**Tobacco smoking is associated with psychotic experiences in the general population of South London**

**Authors**
Vishal Bhavsar[1]
Sameer Jauhar[1]
Robin M Murray[1]
Matthew Hotopf[2, 3]
Stephani L Hatch[2]
Ann McNeill [4]
Jane Boydell[5]
James H MacCabe[1, 3]

**Affiliations:**
1. King's College London, Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience
2. King's College London, Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience
3. South London and Maudsley NHS Foundation Trust, London
4. King's College, London, National Addictions Centre, Institute of Psychiatry, Psychology and Neuroscience and UK Centre for Tobacco and Alcohol Studies
5.Cornwall Partnership Foundation NHS Trust, Cornwall.

**WORD COUNT, EXCLUDING ABSTRACT, REFERENCES, TABLES/FIGURES, APPENDICES AND SUPPLEMENTARY MATERIAL: 3110**

**Abstract**
**Background**: The association between cigarette smoking and psychosis remains unexplained, but could relate to causal effects in both directions, confounding by socioeconomic factors such as ethnicity, or use of other substances, including cannabis. Few studies have evaluated the association between cigarettes and psychotic experiences (PEs) in diverse, inner-city populations, or relationships with number of cigarettes consumed.
**Methods**: We assessed associations and dose-response relationships between cigarette smoking and PEs in a cross-sectional survey of household residents (n=1680) in South East London, using logistic regression to adjust for cannabis use, other illicit substances, and socioeconomic factors, including ethnicity.
**Results**: We found association between any PEs and daily cigarette smoking, which remained following adjustment for age, gender, ethnicity, cannabis and use of illicit stimulant drugs (fully adjusted OR: 1.47; 95%CI: 1.01, 2.15). Fully-adjusted estimates for the association, and with number of PEs, increased with number of cigarettes smoked daily, implying a dose-response effect (P=0.001 and <0.001, respectively). Odds of reporting any PEs in ex-smokers were similar to never-smokers.
**Conclusions**: In this diverse epidemiological sample, association between smoking and PEs was not explained by confounders such as cannabis or illicit drugs. Daily cigarette consumption showed a dose-response relationship with the odds of reporting PEs, and of reporting a greater number of PEs. There was no difference in odds of reporting PEs between ex-smokers and never-smokers, raising the possibility that the increase in PEs associated with smoking may be reversible.

## Introduction

The search for environmental causes for psychosis(Dean and Murray, 2005) in the last three decades has included factors that can be experienced after childhood, for example migration and the use of substances(Morgan et al., 2010). Investigations into the possible causal effects of cannabis have featured prominently in research into substances, with a meta-analysis estimating that cannabis users experienced nearly three times the odds of having psychosis compared to non-users (OR: 2.93, 95%CI: 2.36,3.64,(Semple et al., 2005). More recently, other drugs have been examined, most notably tobacco.

There is a strong positive association between smoking cigarettes and psychotic disorders(de Leon and Diaz, 2005). The most recent meta-analysis of smoking as a risk factor for psychosis estimated the odds ratio for daily smoking to be around 3, based on eleven case-control studies, and the relative risk, from five prospective studies, to be approximately 2(Gurillo et al., 2015). The positive association between tobacco smoking and psychotic illnesses has a number of candidate explanations. These include:

a. self-medication(Kumari and Postma, 2005), for example of psychiatric symptoms(Smith et al., 2002), cognitive deficits(Barr et al., 2008, Sacco et al., 2005, George et al., 2002), or adverse effects of psychiatric drugs(Goff et al., 1992),
b. shared genetic liability to both smoking and psychoses(Lyons et al., 2002, Smith et al., 2008, Chen et al., 2016),
c. a causal effect of smoking on schizophrenia(Kendler et al., 2015, Weiser et al., 2004),
d. a reverse causal effect- mental health problems could result in people who smoke being less likely to quit, for example because of more severe nicotine dependence or more limited access to smoking cessation treatment(Szatkowski and McNeill, 2014), and
e. confounding by other drug use – people who smoke are more likely to take other drugs, including cannabis and stimulants(Morral et al., 2002, Regier et al., 1990), which may be causally associated with psychosis(Large et al., 2011, Semple et al., 2005).

In a recent prospective study, Kendler and colleagues found that smoking was associated with later schizophrenia in two Swedish cohorts, after accounting in the design for shared familial factors between people who developed schizophrenia and those who did not(Kendler et al., 2015). Heavy smokers in discordant monozygotic twin pairs were around 1.7 times more likely to develop psychosis compared to the non-smoking twin, suggesting that genetic factors do not completely explain the relationship between smoking and later psychosis. Strengths of association were not affected by specifying different buffer periods between smoking assessment and first diagnosis, implying that the association did not arise as a result of people smoking as part of the psychosis prodrome.

It is increasingly argued that psychotic disorders represent the extreme end of a phenomenological continuum of psychotic experiences (PEs) which extend into the general, non-clinical population(Johns et al., 2004, Johns and Van Os, 2001, Linscott and van Os, 2013). However, although observational data from a number of sources have indicated high smoking prevalence in people with mental disorders (Royal College of Psychiatrists (RCPSYCH, 2013 ), few studies have addressed the question of whether tobacco smoking is associated with PEs in the general population(Van Gastel et al., 2013, Gage et al., 2014). Furthermore, the extent to which any association is explained by confounding by cannabis or socioeconomic factors is unclear.

This study examined the association between cigarette smoking and PEs in a representative population-based sample of South London.

Our objectives were to:

1. Estimate the association between smoking and PEs and between smoking and the number of PEs reported, taking into account possible confounding by cannabis, stimulant use and ethnicity, and
2. Test for a linear trend in the odds of reporting PEs with quantity of cigarettes smoked per day.

**Methods**

*Sample:*
The South East London Community Health study (SELCoH(Hatch et al., 2011) is a representative household survey of South East London residents collected in 2008-2010. The analytic sample consisted of 1698 people, residing in 1075 households, collected through random sampling of a postcode address file, who were interviewed by lay researchers. Respondents were between the ages of 16 and 90 years of age. Of 2359 people eligible within participating households, 1698 (71.9%) participated.

*Psychotic experiences:*
The rating scale used for the assessment of PEs was the Psychosis Screening Questionnaire (PSQ(Bebbington and Nayani, 1995). The PSQ is a self-report questionnaire designed to be administered by lay interviewers for use in large-scale epidemiological studies, for the purpose of screening respondents for possible psychotic disorder. It is a five-item questionnaire that assesses different positive psychotic symptom domains experienced in the previous year. These comprise: hypomania, strange experiences, persecutory experiences, auditory hallucinations, and thought interferences. Each domain contains an initial "probe" item, which is followed by secondary questions. Because the present study was focused on non-affective psychosis, responses to the hypomania item were not examined. Endorsement of PEs was defined as positive response to items in the four remaining domains. This approach was consistent with a previous analysis of PEs originating from these data(Morgan et al., 2014). Information on the number of domains endorsed was also available. The PSQ displays good correspondence with psychosis items on the Schedules for Clinical Assessment in Neuropsychiatry(Bebbington and Nayani, 1995) and has seen frequent use in population studies(e.g.(Bebbington et al., 2004, Johns et al., 2004, Johns et al., 2002)

*Sociodemographic and clinical measures*
Data on age, gender, employment status (employed, unemployed, student, other), ethnicity (White, Black Caribbean, Black African, Asian, and other), marital status (single, married/cohabiting, divorced/separated, and widowed), social class (measured by the NS-SEC), a composite score of general cognitive ability (details available in Mollon et al. (2016), and highest educational attainment (no qualifications, GCSE, A level, and degree level or above) were available. The presence of symptoms of a common mental disorder in the previous two weeks was defined based on responses to the CISR (Clinical Interview Schedule, Revised(Lewis and Pelosi, 1990)), with a cut-off score of twelve(Lewis et al., 1992).

*Measurement of cigarette smoking:*
Information on cigarette smoking analysed in this study was collected from SELCoH participants at four levels: the category of "never smoked" was based on answering "no" to the question: "have you ever smoked a cigarette?". Ex-smokers were defined as those answering "yes" to the question: "have you ever smoked a cigarette?" and then answering "no" to the question: "do you smoke cigarettes at all nowadays?". Sporadic smoking was based on answering "yes" to the question: "have you ever smoked a cigarette?", then "yes" to the question: "do you smoke cigarettes at all nowadays?", and then reporting a zero daily cigarette intake when asked: "about how many cigarettes a day do you usually smoke?". Finally, daily smokers were defined by answering positively to both prior questions and providing an estimate of the number of daily cigarettes smoked. All participants defined as daily smokers were therefore current smokers.

*Ascertainment of cannabis use:*

Participants were asked about cannabis use frequency and categorised into the following groups: never used, use less frequently than once a week, use more than once a week but less than daily, and use daily.

*Evaluation of stimulant substance use:*
Participants reported use of amphetamines, ecstasy, cocaine and crack use; all were combined into a single variable with three levels - never used, use but not in the previous year, and use in the previous year. All models which adjusted for substance misuse included this three level variable.

*Analysis:*
All analyses were carried out in STATA 14(Stata, 2014) and took account of non-response weights and clustering of responses by household. Inverse probability weights(Pickles et al., 1995) were calculated from logistic regression models for non-response of an eligible individual within households. Predictor variables for non-response were selected for inclusion in the final weights model based on strength of statistical evidence (p-values of less than 0.05) and whether the selected weighting scheme reproduced the means and prevalences of participants with complete data. The final prediction model contained effects of age and gender. Categorical descriptions of the sample by PEs were inspected. Univariate associations between PE status and cigarette smoking, stimulants, and sociodemographic variables (age, gender, and ethnicity) were evaluated and presented. Multivariate models were used to assess and account for confounding. Age and gender were included in all models. Covariates whose inclusion in the model did not deviate the association between PEs and daily cigarette smoking by more than 10% of the unadjusted odds ratio were discarded(Greenland et al., 2016). This left age, gender, and ethnic group as covariates in modelling, alongside stimulant and cannabis use as potential confounders of primary interest. In particular, neither the inclusion of general cognitive ability, marital status, employment status, social class, nor educational attainment altered estimates sufficient for their inclusion. Having identified evidence of strong negative confounding by ethnicity, we explored the association between ethnic group and smoking, presented in table 7 of the supplementary material to this paper. Also presented as supplementary material are descriptive data on the overlap between cigarette smoking and use of cannabis, and of stimulants. Modification of the association between current smoking and reporting any PEs by age, cannabis use and common mental disorder was tested by fitting multiplicative interaction terms for smoking status by age, cannabis use, and common mental disorder in fully adjusted models. Ordinal logistic regressions were used to assess the association between smoking status and number of PEs (range from 0-4). Finally, we examined the possibility of a dose-response relationship by assessing linear trends in the association between the number of cigarettes smoked and a. the odds of reporting any PEs (from logistic regression models), and b. the odds of reporting one further PE (from ordinal logistic regression models).

## Results

After excluding participants with missing data on the modelled variables, 1680 survey participants remained for analysis. Sociodemographic and substance use associations with PEs are shown in table 1. PEs were more frequently reported by younger participants, and those with Black Caribbean and Black African ethnic status. Cannabis, ecstasy, cocaine and other stimulants were associated with PEs. The estimate for crack cocaine, whilst indicating a possible strong association, was imprecise and not statistically significant, as its use was seldom reported. Cannabis use frequency was strongly associated with use of stimulant drugs (see supplementary material, table 6). There was an association between PEs and daily, but not sporadic or past, cigarette smoking. Multivariate models for the odds of reporting any PEs are show in table 2: when sociodemographic variables were included in the model, the estimate increased, indicating positive confounding by age, gender, and ethnicity. Further adjustment for cannabis frequency attenuated the odds ratio for daily smoking on PEs. Finally, adjustment for stimulant use (recent and in the lifetime) modestly reduced the association. No statistical evidence was found for differences in the association between current smoking and the odds of reporting PE within different age groups, or at different levels of cannabis use.

We found strong statistical evidence for a dose-response relationship between the number of cigarettes smoked and the odds of reporting any PEs, and the reporting of a greater number of PEs, in adjusted models. On average an increase in daily cigarette consumption from 0 to 1-9, from 1-9 to 10-19, or 10-19 to 20 or more, was accompanied by a by a 1.04 increase in the overall relative odds of reporting any PEs (95%CI: 1.02,1.07; table 3) and a 1.58 fold increase in the relative odds of reporting one further PE (95%CI: 1.32, 1.90; table 3).

Daily smoking was associated not only with an increased odds of reporting PEs, but also with increasing number of PEs, although this estimate lost precision after adjusting for stimulant use (fully adjusted OR: 1.55, 95%CI: 0.98, 2.47, table 4). The most common PE was strange experiences (6.05%), followed by auditory hallucinations (3.87%), then persecutory experiences (3.27%), with thought interferences the least common PE (1.32%). Individual types of PE were associated with daily smoking, with precise estimates for strange experiences, but not for the other symptoms. In fully adjusted models, associations remained for each symptom, but lost precision. On account of the association between PEs and other symptoms of mental disorder, we estimated associations of PEs with smoking pattern by common mental disorder, shown in table 5 of the supplementary material. No statistical evidence was found for variation in effect estimates by common mental disorder, although this test lacked power. Because of the association between ethnicity and PEs, and the attenuation in estimates observed when it was included in regression models, we described the association between ethnicity and smoking, reported in table 7 (included in supplementary material): all non-White ethnic groups had lower proportions of reported daily, ex-, and sporadic smoking compared to the White reference group ($p<0.001$).

## Discussion

*Summary of findings*
We found evidence of a cross-sectional association between daily cigarette smoking, but not ex-smoking, and PEs in a sample of household residents in South East London. The association was not explained completely by cannabis use frequency, or by use of stimulant drugs, or by ethnicity (ethnicity was strongly associated with daily smoking, see supplementary material, table 7). There was an increasing strength of association observed by number of cigarettes smoked, and increased cigarette consumption predicted a greater number of PEs. We did not find statistical evidence for interaction of smoking with age, cannabis use, or with symptoms of common mental disorder.

*Previous literature*
Smoking is a crucial, potent, and modifiable cause of morbidity and mortality in the UK(Matcham et al., 2017). Although the number of people who smoke in the UK is falling, (Action on Smoking and Health( 2015)), this decline is not reflected in people with mental illness (National Centre for Social Research, (2010)); and data from the Health Survey for England suggests that smoking may be declining more slowly in people with mental health problems compared to those without(Szatkowski and McNeill, 2014). Therefore, identifying the mechanisms by which smoking and mental illness are associated could be beneficial for public health.

Our findings, that PEs and daily smoking are associated, are consistent with a small body of literature suggesting that smoking is more common in people with sub-clinical PEs than the rest of the general population. Firstly, van Gastel et al(2013) reported an analysis of an internet survey, finding that the cross-sectional association between scores on the Community Assessment of PEs and daily smoking for the past month remained apparent despite accounting for cannabis use and for a group of other confounders. Secondly, smokers were 1.3 times more likely to report PEs in the World Health Surveys compared to non-smokers, after adjustments, suggesting the association is consistent across national settings(Koyanagi et al., 2016). Thirdly, Wiles et al(2006) reported association between smoking and PEs in the 2007 UK Adult Psychiatric Morbidity Surveys, but found that the crude association was strongly attenuated by adjustment for cannabis, general cognitive ability and marital status. Fourthly, Saha et al found that daily smoking was associated with reporting delusion-like experiences in an Australian household survey(2011), after adjusting for a broad range of confounders. Fifth, in an analysis of prospective data from the Avon Longitudinal Study of Parents and Children, Gage et al(2014) reported that smoking at aged 16 was predictive of PEs at 18, after accounting for cannabis use frequency and a range of early and mid-life confounders. Overall, few previous studies have assessed dose-response relationship with number of cigarettes smoked or by number of PEs reported, and few studies have adjusted for cannabis use in detail, for example, by including cannabis use frequency in statistical models.

*How our results fit in*
Our results, from a highly socioeconomically and ethnically diverse sample, are consistent with the previous literature suggesting the cross-sectional association between cigarette smoking and PEs is not fully explained by cannabis use, the use of stimulant drugs, or confounding by demographic or socioeconomic status, particularly by ethnic group. Furthermore, we present evidence that the relationship between odds of reporting any PEs, and a greater number of PEs is related to the number of cigarettes smoked per day. Finally, we extend previous literature by presenting evidence that daily smoking predicts the reporting of more PEs on a continuous scale. We also found no evidence of association between PEs and being an ex-smoker, implying that our analysis did not suffer from confounding by non-time-varying characteristics, such as unadjusted sociodemographic factors. The finding of no association between PEs and ex-smoking is consistent with other literature suggesting that

mental health improves following smoking cessation(Taylor et al., 2014) raising the possibility that the increase in PEs associated with smoking may be reversible. Our results are also consistent with smoking being a more persistent behaviour in people with PEs compared to those without, and fit with some evidence that people with psychosis who smoke tend to have more severe positive symptoms and more limited social adjustment(Barnes et al., 2006, Krishnadas et al., 2012).

*Strengths and limitations*
This was a cross sectional study and these associations could be explained by smoking occurring after PEs. Measurement of smoking, PEs, and cannabis use were by self-report in the same survey, and some way of confirming this information in independent data would have improved the validity of the study. Strong collinearity between exposure and a confounder limits the ability of regression methods to correctly adjust for confounding - in this study, the close overlap between cannabis use and cigarette smoking(Amos et al., 2004) might not have fully allowed for the identification of separate effects for these two factors(Greenland et al., 2016, Gage et al., 2014). There were no data on the persistence or timeframe of PEs, further limiting inference. Although we were able to adjust estimates for stimulant use, this was in the form of an aggregated variable across four different stimulants, leaving open the possibility of residual confounding by the use of individual stimulants. However, despite these limitations to the data, the study did allow the assessment of this association in an urban, diverse population with relatively high levels of cannabis and stimulant use, in contrast to previous studies. The generalizability of our results to the rest of the UK population could be limited. However, a previous study based on this data suggested similarity in the distributions of age, gender, economic activity and ethnicity to the overall English population recorded in the UK Census(Hatch et al., 2011). We found evidence that ethnic group was strongly related to the probability of daily smoking, in accordance with other studies(Best et al., 2001, McCambridge and Strang, 2005, Wanigaratne et al., 2003), and adjusted for it as a possible confounder (see supplementary material, table 7).

*Conclusions*
The association between PEs and smoking is apparent in a highly diverse population with relatively prevalent use of cannabis and stimulant drugs. The linear relationship between cigarette consumption and odds of reporting PEs requires urgent explanation in longitudinal studies and diverse populations.

**Acknowledgement**

VB is supported by a Wellcome Clinical Research Training Fellowship (101681/Z/13/Z). This paper represents independent research funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. We acknowledge the assistance of Josephine Mollon and Shirlee MacCrimmon in the preparation of this paper.

**References**

AMOS, A., WILTSHIRE, S., BOSTOCK, Y., HAW, S. & MCNEILL, A. 2004. 'You can't go without a fag . . . you need it for your hash'—a qualitative exploration of smoking, cannabis and young people. *Addiction,* 99**,** 77-81.

ASH 2015. ACTION ON SMOKING AND HEALTH. Smoking statistics: Who smokes and how much?. . Action on Smoking and Health.

BARNES, M., LAWFORD, B. R., BURTON, S. C., HESLOP, K. R., NOBLE, E. P., HAUSDORF, K. & YOUNG, R. M. 2006. Smoking and schizophrenia: is symptom profile related to smoking and which antipsychotic medication is of benefit in reducing cigarette use? *Australian and New Zealand Journal of Psychiatry,* 40**,** 575-580.

BARR, R. S., CULHANE, M. A., JUBELT, L. E., MUFTI, R. S., DYER, M. A., WEISS, A. P., DECKERSBACH, T., KELLY, J. F., FREUDENREICH, O., GOFF, D. C. & EVINS, A. E. 2008. The effects of transdermal nicotine on cognition in nonsmokers with schizophrenia and nonpsychiatric controls. *Neuropsychopharmacology,* 33**,** 480-490.

BEBBINGTON, P. & NAYANI, T. 1995. The psychosis screening questionnaire. *Int J Methods Psychiatr Res,* 5**,** 11-19.

BEBBINGTON, P. E., BHUGRA, D., BRUGHA, T., SINGLETON, N., FARRELL, M., JENKINS, R., LEWIS, G. & MELTZER, H. 2004. Psychosis, victimisation and childhood disadvantage: Evidence from the second British National Survey of Psychiatric Morbidity. *British Journal of Psychiatry,* 185**,** 220-226.

BEST, D., RAWAF, S., ROWLEY, J., FLOYD, K., MANNING, V. & STRANG, J. 2001. Ethnic and Gender Differences in Drinking and Smoking among London Adolescents. *Ethnicity & Health,* 6**,** 51-57.

CHEN, J., BACANU, S.-A., YU, H., ZHAO, Z., JIA, P., KENDLER, K. S., KRANZLER, H. R., GELERNTER, J., FARRER, L., MINICA, C., POOL, R., MILANESCHI, Y., BOOMSMA, D. I., PENNINX, B. W. J. H., TYNDALE, R. F., WARE, J. J., VINK, J. M., KAPRIO, J., MUNAFÒ, M. & CHEN, X. 2016. Genetic Relationship between Schizophrenia and Nicotine Dependence. *Scientific Reports,* 6**,** 25671.

DE LEON, J. & DIAZ, F. J. 2005. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. *Schizophrenia research,* 76**,** 135-157.

DEAN, K. & MURRAY, R. M. 2005. Environmental risk factors for psychosis. *Dialogues in Clinical Neuroscience,* 7**,** 69-80.

GAGE, S., HICKMAN, M., HERON, J., MUNAFÒ, M., LEWIS, G., MACLEOD, J. & ZAMMIT, S. 2014. Associations of cannabis and cigarette use with psychotic experiences at age 18: findings from the Avon Longitudinal Study of Parents and Children. *Psychological medicine,* 44**,** 3435-3444.

GEORGE, T. P., VESSICCHIO, J. C., TERMINE, A., SAHADY, D. M., HEAD, C. A., PEPPER, W. T., KOSTEN, T. R. & WEXLER, B. E. 2002. Effects of smoking abstinence on visuospatial working memory function in schizophrenia. *Neuropsychopharmacology,* 26**,** 75-85.

GOFF, D. C., HENDERSON, D. C. & AMICO, E. 1992. Cigarette smoking in schizophrenia: relationship to psychopathology and medication side effects. *Am J Psychiatry,* 149**,** 1189-94.

GREENLAND, S., DANIEL, R. & PEARCE, N. 2016. Outcome modelling strategies in epidemiology: traditional methods and basic alternatives. *International Journal of Epidemiology,* 45**,** 565-575.

GURILLO, P., JAUHAR, S., MURRAY, R. M. & MACCABE, J. H. 2015. Does tobacco use cause psychosis? Systematic review and meta-analysis. *The Lancet Psychiatry,* 2**,** 718-725.

HATCH, S. L., FRISSA, S., VERDECCHIA, M., STEWART, R., FEAR, N. T., REICHENBERG, A., MORGAN, C., KANKULU, B., CLARK, J. & GAZARD, B. 2011. Identifying socio-demographic and socioeconomic determinants of health inequalities in a diverse London community: the South East London Community Health (SELCoH) study. *BMC public health,* 11**,** 861.

JOHNS, L. C., CANNON, M., SINGLETON, N., MURRAY, R. M., FARRELL, M., BRUGHA, T., BEBBINGTON, P., JENKINS, R. & MELTZER, H. 2004. Prevalence and correlates of self-reported psychotic symptoms in the British population. *British Journal of Psychiatry,* 185**,** 298-305.

JOHNS, L. C., NAZROO, J. Y., BEBBINGTON, P. & KUIPERS, E. 2002. Occurrence of hallucinatory experiences in a community sample and ethnic variations. *The British Journal of Psychiatry,* 180**,** 174-178.

JOHNS, L. C. & VAN OS, J. 2001. The continuity of psychotic experiences in the general population. *Clinical Psychology Review,* 21**,** 1125-1141.

KENDLER, K. S., LÖNN, S. L., SUNDQUIST, J. & SUNDQUIST, K. 2015. Smoking and schizophrenia in population cohorts of Swedish women and men: a prospective co-relative control study. *American Journal of Psychiatry,* 172**,** 1092-1100.

KOYANAGI, A., STICKLEY, A. & HARO, J. M. 2016. Psychotic symptoms and smoking in 44 countries. *Acta Psychiatrica Scandinavica,* 133**,** 497-505.

KRISHNADAS, R., JAUHAR, S., TELFER, S., SHIVASHANKAR, S. & MCCREADIE, R. G. 2012. Nicotine dependence and illness severity in schizophrenia. *The British Journal of Psychiatry,* 201**,** 306-312.

KUMARI, V. & POSTMA, P. 2005. Nicotine use in schizophrenia: the self medication hypotheses. *Neuroscience & Biobehavioral Reviews,* 29**,** 1021-1034.

LARGE, M., SHARMA, S., COMPTON, M. T., SLADE, T. & NIELSSEN, O. 2011. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. *Archives of general psychiatry,* 68**,** 555-561.

LEWIS, G. & PELOSI, A. 1990. Manual of the revised clinical interview schedule (CIS-R). *Institute of Psychiatry, London*.

LEWIS, G., PELOSI, A. J., ARAYA, R. & DUNN, G. 1992. Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. *Psychological medicine,* 22**,** 465-486.

LINSCOTT, R. J. & VAN OS, J. 2013. An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychol Med,* 43**,** 1133-49.

LYONS, M. J., BAR, J. L., KREMEN, W. S., TOOMEY, R., EISEN, S. A., GOLDBERG, J., FARAONE, S. V. & TSUANG, M. 2002. Nicotine and familial vulnerability to schizophrenia: a discordant twin study. *Journal of abnormal psychology,* 111**,** 687.

MATCHAM, F., CARROLL, A., CHUNG, N., CRAWFORD, V., GALLOWAY, J., HAMES, A., JACKSON, K., JACOBSON, C., MANAWADU, D., MCCRACKEN, L., MOXHAM, J., RAYNER, L., ROBSON, D., SIMPSON, A., WILSON, N. & HOTOPF, M. 2017. Smoking and common mental disorders in patients with chronic conditions: An analysis of data collected via a web-based screening system. *General Hospital Psychiatry,* 45**,** 12-18.

MCCAMBRIDGE, J. & STRANG, J. 2005. Can it really be this black and white? An analysis of the relative importance of ethnic group and other sociodemographic factors to patterns of drug use and related risk among young Londoners. *Drugs: Education, Prevention and Policy,* 12**,** 149-159.

MOLLON, J., DAVID, A. S., MORGAN, C., FRISSA, S., GLAHN, D., PILECKA, I., HATCH, S. L., HOTOPF, M. & REICHENBERG, A. 2016. Psychotic experiences and neuropsychological functioning in a population-based sample. *JAMA psychiatry,* 73**,** 129-138.

MORGAN, C., CHARALAMBIDES, M., HUTCHINSON, G. & MURRAY, R. M. 2010. Migration, ethnicity, and psychosis: toward a sociodevelopmental model. *Schizophrenia bulletin,* 36**,** 655-664.

MORGAN, C., REININGHAUS, U., REICHENBERG, A., FRISSA, S., HOTOPF, M. & HATCH, S. L. 2014. Adversity, cannabis use and psychotic experiences: evidence of cumulative and synergistic effects. *The British Journal of Psychiatry,* 204**,** 346-353.

MORRAL, A. R., MCCAFFREY, D. F. & PADDOCK, S. M. 2002. Reassessing the marijuana gateway effect. *Addiction,* 97**,** 1493-1504.

NATCEN 2010. Cigarette smoking and mental health in England:data from the Adult Psychiatric Morbidity Survey 2007. 2010.

PICKLES, A., DUNN, G. & VÁZQUEZ-BARQUERO, J. L. 1995. Screening for stratification in two-phase ('two-stage') epidemiological surveys. *Statistical Methods in Medical Research,* 4**,** 73-89.

RCPSYCH 2013 ROYAL COLLEGE OF PSYCHIATRISTS. Smoking and mental health.Royal College of Psychiatrists Council Report CR178. London: Royal College of Psychiatrists.

REGIER, D. A., FARMER, M. E., RAE, D. S., LOCKE, B. Z., KEITH, S. J., JUDD, L. L. & GOODWIN, F. K. 1990. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. *Jama,* 264**,** 2511-2518.

SACCO, K. A., TERMINE, A., SEYAL, A., DUDAS, M. M., VESSICCHIO, J. C., KRISHNAN-SARIN, S., JATLOW, P. I., WEXLER, B. E. & GEORGE, T. P. 2005. Effects of cigarette smoking on spatial working memory and attentional deficits in schizophrenia involvement of nicotinic receptor mechanisms. *Archives of General Psychiatry,* 62**,** 649-659.

SAHA, S., SCOTT, J. G., VARGHESE, D., DEGENHARDT, L., SLADE, T. & MCGRATH, J. J. 2011. The association between delusional-like experiences, and tobacco, alcohol or cannabis use: a nationwide population-based survey. *BMC psychiatry,* 11**,** 1.

SEMPLE, D. M., MCINTOSH, A. M. & LAWRIE, S. M. 2005. Cannabis as a risk factor for psychosis: systematic review. *Journal of Psychopharmacology,* 19**,** 187-194.

SMITH, M. J., BARCH, D. M., WOLF, T. J., MAMAH, D. & CSERNANSKY, J. G. 2008. Elevated rates of substance use disorders in non-psychotic siblings of individuals with schizophrenia. *Schizophrenia research,* 106**,** 294-299.

SMITH, R. C., SINGH, A., INFANTE, M., KHANDAT, A. & KLOOS, A. 2002. Effects of cigarette smoking and nicotine nasal spray on psychiatric symptoms and cognition in schizophrenia. *Neuropsychopharmacology,* 27**,** 479-497.

STATA, C. 2014. Stata Statistical Software: Release 14. *Special Edition*.

SZATKOWSKI, L. & MCNEILL, A. 2014. Diverging Trends in Smoking Behaviors According to Mental Health Status. *Nicotine & Tobacco Research,* 17**,** 356-360.

TAYLOR, G., MCNEILL, A., GIRLING, A., FARLEY, A., LINDSON-HAWLEY, N. & AVEYARD, P. 2014. Change in mental health after smoking cessation: systematic review and meta-analysis. *Bmj,* 348**,** g1151.

VAN GASTEL, W., MACCABE, J., SCHUBART, C., VREEKER, A., TEMPELAAR, W., KAHN, R. & BOKS, M. 2013. Cigarette smoking and cannabis use are equally strongly associated with psychotic-like experiences: a cross-sectional study in 1929 young adults. *Psychological medicine,* 43**,** 2393-2401.

WANIGARATNE, S., DAR, K., ABDULRAHIM, D. & STRANG, J. 2003. Ethnicity and Drug Use: exploring the nature of particular relationships among diverse populations in the United Kingdom. *Drugs: Education, Prevention and Policy,* 10**,** 39-55.

WEISER, M., REICHENBERG, A., GROTTO, I., YASVITZKY, R., RABINOWITZ, J., LUBIN, G., NAHON, D., KNOBLER, H. Y. & DAVIDSON, M. 2004. Higher rates of cigarette smoking in male adolescents before the onset of schizophrenia: a historical-prospective cohort study. *American Journal of Psychiatry*.

WILES, N. J., ZAMMIT, S., BEBBINGTON, P., SINGLETON, N., MELTZER, H. & LEWIS, G. 2006. Self-reported psychotic symptoms in the general population. *Results from the longitudinal study of the British National Psychiatric Morbidity Survey,* 188**,** 519-526.

**Table 1. Counts and survey-weighted univariate associations between PEs and each variable used in this study, based on the analytic sample of 1680.**

| | Number in each category | Number reporting PEs in category (%) | PE Odds Ratio | 95% CI |
|---|---|---|---|---|
| **Age** | | | | |
| **16-24** | 356 | 85(23.88) | Reference | |
| **25-34** | 401 | 69(17.21) | 0.69 | 0.48, 0.99 |
| **35-44** | 334 | 64(19.16) | 0.76 | 0.52, 1.11 |
| **45-54** | 259 | 57(22.01) | 0.91 | 0.62, 1.34 |
| **55-64** | 157 | 25(15.92) | 0.61 | 0.37, 1.00 |
| **65+** | 173 | 19(10.40) | 0.37 | 0.21, 0.66 |
| **Gender** | | | | |
| **Male** | 730 | 147(20.14) | Reference | |
| **Female** | 950 | 171(18.00) | 0.86 | 0.68, 1.09 |
| **Ethnicity** | | | | |
| **White** | 1045 | 170(16.27) | Reference | |
| **Black Caribbean** | 143 | 45(31.47) | 2.28 | 1.51, 3.47 |
| **Black African** | 229 | 51(22.27) | 1.46 | 1.01, 2.10 |
| **Asian** | 62 | 8(12.90) | 0.71 | 0.35, 1.44 |
| **Other** | 201 | 44(21.89) | 1.43 | 0.98, 2.06 |
| **Smoking pattern** | | | | |
| **Never smoker** | 513 | 84(16.37) | Reference | |
| **Ex-smoker** | 448 | 77(17.19) | 1.06 | 0.75, 1.49 |
| **Sporadic smoker** | 297 | 47(15.82) | 0.97 | 0.65, 1.44 |
| **Daily smoker** | 422 | 110(26.07) | 1.76 | 1.27, 2.42 |
| **Crack use** | | | | |
| **Never** | 1642 | 300(18.27) | Reference | |
| **Yes, not in the last year** | 34 | 16(47.06) | 3.82 | 1.93, 7.61 |
| **Yes, in the last year** | 4 | 2(50.00) | 4.04 | 0.56, 28.91 |
| **Ecstasy use** | | | | |
| **Never** | 1383 | 245(17.72) | Reference | |
| **Yes, not in the last year** | 215 | 50(23.26) | 1.42 | 1.00, 2.02 |
| **Yes, in the last year** | 82 | 23(28.05) | 1.78 | 1.05, 3.02 |
| **Amphetamine use** | | | | |
| **Never** | 1409 | 247(17.53) | Reference | |
| **Yes, not in the last year** | 241 | 61(25.31) | 1.59 | 1.16, 2.18 |
| **Yes, in the last year** | 30 | 10(33.33) | 2.19 | 1.04, 4.63 |
| **Cocaine use** | | | | |
| **Never** | 1308 | 225(17.20) | Reference | |
| **Yes, not in the last year** | 238 | 55(23.11) | 1.45 | 1.03, 2.04 |
| **Yes, in the last year** | 134 | 38(28.36) | 1.87 | 1.22, 2.84 |
| **Any stimulant use** | | | | |
| **Never** | 1234 | 204(16.53) | Reference | |
| **Yes, not in the last year** | 287 | 69(24.04) | 1.80 | 1.25, 2.61 |
| **Yes, in the last year** | 159 | 45(28.30) | 1.94 | 1.31, 2.88 |
| **Cannabis use** | | | | |
| **Never** | 1502 | 255(16.98) | Reference | |
| **Less than once a week** | 74 | 21(28.38) | 1.89 | 1.10, 3.22 |
| **More than once a week but less than daily** | 57 | 22(38.60) | 3.00 | 1.76, 5.16 |
| **Daily** | 47 | 20(42.55) | 3.49 | 1.89, 6.45 |
| **Total** | 1680 | 318(18.93) | - | - |

**Table 2. Odds ratio estimates for smoking pattern on PEs from survey weighted logistic regression. All models based on 1680 participants. Age was adjusted for as a continuous variable.**

| | Model I: Unadjusted | | Model II: Model I adjusted for age, gender, and ethnicity | | Model III: Model II further adjusted for frequency of cannabis use | | Model IV: Model III further adjusted for stimulant use* | |
|---|---|---|---|---|---|---|---|---|
| | **OR** | **95% CI** | **OR** | **95% CI** | **OR** | **95% CI** | **OR** | **95% CI** |
| **Never smoker** | Reference | | Reference | | Reference | | Reference | |
| **Ex-smoker** | 1.06 | 0.75, 1.49 | 1.40 | 0.96, 2.05 | 1.30 | 0.89, 1.90 | 1.25 | 0.78, 1.82 |
| **Sporadic smoker** | 0.97 | 0.65, 1.44 | 1.09 | 0.72, 1.66 | 1.05 | 0.69, 1.59 | 1.03 | 0.68, 1.58 |
| **Daily smoker** | 1.76 | 1.27, 2.42 | 2.05 | 1.44, 2.92 | 1.66 | 1.15, 2.4 | 1.47 | 1.01, 2.15 |

**Table 3. Odds ratio (OR) estimates for the association between a. any PEs (upper panel) and b. the number of PEs (lower panel, reflecting the increase in relative odds for one more PE) with quantity of cigarettes smoked per day. Based on overall analytic sample of 1680. Test statistics (T) are from survey-weighted logistic regression models.**

| **Daily cigarettes smoked** | **Model I: Unadjusted** | | **Model II: Model I adjusted for age, gender, and ethnicity** | | **Model III: Model II further adjusted for frequency of cannabis use** | | **Model IV: Model III further adjusted for stimulant use*** | |
|---|---|---|---|---|---|---|---|---|
| **Any PE** | **OR** | **95% CI** | **OR** | **95% CI** | **OR** | **95% CI** | **OR** | **95% CI** |
| **0** | Reference | | Reference | | Reference | | Reference | |
| **1-9** | 1.51 | 1.06, 2.15 | 1.38 | 0.96, 2.00 | 1.15 | 0.78, 1.69 | 1.05 | 0.71, 1.56 |
| **10-19** | 2.26 | 1.54, 3.31 | 2.36 | 1.59, 3.49 | 1.98 | 1.31, 2.98 | 1.88 | 1.24, 2.84 |
| **20 or more** | 2.13 | 1.24, 3.67 | 2.54 | 1.46, 4.43 | 2.20 | 1.25, 3.89 | 2.04 | 1.15, 3.62 |
| | *T for linear trend=4.19 P<0.001* | | *T for linear trend=4.76 P<0.001* | | *T for linear trend=3.66 P<0.001* | | *T for linear trend=3.32 P=0.001* | |
| **Number of PEs** | | | | | | | | |
| **0** | Reference | | Reference | | Reference | | Reference | |
| **1-9** | 1.65 | 1.03,2.64 | 1.62 | 1.00,2.64 | 1.39 | 0.85,2.29 | 1.36 | 0.83,2.22 |
| **10-19** | 2.52 | 1.61,3.94 | 2.97 | 1.85,4.76 | 2.50 | 1.52,4.11 | 2.37 | 1.43,3.91 |
| **20 or more** | 4.17 | 2.29,7.62 | 5.53 | 3.03,10.09 | 4.70 | 2.50,8.83 | 4.32 | 2.29,8.15 |
| | *T for linear trend=3.32 P=0.001* | | *T for linear trend=6.52 P<0.001* | | *T for linear trend=5.30 P<0.001* | | *T for linear trend=4.98 P<0.001* | |

**Table 4. Models comparing daily smokers to never smokers for an increase in number of PEs, and for separate types of psychotic experience. All models based on 1680 participants. Estimates for ex-smokers and sporadic smokers are not presented.**

| | OR(95%CI) for an increase of one psychotic experience | OR(95% CI) for auditory hallucinations | OR(95% CI) for thought interferences | OR(95% CI) for persecutory experiences | OR(95% CI) for strange experiences |
|---|---|---|---|---|---|
| **Number reporting this symptom (% of sample)** | | 65(3.88) | 22(1.32) | 55(3.30) | 100(6.05) |
| **Model I: Unadjusted** | 1.76(1.19,2.59) | 1.68(0.91,3.08) | 2.17(0.72,6.57) | 1.45(0.76,2.77) | 2.02(1.19,3.42) |
| **Model II: Model I further adjusted age, gender and ethnicity** | 2.12(1.37,3.26) | 2.14(1.05,4.37) | 4.65(1.53,14.09) | 1.62(0.76,3.46) | 2.39(1.37,4.18) |
| **Model III: Model II further adjusted for cannabis use** | 1.70(1.09, 2.66) | 1.78(0.85,3.72) | 3.37(1.04,10.91) | 1.32(0.59,2.96) | 1.89(1.05,3.4) |
| **Model IV: Model III further adjusted for stimulant use*** | 1.55 (0.98, 2.47) | 1.56(0.72,3.39) | 3.25(0.97,10.87) | 1.14(0.51,2.58) | 1.74(0.95,3.18) |