*Psychol Med*. Author manuscript; available in PMC 2018 May 08.

Published in final edited form as:
*Psychol Med*. 2017 July ; 47(9): 1659–1667. doi:10.1017/S0033291717000125.

# Curiosity killed the cat: No evidence of an association between cat ownership and psychotic symptoms at age 13 and 18 years in a UK general population cohort

**F. Solmi**[1], **J.F Hayes**[1], **G. Lewis**[1], and **J.B Kirkbride**[1]

[1]Division of Psychiatry, University College London, London, UK

## Abstract

**Background—**Congenital or early life infection with *Toxoplasma Gondii* has been implicated in schizophrenia aetiology. Childhood cat ownership has been hypothesised as an intermediary marker of *T. Gondii* infection and, by proxy, as a risk factor for later psychosis. Evidence supporting this hypothesis is, however, limited.

**Method—**We used birth cohort data from the Avon Longitudinal Study of Parents and Children (ALSPAC) to investigate whether cat ownership in pregnancy and childhood (4, 10 years old) was associated with psychotic experiences (PEs) in early (age 13; N=6,705) and late (age 18; N=4,676) adolescence, rated from semi-structured interviews. We used logistic regression to examine associations between cat ownership and PEs, adjusting for several sociodemographic and socioeconomic factors, household characteristics and dog ownership. Missing data were handled via multiple imputation.

**Results—**Cat ownership during pregnancy was not associated with PEs at age 13 (adjusted odds ratio [OR]: 1.15, 95% confidence interval [CI]: 0.97-1.35) or 18 years (OR: 1.08, 95%CI: 0.86-1.35). Initial univariable evidence that cat ownership at 4 and 10 years was associated with PEs at age 13 years did not persist after multivariable adjustment (4 years OR: 1.18, 95%CI: 0.94-1.48; 10 years OR 1.12, 95%CI: 0.92; 1.36). There was no evidence that childhood cat ownership was associated with PEs at 18 years old.

**Conclusions—**While pregnant women should continue to avoid handling soiled cat litter, given possible *T Gondii* exposure, our study strongly indicates that cat ownership in pregnancy or early childhood does not confer an increased risk of later adolescent PEs.

### Keywords

Psychotic symptoms; psychosis; cat ownership; ALSPAC; pet ownership

**Corresponding author:** Francesca Solmi, PhD, UCL Division of Psychiatry, 6th Floor, Wing B, Maple House, 149 Tottenham Court Road, London W1T 7NF, francesca.solmi@ucl.ac.uk, P: 02076799643.

**Conflict of Interest**

FS, JH, GL, and JBK currently own or have owned cats (FS, JH, and JBK N=1; GL N=2), but declare that the latter did not have a role in the formulation of the study hypothesis.


Europe PMC Funders Author Manuscripts

## Background

House cats are the primary hosts of *Toxoplasma Gondii (T. Gondii),* a protozoan parasite that can infect various warm-blooded animals, including humans (Tenter *et al.* 2000; Webster *et al.* 2013). Infection can occur *in utero* or postnatally, via ingestion of either the parasite's oocysts – which might be present in soil, water, or food – or tissue cysts from infected animals (e.g., in raw or undercooked meat). In intermediate hosts (e.g., humans or animals other than cats), the parasite exploits lymphocytes to encroach in muscle tissues and, importantly, the brain, where it can form tissue cysts in neurons, microglia, and astrocytes (Carruthers & Suzuki 2007).

Although the evidence is not unequivocal (Sugden *et al.* 2016), data from several epidemiological, experimental, and animal studies suggests that *T. Gondii* infection may be implicated in the aetiology of psychosis. For example, dopaminergic dysfunction and cognitive impairments – similar to those observed in people with schizophrenia – have been observed in infected rodents (Gaskell *et al.* 2009; Prandovszky *et al.* 2011; McConkey *et al.* 2013) and humans (Kannan & Pletnikov 2012); these people may also experience hallucinations during acute infection with the parasite (Sugden *et al.* 2016). A recent meta-analysis of 38 studies found that compared with controls, people with schizophrenia were nearly 3 times more likely to be seropositive for *T. Gondii* antibodies (odds ratio (OR) 2.71; 95% confidence intervals (CI): 1.93 – 3.80) (Torrey *et al.* 2012). Higher seroprevalence and serointensity of *T. Gondii* IgG (but not IgM, an indicator of recent infection) in people with schizophrenia (Cetinkaya *et al.* 2007) and their mothers (Brown *et al.* 2005; Mortensen *et al.* 2007a) suggest that either early life exposure to the parasite, congenital infection, or transmission of maternal antibodies could alter subsequent offspring neurodevelopment.

Assuming a causal relationship between *T. Gondii* infection and later psychosis, some researchers have hypothesised that cat ownership should confer an increased risk of psychotic disorders (Torrey & Yolken 1995; Yuksel *et al.* 2010; Torrey *et al.* 2015). Moreover, this theory has been proposed to explain several epidemiological findings, including higher rates of psychotic disorders in urban populations (with higher cat densities and subsequent possibility for infection) (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015). Nonetheless, robust empirical evidence to support this theory remains limited. Cat ownership or contact during pregnancy (Kapperud *et al.* 1996; Cook *et al.* 2000) and childhood (Taylor *et al.* 1997) do not appear to be associated with *T. Gondii* infection, although handling soiled cat litter is known to be associated with infection (Kapperud *et al.* 1996). Epidemiological studies which have reported an association between cat ownership and psychosis - (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015; Yuksel *et al.* 2010), have generally been hindered by notable methodological limitations (Wolf & Hamilton 2015), including reliance on case-control designs that are susceptible to recall bias, small *ad hoc* samples and weak statistical analyses, which have failed to adequately account for confounding or missing data.

To overcome these issues, we sought to test whether prenatal and childhood cat ownership were associated with an increased risk of developing psychotic experiences (PEs) in early and late adolescence, using longitudinal data from the Avon Longitudinal Study of Parents

Europe PMC Funders Author Manuscripts

and Children (ALSPAC). Psychotic experiences in adolescence are an established risk factor for later schizophrenia, particularly with respect to psychotic symptoms which emerge or persist in late adolescence (Poulton *et al.* 2000; Fisher *et al.* 2013). Since *T. Gondii* infection is proposed to increase psychosis risk by affecting early life neurodevelopment (Mortensen *et al.* 2007b), we restricted cat ownership to the prenatal and early childhood period (at 4 years of age), although we also performed additional analyses using cat ownership at age 10 years to better align with previous research (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015; Yuksel *et al.* 2010).

## Methods

### Sample

The ALSPAC study invited 16,734 pregnant women expected to deliver between 1st April 1991 and 31st April 1992 resident in the former county of Avon in the Southwest of England; of these, 14,541 (87%) enrolled resulting in 14,062 live births and 13,988 children alive at one year of age. The sample was supplemented with 713 additional children (whose mothers were originally eligible for the study) during follow-up between the ages of seven and 18 years. More details on recruitment, follow-up assessments and time-points have been published elsewhere (Boyd *et al.* 2012). All mothers gave informed written consent prior to recruitment and the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees gave ethics approval for this study.

In this study we included children with complete data on psychotic experiences at ages 13 (N=6,705) and 18 (N=4,676). For twin pairs (N=87, 2.6% of the sample at age 12, and N=42, 1.8% at age 18), we excluded one sibling (sibling “B”) to avoid biasing estimates due to shared genetic and environmental exposures; there is no evidence that, in twins, birth order is related to schizophrenia risk (Onstad *et al.* 1992; Kleinhaus *et al.* 2008).

### Exposure variable

Information on pet ownership was reported by mothers via postal questionnaires during pregnancy, and subsequently when their child was eight, 21, 31 and 47 months old. In addition to cat ownership, mothers were asked about the number and type of other pets owned, including: dogs, rabbits, rodents, birds, (all waves), and tortoises and fish (from 21 months). From these questions we created two primary binary exposure variables, indicating whether the mother owned a cat (yes/no): (i) in pregnancy; and (ii) at 47 months of the child (circa 4 years). As a secondary exposure, we employed cat ownership at 10 years (122 months) in order to create an exposure variable comparable with those used in previous studies (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015). We did not test whether a dose-response effect existed between duration of cat ownership and psychotic symptoms, since the majority (89%) of children who reported cat ownership at age 4 years also owned one at eight, 21, and 31 months, as reported by their mothers.

### Outcome variables

At approximately age 13 and 18 years, children attended clinic visits where they were administered the psychotic-like symptoms interview (PLIKSi), a semi-structured

interviewer-rated screening assessment for PEs. The PLIKSi contains six questions on unusual experiences (i.e. derealization, depersonalization, self-unfamiliarity, dysmorphophobia, partial object perception, and other perceptual abnormalities) followed by 12 questions adapted from the Diagnostic Interview Schedule for Children version IV (DISC-IV) (Shaffer *et al.* 2000) and the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) (WHO 1994). These are aimed at assessing the presence of delusions (being spied on, persecuted, having thoughts read, reference, control, grandiose ability, and other delusions), hallucinations (visual and auditory), and intrusive thoughts (thought broadcasting, insertion and withdrawal) (Horwood *et al.* 2008). Total scores were recoded into a binary variable indicating the absence, or the suspected/definite presence of symptoms, consistent with previous investigations of PEs in ALSPAC (Horwood *et al.* 2008; Dorrington *et al.* 2014). Children whose psychotic symptoms could have been attributed to fever or sleep problems were coded as not having the outcome (Zammit *et al.* 2008, 2009; Dorrington *et al.* 2014).

## Other variables

We employed causal diagrams, known as Directed Acyclic Graphs (DAGs) (Textor & Liśkiewicz 2011), to identify variables which could confound the association between cat ownership and psychotic symptoms. We modelled hypothesised associations between a broad initial set of potential child- and mother-based variables, cat ownership in either pregnancy or childhood and PEs using the DAGitty web-based software. (Textor *et al.* 2011) Our DAGs (supplementary figures 1 and 2) suggested that it was inappropriate to control for some of these variables, either because they did not meet criteria for confounding (e.g., child gender, stressful life events, maternal depression, pet ownership other than dogs), or because adjustment for other variables (e.g. paternal age, dog ownership in pregnancy) provided sufficient control for any other causal paths (e.g. maternal age, dog ownership at age four years). From our DAGs we were able to identify the minimal sufficient number of confounders of the relationship between exposure to cat ownership in pregnancy and childhood and PEs at age 13 and 18 years. These included: child ethnicity (white/non-white – including Black African, Black Caribbean, Other Black, Indian, Pakistani, Bangladeshi, Chinese, Other, mixed); paternal age (at the time of mother's pregnancy); maternal marital status in pregnancy (single, separated, divorced, or widowed/married); highest maternal academic education in pregnancy (vocational course/secondary schooling/ university degree or higher); maternal social class (manual vs. non–manual profession); number of house moves up to 47 months (4 years old); housing type (detached, semi-detached, terraced/flats, other); household crowding index (range: 0 – 1); and dog ownership in pregnancy.

The ALSPAC website contains details of all the data that is available through a fully searchable data dictionary available at: http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/

## Statistical analyses

We employed cross-tabulations (with Chi-square tests) and ANOVAs to (i) investigate the presence of selective attrition in the sample, by comparing children with and without missing outcome data on exposure and confounding variables; (ii) describe the sample and

test for differences in the distribution of exposure and confounding variables across outcome levels. We then fitted univariable and multivariable logistic regression models adjusting for all variables identified as relevant confounders using DAGs (supplementary figure 1 and 2), i.e.: dog ownership in pregnancy; housing type; household crowding; maternal education, social class, and marital status; paternal age; number of house moves. When the studied exposure was cat ownership in childhood, we further adjusted for maternal cat ownership in pregnancy.

Since our primary hypothesis was a null association between cat ownership and psychotic symptoms, we conducted power calculations, assuming an alpha of 0.05 to determine the effect size we could reasonably expect to detect, had it existed, given our sample sizes. Our sample had over 90% power to detect an odds of ratio of 1.25 based on the observed exposure distribution and sample sizes.

## Missing data

Analyses were based on participants with complete data at age 13 (N=6,705) and 18 years (N=4,676). Missing main exposures and covariate data varied between 0.04% (pregnancy) to 34.08% (age four), and 0.02% (pregnancy) to 33.58% (age four) at each time point respectively (Supplementary table S1).

We used multiple imputation with chained equations (MICE) and the Stata *ice* command (Royston & White 2011) to impute missing exposure and covariate data, including all observed exposure, covariate and outcome data into our multiple imputation (MI) routine, in addition to several auxiliary variables which could provide information about missing values. These included: gender; stressful life events; maternal depression in pregnancy; other pet (rabbit, rodents, turtles, birds, fish) ownership in pregnancy and age four; two measures of depressive symptoms at age 12 and 18 years assessed via self-reported with the short moods and feelings questionnaire (SMFQ) (Angold *et al.* 1995); a continuous measure of IQ assessed during a clinical assessment at age 8 years using the Wechsler Intelligence Scale for Children third edition (WISC-3); and a measure of family income at 33 months of the child. We also included a variable indicating maternal history of schizophrenia at birth in light of the known genetic heritability of psychosis (Lichtenstein *et al.* 2009). We imputed 100 datasets using linear, logistic, ordinal logistic, and multinomial logistic models according to the nature of the variables whose missing values had to be imputed. As sensitivity analyses we examined the association between cat ownership and adolescent PEs in (i) a complete case analysis, to assess any possible bias introduced when failing to account for missing data, and (ii) using data on the full ALSPAC sample (N=15,023) with multiple imputation on those missing outcome data, to assess possible biases introduced by our main choice of multiple imputation.

All analyses were performed using Stata13 (StataCorp 2013).

# Results

## Missing data

Children with missing outcome data at ages 13 and 18 were more likely to be boys, from a non-white ethnic background, to live in more crowded houses, and have experienced a stressful life event by age 4 years. Children with missing data were also more likely to have younger parents, and a mother who had suffered from probable depression in pregnancy, was less well educated, not married, from a manual occupation, and who had moved house more frequently. At both age 13 and 18 years, children whose mother had owned a cat in pregnancy were less likely to have missing data, although children whose mother had owned a cat in their childhood were more likely to have missing outcome data at age 13 years. Participants with missing outcome data at either age were more likely to have a mother who owned a dog, a bird, a rabbit, or rodent in pregnancy or during childhood (Supplementary Table S1).

## Sample characteristics

A total of 6,705 and 4,676 children had complete data on psychotic symptoms at age 13 and 18 years, respectively, and were therefore included in the analyses. At both ages, the majority of each sample was of female gender, white ethnicity, had a mother who had completed at least A-levels, was married, non-manual profession, and had moved house less than three times between the four years prior to pregnancy and age 4 years of the child (Table 1) In both samples, around one third of mothers owned a cat during pregnancy, and at four and ten years (Table 1). Among children who owned a cat at age 4 years, between 79% and 89% also owned a cat at previous waves of data collection (i.e., at ages 8, 21, and 33 months). Among those who owned a cat at age 10 years, between 62% and 86% also owned a cat at a previous time point (data available from authors).

At age 13 years, a greater proportion of the sample who reported suspected/definite psychotic symptoms owned a cat in childhood, were girls, lived in flats and in crowded home environments, had moved homes more frequently, and had a mother who was younger, less well educated, and of single marital status (Table 1). Similar patterns were generally observed for the sample at 18 years (Table 1), although there was no longer any apparent association between PEs and number of house moves, while non-manual social class and non-white ethnicity were associated with experiencing suspected/definite PEs at this age.

## Cat ownership and psychotic symptoms

Cat ownership in pregnancy was not associated with psychotic symptoms at age 13 or 18 years in either univariable (age 13: OR: 1.15, 95%CI: 0.97-1.35; age 18; OR: 1.08, 95%CI: 0.86-1.35) or in multivariable models (age 13: adjusted OR: 1.15, 95%CI: 0.97-1.36; age 18; OR: 1.08, 95%CI: 0.85 - 1.37), following multiple imputation (Table 2). Owning a cat at age 4 years was associated with higher odds of having PEs at age 13 years in univariable (OR: 1.23, 95%CI: 1.04-1.46), but this effect was no longer significant after multivariable adjustment (OR: 1.18, 95%CI: 0.94-1.48). There was no evidence that cat ownership at age 4 years was associated with PEs at age 18 years (univariable OR: 1.11, 95%CI: 0.88-1.40; adjusted OR: 0.97, 95%CI: 0.71-1.31). These patterns were similar with respect to cat

ownership at age 10 years, with no apparent association with PEs at age 13 years (OR: 1.12; 95%CI: 0.92-1.36) or 18 years (OR: 1.08; 95%CI: 0.82-1.45) after multivariable adjustment (Table 2).

### Sensitivity analyses

In complete case analyses cat ownership in pregnancy was associated with higher odds of PEs at age 13 years in all models (univariable OR: 1.31, 95%CI: 1.04 – 1.65; adjusted OR: 1.34, 95%CI: 1.06 - 1.69), as was cat ownership at age 4 years (univariable OR: 1.44, 95%CI: 1.13 – 1.83; adjusted OR: 1.47, 95%CI: 1.01 – 2.13). Cat ownership at 10 years was only associated with PEs at 13 years in the univariable (OR: 1.30, 95%CI: 1.02 – 1.66), but not in the adjusted ones. We found no evidence of an association between cat ownership and PEs at age 18 years (Supplementary Table 3).

Next, we used the fully imputed dataset to examine the association between cat ownership and adolescent PEs on the whole ALSPAC cohort (N= 15,023). The pattern of these results (Supplementary Table 4) were very similar to the magnitude, direction and general lack of association between cat ownership and adolescent PEs reported in our main results based on imputation of exposures and confounders (Table 2). Together these sensitivity analyses suggested that complete case analyses may lead to biased risk estimates, while our choice of MI routine did not substantially bias our results.

## Discussion

We found no evidence that cat ownership in pregnancy or childhood was associated with PEs in early and late adolescence using prospectively-collected data from a large population-based cohort, following control for several confounders and methods that investigate the likely impact of missing data.

Our findings in relation to PEs are not consistent with the existing literature that has studied cat ownership in people with schizophrenia (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015; Yuksel *et al.* 2010). We suggest that several methodological differences between our study and other investigations, including previous reliance on small, retrospective, convenience samples, may explain the discrepancy.

Our study was based on PEs in early and late adolescence, unlike other studies which were based on a clinical diagnosis of schizophrenia (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015; Yuksel *et al.* 2010). One possible explanation of our null findings is that cat ownership does not affect the population expression of psychosis (i.e. does not shift the continuum), but operates only to increase risk of threshold symptoms for clinical disorder. We consider this explanation unlikely, given that: psychotic symptoms in late childhood and adolescence predict onset of non-affective psychosis and other psychopathology (Poulton *et al.* 2000; Laurens *et al.* 2007; Kelleher *et al.* 2012; Fisher *et al.* 2013) and psychotic symptoms in late adolescence are better predictors of future psychopathology. In line with other literature (Kelleher *et al.* 2012), we observed a decline in the prevalence of PEs between ages 13 and 18 years. If symptoms in later adolescence therefore provide a greater indication of later clinical disorder (Poulton *et al.* 2000; Fisher *et al.* 2013) then our results at age 18 (where




Europe PMC Funders Author Manuscripts

there was no evidence of any association between cat ownership and PEs) may have the strongest implications for likely effects of early life cat ownership on clinical disorder..

Unlike previous studies which investigated cat ownership up until age of 10 or 13 years, (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015; Yuksel *et al.* 2010), we restricted our main exposure variables to cat ownership during potentially sensitive windows of neurodevelopment, namely pregnancy and at age 4 years (47 months). We included cat ownership at age 10 years as a secondary exposure, consistent with previous literature, but our results mirrored those found at age 4 years, generally indicating an absence of association. Our study was sufficiently powered to detect effect sizes previously observed in the schizophrenia literature with respect to cat ownership (odds ratios of 1.25 or more) (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015; Yuksel *et al.* 2010), as evidenced by the initial univariable associations we only observed between childhood exposure and PEs at age 13 years. While our study would have had less power to detect smaller odds ratios, including those we observed between 1.04-1.15, any such small effects, if true, would not warrant particular public mental health attention.

Previous reports of positive associations between cat ownership and schizophrenia may therefore have been attributable to Type I error, particularly given the small sample sizes and lack of control for confounders inherent to some studies. We adjusted for several, theoretically-informed confounders, including ethnicity (Westgarth *et al.* 2010; Kirkbride *et al.* 2012), maternal academic achievement and social class (Mulvany *et al.* 2001; Werner *et al.* 2007; Westgarth *et al.* 2010), and parental age (Sipos *et al.* 2004; Lopez-Castroman *et al.* 2010; Westgarth *et al.* 2010; Petersen *et al.* 2011). We also adjusted for number of house moves in light of evidence of an association between residential mobility and psychotic experiences (Singh *et al.* 2014), crowding index and housing type as a proxies for both social class and greater possibility of contact with *T. Gondii* contaminated litter, and dog ownership as a possible confounder of the association between *T. Gondii* infection (given an increased likelihood to contaminated soils outdoors) and psychosis risk.

Earlier studies also relied on retrospective recall, and hence the potential of recall bias, of cat exposure and did not distinguish between ownership in infancy versus later childhood, making it impossible to attribute risk to specific periods of cat ownership over the early life course.

Finally, we employed multiple imputation techniques in order to account for missing data, which could have otherwise biased our results. Consistent with guidelines (Sterne *et al.* 2009), we included all known exposure, outcome, covariate and auxiliary variables in MI as well as additional variables which had been previously found to be associated with PEs in this sample. Comparing our results with those from complete case analyses suggests that selective participation may potentially bias estimates, and could therefore explain previous positive findings in the literature (Torrey & Yolken 1995; Torrey *et al.* 2000, 2015). This hypothesis is further supported by our results using the fully-imputed sample, where no significant associations were found in line with our main findings.

Europe PMC Funders Author Manuscripts

In conclusion, there is good evidence to support an association between *T. Gondii* infection and later risk of experiencing psychosis, and this research is consistent with possible inflammatory causes of schizophrenia and other psychotic disorders. From a public health perspective, however, it is perhaps reassuringly that data from our prospective longitudinal study were not consistent with the hypothesis that cat ownership in pregnancy or early childhood is a risk factor for later psychosis.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

We are extremely grateful to all the families who took part in this 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.

**Financial Support**

Dr James Kirkbride and Dr Francesca Solmi are supported by a Sir Henry Dale Fellowship to JBK, jointly funded by the Wellcome Trust and the Royal Society (grant number: 101272/Z/13/Z). The UK Medical Research Council and the Wellcome Trust (Grant ref: 102215/2/13/2; Grant ref: GR072043MA MRC G0701503) and the University of Bristol provide core support for ALSPAC. This publication is the work of the authors and will serve as guarantors for the contents of this paper.

## Bibliography

Angold A, Costello EJ, Messer SC, Pickles A, Winder F, Silver D. Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. International Journal of Methods in Psychiatric Research. 1995; 5:237–249.

Boyd A, Golding J, Macleod J, Lawlor D, Fraser A, Henderson J, Molloy L, Ness A, Ring S, Davey Smith G. Cohort Profile: The “Children of the 90s”--the index offspring of the Avon Longitudinal Study of Parents and Children. International journal of epidemiology. 2012; 42:111–127. [PubMed: 22507743]

Brown AS, Schaefer CA, Quesenberry CP, Liu L, Babulas VP, Susser ES. Maternal exposure to toxoplasmosis and risk of schizophrenia in adult offspring. The American journal of psychiatry. 2005; 162:767–73. [PubMed: 15800151]

Carruthers, VB., Suzuki, Y. Schizophrenia bulletin. Vol. 33. Oxford University Press; 2007. Effects of Toxoplasma gondii infection on the brain; p. 745-51.

Cetinkaya, Z., Yazar, S., Gecici, O., Namli, MN. Schizophrenia bulletin. Vol. 33. Oxford University Press; 2007. Anti-Toxoplasma gondii antibodies in patients with schizophrenia--preliminary findings in a Turkish sample; p. 789-91.

Cook AJ, Gilbert RE, Buffolano W, Zufferey J, Petersen E, Jenum PA, Foulon W, Semprini AE, Dunn DT. Sources of toxoplasma infection in pregnant women: European multicentre case-control study. European Research Network on Congenital Toxoplasmosis. BMJ (Clinical research ed.). 2000; 321:142–7.

Dorrington S, Zammit S, Asher L, Evans J, Heron J, Lewis G. Perinatal maternal life events and psychotic experiences in children at twelve years in a birth cohort study. Schizophrenia research. 2014; 152:158–63. [PubMed: 24275580]

Fisher, HL., Caspi, A., Poulton, R., Meier, MH., Houts, R., Harrington, H., Arseneault, L., Moffitt, TE. Psychological medicine. Vol. 43. Cambridge University Press; 2013. Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: a birth cohort study; p. 2077-86.

Gaskell EA, Smith JE, Pinney JW, Westhead DR, McConkey GA. A unique dual activity amino acid hydroxylase in Toxoplasma gondii. PloS one. 2009; 4:e4801. [PubMed: 19277211]

Horwood J, Salvi G, Thomas K, Duffy L, Gunnell D, Hollis C, Lewis G, Menezes P, Thompson A, Wolke D, Zammit S, et al. IQ and non-clinical psychotic symptoms in 12-year-olds: results from the ALSPAC birth cohort. The British journal of psychiatry : the journal of mental science. 2008; 193:185–91. [PubMed: 18757973]

Kannan G, Pletnikov MV. Toxoplasma gondii and cognitive deficits in schizophrenia: an animal model perspective. Schizophrenia bulletin. 2012; 38:1155–61. [PubMed: 22941742]

Kapperud G, Jenum PA, Stray-Pedersen B, Melby KK, Eskild A, Eng J. Risk Factors for Toxoplasma gondii Infection in Pregnancy: Results of a Prospective Case-Control Study in Norway. American Journal of Epidemiology. 1996; 144:405–412. [PubMed: 8712198]

Kelleher I, Keeley H, Corcoran P, Lynch F, Fitzpatrick C, Devlin N, Molloy C, Roddy S, Clarke MC, Harley M, Arseneault L, et al. Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies. The British journal of psychiatry : the journal of mental science. 2012; 201:26–32. [PubMed: 22500011]

Kirkbride JB, Errazuriz A, Croudace TJ, Morgan C, Jackson D, Boydell J, Murray RM, Jones PB. Incidence of schizophrenia and other psychoses in England, 1950-2009: a systematic review and meta-analyses. PloS one. 2012; 7:e31660. [PubMed: 22457710]

Kleinhaus K, Harlap S, Perrin MC, Manor O, Calderon-Margalit R, Friedlander Y, Malaspina D. Twin pregnancy and the risk of schizophrenia. Schizophrenia research. 2008; 105:197–200. [PubMed: 18722752]

Laurens KR, Hodgins S, Maughan B, Murray RM, Rutter ML, Taylor EA. Community screening for psychotic-like experiences and other putative antecedents of schizophrenia in children aged 9-12 years. Schizophrenia research. 2007; 90:130–46. [PubMed: 17207968]

Lichtenstein P, Yip BH, Björk C, Pawitan Y, Cannon TD, Sullivan PF, Hultman CM. Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study. The Lancet. 2009; 373:234–239.

Lopez-Castroman J, Gómez DD, Belloso JJC, Fernandez-Navarro P, Perez-Rodriguez MM, Villamor IB, Navarrete FF, Ginestar CM, Currier D, Torres MR, Navio-Acosta M, et al. Differences in maternal and paternal age between schizophrenia and other psychiatric disorders. Schizophrenia research. 2010; 116:184–90. [PubMed: 19945257]

McConkey GA, Martin HL, Bristow GC, Webster JP. Toxoplasma gondii infection and behaviour - location, location, location? The Journal of experimental biology. 2013; 216:113–9. [PubMed: 23225873]

Mortensen, PB., Nørgaard-Pedersen, B., Waltoft, BL., Sørensen, TL., Hougaard, D., Torrey, EF., Yolken, RH. Biological psychiatry. Vol. 61. Elsevier; 2007a. Toxoplasma gondii as a risk factor for early-onset schizophrenia: analysis of filter paper blood samples obtained at birth; p. 688-93.

Mortensen PB, Nørgaard-Pedersen B, Waltoft BL, Sørensen TL, Hougaard D, Yolken RH. Early infections of Toxoplasma gondii and the later development of schizophrenia. Schizophrenia bulletin. 2007b; 33:741–4. [PubMed: 17329231]

Mulvany, F., O'Callaghan, E., Takei, N., Byrne, M., Fearon, P., Larkin, C., Wiersma, D., Giel, R., De Jong, A., Slooff, C., Argyle, M., et al. BMJ (Clinical research ed.). Vol. 323. British Medical Journal Publishing Group; 2001. Effect of social class at birth on risk and presentation of schizophrenia: case-control study; p. 1398-401.

Onstad, S., Skre, I., Torgersen, S., Kringlen, E. Acta Psychiatrica Scandinavica. Vol. 85. Blackwell Publishing Ltd; 1992. Birthweight and obstetric complications in schizophrenic twins; p. 70-73.

Petersen, L., Mortensen, PB., Pedersen, CB. The American journal of psychiatry. Vol. 168. American Psychiatric Publishing Arlington; VA: 2011. Paternal age at birth of first child and risk of schizophrenia; p. 82-8.

Poulton R, Caspi A, Moffitt TE, Cannon M, Murray R, Harrington H. Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. Archives of general psychiatry. 2000; 57:1053–8. [PubMed: 11074871]

Prandovszky, E., Gaskell, E., Martin, H., Dubey, JP., Webster, JP., McConkey, GA. PloS one. Vol. 6. Public Library of Science; 2011. The neurotropic parasite Toxoplasma gondii increases dopamine metabolism; p. e23866

Royston P, White IR. Multiple Imputation by Chained Equations (MICE): Implementation in Stata. Journal of statistical software. 2011; 45

Shaffer D, Fisher P, Lucas CP, Dulcan MK, Schwab-Stone ME. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. Journal of the American Academy of Child and Adolescent Psychiatry. 2000; 39:28–38. [PubMed: 10638065]

Singh, SP., Winsper, C., Wolke, D., Bryson, A., Poulton, R., Caspi, A., Moffitt, TE., Cannon, M., Murray, R., Harrington, HL., Rossler, W., et al. Journal of the American Academy of Child and Adolescent Psychiatry. Vol. 53. Elsevier; 2014. School mobility and prospective pathways to psychotic-like symptoms in early adolescence: a prospective birth cohort study; p. 518-27.e1.

Sipos A, Rasmussen F, Harrison G, Tynelius P, Lewis G, Leon DA, Gunnell D. Paternal age and schizophrenia: a population based cohort study. BMJ (Clinical research ed.). 2004; 329:1070.

StataCorp. Stata Statistical Software: release 13. StataCorp LP; College Station, TX 13: 2013.

Sterne JAC, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, Wood AM, Carpenter JR. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ (Clinical research ed.). 2009; 338 b2393.

Sugden, K., Moffitt, TE., Pinto, L., Poulton, R., Williams, BS., Caspi, A. PloS one. Vol. 11. Public Library of Science; 2016. Is Toxoplasma Gondii Infection Related to Brain and Behavior Impairments in Humans? Evidence from a Population-Representative Birth Cohort; p. e0148435

Taylor MR, Lennon B, Holland CV, Cafferkey M. Community study of toxoplasma antibodies in urban and rural schoolchildren aged 4 to 18 years. Archives of disease in childhood. 1997; 77:406–9. [PubMed: 9487962]

Tenter AM, Heckeroth AR, Weiss LM. Toxoplasma gondii: from animals to humans. International journal for parasitology. 2000; 30:1217–58. [PubMed: 11113252]

Textor J, Hardt J, Knüppel S. DAGitty. Epidemiology. 2011; 22:745.

Textor, J., Liśkiewicz, M. Adjustment criteria in causal diagrams: an algorithmic perspective; Proceedings of the 27th Conference on Uncertainty in Artificial Intelligence; 2011. p. 681-688.

Torrey, EF., Bartko, JJ., Yolken, RH. Schizophrenia bulletin. Vol. 38. Oxford University Press; 2012. Toxoplasma gondii and other risk factors for schizophrenia: an update; p. 642-7.

Torrey EF, Rawlings R, Yolken RH. The antecedents of psychoses: a case-control study of selected risk factors. Schizophrenia research. 2000; 46:17–23. [PubMed: 11099881]

Torrey, EF., Simmons, W., Yolken, RH. Schizophrenia research. Vol. 165. Elsevier; 2015. Is childhood cat ownership a risk factor for schizophrenia later in life?; p. 1-2.

Torrey EF, Yolken RH. Could schizophrenia be a viral zoonosis transmitted from house cats? Schizophrenia bulletin. 1995; 21:167–71. [PubMed: 7631163]

Webster JP, Kaushik M, Bristow GC, McConkey GA. Toxoplasma gondii infection, from predation to schizophrenia: can animal behaviour help us understand human behaviour? The Journal of experimental biology. 2013; 216:99–112. [PubMed: 23225872]

Werner S, Malaspina D, Rabinowitz J. Socioeconomic Status at Birth Is Associated With Risk of Schizophrenia: Population-Based Multilevel Study. Schizophrenia Bulletin. 2007; 33:1373–1378. [PubMed: 17443013]

Westgarth C, Heron J, Ness AR, Bundred P, Gaskell RM, Coyne KP, German AJ, McCune S, Dawson S. Family pet ownership during childhood: findings from a UK birth cohort and implications for public health research. International journal of environmental research and public health. 2010; 7:3704–29. [PubMed: 21139856]

WHO. SCAN: Schedules for Clinical Assessment in Neuropsychiatry, Version 2.0. Geneva: 1994.

Wolf, PJ., Hamilton, FE. Schizophrenia research. Vol. 168. Elsevier; 2015. Flawed analyses undermine proposed relationship between childhood cat ownership and schizophrenia; p. 596

Yuksel P, Alpay N, Babur C, Bayar R, Saribas S, Karakose AR, Aksoy C, Asian M, Mehmetali S, Kilic S, Balcioglu I, et al. The role of latent toxoplasmosis in the aetiopathogenesis of schizophrenia -

The risk factor or an indication of a contact with cat? Folia Parasitologica. 2010; 57:121–128. [PubMed: 20608474]

Zammit S, Horwood J, Thompson A, Thomas K, Menezes P, Gunnell D, Hollis C, Wolke D, Lewis G, Harrison G. Investigating if psychosis-like symptoms (PLIKS) are associated with family history of schizophrenia or paternal age in the ALSPAC birth cohort. Schizophrenia research. 2008; 104:279–86. [PubMed: 18562177]

Zammit S, Thomas K, Thompson A, Horwood J, Menezes P, Gunnell D, Hollis C, Wolke D, Lewis G, Harrison G. Maternal tobacco, cannabis and alcohol use during pregnancy and risk of adolescent psychotic symptoms in offspring. The British journal of psychiatry : the journal of mental science. 2009; 195:294–300. [PubMed: 19794196]



Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts







**Table 1**

**Sample characteristics**

| *Variables* | **Psychotic experiences age 13** | | | | **Psychotic Experiences age 18** | | | |
|---|---|---|---|---|---|---|---|---|
| | **N (%) N = 6,705** | **None N (%) N= 5,929 (88.43%)** | **Suspected or Definite, N (%) N= 776 (11.57%)** | **P ($\chi^2$)** | **N (%) 4,676** | **None N (%) N = 4,306 (92.09%)** | **Suspected or Definite, N (%) N= 370 (7.91%)** | **P ($\chi^2$)** |
| **Cat Ownership in pregnancy (yes)** | 1,959 (31.66%) | 1,719 (31.35%) | 240 (34.09%) | 0.14 | 1,336 (31.17%) | 1,227 (31.06%) | 109 (32.44%) | 0.60 |
| **Cat Ownership at age 4 (yes)** | 1,620 (28.78%) | 1,407 (28.21%) | 213 (33.23%) | 0.008 | 1,017 (28.54%) | 1,019 (28.47%) | 88 (29.33%) | 0.75 |
| **Cat Ownership at age 10 (yes)** | 1,837 (31.83%) | 1,611 (31.40%) | 226 (35.26%) | 0.05 | 1,232 (31.44%) | 1,134 (31.22%) | 98 (34.15%) | 0.30 |
| **Dog Ownership in pregnancy (yes)** | 1,380 (22.30%) | 1,209 (22.05%) | 171 (24.29%) | 0.18 | 880 (20.53%) | 800 (20.25%) | 80 (23.81%) | 0.79 |
| **Gender (Female)** | 3,420 (51.03%) | 2,995 (50.54%) | 425 (54.77%) | 0.03 | 2,639 (56.45%) | 2,401 (55.77%) | 238 (64.32%) | 0.001 |
| **Ethnicity (Non-white)** | 239 (3.95%) | 209 (3.90%) | 30 (4.34%) | 0.58 | 180 (4.30%) | 159 (4.11%) | 21 (6.56%) | 0.04 |
| **Social class (manual)** | 833 (15.62%) | 728 (15.39%) | 105 (17.38%) | 0.20 | 568 (15.22%) | 507 (14.69%) | 61 (21.71%) | 0.002 |
| **Housing type (flat)** | 812 (13.19%) | 685 (12.55%) | 127 (18.14%) | <0.0001 | 562 (13.16%) | 495 (12.57%) | 67 (20.12%) | <0.0001 |
| **Marital Status (married)** | 5,046 (81.24%) | 4,523 (82.13%) | 523 (74.29%) | <0.0001 | 3,516 (81.63%) | 3,286 (82.73%) | 230 (68.66%) | <0.0001 |
| **Maternal education** | | | | | | | | |
| *Up to A levels* | 3,823 (62.28%) | 3,366 (61.97%) | 457 (64.73%) | 0.03 | 2,628 (61.79%) | 2,437 (62.17%) | 191 (57.36%) | <0.0001 |
| *Degree or higher* | 1,005 (16.37%) | 914 (16.83%) | 91 (12.89) | | 822 (19.33%) | 771 (19.67%) | 51 (15.32%) | |
| **Number of house moves** | | | | | | | | |
| *One to three* | 1,417 (29.23%) | 1,245 (29.00%) | 172 (31.39%) | 0.05 | 993 (29.24%) | 912 (29.02%) | 81 (32.02%) | 0.09 |
| *Four or more* | 629 (13.00%) | 545 (12.67%) | 84 (15.33%) | | 428 (12.60%) | 388 (12.34%) | 40 (15.81%) | |
| ***Crowding Index*** | | | | | | | | |
| *0.25%* | 1,892 (31.03%) | 1,685 (31.16%) | 207 (29.96%) | 0.02 | 1,278 (30.18%) | 1,179 (30.20%) | 99 (30.00%) | <0.0001 |
| *0.75%* | 929 (15.23%) | 814 (15.05%) | 115 (16.64%) | | 599 (14.15%) | 532 (13.63%) | 67 (20.30%) | |
| *1%* | 241 (3.95%) | 200 (3.70%) | 41 (5.93%) | | 161 (3.80%) | 138 (3.53%) | 23 (6.97%) | |
| | | **Mean SD** | **Mean SD** | | **Mean SD** | **Mean SD** | **Mean SD** | |
| ***Maternal Age*** | 29.18 (4.52) | 28.79 (4.51) | 28.19 (4.72) | 0.001 | 29.42 (4.57) | 29.03 (4.53) | 27.69 (5.23) | <0.0001 |
| ***Paternal Age*** | 30.71 (6.72) | 31.33 (5.46) | 31.14 (5.53) | 0.46 | 31.10 (6.76) | 31.59 (5.52) | 30.54 (5.40) | **0.005** |

## Table 2

**Univariate and multivariate Odds Ratios (OR) and 95% confidence intervals (CI) for the association between maternal cat ownership in pregnancy and between the ages of 8 months and 4 years of the child and psychotic symptoms (suspected or definite vs. none) at age 13 and 18 (N includes exposure and confounding variables imputed with multiple imputation with chained equations, N=100 imputations)**

| | Psychotic experiences age 13 (suspected or definite vs. none) N= 6,705 | |
|---|---|---|
| **Exposure variable** | **Crude OR (95%CI)** | **Adjusted OR (95%CI)** |
| **Cat Ownership in pregnancy** | | |
| *No* | Ref | Ref |
| *Yes* | 1.15 (0.97; 1.35) | 1.15 (0.97; 1.36) |
| **Cat Ownership at age 4** | | |
| *No* | Ref | Ref |
| *Yes* | 1.23 (1.04; 1.46) ** | 1.18 (0.94; 1.48) |
| **Cat Ownership at age 10** | | |
| *No* | Ref | Ref |
| *Yes* | 1.19 (1.00; 1.41) ** | 1.12 (0.92; 1.36) |
| | **Psychotic experiences age 18 (suspected or definite vs. none) N= 4,676** | |
| **Exposure variable** | **Crude OR (95%CI)** | **Adjustment 1[a] OR (95%CI)** |
| **Cat Ownership in pregnancy** | | |
| *No* | Ref | Ref |
| *Yes* | 1.08 (0.86; 1.35) | 1.08 (0.85; 1.37) |
| **Cat Ownership at age 4** | | |
| *No* | Ref | Ref |
| *Yes* | 1.11 (0.88; 1.40) | 0.97 (0.71; 1.31) |
| **Cat Ownership at age 10** | | |
| *No* | Ref | Ref |
| *Yes* | 1.15 (0.89; 1.48) | 1.08 (0.82; 1.45) |

** p≤0.05

[a] = Model of cat ownership in pregnancy is adjusted for child ethnicity; maternal education, marital status, and social class; paternal age; number of house moves until age 4, type of house, crowding index. Models of cat ownership in at age four and ten years are further adjusted for cat ownership in pregnancy.