Invisible children: attempting to engage the most vulnerable families

Cullen et al. describe childhood antecedents of schizophrenia: such prospective studies are rare. Retrospective research suggests that as the number of adverse childhood experiences increases, so does the risk for health problems, including alcohol misuse, ischaemic heart disease, suicide attempts and externalising behaviours. However, retrospective studies are prone to the biases associated with recalling early childhood. The best way to fully understand the mechanisms underpinning the relationship between adverse childhood experiences and later development is to follow children prospectively from early childhood.

We had a unique opportunity to achieve this in Glasgow because of the existence of the Women’s Reproductive Health Service (WRHS), which provides antenatal care for some of the most vulnerable women in Glasgow: those affected by problem drug or alcohol use or significant mental health or personality problems. This cohort is well characterised in terms of family adversity.

We conducted a feasibility study to see whether it was possible to assess the mental health of the children of very vulnerable mothers. We selected a random sample of ten women who had received antenatal care from the WRHS 7 years earlier. Of the ten children targeted, one was deceased, two had been adopted and one was uncontactable because the mother was in a woman’s refuge in a secret location. Of the remaining six, three opted out, one was uncontactable despite repeat attempts, and of the two whose mother provided consent, one then became uncontactable and the last opted out. Each woman received a minimum of ten phone calls and five attempted visits with a letter left each time (unless they had opted out in writing or by phone). Despite two members of staff working full time for 8 weeks, it was not possible to conduct any mental health assessments on these children of very vulnerable mothers. Our research team were able to meet with only two out of our target sample of ten women and did not succeed in assessing any of the children. In other words, despite persistent phone calls and home visits, eight of these vulnerable women and all of their children remain invisible.

The considerable resources available to our research team – including the potential to make multiple phone calls and visits – are not usually open to healthcare or social-care professionals. The question we then have to ask is, how do we reach these most vulnerable of families and safeguard the health of their children?


Authors’ reply: Notwithstanding the logistical and ethical issues that make this sensitive research difficult to accomplish, we agree that prospective investigations of children followed from early childhood offer the best prospect for identifying mechanisms underpinning the relationship between childhood adversity and later outcomes such as mental health, social functioning, and educational/occupational attainment.

In response to the query regarding how this important research might be achieved given the challenges Sim et al. identified, we suggest that longitudinal, population record-linkage studies offer excellent capacity to examine these relationships in an unbiased, inclusive, and ethical manner. One such investigation is the New South Wales Child Development Study (http://nswcds.com.au) based at the University of New South Wales. This is a longitudinal investigation following the development of a cohort of 87,026 children who entered full-time schooling in 2009 (representing 99.9% of the population). Via local record-linkage infrastructure provided by the Centre for Health and Record Linkage (http://www.cherel.org.au), and operated under strict privacy provisions, anonymised multi-agency records on the children (including health, education, welfare, birth, and developmental records) have been combined by researchers with records on their parents (including health and criminal records).

As part of this study, diverse measures of childhood adversity are available from population-based government child-protection files. Records were available for 3926 children (4.5%) in the cohort by the age of 5 years. These records, in combination with linked information on mental health and well-being outcomes in childhood (and, in due course, in adolescence and adulthood), offer an excellent opportunity to determine the childhood, adolescent, and adult sequelae of early exposure to adversity. Publications from the initial phase of the investigation (spanning birth to 5 years in the population cohort) are currently in preparation.

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The developmental trajectory of bipolar disorder

The article by Duffy et al.1 in the February issue tests evidence for a clinical staging model of bipolar disorder for the offspring of parents with lithium-responsive illness and the offspring of parents with lithium-non-responsive illness.

In their analyses, Duffy et al. were unable to show a statistically significant difference for the risk of any psychiatric disorder between both subgroups of offspring. Yet they still conclude that the offspring of parents with lithium-non-responsive illness manifest neurodevelopmental disorders in childhood and psychotic disorders in young adulthood. A second problem is that the neurodevelopmental disorder category included cluster A

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traits, which do not readily fit with the others (attention deficit hyperactivity disorder (ADHD) and learning disabilities). A third problem is that schizoaffective disorder was included among the bipolar spectrum disorders in the analyses, a decision that requires further justification.

A fourth problem is that, as described in a previous article, a diagnosis of bipolar affective disorder not otherwise specified was given to participants who presented with manic symptoms meeting threshold DSM-IV diagnostic criteria but not minimal duration criteria. It is possible that this was the reason for a statistically significant difference in the cumulative incidence of bipolar spectrum disorders between the offspring of well parents and the offspring of parents with a bipolar disorder. Finally, 23% of participants in the group of offspring of a parent with bipolar disorder 1 were recruited within families, making it unclear how many participants had a parent who did not have the disorder.


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An oversimplification of psychosis, its treatment, and its outcomes?

Jauhar et al’s meta-analysis1 of randomised controlled trials in cognitive–behavioural therapy for psychosis (CBTp) is broadly consistent with previous results; that is, there is an overall significant but modest impact on psychotic symptoms, with blinded studies showing lower effect sizes than those that are not blinded. However, there are a number of problems with this study and especially with its conclusions.

Jauhar et al conclude that they find the advocacy by government (including NICE) for CBTp ‘puzzling’, bearing in mind the low effect sizes found for psychotic symptoms. However, I find it puzzling that the authors comment on NICE recommendations, since a third of the studies included for their overall symptoms analysis (12/34) were not based on therapies recommended by NICE in the first place (based on what we know is effective from the literature so far): they were either group or brief CBT studies. Three further studies were in Chinese, so their relevance to NICE recommendations is hard to tell.

It is a testament to the far-reaching effects of CBTp that the analyses revealed any effects at all, since the authors looked at outcomes that were not always targeted by the therapy. For instance, only a few of the 34 studies included for negative symptoms actually targeted such symptoms specifically. Furthermore, severity of positive symptoms/hallucinations was used as the outcome for studies that did not hypothesise changes in psychotic symptoms since the target was on compliance with command hallucinations, emotional dysfunction, or social functioning. By contrast, outcomes on depression, anxiety or distress as a result of psychotic symptoms, and trials targeting self-esteem, post-traumatic symptoms, suicidality, or substance misuse, which are all main and legitimate targets in CBTp, were excluded.

The criteria for studies to be included in the final analyses were idiosyncratic. Perhaps the most surprising was the decision to exclude studies that targeted hallucinations specifically from their positive symptoms analyses. A separate ‘supplementary’ meta-analysis was carried out for those studies, with an effect size of 0.34, which is not reported in the abstract (where only the lower – 0.25 effect on positive symptoms is reported). Clinicians familiar with clinical presentations of patients with psychosis might be surprised at their rationale for excluding trials because patients had a dual diagnosis, or had medication-resistant psychotic symptoms but no further diagnosis specification. None of the follow-up data available was included, meaning that the
Sensky et al 160 (non-significant) end-of-study results contribute to the findings, but the (significant) 9-month and 5-year follow-up results do not. 7

Meta-analyses can be highly informative, but they are highly prone to bias. 8 Those with a ‘washing machine’ approach, such as this one (i.e. amalgamating different populations – from acute in-patients to chronic out-patients, from young people with a first episode of psychosis to older adults; different therapies – from 3 sessions of acceptance and commitment therapy to 18 months of weekly cognitive therapy; different modalities – groups or individual; different targets – from compliance with command hallucinations to emotional dysfunction), tell us very little about what works for whom. Unsurprisingly, the heterogeneity statistics were highly significant for all analyses, with I 2 being at 50% or above (i.e. representing ‘substantial heterogeneity’), suggesting that there was too much heterogeneity to obtain meaningful pooled estimates, and that the necessary criteria for rendering a meta-analysis appropriate were not met. 9

The field of CBTp has now progressed such that it is no longer appropriate to simply lump together psychosis patients assuming that clinical presentations are the same, that therapy is for the same problem, and that the type of CBT is the same. Other recent meta-analyses, which focus on treatment-resistant patients, 10 or on individually tailored, formulation-based CBT for hallucinations and delusions, 11 will be more informative to clinicians and researchers about the specific effects of CBTp.

To conclude, the reported analyses reflect an over-simplification of the complexities of psychosis and psychological interventions. The biggest challenges in psychological therapy trial methodology (and in clinical practice) are the quality of adherence to the therapy delivered and the competence of the therapists, none of which was taken into account in this study. A more meaningful reading of the existing research is that the next steps are to investigate which patients benefit on which outcomes at which stages with which types of therapy, and how to ensure therapist competence (and availability).

Declaration of Interest
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Authors’ reply: One of the founding principles of meta-analysis is to pool data from as many studies as possible. 1 Among other benefits this prevents studies being preselected for consideration on arbitrary grounds. It is difficult to imagine anything more arbitrary than restricting a meta-analysis of CBT for schizophrenia to studies that conform to some notion of interpretation of the NICE guideline, as Peters seems to be suggesting, not to mention excluding any that were in Chinese.

Similarly, it would be wrong to exclude studies that used group CBT a priori. Here, though, it is entirely legitimate to examine this issue post hoc; that is, to ask whether use of group v. individual CBT significantly moderates effect size. Carrying out this analysis on our data reveals that the pooled effect sizes for both types of intervention were very similar in the meta-analysis of overall symptoms (effect size in 7 group studies –0.24 v. –0.23 in 24 individual studies; Q = 0.006; P = 0.94); for positive symptoms, group CBT had a non-significantly smaller effect size than individual CBT (effect size in 8 group studies –0.08 v. –0.25 in 23 individual studies; Q = 1.73; P = 0.19) (across both analyses, one study employed both group and individual CBT and three were rated as ‘unclear’). This might or might not be considered evidence that group CBT is less effective than individual CBT, but what it does not mean is that inclusion of group studies in our original meta-analyses somehow acted to dilute the pooled estimate – the effect sizes for studies using individual CBT are similar or lower to those we reported for all studies combined (effect sizes were –0.33 for overall symptoms and –0.25 for positive symptoms).

With regard to some of the other points raised by Peters, our diagnostic criteria were broad and similar to those used by NICE, Wykes et al and the Cochrane Collaboration. We recognised the possibility that Acceptance and Commitment Therapy might be different from regular CBT and presented an analysis in the article excluding two studies using this 2,3 and another where CBT took the form predominantly of coping skills enhancement; 4 this did not materially affect the results. Peters expresses surprise over our decision to exclude studies that specifically targeted hallucinations from the meta-analysis of positive symptoms. As it happens, only three studies of hallucination-directed CBT also reported outcomes for positive symptoms. Adding the data from two of them 5,6 (data cannot be extracted from one study 7) to the positive symptoms dataset makes no difference to the pooled effect size (–0.25; CI –0.36/–0.13).

Peters argues that there was too much heterogeneity among the results to obtain meaningful pooled estimates. In fact, the Cochrane Collaboration article she cites 8 recommends (a) not pooling data using meta-analysis, (b) investigating heterogeneity using subgroup analysis or meta-regression or (c) using a

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References:
Borderline personality disorder and mood

Parker examined whether borderline personality disorder (BPD) is a bipolar or unipolar mood condition and concluded by suggesting that it is probably neither.1 It would like to offer a supplementary interpretation of the literature; that is BPD is in bipolar disorder2 and depression,3 and those who develop bipolar major of patients with established bipolar disorder, even after episodes, might be the core feature of bipolar disorders.5 The evidence that affect or mood instability, as opposed to mood the syndrome. While under- investigated, there is emerging
dysregulation.4 Support that BPD is a mood disorder is also
shifting negativity–euphoria–anger.10 Negative emotional instability is a critical feature of BPD but it is changeable, as is obvious to clinicians who have been charged with the care of people with BPD on in-patient wards.

Affect can be studied on the basis of intensity, frequency of


Gordon Parker makes a powerful case against the hypothesis that borderline personality disorder is really a form of bipolar or unipolar disorder.1 In so doing he is tilting at a windmill in whose
Correspondence has been most damaging, and from the many disorders that give dysregulation from personality disorders, where its infiltration nosology is now to separate the essential core of emotional critiques, I do not claim any connection between bipolar, unipolar history is one of remission rather than persistence. The task of associated with many other mood states; nothing about it is driven by personality. The very name ‘borderline personality disorder’ betrays an abrogation of diagnosis. It overlaps with post-traumatic stress disorder, other personality disorders, anxiety, depression, and dissociative and adjustment disorders, yet does not belong to any of them. By having layer upon layer of diagnostic requirements that allow it to become grossly heterogeneous, it has confused everybody and satisfied none. Personality disorders are trait based and these traits are persistent over time and linked to normal personality variation. There is good evidence that borderline-personality characteristics are closely linked to affective instability, not normal personality variation, and its natural history is one of remission rather than persistence. The task of nosology is now to separate the essential core of emotional dysregulation from personality disorders, where its infiltration has been most damaging, and from the many disorders that give the term ‘comorbidity’ such a bad press. A start has been made in the reclassification of personality disorder in ICD-11, where borderline personality disorder and the other current categories of personality disorder have all been removed, but much more needs to be done.


Declaration of Interest
The author is Chair of the ICD-11 Working Group for the Revision of Classification of Personality Disorders.

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Authors’ reply: Two letters in response to my brief editorial seeking to argue why borderline personality disorder (BPD) is not a mood disorder. One (by Dr Stephen Marwaha) gently offers a ‘supplementary interpretation’ that seemingly positions BPD in an ineffable zone. The other (by Professor Peter Tyrer) is also gracious, but accuses me of ‘tilting at a windmill’. What is it about BPD that promotes intense professional interchanges and risks splitting?

Let me proceed less impulsively. Peter states that he did not claim any connection between ‘bipolar, unipolar and borderline’, but I did not ascribe any such claim to him. Further, he suggests that, in my arguing against BPD as a mood disorder, I was ‘tilting against a windmill’ in whose construction he had ‘absolutely no part’. Here I risk being more coyote-like than Don Quixote-like in recording that Peter did lead me up the path to the windmill. As then Editor of the British Journal of Psychiatry, he invited me (personal communication, 16 July 2013) to write an editorial on the ‘status and relationship of those disorders’, and there observed that he ‘wrote a paper in 2009 saying that BPD was a mood disorder so I have already nailed my placard on the diagnostic wall’.

It would be fairer to Peter, however, to report his actual referenced 2009 paper. Its abstract stated that BPD ‘is better placed with the mood disorders than in odd isolation as a personality disorder’. In the body of the paper, he judged that BPD does not fit within the general descriptors of a personality disorder and, later, in considering whether it were to be ‘accepted as a mood disorder’, he suggested that it might warrant a ‘term such as fluxithymia, or “rapidly changing” mood disorder’. In relation to other points made in his letter, I agree with all but one of his interpretations. Peter states that BPD characteristics are linked closely to affective instability, not normal personality variation. But is not an affective stability/instability dimension a personality dimension? Even if such instability in those with BPD remits with time (as the data show), this does not of necessity eject BPD from a personality home base. If attenuation with age were to discount a personality base, where would we place sociopathy nosologically when it also commonly ‘burns out’?

Marwaha effectively argues that ‘BPD is in large part a mood disorder but is not necessarily a bipolar or unipolar mood variant’. While there is one public figure who has described his mood disorder as a ‘tripolar one’, and there are usually three options in life, our current classificatory systems in psychiatry allow only for unipolar and bipolar disorders. If BPD is a mood disorder, it has to be positioned as one or other: there is no mood condition beyond their borders.

Marwaha proceeds to argue that ‘affect’ nuances allow BPD to be positioned as a mood disorder. Let us consider paranoid personality disorder (PPD) as an analogy for his points. Do not individuals with a PPD temperament experience changes in affect that are ‘intense, frequent, rapid to occur, slow to dissipate’ and with ‘valence’ components weighting anger and emotional dysregulation? If so, as I would argue, would we not, logically, similarly risk positioning PPD (and several other personality disorders) akin to BPD if we accept Marwaha’s arguments? I doubt whether we would feel comfortable with such a suggestion. In essence, if we concentrate on features shared across conditions (especially emotional dysregulation) we will predictably find convergence and risk diagnostic confusion. My editorial adopted the opposite approach: focusing on points of distinction between BPD and mood disorders, and which seek to advance diagnostic differentiation, especially in a clinical context.


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Nothing in between: a multi-faith response to the paper on religion and suicide

As a Liberal Jewish psychiatry registrar and a moderately observant Hindu psychiatry senior house officer, we read with great interest Kleiman & Liu’s fascinating paper on the relationship between religious service attendance and suicide risk.\(^1\) We were also pleased to note that the paper has already generated sufficient interest to give rise to a fascinating editorial by Cook\(^2\) as well as helpful correspondence between the authors and Professor Nebhinani.\(^3\) This seems to attest to the importance of this topic, and we hope that our additional reflections on the methodology of Kleiman & Liu’s study can be part of an evolving dialogue around the interactions between mental health and religion/spirituality.

First, while there are many advantages to the prospective study design, difficulties are produced when the outcome of interest (here, completed suicide) is a relatively rare one. Only 25 completed suicides occurred, and the absolute numbers occurring in the two groups (frequent v. less frequent service attenders) were not specified. Even a very small swing in the distribution of the suicides from one group to the other could significantly alter the apparent magnitude of the protective effect of service attendance.

Second, the absence of any intermediate data between baseline and the end of the study period makes it difficult to draw conclusions about the potential link between religious service attendance and suicide – hence the title of our letter, ‘Nothing in between’. During the follow-up period (12–18 years), much might have changed in people’s lives, behaviours and health. In particular, people’s level of religious observance (in the form of service attendance) might well have varied over the study period – as might their mental health. Moreover, there might well be interactions between these two variables. With only two data-points (baseline self-report and a dichotomous outcome of suicide/not-suicide), it is impossible to know people’s religiosity and mental health across the study period.

Third, this lack of intermediate data might stem from the fact that Kleiman & Liu’s study seems to have ‘piggy-backed’ onto a separate, pre-existing epidemiological survey,\(^4\) the primary objective of which was not the investigation of the relationship between religiosity and suicide. Convenient as it might have been to make use of pre-existing data, it might be that a study set up specifically to address the research question would offer richer information and allow greater extrapolation and clinical application.

Fourth, and also in terms of clinical applicability, we would question whether the focus on completed, as opposed to attempted, suicide is necessarily an advantage. As the authors observe, there do seem to be differences between the clinical profiles of those who complete, compared with attempt, suicide. However, the two are closely related, with previous suicide attempts a sufficiently well-recognised risk factor for suicide completion that it has been controlled for as a potential confounder in Kleiman & Liu’s study, even though it was not found to be ‘a significant predictor of death by suicide’. Moreover, in the clinical setting, suicide attempts are one of the primary risk events of concern, but the study does not provide information on how religious service attendance might relate to these – information which could be of considerable relevance for risk assessment.

Given the above reflections, as well as the study limitations identified by Kleiman & Liu, Cook and Nebhinani, we caution against an over-simplistic reading of the article’s headline finding. In our clinical experience, the relationship between a person’s religiosity and their risk of self-harm/suicide can vary considerably. We therefore urge that clinicians continue to conduct detailed explorations of each patient’s individual dynamic risk factors and not overly focus on particular population-level static risk factors.

Authors’ reply: While we agree with several of the points raised by Yates & Arya, further discussion of several issues is needed. First, we agree that caution is needed when interpreting prediction of a low base-rate occurrence such as suicide. As we note in the paper, although suicide is an infrequently occurring event, the number of suicides in the data-set matches what would be expected from the population during the study period.\(^1\) Considerable effort was taken by the United States Centers for Disease Control and Prevention to guarantee high accuracy of the cause of death data. The authors also noted that ‘the absolute numbers occurring in the two groups (frequent v. less frequent service attenders) were not specified’. This information is available in Table 1 in the paper. Of the 25 people who died by suicide, 8 (32%) attended religious services frequently and the other 17 did not.

Second, our outcome variable (death by suicide) was time-varying (i.e. our analyses examined religious service attendance not only as a predictor of death by suicide but also time to this event, which would differ from decrement to decrement). We agree that intermediate data in between the time an individual reported on their religious service attendance and the end of the study or their death would be desirable. It is important, however, to consider the feasibility of conducting such a multi-wave study with a large enough sample for meaningful analysis of a low-base-rate event, such as death by suicide, as the outcome of interest. Additionally, we believe it is particularly telling that our measure of religious service attendance was able to predict suicide deaths in some cases several years later, despite any intermediate life changes. This might be because of the fact that a large number of participants (42%) in the data-set were over 50; frequency of religious service attendance tends to be relatively stable in that age group.\(^2\) Thus, religious service attendance might not have varied much over the course of the study.

Third, as suggested by Yates & Arya, collecting data on individual (v. population level) time-varying prospective predictors of suicide might be ideal. Such a study, however, would be extremely expensive and resource intensive. Indeed, over 20 000 people were needed for a data-set that had 25 suicides and data-sets such as this are rare. The number of participants needed to test the hypotheses in a fashion suggested by Yates & Arya would be quite substantially more, and the related resources needed to conduct such a study would be magnified with each follow-up assessment.

Fourth, Yates & Arya stated that using suicide deaths as an outcome variable might not be an advantage relative to using attempted suicide, in part because of the greater relevance of the latter to clinical settings. We caution against this view for several reasons. First, as highlighted by Cook, the use of attempted suicide was designed to increase the power of the study. Second, as the authors correctly note, literature suggests a gradient in risk from suicide attempts to suicide completions, such that religious service attendance might be a stronger predictor of the former. Finally, as we noted in our reply, in our clinical practice we find that the relationship between religious service attendance and suicide risk is complex, such that intermediate data would be useful.


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reasons. First, both deaths by suicide and suicide attempts are important public health concerns. Although a prior history of suicidal behaviour is indeed a strong predictor of future suicidal behaviour, a very large proportion of suicide deaths occur with the first attempt. Second, as cited in our manuscript, research finds that although suicide attempters and suicide decedents are overlapping groups, there is still a considerable lack of overlap between the two groups. Over 90% of people who attempt suicide do not go on to die by suicide. Moreover, several studies have assessed religion as a predictor of suicide attempts and thus our focus on death by suicide builds upon this literature.


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Correction

Is depression one thing or many (letter)? BJP, 204, 488. The second author is: A. Odone. The online version of this letter has been corrected post-publication, in deviation from print and in accordance with this correction.

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Retraction

Childhood maltreatment and methylation of the glucocorticoid receptor gene NR3C1 in bipolar disorder. BJP, 204, 30–35. An investigation carried out at the request of the Dean of the Faculty of Medicine of the University of Geneva has concluded that one of the authors (Alain Malafosse) fabricated methylation data. A reanalysis of the DNA reveals no significant correlation between childhood trauma and methylation of the NR3C1 gene. The original conclusions therefore no longer hold true and we wish to retract the paper.

J. M. Aubry, A. Dayer, N. Perroud, C. Piguet, A. Nallet, S. Favre

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