The Psychosocial Effects of Drug-Induced Akathisia

A thesis submitted to the University of Manchester for the Degree of Doctor of Clinical Psychology in the Faculty of Biology, Medicine and Health

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List of Contents

	Word count *Excluding references and appendices but including footnotes, tables and figures*
Paper 1	8,571
Paper 2	8,859
Paper 3	5,989
Total	**23,419**

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Abstract

Overall topic and aim: This thesis explored the psychosocial implications of the drug-induced movement disorder, akathisia. The thesis consists of three papers: 1) a systematic literature review, 2) an empirical study, and 3) a critical appraisal of the research process.

The systematic literature review (Paper 1) is a mixed-methods narrative synthesis looking at the evidence for an association between akathisia and suicidality. 21 studies were identified (13 quantitative studies and eight case reports) from a search of five scientific databases. Seven of the quantitative studies reported a significant association between akathisia and suicidality, and six did not report a significant association. All case reports described an association between akathisia and suicidality. Akathisia and suicidality were associated with both first- and second-generation antipsychotic medications and this relationship was influenced by age, medication-related factors, affective and cognitive issues, and methods of assessing akathisia. The results are discussed in relation to existent research and implications for clinical practice are offered.

The empirical study (Paper 2) explored service user's first-hand experiences of akathisia. Six participants took part in semi-structured interviews which were analysed using Interpretative Phenomenological Analysis (IPA). Three superordinate themes were identified: *'Journey through the mental health system'*, *'adjustment to life with akathisia'*, and *'the internal experience of akathisia'*. Results demonstrated that participants associated akathisia with a plethora of psychological and social implications, including: changes in occupation, interaction, relationships, cognition, identity, psychological wellbeing and suicidality, compounded by negative experiences of mental health services. Findings were consistent with previous research and provide novel insights into the experiences of individuals who develop akathisia. Implications for clinical practice are offered.

Paper 3 is a critical appraisal of the research process, which identifies the rationale for decisions made, evaluation of the methods used, additional strengths and limitations, and the contribution of the research to the literature on akathisia. The researcher's personal reflections are offered throughout.

Declaration

No portion of the work submitted in this thesis has been submitted in support of an application for another degree or qualification of this or any other University or other institute of learning.

Copyright Statement

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Firstly, I would like to thank my research supervisor's, Dr Sara Tai and Ms Yvonne Awenat, for their support, guidance and supervision throughout the research process, which was imperative to the successful completion of this thesis. I would also like to thank the participants who were kind enough to give their time to take part in the research.

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Paper 1: Literature Review

The Association between Akathisia and Suicidality after Neuroleptic Intervention: A Systematic Review of the Evidence

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Prepared in accordance with requirements for submission to the Journal of Human Psychopharmacology (appendix A)

Abstract

Purpose: Akathisia is a drug-induced movement disorder primarily associated with the use of neuroleptic and psychotropic medications. Service users with akathisia report internal feelings of restlessness and experience an inability to sit still. The current review systematically examined existing literature for potential evidence of an association between akathisia and suicidality. Secondary aims were to identify other factors that potentially influence any association and to assess the quality of the available evidence.

Method: A literature search of five electronic scientific databases (PsycINFO, EMBASE, MEDLINE, CINAHL, Web of Science), reference lists and grey literature was completed. All studies were quality appraised and the results were synthesised using a convergent narrative approach.

Results: 21 articles met inclusion criteria for the study: 13 quantitative studies and eight case reports. Seven quantitative studies reported a significant association between akathisia and suicidality and six did not report a significant association. All case reports described an association between akathisia and suicidality. There was variation in the quality and reporting in all quantitative studies and case reports. Akathisia and suicidality were associated with both first- and second-generation antipsychotics, and several forms of suicidality were identified. A range of factors were found to influence the association between akathisia and suicidality, namely: age, medication-related factors, how akathisia is rated and by whom, and affective and cognitive issues.

Conclusions: The results provide partial evidence for an association between akathisia and suicidality. Directions for future research and implications for clinical practice are offered.

Key words: Akathisia, restlessness, agitation, movement disorder, side effects, extrapyramidal, suicidality, suicide.

Introduction

Akathisia (a term coined by Hascovec in 1902 from the Greek meaning, 'not to sit'), is a 'syndrome' characterised by intense feelings of inner-restlessness and an inability to sit still. In the absence of a universally accepted definition and specific set of criteria for akathisia, it is a challenging condition to research (Hansen, 2001; Tachere & Modirrousta, 2017). Researchers generally agree that akathisia consists of both subjective and objective components (Barnes, 1989), often accompanied by a sense of restlessness and feelings of panic, tension, irritability and impatience (Akagi & Kumar, 2002; Kane et al., 2009). Though akathisia is generally considered a 'movement disorder' or 'extrapyramidal side effect' (Lane, 1998; Hamilton & Opler, 1992), others argue that it should be recognised as a sensorimotor disorder, due to the sensory symptoms individuals describe (Lohr, Eidt, Alfaraj & Soliman, 2015; Shear, Frances & Weiden, 1983). Researchers have attempted to classify akathisia into various subtypes, namely: acute, chronic, tardive, and withdrawal-related and pseudo akathisia (Halstead, Barnes & Speller, 1994; Barnes & Braude, 1985; Sachdev, 1995). However, the underlying pathophysiology of akathisia remains incompletely understood (Hansen, 2001).

The American Psychiatric Association (APA) (2013) described akathisia as *'subjective complaints of restlessness, often accompanied by observed excessive movements (e.g. fidgety movements of the legs, rocking from foot to foot, pacing, inability to sit or stand still), developing within a few weeks of starting or raising the dosage of a medication (such as neuroleptic) or after reducing the dosage of a medication used to treat extrapyramidal symptoms'.* Akathisia was initially known to develop as a side effect of neuroleptic medications; specifically, first-generation antipsychotics (FGA's) (Sachdev & Loneragan, 1991). Research has since identified that newer second-generation (or 'atypical') antipsychotics (SGA's) (Avantis & Miller, 1997; King, Burke & Lucas, 1995) are also linked with akathisia, despite some researchers arguing that newer medications produce fewer side effects (Chung & Chiu, 1996)[1]. Several studies have also found antidepressant medications to be

[1] Given the contentious debate around the use of the term 'antipsychotic' (King & Voruganti, 2002), 'neuroleptic' will be used to refer to antipsychotic medication. However, in instances where authors differentiate between FGA's or SGA's, their terminology will not be altered.

linked with akathisia (Lane, 1998; Hansen & Wilkinson, 2001; Olivera, 1996; Gerber & Lynd, 1998); however, it continues to be primarily associated with antidopaminergic neuroleptics (Sabaawi, Holmes & Fragala, 1994; Sachdev & Saharov, 1998; Miller et al., 1998).

Sachdev (1995) estimated that neuroleptic-induced akathisia was present in 25-75% of people with psychiatric diagnoses, making it one of the most common side effects of neuroleptic medication (Lohr et al., 2015). Regarding neuroleptic medications specifically, Van Putten, May and Marder (1984) diagnosed akathisia in 40% of participants within six hours of receiving medication. In their descriptive studies, Healy and Farquhar (1998) found akathisia present in all six individuals receiving neuroleptic medications and King et al (1995) diagnosed 16% of their sample with akathisia. In a review study by Lane (1998) the incidence rates of akathisia from selective serotonin reuptake inhibitor (SSRI) medication ranged between 4.5-25%.

Difficulties in defining akathisia have caused challenges in recognition and treatment (Shear et al., 1983; Hirose, 2003) which likely impacts prevalence rates. For example, Hansen (2001) found that reports focusing on subjective components of akathisia appeared to have higher incidence rates than those targeting objective components. Lohr et al (2015) and Lane (1998) also highlighted that challenges in describing the sensations associated with akathisia can make it difficult for individuals to articulate what they are experiencing, preventing them from reporting symptoms to professionals, and resulting in underdiagnoses. Consequently, akathisia often goes unrecognised (Lane, 1998; Tachere & Modirrousta, 2017) and can be misconstrued for anxiety, agitation, Tourette's syndrome, tardive dyskinesia and neuroleptic-induced dystonia (Lohr et al., 2015).

Several researchers have identified associations between akathisia and increased aggressive and violent behaviour (Keckich, 1978; Leong & Silva, 2003; Galynker & Nazarian, 1997; Azhar & Varma, 1992; Crowner et al., 1990). Akathisia has also been found to trigger an increase in self-injurious behaviour and suicidality (Hansen, 2001; Hamilton & Opler, 1992; Atbasoglu, Schultz & Andreasen, 2001). The seminal report by Shear, Frances & Weiden (1983) on the association between akathisia and suicidality reported on two males who developed suicidal ideation and

behaviours, which they attributed directly to akathisia. The same conclusions have been reported in several other case report studies (Azhar & Varma, 1992; Drake & Ehrlich, 1985; Weiden, 1985; Popli & Gupta, 1993; Weddington & Banner, 1986), case series (Van Putten, 1974; Schulte, 1985; Chouinard, 1991; Rothschild & Locke, 1991; Wirshing et al., 1992) and one prevalence study (Sandyk, Kay, Awerbuch & Iacono, 1991). Previous literature reviews have also proposed links between akathisia and suicidality (Lane, 1998; Margolese, Chouinard, Walters Larach & Beauclair, 2001). In contrast, some researchers have argued that although akathisia is considered to worsen pre-existing suicidal ideation, it cannot be inextricably linked (Chung & Chiu, 1996; Crowner et al., 1990).

A previous literature review by Hansen (2001) examined available evidence and explored the potential association between akathisia and suicidality. A systematic search identified 26 studies, and although the majority of these were case reports concluding that suicidality increased as a result of akathisia, empirical studies also found that individuals with akathisia had increased de novo suicidal, homicidal and violent ideations (e.g. Shaw, Mann & Weiden, 1986; Hamilton & Opler, 1992). Hansen concluded that the available evidence at that time was insufficient to provide a definitive causal link between akathisia and suicidality, and although the possibility could not be excluded, further research was needed.

The association between akathisia and suicidality continues to be a complex and controversial topic, with inconsistent conclusions being drawn across studies (Hansen, Nausheen, Hart & Kingdon, 2013). Some suggest additional factors determine the development of suicidality following onset of akathisia (Lohr et al., 2015), and more recent research has highlighted that medication-related factors, subjective versus objective ratings of akathisia, age, cognitive impacts and affective issues, may influence this association. The current review will explore these in greater detail.

The number of studies published since the Hansen (2001) review warrants an updated review of more recent findings. The aim of the current paper is to undertake a systematic review and narrative synthesis of the research evidence for an association between akathisia and suicidality, thereby contributing to current

scientific knowledge. For the purposes of the current review 'suicidality' will be defined as suicidal ideations (thoughts), suicide plans, suicide behaviour (including attempted suicide), parasuicide, and completed suicide. Suicidality may be captured by self-reports, clinician-reported suicidality, or frequency data (i.e. serious incidents, attempted suicide, completed suicide).

The 'five year forward view for mental health' report by an independent Mental Health Taskforce to the NHS in England, outlined targets to reduce suicides by 10% by 2020 (NHS England, 2016). If evidence does support an association between akathisia and suicidality, it is important to raise awareness of this. Therefore, the current review has the potential to inform policy and regulations on suicidality, provide clinicians with updated information on the development of akathisia and suicidality (including factors potentially influencing the relationship, and current interventions), and ultimately inform the clinical care of individuals who develop akathisia secondary to neuroleptic medication use. The primary review question and objectives are as follows:

Primary Review Question:

Does the available evidence support an association between akathisia and suicidality?

Review Objectives:

1. Synthesise the evidence within the literature for a potential association between akathisia and suicidality.
2. Identify additional factors that might influence any association between akathisia and suicidality.
3. Examine the methods used within studies exploring the association between akathisia and suicidality.
4. Assess the quality of the evidence on the association between akathisia and suicidality.

Method

Literature Search

The search included electronic databases (PsycINFO, EMBASE, MEDLINE, CINAHL, Web of Science) and was restricted to studies with adults (over the age of 16 years) published between 2001 to 2019. No limitations were placed on language. Hand searching of reference lists for selected papers was completed to identify other potentially eligible studies. Following the removal of duplicates the first author (LB) screened the titles and abstracts of the identified studies, with an independent researcher screening 20% of these papers. Full paper screening was also completed by the first author with 20% of these screened by an independent researcher. Inter-rater reliability was calculated at (100%). The final search was completed in December 2019 and downloaded into EndNote X9. The current review and protocol are registered with PROSPERO (Centre for Reviews and Dissemination (CRD) 2020), registration number: CRD42020112001.

Search Strategy

The search strategy included search term combinations of two key blocks of key words: akathisi* OR acathisi* OR restless* OR movement OR agitat* OR "side effects"; AND suicid* OR "self harm" OR "self-injurious behavi*".

Inclusion/ Exclusion Criteria

Inclusion criteria were as follows:

1. Full text articles that included original research investigating the association between akathisia and symptoms associated with akathisia and suicidality
2. Studies including Randomised Controlled Trials (RCT's), quantitative studies, qualitative studies, case report studies, letters to the editor, peer reviewed notes or summary articles
3. Studies on neuroleptic medications
4. Publications from 2001 onwards
5. Research with adults (16 years and over)
6. Articles in English or where an English translation was available
7. Grey literature

8. Articles on human subjects

Exclusion criteria were as follows:

1. Research on non-human participants
2. Research with children or adolescents
3. Studies relating to antidepressant medications

Critical Appraisal

Quantitative studies and case reports were separated at the quality appraisal stage so the evidence could be examined separately, in accordance with recommendations for conducting a systematic literature review with diverse results (Sirriyeh, Lawton, Gardner & Armitage, 2012). It was important to undertake a critical appraisal of the literature to address the overall review question, the objectives, assess for potential bias, and review the overall generalisability of the studies.

Quantitative studies were appraised using the Quality Assessment Tool for Studies with Diverse Designs (QATSDD), a reliable and valid tool for assessing quality in studies with diverse designs (Sirriyeh et al., 2012)[2]. The QATSDD was based on adapted criteria as outlined in Jackson, Cheater and Reid (2008). This tool was considered the most appropriate for assessing for the risk of bias given the heterogeneity in the quantitative studies. Five of the 13 quantitative papers included in the current review were also quality assessed by a second researcher. Inter-rater reliability was calculated at (88%) (kappa = 0.847) showing strong agreement. Any discrepancies were discussed in order to reach consensus.

Tools for appraising the quality of case reports are limited. For the current review, a bespoke tool was created (appendix B), by integrating and adapting items from existing tools; namely the 'CARE' case report guidelines (Riley et al., 2017), the checklist for case reports by the Joanna Briggs Institute (Moola et al., 2017) and the case series and case report assessment tool by Murad, Sultan, Haffar and Bazerbachi (2018). This bespoke tool enabled comparisons to be made between the case reports and for the quality and risk of bias to be assessed.

[2] The QATSDD is a 16-item scale which utilises a 4-point scoring scale from 0-3. The aggregated scores are then calculated to provide an overall percentile.

Synthesis of Findings

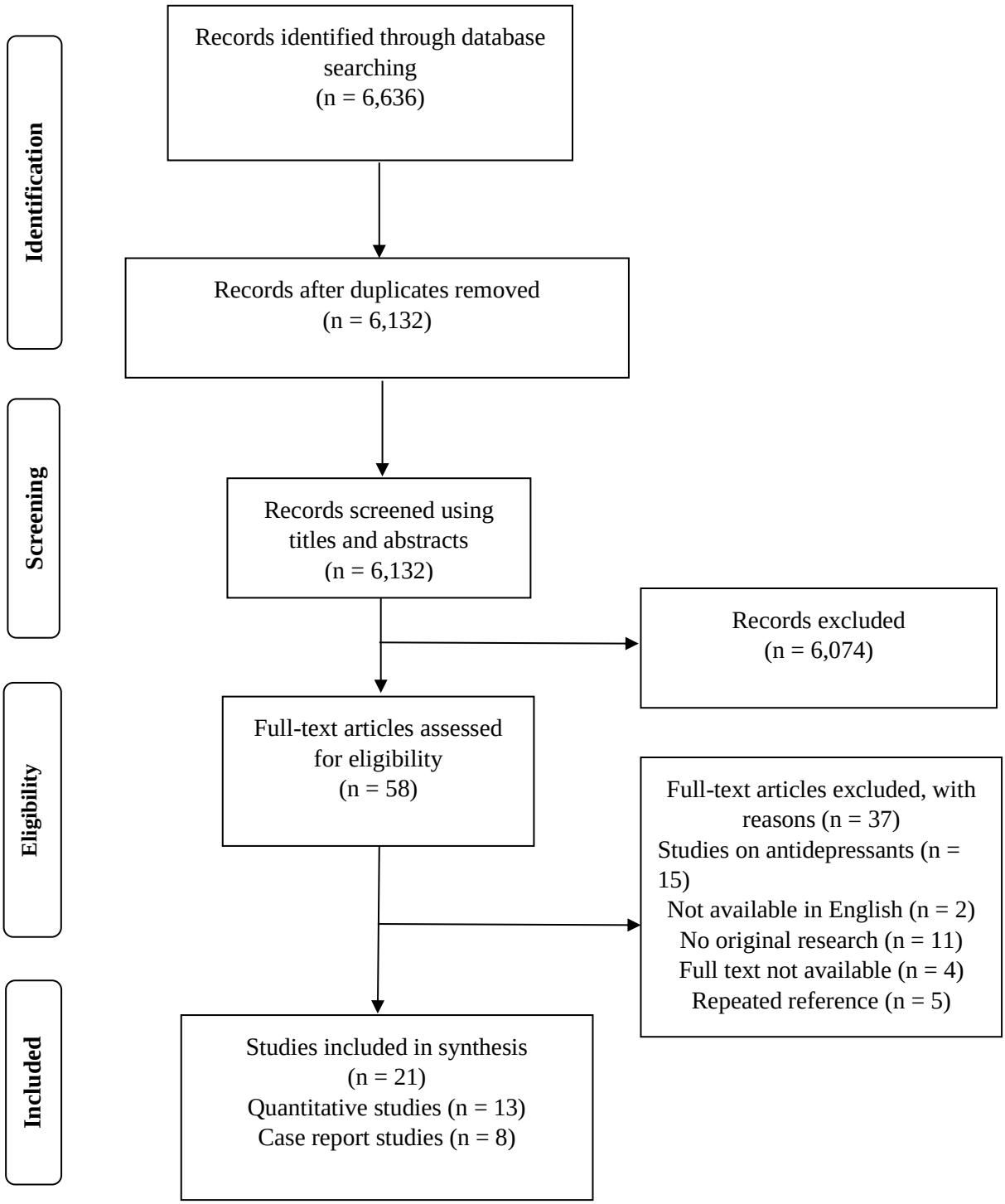
Studies were analysed using a convergent synthesis design (Hong, Pluye, Bujold & Wassef, 2017). This involved data from quantitative studies and case reports being extracted and analysed separately. A formal narrative synthesis approach was completed in accordance with guidance (Popay et al., 2006; CRD, 2008; Ryan, 2013) and coinciding with the outcomes of the review. The methodological heterogeneity of the finalised studies meant that formal statistical methods (e.g. meta-analysis) were not suitable and a narrative synthesis was an appropriate alternative (Campbell, Katikireddi, Sowden, McKenzie & Thomson, 2018).

Results

Characteristics of Included Studies

Searches of electronic databases identified 6,636 potentially relevant studies. Three papers retrieved were published in other languages; one in Russian and two in Turkish. The authors of these papers were contacted and an English translation was provided for the Russian article. The authors of the Turkish papers did not respond. Following screening a total of 21 studies were deemed to meet inclusion criteria and were included in the review. Overall, 2,283 participants were included across all studies. The search for grey literature revealed no results that met inclusion criteria.

Figure 1: PRISMA Flow Diagram



Quantitative Studies

Table 1: Characteristics and Quality of Studies: Significant Association Found

First author and year	Sample and participant characteristics	Aim	Design and relevant measures	Main findings	Additional influencing factors	Quality assessment rating %
Atbasoglu (2001)	68 participants: 49 males, 19 females, diagnosed with schizophrenia or schizophreniform disorder.	To investigate the relationship between drug-induced akathisia, dysphoria, suicidality and feelings of depersonalisation.	Between groups cross sectional design. Akathisia measured using the BARS[3]. Suicidality measured using the HAM-D[4].	Presence of akathisia was significantly associated with suicide and agitation. Greater likelihood of suicidality among participants with akathisia than those without.	Depressed mood and anxiety. Subjective versus objective ratings.	64%
Dong (2005)	92 cases, 92 matched controls.	To describe and identify the risk factors of inpatient suicides during psychiatric inpatient care.	Retrospective 1:1 matched pair's case-control design. Suicide assessed by the Questionnaire for Hong Kong Psychiatric Patients Suicide.	Extrapyramidal side effects and akathisia were significant risk factors for inpatient suicide.	Symptom severity.	81%
[5]Emsley (2003)	555 participants: 277 haloperidol group, 278 risperidone group.	To compare the incidence and severity of akathisia in patients diagnosed with recent onset schizophrenia who were treated with either haloperidol or risperidone. To assess the relationship between akathisia and suicidality.	Randomised Control Trial (RCT) (summary). Akathisia measured by the physician and patient items from the ESRS[6]. Suicidality recorded on an adverse effects reporting form.	Patients who were suicidal during the trial had significantly higher self-reported levels of akathisia at baseline than those who were not. Feelings of inner restlessness, or patient-reported akathisia, predicted subsequent suicidality.	Type of medication received.	N/A

[3] Barnes Akathisia Rating Scale (Barnes, 1989; 2003)
[4] Hamilton Depression Scale (Hamilton, 1960)
[5] The study by Emsley, Davidson & Rabinowitz (2003) was a summary article and was not appropriate for quality assessment
[6] Extrapyramidal Symptom Rating Scale (Chouinard & Margolese, 2005)

Moncrieff (2009)	439 participant comments in total: 223 comments on risperidone, 170 on olanzapine, 46 on older neuroleptics.	To investigate the subjective effects experienced with olanzapine, risperidone and older neuroleptics.	Mixed-methods content analysis. Presence of akathisia and suicidality determined by self-report comments.	Akathisia was strongly associated with suicidal thoughts; particularly for olanzapine. Suicidal thoughts were strongly associated with reporting akathisia: 13.8% of respondents reporting akathisia also reported suicidal thoughts.	Type of medication received. Impact of impaired cognitive abilities.	64%
Pompili (2009)	20 cases, 20 controls: 18 males, 2 females all diagnosed with schizophrenia.	To compare individuals diagnosed with schizophrenia who completed suicide with living individuals with the same diagnosis.	Retrospective matched pairs case-control design. Symptoms of akathisia and suicidality rated according to a bespoke checklist.	Agitation and motor restlessness predicted suicidality.	Medication adherence. Insomnia.	62%
Seemuller (2012a)	296 participants: 148 in risperidone group, 148 in haloperidol group. 40.5% female, 59.5% male *(M = 41 years)*.	To compare risperidone and haloperidol on the relationship between akathisia and suicidality in patients diagnosed with first-episode schizophrenia.	RCT. Randomly assigned to treatment groups in 1:1 ratio. Akathisia measured by the HAS[7]. Suicidality measured by the HAM-D.	Suicidal ideation was significantly associated with clinically observed akathisia. The findings suggest a promoting effect of akathisia on suicidal ideation cannot be ruled out in patients diagnosed with first-episode schizophrenia.	Medication differences. Subjective versus objective ratings. Depression.	69%
Seemuller (2012b)	10 participants with suicidality: 6 from the risperidone group, 4 from haloperidol group. 8 males, 2 females *(M = 24 years)*.	To analyse on a single case basis the relationship between a sudden increase in suicidality, anxiety symptoms, medication dosing and clinician and patient-rated akathisia.	Case series design taken from the data from a larger RCT. Akathisia measured by the HAS. Suicidality measured by the HAM-D.	Found a positive relationship between suicidality and akathisia scores within the titration period of the study medication.	Subjective versus objective ratings. Age.	45%

[7] Hillside Akathisia Scale (Fleischhacker et al., 1989; Fleischhacker, Miller, Schett, Barnas & Ehrmann, 1991)

Table 2: Characteristics and Quality of Studies: No Significant Association Found

First author and year	Sample and participant characteristics	Aim	Design and relevant measures	Main findings	Additional influencing factors	Quality assessment rating %
Hansen (2004)	86 participants divided into two groups: akathisia present, akathisia absent.	To investigate whether there is an association between akathisia or parkinsonism and suicidality.	Sub-analysis from a RCT. Longitudinal, between groups design. Akathisia measured by the BARS. Suicidality measured by the CPRS[8].	At no time point was there a significant association between akathisia and depression/ suicidality or distress associated with akathisia and suicidality. No difference between suicidality scores in the two groups was found at Time 1 or Time 2.	N/A	52%
Hansen (2013)	70 patients diagnosed with schizophrenia: 54 males, 16 females *(M = 38 years).*	To investigate the relationships between drug and alcohol use and extrapyramidal symptoms in people diagnosed with schizophrenia.	Cohort design. Akathisia measured by the BARS. Suicidality measured by subscale from HONOS[9].	Suicidality was not linked with akathisia.	Possible links between gender and the development of extrapyramidal symptoms.	64%
Kornetova (2018)	71 patients: 37 males, 34 females. 27 participants with akathisia, 44 participants not with akathisia.	To identify the relationship between parasuicides in history, hopelessness, akathisia and key clinical-dynamic indicators in patients diagnosed with schizophrenia.	Cross sectional, between groups design. Akathisia measured by the BARS. Suicidality measured by BHS[10].	It was not possible to establish a link between parasuicides in the past, hopelessness and akathisia at the time of the survey. No significant statistical differences noted on the BHS between those with and without akathisia.	Age.	62%

[8] Comprehensive Psychopathological Rating Scale (Asberg, Montgomery, Perris, Schalling & Sedvall, 1978)
[9] Health of the Nation Outcome Scales (Wing et al., 1998)
[10] Beck Hopelessness Scale (Beck, Weissman, Lester & Trexler, 1974)

Lukaschek (2014)	101 cases, 101 controls matched on: gender, age, admission date and inpatient treatment, primary psychiatric diagnosis. Sample was 63.4% male *(M = 40 years).*	To identify determinants of railway suicides in individuals receiving in-patient psychiatric treatment.	Retrospective, matched pair case-control design. Bespoke measure of sociodemographic information.	Neither restlessness nor impulsivity predicted in-patient suicide. Difference between cases and controls regarding restlessness was not significant.	Changes in therapist.	71%
[11]Mlodozeniec (2009)	86 participants diagnosed with schizophrenia or schizoaffective disorder.	To explore the possible association between akathisia and suicidality.	Cross sectional, between groups design (summary). Suicidality measured by the ISST[12] and the CGI-SS[13]. Akathisia measured on the BARS.	No significant association found between the presence of akathisia and suicidality measured on the ISST.	N/A	N/A
Reutfors (2016)	84 cases, 84 matched controls. Suicide cases: 45 males, 39 females. Matched controls: 50 males, and 34 females.	To explore the risk of suicide in response to symptoms that are known to emerge from taking neuroleptic medication.	Retrospective population-based, matched pairs nested case-control design.	Akathisia was not significantly associated with increased suicide risk, though it did constitute an increased risk for suicidality.	Medication adherence. Polypharmacy.	64%

[11] The study by Mlodozeniec et al (2009) was a summary article and was not appropriate for quality assessment
[12] InterSePT Scale for Suicidal Thinking (Lindenmayer et al., 2003)
[13] Clinical Global Impression Scale for Severity of Suicidality (Busner & Targum, 2007)

Case Reports

Table 3: Characteristics and Quality of Included Studies

First author and year	Participant characteristics	Relevant history	Reported symptoms	Relevant measures	Report summary and main findings	Quality assessment rating %
Cheng (2013)	Male, 38 years	Diagnosis of schizoaffective disorder, traumatic brain injury, no prior suicidality.	Restlessness, frustration, agitation and secondary low mood.	Mental state examination.	Reports on an individual who developed akathisia after commencing pipotiazine, after which they shot themselves in the mouth. After medication changes and being prescribed risperidone and lorazepam, they reported no suicidal ideation or akathisia. Concludes that clinicians should consider akathisia developing whenever alterations are made to medications.	81%
Hansen (2001)	Male, 83 years	Depression.	Urge to move, not being able to keep lower limbs still.	BARS.	Reports that after commencing risperidone the individual developed symptoms of akathisia and suicidal ideation due to the restlessness. Electro convulsive therapy (ECT) was administered and they remained on a low dose of risperidone. Subjective complaints of akathisia dissipated after ECT. Concludes that in extreme cases neuroleptics can lead to suicidal ideation and behaviour.	89%
Inoue (2010)	Female, 37 years	Receiving chemotherapy for breast cancer.	Restlessness, fidgety movements, inability to sit or stand still.	N/A	Reports that after receiving prochlorperazine symptoms of akathisia developed. After prochlorperazine was discontinued akathisia symptoms dissipated. The individual also received psychotherapy. Concludes the increase in prochlorperazine triggered akathisia and domperidone should be substituted in the treatment of individuals with cancer.	77%
Kertesz (2018)	Female, 81 years	Postpartum depression accompanied by suicidal ideation.	Anxious, continuous vocalisations, could not sleep, inner-restlessness, urge to make sounds.	Psychiatric examination.	Reports an individual who developed repetitive vocalisations when treated with risperidone. After substituting this for quetiapine, the individual's symptoms intensified. Tetrabenazine was added and symptoms subsided within a week. Concludes that the levels of distress related to akathisia constitute a risk factor for suicidality.	81%

Padder (2006)	Male, 23 years	Diagnosed with mood disorder, substance misuse, anger.	Restlessness, irritability, inability to sit still, constant desire to move.	Initial mental status examination.	Reports how after increasing the dosage of aripiprazole akathisia developed. Aripiprazole was discontinued and propranolol and benzodiazepines commenced, symptoms of akathisia then dissipated. Concludes that further studies should look into the development of akathisia and suicidality for individuals treated with aripiprazole.	77%
Penders (2013)	Female, 67 years	Depression, Diagnosis of bipolar II.	Anxiety, restlessness, unable to sit still, pervasive insomnia, subjective despondency.	Suicidality: QIDS[14]	Reports on an individual prescribed ziprasidone and soon after, clozapine. Five days after clozapine was added they developed akathisia and suicidal ideation. After several medication alterations akathisia resolved over a three-week period. Concludes that second-generation neuroleptic drugs can cause akathisia and clinicians should be aware of this.	85%
Ponde (2015a)	Female, 29 years	Trauma, abuse, psychosis, depression, suicidal ideation and behaviour.	Inability to sit still, anxiety, insomnia, anguish.	N/A	Reports after being treated with aripiprazole the individual developed akathisia. The dosage was increased twice and as the symptoms worsened suicidal ideation increased. All medications were discontinued and symptoms improved after the introduction of clozapine.	81%
Ponde (2015b)	Male, 56 years	Childhood abuse and social withdrawal.	Psychomotor agitation, increased anxiety, restlessness, unable to remain still.	N/A	Reports akathisia began after risperidone commenced. As a result, suicidal ideation intensified. Akathisia dissipated after all other medications were discontinued and clozapine was prescribed.	73%

[14] Quick Inventory of Depressive Symptomatology (Rush et al., 2003)

What evidence can be found within the literature of potential associations between akathisia and suicidality?

Quantitative Studies

Seven studies reported a significant association between akathisia and suicidality. Atbasoglu et al (2001) found that the presence of akathisia was significantly associated with general suicidality[15] *(x2 = 7.38, df = 1, p = 0.007),* and Dong, Ho & Kan (2005), who sought to investigate risk factors for completed inpatient suicides, reported that akathisia was a significant risk factor that predicted inpatient suicide *(OR = 10.8, 95% CI = 1.75-66.7, p = 0.02).* Pompili et al (2009), who also investigated risk factors for completed suicides, found that agitation and motor restlessness were factors that significantly predicted subsequent suicidality *(OR = 3.66, 95% CI = 0.95-14.02, z = 1.90, p = 0.05).* Emsley et al (2003) investigated general suicidality and found that individuals who exhibited suicidality had significantly higher self-reported levels of akathisia than those not exhibiting suicidality. In the study by Moncrieff, Cohen & Mason (2009), the presence of akathisia was found to be significantly associated with suicidal ideation *(x2 = 3.12, df = 1, p = < 0.001).* Seemuller et al (2012a) found that suicidal ideation was also significantly associated with clinician-observed akathisia *(p = 0.02),* and Seemuller et al (2012b) found a positive relationship between emergent suicidality and akathisia scores, when participants were analysed on a single case basis.

Six studies did not report an association between akathisia and suicidality. Hansen, Jones and Kingdon (2004) did not find a significant association between akathisia and suicidality at time one (baseline) *(r = -0.346, p = 0.728, SD = 1.07)* or time two (nine months) *(r = -0.425, p = 0.671, SD = 1.00)* of their study, which investigated suicidal ideation; however, no results were provided for time three (18 months) as they had insufficient ratings for interpretation. They also noted a trend that suicidality had decreased in both the akathisia present and akathisia absent groups between time one and time two. Hansen, Nausheen, Hart and Kingdon (2013) also found no significant association between suicidality and akathisia when investigating general suicidality. Kornetova et al (2018) found that there were no significant

[15] 'General suicidality' refers to suicidal ideation and suicidal behaviour.

differences between those with and without akathisia in their study investigating parasuicide *(p = 0.954).* In a study investigating risk factors for completed suicide, Lukaschek et al (2014) found that neither restlessness nor impulsivity were significant predictors of inpatient suicide (*p = 0.19*), and Mlodozeniec et al (2009) found no statistically significant association between individuals with and without akathisia when investigating suicidal ideation. The study by Reutfors et al (2016) investigating risk factors for suicide found that although there was a trend of akathisia being associated with an increased risk for suicide, this was not statistically significant (*OR = 1.29, CI = 0.48-3.45*)[16].

Case Report Studies

Eight case reports were included in the review and all aimed to provide novel information regarding the development of akathisia and increased suicidality, and the interventions undertaken thereafter. All case reports concluded that suicidality increased subsequent to the development of akathisia. 'Patients' were described as attributing the increase in suicidality to symptoms of akathisia, which they in-turn attributed to medications. Individuals reported experiencing a range of symptoms related to akathisia such as restlessness, agitation, fidgetiness, inability to sit still, an urge to move, anxiety and anguish. Suicidality was described within the reports as involving suicidal ideation and attempts to end one's own life. The reports included four males and four females ranging in age from 23 years to 83 years *(M = 51 years).* Medications associated with the development of akathisia were all SGA's, including: pipotiazine, risperidone, prochlorperazine, aripiprazole, clozapine and ziprasidone. Though case reports have limited generalisability, they provide useful clinical information to inform the care and treatment of individuals who develop akathisia secondary to neuroleptic intervention. Table 3 provides an overview of the reports, the conclusions made, measures used, symptoms described and the demographics of service users.

[16] Some studies that did not find a significant association between akathisia and suicidality noted trends. However, for most quantitative studies the association between akathisia and suicidality formed one aspect of a wider study, and further interpretation of results was not always provided.

What additional factors have been found to influence any association between akathisia and suicidality?

Quantitative Studies

Several studies highlighted factors that were demonstrated or hypothesised to influence an increase in suicidality following the development of akathisia. Kornetova et al (2018) found that individuals who had akathisia and developed parasuicide had a younger mean age in comparison to individuals who did not. Seemuller et al (2012b) also reported that individuals who developed suicidality in response to akathisia were significantly younger and exhibited higher levels of suicidality by the end of the study period.

Several studies highlighted the impact that medication had on the development of akathisia and suicidality. Pompili et al (2009) demonstrated a significant association between suicidality and lower adherence to medication after the development of akathisia. Reutfors et al (2016) reported that although their findings did not show a significant association between akathisia and suicidality, this was likely due to greater levels of adherence with prescribed medication during the study. Regarding types of medication described in the studies, Seemuller et al (2012a) found that individuals treated with haloperidol experienced significantly more akathisia, as measured by the HAS, when compared to risperidone; although medication type was not analysed in relation to akathisia and suicidality specifically. Moncrieff et al (2009) demonstrated that significantly more individuals taking olanzapine *($x2 = 46.7, df = 1, p < 0.001$)* experienced suicidal ideations associated with akathisia compared to risperidone. Emsley et al (2003) also found risperidone to be associated with a lower risk of patient-reported and physician-assessed akathisia and suicidality, compared with haloperidol. Seemuller et al's (2012b) results reported that seven individuals with akathisia received increased dosages of either risperidone or haloperidol close to the time of suicidality developing.

Three studies highlighted differences in subjective and objective ratings of akathisia in relation to the development of subsequent suicidality. Seemuller et al (2012b) found that there was a significantly higher number of individuals who reported increased subjective ratings of akathisia related to suicidality, in comparison to

clinician-rated akathisia and suicidality. They also found that subjective ratings of akathisia occurred more frequently in those with suicidality when compared to non-suicidal patients. The study by Atbasoglu et al (2001) found that suicidality was related with subjective ratings of akathisia; however, it was not significantly associated with objective ratings by clinicians. In contrast, Seemuller et al (2012a) found clinician-rated akathisia was significantly associated with akathisia and suicidality, whereas subjective ratings were not. Regarding the severity of akathisia, Dong et al (2005) hypothesised that the mild nature of the akathisia experienced by individuals within their study may have minimised their results, and Hansen et al (2004) also concluded that the mild levels of akathisia in their study may *'not have been sufficient to cause an increase in suicidality'* (p. 387).

More generally, Atbasoglu et al (2001) reported that anxiety and depression scores for individuals with akathisia were significantly higher in people who were suicidal compared to people who were not suicidal. They also found that depressed mood and subjective awareness of akathisia were predictors of suicidality. Depressed mood was significantly associated with the development of suicidality in individuals experiencing akathisia in Seemuller et al (2012a), and Pompili et al (2009) reported that insomnia induced by restlessness was a predictor of suicidality; although, no specific analysis was conducted on insomnia, restlessness and akathisia. Both studies by Seemuller et al (2012a, 2012b) found that suicidality occurred after the development of akathisia, except in one case where akathisia developed subsequent to suicidality. Also, no association between anxiety and suicidal ideation was found; which may indicate that suicidal ideation was a direct result of akathisia (Seemuller et al., 2012b). Moncrieff et al (2009) described how impaired cognition, including slowing of mental processes, mental clouding, and feelings of reduced intelligence, were reported by individuals who experienced suicidality subsequent to the development of akathisia. Lukaschek et al (2014) also demonstrated how retirement, previous suicide attempts and longer duration of mental illness, significantly increased suicide risk for patients with akathisia. This potentially contrasts with findings by Seemuller et al (2012a, 2012b) that individuals experiencing a first episode of psychosis were more likely to exhibit increased suicidality after the development of akathisia.

Case Report Studies

A common theme across case report studies was polypharmacy. All case reports identified that individuals were prescribed several medications simultaneously, and although the authors specify which medication they attributed to cause akathisia, it remains difficult to definitively identify a specific medication overall. A second theme is that in seven of the case reports individuals were found to have a history of mental health issues, including diagnoses of depression or bipolar disorder, trauma, psychosis and substance misuse (Cheng, Park & Hernstadt, 2013; Hansen & Wilkinson, 2001; Kertesz & Maze, 2018; Padder et al., 2006; Penders, Agarwal & Rohaidy, 2013; Ponde & Freire, 2015a, 2015b). This could indicate a propensity for individuals with a history of psychological difficulties to find managing the symptoms of akathisia more challenging. Other studies reported that the development of akathisia precipitated increased depression which then led to suicidality (Hansen & Wilkinson, 2001; Cheng et al., 2013; Inoue, Takahashi, Hosoda & Koyama, 2010; Kertesz & Maze, 2018; Penders et al., 2013; Ponde & Freire, 2015a). A third theme within the case reports was that akathisia developed after medication dosage was increased (Inoue et al., 2010; Padder et al., 2006; Penders et al., 2013; Ponde & Freire, 2015a) and after changes in neuroleptic medication (Cheng et al., 2013; Kertesz & Maze, 2018). Just two of the studies in the review involved individuals who had previous suicidality (Ponde & Freire, 2015a; Kertesz & Maze, 2018), suggesting that previous history of suicidality is not necessary for emerging suicidality to develop after akathisia. Table 3 provides details of the medications associated with the onset of akathisia in the case reports.

Which methods have been used to study the association between akathisia and suicidality?

Quantitative Studies

Of the studies which found a significant association between akathisia and suicidality, two used observational case-control designs (Dong et al., 2005; Pompili et al., 2009), two used data from RCT's (Emsley et al., 2003; Seemuller et al., 2012a), one used a cross sectional between groups design (Atbasoglu et al., 2001), one used a case-series design (Seemuller et al., 2012b), and one was a mixed-methods study (Moncrieff et al., 2009). To measure akathisia, three studies used

validated measures (Atbasoglu et al., 2001; Seemuller et al., 2012a, 2012b), which involved both self-report and clinician-rated items to assess subjective and objective components of akathisia (BARS, HAS), one used a clinician-rated observation measure (ESRS) (Emsley et al., 2003), one used self-report data from online entries (Moncrieff et al., 2009), and two used bespoke questionnaires (Dong et al., 2005; Pompili et al., 2009). To measure suicidality, three studies used self-report measures (HAM-D) (Atbasoglu et al., 2001; Seemuller et al., 2012a, 2012b), two used bespoke checklists (Dong et al., 2005; Pompili et al., 2009), one used an adverse event reporting form (Emsley et al., 2003), and one used self-report data from online entries (Moncrieff et al., 2009).

Of the studies that did not find a significant association between akathisia and suicidality, two used observational case-control designs (Lukaschek et al., 2014; Reutfors et al., 2016), two used a cross sectional between groups design (Kornetova et al., 2018; Mlodozeniec et al., 2009), one used a retrospective cohort design (Hansen et al., 2013), and one was a sub-analysis of an RCT (Hansen et al., 2004). To measure akathisia, four of the studies used valid and reliable self-report and clinician-rated measures (BARS) (Hansen et al., 2004; Hansen et al., 2013; Kornetova et al., 2018; Mlodozeniec et al., 2009), one used a bespoke clinician-rated measure (Lukaschek et al., 2014), and one did not specify a measure (Reutfors et al., 2016). To measure suicidality, three studies used self-report measures (BHS, CPRS, HONOS) (Hansen et al., 2004; Hansen et al., 2013; Kornetova et al., 2018), one used both a self-report and clinician-rated measure (ISST, CGI-SS) (Mlodozeniec et al., 2009), one used a bespoke clinician-rated measure (Lukaschek et al., 2014), and one did not specify (Reutfors et al., 2016).

Seven studies were observational in design and six were experimental. All used purposive, convenience or continuous sampling methods, and recruited individuals from mental health services with specific diagnoses who had received specified medications, or had exhibited akathisia and suicidality. Of the studies that found a significant association between akathisia and suicidality, three were multi-centre (Dong et al., 2005; Seemuller et al., 2012a, 2012b), two were single-centre (Pompili et al., 2009; Atbasoglu et al., 2001), one utilised a single website (Moncrieff et al., 2009) and one did not specify where the sample was obtained (Emsley et al., 2003).

Of the studies that did not find a significant association, four were multi-centre (Lukaschek et al., 2014; Hansen et al., 2013; Hansen et al., 2004; Reutfors et al., 2016), one was single-centre (Kornetova et al., 2018), and one did not specify where the sample was obtained (Mlodozeniec et al., 2009). Geographically, the studies were based in Hong Kong, Russia, Germany, Sweden and the United Kingdom. The common usage of multi-centre recruitment combined with the variety of geographical locations increases the generalisability of the evidence.

Case Report Studies

All case reports were based on retrospective accounts of individuals who developed akathisia and thereafter experienced an increase in suicidality. All were written as single case studies based on direct observation. The case reports were from the United States of America (USA), Israel, Australia, Japan, Brazil and the United Kingdom. Only one of the studies reported using a recognised valid and reliable measure (BARS) to assess for the presence of akathisia (Hansen & Wilkinson, 2001). Only one reported using a validated and reliable measure (QIDS) to assess for the presence of suicidality (Penders et al., 2013). Three of the case reports stated that a psychiatric evaluation was conducted (Cheng et al., 2013; Kertesz & Maze, 2018; Padder et al., 2006), and three did not identify any specific assessment being undertaken beyond observation and self-report (Inoue et al., 2010; Ponde & Freire, 2015a, 2015b). The majority of the reports had utilised more than one data source to gather information. However, for all reports the post-treatment outcomes and cessation of symptoms were drawn from observations and self-reports. There was little evidence to demonstrate that pre and post measures were taken as part of on-going assessment. The treatment that individuals received for akathisia was generally well reported and information on medication alterations, dosages and timescales were present in all reports. All reports also provided a background of the literature pertaining to akathisia and suicidality.

What is the quality of the evidence on the association between akathisia and suicidality?

Quantitative Studies

The quantitative study quality assessment scores ranged from 19 (45%) to 34 (81%). The mean percentage for studies that found a significant association between akathisia and suicidality was (*M = 64%*) and the mean score for those that did not find a significant association was (*M = 62%*). All studies met criteria for there being a fit between the research question and the method of analysis. The studies demonstrated that the method of analysis had been considered in addressing the research question/s and was generally the most suitable approach. The studies obtained higher combined scores on the criteria which concerned there being a fit between the stated research question and the method of data collection, with all studies achieving a score of two or more. However, there were several areas in which the studies generally obtained lower scores. None of the studies provided evidence of service user involvement in the design process, and the majority showed no evidence that the sample size had been considered for the purpose of analysis; overall, the scores for this criterion were 10 out of 39 (25%). The majority of studies included also had limited information concerning the statistical assessment of reliability and validity of the measurement tools used. 10 of the 13 studies obtained scores on this criterion; however, only the study by Dong et al (2005) achieved a score of two. Please see tables 1 and 2 for further information on quality appraisal scores, and appendix C for a breakdown of individual scores per criterion.

Case Report Studies

Quality assessment scores for case reports ranged from 19 (73%) to 23 (89%). The highest scoring reports were by Hansen and Wilkinson (2001) (89%) and Penders et al (2013) (85%). All case reports achieved maximum scores for outlining relevant medical and social history and for describing unanticipated events in the individual's treatment. One of the lowest scoring areas for all case reports was a lack of reporting of standardised measures being used pre and post treatment. Some of the studies did refer to using 'measures' or 'tools'; however, these were often unidentified. Additionally, none of the case reports stated that informed consent had been obtained. More generally, all case reports achieved scores on the following areas: clearly describing the individuals demographics, clearly describing the individual's current clinical condition, defining the key concepts of akathisia and suicidality, exploring alternative diagnoses, describing the results of assessments (even where

specific tools were not identified), clearly describing the intervention or treatment procedure, outlining the post-intervention clinical condition, describing the case in sufficient detail so as to allow clinicians to make inferences about their own practice, and providing takeaway lessons. Please see table 3 for further information on individual quality appraisal scores.

Discussion

This review aimed to investigate whether the available evidence supports an association between akathisia and suicidality. Seven quantitative studies found a significant association between akathisia and suicidality, and six studies did not report a significant association. All case reports indicated that akathisia leads to an increase in suicidality after the receipt of neuroleptic medication. The results showed that the development of akathisia and suicidality was associated with FGA's and SGA's, and several forms of suicidality were reported within the studies. Additionally, a range of factors were found to influence the association between akathisia and suicidality, including: age, medication-related factors, subjective versus objective ratings of akathisia, psychiatric history, and affective, sleep-related and cognitive issues. Methodologically, the variation in designs, sample characteristics, measures, analyses and reporting of results within the quantitative studies, meant that few comparisons could be drawn between studies that did and did not report a significant association.

Consistent with the findings of the previous review (Hansen, 2001), all case reports reported that the development of akathisia precipitated an increase in suicidality. Our findings also demonstrate that akathisia can lead directly to the emergence of new suicidality; even for those without a previous history of suicidality. These findings are in contrast to other studies which reported that akathisia simply exacerbates pre-existing suicidality, but does not lead directly to the emergence of new suicidality (Chung & Chiu, 1996; Crowner et al., 1990). The finding that other factors (outlined above) influence the association between akathisia and suicidality also supports previous literature, which suggests that some individuals who develop akathisia may be more vulnerable of developing suicidality than others (Lohr et al., 2015; Hansen, 2001; Hamilton & Opler, 1992). In contrast to other studies included in this review

that identified age as a factor that influences the association between akathisia and suicidality, Atbasoglu et al (2001) and Pompili et al (2009) found no significant effects for age in relation to the development of akathisia and suicidality. Seemuller et al (2012b) and Kornetova et al (2018) also reported no significant differences on the basis of gender and the association between akathisia and suicidality.

Hansen (2001) and King et al (1995) reported differences between objective and subjective ratings of akathisia. The findings of the current review are that, in some cases, clinician-rated (objective) akathisia scores were significantly lower than patient-rated (subjective) akathisia scores. These differences may be attributed to difficulties articulating the experiences of akathisia for service users, which can result in underdiagnoses (Lohr et al., 2015). These findings are, however, in contrast with Seemuller et al (2012a), who reported that clinician-rated akathisia was significantly associated with akathisia and suicidality, whereas subjective ratings were not.

Eight case reports were included in the review and all identified that polypharmacy and medication changes were observed in people who developed akathisia and subsequent suicidality; consistent with previous research (Pringsheim et al., 2018). Furthermore, there is a possibility that certain neuroleptics are more likely to increase the onset of akathisia-related suicidality than others. These findings, combined with the findings of the quantitative studies, support previous research which indicates that akathisia can develop following treatment with both SGA's (Avantis et al., 1997; King et al., 1995) and FGA's (Sachdev, 1995). Regarding medication, Atbasoglu et al (2001) concluded that there were no significant differences between duration of taking neuroleptics and the development of akathisia and suicidality and secondly, that the severity of akathisia did not relate to suicidality. However, evidence is provided in the case reports that alterations in dosage and changes in medication could potentially precipitate the development of akathisia and thereafter, suicidality.

A strength of the current review is that several search terms related to akathisia and suicidality were used. This was following review of relevant medical subject headings (MeSH), terminology used within published literature, descriptions from

the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (APA, 2013) and the International Classification of Diseases (ICD.10) (World Health Organisation, 1992), and published medication leaflets. Improvements on the previous review by Hansen (2001) also include using five relevant databases instead of three to broaden the search. This review also focused solely on the association between akathisia and suicidality. As no search limitations were placed on language, attempts were made to obtain English translations of studies in other languages, and in addition to including studies from any geographical location, this increased the potential for generalisability of the review. Undertaking a structured narrative synthesis also allowed for all studies returned from the search to be included, thus providing an overall synthesis of published research. Using a validated tool to assess the quality of quantitative studies and a bespoke tool to assess the case reports also allowed for the risk of bias to be evaluated.

There are some limitations to the current review. Studies involving participants prescribed antidepressant medication alone were excluded as individuals experiencing affective issues have a higher propensity for suicidality (Bradvik, 2018). Additionally, individuals experiencing affective issues have been found to be more likely to engage in suicidal behaviour compared to people given other psychiatric diagnoses (Healthcare Quality Improvement Partnership, 2017). Excluding these studies enabled the review to focus on examining suicidality and akathisia related to neuroleptic medication, but limits the ability to make inferences about the impact of akathisia on suicide in relation to other drugs. Two of the studies included in the review could not be quality assessed as they were summary articles. One of these articles reported a significant association between akathisia and suicidality and the other did not report a significant association.

Quantitative studies used appropriate methodological approaches to investigate study aims. However, none of the studies reported evidence of service user involvement and few stated explicitly that sample size had been considered, with several studies highlighting that smaller sample sizes limited the representativeness of their findings. Four studies used retrospective designs which may have introduced bias, few differentiated between severities of akathisia and suicidality, and several did not utilise valid and reliable assessment tools. The reporting of the findings across all

quantitative studies also lacked consistency, with some studies either reporting no results, or reporting significance values without effect sizes, which did not allow for comparison of the magnitude of effects. Studies that found a significant association reported more statistical evidence than those that did not. The heterogeneity of the studies meant that many used different measures for akathisia and suicidality, had different designs and assessed individuals across different time points which, coinciding with the lack of consistency in reporting results, impacts the interpretability of the findings. Several of the studies also incorporated other variables into their designs but reported not having sufficient power for analysis, and few focused solely on akathisia and suicidality.

Case reports contained sufficient information to allow clinicians to make inferences regarding their own practice and were clearly written, including relevant patient histories and thorough explanations of the interventions provided. This is in contrast to the findings of the previous review (Hansen, 2001). However, none of the case reports identified whether informed consent had been obtained which may have potential ethical implications. A lack of standardised assessment measures used pre and post treatment across studies increases the subjective risk of observer bias. Reliance on patient self-report also poses the potential for recall bias; however, research generally suggests that subjective ratings of akathisia result in increased incidence rates compared to clinician ratings (Hansen, 2001; Seemuller et al., 2012b). Reporting on single incidences also limits the generalisability of the findings. However, generally the case reports provide useful clinical information that will help guide clinical decision making.

Conclusion

In conclusion, this review provides evidence of a likely but partial association between akathisia and suicidality. Methodological issues across quantitative studies may have produced false positive or false negative results. All case studies reported an association between akathisia and suicidality. The findings also suggested that akathisia can lead to several forms of suicidality, including general suicidality, emergent suicidality, suicidal ideation and can be a risk factor for completed suicide. However, in the absence of clear defining features of akathisia, limitations with

assessment, and lack of clarity of pathophysiology, akathisia frequently goes undetected, making it a challenging area of research. Future research should examine the association between akathisia and suicidality using standardised methods and reporting. Future research should also be conducted on how the development of akathisia impacts individual's psychological wellbeing. An up to date review of the evidence for an association between akathisia and suicidality resulting from antidepressant medications is also necessary. The current review provides evidence that akathisia can be associated with increased suicidality. Though there are several factors that can influence this association, such as age, medication-related factors, methods of rating akathisia, psychiatric history, and affective, cognitive and sleep-related issues, further investigation is required to prevent future loss of life.

Clinical Implications

- Clinicians should be mindful that the development of akathisia may lead to increased suicidality. Additionally, akathisia can develop in response to both FGA'S and SGA's.
- Suicidality, which may develop subsequent to akathisia, can take several forms, from suicidal ideation to suicidal behaviour (including attempts to take one's own life). Individuals who develop akathisia should be closely monitored for increased suicidality and risk assessments should be completed on a regular basis. Additionally, regular assessment for akathisia should always be completed for service users receiving neuroleptic medications, with particular focus at times of alterations in medication, polypharmacy and questionable adherence.
- Service users may be at greater risk of developing suicidality following onset of akathisia if they are younger, experiencing mental health issues for the first time, experiencing affective problems (i.e. anxiety, depression), not sleeping well, and during significant life changes. Akathisia may also affect cognition which may impact service users' abilities to cope with distress.
- Clinicians should be mindful that service users will likely find it difficult to articulate their experience of akathisia. Training should be provided to both qualified clinicians and trainees on how to better recognise the symptoms and signs of akathisia.

- The BARS and HAS are the most commonly used scales for assessing the presence of akathisia. Yet, subjective and objective components of these measures should be assessed and interpreted with caution, as individuals experiencing akathisia may not always exhibit objective signs. Any future research on akathisia should also be used to develop updated assessment measures.
- Service users should be fully informed of the potential for the development of side effects before providing informed consent to receiving neuroleptic medication. Detailed information should be given on what side effects are possible and the distress and discomfort they can cause.
- Clinician's working in physical health settings (i.e. oncology) should be mindful that some medications frequently used within such settings (i.e. prochlorperazine) can also cause akathisia.

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Paper 2: Empirical Study

Service User's First-Hand Experiences of the Psychosocial Effects of Akathisia

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Abstract

Akathisia is a medication-induced movement disorder caused by neuroleptic and psychotropic medications. The purpose of this study was to investigate psychosocial experiences of service users who have developed akathisia. Individual semi-structured interviews were conducted and analysed using Interpretative Phenomenological Analysis (IPA). Six participants were recruited from an NHS Trust and a third-sector organisation in the North West of England. Three superordinate themes were identified: *'Journey through the mental health system'* related to the experiences of care, treatment and support participants received. *'Adjustment to life with akathisia'* related to the experiences of akathisia and the social changes and coping mechanisms participants employed, and *'the internal experience of akathisia'* related to cognitive and affective changes, and the implications of akathisia for identity and suicidality. The results demonstrate that akathisia can be a highly distressing condition with a myriad of social and psychological implications for service users. Recommendations for future research and clinical implications are offered.

Key words: Akathisia, restlessness, movement disorder, qualitative, interpretative, experience, psychological, social, identity, suicide.

Introduction

Akathisia is an iatrogenic medication-induced movement disorder where individuals report subjective symptoms of inner-restlessness, agitation, irritability, discomfort and an inability to remain still, which may lead to objective signs of pacing, rocking, and shifting positions (Kane et al., 2009; Lohr, Eidt, Alfaraj & Soliman, 2015). Although a universally accepted definition and precise diagnostic criteria for akathisia has yet to be established (Hansen, 2001; Tachere & Modirrousta, 2017), attempts to classify akathisia into subtypes of acute, chronic, pseudo, tardive, and withdrawal akathisia exist (Halstead, Barnes & Speller, 1994; Barnes & Braude, 1985; Sachdev, 1995). Akathisia is now a recognised condition in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013) and the International Classification of Diseases (ICD.10) (World Health Organisation, 1992), yet specific criteria required for diagnosis remain unidentified.

For several years akathisia was considered to develop solely in response to neuroleptic medications such as first generation 'typical antipsychotics' (FGA's) (Sachdev & Loneragan, 1991; Sachdev, 1995). More recent research has found it also develops in response to second generation 'atypical antipsychotics' (SGA's) (Kane et al., 2009). It is now widely accepted that akathisia can also result from antidepressant medications (Lipinski, Mallya, Zimmerman & Pope, 1989; Lane, 1998; Hansen & Wilkinson, 2001; Salem, Nagpal, Pigott & Teixeira, 2017). Though the underlying pathophysiology of akathisia remains incompletely understood (Hansen, 2001), it is proposed to result from a blockade in dopamine (DA) pathways; a known effect of neuroleptic and some psychotropic medications. There is on-going debate about whether this blockade occurs at the pre- or post-synaptic level (Sachdev & Loneragan, 1991). Other hypotheses proposed for akathisia include imbalances in the serotonergic and noradrenergic neurotransmitter systems, and mechanisms related to iron deficiency (Salem et al., 2017).

Akathisia has been found in approximately 20% of service users during the first weeks of commencing neuroleptic interventions (Juncal-Ruiz et al., 2017). The first line of treatment for akathisia has traditionally involved medications such as benzodiazepines, betablockers, anticholinergics, antihistamines or lower potency

neuroleptics (Iqbal, Lambert & Masand, 2007; Hansen, 2001). Salem et al (2017) and Pringsheim et al (2018) have produced guidance for the treatment of akathisia, within which it states that interventions should be personalised according to individual responses. Distress caused by akathisia can result in non-adherence to medication (Hansen, 2001) and some studies have reported on the use of electro-convulsive therapy (ECT) as intervention (Chung & Chiu, 1996; Hansen & Wilkinson, 2001). Inoue, Takahashi, Hosoda & Koyama (2010) proposed that psychotherapy may be beneficial in helping service users manage akathisia related distress. There are no definitive timescales for the cessation of symptoms of akathisia, regardless of interventions, although this may be influenced by dosage, medication type, and individual withdrawal responses (Caroff, Hurford, Lybrand & Campbell, 2011).

Several researchers describe clinical challenges in diagnosing akathisia (Lohr et al., 2015) which is often misidentified as anxiety, agitation, tardive dyskinesia and tardive dystonia (DiMartini, Trzepacz & Daviss, 1996; Van Harten, Hoek, Matroos, Koeter & Kahn, 1997; Ponde & Freire, 2015; Lohr et al., 2015). There has also been on-going debate surrounding the differentiation between akathisia and 'restless legs syndrome' (RLS) (Braude, Barnes & Gore, 1983; Sachdev & Loneragan, 1991; Turk, Gunduz & Kiziltan, 2018; McCall et al., 2014; Tan, 2018). Other challenges in identifying akathisia include difficulties for service users articulating their experiences (Jong-Hoon et al., 2002), and the subjective distress of akathisia being present without objective movements. These challenges can lead to misdiagnosis and increased dosages of medication, which usually exacerbates symptoms (Salem et al., 2017). The absence of a universally accepted definition and diagnostic criteria for akathisia, in addition to the challenges above, make conducting research on akathisia, difficult.

Research on akathisia has primarily had a pharmacological focus, with fewer studies investigating the psychological manifestations of the condition (Jong-Hoon et al., 2002). Akathisia has been described to be associated with increased psychopathology, depression and psychomotor agitation (Duncan, Adler, Stephanides, Sanfilipo & Angrist, 2000; Chouinard, 2006; Sabaawi, Holmes & Fragala, 1994). Jong-Hoon et al (2002) reported that akathisia was significantly

associated with depression, attentional impairment and reduced mental tracking[17], and a further study demonstrated that individuals with akathisia had significantly higher scores for anxiety and subjective cognitive dysfunction, which negatively affected their ability to carry out everyday tasks (Jong-Hoon & Hee-Jung, 2007). Studies by Jouini et al (2017) and Penn, Hope, Spaulding and Jucera (1994) found that akathisia increased social anxiety, indicating negative effects on social interactions and individuals' beliefs about how they are perceived by others.

Few studies have explored service users' views of their experiences of akathisia despite the fact that their perception of akathisia may, in turn, influence their subjective experiences. Gruber, Northoff and Pflug (1998) found that the subjective distress from akathisia led to an *'inner compulsion to move; lack of control over motor behavior; feelings of inhibition of purposeful action; and subjectively close or inseparable relationship between inner-restlessness and restless movements'* (p. 1). Moncrieff, Cohen and Mason (2009) found that individuals with akathisia reported loss of motivation, feelings of reduced intelligence, slowing of mental processes and emotional flattening, and several studies highlight an association between akathisia, aggressiveness and suicidality (Schulte, 1985; Pompili et al., 2009; Seemuller et al., 2012a, 2012b; Dong, Ho & Kan, 2005; Atbasoglu, Schultz & Andreasen, 2001). Available evidence suggests that akathisia affects service users' wellbeing and functioning. However, no studies to date have explored the social and psychological experiences of service users who develop the condition. The current study aims to address this gap and inform clinical practice by providing first-hand accounts of the psychosocial experiences of service users living with akathisia.

Aims

The aim of this study was to contribute to existing literature by exploring the psychosocial effects of akathisia, and how service users make sense of their experiences, using qualitative methods. We aimed to understand the psychosocial factors that require consideration for the recognition and treatment of akathisia, and

[17] 'Mental tracking' refers to prediction '*of an objects position given the previous environmental state and motor commands, and the current environment state resulting from movement*' (Hiraki, Sashima & Phillips, 1997, p. 1).

identify how clinicians might help improve the mental health and wellbeing of service users with the condition.

The primary research question was ***'how do service users understand and make sense of their experiences of living with akathisia?'*** The secondary research objectives were to address the following questions:

1. How do participants describe the experience of akathisia?
2. What are participants' perceptions of any information they received about medication?
3. What are participants' perceptions of any support they received to manage akathisia?
4. What psychological and social implications did akathisia have for participants?

Method

Participants

Six individuals were recruited for the study. One participant was recruited from an NHS neurology service and five from the 'Hearing Voices Network'; a third-sector organisation[18]. Participants included an equal ratio of male and female participants aged between 26 and 63 years (*M = 44*). All participants resided in the UK and were British citizens. Four participants were White British (three English, one Irish) and two were Black British from Caribbean descent. All participants were unemployed and five had attended secondary school. Five of the participants lived with family and one resided in an inpatient psychiatric hospital (voluntary basis). Participants self-reported receipt of psychiatric diagnoses including schizophrenia, bipolar disorder, personality disorder, anxiety, and depression. All participants self-reported taking medication associated with akathisia and experiencing subjective symptoms and objective signs of akathisia. Five participants were experiencing akathisia at the time of their interview and one experienced akathisia on two separate occasions several years prior.

[18] The Hearing Voices Network provides advice and support for individuals who hear voices, and aims to promote more positive relationships and acceptance of the voices.

Inclusion Criteria:

To be eligible to take part in the study participants were required to be English speaking adults (over 18 years of age) with capacity to provide informed consent to take part in the study, who self-identified as having experienced at least one symptom of akathisia within the last six months or more. Participants were required to have received a current or previous diagnosis of a mental health problem for which they were prescribed a drug associated with akathisia. Service users who experienced other organically-based mental health problems (i.e. dementia) were not eligible to take part as the physical symptoms they experienced may overlap with those of akathisia.

Procedure

Individuals who self-reported experiences of akathisia during a routine NHS outpatient clinic appointment were informed about the study by their health professional. The first author (LB) also attended meetings of the 'Hearing Voices Network' to inform attendees about the study. Potential participants were required to sign a consent to contact form (appendix E) and an eligibility screening checklist (appendix F) was completed with the first author. Eligible people received an information sheet (appendix G) about the study. Prior to commencing the interviews participants gave verbal or written informed consent (appendix H) and were asked to complete a demographics questionnaire (appendix I). Participants could choose to have the interview in their own home, at the University of Manchester, on NHS premises or by phone. Four interviews were conducted face-to-face and two by telephone. Protocols were developed to address any risks that arose (appendix J).

Design and Analysis

Interpretative Phenomenological Analysis (IPA) is a qualitative method based on an inductive, data-driven approach to make sense of individuals' experiences (Smith, 1996, 2004, 2011). IPA incorporates three key elements of phenomenology, hermeneutics and idiography. 'Phenomenology' is concerned with how individuals experience the world, 'hermeneutics' relates to how information is interpreted, and 'idiography' refers to the in-depth and detailed investigation of phenomena (Smith, Flowers & Larkin, 2009). IPA involves a double-hermeneutic approach whereby the researcher attempts to 'decode' and make sense of participants making sense of their

experiences (Pietkiewicz & Smith, 2012). Employing this approach enabled the extraction of detailed first-hand accounts of the psychosocial effects of akathisia, consistent with the aims of the study.

A bespoke semi-structured topic guide was developed (appendix K), designed to explore a broad variety of potential social and psychological experiences, informed by the literature on akathisia. Interviews were recorded on an encrypted recording device and transcribed verbatim by the first author (LB). All identifiable information was removed. Consistent with an IPA approach (Smith et al., 2009) analysis began by reading and re-reading each transcript after which initial exploratory coding of the data examining descriptive, linguistic and conceptual content was conducted. Emergent themes were identified from individual transcripts which were ordered chronologically, clustered into related themes, and given a specific label. Cross case analysis of the clustered themes was conducted to compare and contrast across transcripts to look for potent themes and connections. These were then developed into subordinate and superordinate themes[19]. Sections of transcripts and all identified themes were discussed amongst the research team to ensure a reflexive approach. The second and third authors (YA and ST) also acted as secondary coders before finalised interpretations were agreed.

Epistemology and Ontology

The researchers aligned with a constructionist ontology which as opposed to being 'fixed', views 'reality' as fluid and better understood through the exploration of everchanging human perceptions and interpretations. It considers that multiple ways of perceiving reality exist, and highlights the importance of understanding individuals' subjective perceptions of the world to uncover meaning. Though IPA lends itself to several epistemological positions (Larkin, Watts & Clifton, 2006), an interpretive epistemology was adopted in the current study; consistent with the phenomenological foundations of IPA (Husserl, 1982). From this perspective, the researcher is an active participant in the analytic process (Chowdhury, 2019), which complements the inductive, idiographic focus of participants' experiences inherent to IPA, and the double-hermeneutic and reflexive process underpinning the approach.

[19] Please see appendix L for a table that identifies recurrent themes for participants.

The primary author (LB) is a third-year trainee clinical psychologist who works in mental health services with individuals across the lifespan. LB's clinical research experience has primarily focused on the development of psychological formulation practices for people with learning disabilities. YA's research interests have mainly focused on the development of psychological interventions for suicide prevention, and understanding of implementation/ acceptability factors of various models of psychotherapy from the perspective of professionals and service users. ST is a reflexive scientist practitioner, therapist, educator and researcher who works clinically with people experiencing psychosis, many of whom also experience akathisia. Her research focuses on the science and practice of psychological interventions, including cognitive theory with people experiencing serious and enduring problems affecting their mental health.

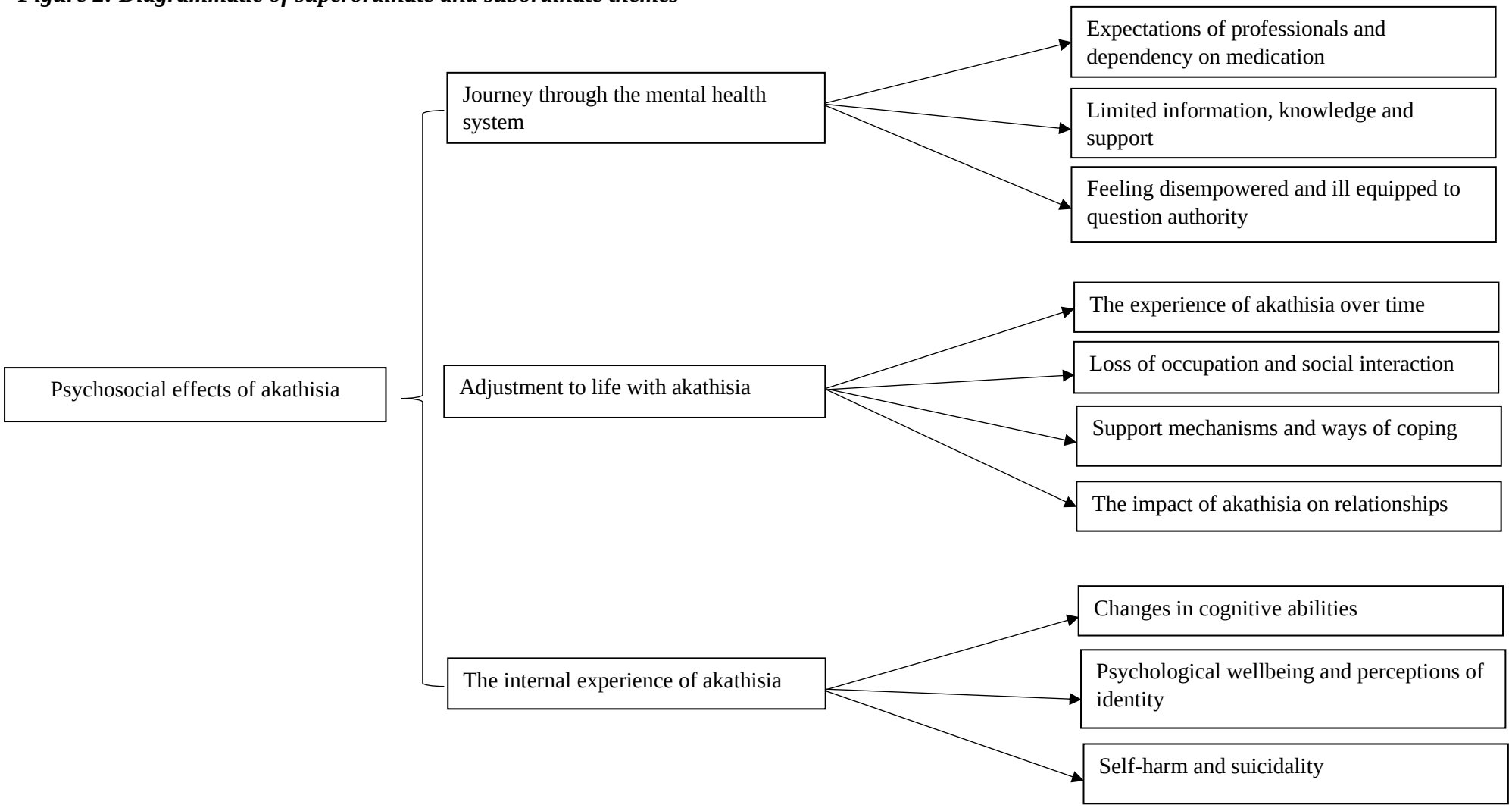
Ethics

Approval for this study was granted by the North West Greater Manchester East Research Ethics Committee (REC reference: 19/NW/0226) (see appendix M).

Results

Three superordinate themes were identified which encapsulated participants' experiences of akathisia: i) 'journey through the mental health system', ii) 'adjustment to life with akathisia', and iii) 'the internal experience of akathisia'. Pseudonyms have been used for the analysis to ensure anonymity. Please see appendix N for examples of analysed transcripts. Figure 2 overleaf displays a diagrammatic representation of the superordinate and subordinate themes:

Figure 2: Diagrammatic of superordinate and subordinate themes



Superordinate theme 1: Journey through the mental health system

Three subordinate themes relate to participants' journeys through the mental health system: i) 'expectations of professionals and dependency on medication', ii) 'limited information, knowledge and support', and iii) 'feeling disempowered and ill equipped to question authority'.

Subordinate theme 1: Expectations of professionals and dependency on medication

This theme relates to participants' expectations of medication and professionals to help them overcome the symptoms of akathisia. Some participants reported having several medication changes, yet continuing to have faith in eventually finding the right medication:

'They [psychiatrists] need to find one that works properly for me…they need to mix it and blend it to get the right one to get me off the movements and that'. (Samuel)

Samuel's language illustrates his belief that the 'right' medication for him would be found. His willingness to experiment with medication and tolerate polypharmacy reflected his willingness to trust the advice provided by his psychiatrist; despite polypharmacy being found to increase akathisia. This demonstrates Samuel's limited knowledge around polypharmacy and his hopes and expectations of his psychiatrist to find a successful pharmacological intervention. All participants referred to polypharmacy, indicating a wider issue around the use of multiple medications. Some participants expressed beliefs that their medication helped them cope with akathisia. Amy reported:

'I thought these medications were going to work and I think now if I didn't have my diazepam…I told them "you better not touch my diazepam because they're the only ones that are helping me cope"'. (Amy)

This illustrates Amy's dependency on medication, and the sense of threat she experienced at the prospect of this being taken away. Her tone conveyed desperation and fear around losing her primary coping mechanism, which speaks to the limited

options of help available and the importance participants generally placed on pharmacological intervention. Mark believed that medication would address a 'chemical imbalance' in his brain, which he believed made him vulnerable to akathisia:

'It must be some sort of chemical imbalance in my mind in my brain, and the tablets if you like are the chemical that helps to…balance things out. They stop the imbalance. Well they don't stop the imbalance, they help it, until you're feeling strong enough to do things for yourself…I'd be frightened of stopping the medication anyway'. (Mark)

This extract depicts Mark's fear around the potential consequences of stopping medication, as he had few other coping strategies. His use of medicalised language and reference to 'chemical imbalance' emphasises his trust and acceptance, even of inaccurate medical information. His reports suggest that this was perpetuated by psychiatric professionals who encouraged the belief that medication would 'fix' him. Yet, Mark's hesitancy and the pauses in his speech indicated his simultaneous doubt of medical perspectives.

Some participants reported placing trust in their psychiatrist to help them overcome the symptoms of akathisia. Samuel described his faith that they would ***'give me the right tablets'*** and Diane reported needing to ***'listen to what the staff were saying'***. These comments illustrate how participants felt strongly about heeding the advice of professionals, and placing trust in them to find a solution:

'It gives me a boost does going and seeing a specialist {neurologist} in the fact that this might just be the time where we come up with something. I think because they've studied for so long, they know and believe in what they are doing'. (Mark)

This demonstrates the trust and high regard in which Mark held his neurologist; a sentiment echoed by other participants. However, his use of 'we' also suggests he had a positive and active role in finding a solution for akathisia. Contrastingly, other participants felt their reliance on professionals resulted in a loss of autonomy, helplessness, and a sense of placing their destiny in someone else's hands.

Subordinate theme 2: Limited information, knowledge and support

This theme is about participants' perceptions of there having been a lack of information about potential side effects of medication, why they developed akathisia, and limited guidance and support to manage the manifestations. Diane outlined the lack of communication she experienced:

'I don't recall them [psychiatrist] ever really having a conversation about it [side effects of medication] …I don't think at the time I really knew what was going on. I did not feel supported'. (Diane)

The limited information and contact participants received made them feel disconcerted and uncertain. Participants also reported feeling unsupported, which exacerbated feelings of loneliness. Other participants, such as Jessica, questioned the competence of psychiatrists who were supposed to be 'caring' for them. This contrasted with the trust and confidence some participants initially reported. Jessica described how the rationale for medication had never been explained:

'They [psychiatrist] never actually sat down and explained to me in full detail…That's what gets me, makes me angry, because they didn't tell me'. (Jessica)

Jessica was overtly emotional about the lack of information she encountered, which caused her to feel vulnerable, deceived, and resulted in the development of frustration and anger towards her psychiatrist. Other participants spoke of how they received little support from mental health teams, which provoked feelings of being discarded, dismissed, and added to their existing confusion:

'I mean, she [GP] said "it shouldn't be doing that but we'll keep monitoring you" …They [mental health team] took five months to reply to me and get involved'. (Amy)

The lack of support described by Amy was echoed by all participants; illustrating how they felt 'voiceless' and 'unheard' within the mental health system. For some participants, being told that medication was unlikely to cause their symptoms

strengthened the belief of there being something wrong with 'me'. This exacerbated participants perceptions of being 'different' to others and perpetuated feelings of abnormality and defectiveness. Participants also described receiving little or no explanation as to why akathisia might have developed:

'I haven't really ever had an explanation off them why they [neurologist/ GP] think it [restlessness] comes around…I'm not really any the wiser why it happened. I don't know whether it's part of what is in my body, or whether it's the tablets I've taken that have contributed towards it. They've not got enough time to sit and talk'. (Mark)

This extract demonstrates how the lack of explanation and communication with professionals increased participants' confusion, causing them to feel unimportant and abandoned; often with detrimental effects on self-worth. Participants communicated a paradox between their beliefs and expectations that professionals and medication could help, yet receiving little information about why akathisia occurred. Lack of guidance and advice on how to manage akathisia was common to all participants, reinforcing feelings of being uncared for:

'No not really nothing erm, anything else has always been what I've tried myself you know. There is nobody to help you and stop you and you're having to take it all on your own because you know, people can't do anything to help you. I feel like I'm drowning and no one is listening…I feel like I'm trying to tell people and no one is listening'. (Mark)

Mark's experience was reminiscent of other participants' feelings of having to cope alone due to lack of support. The sense of 'drowning' that Mark described speaks to his feelings of being all consumed, trapped, and suffocated by akathisia, alongside the complexity of navigating the mental health system as a 'patient'.

Subordinate theme 3: Feeling disempowered and ill equipped to question authority

This theme relates to the treatment participants received in mental health services. All participants reported feeling unable to question authority figures which, in addition to the lack of information, caused them to question their internal experience

of akathisia. Some participants reported that the dismissal of their experiences by professionals left them feeling invalidated and disempowered:

'I was actually in a hospital and I was annoying them [staff] walking up and down the corridor. They kept saying "would you just go and sit down", "no I can't", "would you just go and sit down", "no I can't". It made me think "oh gosh, I'm doing something that I shouldn't be doing" …I thought it was the quetiapine but the doctor said it couldn't be that. But at the time I did think "you know, I was alright until you [psychiatrist] put me on this"'. (Diane)

This conveys a lack of basic compassion, empathy and understanding Diane received from staff. She described her experience being like that of a child chastised for unacceptable behaviour. The verbiage 'you put me on this' also communicates Diane's frustration at the lack of acknowledgement and ownership she perceived her psychiatrist had in relation to her distress. Repetition of the phrase 'I can't' also communicates her desperation and the lack of control she experienced over her urge to pace. Dismissal by professionals was reported by all participants, which developed into limited trust for those 'caring' for them. For most participants, the lack of support caused additional distress. David reported questioning if his medication caused akathisia:

'I thought it [akathisia] was the clozapine but they [psychiatrists] turned around to me and said "it's not the clozapine", it's not the clozapine that caused the symptoms I'm getting. It's because of the tablets [neuroleptics], I don't know, it must be… Just taking the tablets is all I can say, simple as that'. (David)

Responses like these caused participants to question their judgement of their own internal experiences. In David's case, after sensing his concerns were dismissed, alternative treatment was not offered and his distress over akathisia was ignored. Such dismissals made participants feel they had less autonomy and involvement in their treatment. Amy was told her symptoms related to her mental health diagnoses:

'She [GP] knows about the pacing but she said it could be my diagnoses what I've got and how I'm feeling'. (Amy)

Being told that akathisia was a symptom of mental health caused participants additional doubt over trusting their own judgements, leading to them underreporting their concerns. This also illustrates participants' perceptions of being within a system where any issues are interpreted through a lens of 'mental health diagnoses'. Mark spoke of how his concerns about medication and akathisia were dismissed:

'Now I don't mean to be disrespectful to anybody but medication does not seem to have helped me in any way. When I've mentioned my thoughts of the tablets it's just been "no no that's okay it's not a problem that", as if I'm totally wrong in what I'm thinking…They [GP, neurologist] don't really give you any suggestions they just sort of tell you it's okay'. (Mark)

In addition to dismissing Mark's concerns, the extract suggests an unwillingness by professionals to accept ownership for his distress. Initially, Mark said he communicated his concerns in a tentative and almost apologetic manner; as did most participants when reporting questioning professionals, illustrating their reluctance to offend or question authority. This epitomises the probable power dynamics present within the mental health system.

Superordinate theme 2: Adjustment to life with akathisia

Four subordinate themes identify how akathisia impacted participants' lifestyles and the adjustments they made to try and cope: i) 'the experience of akathisia over time', ii) 'loss of occupation and social interaction', iii) 'support mechanisms and ways of coping', and iv) 'the impact of akathisia on relationships'.

Subordinate theme 1: The experience of akathisia over time

This theme relates to participants' experiences of akathisia; the onset and development of symptoms, including duration and frequency. Participants' descriptions of subjective symptoms of akathisia included: feeling uneasy, racing mind, agitation, anxiety, restlessness, a surge of energy, unable to relax, lack of control, irritability, constant need to move, feeling jittery and an internal sense of anticipation. Participants reported these symptoms were highly distressing, frustrating, despairing, hard to deal with and 'horrible'. The objective manifestations included: inability to remain still, pacing, involuntary movements (arms and legs),

struggles balancing, shaking fingers, twitching, and fidgeting and rocking. Most participants experienced difficulties in articulating their experiences of akathisia and in response to the question ***'can you explain what akathisia feels like?'***, Samuel stated '***that's such a hard question man. It's hard to explain*'.** Other participants described their experiences using metaphors:

'It was like butterflies in my stomach' (Diane), ***'it's like being on a motorway and my heads not stopping its whizzing, its whizzing all the time' (Amy)***, ***'I need to break out of my body' (David)***, and ***'it feels like I'm going to explode' (Mark)***.

These metaphors, in addition to demonstrating variability and challenges articulating the experience of akathisia, suggest a sense of urgency, exasperation, confusion, uncontrollability, a build-up of energy, an unstoppable urge to move and physiological changes. Participants reported the onset of akathisia occurring after days or weeks after starting either neuroleptic or antidepressant medication. Participants described it lasting from two to ten years (the latter being ongoing), and some reported increased symptom severity after increases in medication.

Mark spoke of how ***'without a doubt it has gotten worse over time…I have come to live with it'*** and Samuel felt that akathisia had lasted for so long that ***'I don't notice I'm doing it half the time. They're [the movements] just always there'***. For some participants continuing to live long-term with akathisia felt like an inevitability. All reported that symptoms occurred day and night, causing difficulties sleeping due to the need to pace ***'it's a [expletive] getting to sleep' (Samuel)***, and ***'I can't sleep and stuff like that' (Jessica)***. For some participants this meant that a key form of escapism was taken away, and lack of sleep may also have impacted their mood. Participants also spoke of the uncontrollability of the movements ***'it's like an involuntary thing' (David)***, which elicited feelings of powerlessness. The drugs participants attributed to akathisia included: clozapine, amisulpride, quetiapine, aripiprazole and fluoxetine.

Subordinate theme 2: Loss of occupation and social interaction

This theme illustrates how akathisia impacted participants' abilities for self-care, daily living skills, travel, and a loss of social interaction and engagement in

pleasurable activities. This led to a sense of being isolated and alone. Diane spoke of how ***'I couldn't get in the bath'*** as she found it difficult to remain still long enough to bathe, and Mark reported that he found it difficult to do daily chores ***'I'll only do probably 10 minutes or something like that and I need to then get on my bed and lie down and rest again'.*** Though akathisia is associated with increased activity, Mark felt it was sometimes soothing to lie down and try to rest; again, highlighting the variability in experiences. He also reported that the restlessness impeded his ability to travel:

'I won't travel now more than 40 to 45 minutes anywhere. I will wait until the traffic has died down to get a clear passage through…Going on the plane is one of the worst experiences of my life now'. (Mark)

Mark's slowed speech and emphasis on each word reflected his sense of dread at the prospect of travelling long distances, and he reported planning journeys in advance due to his need to move. The ability of akathisia to limit participants' daily movement emphasised the intense control it had over them. The inability to remain still also meant that participants kept themselves isolated. All reported no longer doing some activities due to the effects of akathisia:

'I do a lot of crafting and I found it hard to sit down. I was feeling that I had to stand up and sit down and stand up and sit down. I found that quite hard to cope with really'. (Diane)

'I used to go the cinemas, can't do that anymore, I used to go for long walks, can't do that anymore, swimming, I don't do that anymore. Everything that is social… I'm sat in a room all day; I get cooped up and can't go out'. (Samuel)

Diane's use of repetition 'stand up and sit down' conveyed an image of her constant need to move. For Samuel, the extract demonstrates how akathisia caused him to feel trapped, isolated and unable to engage in meaningful activity; a sentiment echoed by other participants. The 'all or nothing' language ('everything') Samuel used suggested attempts to communicate the extent of the lack of activity. Amy reported that her limited activity was triggered by not wanting to interact with others:

'I'll think, do I have to face people today? I don't want to speak to people. I want to keep it to myself. Even relaxation used to help me…I've stopped doing arts and crafts. I think to myself "have your relaxation you deserve it" but I want to pace'. (Amy)

This illustrates how Amy felt unable to socialise as she had previously; suggesting a sense of loss. There was also an internal conflict present, between managing competing goals of wanting to engage in activities, but also needing to pace. Diane spoke of how she was unable to attend church due to pacing, and her experience also impacted interactions with friends:

'I'd see my friend and we could sit in silence for an hour. I wouldn't know what to say…I just sort of switched off into my own little mind and no one could get to me...I didn't interact with anyone I don't think'. (Diane)

This extract suggests wider issues around the stigma faced by individuals experiencing psychological difficulties and, in this instance, akathisia. Diane found it difficult to discuss her experiences with friends, which in addition to preventing her maintaining religious practices, caused her to question her sense of identity and belonging. Her language also conveys feelings of hopelessness and potentially, having given up. For participants, akathisia symbolised an introverted version of themselves, who felt unable to interact and alienated from society. This may relate to previous dismissals by professionals and the 'silence' around the condition.

Subordinate theme 3: Support mechanisms and ways of coping

This theme relates to participants attempts to cope with the distress caused by akathisia. All participants identified that pacing was both a symptom of akathisia and a coping mechanism to try and minimise their distress:

'I don't know I just feel better pacing. I open the door and walk along the passageway. Up and down the passageway. After I've done that, I feel a bit better. Well, that's what I tell myself. I don't know if I am though but that's what I tell myself'. (David)

David's report echoed those of other participants who used pacing as a self-soothing activity. His use of language 'that's what I tell myself' suggests he utilised self-speech as a coping mechanism, which may relate to having few people to talk to. Other participants reported using avoidance as their primary coping strategy:

'I just switched off. I think that was my coping strategy that, you know, I'm not doing anything I'm not saying anything and will avoid going out'. (Diane)

The use of self-isolation and avoidance were strategies identified by other participants. Such disengagement is a common determinant of a deterioration in psychological wellbeing, and Diane's language ('switch off') suggested an attempt to detach or 'dissociate' from reality. The experiences of akathisia caused such distress that participants felt they needed to distance themselves for self-preservation. Amy identified several strategies to try and alleviate her symptoms, including: trying to do relaxing activities, kicking legs, throwing stones and self-altering medication, and Mark reported being ***'willing to try anything'*** to prevent akathisia, suggesting a feeling of desperation to quell the symptoms.

For some participants, family members were their primary source of support. Although David had a support worker, he felt unable to engage with them due to personality differences, and despite having support from a psychiatrist and neurologist, Samuel and Mark felt isolated and that they needed to cope alone:

'Like I said it's [akathisia] just a side effect isn't it and I have to cope with it'. (Samuel)

'It's like you are drowning. There is nobody there to help you and stop you and you're having to take it all on your own because you know, people can't do anything to help you'. (Mark)

The extracts from Samuel and Mark illustrate their feelings of resignation, loss of hope, and a sense of desolation, unhappiness and loneliness. Samuel's use of the word 'just' indicates an attempt to minimise the impact of akathisia, which suggests a use of dissonance and avoidance as coping strategies. He also alluded to the

distress of akathisia being like a penance he needed to cope with, due to the guilt and shame of being diagnosed with a mental health problem.

Subordinate theme 4: The impact of akathisia on relationships

This theme relates to akathisia having negative impacts on participants sustaining existing and forming new relationships, and experiencing others as stigmatising or judgemental. Amy reported feeling misunderstood by others:

'I don't want to be around people who hurt my feelings or being quite nasty to me. I've got people telling me like "will you sit down because you're making me dizzy" and I want to say "will you just shut up". It just feels like people don't understand what's going on in my mind and why I need to pace up and down'. (Amy)

Amy's language indicated the frustration and turmoil of not feeling understood by individuals with whom she had existing relationships. Samuel also felt his ability to form new relationships was compromised in addition to the loss of previous friendships ***'well I don't really ever see anyone anymore the only people I see are my mother and my sister. I've not really got any mates left now'***, and Diane reported that pacing had negative impacts on her marriage and familial relationships:

'He [husband] couldn't cope with the pacing up and down either. That was the other thing he got annoyed at me because I'd constantly be moving my legs. I didn't have as much contact with family as normal. I was embarrassed and thinking that I was being stupid and what's wrong with me?' (Diane)

This extract demonstrates how the impacts of akathisia extended beyond the individual to other relationships; suggesting a negative impact on relational dynamics between participants and others. The annoyance Diane felt from her husband coupled with her thoughts she was 'being stupid', represented a self-deprecating perception which was reinforced by others. Mark too identified significant impacts on his relationship resulting from his need to move, and though his partner showed humility, he had suggested terminating their relationship:

'She has been understanding…but it's spoiling her life as well. It's embarrassing for one, embarrassing but also frustrating that I can't just do something to stop it. I've discussed it with her if she wanted to go elsewhere because of how I am. I do understand that, that would be very hard to take'. (Mark)

Participants felt ashamed and embarrassed of how they appeared to others, and perceived themselves as a burden. For all the male participants, their embarrassment and frustration were exacerbated by difficulties engaging in sexually intimate behaviour due to their need to move, which had detrimental effects on self-esteem:

'I might get up in the morning and go and have 10 minutes just cuddling up to her, but once my legs start going which they will, I've got to go back to my own bed…You're never able to get close enough to be intimate'. (Mark)

Superordinate theme 3: The internal experience of akathisia

Three subordinate themes depict changes in participants' internal experiences resulting from akathisia: i) 'changes in cognitive abilities', ii) 'psychological wellbeing and perceptions of identity', and iii) 'self-harm and suicidality'.

Subordinate theme 1: Changes in cognitive abilities

This theme relates to participants' perceptions of changes in cognitive functioning and affect resulting from akathisia. All participants reported changes in memory since the onset of symptoms:

'I just can't like, I forget things. Like you'll tell me something and I'll go out of the building and I'll tend to forget. Yes, it's affected my memory, it has'. (David)

David's use of language ('it has'), conveys how he was grappling with the changes in memory he experienced during the interview. Participants also reported challenges maintaining attention and concentration, which impacted their ability to conduct everyday tasks:

'Yes, I can't concentrate anymore. I've sat and tried to read the same book, and read a few pages and that and then I put it down, and then I pick the book back up again and I've already forgot what I've read'. (Samuel)

Samuel's use of language depicts his feelings of an absolute inability to concentrate. This reflects the earlier feelings of hopelessness he described, which were linked to his attempts to engage in activities. It may also be that low mood, likely resulting from the isolation, withdrawal and lack of sleep participants described, negatively impacted their ability to attend and concentrate. Jessica also noted changes in cognition:

'It's difficult for me to focus on anything. Everything has changed since I started taking this medication, my brain function as well. Everything goes slower. I don't have a good memory'. (Jessica)

Jessica thought that medication impacted her processing speed and ability to focus. It is unclear whether this related solely to akathisia, or to the effects of medications themselves, and other participants reported quickening of cognitive processes. Jessica's use of the word 'everything' also conveys the extent she felt her usual functions had been negatively affected. Amy identified how the cognitive changes she attributed to akathisia impacted her ability to complete tasks:

'I was pacing and then I tried to make a cup of coffee. The milk was going everywhere so I spilt it then wiped it up'. (Amy)

For Amy, the symptoms of akathisia impacted her motor performance and skills, and during the interview, she demonstrated how this happened and showed that she was shaking when trying to pour milk. She also thought other people were watching what she was doing, which caused further embarrassment and additional anxiety.

Subordinate theme 2: Psychological wellbeing and perceptions of identity

This theme is about the emotional distress and changes to identity participants experienced after developing akathisia. Samuel spoke about how uncontrollable movements caused him to feel embarrassed and depressed:

'It's not nice, it's embarrassing but, here we are, it's down to the meds. Other than that, it makes me feel depressed and you know what I mean, it's horrible'. (Samuel)

Here, Samuel made a direct link between akathisia and medication, demonstrating his awareness of medication being implicit in his experiences. His language indicated a sense of defeat and resignation over his situation, and he attempted to elicit reassurance and understanding from the interviewer, which he rarely received from others. Similarly, Diane spoke about how akathisia caused anxiety:

'I was very anxious about it. I think it's just the worry that you don't know whether it's something serious'. (Diane)

This extract depicts Diane's ongoing uncertainty about her symptoms and concerns of having a serious health problem. All participants indicated that as a result of their efforts to be compliant with their 'treatment', many of their concerns remained unspoken; resulting in heightened anxiety. Other participants commented on the connection between affective changes and changes in their sense of identity:

'It's like I'm stuck and can't get out. My mood is at 2% at the moment which is very low really…I feel like I've lost my self-esteem and my confidence. It might not seem it but I feel it coz I feel like I want to tell people "I can't do it" …Sometimes when I wake up I don't know who I am'. (Amy)

Here, Amy's language illustrates her sense of being trapped with no escape. All participants described wanting to escape from akathisia but feeling unable to. For Amy, akathisia caused the loss of key aspects of her identity, and the extract also suggests a conflict between her need to self-present, and desperately wanting to explain how akathisia was limiting her.

Mark spoke specifically of changes in his personality ***'I don't do none of that now because my personality has changed. I'm not as, erm, I'm not as outgoing and I wouldn't try things now that I would have before',*** and Samuel reported that ***'I used to be the life and soul of the party'***. These were similar to reports of other

participants who described a loss of identity and a 'changed self'. It conveys how akathisia prevented participants trying new things, which concurred with Amy's feelings of a loss of confidence. For Mark, the symptoms of akathisia meant he became more cautious; an additional factor preventing him from interacting socially.

Subordinate theme 3: Self-harm and suicidality

This theme relates to akathisia causing ideations and behaviours of self-harm and suicidality. All participants reported experiencing suicidal ideations which they directly attributed to akathisia. Some had made plans or previous attempts to end their own lives, and some had self-harmed; epitomising the extent of their distress. For example, Diane and Mark spoke about suicidal ideation:

'Yes, I got very down and my mood was really low. Yes, it was just sheer, erm, despair, thinking I was going to be like this for the rest of my life. The thoughts [ending own life] started happening quite quickly I'd say, within two or three months'. (Diane)

'I've got to say it's put me on edge. I've had the thoughts of suicide I can't say I haven't because I have. It's horrendous it really is…I get in depressions that make me feel this is never going to end and there's only one way to end it'. (Mark)

Diane's omission of referring overtly and directly to suicidal ideation may indicate her sense of shame and embarrassment, which was echoed by other participants. Some participants spoke of their regret of having put loved ones through this experience, in addition to their guilt of others having to live alongside them with akathisia. The sense of 'no escape' and hopelessness akathisia caused resulted in participants experiencing ideations, forming plans or making attempts to end their own lives. The emotional turmoil, mood and personality changes, social isolation and feelings of hopelessness caused by akathisia, all associated with suicidality, were clear in participants' language, which conveyed desperation concerning the inevitability and prospect that akathisia had become a permanent part of their existence.

Discussion

This is the first study to investigate the psychosocial effects of akathisia from the perspective of people with lived experience. Results demonstrate that akathisia extends beyond the inner-subjective symptoms and objective signs, with effects on multiple aspects of service users' lives, and their social and psychological functioning. Participants generally reported negative experiences of mental health services, receiving inadequate information and support and feeling unable to question the authority of medical professionals. The onset of akathisia was generally attributed to medication, and all participants experienced akathisia as a highly distressing condition that caused suicidality.

All participants reported perceived changes in cognitive functioning, such as difficulties with memory and concentration, that occurred after akathisia developed. These findings are based on participants' self-reports, as opposed to neuropsychological evidence, and may need to be interpreted with caution; yet results are consistent with previous literature which associates akathisia with cognitive dysfunction (Jong-Hoon et al., 2002; Jong-Hoon & Hee-Jung, 2007). Participants also reported affective changes (i.e. feeling depressed and anxious), which have been linked to several domains of cognitive dysfunction (Lam, Kennedy, McIntyre & Khullar, 2014; Yang et al., 2015) such as processing speed, memory, attention and concentration. The affective changes reported by participants also coincide with previous research which identifies that akathisia causes emotional flattening, loss of motivation and increased psychopathology (Moncrieff et al., 2009; Duncan et al., 2000; Jong-Hoon et al., 2002; Chouinard, 2006).

Cognitive and emotional changes reported by participants were linked to decreased social interaction and feeling a need to isolate themselves; coinciding with the findings of Penn et al (1994) and Jouini et al (2017). The anxiety participants reported around involuntary movements could be interpreted using the Clark and Wells (1995) model of social phobia, as participants believed they were perceived negatively by others, which led to them adopting several 'safety behaviours', such as self-isolation and avoidance. Emotional experiences reported by participants (i.e. hopelessness) coupled with social isolation and withdrawal, are also psychological

determinants associated with suicidality (Osgood, 1991), and our findings support previous research reporting an association between akathisia and suicidality (Pompili et al., 2009; Seemuller et al., 2012a, 2012b; Dong et al., 2005; Atbasoglu et al., 2001).

Research has highlighted challenges for clinicians diagnosing and differentiating akathisia from other issues (Lohr et al., 2015), exacerbated in the absence of objective signs and difficulties for service users articulating their experiences (Jong-Hoon et al., 2002). All participants reported difficulties articulating their experience of akathisia, which may be reminiscent of 'alexithymia'[20]. It is possible that the neurological implications of akathisia, in addition to other dysfunctions, cause difficulties processing emotional information. Participants described a conflict between attributing their internal experiences to their mental health diagnoses, as was often implied by professionals, or to the medication they were prescribed. Others reported attributing their difficulties to a 'chemical imbalance', which may relate to popularised and colloquial explanations for experiences such as depression. Many participants felt professionals did not take the severity of their distress seriously which caused feelings of invalidation. This led to them questioning the expertise of professionals, and also suggests challenges for clinicians recognising akathisia; potentially derived from a lack of knowledge and training around medication-induced conditions.

All participants reported personal experiences of polypharmacy, which creates challenges in identifying which medication precipitated akathisia. Most participants reported akathisia occurring after taking neuroleptics, antidepressants, or a combination of both; consistent with literature (Kane et al., 2009; Lipinski et al., 1989; Lane, 1998; Hansen & Wilkinson, 2001; Salem et al., 2017; Hansen, 2001). Participants reported differences in the time scales for the onset and cessation of symptoms and changes in symptoms over time; however, most reported a progression in frequency, severity and intensity. This supports literature that suggests the dissolution of akathisia is dependent on several factors, such as dosage

[20] Alexithymia is used to describe individuals experiencing an *'inability to identify or verbally describe his or her feelings'* (Zaidel & Kaplan, 2007, p. 1).

and medication type (Caroff et al., 2011). However, such investigation was beyond the scope of this study.

The results also highlight several effects of akathisia not previously investigated. Firstly, they demonstrate that akathisia has detrimental effects on service users' social lives, including functional skills and abilities, a loss of social engagement and interaction, strain on relationships and intimacy, and a need to independently adopt novel coping mechanisms and strategies to try and manage the distress. These factors combined led to participants experiencing a loss of autonomy and self-determination, predominantly due to increased reliance on others. The literature on akathisia and RLS also suggests that akathisia does not impact sleep like RLS does (Salem et al., 2017). In contrast, all participants in this study reported significant difficulties sleeping because of their constant need to move. It is likely that sleep deprivation, in addition to the neurobiological underpinnings of akathisia, has negative effects on cognitive functioning as identified in neuroscientific research (Killgore, 2010; Alhola & Polo-Kantola, 2007; Lam, Kennedy, McIntyre & Khullar, 2014).

Participants described oscillating between beliefs that professionals and medication could help, and beliefs that medication caused akathisia. This was compounded by the lack of information, empathy and support they received. The impacts of basic needs like safety and security being unmet can be understood by Maslow's (1943) 'hierarchy of needs', as unmet primary needs can prevent individuals progressing to achieve psychological growth; an experience described by all participants. Participants' feelings of abandonment by professionals and the lack of information they received about akathisia, whilst raising ethical concerns around informed consent, also had negative consequences for the 'doctor-patient' relationships (Reandeau & Wampold, 1991).

The reports of participants feeling disempowered and needing to comply with professionals' advice are reminiscent of Milgram's (1963) studies on obedience, which suggest that during childhood socialisation processes *'we are taught to obey authority and are rewarded for doing so'* (Miller, Collins & Brief, 1995, p. 9); particularly for professions regarded highly by society. These ideas were mirrored in participants sentiments around feeling they needed to follow the advice of

professionals as ‘experts’, and place trust in them, even if they felt medication was causing distress. Peng, Cao, Li and Wu (2018) also found individuals high in social anxiety (as described by participants in this study) were more likely to *‘pursue social acceptance and possibly avoid social rejection’* (p. 1).

Recruiting a sample of participants with an equal ratio of binary gender and variance in age and ethnicity is a strength of this study. Purposely, we did not seek to include or exclude participants on the grounds of severity of akathisia, medication-type or specific symptoms. Utilising an IPA framework also allowed in-depth exploration of participants’ experiences coinciding with the research aims, whilst being mindful of the impact of the researcher on the analytic process. Though using measures to determine the severity of akathisia was not appropriate for this qualitative study, future research should seek to investigate whether the severity of akathisia impacts the experiences of service users, and a replication study with a larger sample would be fruitful to gather additional information about the effects of akathisia. Future research should also seek to investigate clinician’s abilities to recognise and diagnose akathisia, in addition to exploring their knowledge of medication-induced movement disorders.

Conclusion

The results of this study confirm that akathisia, in addition to being a highly distressing experience for service users, is a complex condition that creates a multitude of psychosocial effects. For the participants in this study, the development of akathisia, in addition to being difficult to articulate, meant significant life changes and a need to adapt through active problem-solving and adjustment. Akathisia can cause negative effects on relationships, occupation and activity, and also lead to significant implications for cognitive functioning, psychological wellbeing and suicidality, which are often exacerbated through negative experiences of the mental health system.

Clinical Implications

- Professionals should ensure service users are involved in care planning and are provided with explicit information about potential side effects of medications, coinciding with guidance on informed consent by the General Medical Council (GMC, 2008). Clinicians should adjust their communication accordingly, using language free of medical jargon and make reasonable adjustments to increase service users' understanding.
- All mental health staff should be given additional training on medication-induced conditions. Such training should be extended to all staff training or working within mental health services.
- The psychosocial implications of akathisia identified from this study should be considered when developing any future definitions or diagnostic criteria for akathisia.
- The National Institute of Clinical Excellence (NICE) recommends therapeutic interventions as a first-line treatment for affective issues (2011) and psychosis (2014). Evidence suggests that psychotherapy may have benefits for individuals with akathisia (Inoue et al., 2010). Further research should be conducted to begin to develop therapies to help service users manage the challenges of akathisia, and support groups for individuals who develop medication-induced movement disorders may have utility. Individually tailored psychological formulations, interventions and care plans may also be indicated in helping reduce psychological distress.
- The results demonstrate the extensive social implications of akathisia. Clinicians should be mindful of the potential social needs of service users who develop akathisia, and recommend appropriate sources of support. Thorough idiosyncratic risk assessments should also be completed given the propensity of individuals with akathisia to experience suicidality.
- The most commonly used measures for identifying akathisia (BARS[21], HAS[22]) require subjective symptoms and objective signs for diagnoses. Most participants considered pacing a coping mechanism to manage the inner-restlessness. It is important to create awareness that subjective experiences of akathisia can be

[21] Barnes Akathisia Rating Scale (Barnes, 1989; 2003)
[22] Hillside Akathisia Scale (Fleischhacker et al., 1989, 1991)

present without objective signs, and clinicians should ensure such experiences are thoroughly investigated.

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Paper 3: Critical Appraisal

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Word count: 7,876 (complete text including references), 5,989 (main text excluding references)

Introduction

In this chapter the researcher will provide a critical appraisal of the systematic literature review and empirical studies. They will evaluate the design of the studies, the methods used, and demonstrate how scientific rigour and reflexivity was maintained. They will reflect on the rationale for decisions made and offer any additional strengths and limitations of the research in addition to those identified in Papers 1 and 2. The researcher will also offer reflections of their experiences of the research process throughout, provide information on the challenges they experienced, and identify how their learning and knowledge has developed.

Paper 1: The Association between Akathisia and Suicidality after Neuroleptic Intervention: A Systematic Review of the Evidence

Topic Rationale

Whilst research on akathisia has increased in recent years (Salem, Nagpal, Pigott, & Teixeira, 2017), since it was acknowledged by Haskovec in 1902, the research base on akathisia has been considered limited (Sethi, 2004). Prior to finalising the focus of the review, the researcher conducted several scoping searches on scientific databases. It became apparent from these searches that there was limited research on akathisia, which presented challenges identifying a suitable topic. After reviewing several potential topics, the researcher found there were a sufficient number of studies published on the association between akathisia and suicidality, since a previous literature review by Hansen (2001), to warrant an updated review of the evidence. It was considered the review would provide valuable evidence on the association between akathisia and suicidality to inform the scientific evidence base, and inform policy and guidelines on suicidality.

Following examination of the previous review (Hansen, 2001) the researcher noted several limitations, including: i) it used limited search terms and scientific databases, ii) it did not solely focus on akathisia and suicidality, iii) it provided limited information on the case studies, iv) there was no evidence to suggest an appraisal of the literature was conducted, and v) when the review was conducted there were minimal quantitative research studies on akathisia and suicidality. Given there were

21 published studies on akathisia and suicidality focusing on neuroleptic medication since the previous review, the researcher thought they could improve on these limitations. The researcher also felt there was synergy between the review topic and their empirical study.

Literature Search

Research suggests that narrow searches provide incomplete results in systematic reviews (Atkinson & Capriani, 2018), and the need for robust and explicit search strategies to overcome the challenges of identifying all relevant studies from databases has been highlighted (Hopewell, Clarke, Lefebvre & Scherer, 2007). After extensive reading of the literature, the researcher decided to expand the search terms used in the previous review ('akathisia' and 'suicidality') (Hansen, 2001), to broaden the scope of the search and thus, improve on the previous search strategy. The researcher included terms and descriptors commonly associated with akathisia (identified in Paper 1), and endeavoured to ensure that all relevant articles on akathisia and suicidality were returned.

Absence of an internationally recognised definition of akathisia and diagnostic criteria (Hansen, 2001; Tachere & Modirrousta, 2017), presented challenges in establishing the search terms. To address this issue, the researcher utilised a number of appropriate sources, including: i) terms for akathisia and suicidality frequently used in published research, ii) descriptors of the manifestations of akathisia published by the Royal College of Psychiatrists (RCPSYCH), the Diagnostic and Statistical Mental of Mental Disorders (DSM-5) (American Psychiatric Association, 2013) and the International Classification of Diseases (ICD.10) (World Health Organisation, 1992), and iii) a search of medical subject headings (MeSH) on scientific databases. In conducting the final searches, the researcher used the descriptors associated with 'akathisia' and 'suicidality' with the Boolean operators 'and' or 'or'. They also improved on the previous review (Hansen, 2001) by searching five relevant scientific databases (PsycINFO, EMBASE, MEDLINE, CINAHL, Web of Science), to maximise the probability of retrieving all relevant evidence as advised in research (Bramer, De Jonge, Rethlefsen, Mast & Kleijnen, 2018). These databases were selected as they had the potential to include studies on

akathisia and suicidality, and specialised in psychology, medicine, biomedical science, nursing and allied healthcare professions.

The final searches provided relevant papers that were not in English. As the researcher felt it was important to be inclusive as possible, no limitations were placed for articles in English during the final searches, which they consider a strength of the review. In an attempt to obtain English copies of these papers, the researcher made requests to the University Library services, and the authors of the papers were contacted via 'Research Gate'. Unfortunately, only one of the authors provided a fully translated version of their article (Kornetova et al., 2018), which was originally in Russian.

Paez (2017) identified the importance and benefits of including grey literature within systematic reviews to provide a comprehensive overview of all relevant evidence. Another strength of the review was that a search of grey literature was conducted. This was conducted on 'Google' using the same search terms used for the database searches. Unfortunately, the search returned no results that met inclusion criteria. A second strength was that screening of titles and abstracts at full text level was undertaken by a second reviewer as recommended in research (Stoll et al., 2018). There were few discrepancies noted from this process, which suggests the search terms were clear and results yielded appropriate articles.

Inclusion and Exclusion Criteria

Participants below the age of 16 were excluded from the study as the aim was to limit the focus to adult individuals who developed akathisia secondary to neuroleptic medication use. As the previous review was published in 2001, the search criteria were set from 2001 onwards to provide relevant articles. A strength of the review was the inclusion of quantitative studies and case reports, and no articles were excluded on the grounds of methodology or design. This was pertinent as research reports an increase of systematic reviews including studies with diverse designs to address a wider range of research questions (Gough, 2015). Dixon-Woods and Fitzpatrick (2001) also highlight the importance of including studies from a range of methodological approaches, and Peinemann, Tushabe and Kleijnen (2013) state that *'the integration of multiple study designs in systematic reviews is required if patients*

should be informed on the many facets of patient relevant issues of health care intervention' (p. 10).

As identified in Paper 1, a potential limitation of the review involved the inclusion of summary studies that were unsuitable for quality appraisal. As this evidence was peer reviewed and met the other inclusion criteria they were included, however, they contained limited detail. One of these studies found a significant association between akathisia and suicidality and one did not find a significant association. Had these not been included in the review, there would have remained six studies that found a significant association between akathisia and suicidality overall, in addition to the case reports, and five that did not. The researcher concluded that including these studies provided useful evidence on the association between akathisia and suicidality.

Quality Appraisal

It is acknowledged that case reports provide useful contributions to healthcare research and practice (Meyer, 1985), however due to their general non-comparative nature which can increase the chance of bias, it is considered that '*certainty in the evidence derived from case series/ reports will be very low*' (Murad, Sultan, Haffar & Bazerbachi, 2018, p. 62). Becoming aware of the limited tools to assess for the quality and risk of bias in case reports, the researcher decided to produce a bespoke tool. The aim of this tool was not to include or exclude studies based on the scores they achieved, but rather to ensure the quality of the studies could be compared and contrasted. The tool was adapted from the CARE guidelines for case reports (Riley et al., 2017), the checklist for case reports from the Joanna Briggs Institute (Moola et al., 2017) and the case series and case report assessment tool by Murad et al (2018). The researcher also reviewed the Pierson (2009) criteria which outlines expected standards for case reports, and the Newcastle Ottawa Scale (Wells, Shea & O'Connell, 2011) to look for other potential criteria, and endeavoured to create a tool based on the available literature that would apply to the case reports in the review.

Prior to producing the bespoke tool, the researcher first used the checklist developed by Murad et al (2018) to appraise the case reports. After completing this process, it became clear that this tool focused on quality appraising case reports written to

document experimental medical interventions and trials. For example, the Murad et al (2018) tool contained questions about 'challenge and re-challenge phenomena'; a medical testing protocol whereby drugs are intentionally administered, withdrawn, then re-administered, whilst monitoring for effects. As the case reports retrieved from the search were reporting on the development of suicidality secondary to akathisia, the researcher decided that developing a bespoke tool would have greater utility and applicability.

A report by the Agency for Health Research Quality (AHRQ) concluded that there were 93 critical appraisal tools available for quantitative studies (Katrak, Bialocerkowski, Massy-Westropp, Kumar & Grimmer, 2004). Research highlights that the majority of these tools are often aimed at appraising specific study designs, such as Randomised Control Trials (RCT's) (Sirriyeh, Lawton, Gardner & Armitage, 2012). Given the heterogeneity in the designs of the quantitative studies retrieved, following consultation with the research team, it was decided that the Quality Assessment Tool for studies with Diverse Designs (QATSDD) (Sirriyeh et al., 2012) was the most appropriate tool to appraise the evidence, as it is specifically designed to assess quality and risk of bias in studies with diverse designs. Overall, the researcher found this tool valuable in assessing the quality of the papers and 'strong' inter-rater reliability scores were obtained from the secondary reviewer. However, the researcher did note that whilst discussing scores with colleagues, there were minor differences in how some of the criteria were interpreted, and what constituted specific scores. To rectify this the researcher held discussions with the secondary reviewer; any discrepancies in interpretation were discussed until consensus was reached.

Data Synthesis

Charrios (2015) argues that although systematic reviews are often considered synonymous with meta-analyses, not all systematic reviews have the data available to *'generate summary numeric results'* (p. 144). In our review, it was considered that employing a convergent synthesis design (Hong, Pluye, Bujold & Wassef, 2017) and utilising a narrative synthesis approach provided an adaptable framework to evaluate the evidence. Conducting a narrative synthesis enabled the researcher to address the primary review question and secondary objectives, and accommodated synthesising

the information from the quantitative studies and case reports. To ensure a good quality narrative approach, the researcher consulted guidelines by Popay et al (2006), the Centre for Reviews and Dissemination (CRD, 2008) and Ryan (2013). Campbell, Katikireddi, Sowden, McKenzie and Thomson (2017) argue that narrative synthesis is a method used when '*it may not be appropriate, or possible, to meta-analyse estimates of intervention effects*' (p. 1). There were several reasons why conducting a meta-analysis was inappropriate: i) the heterogeneity of the quantitative studies, both in terms of statistical reporting and methodological variations, meant that aggregation of the results and statistical pooling would not have provided overall effects, ii) the studies investigated varying forms of suicidality, the primary outcome of the review, which caused a lack of consistency as to how this was assessed across studies, and iii) the studies did not differentiate between different severities of akathisia. Additionally, the researcher was keen to include the case report studies, and although this would not have inhibited undertaking meta-analyses, the inclusion of the case reports also aligned with a narrative synthesis approach.

Learning and Development

In addition to the results gained from the review, the researcher reflected on how the review process had enhanced their knowledge. From the outset of the process, the researcher was mindful they had no prior experience of undertaking a systematic review. In this regard, the researcher found the guidance from the CRD (2008) an invaluable resource that provided detailed descriptions of the various processes involved in undertaking a review. The researcher also reflected on the extensive knowledge they acquired throughout the process, which included: i) how to develop a robust and effective search strategy, ii) increased knowledge of the various platforms, scientific databases and how to appropriately conduct searches, iii) completing a review protocol and the process of registering this with an appropriate database, iv) knowledge around conducting quality assessment and appraising literature, and v) becoming familiar with the processes of narrative syntheses. In completing the review, the researcher also reflected on how their knowledge of psychotropic and neuroleptic medication had been enhanced, and considered the benefits that this knowledge will bring to their future clinical practice.

Paper 2: Service User's First-Hand Experiences of the Psychosocial Effects of Akathisia

Studying Akathisia

Akathisia is estimated to affect 20-75% of service users (Shahidi, Rohani, Munhoz & Akhoundi, 2018; Donaldson, Marsden, Schneider & Bhatia, 2012) making it one of the most prevalent side effects of neuroleptic and other psychotropic medications. Yet, it remains one of the most underreported (Csernansky, 2002) and under researched (Jong-Hoon et al., 2002). Salem et al (2017) state that researching akathisia '*poses unique challenges and limitations'* (p. 791), which result from issues in its identification and diagnosis (Hirose, 2003), challenges in service users articulating their experiences (Lohr, Eidt, Alfaraj & Soliman, 2015), having no universally accepted definition or specific diagnostic criteria, and an incomplete understanding of its neurobiological basis (Hansen, 2001; Sachdev & Loneragan, 1991; Salem et al., 2017). Although some previous studies have explored the effects of akathisia on service users (identified in Paper 2), none have investigated the psychosocial experiences of service users, using qualitative methodologies. Undertaking a novel study that aimed to explore and make sense of service users' experiences of akathisia, would add to the literature base on this under researched area, and highlight how akathisia effects the lives and wellbeing of service users.

From the outset the researcher was aware of controversial issues related to studying akathisia. For example, an article by Breggin (2006), reported that the pharmaceutical company 'GlaxoSmithKline', attempted to suppress his reports, which contained information on the association between akathisia and suicidality. This illustrated the contentious nature of researching akathisia, and highlighted the potential vested interest and motivation of particular parties in wanting to minimise the acknowledgement of side effects that develop as a result of pharmacological intervention. The researcher also reflected how the majority of research on akathisia to date had a medical focus, investigating what additional pharmacological interventions would help address the condition.

Ethical Considerations and Ethical Approval Process

The maintenance of ethical standards was considered throughout the study. Prior to applying for ethical approval, the researcher consulted with the Community Liaison Group (CLG) from the University of Manchester to discuss the study, and gain the perspectives of service users on any potential ethical issues they thought were present. Thereafter, approvals were granted by a local NHS Research Ethics Committee (REC).

During the study, participants were provided with the necessary information about what they would be asked to do and how their data would be stored, via the participant information sheet, prior to giving informed consent. The researcher answered any questions they had. The researcher also ensured confidentiality was maintained by anonymising the transcripts during the transcription process and using pseudonyms throughout the write-up of the analysis. Coinciding with the National Institute of Clinical Excellence (NICE, 2018) guidance on capacity, the researcher assumed capacity unless there was evidence to suggest otherwise, as outlined by the principles in the Mental Capacity Act (MCA, 2019).

The researcher ensured that they were familiar with the risk and distress protocols prior to undertaking the interviews. They ensured that they had relevant contact details for professionals working with participants referred through the NHS and for those who self-referred, in the event these were required. Any risks that arose were discussed with their primary research supervisor (ST) as per protocol. The researcher reflected on the comparisons between managing risk as a clinician in training, and their role as a researcher. Supervision was used to reflect on how within their clinical role, the researcher would usually provide advice and support when presented with risk issues. However, within their role as a researcher, they were unable to directly provide necessary advice and support, and were required to signpost participants to relevant services. This juxtaposition gave rise to some internal conflicts for the researcher, which they found useful to explore with their supervisors.

Research has highlighted the challenges in recruiting participants from the NHS (Thompson & France, 2010). The researcher found the process of gaining ethical approval valuable in identifying additional areas of potential ethical concern that

could be addressed prior to commencing the study. They also found the initial ethical approval process relatively streamlined and straightforward. Throughout the approvals process in its entirety however, the researcher experienced approximately 20 weeks of additional delays beyond stipulated feedback times, which invariably impacted their ability to begin recruitment. For example, the researcher experienced a five-week delay after being informed they needed to submit a substantial amendment to add non-NHS sites to an approved project. Following response from the Health Research Authority (HRA), it became clear that the HRA do not oversee the addition of non-NHS sites and thus, this was a preventable loss of time. If the researcher was to conduct the study again, they reflected on how they would include the contingency plan within the original application to the REC, which would have avoided some additional delays.

Recruitment

Research highlights several issues in recruiting research participants from the NHS. Adams, Caffrey and McKevitt (2015) found that the pressures staff reported in facilitating recruitment whilst managing competing clinical caseloads had negative impacts on successful recruitment and retention of participants. They also found that staff questioned the benefits versus burdens of service users taking part in research. The limited resources within the NHS have also been highlighted as one factor impacting recruitment; including the retention and attrition of participants (Skea, Treweek & Gillies, 2017). Throughout the recruitment process, the researcher had first-hand experiences of these challenges, and clinicians helping with recruitment expressed how competing demands were preventing them engaging. The researcher reflected on the pressures facing professionals in the NHS, and how this creates a potential conflict with guidance that stipulates service users should have the opportunity to be informed about research (Department of Health, 2017).

Upon the addition of adding third-sector agencies to the study, the researcher found recruiting participants more accessible. After attending several weekly groups and speaking with potential participants at the 'Hearing Voices Network', several service users were keen to take part in the study and share their experiences of akathisia. The researcher reflected on how the study may have been enhanced by recruiting

participants from more than one of the third-sector agency groups; unfortunately, this was not possible within the recruitment window.

Participants

Despite challenges in recruitment, the researcher recruited one participant from the NHS and five from the third-sector organisation. Though there is no definitive sample size propagated for studies using Interpretative Phenomenological Analysis (IPA) (Smith & Osborn, 2003; Brocki & Wearden, 2006), research posits that approximately four to 10 participants should be obtained for professional doctorate studies utilising an IPA framework (Smith, Flowers & Larkin, 2009; Pietkiewicz & Smith, 2014). There also exists a consensus within IPA researchers that larger samples can result in losing *'potentially subtle inflections of meaning'* (Collins & Nicolson, 2002, p. 626). Therefore, aiming to recruit six to eight participants from the outset of the study fulfilled the criteria above, allowed for potential attrition, and aligned with other psychological research using IPA (Todd, Simpson & Murray, 2010; Knudson & Coyle, 2002). The researcher felt that the eventual recruitment of six participants was sufficient for their IPA analysis, and enabled the detailed case-by-case analysis pertinent to this approach (Smith et al., 2009). The range of participants that wished to take part in the study resulted in an equal split of binary gender, and provided participants from a variety of ethnic, cultural and educational backgrounds and ages; overall providing good variation in the sample.

Establishing Akathisia

The lack of a universally accepted definition or specific diagnostic criteria for akathisia, in addition to making it a difficult area to research, led to the researcher developing strategies for ensuring participants had experienced akathisia, and were eligible to take part in the research. The researcher developed a screening checklist to ensure individuals taking part self-reported experiencing subjective symptoms and objective signs of akathisia, after receiving a medication found to be associated with akathisia (Lane, 1998; Bazire, 1995; Sachdev, 1995; Lohr et al., 2015). In developing the screening checklist, in addition to consulting with the research team and relevant literature, the researcher reviewed medication leaflets by the Royal College of Psychiatrists (RCPSYCH), retrieved from (https://www.rcpsych.ac.uk/).

The research team decided it would be inappropriate to use a specific measure to identify akathisia for several reasons. Firstly, the Barnes Akathisia Rating Scale (BARS) (Barnes, 1989, 2003) and the Hillside Akathisia Scale (HAS) (Fleischhacker et al., 1989), the most commonly used measures to identify akathisia, require the presence of both subjective symptoms and objective signs to be present for diagnosis. As research highlights that the subjective symptoms of akathisia may not be accompanied by objective signs (Hirose, 2003), it was felt using a measure would have limited utility in this instance. Instead, using a screening tool allowed for participants to highlight their own internal sensations and movements they experienced with akathisia. Secondly, as the BARS and HAS require observation of service users for extended periods of time, they are more suited to inpatient settings; given this was a field study, the researcher did not have the ability to do this. Thirdly, whilst such measures are useful for experimental research looking to establish causality, as this was a qualitative study, it was not deemed necessary. Hirose (2003) argues that attempts to define and provide diagnostic criteria for akathisia have had counterproductive effects of raising the threshold for diagnoses. The fourth reason for not using a measure related to the researcher being mindful of the potential impact, distress and rejection participants who volunteered to take part in the study may experience, if they felt 'their' experience of akathisia was not extensive enough to meet specific criteria.

Developing a Topic Guide

In developing the topic guide, the researcher consulted the Smith et al (2009) and Smith and Osborn (2015) texts, and used open-ended questions as advised in research (Jamshed, 2014). The topic guide for this study was designed to cover a broad range of social and psychological factors, to ultimately explore participants' experiences of living with akathisia. The researcher also conducted mock interviews with members of the research team prior to undertaking the interviews, which helped familiarise themselves with the content. Whilst developing the topic guide, the researcher considered if conducting a focus group would have utility. Smith (2004) and Brocki and Wearden (2006) argue that whilst focus groups may be useful for eliciting information on neutral topics, participants may not feel comfortable sharing experiences of a more personal nature in such forums. As IPA aims to elicit personal experiences and it was envisaged matters of a personal nature would be discussed

during the interviews, the researcher concluded that facilitating a focus group would yield limited benefit to the development of the topic guide.

To ensure participants had the opportunity to discuss pertinent matters, they were asked at the end of the interview if there was anything more they wished to share. However, no participants provided additional information, and some commented that the content of the interview included a broad range of areas coinciding with their experiences. Following completion of the interviews, the researcher reflected on additional areas of investigation that may have been useful. These included: i) further exploration of specific adjustments participants made to cope with akathisia, and ii) further exploration of how akathisia impacted participants' perceptions of themselves and their sense of identity specifically, as all participants reported changes in these areas during the interviews.

Interviews

Semi-structured interviews are commonly used within qualitative research (Jamshed, 2014; DiCicco-Bloom & Crabtree, 2006) and are recommended for IPA studies (Smith et al., 2009; Smith & Osborn, 2003). Utilising this approach enabled the aims and objectives of the research to be fulfilled, whilst allowing flexibility to facilitate participants exploring their experiences of akathisia. The researcher felt that using this technique enabled them to form appropriate and necessary rapports, which was important given the emotive nature of the topic. The researcher felt that participants engaged well during the interviews, which was reflected by the rich data obtained, and the duration of the interviews ranged from 36 to 83 minutes *(M = 49.5 minutes)*.

To ensure inclusivity, the researcher endeavoured to take a flexible approach, making reasonable adjustments throughout the interviews as necessary, which included: i) adapting their communication using simplified language free of medicalised jargon, ii) being flexible in the choice of venue and format of the interviews, and iii) reassuring participants they were able to take breaks when necessary. Murray (2003) highlights the potential therapeutic benefits that can be gained from the researcher-participant relationship, during which participants share difficult and emotional life experiences. The researcher reflected on their role as a trainee clinical psychologist, and the usefulness of their therapeutic skills in

providing reflections and conveying empathy, during the interviews. All participants reported it was helpful to speak about their experiences, as in many cases, they felt they had not had this opportunity previously. During supervision, the researcher reflected on the importance of developing appropriate rapports in non-therapeutic settings during research.

The researcher also reflected on their observations and the challenges encountered during the interviews. As participants were experiencing akathisia, they invariably found it difficult to remain stationary throughout the duration of the interview. Participants frequently reported a need to pace, and whilst the researcher reassured them this was fine, the possibility remains that this may have impacted their ability to attend and concentrate and thus, fully share their experiences. In addition to akathisia, several participants were experiencing symptoms associated with psychosis during the interviews; particularly 'hearing voices'. The researcher considered how this may also have impacted participants' abilities to recount their experiences, and it is conceivable that if such challenges were not present, more data may have been obtained. Participants reported it was useful for some questions to be repeated, and the researcher checked throughout that the experiences participants described related to akathisia.

Methodology and Data Analysis

IPA is an approach which is *'committed to the examination of how people make sense of their major life experiences'* (Smith et al., 2009, p. 1), and is based on the principles of phenomenology, hermeneutics and idiography. IPA requires the researcher to take a reflexive approach, whereby both *'the participants' and researchers' interpretation of phenomena is taken into account in the process of analysis'* (Pietkiewicz & Smith, 2014, p. 361). As this was the first study to explore service users' first-hand experiences of akathisia, the researcher considered that the theoretical orientation and phenomenological epistemology of IPA (McLeod, 2001) aligned with the aims of the research. It was also considered that IPA would enable an in-depth insight into the psychosocial experiences of service users with akathisia, through the acquisition of personal perceptions, experiences and meanings.

Upon reviewing alternative analytic approaches, the researcher concluded that Thematic Analysis (TA) (Braun & Clarke, 2006) was inappropriate, as TA generally looks at themes across the whole data set, as opposed to the dual focus of IPA, which propagates and in-depth case-by-case analysis to draw patterns of meaning across participants (Larkin, Watts & Clifton, 2006). Additionally, TA as a method is not bound by any particular theoretical orientation and generally has larger sample sizes, which would not allow for the quality and depth of interpretation this study aimed to acquire. The researcher also considered Grounded Theory (GT) (Strauss & Corbin, 1990; Glaser, 1992) as an alternative methodology. Smith et al (2009) argue that although IPA and GT both involve an inductive approach, IPA is likely to offer *'more detailed and nuanced analysis of the lived experience of a small number of participants with an emphasis on the convergence and divergence between participants'* (p. 202). This is in opposition to GT that often uses larger sample sizes with the aim of producing a theory or model of the phenomena being studied, by which to generalise the findings to larger heterogeneous samples (Tie, Birks & Francis, 2019). As such, IPA was considered more appropriate.

The data analysis process in IPA is known for being *'detailed and very time consuming'* (Pietkiewicz & Smith, 2014, p. 364). The researcher found the stages for analysis outlined in Smith et al (2009) an invaluable resource throughout the analysis process, and that they were able to align their analysis closely to the guidelines. The researcher also appreciated the rich and detailed information that the multi-stage analysis provided, particularly during write-up of the results. They found one of the first stages of analysis which focused on descriptive, linguistic and conceptual elements, though time consuming, added depth and clarity to their understanding and interpretations of participants' experiences. The researcher reflected on how revisiting the transcript after breaks, also aided the generation of new ideas, reflections and perspectives. The researcher found it incredibly helpful to consult with the research team during the development of the subordinate and superordinate themes, particularly as they had a vast data set which required multiple reviews to arrive at the identified themes.

Reflexivity

Reflexivity refers to how '*the researcher's involvement with a particular study influences, acts upon and informs such research*' (Nightingale & Cromby, 1999, p. 228). Palaganas, Sanchez, Molintas and Caricativo (2017) argue that although the concept of reflexivity is '*poorly described and elusive*' (p. 426), it involves a '*continuous process of reflection by researchers on their values…*' (p. 427) and Shaw (2010) asserts taking a reflexive approach involves '*explicit evaluation of the self*' (p. 324). The researcher felt that the concept and process of reflexivity melded well with the phenomenological, idiographic and double-hermeneutic principles underpinning IPA (Smith et al., 2009). They also accepted the inevitable subjectivity and bias inherent in their interpretations of the data, driven by their own perspectives and world view (Shaw, 2010).

The author (LB) remained cognizant throughout the research process of their status as a white British male in their final year of professional training in clinical psychology. They were mindful of having no prior personal experience of being a service user in mental health settings, nor had they previously been diagnosed or received any medication for a mental health problem. They also had no prior experience living with akathisia. The researcher was also mindful of their professional position during the interviews, and reflected during supervision on how this may have impacted what participants felt comfortable to disclose.

The researcher found supervision a valuable space to think about their values, background and life experiences, and other subjective factors that could potentially influence the research and analysis. Yanos and Ziedonis (2006) highlight the challenges and potential conflicts that can occur for individuals in simultaneous 'patient-orientated clinician-researcher' roles, which social psychologists' term 'inter-role conflict' (Polasky & Holohan, 1998). To address these potential issues, the researcher found it helpful to distinguish boundaries and provide clarity of their role with participants, prior to them providing informed consent. The researcher thought that taking this approach helped maintain boundaries and focus on the interview topic, whilst creating a space where participants felt safe to share their experiences. Supervision was also used to reflect on how the emotions that were

evoked for the researcher during the interviews, may relate to their own life experiences.

To maintain a reflexive approach during the analysis, the researcher was mindful this was their first time conducting IPA, and they attended additional research tutorials to discuss the theoretical underpinnings of IPA, and the comparisons between IPA and other qualitative approaches (i.e. TA and GT). Within the tutorials the analytic process of IPA was discussed in detail and the researcher's thoughts and perspectives of IPA's theoretical underpinnings were explored. The researcher maintained a reflective diary throughout the research process (Smith, 1999) and made anonymised notes after each interview, which helped them reflect on potential subjectivities, their emotional responses and thoughts as advised in research (Holmes, 2014). These notes were useful during the analysis process (Elliott, Ryan & Hollway, 2012). The research team reviewed transcript extracts to help make sense of the experiences of participants, and subordinate and superordinate themes were reviewed and revised on several occasions on consultation with the research team, in line with IPA guidance (Smith et al., 2009; Smith & Osborn, 2015); helping to ensure validity and scientific rigour.

Learning and Development

In addition to the results gained from the empirical study, the researcher reflected on how their knowledge of the processes of conducting clinical research had progressed. The researcher reflected on the challenges of navigating within multiple organisations and systems, and one of their biggest learning experiences has been an increased understanding of the intricacies of the research process, the roles of the different organisations, and the complexities of designing and implementing research within the NHS and third-sector organisations. The researcher felt their knowledge of different qualitative methodologies and methods, particularly IPA, had been enhanced significantly throughout the process. They considered that such experiences will be invaluable when undertaking any future research in clinical settings.

Personal Reflections

Throughout the research process, the researcher reflected on the challenges of undertaking research on akathisia, which had mostly been researched by medical professionals and the pharmaceutical industry. Through absorbing themselves in the literature, the researcher found they became better acquainted with medicalised language, and reflected on how the majority of research on akathisia sought to find additional pharmacological interventions. The researcher felt there existed a general lack of acknowledgement within the literature about the distress akathisia causes for service users, which made them reflect on the medicalised nature of mental health services, and what clinical psychology can offer as a profession.

During the research process, there were instances where the challenges of competing demands of the clinical psychology doctorate, in parallel with the requirements and challenges of the research and trying to balance personal commitments, felt particularly difficult to manage for the researcher, and required determination and perseverance. The researcher found supervision extremely helpful as a forum to explore and reflect on the challenges they encountered and valued the shared experiences of colleagues. On balance, the researcher felt that the research process, whilst challenging, has been an invaluable learning opportunity which outweighs the challenges encountered, and they are confident the experience will be beneficial to their future career.

Implications of the Research

The findings from the systematic literature review and empirical studies advance the overall knowledge-base and understanding of drug-induced akathisia. As the implications of the research are highlighted within Papers 1 and 2, they will not be repeated here. However, the general recommendations from the research centre around better recognition and interventions for akathisia, additional training for clinical staff, and an increased awareness of the psychological and social distress akathisia causes. As the first study of its kind, this research provides a novel psychological perspective and insight of the lives of service users who develop akathisia, that it is hoped can inform the development of a universally accepted

definition and set of specific diagnostic criteria, the knowledge of clinicians working in healthcare settings about the needs of service users who develop akathisia, the development of comprehensive treatment models for akathisia, and guidelines on the prevention of suicidality, medication, and needs of individuals with mental health problems.

Dissemination Plans

It is planned that Paper 1 will be submitted for publication to the *Journal of Human Psychopharmacology*. It is planned that Paper 2 will be submitted for publication to the *Journal of Qualitative Health Research.* The researcher also plans to produce a poster of the empirical study and to submit and present this at a relevant conference.

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Appendices

Appendix A: Submission guidelines for the *Journal of Human Psychopharmacology*

Data Protection and Privacy

By submitting a manuscript to, or reviewing for, this publication, your name, email address, institutional affiliation, and other contact details the publication might require, will be used for the regular operations of the publication, including, when necessary, sharing with the publisher (Wiley) and partners for production and publication. The publication and the publisher recognize the importance of protecting the personal information collected from users in the operation of these services, and have practices in place to ensure that steps are taken to maintain the security, integrity, and privacy of the personal data collected and processed. You can learn more at https://authorservices.wiley.com/statements/data-protection-policy.html.

Preprint Policy

Human Psychopharmacology: Clinical and Experimental will consider for review articles previously available as preprints. Authors may also post the submitted version of a manuscript to a preprint server at any time. Authors are requested to update any pre-publication versions with a link to the final published article.

1. AIMS & SCOPE

Human Psychopharmacology: Clinical and Experimental (HUP) provides a forum for the evaluation of clinical and experimental research on both new and established psychotropic medicines. Experimental studies of other centrally active drugs, including herbal products, in clinical, social and psychological contexts, as well as clinical/scientific papers on drugs of abuse and drug dependency will also be considered. While the primary purpose of the Journal is to publish the results of clinical research, the results of animal studies relevant to human psychopharmacology are welcome. The following topics are of especial interest to the editors and readers of the Journal:

- All aspects of clinical psychopharmacology
- Efficacy and safety studies of novel and standard psychotropic drugs
- Studies of the adverse effects of psychotropic drugs
- Effects of psychotropic drugs on normal physiological processes
- Geriatric and paediatric psychopharmacology
- Ethical and psychosocial aspects of drug use and misuse
- Psychopharmacological aspects of sleep and chronobiology
- Neuroimaging and psychoactive drugs
- Phytopharmacology and psychoactive substances
- Drug treatment of neurological disorders
- Mechanisms of action of psychotropic drugs
- Ethnopsychopharmacology

• Pharmacogenetic aspects of mental illness and drug response
• Psychometrics: psychopharmacological methods and experimental design

2. ETHICAL GUIDELINES

HUP has adopted the following ethical guidelines for publication and research.

2.1 Original Publication

Submission of a manuscript will be held to imply that it contains original unpublished work and is not being submitted for publication elsewhere at the same time. The author must supply a full statement to the Editor-in-Chief about all submissions and previous reports that might be regarded as redundant or duplicate publication of the same or very similar work.

2.2 Authorship and Acknowledgements

Authorship: Authors submitting a paper do so on the understanding that the manuscript has been read and approved by all authors and that all authors agree to the submission of the manuscript to the Journal.

HUP adheres to the definition of authorship set up by The International Committee of Medical Journal Editors (ICMJE). According to the ICMJE authorship criteria, all named authors should meet the following conditions: 1) substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data, 2) drafting the article or revising it critically for important intellectual content and 3) final approval of the version to be published. Participation solely in the acquisition of funding or the collection of data does not justify authorship. All people who fulfil the criteria for authorship should be listed as authors.

The Editors recognise that complex, large-scale and multi-centre research will often result in a significant number of people fulfilling the authorship criteria. However, they reserve the right to ask the lead author to justify the inclusion of more than six authors.

Acknowledgements: Authors can declare grant funding, additional assistance from individuals or bodies, or any other aspect where it is felt that those individuals or bodies should be given credit. Do not mention conflicts of interest in the Acknowledgements.

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HUP requires that sources of financial support for the work reported within the manuscript are fully acknowledged, and any potential conflicts of interest noted.

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When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 1983. Do not use patients' names, initials or hospital numbers, especially in illustrative material. When reporting experiments on animals, indicate whether the institution's or a national research council's guide for, or any national law on, the care and use of laboratory animals was followed. A statement describing explicitly the ethical background to the studies being reported should be included in all manuscripts in the Materials and Methods section. Ethics committee or institutional review board approval should be stated.

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HUP attempts to keep the review process as short as possible to enable rapid publication of new scientific data. In order to facilitate this process, please suggest one reviewer from outside the country where the author is based.

4. MANUSCRIPTS TYPES ACCEPTED

HUP invites the following types of submission. All submissions are subject to peer review:

Research Articles

Research Articles are the Journal's primary mode of scientific communication.

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Authors who wish to submit an unsolicited review should first contact the Editor-in-Chief to determine its suitability for publication in the Journal.

Short Communications

Short research pieces and practical inferences from clinical observations will be considered, but should not exceed 1500 words.

Case Reports

The journal does not accept case reports for publication. Authors of case reports are encouraged to submit to the Wiley Open Access journal, Clinical Case Reports www.clinicalcasesjournal.com which aims to directly improve health outcomes by identifying and disseminating examples of best clinical practice.

5. MANUSCRIPT PREPARATION

5.1 Format

Language: The language of publication is English. Authors for whom English is a second language should have their manuscript professionally edited by an English speaking person before submission to make sure the English is of high quality. You may wish to consider using our editing services which are described at http://wileyeditingservices.com/en/. All services are paid for and arranged by the author, and use of this or a similar service does not guarantee acceptance or preference for publication.

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Borstrøm, I., & Elbro, C. (1997). Prevention of dyslexia in kindergarten: Effects of phoneme awareness training with children of dyslexic parents. In C. Hulme & M. Snowling (Eds.), Dyslexia: Biology, cognition and intervention (pp. 235–253). London, UK: Whurr.

Balakrishnan, R. (2006, March 25-26). Why aren't we using 3d user interfaces, and will we ever? Paper presented at the IEEE Symposium on 3D User Interfaces. doi:10.1109/VR.2006.148

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Appendix B: Quality appraisal tool for case reports

V1. 24/01/2020

Adapted Quality Appraisal Checklist for Case Report Studies

The following quality appraisal tool which has been designed to assess the risk of bias in case report studies has been adapted from the CARE guidelines for case reports (Riley et al., 2017), the checklist for case reports from the Joanna Briggs Institute (Moola et al., 2017) and the case series and case report assessment tool by Murad, Sultan, Haffar & Bazerachi (2018).

Reviewer:	**Date:**
Author:	**Year:**

Criteria	**No (0 points)**	**Partial (1 point)**	**Yes (2 points)**	**Not Applicable**
1. Were the individual's demographic characteristics clearly described?				
2. Was the individual's history clearly described and presented?				
3. Was the current clinical condition of the individual and their main symptoms on presentation clearly described?				
4. How well defined are the key concepts within the case report?				
5. Were alternative diagnoses or causes that may explain the individual's presentation ruled out?				

1

6. Were standardised assessment or measures used to collect information regarding the presenting problem(s) and outcomes?				
7. Were diagnostic tests or assessment methods and the results clearly described?				
8. Was the intervention or treatment procedure clearly described?				
9. Was the post-intervention clinical condition clearly described?				
10. Were adverse or unanticipated events identified and described?				
11. Is the case described with sufficient detail so as to allow clinicians to make inferences related to their own practice?				
12. Does the case report provide takeaway lessons?				
13. Is there evidence of informed consent being gained within the case report?				

Total Score out of 26: **Percentage:**

Guidance for Completion of the Adapted Quality Appraisal Checklist for Case Report Studies

1.	Does the case report clearly describe the individual's age, sex, race, social demographics, relevant medical history, diagnosis and medications? The setting and context may also be described (Moola et al., 2017).
2.	A good case report will clearly describe the history of the individual, their medical, family and psychosocial history including relevant medical information, as well as relevant past interventions and their outcomes (Moola et al., 2017; Riley et al., 2017).
3.	The current clinical condition of the individual should be described in detail including the uniqueness of the condition, symptoms, frequency and severity (Moola et al., 2017).
4.	Does the case report provide working definitions or diagnostic criteria for the key concepts of akathisia and suicidality?
5.	Is there evidence within the case report of alternative or differential diagnoses being considered and excluded? (Riley et al., 2017).
6.	A case report is enhanced if it makes reference to specific valid and reliable measures or standardised tests which have been used to identify the presenting problems and outcomes.
7.	The reader of the case report should be provided sufficient information to understand how the patient was assessed. It is important that all appropriate tests and measures are ordered to confirm a diagnosis and therefore the case report should provide a clear description of any tools used (whether a 'gold standard' or alternative/ adapted test) (Moola et al., 2017).
8.	It is important to clearly describe treatment or intervention procedures as other clinicians will be reading the paper and therefore require a clear description of the treatment protocol. The report should describe the treatment/ intervention protocol in detail (Moola et al., 2017).
9.	A good case report should clearly describe the clinical condition post-intervention in terms of the presence or lack thereof symptoms (Moola et al., 2017).
10	With any treatment intervention or drug it is likely there will be some adverse events and in some cases, these may be severe. It is important that adverse

	events are clearly documented and described, particularly when a new or unique condition is being treated or when a new drug or treatment is used. In addition, unanticipated events, including any that may yield new or useful information should be identified and clearly described (Moola et al., 2017).
11	A case report that is described with a sufficient amount of detail will enable other practitioners to apply the evidence derived from the case in their clinical practice. Alternatively, a case report that is not adequately described will likely not be helpful to a clinician's clinical practice (Murad, Sultan, Haffar & Bazerachi, 2018).
12	Case reports should summarise key lessons learned from a case in terms of the background of the condition and clinical practice guidance for clinicians when presented with similar cases (Moola et al., 2017).
13	A good case report should demonstrate that informed consent was obtained from the individual or, if it was not possible to obtain signed consent, all possible attempts should be made to obtain this and an explanation given as to why it was not possible for this to be obtained. In exceptional circumstances or where the patients are unable to provide consent, consent may be obtained from a close relative (Riley et al., 2017).

Appendix C: Quantitative study quality assessment scores

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q
1	Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Total	Percentile
2	Reutfors (2016)	1	3	3	2	3	2	0	3	0	3	3	2	0	2	27	64.28%
3	Dong, Ho & Kan (2005)	2	3	3	2	3	3	3	3	2	3	3	1	0	3	34	80.95%
4	Moncrieff (2009)	2	3	2	1	2	3	1	2	0	3	3	2	0	3	27	64.28%
5	Lukaschek (2014)	2	3	3	2	2	2	2	3	1	2	3	3	0	2	30	71.42%
6	Kornetova (2018)	2	3	3	0	2	2	2	3	1	3	2	1	0	2	26	61.90%
7	Seemuller et al (2012a)	2	2	3	2	2	3	3	1	1	2	3	3	0	2	29	69.04%
8	Atbasoglu (2001)	2	2	3	0	2	2	2	2	1	3	3	2	0	3	27	64.28%
9	Pompili (2009)	2	3	3	1	1	3	2	2	0	2	3	2	0	2	26	61.90%
10	Emsley (2003)																N/A
11	Mlodozeniec (2009)																N/A
12	Seemuller et al (2012b)	2	2	1	0	2	1	1	2	1	2	2	1	0	2	19	45.23%
13	Hansen (2013)	2	3	3	0	2	2	3	1	0	2	3	3	0	3	27	64.28%
14	Hansen (2004)	1	3	2	0	1	3	1	2	1	3	2	1	0	2	22	52.38%
15																	
16																	

Appendix D: Submission guidelines for the *Journal of Qualitative Health Research*

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6.4 Promoting your article
Publication is not the end of the process! You can help disseminate your paper and ensure it is as widely read and cited as possible. The SAGE Author Gateway has numerous resources to help you promote your work. Visit the Promote Your Article page on the Gateway for tips and advice.

Appendix E: Consent to contact form

MANCHESTER 1824
The University of Manchester

Version 1. 03/05/2019
IRAS ID: 257977

Study Title: The psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences

Researcher: Luke Beardmore

If you are interested in taking part in this study and would like the researchers to contact you please give your details below. You should only provide the information if you are happy to be contacted in that way. For example, if you do not want to be contacted by phone then do not provide a phone number.

Please note the following points in relation to the processing of your data:

- Data will be held securely by the research team on behalf of the University of Manchester according to the University's data protection and information security policies. A copy of the University's Privacy Notice can be found at: http://documents.manchester.ac.uk/display.aspx?DocID=37095
- Access to the data will be restricted to the research team for the sole purpose of contacting you about this study.
- Your data will not be shared with any third party without your written permission.
- The details collected will only be stored for as long as required to find out if you wish to take part in the study. Once no longer needed, that data will be destroyed securely.
- If you decide to change your mind about being contacted about the study or would like your details to be destroyed you can contact Luke Beardmore on luke.beardmore@postgrad.manchester.ac.uk

Once you have completed your details, please ensure that you have added your signature. You can then tear off the slip below and give it to the clinician that informed you about the study. You can keep the top half of this form for your information.

✂----------

I am happy **to provide/for my health care professional to provide** (delete as appropriate) my personal details so that I can be contacted about this study.

Name	
Signature	
Today's date	

Please complete the details below or hand back to your health care provider to complete on your behalf

Contact by letter	Address	
	Post Code	
Contact by phone	Preferred contact number	
	When would you prefer to be contacted? (please circle)	Morning/ Afternoon/ Evening/ Don't Mind
Contact by email	Email address	

Appendix F: Eligibility screening checklist

Study: The Psychosocial Effects of Akathisia after Neuroleptic Use: A Qualitative Exploration of Real Life Experiences

Eligibility Screening Checklist

Criteria	Criteria met	
	Yes	No
1. Participant self-identifies as having experienced any of the symptoms associated with akathisia in the past 6 months or more.		
2. Participant has experienced at least one of the symptoms associated with akathisia such as uncomfortable restlessness, pacing, irritability, unable to sit still, feeling the need to move, difficulty sleeping, pacing and agitation as outlined in the literature.		
3. Participant is an adult (18 years of age or above).		
4. Participant possesses mental capacity to be able to provide informed consent to take part in the study.		
5. Participant has a current or previously diagnosed mental health problem as identified in the Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD) manuals.		
6. Participant has received a neuroleptic medication associated with the onset of akathisia (i.e. typical or atypical antipsychotics, antidepressants) as highlighted within the current literature base.		
7. Participant is an English speaker.		

Appendix G: Participant information sheet

MANCHESTER 1824
The University of Manchester

Version 5. 24.09.2019
IRAS ID: 257977

Participant Information Sheet (PIS)

Study: The psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences

This PIS should be read in conjunction with The University privacy notice
http://documents.manchester.ac.uk/display.aspx?DocID=37095

We would like to invite you to take part in a research study as part of a student project for a Doctorate in Clinical Psychology (ClinPsyD). Before you decide whether to take part, it is important for you to understand why the research is being carried out and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. After reading this information sheet you will have at least 24 hours to decide whether you wish to take part in the study. The researcher will contact you to ask if you would like to take part.

Who will conduct the research?

This research will be carried out by Luke Beardmore who is a Trainee Clinical Psychologist from the University of Manchester. Please find contact details below:

Name: Luke Beardmore
Role: Chief Investigator & Trainee Clinical Psychologist
Address: Faculty of Biology, Medicine and Health; School of Health Sciences; Division of Psychology and Mental Health; 2nd Floor, Zochonis Building; The University of Manchester; Oxford Road; Manchester; M13 9PL.
Email: luke.beardmore@postgrad.manchester.ac.uk
Tel No: 0161 306 0400

The research is supervised by Dr Sara Tai (Consultant Clinical Psychologist), Yvonne Awenat (Registered Nurse & Clinical Research Fellow), and Dr Christopher Murphy (Consultant Neurologist). The 4 individuals named above form the 'research team'. This research is sponsored by the University of Manchester.

What is the purpose of the research?

The purpose of this study is to gain a better understanding of people's experiences of developing symptoms of akathisia. Akathisia is a movement disorder that can develop after taking some medications for mental health problems. In addition to a number of other symptoms, people who develop akathisia describe having feelings of inner restlessness and experience agitation and an inability to sit still.

As there is little known about akathisia, we would like to find out more about how this condition affects people's lives. We hope to use the knowledge gained from this study to improve the care and treatment that people who develop akathisia receive.

Why have I been chosen?

You have been invited to take part in the study because you expressed an interest in taking part, are over 18 years of age, are an English speaker and have received medication for a diagnosed mental health problem. After receiving this medication, you reported developing at least one of the symptoms known to be associated with akathisia. We hope to recruit approximately 7 other people to take part in the study.

What would I be asked to do if I took part?

If you agree to take part in the study you will be asked to sign a consent form. You will be offered a copy of this form. You will also be asked to complete a demographics form which records characteristics on ethnicity, gender, age, education level and a brief medical history relevant to the inclusion criteria for the study. If you have self-referred to take part in the study you will also be asked to consent to the chief investigator contacting a professional involved in your care to gain any relevant risk-related information prior to taking part in the study; this will be optional and dependent on whether you are currently open to or seeing, a professional from another service. If you wish to take part in this study the researcher will arrange to meet you at a time and place convenient for you to conduct an interview which will last for up to 60 minutes. The interview may take place in your home, at the University of Manchester, at a designated NHS building or on the telephone, depending on your preference. For face to face interviews, the interviews will be audio recorded and later transcribed. In the event that you would prefer for the interview to be conducted via telephone, the chief investigator will audio record consent by recording each point of the consent form in audio format along with your name and your agreement to take part in the study. To ensure confidentiality interviews conducted via telephone will take place in private rooms at the University of Manchester. Any care you are currently receiving will not be altered in any way as a result of taking part in the study. It will not be possible to remove your information from the project once it has been anonymised. All data will be fully anonymised after 48 hours of the interview, after which point it will not be possible to withdraw your data. If you wish the researcher will arrange to send you a summary of the results of the study after it has finished. The research project will last for approximately 6 months in total.

During the interview you will be asked questions related to the symptoms you have experienced and how these symptoms may have impacted your life and your abilities. You will also be asked what medication/s you are currently taking, or have taken, over the last twelve months. At the end of the interview, you will be invited to speak about any other experiences you have. You will have the opportunity to provide information related to akathisia that the researcher did not directly question you about.

What are the risks of taking part?

It is not anticipated that you will experience any distress from taking part in the interview. However, we appreciate that for some people discussing their experiences has the potential to be upsetting. You will be able to take a break at any point throughout the interview or terminate the interview should you wish. In case you do experience distress following the interview, the researcher will provide information of where you can seek additional support.

What are the benefits of taking part?

There are no immediate benefits of taking part in the research, however, it is hoped that through the information gained from the study professionals will have a better understanding of the effects of akathisia leading to future improvements in care.

What will happen to my personal information?

In order to undertake the research project, we will need to collect the following personal information from you:

- Name and signature for consent purposes.
- Contact details e.g. email address, telephone number or address.
- Demographics form.
- Audio recordings of the interview session.
- Contact details of your GP and other Health Care Professional.

We are collecting and storing this personal information in accordance with the General Data Protection Regulation (GDPR) and Data Protection Act 2018 which legislate to protect your personal information. The legal basis upon which we are using your personal information is "public interest task" and "for research purposes" if sensitive information is collected. For more information about the way we process your personal information and comply with data protection law please see our privacy notice for research participants. http://documents.manchester.ac.uk/display.aspx?DocID=37095

The University of Manchester as Data Controller for this project, takes responsibility for the protection of the personal information that this study is collecting about you. In order to comply with the legal obligations to protect your personal data, the University has safeguards in place such as policies and procedures and all researchers are appropriately trained.

Only the research team at the University of Manchester will have access to your personal identifiable information. This is data that could identify you. It may also be necessary for the research team to access this information for the purposes of 'lone working' when the chief investigator conducts the interview. All personal identifiable information from the interviews will be removed during the write-up (transcription) process and will be fully anonymised as soon as is practical. The original audio recordings will then be deleted. All personal information (i.e. address, name, demographics forms) will be stored in secure filing cabinets at the Division of Psychology and Mental Health at the University of Manchester throughout the study, after which they will be destroyed. Consent forms to participate in the study will be retained for up to 5 years. If you provided audio recorded consent to taking part in the study for the purpose of having the interview conducted via the telephone, these recordings will also be retained for up to 5 years. The audio recorded consent files will be stored separately to the research data in line with personal data requirements and will be destroyed after completion of the study.

Individuals from the University of Manchester, NHS Trust or regulatory authorities may need to look at the data collected for this study to make sure the project is being carried out as planned. This may involve looking at identifiable data, but all individuals involved in auditing and monitoring the study will have a strict duty of confidentiality to you as a research participant.

You have a number of rights under data protection law regarding your personal information. For example, you can request a copy of the information we hold about you, including audio recordings. This is known as a Subject Access Request. If you would like to know more about your different rights, please consult our privacy notice for research and if you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to The Information Governance Office, Christie Building, University of Manchester, Oxford Road, M13 9PL. at the University and we will guide you through the process of exercising your rights.

You also have a right to complain to the Information Commissioner's Office, Tel 0303 123 1113

Will my participation in the study be confidential?

Yes, your participation in the study will be kept confidential. In the event that there are concerns about your safety or the safety of others the researcher may need to 'break confidentiality.' In the event that a disclosure was made that would require further action, the researcher may need to contact your named health professional, GP, or other relevant authorities in order to ensure the safety of yourself and of others. The researcher will remind you of this before the interview begins and will tell you if they need to break confidentiality.

Any personal information that you are asked to provide will be kept confidential. However, relevant authorities may need to carry out audits on the project which may involve reviewing confidential information. Any personal identifiable information will be kept in secure filing cabinets at the Division of Psychology and Mental Health at the University of Manchester throughout the study. At the end of the study all personal identifiable information will be destroyed.

The audio recordings of the interviews will be made on an encrypted University device and will be transferred to a secure server at the University of Manchester. Audio recorded consent will also be taken using the same encrypted recording device used for face to face interviews. Only members of the research team will have access to the recordings. The audio recordings will be written out (transcribed) in full by the researcher who will remove all names and personal identifiable information from the transcription. The original recordings will then be deleted. Copies of the transcriptions will be kept on the secure server at the University of Manchester for up to 5 years. You will be asked whether or not you consent for the transcriptions to remain on file for the purposes of future research, in which case they will be retained for up to 15 years. The consent form that you signed to take part or the audio recorded consent file will be retained for up to 5 years.

What happens if I do not want to take part or if I change my mind?

Your participation in this study is entirely voluntary and it is your decision whether you wish to take part. If you choose not to take part the care that you receive will not be affected in any way. As the recordings of the interviews are an essential part of your participation, if you do not consent to this, you will be withdrawn from the study. If you give consent to take part and change your mind you can withdraw from the study or stop the interview at any time, without providing a reason or affecting your data protection rights. All data will be fully anonymised after 48 hours of the interview, after which point it will not be possible to withdraw your data.

Will I be paid for participating in the research?

You will receive a high street shop voucher to the value of £10 for taking part in the study. You will also receive reimbursement for your travel costs should you need to travel for the interview.

Will my data be used for future research?

When you agree to take part in a research study, the information about you may be provided to researchers running other research studies in this organisation. The future research should not be incompatible with this research project and will concern healthcare experiences. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research. https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you regarding any other matter or to affect your care. It will not be used to make decisions about future services available to you.

Will the outcomes of the research be published?

The results of the study will be written up as part of a doctoral level thesis. This piece of work will be submitted to the University of Manchester for marking and evaluation. The research team hope to publish the results of the study in a relevant scientific journal and may present oral or poster presentations at conferences. Your identity will not be revealed in any publication, however direct quotes which do not contain any identifiable information may be used. You will be asked to give consent for this. The results of the study will also be fed back to internal and external researchers and lay community audiences.

Who has reviewed the research project?

The study was initially reviewed by the University of Manchester, Department of Clinical Psychology research subcommittee. All research within NHS settings has also been approved by a Research Ethics Committee (REC). A REC is a group of health professionals who review the research proposal to ensure that it is ethically and scientifically sound. Approval for this study has been granted from the North West – Greater Manchester East Research Ethics Committee. Approval for the study has also been granted by Salford Royal NHS Foundation Trust.

What if I want to make a complaint?

Minor complaints

If you have a minor complaint then you need to contact the researcher(s) in the first instance.

Contact details:

Name: Luke Beardmore
Role: Chief Investigator & Trainee Clinical Psychologist
Address: Faculty of Biology, Medicine and Health; School of Health Sciences; Division of Psychology and Mental Health; 2nd Floor, Zochonis Building; The University of Manchester; Oxford Road; Manchester; M13 9PL.
Email: luke.beardmore@postgrad.manchester.ac.uk
Tel No: 0161 306 0400

Name: Dr Sara Tai
Role: Primary Academic Supervisor/ Consultant Clinical Psychologist & Academic Director
Address: Faculty of Biology, Medicine and Health; School of Health Sciences; Division of Psychology and Mental Health; 2nd Floor, Zochonis Building; The University of Manchester; Oxford Road; Manchester; M13 9PL.
Email: sara.tai@manchester.ac.uk
Tel No: 0161 306 0400

Name: Yvonne Awenat
Role: Academic Supervisor/ Registered Nurse & Clinical Research Fellow
Address: Faculty of Biology, Medicine and Health; School of Health Sciences; Division of Psychology and Mental Health; 2nd Floor, Zochonis Building; The University of Manchester; Oxford Road; Manchester; M13 9PL.
Email: yvonne.awenat@manchester.ac.uk
Tel No: 0161 306 0400

Formal Complaints

If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers in the first instance then please contact:

The Research Governance and Integrity Manager, Research Office, Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 275 2674.

What Do I Do Now?

The researcher will make contact with you either by phone or by email within approximately 24 hours of receiving this information which has been sent to you either by letter or by email. You are encouraged to ask any questions you have either in relation to the information in this form, or about the project or your involvement in the study. You will also be asked whether or not you wish to take part in the study.

Thank you for taking the time to read this information sheet

Appendix H: Participant consent form

MANCHESTER 1824
The University of Manchester

Version 2. 16.02.2019
IRAS ID: 257977

The Psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences

Consent Form

If you are happy to participate please complete and sign the consent form below:

	Activities	Initials
1	I confirm that I have read the attached information sheet (Version x, xx/xx/xxxx) for the above study and have had the opportunity to consider the information, to ask questions and had these answered satisfactorily.	
2	I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving a reason and without detriment to myself. I understand that my data will be fully anonymised after 48 hours of the interview, after which point it will not be possible to withdraw my data. I agree to take part on this basis.	
3	I agree to the interviews being audio recorded.	
4	I agree that any information collected, including quotes from interviews, may be published in anonymous form in academic work, books, reports or journals.	
5	(Optional) I agree that the researchers may retain my contact details for the duration of the study in order to provide me with a summary of the findings for this study.	
6	(Optional) I agree that anonymised transcripts can be retained for use in future research projects for up to 15 years.	
7	I understand that consent forms will be kept for up to 5 years and data transcripts will be kept for up to 5 years.	
8	I understand that if I gave information about myself (or someone else) potentially being harmed, the researchers could not keep this information to themselves. If I or someone else (e.g. a child) were at risk of being harmed, the researchers might need to break confidentiality and contact relevant services to protect me. Other services might include mental health services, social services or the police, for example.	

9	I understand that data collected during the study may be looked at by individuals from the University of Manchester, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.	
10	I agree to take part in this study.	

Data Protection

The personal information we collect and use to conduct this research will be processed in accordance with data protection law as explained in the Participant Information Sheet and the Privacy Notice for Research Participants. http://documents.manchester.ac.uk/display.aspx?DocID=37095

Name of Participant	Signature	Date
Name of the person taking consent	Signature	Date

1 copy of this form will be retained by the research team (original) and 1 copy will be offered to the participant.

Appendix H continued: Participant consent form for self-referral

MANCHESTER 1824
The University of Manchester

Version 3. 24.09.2019
IRAS ID: 257977

The Psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences

Consent Form for Self-Referrals

If you are happy to participate please complete and sign the consent form below:

	Activities	Initials
1	I confirm that I have read the attached information sheet (Version x, xx/xx/xxxx) for the above study and have had the opportunity to consider the information, to ask questions and had these answered satisfactorily.	
2	(Optional) I give consent for the chief investigator to make contact with my current health professional or GP to obtain any relevant risk information prior to taking part in the study.	
3	I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving a reason and without detriment to myself. I understand that my data will be fully anonymised after 48 hours of the interview, after which point it will not be possible to withdraw my data. I agree to take part on this basis.	
4	I agree to the interviews being audio recorded.	
5	I agree that any information collected, including quotes from interviews, may be published in anonymous form in academic work, books, reports or journals.	
6	(Optional) I agree that the researchers may retain my contact details for the duration of the study in order to provide me with a summary of the findings for this study.	
7	(Optional) I agree that anonymised transcripts can be retained for use in future research projects for up to 15 years.	
8	I understand that consent forms will be kept for up to 5 years and data transcripts will be kept for up to 5 years.	

9	I understand that if I gave information about myself (or someone else) potentially being harmed, the researchers could not keep this information to themselves. If I or someone else (e.g. a child) were at risk of being harmed, the researchers might need to break confidentiality and contact relevant services to protect me. Other services might include mental health services, social services or the police, for example.	
10	I understand that data collected during the study may be looked at by individuals from the University of Manchester, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.	
11	I agree to take part in this study.	

Data Protection

The personal information we collect and use to conduct this research will be processed in accordance with data protection law as explained in the Participant Information Sheet and the Privacy Notice for Research Participants. http://documents.manchester.ac.uk/display.aspx?DocID=37095

Name of Participant	Signature	Date
Name of the person taking consent	Signature	Date

1 copy of this form will be retained by the research team (original) and 1 copy will be offered to the participant.

Appendix I: Demographics questionnaire

MANCHESTER 1824
The University of Manchester

Version 1. 23.08.2019

IRAS ID: 257977

Date of Interview	

Demographic Questionnaire

Title of Project: The psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences

This questionnaire is designed to gather some more information about you. Please ask the researcher if you have any questions or if you would prefer them to complete this questionnaire with you.

Age		
Gender		
Ethnicity *(Choose one which best describes your ethnic group or background)*	English/Welsh/Scottish/Northern Irish/British Irish	
	Irish	
	Gypsy or Irish traveller	
	Any other white background	
	White and Black Caribbean	
	White and Black African	
	White and Asian	
	Any other mixed/multiple ethnic background	
	Indian	
	Pakistani	
	Bangladeshi	
	Chinese	
	Any other Asian background	
	Black/African/Caribbean/Black British	
	African	
	Caribbean	
	Any other Black/African/Caribbean/Black British background	
	Any other ethnic group (Please describe):	
Higher education level *(e.g. Secondary school)*		
Living Status *(e.g. living alone, cohabiting)*		

1

Date of Interview	

Demographic Questionnaire

Employment status *(Choose one which best describes you currently)*	Employed	
	Unemployed	
	Student	
	Retired	
	Unable to work	
	Other (Please explain):	
Service currently providing your care		
Medication/s prescribed over the past 6 months *(e.g. Risperidone)*		
Symptoms experienced over the past 6 months *(e.g. restlessness, agitation)*		
Mental health diagnoses *(e.g. psychosis, depression etc)*		

Thank you for taking the time to fill this in.

Appendix J: Distress and risk protocols

School of Health Sciences
Faculty of Biology, Medicine and Health
2nd Floor Zochonis Building
The University of Manchester
Brunswick Street
Manchester, M13 9PL

Distress Protocol

Study: The Psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences

Distress: Participant shows signs that they are experiencing distress or exhibits behaviours associated with distress such as crying. This might indicate that the questions asked or the responses given have elicited challenging emotions for the participant and triggered upsetting thoughts or memories. The researcher will also be mindful of symptoms related to akathisia, such as uncomfortable restlessness, pacing or agitation throughout the duration of the interviews.

Should a participant become distressed during the interview the following will occur:

Step 1:

- Researcher to offer participant immediate emotional support, understanding and reassurance.
- Ask participant if they would like to take a break from the interview
- If yes, stop the interview for a couple of minutes. Offer the participant a drink and see if they would like to leave the room or take a short walk
- If no, continue with the interview but reassure the participant they can stop the interview at any time

Step 2:

- Upon returning from a break the researcher will ensure the participant wishes to continue with the interview and will offer continued support
- The researcher will reassure the participant they can stop the interview at any time
- If risk is highlighted, assess and proceed to follow risk protocol
- If the participant would like to discontinue the interview or continues to experience distress, the researcher should follow the actions outlined in **Step 3**

Step 3:

- Stop the interview. Provide the participant with support, empathy and reassurance
- Stay with the participant until they are calm
- Recommend that the participant contacts their GP if they continue to experience on-going distress/ encourage participant to use the support numbers provided
- Ask the participant if they would like their care co-ordinator/ health professional to contact any family members/ next of kin
- Reassure participant that stopping the interview will not affect their care in any way

- Researcher to seek support from supervisors

Follow up:

- If participant consents, follow up with a courtesy call or email the next day
- Encourage participant to use provided support numbers

School of Health Sciences
Faculty of Biology, Medicine and Health
2nd Floor Zochonis Building
The University of Manchester
Brunswick Street
Manchester, M13 9PL

Risk Protocol

Study: The Psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences

Should a participant disclose information that implies a risk to the participant or someone else the following steps will be taken:

Risk: Participant discloses information which implies risk to themselves or others

Step 1:

- Researcher will accurately document the information disclosed
- Researcher will contact their research team supervisor to discuss the information disclosed and the most appropriate course of action

Step 2:

- If action is felt to be required the researcher will immediately report these concerns to the participant's allocated health professional/ care co-ordinator
- If the participants health professional is not available the researcher will report their concerns to the most appropriate adult or child safeguarding team if necessary
- Where possible, any concerns would be discussed with the individual and they will be informed that the researcher will be sharing information to respect confidentiality
- All actions will be completed with priority and will be done so at the soonest available opportunity
- The researcher will maintain a clear written record of the concern and all steps taken to deal with the matter, for example, who the concern has been raised with and on what date/ time

Should participants behave in a way (e.g. exhibit violent or aggressive behaviour) that poses a risk to the researcher during the interviews the following steps would be taken:

Risk: Participant poses a risk to the researcher

Step 1:

- The researcher will discontinue the interview immediately and leave the room to give the participant the opportunity to calm down
- If the risk was imminent, the researcher would immediately vacate the area and call the police

Step 2:

- The researcher would contact the research team supervisor to discuss the risk and whether any further actions needed to be taken
- The researcher would accurately document the risk that had taken place

Appendix K: Topic guide

MANCHESTER 1824
The University of Manchester

Version 2. 03.05.2019
IRAS ID: 257977

Project Title:

The psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences

Topic Guide

What follows is a guide: -

The order and exact content of the questions will be determined by the participant and will be influenced by the ongoing analysis so the order of the questions may vary as the interview develops.

The following topics and prompts serve as an interview guide.

Explanation of use of symbol 'X' in the topic guide. As the term 'akathisia' may be unfamiliar to some participants the interviewer will adopt the terminology used by the participant (e.g., restlessness, restless legs, etc) to describe akathisia and its symptoms during the interview.

- **I am interested in hearing about your experiences of your problem of X. Thinking about X, can you tell about how you became aware of this?**
  - What do you understand about how X came about?
  - How long has X been a problem for you?

- **What medication/s are you currently taking, or have you taken, over the past twelve months?**

- **How do you think the development of X is linked to the medication?**
  - Could you tell me what you understood about the medication you were prescribed? E.g., reason for prescription, information given by prescriber or from medication patient information leaflet of any warnings of possible side effects

- **What kind of symptoms did you experience?**
  - What parts of your body were affected by the symptoms? (E.g. legs, arms, skin etc.)
  - How frequently would you experience such symptoms?
  - At what particular times of the day or night would the symptoms occur?

- **How severely would you say the symptoms affected you before and after you started taking the medication?**
  - How soon after you started taking the medication did the symptoms develop?
  - How soon after you stopped taking the medication did the symptoms decrease?
  - How did the symptoms affect your life? (sleep, mood, appetite etc.)

- **Sometimes, people who develop X and symptoms related to X report experiencing suicidal thoughts or thoughts of causing harm to themselves. Did you experience any thoughts like this?**
  - At what point did you begin to have thoughts like these?
  - Had you experienced thoughts like these before?

1

- How often would you say you had these thoughts?
- Did you ever harm yourself or attempt suicide?

- **Could you tell me more about the ways in which the development of X impacted your life?**
  - Did this affect what you were able to do?
  - What was that experience like for you?
  - How did this make you feel?
  - How did you respond to this?

- **Please tell me about any differences you noticed in day to day life or functioning as a result of developing X?**
  - **Social life:** How did the development of X affect you socially?
  - **Leisure/ activities:** How did the development of X affect things that you usually liked to do? (E.g. activities, sports, socialising etc.)
  - **Work / study:** How did X impact on your work or study?
  - **Relationships:** Can you tell me if the development of X impacted on your relationships with others?
  - **Task completion/ usual functioning:** Call you tell me more about how X affected your ability to do things that you would usually do? (E.g. reading, driving, domestic tasks, caring for others etc.)
  - **Travel:** Were there any difficulties with travelling by car, bus, train, aircraft or other means of travel?
  - **Sleep:** Were there any effects on your sleep?
  - **Other areas affected?**
  - General prompts for all of the above:
    - What was this experience like for you?
    - What did this mean to you?
    - How did this make you feel?
    - How did you respond to these changes?

- **Can you tell me how you managed the symptoms that you experienced?**
  - What did you find helped to prevent / reduce / stop these symptoms?
  - Did you ever use alcohol or recreational/ street drugs to help relieve the symptoms of X?
  - Were there certain things that you found that you had to avoid?

- **What advice were you given by the person who prescribed the medication?**
  - Did the prescriber warn you of the possibility that the medication could cause such side effects?
  - What advice did the prescriber give you about how to manage the symptoms?
  - Did they advise to reduce or stop this medication?
  - Were you prescribed any other medication to control the symptoms?
    - If so, what was the name of that medication?
    - Did it help?

- **Were any other suggestions made of how to control your symptoms?**
  - E.g. Acupuncture or other alternative therapies?
  - If so: - What was the impact of this?

- **Did you seek help from anyone other than the prescriber?**
  If so, who? (GP, Nurse, Charity / User organisation (E.g. Restless Legs Society)
- **Is there anything else you think is relevant about your experience of X that I have not asked you already?**

- **How have you found discussing these things today?**
  - Was there anything that was difficult to talk about?

Appendix L: Table of recurrent themes

Superordinate themes	David	Diane	Jessica	Samuel	Amy	Mark	Present in over half sample?
Journey through the mental health system	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adjustment to life with akathisia	Yes	Yes	Yes	Yes	Yes	Yes	Yes
The internal experience of akathisia	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Appendix M: Ethics approval letters

Health Research Authority

North West - Greater Manchester East Research Ethics Committee

3rd Floor, Barlow House
4 Minshull Street
Manchester
M1 3DZ

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

10 June 2019

Mr Luke Beardmore
Flat 2, 87-89 Northen Grove
Didsbury
Manchester
M202JL

Dear Mr Beardmore

Study title:	**The psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences.**
REC reference:	**19/NW/0226**
Protocol number:	**NHS001509**
IRAS project ID:	**257977**

Thank you for your letter of 08 May 2019, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Study Poster]	1	22 December 2018
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Evidence of insurance]	1	21 February 2019
Interview schedules or topic guides for participants [Topic Guide]	2	03 May 2019
IRAS Application Form [IRAS_Form_22032019]		22 March 2019
Letter from sponsor [Letter from sponsor]	1	21 February 2019
Other [Combined liability]	1	07 May 2018
Other [Distress & Risk Protocol]	1	02 December 2018
Other [Lone Working Protocol]	1	11 January 2019
Other [Risk Assessment]	1	15 January 2019
Other [Yvonne Awenat Full CV]	1	11 March 2019
Other [EL Certificate]	1	11 March 2019
Other [Insurance Broker]	1	31 May 2018
Other [Consent to contact form]	1	03 May 2019
Other [LB ethical review further information re-submission table]	1	07 May 2019
Participant consent form [Participant Consent Form]	2	16 February 2019
Participant information sheet (PIS) [Participant Information Sheet]	3	03 May 2019
Research protocol or project proposal [Research Protocol]	3	03 May 2019
Summary CV for Chief Investigator (CI) [LB CV]	1	08 March 2019
Summary CV for student [LB CV]	1	08 March 2019
Summary CV for supervisor (student research) [Dr Sara Tai CV]	1	11 March 2019

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at:
https://www.hra.nhs.uk/planning-and-improving-research/learning/

19/NW/0226	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Signed on behalf of
Mr Simon Jones
Chair

Email:nrescommittee.northwest-gmeast@nhs.net

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Mr Luke Beardmore
Flat 2, 87-89 Northen Grove
Didsbury
Manchester
M202JL

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

10 June 2019

Dear Mr Beardmore

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**The psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences.**
IRAS project ID:	**257977**
Protocol number:	**NHS001509**
REC reference:	**19/NW/0226**
Sponsor	**University of Manchester**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **257977**. Please quote this on all correspondence.

Yours sincerely,

Amber Ecclestone
Approvals Specialist

Email: hra.approval@nhs.net

Copy to: *Ms Lynne Macrae*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Study Poster]	1	22 December 2018
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Evidence of insurance]	1	21 February 2019
HRA Schedule of Events	1	01 April 2019
HRA Statement of Activities	1	01 April 2019
Interview schedules or topic guides for participants [Topic Guide]	2	03 May 2019
IRAS Application Form [IRAS_Form_22032019]		22 March 2019
Letter from sponsor [Letter from sponsor]	1	21 February 2019
Other [Combined liability]	1	07 May 2018
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Health Research Authority

North West - Greater Manchester East Research Ethics Committee
3rd Floor, Barlow House
4 Minshull Street
Manchester
M1 3DZ

Tel: 02071048199
Fax:

08 October 2019

Mr Luke Beardmore
Flat 2, 87-89 Northen Grove
Didsbury
Manchester
M202JL

Dear Mr Beardmore

Study title:	**The psychosocial effects of akathisia after neuroleptic use: A qualitative exploration of real life experiences.**
REC reference:	**19/NW/0226**
Protocol number:	**NHS001509**
Amendment number:	**01**
Amendment date:	**20 August 2019**
IRAS project ID:	**257977**

Summary of amendment
The above amendment was reviewed the Sub-Committee in correspondence.

Ethical opinion

With regards to recruitment advertising on twitter, the Sub-Committee wanted to know if it will be shared by other organisations on Twitter such as the university of Manchester and other NHS trusts The committee had also requested that this should be made clear.

The researcher responded with corresponding updated forms, including: the consent form for participants who self-refer. A poster advertising the study to participants stipulating they can self-refer. An updated study protocol and participant information sheet outlining where on Twitter the study will be advertised and information on participants who self-refer.

After reviewing these changes the members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*

NHS
Health Research Authority

Copies of advertisement materials for research participants [Study poster]	2	24 September 2019
Non-validated questionnaire [Demographics questionnaire]	1	23 August 2019
Notice of Substantial Amendment (non-CTIMP)	01	20 August 2019
Other [Response to committee]		24 September 2019
Participant consent form [Self-referral consent form]	3	24 September 2019
Participant information sheet (PIS) [PIS]	5	24 September 2019
Research protocol or project proposal [Protocol]	5	24 September 2019

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

19/NW/0226:	**Please quote this number on all correspondence**

Yours sincerely

Pp

Mr Simon Jones
Chair

E-mail: nrescommittee.northwest-gmeast@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Appendix N: Examples of analysed transcripts

Experience of mental health settings Impact on others/ perceptions of others Not believed/ lack of empathy/ understanding from staff Helplessness Guilt/ self-blame Questioning self-experience Powerlessness over symptoms/ side effects Pacing Articulating akathisia- metaphor	30. Erm, I was actually in hospital and I was annoying them walking up and down the corridor… R: 31. I see… P: 32. They kept saying '(insert name) would you just go and sit down'… 33. 'no I can't'… 34. 'Would you just go and sit down' 35. 'No I can't' R: 36. I see… P: 37. And they were quite sort of, I don't know. It made me think 'oh gosh, I'm doing something that I shouldn't be doing' R: 38. Okay. So the response they gave was to go and sit down when you felt like you couldn't? P: 39. Yes R: 40. What did you feel that you needed to do? P: 41. I needed to pace up and down. I could sit down for a minute or two and then I'd think '(insert name) I've got to walk'… R: 42. I understand. So how did those sensations feel inside? P: 43. It was like butterflies in my stomach R: 44. Butterflies in your stomach? P: 45. Yeah	In hospital- annoying to others- walking up and down. Important for P to talk about hospital experience *Personalised- felt they were being 'annoying' perceived as annoying by others. 'Up and down': repetitive action conveyed in language, maybe to convey an image?* Was repeatedly told to sit down in hospital- not believed. Sounded distressed and upset in voice/ tone whilst speaking about this *Language depicts desperation and helplessness. The word 'can't' referred to multiple times. Use of the word 'they' talking about staff as a collective group of individuals- felt bullied? Slows tone down on second 'No I can't', possibly to convey emphasis* Not being listened to by staff- like they did not understand. Is this reminiscent of people's experiences with mental health contexts? Suggestive of a level of confusion about how they were being treated *Difficult to articulate how 'they' were? Staff reaction led to self-blaming. 'Oh gosh' reflects how concerned they were in response to staff response. Like being chastised as a 'child' by a parent* The actions of others made them question themselves and whether they were acting appropriately. Thought they were doing something they should not have been doing. Suggests staffs response made them more concerned. Not being believed or listened to Needed to pace- could only sit for a minute *'Needed', similar to 'can't'- language conveys little option. Links to powerlessness in situation and settings- language conveys necessity* *Use of metaphor- like butterflies in my stomach- used to convey sensations experienced* Possibly highlights difficulties articulating experience of akathisia

Impact of akathisia/ relationships Communication Social activity/ isolation Metaphor	P: Right okay. So I kind of stopped, stopped talking a lot. Erm you know, I'd see my friend and we could sit in silence for an hour. I wouldn't know what to say and you know, going to church people would want to know how I was and I just couldn't tell them. I just sort of switched off into my own little mind and no one could get to me. I didn't interact with anyone I don't think	Relationships- stopped talking, would sit in silence and not know what to say. Impacts for socialising with others. *Language suggests a fear of being judged/ not knowing how to explain. Wouldn't know what to say- switched off into my own little mind- emphasis on the word 'little'- again does this link to powerlessness/ not feeling important/ worthlessness? Image- closed in, boxed off from others- no one could get to me* *All or nothing- did not interact with 'anyone'* *I just couldn't tell them- does this show a degree of feeling isolated from others and not able to share experiences? Spoken in a soft, slow tone* May suggest potential links to stigma associated with having a mental health issue. Does this link with religious culture? Are there links here to a 'powerful other' being played out in the relationship with their psychiatrist also? Did akathisia impact confidence interacting with others/ awkwardness around communication?
	R: I see. And you would have interacted with them before?	
	P: Yes	
	R: Okay so the symptoms made you feel like you needed to sort of not tell people how you were doing and to switch off?	
	P: Yes	
	R: I see. What was it like feeling like that? It sounds like that might have been a difficult experience?	
Limited knowledge/ understanding Relationships Dissociation? Avoidance	P: Yeah, yes it was. I mean I, I, I, I don't think at the time I really knew what was going on and I don't think I, you know, looking back on it, and sort of my husband telling me and my friend telling me what I was like on it, you know I, erm, see my friend said I wasn't really with it I just switched off	Lack of awareness about what was happening. Other people telling them what they were like at the time. Reminiscing about the experience. *Repetition 'I', 'yes'. Metaphor- switched off/ not really with it- almost sounds like this was an out of body experience separate to themselves* Coping strategies: 'switch off'? Coping strategy: not doing anything/ saying anything- links to avoidance? Was there a degree of shame involved in having these side effects? Almost like they became frozen and wanted to be invisible. Wanting to avoid negative judgement from others? Avoidance
	R: Okay, so you felt like you switched off. And do you think that helped?	
Coping strategy	P: Yeah I think so. I just switched off. I think that was my coping strategy that, you know, I'm not doing anything I'm not saying anything and will avoid going out	

Side effects- impacts Relationship difficulties Annoying others/ perceptions of others Disruptions on personal life Social impacts Support/ partner Impacts on others/ relationships Suicidality Hope in medical professionals Coping mechanism/ trying to problem solve	P: 64. It's very erm, intrusive into my life its, I've got a partner, well, I say I've 65. Got one I think I've got one, erm, she lives in (insert place) I 66. live in (insert place). We see one another every weekend, but during the 67. Week if we've got something on. *Sigh*, we are engaged but we don't 68. Live together, erm, but it's got to a stage that if we sat somewhere and 69. My legs are shaking it gets so annoying for her. Even if it's like in a quiet 70. Room and she can hear erm, my legs rubbing against the settee or me 71. Jeans rubbing against one another or what have you, erm you know… 72. And the more I try to stop it the worse it gets. But it's got to the point 73. Where I think I mean, I know this might sound personal, but we don't 74. Even sleep in the same bed R: 75. Okay, I see… P: 76. We haven't done for a long time because of my restlessness R: 77. And how has that impacted your relationship? P: 78. Erm, it's just, it has come between us, erm, she was very understanding 79. And I think she has been understanding. I will give her her due she has 80. Been very understanding, but, its spoiling her life as well R: 81. Mm I see…And what is that like (insert name) thinking about that? 82. How does that make you feel when you're experiencing these 83. Symptoms and they're impacting on your relationship? P: 84. Erm, I've got to say it's put me on the edge. I have had the thoughts of 85. Suicide I can't say I haven't because I have. Erm, because I cannot see 86. Every time I go to see a doctor or a specialist, I think maybe they will 87. Sort it and when I come home and I tell them 'they've said this or 88. They've said that' that maybe things are coming to a head, yet we've 89. Never ever got the point to solve it, so…	Side effects- intrusive. Talks about partner *Sigh- sense of feeling disheartened when speaking about partner and the impacts the side effects have had on their relationship* Relationship- legs shaking causes annoyance to partner. Causing annoyance to others (moving legs causes rubbing noises) Trying to stop it makes it worse. Not sharing bed with partner due to side effects Seems like there has been a significant impact on P's ability to be intimate with their partner due to symptoms- possible implications for self-esteem/ socialisation. Possible links to values and beliefs Describes manifestations of symptoms *'It' has come between us- interesting language use- almost like the restlessness is an entity in its own right/ the enemy?* Partner is understanding/ relationships Social- impacting other people's lives *Metaphor- 'on the edge'- reminiscent of feeling like they're just 'holding on'- link with suicidal thoughts. Suggests hopelessness* Need to think about the context of having experienced this for 10 years- I do not think at any point P acknowledges how well they have done to cope with these things- given how much they have tried Thoughts of suicide- cannot see a way out *Sense of hopelessness- no solution yet- not been able to 'solve the problem'*

Social/ activity Loss of activity Social/ loss Psychological impacts/ concentration Loss of activity Akathisia/ side effects Inability to sit still	P: 296. 297. 298. R: 299. P: 300. 301. R: 302. P: 303. R: 304. 305. 306. P: 305. R: 306. P: 307. 308. 309. 310. P: 311. 312. R: 313. 314.	Well erm, err, yeah, I mean I used to go the cinemas, can't do that Anymore, I used to go for long walks, can't do that anymore, Erm, swimming… Yes… I don't do that anymore. Everything that's social. I'm sat in a room all day and get cooped up and can't go out I see You know what I mean? Yes, I understand. So, can you tell me, have the side effects had any psychological impacts that prevent you from being able to do activities? Yes, I can't concentrate anymore I see… Do you know what I mean I've sat and tried to read the same book, And read a few pages and that and then I put it down, and then I Pick the book back up again and I've already forgot what I've read So I've started the same book about 4 times I've got a few books in me room but like you say I just, can't Concentrate. I can't keep still for that long. Okay, so the side impact things like you sitting down reading A book which is something you used to enjoy doing?	Social- P identifies things they cannot do anymore- cinema, long walks, swimming Side effects have prevented these things *'Erm'- hesitation, thinking, trying to recall information- links to memory? Repetition of 'can't do that anymore'- suggests definitive 'can't' do something now even if they wanted to. Does this relate to a degree of powerlessness? 'Cooped up' almost like being trapped due to side effects and symptoms related to MH* Social- does nothing now- isolation *All or nothing language/ thought processes* *Also refers to a degree of 'loss' about not being able to do 'anything' social now* *Trying to seek reassurance/ empathy understanding from interviewer?* Does this relate to a lack of support from professionals or understanding about P's challenges? Cognitive- struggles to concentrate *All or nothing language used again- 'can't'* Social/ activity- reading- forgets what they have just read. Detailed explanation of how frustrating this process has felt of trying to start a book *Language conveys a possible sense of frustration- trying to read the same book over and over* Relates to something the majority of people take for granted but due to the meds and side effects even beginning a book is difficult for P