Evidence that supports using birth size as a phenotypic marker of gene-dosage variation *in utero*. Disruption to the imprinted gene IGF2 and IGF2r can cause opposite outcomes for fetal growth/birth size and later psychiatric disorders, consistent with their respective imprints being of paternal and maternal origin [1, 2]. Further, birth size has been used in mouse model studies measuring the phenotypic outcomes of early-life perturbations to imprinted genes [3-5], making it reasonable to expect a similar influence of imprinted genes on human birth size [6] and possible associations with variation in cognitive development and functioning in childhood and adolescence [7, 8]. These studies suggest that fetal growth and early neurodevelopment may be correlated through similar gene-dosage disruptions [9], just as opposing morphological and behavioral differences are both induced by modified IGF2/IGF2r [10, 11] and Peg3 [12] expression. Therefore, such gene-dosage variation expressed in the placenta and developing brain may be correlated, which would imply a connection between variation in birth size to variation in postnatal behavior.

Sources and validation of data on birth size and mental illness. Offspring born between 1978 and 2009 were classified as having a mental illness if they had been admitted as an inpatient or had been in outpatient care. From 1969 to 1993, the diagnostic system used was the Danish modification of the International Classification of Diseases, 8th revision (ICD-8), and from 1994 on, the 10th revision (ICD-10)(table S2). At least one year (and up to 30 years) of follow-up was available for each offspring up until 2009. Those suspected of having a mental illness are referred by general practitioners or school psychologists (if suspected in childhood) to a psychiatric clinic where they are diagnosed and treated by psychiatrists.

To improve the accuracy of diagnoses and to remove effects of mis-diagnoses or changes of diagnoses due to changes in the ICD coding structure, we used the following procedures. Out of all psychiatric diagnoses that an individual accumulated in the psychiatric registry between 1979 and 2009, the date of the first diagnosis was used as the censor time (from date of birth to date of incidence) and the last recorded diagnosis was used to define the disorder with which that person was diagnosed. Any parents of offspring (born between 1978 and 2009) were also scanned for the same set of psychiatric disorder groups and binary (presence/absence) markers were included in these analyses to represent the known familial component for each of these disorders.

For each analysis, all offspring with non-target psychological disorders were removed to limit potentially confounding of the comparisons between offspring with the target psychological disorder and the control group of offspring with no history of mental illness. This also meant that risk patterns could be compared directly for specific psychological disorder groups with no overlap in their ICD codes.

To avoid the potential confounding of psychoactive substance use on risk of psychiatric disorders, individuals (parents or offspring) were excluded if they were

ever diagnosed as having a psychiatric disorder due to drug or alcohol use (ICD-10 codes F10-F19; ICD-8 codes 291.09, 291.19, 291.29, 291.39, 291.99, 303.09, 303.19, 303.20, 303.28, 303.29, 303.90, 303.91, 303.99, 304.09, 304.19, 304.29, 304.39, 304.49, 304.59, 304.69, 304.79, 304.89, 304.99).

In an additional analysis where gestation length was also categorized (figure S3), AS and SS risk patterns remained consistently similar across birth weight and length ranges, providing additional support for the risk patterns presented in the main paper (figure 3).

Missing data removed. The sample of singleton births was reduced from 1,787,447 to 1,757,770 due to missing values for birth weight (n=532), paternal (n=11,699) and maternal (n=41) age, parity (n=84), APGAR 5 score (n=10,802); extreme birth weight values < 1,850 and > 5,400 grams (n=1263); extreme paternal (< 16 and > 60 (n=889)) and maternal age (< 15 and > 46 (n=206)) values; and very short gestation (< 30 weeks (n=4,161)).

Covariates included in the analyses. Covariate data were obtained from the Danish birth, psychiatric, person and household registries covering the period of 1978-2009. Parental covariates (table S1) included: a binary (1-0, presence-absence) marker indicating whether either parent had been diagnosed with the same psychological disorder as the child to account for familial transmission; the age (in years) of each parent at the time of the child's birth; binary (1-0) markers indicating whether mothers had any pre-existing hypertension (i.e. primary or secondary hypertension, hypertensive heart or renal disease; table S3), pre-existing diabetes (i.e. type-I or type-II, malnutrition-related, other or unspecified; table S3), previous spontaneous or induced abortions, combined highest education (in years) of parents, and combined average income (in Dkr) of parents.

Maternal pregnancy-related covariates (table S1) included: gestation length (in weeks); binary (1-0) markers indicating whether mothers experienced any maternal bleeding (i.e. haemorrhage, placenta praevia; table S3), fetal oxygen deprivation (i.e. hypoxia, asphyxia; table S3), pregnancy oedema, and gestational diabetes or gestational hypertension (i.e. pregnancy-induced hypertension, preeclampsia, eclampsia; table S3). Other birth-related influences included APGAR 5 (Appearance, Pulse, Grimace, Activity, Respiration), a score of 1-10 (maximally 2 points for each category) given to babies shortly after birth ranging from poor to excellent health.

Other factors that our analyses adjusted for (table S1) related to the child and included: sex (1=female, 0=male); birth season (calendar month, 1 to 12); birth year (3-year cohorts between 1978 - 2008) to account for changes in diagnostic criteria over time; country of origin (0 = Danish national, 1 = immigrant); demographic parity (born first, second, third, fourth or higher), split into groups coded as binary variables with the first born group set as reference; region within Denmark (Hovedstaden = Copenhagen Area, Sjælland, Syddanmark, Midtjylland and

Nordjylland) in which the child had resided for the longest as of 2009, split into groups with Hovedstaden set as reference to account for possible differences in diagnostic practices regionally.

Model diagnostic procedures. These were assessed for all Cox regressions, which included checking for violation of the assumption of proportional hazards, for disproportional data, and for nonlinearity in the relationship between the log hazard and the covariates. All tests were passed and are standard for checking whether a fitted Cox regression adequately describes the data.

Risk trends for covariates. Some covariates consistently increased or decreased risk for most disorders. Factors associated with increased risks included: whether either parent had been diagnosed with the same disorder, confirming a familial component; being born more recently; presence of maternal bleeding during pregnancy; and whether mothers had any previous induced or spontaneous abortions (figure 4). Factors related to decreased risk of most mental illnesses included: having parents with higher average income; being foreign rather than native born; being born outside of the Copenhagen (Hovedstaden) area except for Midtjylland (including Denmark's second largest city Aarhus), where bipolar disorder was significantly more frequent.

Other covariates significantly modified risks for autistic but not schizophrenic disorders. Being born from a pregnancy that had any form of gestational hypertension increased risk of autistic disorders, whereas being born with a higher APGAR score decreased it.

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