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## Childhood psychotic symptoms: link between non-consensual sex and later psychosis

Michael Daly

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## Correspondence

Edited by Kiriakos Xenitidis and  
Colin Campbell

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### How to interpret different results for CRHTT data

Jacobs & Barrenho<sup>1</sup> used the same data as Glover *et al*<sup>2</sup> when they were comparing admissions in primary care trusts with and without crisis resolution and home treatment teams (CRHTTs). However, they employed different methods for their analysis and reached conflicting conclusions. According to Jacobs & Barrenho, the introduction of CRHTTs did not have a statistically significant influence on the number of admissions, while Glover *et al* found a significant reduction especially for CRHTTs which offered a 24-hour service.

In their article, Jacobs & Barrenho<sup>1</sup> do report a reduction in admissions (e.g. Fig. 4) but state that it was not statistically significant. They do not mention power calculations. There were usable data available from 229 primary care trusts (PCTs) and the authors conducted various complex analyses by using a number of control factors and by studying trends over time. It could be that their lack of statistically significant findings is because of a lack of power. If this is the case, there is no fundamental difference between their findings and the previous analysis.<sup>2</sup>

At the end of their article, the authors make the suggestion that perhaps data should be analysed at the level of CRHTTs and not at the level of PCTs, given that there is huge variation between CRHTTs. We concur with that suggestion and we would like to go even further and suggest that future studies look at the service actually provided to individual patients in terms of how many visits are undertaken over a specified number of days. This information is readily available from most electronic notes systems. Further study is needed to investigate the types of interventions provided, such as whether medication was prescribed and administered, whether specific psychological treatments were offered, and so on. The availability of such data will allow an informed decision to be made about what is required to avoid admission to hospital and whether a CRHTT is the best organisational format to deliver that care.

1 Jacobs R, Barrenho E. Impact of crisis resolution and home treatment teams on psychiatric admissions in England. *Br J Psychiatry* 2011; **199**: 71–6.

2 Glover G, Arts G, Babu KS. Crisis resolution/home treatment teams and psychiatric admission rates in England. *Br J Psychiatry* 2006; **189**: 441–5.

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**Authors' reply:** Power calculations are seldom used in the multiple regression context, particularly with panel data and population-level data. These tend to be rather made with trial-based data to estimate appropriate sample sizes. Many would argue that *post hoc* power calculations are misleading and irrelevant.<sup>1–3</sup> Nevertheless, a *post hoc* power calculation based on the ordinary least squares model which uses the total number of valid cases used in the analysis, the total number of predictors in the model, the model *R*-squared, and the assumed *P*-value (set at 0.05), suggests that for all models the power is 1.00. By convention, this value should be greater than or equal to 0.80.

More importantly though, the benefit of the difference-in-difference methodology is that it provides for more precise estimates than the previous analysis and also allows for the simultaneous inclusion of covariates such as the team fidelity criteria (e.g. crisis resolution and home treatment teams (CRHTTs) offering a 24-hour service) as well as overall time trends. There are fundamental differences between the two types of analyses with the difference-in-difference methodology being a far more potent and robust policy evaluation tool.

We agree that future studies should ideally look at analysing admissions (and potentially other factors) at CRHTT level. We explored the possibility of doing this by contacting several teams to ask about their geographical boundaries, but found, surprisingly, that many teams were in fact unable to clearly delineate their geographical 'patch' and that even if they could define their current boundaries, these had often changed over time, making an analysis of long-term trends with difference-in-difference methodology unfeasible. Moreover, a large-scale national longitudinal study would require data from before the policy change (circa 1998) to effectively assess the policy impact, for which routine administrative data is more suited than data from individual electronic records systems, which have huge variation in detail, quality and method of collection.

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### Need to identify modifiable risk factors of dementia in the older UK African–Caribbean population

The article by Adelman and colleagues<sup>1</sup> made an important contribution in exploring dementia in older people of African–Caribbean origin in the UK. This article paves a way for policy makers in assessing the public health implications of this ubiquitous condition in terms of care burden and economic impact. However, this research study raises important issues.

Previous studies<sup>2</sup> consistently indicate increased prevalence of dementia in older African–Caribbean people when compared with the indigenous White population in the UK. The magnitude of this difference between these populations is not clear. Hence, there is a definite need for well-planned epidemiological studies to determine the actual burden of disease. Surprisingly, Adelman *et al*'s study<sup>1</sup> presumed that vascular factors such as hypertension and type 2 diabetes are likely to increase the burden of dementia in the African–Caribbean population. However, the possibility of other risk factors such as depression, illiteracy and prevalence of apolipoprotein 4, which, presumably, increase the chances of subsequent dementia, needs more emphasis.<sup>3,4</sup> Current data from sub-Saharan Africa and India<sup>4</sup> suggest that age-adjusted dementia prevalence estimates in 65-year-olds are low (1–3%) compared with other low- and middle-income countries. It appears that there is a need to identify potentially modifiable environmental/genetic factors to explain the increased prevalence of dementia when this population migrated to the UK. Therefore, future studies are needed to identify these risk factors in this migrant population.

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**Authors' reply:** We agree that it is helpful to emphasise that we do not know whether vascular factors are the primary aetiology behind the increased prevalence of dementia in this population. We considered literacy to be a risk, and this (like our earlier study) controlled for education<sup>1</sup> and found no difference between ethnic groups. Similarly, depression rates in older Black and minority ethnic populations have not been found to be raised;<sup>1</sup> nor has the prevalence of apolipoprotein 4 when compared with their White counterparts.

However, there are contradictory findings about whether the expression may be the same.<sup>2–5</sup> Thus, although all these factors may relate to the rates of Alzheimer's dementia, there was no clear evidence to suggest they are responsible for the increased rate in the African–Caribbean group. Finally, there is no evidence that the prevalence of dementia in the participant's country of birth (Caribbean Islands) is lower than that for the UK. A Delphi consensus study estimated that the rates for Latin America and the Caribbean are at least as high as for Western Europe.<sup>6</sup> We agree, however, that more research is needed to consider the possible aetiology and modifiable risk factors.

Declaration of interest

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## Internet-based CBT for severe health anxiety

Having appraised the evidence regarding the article by Hedman *et al*,<sup>1</sup> we write to comment as follows.

First, it is not possible, from the article,<sup>1</sup> to tell whether the comparison group was similar to the experimental group, as no statistical tests were done.

Second, the treatment described by the authors as internet-based cognitive–behavioural therapy (CBT) involved components of mindfulness and may have been more appropriately described as internet-based modified CBT.

Third, given that defined psychological approaches, including CBT are accepted as treatment for health anxiety,<sup>2–5</sup> CBT delivered as usual may have been a more appropriate control treatment than the online discussion forum. An online discussion forum is not recognisable or recommended treatment for health anxiety.

Fourth, the description of participant recruitment is contradictory: 'There were no advertisements in newspapers or in other media. However, an article about the study was published in a major nationwide newspaper'.

Fifth, we note that the power in per cent is not stated explicitly in the study such as to inform respective clinician's appraisal of this study as regards applicability of results to various clinical settings.

In light of the above, there is a need for cautious interpretation of the evidence presented, which we feel has limited therapeutic value in the acute psychiatry settings, such as crisis resolution and home treatment teams and in-patient wards, in which we work. However, we value this paper as adding to the limited body of knowledge available about treatments for health anxiety and expanding the notion that this disorder is treatable.

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**Author's reply:** There were no statistically significant differences between the groups at pre-treatment (as can be read from Table 2, means and standard deviations were very similar across groups). However, for several reasons we found it appropriate not to report *P*-values of baseline data. Analyses were conducted using ANCOVAs, holding pre-treatment values as covariates. Moreover, when *n* is small, considerable variation between groups can be the case without reaching statistical significance, because of limited power. Consequently, several scientific journals (e.g. *Annals of Internal Medicine*<sup>1</sup>), advise against the use of *P*-values when comparing baseline data in randomised controlled trials.

As for the name of the treatment, we view the term internet-based cognitive-behavioural therapy (CBT) as most suitable. The treatment's theoretical foundation and its components are based on learning theory and cognitive theory. As stated in the Method and the Discussion sections, the rationale for including a mindfulness exercise was to reduce avoidance behaviours related to bodily sensations and to enhance exposure. Also, as the term CBT has been used for describing a plethora of treatments with substantial inter-treatment variability, the addition of 'modified' would probably be misleading rather than clarifying. In fact, a recent paper presents mindfulness-based cognitive therapy as 'a newer variation of cognitive behavioral therapy'.<sup>2</sup>

Regarding the control group, I agree that participating in a discussion forum hardly can be viewed as the optimal control condition. However, as the present study is the first ever to investigate internet-based CBT for health anxiety, a comparison with conventional CBT would have been premature. Such a comparison would have meant conducting a non-inferiority trial presenting difficulties regarding criteria for non-inferiority as well as the inherent assay sensitivity problem. In addition, far more participants would have needed to be randomised to internet-based CBT (because of power issues), which would have been ethically questionable. That is, far more patients would have been exposed to a potentially non-effective or even unsafe treatment. As I see it, the ideal control condition would rather have been an internet-based psychological placebo arm providing the same amount of therapist attention and treatment credibility without targeting the central proposed mechanisms of change.

When it comes to recruitment, I consider advertisements and an article in a newspaper as two quite different forms of attention. The former is under complete control of the researcher while the latter is not. As a consequence, I find it reasonable to assume that the two forms of attention have differential effects in terms of recruitment and that they therefore should be reported separately.

As for generalisability of the findings, Udo *et al* state that our paper tells us little as to whether internet-based CBT works in acute psychiatry settings or in an in-patient psychiatric context. I can only say that I absolutely agree. The clinic at which the present study was conducted is an out-patient clinic and internet-based CBT is not different from conventional CBT in the sense that one should be vary cautions in generalising findings from one healthcare context to another.

## Childhood psychotic symptoms: link between non-consensual sex and later psychosis

Numerous studies have established a link between trauma early in life and psychosis in adulthood.<sup>1</sup> In particular, non-consensual sex in childhood appears to robustly predict the occurrence of psychotic symptoms later in life.<sup>2</sup> Bebbington *et al*<sup>3</sup> add to this literature by demonstrating a large potential role of non-consensual sex in the development of psychosis in a large representative sample of English adults. However, although the authors take several steps to adjust for residual confounding, they make no attempt to correct for the presence of psychotic symptoms in childhood. This is a potentially critical error as reverse causation remains a distinct possibility. Children who exhibit psychotic symptoms may be at high risk of sexual victimisation owing to their poor social skills, paucity of social relationships, and for numerous other reasons. Thus, initial mental health may explain the link between sexual abuse and adult psychosis.

In an analysis of over 3500 British adults reported elsewhere,<sup>4</sup> I showed that non-consensual sex at age 16 or earlier placed females at a substantial risk of auditory and visual hallucinations at age 29 (OR = 8.51, 95% CI 0.99–73.28). However, females who experienced hallucinations in childhood were also likely to have been forced to have sex by age 16. When the presence of initial psychotic symptoms was taken into account the link between non-consensual sex in childhood and hallucinations in adulthood was diminished to non-significance (OR = 2.43, 95% CI 0.09–62.88). These findings suggest that childhood sexual abuse may not be related to psychosis in adulthood over and above psychotic symptoms in childhood, at least in the domain of visual and auditory hallucinations.

Thus, when patent non-causal explanations have not been tested, vigilance is required prior to inferring that the link between sexual abuse and psychosis may be causal. Although the design utilised by Bebbington *et al* was cross-sectional, it would have been possible to ask participants to retrospectively gauge the age at onset of their psychotic symptoms. This would have allowed the researchers to produce a more methodologically robust assessment of the potential causal effect of sexual abuse.

Bebbington *et al* also identified anxiety and depression as partial mediators of the relation between sexual abuse and psychosis. However, poor initial mental health may have determined both childhood abuse and later experiences of depression, anxiety and psychosis. It is therefore of the utmost importance that those assessing the role of environmental risk factors in predicting psychosis endeavour to assess the presence of psychosis and subclinical psychotic symptoms and mental health more generally at baseline. This will allow the contribution of early environmental risk factors to psychosis to be evaluated and will provide a robust evidence base for clear policy-relevant recommendations.

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**Author's reply:** Dr Daly argues that the link between child sexual abuse and adult psychosis may be the result of confounding by psychotic symptoms in childhood or adolescence. He adduces evidence for this from his secondary analysis of data from the 1970 British Birth Cohort sample.<sup>1</sup> Of the female sample, 1.6% indicated that they had been forced to have sex by the age of 16, and this was associated with an elevated risk of visual and auditory hallucinations at age 29 (OR=8.5). However, after controlling for the experience of such quasi-psychotic symptoms before the age of 16, the odds ratio fell to a non-significant 2.4. Daly interprets this as indicating that this relationship exists because children with quasi-psychotic symptoms are more at risk of abuse and also at greater risk of developing psychosis as adults.

Nevertheless, Dr Daly's conclusion must equally be tentative. First, the British Birth Cohort sample apparently does not provide temporal discrimination between the occurrence of sexual abuse and the development of quasi-psychotic symptoms. Second, given that this is so, the diminution of the odds ratio after controlling for quasi-psychotic symptoms in adolescence could indicate mediation. In other words, the sexual abuse leads to adolescent symptoms which are then associated with adult symptoms. I find this explanation more plausible than the suggestion that psychotic symptoms themselves have a major effect in increasing vulnerability to abuse. There is some evidence that psychotic symptoms in adolescence are associated with prior abuse.<sup>2</sup>

It would be good to resolve this argument with appropriate data from a cohort study. However, this might not be possible: there are considerable ethical difficulties in contemporaneous enquiry about sexual abuse in child and adolescent epidemiological samples. Current research has provided some indication that the psychological consequences of abuse show similarities to psychological antecedent and maintaining factors in psychosis,<sup>3,4</sup> and this does add plausibility to the aetiological role of sexual abuse. The particular association of early trauma with psychotic disorders (schizophreniform or bipolar) characterised by hallucinations is also difficult to explain in terms of confounding.<sup>5,6</sup>

The final worry about Dr Daly's argument is that it may detract attention from therapeutic engagement with the consequences of sexual abuse and other trauma in people with psychosis.

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### Revascularisation in patients with mental illness

Mitchell *et al* must be congratulated on their systematic review of myocardial revascularisation in patients with mental illness.<sup>1</sup> As physicians performing revascularisation procedures, we were disappointed by the inferior treatment received by patients with mental health problems. Fortunately, these patients account for only a minority of those presenting to acute cardiology services with symptoms and signs suggestive of acute coronary syndrome. However, when they do attend, they present cardiologists with a number of challenges, which ultimately can influence the decision regarding treatment.

Revascularisation remains an important treatment for those patients with myocardial necrosis, providing both symptomatic and prognostic benefit.<sup>2</sup> Importantly, however, it can only be performed following invasive coronary angiography – a procedure which carries a risk of vascular complication, myocardial infarction, stroke or even death of 0.2–1.0%. Clearly, patients must give appropriate consent before coronary angiography is undertaken, and this can represent an important hurdle when treating patients with mental health problems.

A second important challenge which should be considered prior to undertaking angiography, and must be considered prior to performing definitive revascularisation, is the issue of adherence to medication. Frequently, revascularisation can be performed percutaneously at the time of angiography. This procedure usually necessitates the implanting of coronary stents, which are small permanent metal scaffolds that help maintain coronary vessel patency. There are many advantages to using these devices; however, in recent times stent thrombosis has emerged as the most serious and worrying complication of their use.<sup>3</sup> This condition is fortunately rare, but it remains a devastating, unpredictable event that has a significant morbidity and mortality; up to a third of patients will die. Research has identified that early or premature discontinuation of dual antiplatelet therapy is one of the most important risk factors in stent thrombosis.<sup>4</sup> Consequently, cardiologists are reluctant to implant stents in patients who they feel are unlikely to comply with dual antiplatelet therapy. Unfortunately, patients with mental illness have been shown to be less adherent to medication,<sup>5</sup> a factor which certainly has as an influence on revascularisation decisions.

These issues represent important challenges (and not excuses), which must be overcome to allow our patients to receive the most appropriate treatment. The differences in treatment certainly deserve to be highlighted and as recommended by Mitchell *et al* the reasons behind them require more in depth investigation, especially within the confines of the National Health Service.

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**Authors' reply:** We thank Drs Garg & Garg for their insightful comments from a cardiologist's perspective. The purpose of our paper was in part to stimulate others to examine more precisely what factors underlie these apparent deficits in received cardiac care. Garg & Garg raise two issues that we agree deserve further investigation – consent to undertake invasive procedures, and compliance with follow-up care. Regarding consent, we are not aware of any studies on refusal of medical procedures particularly following on from an acute psychiatric episode. However, there are some data on refusal to start medication in psychiatric settings which may be a useful point of comparison.<sup>1,2</sup> Kasper *et al* found that in newly admitted psychiatric in-patients 12.9% refused treatment but that 90% of these ended their refusal within 4 days suggesting persistent refusal may be overestimated, accounting for perhaps 1% of treatment problems.<sup>2</sup> It is worth noting that non-adherence rates among patients with severe mental illness is probably lower for hypoglycaemic and antihypertensive drugs than for antipsychotics.<sup>3</sup> One important question here is whether the very small proportion of patients who cannot initially consent because of acute mental illness are always given a second chance to consent once well? Better links between physicians and psychiatrists would no doubt help here. Even in those with mental ill health, the vast majority of problems with day-to-day adherence are caused by accidental omissions and rational non-adherence and not ongoing florid psychiatric illness.<sup>4</sup>

The second issue raised was provider caution owing to the possibility of future non-adherence. Garg & Garg rightly highlight that non-adherence to cardiovascular medication is sometimes higher in those with mental ill health, although this is not always the case. Contrary to popular opinion, non-adherence (to medical drugs) is sometimes lower, not higher, in people with mental illness.<sup>5</sup> In truth, we do not know whether there is a low prescribing rate or a low uptake rate or both. Focusing on anti-platelet drugs, an unpublished meta-analysis presented by Mitchell at the Royal College of Psychiatrists' Faculty of Liaison Faculty Meeting (2011) found no difference in receipt of antiplatelet drugs in those with *v.* without broadly defined mental illness, but there was a slight effect in those with severe mental illness (OR = 0.91, 95% CI 0.84–0.99), suggesting that patients with severe mental illness are indeed receiving slightly less medication for cardiovascular indications. A caution is that these studies are based on prescribed medication rates not actual adherence with medication.

Documenting these inequalities is only the initial step. Are we taking appropriate actions to compensate for these difficulties? For instance, we would not consider a patient with visual impairment to be non-adherent because they cannot read a patient instruction sheet. We would make extra effort to give the information in another format. Surely, where medical treatment is indicated, we (i.e. all healthcare professionals) must make some effort to compensate for the difficulties faced by patients with comorbid conditions and ensure our facilities and treatments are acceptable and understandable even when it is expensive or inconvenient to do so. Collaborative care, attached professionals and peer-support models have shown promise in some areas. Could cardiologists and psychiatrists working together establish whether these are useful in the aftercare of patients with mental ill health who require cardiac surgery?

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## Generalised spike-and-slow-wave complexes without seizures in schizophrenia

There has been long discussion about the increased prevalence of electroencephalogram (EEG) abnormalities and their significance in patients with schizophrenia.<sup>1–4</sup> Although interictal epileptiform discharges presumably indicate a higher risk for seizures,<sup>5</sup> such abnormalities alone in a clinical case of schizophrenia are generally not regarded as having strong implications for antipsychotic therapy.

Here, we report the case of a 17-year-old student who over a period of several months developed a paranoid-hallucinatory syndrome, feeling persecuted, sidelined and out-casted by his peers. He also experienced changes in auditory perception, reported supersensitive hearing and auditory hallucinations of backbiting whispering voices of his peers. There was a prodromal phase with increasing social withdrawal, affective flattening and a drop in school grades over a period of 2 years prior to the diagnosis of schizophrenia by an out-patient psychiatrist. Treatment with 250 mg quetiapine led to some improvement but not remission. Aged 13 he had been in a road traffic accident, with subtle contusions and subarachnoid bleeding which fully recovered without any other neurological, psychiatric, cognitive or magnetic resonance imaging symptoms or signs. A routine clinical EEG showed infrequent 3 Hz spike-and-slow-wave complexes (SWCs). Video telemetry for 3 days clearly showed 3 Hz SWCs with a duration of between 200 and 3500 msec and an average frequency of about 8 per hour and a peak frequency of 18 per hour without clinical seizure correlates. Assuming

that the EEG findings might play a role in the genesis of schizophreniform syndrome, medication was changed to valproate monotherapy. This resulted in full clinical and cognitive remission and considerable improvement of the EEG within a few weeks. Subsequently, the patient's school grades returned to top levels.

The clinical relevance of such an EEG finding in a patient with schizophrenia is still an unresolved question.<sup>6</sup> In spite of an intensive historical discussion of this issue, to our knowledge this is the first description of a clinical case of schizophrenia with generalized 3 Hz SWCs and excellent clinical response to valproate monotherapy. In our view, this case illustrates three clinically important points: (1) it is worthwhile doing EEG studies in patients with schizophrenia; (2) non-ictal SWCs might play a pathogenetic role in a small subgroup of patients with schizophrenia; and (3) in clear-cut cases of SWCs in patients with schizophrenia but without clinical seizures, a therapeutic trial with anticonvulsant medication might be warranted.

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