59)	2.30 (1.46, 3.62)	2.28 (1.32, 3.95)	2.29 (1.33, 3.96)
Depressive symptoms	0.99 (0.89, 1.10)	0.98 (0.89, 1.08)	0.98 (0.86, 1.13)	0.97 (0.86, 1.10)
Anxiety symptoms	1.00 (0.98, 1.03)	1.00 (0.98, 1.03)	0.98 (0.93, 1.02)	0.98 (0.93, 1.02)
Mental well-being	0.98 (0.94, 1.02)	0.97 (0.93, 1.02)	1.00 (0.97, 1.03)	1.00 (0.97, 1.03)

Abbreviations: RR = risk ratio, RD = relative difference, CI = confidence interval. Notes: Parental depressive symptoms, anxiety symptoms, and mental well-being were assessed as continuous variables. Lower scores on mental well-being indicates better mental health. The adjusted models controlled for youth sex and age, parental education and parental occupation. Only psychotic experiences reported as 'definitely present' were included.

Methodological considerations

The current study benefited from a large sample size of parents and their offspring that were assessed independently yet using the same measure for psychotic experiences. The findings were consistent and robust across numerous statistical models, increasing the confidence in the findings. However, some limitations should be considered. First, regarding measurement of psychotic experiences, self-report measures of psychotic experiences might be considered overinclusive, yet the overlap between self-reported and clinically assessed psychotic experiences is reasonable (Gundersen et al., 2019; Kelleher, Harley, Murtagh, & Cannon, 2011), and even psychotic experiences that are not verified clinically seem to have clinical importance in both adults and youths (Monshouwer et al., 2023; Rimvall et al., 2019). However, clinically important information about the degree of distress due to psychotic experiences (Karcher et al., 2018), was not thoroughly assessed in the current study using a shortened version of the PLIKSq. Further, although the questions for the PLIKS-interview were based on questions from Diagnostic Interview Schedule for Children–IV (DISC–and the Schedules for Clinical Assessment in Neuropsychiatry (SCAN), the PLIKSq lacks formal validation. Second, the recurrence of psychotic experiences (as opposed to remitting psychotic experiences) is an important marker of clinical severity (Staines et al., 2023), which could not be considered in parents nor youths, given the cross-sectional nature of the current study. Third, information on diagnosed/diagnosable psychotic disorders was not available for neither parents nor youths or other relatives, and we cannot rule out, that the findings in part might reflect associations between parental and offspring psychotic symptomatology higher on the continuum than the level of subclinical psychotic experiences. Further, we could not assess to which degree the findings that psychotic experiences clustered in families were due to genetic effects or environmental effects within the families or more broadly. Also, potential (sub)culturally accepted expression of psychotic experiences, e.g. specific religious or paranormal beliefs, which might cluster in families, was not assessed. Fourth, due to non-participation, there is a risk of selection bias. Prior attrition analyses based on half of all participants in the LOFUS cohort (Jepsen et al., 2020b), showed that participants were more often

Table 3. Multivariate models: Associations between parental factors (mutually adjusted) and offspring psychotic experiences for mothers and fathers separately

	One or more psychotic experiences in offspring Risk ratio (95% CI)	Number of psychotic experiences in offspring (0,1,2, ⩾3) Relative difference (95% CI)
Maternal analyses (including 700 mothers and 901 offspring)		
Psychotic experiences	2.25 (1.60, 3.19)	2.23 (1.48, 3.35)
Depression symptoms	0.99 (0.92, 1.06)	0.97 (0.90, 1.05)
Anxiety symptoms	1.00 (0.98, 1.03)	1.01 (0.97, 1.04)
Mental well-being	0.97 (0.93, 1.02)	0.96 (0.91, 1.02)
Paternal analyses (496 father and 652 children)		
Psychotic experiences	2.44 (1.50, 3.96)	2.50 (1.34, 4.65)
Depression symptoms	0.92 (0.78, 1.08)	0.91 (0.74, 1.14)
Anxiety symptoms	0.99 (0.95, 1.04)	0.99 (0.94, 1.04)
Mental well-being	0.96 (0.89, 1.02)	0.96 (0.89, 1.04)

Abbreviations: CI = confidence interval. Notes: Parental depressive symptoms, anxiety symptoms and mental well-being were included in the models as continuous variables. Lower scores on mental well-being indicates better mental health. All models were further adjusted for youth sex and age, parental education and parental occupation. Only psychotic experiences reported as 'definitely present' were included.

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female and had fewer socioeconomic adversities compared to non-participants, likely resulting in less variation and somewhat biasing the reported associations towards the null. Because register data for the entire cohort is not yet available, we could not conduct specific attrition analyses for the current sample, yet we can fairly assume that our sample was similarly subject to differential attrition and positively selected. Additionally, further selection bias could have been introduced as fathers were particularly underrepresented in the current sample compared to mothers, likely largely attributable to the fact that more than 80% of children of divorced parents in Denmark have their household address with their mothers (Ottosen, Stage, & SFI - Det Nationale Forskningscenter for Velfærd, 2012). Lastly, although reliable administrative data was utilized to link family members (Pedersen, 2011), a *genetic* link between the youth and both parents is not ensured (nor tested) in all cases, but this would be the case in the vast majority of participants.

Finally, the rural context of the current cohort could be considered, as evidence suggests that psychotic disorders are less prevalent in rural areas (Vassos, Pedersen, Murray, Collier, & Lewis, 2012). However, the evidence for an association between urbanicity and psychotic experiences is not as strong (DeVylder et al., 2018), and the prevalence of definite psychotic experiences according to PLIKSq among 11-17-year-olds in LOFUS (17.2%) was almost identical with a report from the Danish Copenhagen Child Cohort 20000 (16.7%) from a mainly suburban population (Rimvall et al., 2020b).

Interpretation

While prior findings from general population- and high risk cohorts are not entirely consistent in showing an association between parental psychotic disorders and offspring psychotic experiences, our findings corroborate the majority of studies indicating a transgenerational transmission of psychotic symptoms/experiences (Gregersen et al., 2022; Jeppesen et al., 2015b; Karcher et al., 2018; MacKenzie et al., 2016; Polanczyk et al., 2010). Additionally, in keeping with our findings, a prior study has shown clustering of positive psychosis symptomatology across the psychosis continuum within families in a smaller study of adults (Hanssen et al., 2006). A key argument behind the idea that psychosis can advantageously be viewed on a continuum in the population, is the presence of shared environmental and genetic risk factors between psychotic experiences and psychotic disorders (van Os, Kenis, & Rutten, 2010). The current findings, that psychotic experiences in parents were robustly associated with psychotic experiences in offspring, lend support to the idea that the familial effects of positive psychotic phenomena should be considered on a continuum.

Evidence clearly indicates that psychotic experiences by no means solely reflect (risk of) psychotic disorders in youths and adults alike (Healy et al., 2019; Kaymaz et al., 2012), and subclinical psychotic symptomatology is likely more advantageously viewed as a transdiagnostic phenotype (van Os & Reininghaus, 2016). However, several studies do indeed indicate some specificity of psychotic experiences across generations (Gregersen et al., 2022; Jeppesen et al., 2015b), as well as larger effects of psychotic experiences in youths on psychotic *v.* non-psychotic disorders later in life according metanalytic evidence (Healy et al., 2019). Regarding genome-wide informed studies, meta-analytic evidence suggests shared genetic vulnerability between schizophrenia and psychotic experiences (Ronald & Pain, 2018). Subsequently, evidence from more than 100 000 individuals using data from the UK biobank showed that polygenic risk score for schizophrenia were indeed associated with psychotic experiences (Legge et al., 2019). However, there was strong evidence of non-specificity, given that polygenic risk scores for depression, bipolar-, and neurodevelopmental disorders were all associated with psychotic experiences (Legge et al., 2019). The evidence of non-specificity of the polygenic risk scores strengthens the notion of psychotic experiences as also environmentally dependent (on factors such as substance misuse, socioeconomic adversities in the family, and trauma) markers of transdiagnostic risk of mentally ill health (van Os & Reininghaus, 2016). Such environmental factors likely explain an important part of the variance in the findings in the current study.

Strikingly, in this general population sample we showed that psychotic experiences were indeed strongly and robustly associated across generations, whereas the role of parental depression, anxiety, and mental well-being were not independently associated with psychotic experiences in offspring in the mutually adjusted statistical models. Also, after further adjustment for general mental health problems of the child, the association between parental and youth psychotic experiences remained. Hence, the current study adds to the notion of specificity of subclinical psychotic expression by presenting novel evidence of familial clustering of psychosis at the lower end of the psychosis continuum. The findings in the current study might both reflect primary genetic effects of psychotic psychopathology as well as psychosocial distress and other detrimental social and environmental factors that might cluster in families (Bolhuis et al., 2022; Newbury et al., 2022; Taylor, Freeman, Lundström, Larsson, & Ronald, 2022), and are likely to interact (Taylor et al., 2022). The dose-response finding in the current study (increased risk of psychotic experiences in youths when both parents reported psychotic experiences) might also reflect both shared genetic and environmental vulnerabilities. While it is well appreciated that prediction of clinical psychosis syndromes through clinical high-risk paradigms for psychosis is a very challenging task, especially in youths (Catalan et al., 2021; Lång et al., 2022), the assessment of subclinical psychosis expression could improve the early identification of vulnerable youths, and wide-spread assessment of psychotic experiences has been suggested to inform identification of younger individuals at increased risk of developing severe psychopathology broadly (Cotter, Healy, Staines, Mongan, & Cannon, 2022).

The current study further calls for systematic consideration of the family systems that the youths are part of in clinical practice, as well as a family history of mental health problems beyond merely considering clinical diagnoses in relatives. Although we have presented evidence of specificity of psychosis vulnerability, based on the larger body of literature, we warn against assuming *diagnostic* specificity of psychotic experiences in families, but rather as vulnerability markers that should be considered within the broader context of the familial and social risks. Future studies may benefit from describing longitudinal patterns of psychotic experiences within family systems to further advise us on whether assessment of psychotic experiences in youths can contribute to targeting more in-depth assessments and possible service provision, particularly in families with clustering of psychotic experiences.

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