DOCTOR OF PHILOSOPHY

Sleep, Digital Health Technologies and Psychotic Symptoms

Clarke, Stephen

Award date:
2019

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Sleep, Digital Health Technologies and Psychotic Symptoms.

Stephen Clarke (B.A., MSc).

Submitted in part fulfilment for the requirements of the degree of Doctorate in Clinical Psychology (DClinPsy).

School of Psychology, Queen’s University Belfast.

July 2019.
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List of Abbreviations:

APP Application
APS Attenuated Psychotic Symptoms
ARMS At-Risk Mental State
CACR Computer Assisted Cognitive Remediation
DHT Digital Health Technology
SMS Short Message Service
TAU Treatment as Usual
UHR Ultra-High Risk
VR Virtual Reality
Acknowledgements.

I would like to take this opportunity to thank Dr Donncha Hanna, Dr Ciaran Shannon, Dr Ciaran Mulholland, Dr Sarah Davidson and Dr Callum Urquhart for their support in the completion of this research portfolio. I also wish to thank my wife, Louise, and my children, Niamh and Niall for their support.
A systematic review and meta-analysis of digital health technologies effects on psychotic symptoms in adults with psychosis.

The follow paper has been published in ‘Psychosis’ and is available at the following doi: 10.1080/17522439.2019.1632376

Abstract

Objective: To conduct a systematic review and meta-analysis of controlled studies to determine the effect of digital health technologies on psychotic symptoms.

Method: Electronic databases were searched up to March 2019. A narrative synthesis and meta-analyses of subcategories were completed.

Results: Twenty-one articles met inclusion criteria, covering three DHT types: avatar therapy, phone apps and computer-assisted cognitive remediation (CACR). In the latter, psychotic symptoms were secondary outcomes and only one of nine CACR studies demonstrated an effect on these symptoms. All four of the avatar trials and one of three phone app studies provided preliminary evidence of effectiveness in reducing psychotic symptoms.

Conclusion: Although effectiveness of DHTs for reducing psychotic symptoms cannot yet be conclusively established, the emerging literature suggests that DHTs using immersive avatar therapy holds most promise.

Keywords: Psychotic symptoms, digital health technologies, avatar therapy, phone apps, computerised cognitive remediation
1.0 Introduction.

With health services under pressure from increased demand for services (Hollis et al., 2015), digital health technologies (DHTs), such as apps, software and online platforms (NICE, 2019), may provide a cost-effective line of interventions, and with individuals using apps and Internet-based technology for symptom relief (Gay, Touros, Joseph, Pandya, & Duckworth, 2016), a review of the effects of DHTs on psychotic symptoms is warranted. An early review demonstrated the acceptability and feasibility of augmenting clinical care with technology (Kasckow et al., 2014), but from 12 articles meeting inclusion criteria in a systematic review of user-led Internet and mobile-based interventions only one RCT reported effects on psychotic symptoms (Alvarez-Jimenez et al., 2014).

A more recent review found some efficacy in clinical outcomes with ecological momentary interventions, but the authors could not complete a meta-analysis due to the lack of controlled studies (Bell, Lim, Rossell, & Thomas, 2017). Another recent systematic review (Gire et al., 2017) examined 18 articles on mobile devices and reported on two articles where native apps or SMS were efficacious in reducing psychotic symptoms, but this review did not include apps that have been recently developed specifically for individuals with psychosis (e.g. Actissist, FOCUS), which were also absent from a systematic review by Bonet et al., (2017). Further, Välimäki et al., (2014) highlighted the need for high-quality trials of novel interventions (e.g. virtual reality) and described how previous reviews could not draw firm conclusions due to heterogeneity and poor quality (e.g. uncontrolled) studies.

Therefore, given that the field has progressed with more controlled studies covering a wider area of DHTs, the present review aimed to broaden the scope of previous reviews by including various types of DHT (e.g. avatar therapy, virtual reality) and include only controlled trials in order to perform a meta-analysis to estimate overall effects of DHTs on psychotic symptoms.
2.0 Method

This review was pre-registered on PROSPERO (registration number: CRD42018108760) before completing the following procedure.

2.1 Literature Search.

Searches were completed on ‘Web of Science’, ‘PubMed’ and ‘PsychINFO’, and were limited to English language, peer reviewed journal articles involving adult participants in clinical trials. Date fields were January 2005 to March 2019, using the following search terms: phone app OR avatar therapy OR virtual reality OR VR OR computer-assisted therapy OR technology-enabled interventions OR digital health interventions OR eHealth OR mHealth OR serious computer games OR smartphone OR mobile app OR internet OR online OR computer OR web-based OR digital mental health AND schizophrenia OR psychosis. Truncations and wild cards were used to identify mutations of search terms. Search results were exported to RefWorks (The Quorum, Cambridge, UK; http://www.refworks.com) for removal of duplicates and exclusion of irrelevant studies through screening titles/abstracts, before assessing full text articles against eligibility criteria. The reference sections of eligible papers were searched for potentially relevant articles.

2.1.1 Eligibility Criteria.

Articles were included if:

1) They met criteria for evidence tier 3b of the Evidence Standard Framework for Digital Health Technologies, i.e. RCTs comparing DHTs with a relevant comparator, measuring clinical outcomes in a target population, using validated condition-specific outcome measures (NICE, 2019), with the target population in this case being adults with psychosis.
2) Studies were included if the primary outcome was not a change in psychotic symptoms, but this was reported as a secondary outcome.

3) Articles that included other presentations or children/adolescents were included if the data of adults with psychosis could be extricated from the overall sample.

Studies were excluded if:

1) Participants were exclusively children/adolescents.

2) The DHT was not an intervention e.g. DHTs used for assessment only (e.g. passive data collection DHTs), or for use in exploring the onset and maintenance of psychosis, and those reporting on intervention development without a trial component to the study.

3) The study involved DHTs not specifically developed for psychosis, e.g. generic mental health apps, such as transdiagnostic CBT apps, native apps (e.g. SMS) and DHTs that can be downloaded directly by users through app stores (e.g. mindfulness apps).

2.1.2 Screening, data abstraction and meta-analysis.

Titles and abstracts were screened by SC, and the full text of studies potentially meeting inclusion criteria were reviewed by SC & CU. A kappa coefficient calculation was completed to assess agreement. Disagreement was resolved by discussion between SC & CU. For each article meeting the inclusion criteria the following details were entered onto a standardised data extraction form: country, participant demographics, intervention, control, completion/attrition rates, and outcomes with times of measurement. The Cochrane Risk of Bias Tool was used by SC and CU to assess trial quality on selection, performance, attrition and reporting. Random effects meta-analyses models were completed using Review Manager 5.3 (Cochrane Informatics, 2014).
3.0 Results

From 843 articles retrieved (PsychINFO: 275; Web of Science: 420; PubMed: 146; others: 2), 602 remained after duplicate removal, of which 551 were excluded following title/abstract screening, leaving 51 full text articles for assessment (Figure 1). With strong agreement between reviewers ($\kappa = .82$), 21 articles met inclusion criteria.

Figure 1. PRISMA flow diagram of systematic search and study selection.
3.1 Summary of sample and study characteristics.

The studies had a total of 1,535 participants, and a mean sample size of 73 (range: 19 to 179). Table 1 presents the main characteristics of the studies, showing that 81% were conducted in Europe and North American. Almost half the articles were published in 2018. Males outnumbered females in all but two studies. Most studies did not report on adverse effects, but of the six reporting this variable, all reported no adverse effects. The number of sessions ranged from six in avatar therapy to eighty hours in cognitive remediation. Time between baseline and final assessment ranged from six weeks to twelve months, with completion rates ranging from 40% to 100%. Thirteen studies compared DHTs to TAU/waitlist, six studies compared DHTs with an active comparator (one being a head-to-head with another evidence-based treatment), and the remaining studies had three arms comparing DHTs to active comparators and TAU.

3.1.1. Trial quality.

Trial quality was assessed independently by SC and CU, and with strong agreement between reviewers (κ = .81), a third of trials were judged to be at high overall risk of bias. Given the nature of the interventions, all trials suffered from lack of blinding of participants, and only 62% of studies maintained blinding of assessors. Other than non-blinding, the main risk of bias was random sequence generation, with 38% of studies failing to adequately describe the method used to generate the allocation sequence. Approximately half the studies (52%) reported a dropout rate higher than 15%, which Wykes, Huddy, Cellard, McGurk, & Czobor (2011) report could undermine the validity of the findings.
<table>
<thead>
<tr>
<th>Authors, year, location &amp; design.</th>
<th>DHT</th>
<th>Control</th>
<th>Completion Rate</th>
<th>Adverse Effects</th>
<th>Risk of bias (overall)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ben-Zeev et al., (2018). U.S.A. RCT.</td>
<td>FOCUS. $n=82$ (60% male); mean age=49(SD:10.1); 65% African-American.</td>
<td>WRAP. $n=81$ (58% male); mean age=49(SD:9.8); 66% African-American.</td>
<td>56% of FOCUS group completed all assessments versus 40% of controls.</td>
<td>0</td>
<td>Low</td>
<td>No significant between-group differences in PSYRATS scores at 6-month assessment.</td>
</tr>
<tr>
<td>Bryce et al., (2018). Australia. RCT.</td>
<td>CACR(COGPAK) $n=29$, (66% male); mean age=40.34(SD:9.62)</td>
<td>Computer games. $n=27$(74% male); mean age=41.78(SD:9.35)</td>
<td>76% of CACR group completed all assessments versus 78% of controls.</td>
<td>0</td>
<td>Low</td>
<td>No significant between-group differences in PANSS scores at 3-month assessment.</td>
</tr>
<tr>
<td>Bucci et al., (2018). U.K. RCT.</td>
<td>Actissist. $n=24$ (62.5% male); mean age=20.21(SD:7.37); 87.5% white British/Irish.</td>
<td>ClinTouch plus TAU. $n=12$ (75% female); mean age=18.33(SD:7)</td>
<td>100% of Acissist group completed all assessments versus 97% of controls.</td>
<td>0</td>
<td>Low</td>
<td>Improvements in PANSS general score and total score at post-intervention were not maintained at 22-week assessment.</td>
</tr>
<tr>
<td>Craig et al., (2018). U.K. RCT.</td>
<td>Avatar therapy. $n=75$ (76%male); mean age: 42.5(SD=10.1); 56% British.</td>
<td>Supportive counselling. $n=75$ (60% male); mean age:42.9 (SD:11.2); 58% British.</td>
<td>67% of avatar group completed 24 weeks versus 78% of controls.</td>
<td>0</td>
<td>Low</td>
<td>No significant between-group differences at 24-week assessment.</td>
</tr>
<tr>
<td>du Sert et al., (2018) Canada. RCT.</td>
<td>VR therapy. $n=19$ (66.7% male); mean age = 42.9 (SD=12.4); 86.7% white.*</td>
<td>TAU/delayed therapy. $n=19$ (66.7% male); mean age = 42.9 (SD=12.4); 86.7% white.*</td>
<td>79% completed all assessments.*</td>
<td>0</td>
<td>High</td>
<td>Reduction in severity of AVHs(PSYRATS) was significantly greater for intervention group than controls at 3-month assessment.</td>
</tr>
</tbody>
</table>
### Table 1 continued.

<table>
<thead>
<tr>
<th>Authors, year, location &amp; design.</th>
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<th>Risk of bias (overall)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Galderisi et al., (2010) Italy. RCT.</td>
<td>CACR-SSANIT. ( n=26 ) (gender not reported); mean age=40.31(SD:8.77); ethnicity not reported.</td>
<td>SLA. ( n=23 ) (gender not reported); mean age=39.17(SD:8.71); ethnicity not reported.</td>
<td>88% of SSANT completed all assessments versus 65% of controls.</td>
<td>Not reported</td>
<td>Low</td>
<td>No significant between-group differences in psychotic symptoms (SANS/SAPS) at 6-month assessment.</td>
</tr>
<tr>
<td>Garety et al., (2015) UK. RCT.</td>
<td>Maudsley Review Training Program ( n=51 ) (60.4% male); mean age= 41.6 (SD:11); 61% white*</td>
<td>Interactive computer tasks. ( n=50 ) (60.4% male); mean age= 41.6 (SD:11); 61% white*</td>
<td>92% of both groups completed all assessments</td>
<td>Not reported</td>
<td>High</td>
<td>Reduction in state paranoia (Paranoid Thoughts Scale) was significantly greater for intervention group than controls at 2-week assessment.</td>
</tr>
<tr>
<td>Gottlieb et al., (2017). U.S.A. RCT.</td>
<td>Internet-based ‘Coping with Voices’ ( n=19 ) (52.6% female); mean age=43.79 (11.16); 78.9% white.</td>
<td>TAU. ( n=18 ) (77.8% male); mean age=40.28(SD:11.69); 55.6% white.</td>
<td>Completion across all groups was 81% at 3-month assessment. *</td>
<td>Not reported</td>
<td>Low</td>
<td>No significant between-group differences in auditory hallucinations (PSYRATS-AH) at 3-month assessment.</td>
</tr>
<tr>
<td>Lee (2013) Korea. RCT.</td>
<td>CACR (Cog-Trainer). ( n=33 ) (53% male); mean age= 43.53 (SD:4.87); ethnicity not reported.</td>
<td>TAU. ( n=33 ) (57% male); mean age=43.36(SD:3.53); ethnicity not reported.</td>
<td>91% of both groups completed all assessments*</td>
<td>Not reported</td>
<td>Low</td>
<td>No significant between-group differences in PANSS at 3-month assessment.</td>
</tr>
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Table 1 continued.

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</thead>
</table>
  n=14; gender, age and ethnicity not reported. | TAU/delayed therapy.  
  n=12; gender, age and ethnicity not reported. | 57% of avatar therapy group completed all assessments versus 67% in TAU/delayed therapy. | Not reported. | High | Significant improvement in PSYRATS at 3-month assessment (for both immediate and delayed therapy). |
  n=25 (72.7% male); mean age=37.3(SD:11.7); ethnicity not reported. | Health controls  
  n=27 (69.9% male); mean age=37.7(SD:11.1).  
  Active comparator (table soccer).  
  n=26 (71.4% male); mean age=35.8(SD:14.4) | 88% of CACR group completed all assessments versus 85% healthy controls and 81% active comparator. | Not reported. | High | No significant between-group differences in PANSS at 3-month assessment. |
  n=30 (80% male); mean age:38.47(SD=7.88); ethnicity not reported. | TAU;  
  n=31 (74.2% male); mean age=39.87(6.12). | 100% of e-Motional Training group completed all assessments versus 96.7% controls. | Not reported. | High | Reduction in PANNS negative score was significantly greater for intervention group than controls. |
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Matsuda et al. (2018) Japan. RCT</td>
<td>CACR-JCORES and group work. n=31 (54.8% male); mean age=36.39(SD:8.53); ethnicity not reported.</td>
<td>TAU; n=31 (58.1% male); mean age=37.77 (SD:9.12).</td>
<td>77.4% of CACR group completed all assessments versus 54.8% controls.</td>
<td>Not reported.</td>
<td>Low</td>
<td>Reduction in PANNS-general score was significantly greater for intervention group than controls.</td>
</tr>
<tr>
<td>Morimoto et al., (2018). Japan. RCT.</td>
<td>CACR-JCORES. n=16 (62.5% male); mean age=36.1 (SD:7.7); ethnicity not reported.</td>
<td>TAU, n= 15 (60% male); mean age=37.4(SD:=11)</td>
<td>100% completion.</td>
<td>Not reported.</td>
<td>Low</td>
<td>No significant between-group differences in PANSS change scores at final assessment.</td>
</tr>
<tr>
<td>Pot-Kolder et al., (2018). Netherlands RCT.</td>
<td>VR-CBT,n=58 (69% male); mean age=36.5 (SD: 10); ethnicity not reported.</td>
<td>Wait-list. n=58 (72.4% male); mean=age: 39.5(SD: 10).</td>
<td>79.3% of VR-CBT group completed all assessments versus 91.4% of controls.</td>
<td>0</td>
<td>Low</td>
<td>Reduction in levels of ideas of persecution was significantly greater for the intervention group than controls at 6-month assessment.</td>
</tr>
<tr>
<td>Priebe et al., (2015) UK. RCT.</td>
<td>Dialog+, n=94 (70.2% male); mean age=41.5(SD:10.7); 40% black.</td>
<td>Dialog+ assessment only, n=85 (67.1% male); mean age=41.7(SD:9.3); 38% black</td>
<td>Completion across groups was 72.1% at 12 assessment.*</td>
<td>Not reported</td>
<td>High</td>
<td>Reduction in general psychopathology symptoms was significantly greater for the intervention group than controls.</td>
</tr>
</tbody>
</table>
Table 1 continued.

<table>
<thead>
<tr>
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<th>DHT</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Rotondi et al., (2010) U.S.A. RCT.</td>
<td>SOAR n=16 (38% male); mean age=38(SD:11); 56% Caucasian.</td>
<td>TAU n=15 (27% male); mean age=38(SD:11); 40% Caucasian</td>
<td>93.8% of SOAR group completed all assessments versus 73.3% controls.</td>
<td>Not reported</td>
<td>High</td>
<td>Reduction in positive symptoms was significantly greater for the intervention group than controls at 12-month assessment.</td>
</tr>
<tr>
<td>Schlosser et al., (2018) U.S.A., Canada &amp; Australia. RCT.</td>
<td>PRIME, n=22 (60% male); mean age=24.32 (SD: 2.6); 50% Caucasian.</td>
<td>TAU/WL n=21 (65% male); mean age=23.79 (SD: 4.5); 55% Caucasian.</td>
<td>77.3% of PRIME group completed all assessments versus 71.4% controls.</td>
<td>Not reported</td>
<td>Low</td>
<td>No significant between-group differences in PANSS scores at final assessment.</td>
</tr>
<tr>
<td>Subramaniam et al., (2012) U.S.A. RCT.</td>
<td>CACR, n=31 (83.9% male); mean age=40(SD:1.17); ethnicity not reported.</td>
<td>Health controls, n=16 (68.8% male); mean age=45(SD:11.6)</td>
<td>51.6% of CACR group completed all assessments, versus 87.5% in controls</td>
<td>Not reported</td>
<td>Low</td>
<td>No significant between-group differences in PANNS scores at 6-month assessment.</td>
</tr>
<tr>
<td>Vauth et al., (2005) Germany. RCT.</td>
<td>CACR-CAST plus vocational rehabilitation, n=47 (61.7% male); mean age=28.5 (SD:6.6); ethnicity not reported.</td>
<td>TSSN, n=45 (71.1% male); mean age=28.5(SD:6.5).</td>
<td>78.7% CAST group completed all assessments versus 77.7% in TSSN group and 60.9% in VRA group.</td>
<td>Not reported</td>
<td>Low</td>
<td>No significant between-group differences in PANNS scores at 6-month assessment.</td>
</tr>
</tbody>
</table>
Table 1 continued.

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Vita et al., (2011) Italy. RCT.</td>
<td>CACR (IPT-Cog), n=26 (80.8% male); mean age=37.15(SD:9.1); CACR, n=30 (60% male); mean age=36.76(SD:11.4).</td>
<td>REHAB, n=28 (64.3% male); mean age=43(SD:7.76); ethnicity not reported.</td>
<td>96.4% of both CACR groups completed all assessments versus 100% of controls.</td>
<td>Not reported.</td>
<td>High</td>
<td>Reduction in PANSS scores was significantly greater in both CACR groups than controls.</td>
</tr>
</tbody>
</table>

*Did not report participant characteristic/completion rates separately for intervention and control.*
3.2 Study synthesis and meta-analysis.

The studies were broken into type of DHT (Figure 2) for narrative and meta-analysis. Two-thirds of articles focused on computer-assisted therapies, with avatar therapy and phone apps having four and three articles respectively.

**Figure 2. Breakdown of studies by DHT.**

3.2.1 Computer-based DHTs.

There were mixed results in the computer-based DHTs category, with Figure 3 showing a non-significant standard mean difference (SMD -.15 [-.47, .17], \( p=.36 \)). In nine of the fourteen studies on computer-based DHTs, the primary outcome was cognitive remediation, with psychotic symptom reduction being a secondary outcome. Only one of these CACR studies demonstrated significant improvements in psychotic symptoms (Matsuda et al.,...
Three of the remaining five non-CACR studies demonstrated positive results. SOAR (Schizophrenia Online Access to Resources) is a web-based programme that focuses on managing positive symptoms, which demonstrated significantly better improvement in psychotic symptoms than the TAU group (Rotondi et al., 2010). However, although participants using another web-based intervention (Coping with Voices) reported that the programme helped (67%) or very much helped (33%) symptom management, there was no significant difference between the intervention and control groups on auditory hallucination measurements at post-intervention (Gottlieb et al., 2017). Dialog+ promotes patient-clinician communication with a solution-focused therapy approach, and at 12-months assessment, patients in the experimental condition reported significantly lower symptoms (PANSS-general) (Priebe et al., 2014). In an experimental investigation targeting reasoning biases Garety et al., (2014) found their intervention to be efficacious in reducing paranoia.

Figure 3. Forest plot for computer-based DHTs.

### 3.2.2 Avatar-based DHTs.

Avatar-based therapy is based on inter-personal relating, with the original trial being led by the therapy developers (Leff et al., 2013). Participants created an avatar to give a face to their auditory verbal hallucinations (AVHs) and software was used to alter the avatar’s voice to sound like the participant’s persecutory AVHs, which were spoken by the therapist and transformed in real time. During therapy, participants were encouraged to become more
assertive, leading to a reduction in hostility and an increase in supportive comments from the avatar; the premise being that the experience would transfer to participants’ actual AVHs. At post-treatment there was improvement in PSYRATS-AH scores, with three participants no longer hearing voices. Further improvement was recorded at three-month follow up, but there was a 34.6% drop-out rate indicating a possible acceptability issue.

Craig et al. (2018) improved on this study with a larger (powered) sample, using an active control (supportive counselling) rather than TAU to control for time and attention given to participants receiving therapy. The dropout rate was lower than Leff et al.’s (2013) trial, with 84% of participants in the avatar group completing the 12-week assessments, where fourteen participants reported an absence of AVHs. However, at 24-weeks the supportive counselling also demonstrated improvements in the frequency of AVHs, with the final results showing no significant differences between the two groups on these domains.

The two latest trials (du Sert et al., 2018; Pot-Kolder et al., 2018) used avatars in immersive virtual reality (VR), as the investigators believed that immersive VR paradigms may increase the feeling of presence and emotional arousal. The investigation by du Sert et al., (2018) focused on refractory AVHs and reported a large reduction on the PSYRATS total score. In the study by Pot-Kolder et al., (2018), participants were randomised to virtual reality cognitive behaviour therapy (VR-CBT) or waitlist. The virtual environment consisted of four scenarios where the participant could control their position with a gamepad. Participants were encouraged to use cognitive/behavioural strategies to navigate the environment to reduce cognitive biases and safety behaviours in-virtuo. Scores on the Paranoid Thoughts Scale showed that those in the VR-CBT condition reported lower levels of persecution than the control group at 6-month follow-up. Although the VR studies focus on exposure rather than the relationship someone has with their voices, they have been included in this section as
avatars were used in the VR environments. The meta-analysis of avatar therapies (Figure 4) found a significant standard mean difference (SMD -0.34 [-0.61,-0.06], p=.02.).

Figure 4. Forest plot for avatar therapies.

3.2.2 Phone apps.
The three phone apps were PRIME (personalized real-time intervention for motivational enhancement), FOCUS and Actissist. Although PRIME was designed to improve motivation and quality of life, psychotic symptoms were measured as a secondary outcome measure. Participants were paid for completing assessments, but were not monetarily incentivised to use the app. Despite the results indicating that the app was efficacious for the primary outcome, there was no significant difference between the changes in PANSS scores between the groups at three-month follow-up.

Ben-Zeev et al., (2018) reported on a head-to-head comparison of ‘FOCUS’ and the Wellness Recovery Action Plan (WRAP). There was no monetary incentive in the study, but all participants were provided with smartphones to generalise their experience. The PSYRATS was used to assess psychotic symptoms as a secondary clinical outcome (the primary outcome being general psychopathology measured by the Symptom Checklist-9). Although FOCUS was not superior, the authors noted that FOCUS compared favourably with an evidence-based intervention (WRAP) on other variables, despite neither having a significant effect on PSYRATS scores.
A three-arm study evaluated Actissist against TAU and the symptom monitoring app ClinTouch, which was used to control for non-specifics of smartphone use and for having a similar look and functionality of Actissist (Bucci et al., 2018). Participants were provided with a smartphone with £10 data per month or were provided the £10 monthly top-up for their own smartphone. All participants were given a £10 shopping voucher per fortnight. The Actissist app consists of on-demand functions and daily prompts to engage with the app. Self-assessment questions lead the app to offer normalizing messages and cognitive/behavioural strategies to cope with experiences. There was 100% completion rate of the 12-week intervention with the Actissist group showing significant within-group improvement in both PANSS and PSYRATS scores, and greater improvement than the ClinTouch group. The completion rate remained reasonably high (83%) at the 22-week follow-up but treatment effects were not maintained. The meta-analysis of avatar therapies (Figure 5) demonstrated a non-significant summary standard mean difference (SMD -0.04 [-0.98,0.89], p=93).

4.0 Discussion.
This review examined the effect of DHTs on psychotic symptoms as an indicator of effectiveness, as research shows that individuals are turning to technology for symptom relief (Gay, Touros, Joseph, Pandya, & Duckworth, 2016). The most common DHT reviewed was CACR. Whilst the primary outcome in these trials was cognitive remediation, studies show that cognitive remediation may impact psychotic symptoms (e.g. McGurk et al., 2007), with
suggestions that improved symptomatology may be mediated through improved self-efficacy from completing cognitive remediation programmes (Lee, 2013; Rotondi et al., 2010). However, only one CACR study reviewed demonstrated improvement in psychotic symptoms. This is similar to findings of a meta-analysis that included non-computerised cognitive remediation in schizophrenia, which showed a small significant effect on symptoms at posttreatment, but the significance disappeared at follow-up (Wykes, Huddy, Cellard, McGurk & Czobor, 2011).

In the avatar therapies the avatars were controlled by therapists to elicit emotions, cognitions and behaviours in-virtuo, allowing participants to challenge threat beliefs in real-time; a practice that can be difficult to achieve in regular clinical settings (Rus-Calafell, Garety, Sason, Craig & Valmaggia, 2018). Whilst the reduction in voice hearing (sometimes a complete cessation of voice hearing) is welcomed, the most recent trial (Craig et al., 2018) reported no significant difference between the avatar group and supportive counselling at 24-week follow-up. A further issue, acknowledged by the developers, is that it requires a trained therapist to voice the avatar, which possibly negates the capability of this DHT to be rolled out to larger numbers in a cost-effective manner.

Despite high completion rates, which may be attributable to participants being provided with smartphones and/or Internet access, none of the phone apps were effective in reducing psychotic symptoms. However, their development is in its infancy, with all the phone app trials being published in 2018, reflecting the novelty of such interventions. Indeed, all avatar-based trials were also published in 2018, which may be an indication that the pace of DHT development is beginning to accelerate, and therefore a limitation of the current review is that it may soon be outdated.
This is linked to limitations of the studies included in the review, i.e. they have mostly been pilot and proof-of-concept trials. As such, they may make type-II errors by not being adequately powered (except Craig et al., 2018). Therefore, it would be beneficial for developers to provide other researchers with access to their DHTs to enable phase III head-to-head trials to be completed. Only one study in the present review did this (Ben-Zeev et al., 2018), comparing a novel DHT (FOCUS) with an evidenced-based intervention (WRAP), and thus it is not possible to state which DHTs may be most effective. Therefore, a further limitation of this review is being unable to make recommendations for clinical practice.

However, recommendations for future research include establishing effectiveness and exploring which components of DHTs (e.g. technology type, theoretical background) are related to symptom improvement, as well as examining relationships between effectiveness of DHT type and other variables (e.g. patient characteristics, clinical setting, illness duration). Further, the present review did not assess access and cost-effectiveness so future research from a health economics perspective would be welcome.

In conclusion, the evaluation of DHTs in ameliorating psychotic symptoms is in its infancy. CACR has no impact on psychotic symptoms, whilst web-based CBTp programmes and phone apps such as Actissist may hold potential, and avatar-based therapies appear to hold most promise. This would be expected given that the three categories in the review adopt different approaches, e.g. CACR posits that cognitive remediation may secondarily improve psychotic symptoms, whereas avatar therapy addresses psychotic symptoms directly. As DHTs have mainly been subjected to pilot and proof-of-concept trials, future research involving larger sample sizes and lower risks of bias are required before effectiveness can be established.

Disclosure of Interest: The authors report no conflict of interest.
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Appendix A: Author instructions from Psychosis.

Structure: Your paper should be compiled in the following order: title page; abstract; keywords; main text introduction, materials and methods, results, discussion; acknowledgments; declaration of interest statement; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figures; figure captions (as a list).

Word Limits: Please include a word count for your paper. The maximum word length for an Article in this journal is 6000 words (this limit includes tables, references and figure captions).

Style Guidelines: Any spelling style is acceptable so long as it is consistent within the manuscript. Please use double quotation marks, except where “a quotation is ‘within’ a quotation”. Please note that long quotations should be indented without quotation marks.

Formatting and Templates: Papers may be submitted in Word format. Figures should be saved separately from the text.

Checklist: What to Include:

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the new affiliation can be given as a footnote. Please note that no changes to affiliation can be made after your paper is accepted. Read more on authorship.

2. Should contain a structured abstract of 200 words.

3. You can opt to include a video abstract with your article. Find out how these can help your work reach a wider audience, and what to think about when filming.

4. Between 5 and 6 keywords. Read making your article more discoverable, including information on choosing a title and search engine optimization.

5. Funding details: Please supply all details required by your funding and grant-awarding bodies as follows.

6. Disclosure statement: This is to acknowledge any financial interest or benefit that has arisen from the direct applications of your research. Further guidance on what is a conflict of interest and how to disclose it.

7. Data availability statement: If there is a data set associated with the paper, please provide information about where the data supporting the results or analyses presented in the paper can be found. Where applicable, this should include the hyperlink, DOI or other persistent identifier associated with the data set(s). Templates are also available to support authors.

8. Data deposition: If you choose to share or make the data underlying the study open, please deposit your data in a recognized data repository prior to or at the time of submission. You will be asked to provide the DOI, pre-reserved DOI, or other persistent identifier for the data set.

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10. **Figures**: Figures should be high quality (1200 dpi for line art, 600 dpi for grayscale and 300 dpi for colour, at the correct size). Figures should be supplied in one of our preferred file formats: EPS, PS, JPEG, GIF, or Microsoft Word (DOC or DOCX). For information relating to other file types, please consult our Submission of electronic artwork document.

11. **Tables**: Tables should present new information rather than duplicating what is in the text. Readers should be able to interpret the table without reference to the text. Please supply editable files.

12. **Equations**: If you are submitting your manuscript as a Word document, please ensure that equations are editable. More information about mathematical symbols and equations.

13. **Units**: Please use SI units (non-italicized).

**Disclosure Statement**: Please include a disclosure statement, using the subheading “Disclosure of interest.” If you have no interests to declare, please state this (suggested wording: *The authors report no conflict of interest*). For all NIH/Wellcome-funded papers, the grant number(s) must be included in the declaration of interest statement. Read more on declaring conflicts of interest.
Chapter 2.

The Association Between Sleep Quality and Attenuated Psychotic Symptoms in a Community Sample.

**Aim:** To determine if poor sleep quality makes a unique contribution to predicting the number of attenuated psychotic symptoms endorsed in a prodromal questionnaire and the level of distress associated with the symptoms, when controlling for demographics, depression and drug/alcohol use.

**Method:** An online survey was conducted using Amazon’s online crowdsourcing service Mechanical Turk (MTurk). The sample was 1,013 adults (18 to 36 years) from the general population in the USA. The survey consisted of the Prodromal Questionnaire 16 (PQ-16), the Pittsburgh Sleep Quality Index, the Patient Health Questionnaire 9 (PHQ-9), the DAST-10 and the AUDIT. Regression analyses were performed with the PQ-16 as the dependent variable, and sleep quality as the predictor variable, holding constant sociodemographic variables, depression, and alcohol/drug abuse.

**Results:** 37% of the sample endorsed six or more PQ-16 items, which may be suggestive of an at-risk mental state, with sleep disturbance significantly increasing the likelihood (Odds ratio 2.09 <.001) of endorsing six or more PQ-16 items. After controlling for socio-demographic variables, depression and drug/alcohol abuse, poor sleep quality made a unique contribution of 5.8% of the variance accounted for in level of distress experienced by attenuated psychotic symptoms.

**Conclusion:** The results add to the evidence that sleep disturbance is a contributory factor in attenuated psychotic symptoms. Effective treatment of sleep disturbance may reduce the likelihood of developing an at-risk mental state.

**Keywords:** psychotic symptoms, sleep disturbance, at-risk mental state, depressive symptoms

**Practitioner points:**
- A significant number of young adults in the general population may have an at-risk mental state.
- Sleep disturbance, as a strong predictor of attenuated psychotic symptoms, should be treated as recommended by clinical recommendations.
- Further research is required to investigate the possible mechanisms (e.g. impaired cognitive processes) through which poor sleep influences attenuated psychotic symptoms.
1.0 INTRODUCTION.

Psychotic disorders, such as schizophrenia, are usually preceded by a prodromal phase, where individuals experience psychological, perceptual and behavioural anomalies (Yung, McGorry, McFarlane, Jackson, Patton & Rakkar, 1996). However, experiencing such phenomena does not make it inevitable that an individual will transition to a psychotic disorder and, consequently, the prodrome terminology can only be applied retrospectively, following a confirmed diagnosis of psychotic disorder. When considering such experiences prospectively, as risk factors for developing psychosis, the nomenclature At-Risk Mental State (ARMS) was proposed by McGorry and Singh (1995). To be categorised as having an at-risk mental state, at least one of the following criteria devised by Yung et al. (2005) must be met: 1) experience of attenuated psychotic symptoms during the past year; 2) experience of brief limited intermittent psychotic symptoms lasting a week or less which have resolved or lessened; 3) have a first-degree relative with a psychotic disorder and have experienced nonspecific symptoms such as lowered mood with a decline in functioning over the past year.

Mills, Fusar-Poli, Morgan, Azis, & McGuire (2017) sought to estimate the prevalence of ARMS in the general population, and reported an estimated weighted prevalence of 14.4%. An estimated 20-45% of individuals meeting ARMS criteria transition to psychosis (Nelson et al., 2008; Oliver et al., 2019). By understanding experiences of those meeting ARMS criteria, we may develop a better understanding of the aetiology of psychosis. The present study aimed to add to the knowledge base by focusing on the first criterion above (attenuated psychotic symptoms), which are subclinical symptoms on a continuum with frank psychosis but are of lower intensity, frequency or duration (Yung et al. 2005). The reason for focusing on attenuated psychotic symptoms (APS) is that they are present in both clinical settings and the general population (Bentall, Claridge & Slade, 1989; Johns & van Os, 2001), suggesting that they may be a very early indicator of psychosis risk. And, although most people
experiencing APS do not transition to psychosis, a meta-analysis of 26 factors concluded that APS meet the criterion of highly suggestive evidence for transition to psychosis (Oliver et al., 2019). With APS having such an important role within the aetiology of psychosis, it is important to study factors that may be involved in these symptoms.

One factor known to be associated with APS is poor sleep (Davies, Haddock, Yung, Mulligan & Kyle, 2017), but it is not known if poor sleep increases the likelihood of experiencing multiple APS, which research suggests may be suggestive of an ARMS. For example, when investigating the validity of a 16-item version of the Prodromal Questionnaire (Loewy et al., 2005) in the general population, Ising et al. (2012) found that endorsing six or more items produced correct classification of ARMS in 44% of cases when interviewed using the Comprehensive Assessment of At-Risk Mental State. Therefore, establishing if poor sleep increases the likelihood of experiencing six or more APS would be clinically important. However, rather than focusing exclusively on the number of APS, cognitive models of psychosis (e.g. Garety, Kuipers, Fowler, Freeman & Bebbington, 2001) posit that it is the distress associated with APS that leads to a need for care, rather than the experience of APS per se (Ward, Gaynor, Hunter, Woodruff, Garety, & Peters, 2014), highlighting the importance of also establishing if poor sleep plays a role in the distress associated with APS. Before estimating any effect that poor sleep might have on the experience of APS and associated distress, it is necessary to consider other factors known to be related to APS, so that their effect may be controlled for.

Socio-demographic factors have consistently been found to be associated with the development of psychosis (Kendler, Gallagher, Abelson & Kessler, 1996; Brucato et al., 2017) and their respective risk/protective factors in relation to APS are reviewed below. Additionally, given that almost nine in every ten individuals diagnosed with psychosis also meet DSM-IV criteria for another mental health condition (Kessler et al., 2005) it is
important to control for the presence of mental health problems that have been shown to be predictive of psychosis. Although post-traumatic stress disorder and anxiety disorders (obsessive compulsive disorder, social anxiety disorder) are frequently found to be comorbid with psychosis (Hardy & Mueser, 2017; McEnery et al., 2019; Niendam, Berzak, Cannon & Bearden, 2009), the two most common comorbid disorders are depression and drug/alcohol dependence (Kessler et al., 2004), which are also strongly related to sleep disturbance, as outlined below.

1.1 Socio-demographic factors.
A modest relationship has been found between socio-demographic variables (age, sex education, relationship status) and APS. Age is an inverse predictor, whilst individuals with lower educational attainment and those who are not married/cohabiting are more likely to endorse APS, and females are more likely to have severe distress ratings than males (Guadiano & Zimmerman, 2013; Waford et al., 2016). However, the relationship between ethnicity and APS is unclear, with results showing that individuals from ethnic minorities endorse more APS (Guadiano & Zimmerman, 2013) and are more likely to develop an at-ARMS (Velthorst et al., 2012); whereas others suggest possible benefits of having a strong identity with an ethnic group when faced with discrimination, which may serve as a protective factor against APS (Anglin, Lui, Espinosa, Tikhonov, & Ellman, 2018). With such equivocal and modest relationships, it is necessary to consider variables that have a stronger relationship with APS.

1.2 Depression.
The link between depression and schizophrenia is well recognised. In a review of comorbidities in schizophrenia, Buckley, Miller, Lehrer and Castle (2009) reported that around half of patients also met criteria for a diagnosis of depression. When considering
individuals with an ARMS profile, early studies found depression to be a risk factor for transitioning to psychosis within 130 days. (Yung et al., 2003). When investigating links between depression and APS in non-clinical samples, Ohayon and Schatzberg (2002) studied community samples across five European countries and reported that 16.5% of the 18,980 participants reported at least one depressive symptom, and 12.5% of these participants also reported psychotic symptoms. Although these studies confirm a relationship between depression and psychotic symptoms they do not establish the direction of the relationship, which is required if depression is to be considered as a predictor variable to be controlled for in the present study. However, in their study of causal associations between depressive symptoms and schizophrenia, Häfner, Maurer, Trendler, an der Heide, Schmidt and Könnecke (2005) recruited a group of 232 patients presenting with a first episode of psychosis and compared their symptoms with a group of 130 demographically matched patients with depression and a third group of 130 healthy controls. When comparing the 10 most frequently endorsed initial symptoms of both patient groups, they found an overlap of 13 symptoms, eight of which did not differ significantly in frequency. In those diagnosed with psychosis, depressed mood was the most frequent initial presentation, appearing four years before first admission to hospital with a first episode of psychosis. The two patient groups only differentiated from the depressive core syndrome as the psychosis group started to experience more positive symptoms approaching admission to hospital, with the authors concluding that depression might be an early stage of the same neurobiological processes that are involved in the onset of psychosis. Therefore, with depressive symptoms being an important feature of psychosis and temporally tending to appear before transition to psychosis, it is important to consider depressive symptoms as a variable to be controlled for when assessing the relationship between poor sleep quality and APS.
1.3 Drug and alcohol abuse.
Drug and alcohol abuse is prevalent among both the general population and people diagnosed with psychotic disorders (Merikangas & McClair, 2012; Moore, Mancuso, Slade, Galletly & Castle, 2012). There is also a relationship between alcohol use and sleep, with alcohol commonly associated with drowsiness after consumption, but sleep maintenance problems are more noticeable after alcohol has been completely metabolised, so that with moderate alcohol consumption, sleep maintenance difficulties are more common in the second half of 8 hours sleep, when the alcohol has been completely metabolised (Roehrs & Roth, 2001). A study by Sivertsen, Skogen, Jakobsen, & Hysing (2015) found a dose-response between drug and alcohol use and sleep disturbance. Cannabis use has been found to be associated with APS (Kuepper et al., 2011), with suggestions that its use may have psychotogenic effects in those with an ARMS (Corcoran et al., 2008), and findings that APS are more prevalent in cannabis users versus non-users in the general population (van Os et al., 2009; Ruiz-Veguilla et al., 2013). Therefore, alcohol consumption and drug use must be controlled for when considering poor sleep as a predictor, given that they are related to both poor sleep and psychotic symptoms.

1.4 Sleep quality.
As the present study aims to assess if poor sleep predicts the number of APS and associated distress after controlling for the above factors, it is necessary to establish the theoretical basis for considering sleep as a predictor variable. With rates of sleep disturbance reported as high as 80% among individuals diagnosed with schizophrenia (Anderson & Bradley, 2013; Reeve, Sheaves, & Freeman, 2015), it is plausible that psychotic symptoms and associated distress are a cause of poor sleep, rather than a predictor of psychotic symptoms. However, the evidence suggests the inverse relationship, with poor sleep precipitating psychotic symptoms (Freeman et al., 2017; Reeve, Emsley, Sheaves & Freeman, 2018; Reeve, Sheaves &
Freeman, 2015; Wright, 1993). For example, in patients diagnosed with schizophrenia, sleep disturbance was a predictor of next-day psychotic symptom severity (Mulligan, Haddock, Emsley, Neil, & Kyle, 2016).

Although poor sleep has been extensively researched in schizophrenia (for a review see: Robertson, Cheung & Xiaoduo, 2019), any attempt to research potential aetiological factors requires examination of the earlier stages of psychosis development. Studies have shown that individuals with an ARMS presentation have increased sleep onset latency than healthy controls (Keshavan et al., 2004) and poor sleep quality is related to the transition to future psychosis in adolescents and young adults (Lunsford-Avery, LeBourgeois, Gupta & Mittal, 2015; Lee et al., 2012; Ruhrmann et al., 2010; Yung, McGorry, McFarlane, Jackson, Patton, & Rakkar, 1996). In studies with non-clinical groups, research has found a positive association between insomnia and paranoid experiences in a community sample of 300 people (Freeman et al., 2009), whilst experimental sleep deprivation was found to induce perceptual distortions (Petrovsky et al., 2014). Using data from the British Psychiatric Morbidity Surveys, Sheaves et al. (2016) reported that insomnia was predictive of de novo hallucinations at 18-month follow-up, and Hennig and Lincoln (2018) found that shorter sleep predicted paranoia, but paranoia did not predict insomnia. Therefore, poor sleep warrants examination as a potential precipitant of psychotic experiences.

Additionally, as cognitive models of psychosis (e.g. Garety, Kuipers, Fowler, Freeman & Bebbington, 2001) suggest that it is not the experience of APS per se that leads to a need for care, but rather it is the distress associated with the symptoms (Ward, Gaynor, Hunter, Woodruff, Garety, & Peters, 2014), the present study also sought to examine if poor sleep contributes to distress associated with APS.
In summary, research suggests that six or more APS is suggestive of an ARMS (Ising et al., 2012), and there may be a significant number of young adults in the general population with an ARMS not being seen by specialist psychosis prevention/early intervention services (Mills, Fusar-Poli, Morgan, Azis, & McGuire, 2017). The present study sought to confirm this high prevalence rate and explore if poor sleep predicts APS and associated distress after controlling for potential confounding factors known to predict APS. The specific questions were:

Research Question 1) Will a large community-based sample replicate the findings of Mills, Fusar-Poli, Morgan, Azis, & McGuire (2017) by finding a high prevalence of young adults endorsing APS and, if so, what are the characteristics of those symptoms?

Research question 2) After controlling for socio-demographic factors, depression, and drug/alcohol abuse, does poor sleep increase the likelihood of someone endorsing six or more APS, which is suggestive of an ARMS?

Research question 3) Does poor sleep quality have predictive power in determining the level of distress experienced from APS, after controlling for demographic factors, depression, and drug/alcohol abuse?

2.0 METHOD.

The Northern Health and Social Care Trust in Northern Ireland provided funding for the study, which was approved by the Research Ethics Committee in the School of Psychology, Queen’s University Belfast (Appendix C).
2.1 Participants.
The sample consisted of 1,013 adults in the USA (aged 18 to 36 years), recruited through Mechanical Turk (MTurk), an Internet-based crowd sourcing service provided by Amazon.com Inc. that offers registered users payment for completing human intelligence tasks (HITs).

2.2 Procedure.
MTurk allows filters to be applied. To increase the likelihood of quality data, a filter was applied so that only users with a 95% acceptability rating from previous HITs could see the current study in MTurk’s listing of available HITs. Participants read an information sheet (Appendix D) before deciding to participate. The information sheet provided full details of the study, i.e. the voluntary nature of participation, the right to withdraw, the type of information that would be asked (sleep pattern, depressive symptoms, APS etc.), how to contact the research team and information about remuneration, which would be processed using MTurk ID codes, with no personal information being stored or analyzed. Anyone wishing to participate confirmed their wish to do so by completing the HIT, on the understanding that doing so confirmed that they had read and understood the information sheet, that they were willing to be a participant, and that they agreed to anonymous data being used in scientific analysis and publication. Upon satisfactory completion of the survey, participants were paid approximately $2.00 (based on a rate of $9.00 per hour). Incomplete data was rejected, whilst anonymous data from completed HITs was exported to an MS Excel spreadsheet for scoring on a password protected computer, before being exported to SPSS (Version 25) for analysis.

2.3 Measures.
Participants were asked to provide socio-demographic data (age, gender, relationship status, education and employment status), before being asked to complete the questionnaires below.
Five attention questions embedded within the questionnaires. An example of an attention question was, “I eat for more than 25 hours per day: True/False/Unsure.”

2.3.1. The Prodromal Questionnaire (PQ-16).
The PQ-16 is a self-report measure for screening unusual experiences (APS) associated with the psychosis prodrome. Its use in several settings has been established in a systematic review (Savill, M., D’Ambrosio, J., Cannon, T., & Loewy, 2017). The subscales consist of perceptual abnormalities/hallucinations (9 items), unusual thought content/delusional ideas/paranoia (5 items) and two items related to negative symptoms. It has high sensitivity (87%) and specificity (87%) in distinguishing between meeting criteria and not meeting criteria for having an ARMS, as assessed using the Comprehensive Assessment of At-Risk Mental State (CAARMS; Yung et al., 2005), and has good internal consistency with Cronbach’s α = .8 (Ising et al., 2012). The presence of APS is assessed on a 2-point scale (true/false), with items endorsed then measuring distress on a 4-point scale (no distress, mild, moderate and severe distress). The total score is achieved by adding up all true items, with total scores of six or more being suggestive of an at-risk mental state (Ising et al., 2012).

2.3.2. Pittsburgh Sleep Quality Index (PSQI).
The PSQI is a 19-item self-report questionnaire with 7 subscales (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, day-time function and use of medication) with good internal consistency (Cronbach’s α = .83), good test-retest reliability and good validity (Buysse et al., 1989). Scoring is based on a 0 to 3 scale, with 0 indicating no difficulty and 3 indicating severe difficulty. A total score is achieved by summing all subscales, with ‘good sleepers’ being differentiated from ‘poor sleepers’ at the cut-off score of 6 (Buysse et al., 1989).
2.3.3. Patient Health Questionnaire 9 (PHQ-9).
The PHQ-9 is a self-report questionnaire used to assess the presence and severity of depressive symptoms in the two weeks prior to its completion, with good internal consistency (Cronbach’s alpha = .89) found in 3,000 primary care patients, and criterion validity having 88% sensitivity and 88% specificity when measuring PHQ-9 scores from 580 participants against depression diagnoses validated by a mental health professional (Kroenke, Spitzer & Williams, 2001).

2.3.4. Alcohol Use Disorders Identification Test (AUDIT).
The AUDIT was developed by the World Health Organization and has been extensively validated globally. A 2007 review showed that the tool has a median reliability coefficient of 0.83 across 18 studies produced in the preceding five years (Reinert & Allen, 2007). It is a ten-item scale assessing alcohol consumption and related problems, with suggested cutoff scores of 8 distinguishing harmful users and 11 classifying alcohol dependence (Tsai, Tsai, Chen & Liu, 2005).

2.3.5. Drug Abuse Screening Test 10 (DAST-10).
The DAST-10 is a self-report scale examining problematic substance use which has been used across a number of participant groups. It has good internal consistency (Cronbach’s alpha approaching .9) (Yudko, Lozhkina, & Fouts, 2007). Sensitivity and specificity was found to be .98 and .91 respectively, when using 4 as the cut-off point (Evren, Ovali, Karabulut, & Cetingok, 2014).

2.4 Data analysis.
Before conducting analyses, a check of the data was completed and cases with missing data or incorrect answers to the attention questions were removed. Data analyses were performed on IBM® SPSS® Statistics. Descriptive statistics of all measures were reported and tests for
normal distribution were conducted to ensure that this assumption was met for parametric analyses. Residual and scatter plots were inspected to ensure that the assumptions of normality, linearity and homoscedasticity were met, whilst inspection of variance inflation factor (VIF) and Tolerance indicated that multicollinearity was not an issue, and Cook’s distance values indicated that there were no influential outliers (Field, 2018; Menard 1995; Myers, 1990). Hierarchical logistic regression analysis was performed to examine if poor sleep quality increased the likelihood of endorsing six or more PQ-16 items when controlling for demographic factors, depression, and drug/alcohol abuse. Hierarchical multiple regression analyses were completed to calculate if poor sleep quality predicted APS distress level when controlling for socio-demographic factors, depression and drug/alcohol abuse.

3.0 RESULTS.
After rejecting incomplete cases ($n=52$) and those with incorrect answers to attention questions ($n=2$), the total sample analysed consisted of 1,013 participants. It was not possible to test for differences between completers and non-completers due to insufficient data available from non-completers. Socio-demographic information is presented in Table 1. There was no significant difference between the number of males and females, and almost half the sample was single, with approximately a third being married. Most participants were in full-time employment, and the vast majority were white/Caucasian.

| Table 1: Demographic information of sample ($n=1,013$).  |
|---------------------------------|------------------|
| **Mean Age (SD)**               | 29.7 (3.83).     |
| **Gender (%)**                  |                  |
| Female                          | 50.9             |
| Male                            | 49.1             |
### Relationship status (%)

- **Single, never married**: 45.1
- **Married**: 34.4
- **Single, but cohabiting with partner**: 14.2
- **Domestic partnership / civil union**: 4.2
- **Divorced**: 1.2
- **Separated**: .8
- **Widowed**: .1

### Education (%)

- **Bachelor degree**: 43.2
- **Some college but no degree**: 20.4
- **Graduate degree**: 14.3
- **Associate degree**: 11.2
- **High school degree or equivalent**: 10.5
- **Less than high school**: .4

### Employment status (%)

- **Employed full-time**: 70.3
- **Employed part-time**: 17.1
- **Not employed, seeking work**: 6.1
- **Not employed, not seeking work**: 5.9
- **Retired**: .6
- **Disabled, not able to work**: 0

### Ethnicity (%)

- **White / Caucasian**: 76
- **Asian / Pacific Islander**: 9.2
- **Hispanic**: 5.9
- **Black or African American**: 5.4
- **Multiple ethnicity**: 2.8
- **American Indian / Native Alaskan**: .7

Table 2 displays the descriptive statistics for the measures used. The PQ-16, the PHQ-9 and the DAST-10 achieved the full range of scores. The PSQI and AUDIT achieved an acceptable range of scores. The internal consistencies of the PQ-16, PHQ-9 and the DAST-10
were excellent and the internal consistencies of the PSQI and the AUDIT were approaching excellent. The mean total score (7.52) for the PSQI in this sample was above the cut-off score of 6, which has been found to differentiate good and poor sleepers. The mean total score (7.24) for the PHQ-9 is within the mild depressive symptoms range, whereas the mean score of 5.08 on the PQ-16 was below the cut-off score of 6 that has been found to be suggestive of an ARMS (Ising et al., 2012). The mean score for the DAST-10 was 5.39, which is above the suggested cut-off point of 4 (Evren, Ovali, Karabulut, & Cetingok, 2014), whilst the mean score for the AUDIT (4.63) is below the suggested cut-off for harmful use (Tsai, Tsai, Chen & Liu, 2005).

Table 2: Descriptive statistics for the measures used.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean total score</th>
<th>SD</th>
<th>Achieved range</th>
<th>Cronbach’s alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td>PQ-16 Total score.</td>
<td>5.08</td>
<td>4.22</td>
<td>0-16</td>
<td>.91</td>
</tr>
<tr>
<td>Pittsburgh Sleep Quality Index (PSQI)</td>
<td>7.52</td>
<td>4.03</td>
<td>0-20</td>
<td>.86</td>
</tr>
<tr>
<td>Patient Health Questionnaire 9 (PHQ-9)</td>
<td>7.24</td>
<td>5.99</td>
<td>0-27</td>
<td>.91</td>
</tr>
<tr>
<td>Alcohol Disorders Identification Test (AUDIT)</td>
<td>4.64</td>
<td>5.03</td>
<td>0-31</td>
<td>.89</td>
</tr>
<tr>
<td>Drug Abuse Screening Test 10 (DAST-10)</td>
<td>5.39</td>
<td>3.29</td>
<td>0-10</td>
<td>.91</td>
</tr>
</tbody>
</table>

Research Question 1).

More than a third (37%) of the sample endorsed six or more PQ-16 items. Summary statistics for the responses to the PQ-16 are in Table 3. The mean number of APS endorsed was 5.08 and the full range of items (0-16) was achieved. Almost 10% of the sample reported experiencing zero APS. The modal number of items endorsed by participants was two. There were no significant differences for the total number of items endorsed between males ($M = 4.88$; $SD = 4.37$) and females ($M = 5.28$; $SD = 4.07$). Age did substantially correlate ($r \geq .1$)
with total PQ-16 score. Of the 90.3% of individuals endorsing at least one PQ-16 item, the most frequently endorsed was intense anxiety when meeting people for the first time, whilst the item least frequently endorsed was seeing faces change.

Table 3: Descriptive statistics for PQ-16 responses.

<table>
<thead>
<tr>
<th>PQ-16 item</th>
<th>Percentage endorsing item.</th>
<th>Total number of items endorsed.</th>
<th>Percentage endorsed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety meeting new people.</td>
<td>69.5</td>
<td>0</td>
<td>9.7</td>
</tr>
<tr>
<td>Lack of interest.</td>
<td>55.9</td>
<td>1</td>
<td>11.6</td>
</tr>
<tr>
<td>Déjà vu.</td>
<td>52.4</td>
<td>2</td>
<td>11.9</td>
</tr>
<tr>
<td>Hearing own thoughts.</td>
<td>36.3</td>
<td>3</td>
<td>11.7</td>
</tr>
<tr>
<td>Distraction by distant sounds.</td>
<td>33.5</td>
<td>4</td>
<td>10.3</td>
</tr>
<tr>
<td>Auditory hallucinations.</td>
<td>32.4</td>
<td>5</td>
<td>7.7</td>
</tr>
<tr>
<td>Confusing differentiating reality.</td>
<td>30.8</td>
<td>6</td>
<td>6.6</td>
</tr>
<tr>
<td>Unable to control thoughts.</td>
<td>30.7</td>
<td>7</td>
<td>5.8</td>
</tr>
<tr>
<td>Olfactory/taste hallucinations.</td>
<td>30.4</td>
<td>8</td>
<td>3.8</td>
</tr>
<tr>
<td>Inferring meaning.</td>
<td>24.8</td>
<td>9</td>
<td>4.4</td>
</tr>
<tr>
<td>Sensing invisible force.</td>
<td>24.6</td>
<td>10</td>
<td>4.5</td>
</tr>
<tr>
<td>Paranoia.</td>
<td>24.2</td>
<td>11</td>
<td>2.6</td>
</tr>
<tr>
<td>Sensing bodily changes.</td>
<td>23.4</td>
<td>12</td>
<td>1.4</td>
</tr>
<tr>
<td>Visual hallucination.</td>
<td>15.5</td>
<td>13</td>
<td>.8</td>
</tr>
<tr>
<td>Hearing voices.</td>
<td>14.5</td>
<td>14</td>
<td>2.5</td>
</tr>
<tr>
<td>Facial hallucination.</td>
<td>9.4</td>
<td>15</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Summary statistics for the subscales of the PSQI are displayed in Table 4. The full range of scores (0 to 3) was achieved for all subscales. Almost a third of participants regularly took up to 30 minutes to fall asleep. Three quarters of the sample stated that they did not use sleep medication during the past month. Two-thirds of the sample reported sleeping between 5 and 7 hours per night, which is below the recommended seven to nine hours sleep recommended for optimal health (Walker, 2017).

Table 4: Descriptive statistics for PSQI subscales.

<table>
<thead>
<tr>
<th>PSQI subscale</th>
<th>Percentage of items endorsed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep latency</td>
<td></td>
</tr>
<tr>
<td>Up to 15 minutes</td>
<td>19.5%</td>
</tr>
<tr>
<td>16 to 30 minutes</td>
<td>29.0%</td>
</tr>
<tr>
<td>31 to 60 minutes</td>
<td>25.2%</td>
</tr>
<tr>
<td>More than 60 minutes</td>
<td>26.3%</td>
</tr>
<tr>
<td>Subjective sleep quality</td>
<td></td>
</tr>
<tr>
<td>Very good</td>
<td>8.0%</td>
</tr>
<tr>
<td>Fairly good</td>
<td>45.0%</td>
</tr>
<tr>
<td>Fairly bad</td>
<td>41.8%</td>
</tr>
<tr>
<td>Very bad</td>
<td>5.2%</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td></td>
</tr>
<tr>
<td>No problem at all</td>
<td>4.9%</td>
</tr>
<tr>
<td>Very slight problem</td>
<td>69%</td>
</tr>
<tr>
<td>Somewhat of a problem</td>
<td>24.3%</td>
</tr>
<tr>
<td>A very big problem</td>
<td>1.8%</td>
</tr>
<tr>
<td>Sleep duration</td>
<td></td>
</tr>
<tr>
<td>More than 7 hours</td>
<td>28.3%</td>
</tr>
<tr>
<td>6 to 7 hours</td>
<td>31.0%</td>
</tr>
<tr>
<td>5 to 6 hours</td>
<td>33.5%</td>
</tr>
<tr>
<td>Fewer than 5 hours</td>
<td>7.2%</td>
</tr>
<tr>
<td>Daytime dysfunction</td>
<td></td>
</tr>
<tr>
<td>No problem at all</td>
<td>51.1%</td>
</tr>
<tr>
<td>Very slight problem</td>
<td>24.7%</td>
</tr>
<tr>
<td>Somewhat of a problem</td>
<td>16.6%</td>
</tr>
<tr>
<td>A very big problem</td>
<td>7.6%</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td></td>
</tr>
<tr>
<td>Greater than 85%</td>
<td>58.1%</td>
</tr>
<tr>
<td>75 to 84%</td>
<td>21.6%</td>
</tr>
<tr>
<td>65 to 74%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Less than 65%</td>
<td>10.6%</td>
</tr>
<tr>
<td>Use of sleep medication</td>
<td></td>
</tr>
<tr>
<td>Not during past month</td>
<td>73.5%</td>
</tr>
<tr>
<td>Less than once a week</td>
<td>9.1%</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>7.5%</td>
</tr>
<tr>
<td>Three or more per week</td>
<td>9.9%</td>
</tr>
</tbody>
</table>
Research Question 2:
A hierarchical logistic regression analysis was completed to determine if poor sleep increased the likelihood of endorsing six or more PQ-16 items, whilst controlling for socio-demographic factors, depression, and drug/alcohol abuse. Socio-demographic variables were entered in the first model (Table 5), which was statistically significant ($\chi^2(6) = 17.98, p = .006$) and accounted for 2.4% (Nagelkerke $R^2$) of the variance in the likelihood of endorsing six or more PQ-16 items. The only socio-demographic variable reaching significance was level of education, with higher education predicting a lower likelihood of endorsing six or more PQ-16 items. After entering depression (PHQ-9 total score), the second model accounted for a further 26.6% of the variance explained. In this model none of the socio-demographic variables reached significance but increasing PHQ-9 scores increased the likelihood (Odds Ratio 1.21, $p < .001$) of endorsing six or more PQ-16 items. Adding drug and alcohol abuse (DAST-10 and AUDIT scores) in the third step accounted for a further 1.5% of variance explained by the model, but only the DAST-10 scores made a statistically significant difference. In the final model, all predictor variables accounted for a total of 36.8% of variance, with the components of the PSQI having a unique contribution of 6.3% when all other variables were held constant. Of the seven subscales of the PSQI, sleep disturbance was the most significant predictor, with individuals reporting sleep disturbance being 1.5 to 3 times more likely to endorse six or more PQ-16 items.

Table 5: Logistic regression models for predictors of endorsing six or more PQ16 items.

<table>
<thead>
<tr>
<th>Model 1</th>
<th>$R^2 = 2.4%$ (Nagelkerke); $\chi^2(6) = 17.98, p = .006$</th>
<th>95% Confidence Interval</th>
<th>Odds Ratio</th>
<th>Upper</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta</td>
<td>Lower</td>
<td>Odds Ratio</td>
<td>Beta</td>
<td>Lower</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>Age</td>
<td>-.01</td>
<td>.96</td>
<td>.99</td>
<td>1.03</td>
<td>.714</td>
</tr>
<tr>
<td>Gender</td>
<td>-.18</td>
<td>.64</td>
<td>.84</td>
<td>1.09</td>
<td>.185</td>
</tr>
<tr>
<td>Marital status</td>
<td>.01</td>
<td>.96</td>
<td>1.01</td>
<td>1.06</td>
<td>.788</td>
</tr>
<tr>
<td>----------------</td>
<td>-----</td>
<td>-----</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Education</td>
<td>-.16</td>
<td>.77</td>
<td>.85</td>
<td>.95</td>
<td>.003</td>
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<tr>
<td>Employment status</td>
<td>.11</td>
<td>.96</td>
<td>1.11</td>
<td>1.28</td>
<td>.151</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>.06</td>
<td>.93</td>
<td>1.06</td>
<td>1.21</td>
<td>.356</td>
</tr>
</tbody>
</table>

### Model 2

$R^2 = 29\%$ (Nagelkerke);

$\chi^2(7) = 241.85, p < .001$

<table>
<thead>
<tr>
<th></th>
<th>95% Confidence Interval</th>
<th>Beta</th>
<th>Lower</th>
<th>Odds Ratio</th>
<th>Upper</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>.01</td>
<td>.97</td>
<td>1.01</td>
<td>1.05</td>
<td>.769</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td>.23</td>
<td>.93</td>
<td>1.26</td>
<td>1.71</td>
<td>.144</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td>-.03</td>
<td>.91</td>
<td>.93</td>
<td>1.02</td>
<td>.248</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td>-.08</td>
<td>.82</td>
<td>.93</td>
<td>1.05</td>
<td>.228</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td>-.01</td>
<td>.84</td>
<td>.99</td>
<td>1.17</td>
<td>.892</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td>.04</td>
<td>.90</td>
<td>1.04</td>
<td>1.21</td>
<td>.576</td>
</tr>
<tr>
<td>PHQ-9 score</td>
<td></td>
<td>.19</td>
<td>1.18</td>
<td>1.21</td>
<td>1.25</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

### Model 3

$R^2 = 30.5\%$ (Nagelkerke);

$\chi^2(9) = 256.08, p < .001$

<table>
<thead>
<tr>
<th></th>
<th>95% Confidence Interval</th>
<th>Beta</th>
<th>Lower</th>
<th>Odds Ratio</th>
<th>Upper</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>.01</td>
<td>.97</td>
<td>1.01</td>
<td>1.05</td>
<td>.741</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td>.18</td>
<td>.87</td>
<td>1.21</td>
<td>1.63</td>
<td>.263</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td>-.03</td>
<td>.91</td>
<td>.97</td>
<td>1.03</td>
<td>.285</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td>-.07</td>
<td>.82</td>
<td>.93</td>
<td>1.05</td>
<td>.247</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td>.15</td>
<td>.86</td>
<td>1.01</td>
<td>1.21</td>
<td>.859</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td>.03</td>
<td>.89</td>
<td>1.03</td>
<td>1.21</td>
<td>.691</td>
</tr>
<tr>
<td>PHQ-9 score</td>
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<td>.19</td>
<td>1.17</td>
<td>1.21</td>
<td>1.24</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>DAST-10 score</td>
<td></td>
<td>.08</td>
<td>1.03</td>
<td>1.08</td>
<td>1.13</td>
<td>.001</td>
</tr>
<tr>
<td>Model 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Beta</td>
<td>Lower</td>
<td>Odds Ratio</td>
<td>Upper</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.01</td>
<td>.95</td>
<td>.99</td>
<td>1.04</td>
<td>.730</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>.21</td>
<td>.89</td>
<td>1.24</td>
<td>1.71</td>
<td>.205</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
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<td>.93</td>
<td>.99</td>
<td>1.01</td>
<td>.699</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>-.07</td>
<td>.82</td>
<td>.93</td>
<td>1.06</td>
<td>.277</td>
<td></td>
</tr>
<tr>
<td>Employment status</td>
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<td>.84</td>
<td>.98</td>
<td>1.19</td>
<td>.981</td>
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</tr>
<tr>
<td>Ethnicity</td>
<td>.04</td>
<td>.89</td>
<td>1.04</td>
<td>1.22</td>
<td>.606</td>
<td></td>
</tr>
<tr>
<td>PHQ-9 score</td>
<td>.14</td>
<td>1.11</td>
<td>1.16</td>
<td>1.21</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>DAST-10 score</td>
<td>.08</td>
<td>1.03</td>
<td>1.09</td>
<td>1.13</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>AUDIT score</td>
<td>.01</td>
<td>.98</td>
<td>1.01</td>
<td>1.05</td>
<td>.483</td>
<td></td>
</tr>
<tr>
<td>Subj. sleep qual.</td>
<td>-.56</td>
<td>.43</td>
<td>.58</td>
<td>.78</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Sleep latency</td>
<td>.03</td>
<td>.87</td>
<td>1.03</td>
<td>1.22</td>
<td>.756</td>
<td></td>
</tr>
<tr>
<td>Sleep duration</td>
<td>.46</td>
<td>1.23</td>
<td>1.51</td>
<td>1.86</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>-.14</td>
<td>.72</td>
<td>.87</td>
<td>1.05</td>
<td>.137</td>
<td></td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>.74</td>
<td>1.49</td>
<td>2.09</td>
<td>2.93</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Sleep medication</td>
<td>.16</td>
<td>1.00</td>
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<td>Daytime dysfunction</td>
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<td>1.11</td>
<td>1.37</td>
<td>1.69</td>
<td>.003</td>
<td></td>
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</table>

Research Question 3.
A hierarchical multiple regression analysis was performed to estimate the unique contribution of poor sleep quality in predicting distress associated with APS, when controlling for socio-demographic factors, depression and drug/alcohol abuse. Socio-demographic variables were entered in the first model, which was significant ($F(6,1006) = 6.37; p < .001$) and accounted
for 3.1% of the variance in PQ-16 distress score, with age and education being the only significant (negative) predictors (Table 6). Adding depression (PHQ-9) in the second model resulted in a further 38.6% of the variance ($F(1,1005)=104.26; p < .001$), whilst entering drug/alcohol abuse in the third model accounted for a further 1.6% ($F(2,1003) = 87.02; p < .001$). The final model, with the components of the PSQI included, explained a total 49.1% of the variance of PQ-16 distress scores ($F(7,996) = 62.02; p < .001$), with the components of the PSQI accounting for 5.8% unique variance in the model.

Regarding the PSQI subscales, subjective sleep quality and habitual sleep efficiency significantly predicted (negatively) PQ-16 distress, and sleep onset latency had a non-significant negative association with distress. The remaining four components of the PSQI (sleep duration, sleep disturbances, use of sleep medication and daytime dysfunction) all significantly positively predicted PQ-16 distress score, with sleep disturbance having the largest beta value ($\beta = 3.91, p < .001$).

Table 6: Regression models for predictors of PQ16 distress score.

<table>
<thead>
<tr>
<th>Model 1 Predictors: demographic variables.</th>
<th>Beta</th>
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<th>t</th>
<th>P</th>
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</thead>
<tbody>
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Model 2 Predictors: Demographic variables and PHQ9 score

<table>
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<tr>
<th>$F(1,1005)=104.26; p &lt; .001; R^2=42.1%, Adj R^2=41.7%$</th>
<th>Beta</th>
<th>Standardised B</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
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<td>-------</td>
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<tr>
<td>PHQ-9 score</td>
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<td>.65</td>
<td>25.81</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**Model 3** Predictors: Demographic variables, PHQ-9, DAST-10, AUDIT

\[
F(2,1003) = 87.02; p < .001; R^2 = 43.8\%, \quad \text{Adj} R^2 = 43.3\%
\]

<table>
<thead>
<tr>
<th>Predictor</th>
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<th>t</th>
<th>P</th>
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<td>Gender</td>
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</tbody>
</table>

**Model 4** Predictors: Demographic variables, PHQ9, AUDIT, DAST-10 and PSQI subscales.

\[
F(7,996) = 62.02; p < .001; R^2 = 49.9\%, \quad \text{Adj} R^2 = 49.1\%
\]

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Beta</th>
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<td>PHQ-9 score</td>
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<td>DAST-10 score</td>
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<td>3.43</td>
<td>.001</td>
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<td>AUDIT</td>
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<td>Daytime dysfunction</td>
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<td>2.46</td>
<td>.014</td>
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</tbody>
</table>

### 4.0 DISCUSSION.

The present study replicates findings showing a high incidence of APS in the general population (Johns & van Os, 2001; Mongan, Shannon, Hanna, Boyd & Mulholland, 2019). Like previous research (Schultze-Lutter, Ruhrmann, Berning, Maier, & Klosterkoetter, 2010) increasing age and level of education was associated with lower likelihood of psychotic symptoms in the first model. However, socio-demographic factors were no longer significant when depression and drug/alcohol abuse were added to the models.

With the primary aim of the study being to assess the effect of poor sleep on number of APS endorsed and related distress, it is significant that PSQI subscales made a unique contribution in the regression models. Although greater than the combined contribution of socio-demographic variables and drug/alcohol abuse, the unique contribution made by poor sleep was modest (compared to the contribution made by depression) and, therefore, the following potential implications are discussed on the understanding that further research is required to establish the association between poor sleep and psychosis risk.
**Implications:** In addition to supporting previous observational and experimental studies showing that sleep deprivation is predictive of perceptual distortions and hallucinations (Freeman et al., 2009; Petrovsky et al., 2014; Sheaves et al., 2016), the current study also found that poor sleep significantly predicted PQ-16 distress. One possible explanation for this is that poor sleep is known to contribute to more negative cognitive biases (Walker, 2018), so it could be that poor sleep negatively impacts on social cognition. For example, in a study by Gujar, McDonald, Nishida and Walker (2011), healthy participants who had insufficient REM sleep demonstrated a fear bias in an emotional face recognition task. Additionally, cognitive processes that have been shown to be involved in psychosis development, e.g. the jumping to conclusion bias (Garety et al., 2005) may be affected by sleep disturbance, although further work would be required to investigate this.

Regarding specific components of sleep difficulty, the present study did not demonstrate a significant relationship between sleep latency and number of APS or distress, which contrasts with previous research (Keshavan et al., 2004). Sleep disturbance made the most significant contribution in both regression models. The subscale measuring sleep disturbance is composed of items related to sleep maintenance (e.g. getting up to use the bathroom; being too cold/hot). From a clinical viewpoint, these difficulties may be easily ameliorated through reducing fluid intake and temperature management.

Another clinical implication is that the findings support the assertion by Mills, Fusar-Poli, Morgan, Azis, & McGuire (2017) that there may be a large number of young adults in the general population with an at-risk mental state who are not being seen by specialist psychosis prevention / early intervention services, and their recommendation is reiterated for further investment in services aimed at psychosis prevention / early intervention to enable greater presence in communities. It is also recommended that such services routinely assess...
for sleep difficulties, which if treated early and effectively may help prevent the worsening of symptoms and associated distress, thus potentially reducing development of an ARMS.

Further, as patients are not referred to specialist psychosis prevention services when presenting with only sleep difficulties, it is suggested that when they present to universal services (e.g. general practice) that they are asked about APS, which with other indicators (e.g. depression / decline in functioning) may warrant referral to specialist services for assessment of a potential ARMS presentation. Although this will rule out the risk of psychosis in most cases, it may help early detection of individuals who may progress to an ARMS, which may be prevented with effective treatment of sleep problems. For example, in a randomised control trial investigating the effects of improving sleep on mental health, participants whose sleep improved showed sustained reductions in paranoia and hallucinations (Freeman et al., 2017). Although this trial demonstrates that effective treatment for sleep problems may decrease risk of developing an at-risk mental state, a recent survey of clinicians found that the provision of evidence-based sleep treatments is rare (Rehman, Waite, Sheaves, Biello, Freeman, & Gumley, 2017). Even when treatment for poor sleep is offered, it is often not the treatment recommended by guidelines. Reeve, Sheaves and Freeman (2019) found that 61.8% of a sample reporting sleep disturbance were prescribed medication, rather than the recommended first-line treatments of cognitive and behavioural therapies (NICE, 2015). The current study echoes the recommendation for use of evidence-based treatments for sleep problems, given that sleep difficulties may be considered a contributory causal factor in the development of psychosis (Freeman et al., 2017).

Limitations: Although recent research in this area has used similar online crowdsourcing methods, such as Crowdflower (Jaya, Ascone, & Lincoln, 2017), there may be concerns regarding self-selection in this methodology. For example, in the current study, the mean total score of 7.52 for the PSQI in this sample was above the cut-off score of 6, which
differentiates good and poor sleepers. Therefore, it is possible that a higher proportion of MTurk users who view their sleep as poor opted to participate in this study rather than another non-sleep related study on MTurk’s list. However, previous studies using crowdsourcing such as MTurk found the data to be as reliable as data from convenience sampling, meeting the standards expected in published research, with the caveat that there may be a trend towards fewer black and Hispanic participants in university student samples, as well as having higher educational attainment than non-student samples in the U.S.A. (Berinsky, Huber, & Lenz, 2012; Buhrmester, Kwang, & Gosling, 2011). In the present sample, 11.3% were black or Hispanic, and more than two-thirds were educated to at least degree level, whereas black and Hispanic people constitute 30.2% of the United States population and only a third of the total population of the United States are educated to degree level according to 2018 census data. A further potential limitation of the study was the use of a self-report measure of poor sleep quality (PSQI) rather than using objective measures, e.g. polysomnography. However, previous studies have shown self-report measures to be reliable when polysomnography is also used for comparison (e.g. Reeve, Sheaves & Freeman, 2019).

**Future research:** Although the regression models show poor sleep predicting APS, the current study used a cross-sectional design and, therefore, future research should consider longitudinal designs to confirm the temporal relationship between poor sleep quality and APS. Further, as noted above, future research investigating the possible impact of sleep disturbance on cognitive processes (e.g. social cognition, jumping to conclusion bias) may demonstrate possible mechanisms through which poor sleep predicts APS. Additionally, future research may investigate if deficits in specific sleep stages (e.g. REM / Non-REM) impacts on the distress experienced by APS.

**Conclusion:** The present study found a modest relationship between poor sleep and APS (and associated distress) after controlling for other variables known to predict ARMS
status. Further research is required to establish the significance of poor sleep in predicting APS and to investigate potential mechanisms involved. It is recommended that individuals with sleep problems be treated using evidence-based treatments.

Funding.
Funding from the Northern Health & Social Care Trust was awarded for payment to participants.
References.


Keshavan, M., Cashmere, D., & Yeragani, V. (2004). Decreased nonlinear complexity and chaos during sleep in first episode schizophrenia. *Biological Psychiatry, 55*, 221S-221S.


Appendix B: Author instructions from the British Journal of Clinical Psychology.

**Parts of the Manuscript.**

Contributions must be typed in double spacing. All sheets must be numbered. The manuscript should be submitted in separate files: title page; main text file; figures/tables; supporting information.

Title Page

The title page should contain:

i. A short informative title containing the major key words. The title should not contain abbreviations (see Wiley's best practice SEO tips);
ii. A short running title of less than 40 characters;
iii. The full names of the authors;
iv. The author's institutional affiliations where the work was conducted, with a footnote for the author’s present address if different from where the work was conducted;
v. Abstract;
vi. Keywords;
vii. Practitioner Points;
viii. Acknowledgments.

**Authorship:** Please refer to the journal’s Authorship policy in the Editorial Policies and Ethical Considerations section for details on author listing eligibility. When entering the author names into Editorial Manager, the corresponding author will be asked to provide a CRediT contributor role to classify the role that each author played in creating the manuscript. Please see the Project CRediT website for a list of roles.

**Abstract:** Please provide a structured abstract of up to 250 words under the headings: Objectives, Methods, Results, Conclusions.. The 'Methods' section for systematic reviews and theoretical papers should include, as a minimum, a description of the methods the author(s) used to access the literature they drew upon. That is, the abstract should summarize the databases that were consulted and the search terms that were used.

**Keywords:** Please provide appropriate keywords.

**Practitioner Points:** All articles must include Practitioner Points – these are 2-4 bullet points, following the abstract, with the heading ‘Practitioner Points’. These should briefly and clearly outline the relevance of your research to professional practice. (Please include the 'Practitioner Points' in your main document but do not submit them to Editorial Manager with your abstract.)

**Acknowledgments:** Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.
Main Text File

As papers are blind peer reviewed, the main text file should not include any information that might identify the authors.

The main text file should be presented in the following order:

i. Title
ii. Main text
iii. References
iv. Tables and figures (each complete with title and footnotes)
v. Appendices (if relevant)

Supporting information should be supplied as separate files. Tables and figures can be included at the end of the main document or attached as separate files but they must be mentioned in the text.

- As papers are double-blind peer reviewed, the main text file should not include any information that might identify the authors. Please do not mention the authors’ names or affiliations and always refer to any previous work in the third person.
- The journal uses British/US spelling; however, authors may submit using either option, as spelling of accepted papers is converted during the production process.

References: References should be prepared according to the Publication Manual of the American Psychological Association (6th edition). This means in text citations should follow the author-date method whereby the author’s last name and the year of publication for the source should appear in the text, for example, (Jones, 1998). The complete reference list should appear alphabetically by name at the end of the paper. Please note that for journal articles, issue numbers are not included unless each issue in the volume begins with page 1, and a DOI should be provided for all references where available.

For more information about APA referencing style, please refer to the APA FAQ.

Reference examples follow:


Tables: Tables should be self-contained and complement, not duplicate, information contained in the text. They should be supplied as editable files, not pasted as images. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes.
Footnote symbols: †, ‡, §, ¶, should be used (in that order) and *, **, *** should be reserved for P-values. Statistical measures such as SD or SEM should be identified in the headings.

**Figures:** Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted.

Legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement.

**Colour figures.** Figures submitted in colour may be reproduced in colour online free of charge. Please note, however, that it is preferable that line figures (e.g. graphs and charts) are supplied in black and white so that they are legible if printed by a reader in black and white. If an author would prefer to have figures printed in colour in hard copies of the journal, a fee will be charged by the Publisher.

**Supporting Information:** Supporting information is information that is not essential to the article, but provides greater depth and background. It is hosted online and appears without editing or typesetting. It may include tables, figures, videos, datasets, etc.

Note: if data, scripts, or other artefacts used to generate the analyses presented in the paper are available via a publicly available data repository, authors should include a reference to the location of the material within their paper.

**General Style Points:** For guidelines on editorial style, please consult the APA Publication Manual published by the American Psychological Association. The following points provide general advice on formatting and style.

- **Language:** Authors must avoid the use of sexist or any other discriminatory language.
- **Abbreviations:** In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Initially, use the word in full, followed by the abbreviation in parentheses. Thereafter use the abbreviation only.
- **Units of measurement:** Measurements should be given in SI or SI-derived units. Visit the Bureau International des Poids et Mesures (BIPM) website for more information about SI units.
- **Effect size:** In normal circumstances, effect size should be incorporated.
- **Numbers:** numbers under 10 are spelt out, except for: measurements with a unit (8mmol/l); age (6 weeks old), or lists with other numbers (11 dogs, 9 cats, 4 gerbils).
Appendix C: Research governance and ethical approval.

Date: 28 February 2019
To: Dr Donncha Hanna
Faculty REC Reference Number: EPS 19_63
Full Title: Sleep and the At Risk Mental State
Decision: APPROVED

Thank you for your application which was reviewed by the EPS Faculty Research Ethics Committee (Faculty REC) in accordance with the Proportionate Review process.

The application and supporting documents have been reviewed and approved.

Conditions of the Approval

The Faculty REC approval is subject to the following conditions:

(i) The study must be conducted in accordance with all relevant legislation. All relevant management approvals from organisations involved in the research must be obtained.
(ii) When the research involves human volunteers the study must be entered on the University’s Insurance Database.
(iii) Monitoring and auditing process must be complied with including submission of annual progress reports to the Faculty REC.

It is the Chief Investigator’s responsibility to ensure the study is conducted in accordance with the conditions stipulated.

Any future changes to any part of the submitted application, protocol or supporting documentation must be notified to the Committee prior to these changes taking place.

Approved Documents

The documents approved by the Faculty REC are listed in the table below.

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<th>Date</th>
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<td>Received 25 February 2019</td>
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<tr>
<td>Study Protocol</td>
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<td>22 February 2019</td>
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<td>Participant Information Sheet</td>
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<td>11 February 2019</td>
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<td>Debrief Sheet</td>
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<td>28 November 2018</td>
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</table>

If you would like to discuss this further please contact the Research Ethics Officer, Miss Kathryn Taylor, at facultyrecops@qub.ac.uk or by telephone on 028 90972529.

Yours sincerely

KK

pp Dr Brendan Murtagh
Chair, EPS Faculty REC
Appendix D: Participant Information Sheet.

This information sheet provides details of a research study being carried out by the School of Psychology at Queens University Belfast and has ethical approval from the University. The purpose of this study is to look at sleep quality and unusual experiences in people from the general population. Previous research suggests that problems with sleep may be associated with unusual experiences and thoughts in the general population. You must be aged 18 or over to participate in this study. If you decide to take part in this study you will be asked to complete 88 questions that enquire about your demographic details, your sleep quality, any alcohol, drug, nicotine and caffeine use, your level of physical activity, and the level of unusual experiences you may experience. The survey should take about 15 minutes to complete. The risks involved in participation are minimal. However, the questionnaires regarding alcohol and drug use may be distressing for some people. If this is the case you should stop completing the survey immediately, and your data will not be analysed or used in the study. If you feel you would like to talk to someone about any distressing experiences you may have had, you may wish to contact local services available in your area. Alternatively, you can contact Befrienders Worldwide (www.befrienders.org) which offers emotional support and advice by hotline, internet or face-to face, or IFOTES (www.ifotes.org) who also offer hotline support and advice to those in distress. The National Council on Alcohol and Drug Dependence (NCADD) offers online signposting to local support for people who are worried about their alcohol and drug use (www.ncadd.org). It is entirely up to you to decide if you would like to participate in the study. You are free not to participate or to withdraw at any time, for whatever reason. However, once you submit the HIT then this data cannot be withdrawn from the study. By accepting to complete and return the HIT, you will be confirming that you have read and understood the information sheet, that you are willing to participate in the research, and that the data you provide can be used in scientific publications. By participating in the study and completing all questions you will be paid via the MTurk interface. While payment will be made using your MTurk identification code, there will be no attempt to access any personal information about you from your ID codes, and they will not be used to store or analyse data. If you require any more information about the study, or if you have any questions as regards what your participation entails or the questionnaires you will be asked to complete, you may contact:

Dr Ciaran Shannon: ciaran.shannon@northerntrust.hscni.net
Prof. Ciaran Mulholland: c.c.mulholland@qub.ac.uk
Stephen Clarke: sclarke03@qub.ac.uk

By clicking through to the questionnaires, it is assumed that you have read the Participant Information Sheet and that you consent to completing the questionnaires and for your data to be used for research purposes. The survey is completely voluntary, and you can withdraw your consent at any time by exiting the survey. If you exit the survey, your data will not be used for research purposes.
Appendix E: Reflections on DClinPsy research experience.

The following reflections begin with why I became interested in psychosis, followed by reflections on the process of developing my research ideas and the stages of the research process, before reflecting on how this has impacted on my desire to continue to be active in research in the future.

My interest in psychosis began during five years working as a support worker, where I supported individuals with a diagnosis of a psychotic disorder who were being discharged from inpatient care back to the community. During this role I built strong relationships with clients, and whilst I could advocate on their behalf with various agencies (e.g. housing, health, police) I felt ill-equipped to fully support their mental health, as I had no formal training in therapeutic modalities. This prompted me to complete an MSc in Applied Psychology with a view to gaining a place on the DClinPsy course, where I hoped to increase my knowledge and clinical skills in relation to psychosis (amongst other conditions), given that I could see that my clients’ traumatic life experiences must have had an impact on their mental health, but I was unsure of why they developed psychosis rather than another condition.

During the first semester of the DClinPsy course our class had to list three broad areas of interest to enable the course team to match trainees with supervisors. I was pleased to be allocated supervisors for my first preference (psychosis), and during the second semester I began working on research ideas. With the observation that clients in my support worker role had all experienced various horrific traumas I was keen to include trauma as a variable. And, when my supervisor mentioned research linking inflammation to the development of psychosis, I developed the idea of testing if cognitive factors (e.g. attentional biases, trauma appraisals and coping style trauma) might mediate the relationship between trauma and inflammation. To do this, I planned to measure cytokine levels in blood samples, and
measure trauma, cognitive architecture, and coping styles by questionnaires, in the following three groups: 1) healthy controls (students), 2) individuals at ultra-high risk of developing psychosis, and 3) individuals who have experienced first episode psychosis.

As my project involved taking blood samples, I thought that ethical approval might take a bit longer than other projects, as I needed to complete training in Human Tissue Act legislation, so I submitted my ethics application as early as possible in second year. I was then surprised but pleased that following only minor amendments to my protocol the project was given ethical approval early on. Buoyed by such a quick approval I was hopeful that governance approval would also be swift, and I would be able to begin recruitment. However, I became very frustrated when one of the health trusts took eleven months to grant governance approval. As I was unable to recruit participants during this time, I ensured that time was not wasted and completed my systematic review on the effects of digital health technologies on psychotic symptoms, which I was delighted to get published.

When governance approval was granted, recruitment of the student sample was quick and easy through a university system and, although the recruitment in the clinical groups was slower and frustrating at times, I managed to recruit enough participants for statistical analyses. Conducting the research involved a lot of logistical planning (e.g. ensuring a suitable timeslot for each participant, ensuring that the clinical room in the regional research facility was available and the time suited the psychiatrist to take the blood samples). Although there were some difficulties (e.g. equipment breaking, some participants not turning up, unable to get blood from some participants), I managed to get enough blood samples, trauma data and cognitive data to allow analysis to start. I, therefore, contacted the laboratory to get the blood analysis results, as the cytokines levels were to be the outcome variables. However, I was shocked to hear that, due to technical and administrative issues, the
laboratory could not analyse the bloods for several months, which would be after the deadline for submission as part of the DClinPsy course.

This required me to draw on one of my personal strengths, resilience, as I had to change direction when nearing completion of my original project, in which I had invested so much time and effort. This episode has taught me the value of having contingency plans when completing research, as unexpected events can and do happen. Luckily, I was in a placement where the scientist practitioner model was alive and well, with weekly research meetings, where new research ideas could be discussed along with monitoring progress of ongoing projects. During this placement, prior to discovering the problems with the laboratory, a colleague and I had discussed the idea of examining sleep problems and psychosis. With a large dataset easily obtainable in a short space of time, using MTurk, I was able to complete a project on this topic for submission as part of my DClinPsy course, whilst still pursuing my original project, which I hope to complete, and hopefully have published, within the next twelve months.

As I had hoped to submit my original study for a viva exam in June, I was initially irritated when the issue with the laboratory arose, meaning that I had to submit later than intended, and had to complete the sleep project in a shorter timescale than I would have liked. As I reflect on this, I am reminded of fellow trainees asking me if I regret embarking on such a complex project (the cytokines project) as part of the DClinPsy course, suggesting it might have been easier and less stressful to do a more straightforward project. However, given my interest in research, and the fact that I was on placement where research was strongly encouraged, I was confident that I would be able to get another project done within the timescale of the DClinPsy course. Therefore, when I have been asked about regretting starting my original project, I reply that I will still complete my original study after completing the DClinPsy course, and with another project done for the course my research
output is going to be higher than it would have been otherwise. Therefore, although it was a bit stressful having to complete a second project, I was not too troubled by it, as I enjoy research, and doing two projects supervised by QUB staff helped me to develop more research skills than I might have gained with only one project. Therefore, rather than regretting this decision, I view it as a bonus to get two projects done and a systematic review published.

Reflecting on the three years, I can see how my confidence in conducting research has increased, so much so that I have joined with two other trainees and qualified psychologists in recently setting up a research group with some ideas for projects we are keen to progress, and hope to publish in years to come. This last point has prompted a final reflection in that I started my research journey on the DClinPsy course with some fears about conducting research. My fears were not about research *per se*, but the possibility of unexpected events when timescales are so important when completing university courses. This was due to my experience during the MSc course that I completed, where I had to change project halfway through the course because the programme I was evaluating for my research was discontinued by the mental health charity providing it. Whilst this caused stress at the time, I was able to get another project done, which I discussed at conferences and in the media. Therefore, although this experience on the MSc course had contributed to some anxiety about something similar happening on the DClinPsy course, it also allowed me to see that contingency planning is essential. Therefore, learning from previous research experience has helped me on the DClinPsy course, and even though the journey has been stressful at times, I have mostly enjoyed the process of developing skills that I had hoped to develop (e.g. statistical analyses), and I now hope to continue to engage in research for many years to come.
ADDENDUM:
The empirical paper investigating the association between poor sleep and psychotic experiences was completed following issues at the laboratory that prevented completion of the original empirical paper within the timeframe of the DClinPsy course. The following addendum outlines the work that has been completed to date in the original study.

Original Empirical Paper.
Exploring the role of trauma, pro-inflammatory cytokines, and cognitive processes in psychosis.

1.0 Introduction.
1.1 Factors involved in psychosis.
Research throughout the twentieth century focused primarily on biogenetic causes of psychosis, viewing psychotic disorders such as schizophrenia as discreet categories of mental illness with biological causes (Kuipers et al., 2006). However, research in recent decades points to a multifactorial aetiology, with psychosocial factors being identified as contributing to the onset and maintenance of psychotic symptoms. For example, in their chapter entitled “Schizophrenia is not an illness”, Read, Mosher and Bentall (2004) argue that the unusual experiences, distress, despair and confusion that some people face are not symptoms of a medical illness, but may be better understood by considering what is going on (and has gone on) in the lives of people experiencing such phenomena. However, biological factors cannot be ignored, as neurotransmitters have been known to be involved in psychosis since the 1950s, when Carlsson found that dopamine agonists (e.g. amphetamines and L-dopa) could produce phenomena such as hallucinations and delusions, whereas dopamine antagonists, such as chlorpromazine and haloperidol, were found to reduce hallucinations and delusions (Yeragani, Tancer, Chokka & Baker, 2010). Further support for the role of biology was seen in the fact that schizophrenia tends to run in families, with first degree relatives of someone diagnosed with schizophrenia being 18 times more likely to also receive a diagnosis of the disorder (Kendler et al., 1985). Yet, first degree relatives also tend to share similar environments, so this finding is not conclusive that genes alone cause psychosis. However, concordance studies show that rates of schizophrenia for monozygotic twins raised apart in different environments are similar to rates for monozygotic twins raised together (Shields, 1962), suggesting that genes do play an important role, whether there is a shared environment or not. And, further support for a genetic component to psychosis was seen when individuals
who were adopted by parents without schizophrenia still showed higher rates of schizophrenia than the general population if their biological parents had a diagnosis of the disorder (Kety et al., 1994).

Whilst these twin and adoption studies provide strong evidence for the role of genetics in psychosis, the same concordance studies also show that the match is not perfect, with monozygotic twins having only a 48% concordance rate (McGue & Gottesman, 1991), suggesting that factors other than genetics are also involved. The stress-vulnerability model (Zubin & Spring, 1977) accommodated this by suggesting that a vulnerability (which may be biological (e.g. genes), psychological or social) interacts with stress to cause psychosis. During the past two decades, there has been an increased interest in psychosocial stresses, with many factors being identified as contributing to the onset and maintenance of psychosis, e.g. ethnicity (Fearon et al., 2006), poverty and inequality (Bosqui, Hoy & Shannon, 2014), urbanicity (Pedersen & Mortensen, 2001), and trauma (Bebbington, 2004). But, how do such social factors interact with genetics and other biological mechanisms to lead to psychosis as the stress-vulnerability model suggests? Since the turn of the millennium there has been an increased focus on the role of psychological processes as serving a mediating role in the onset and maintenance of psychosis, in a manner that might embrace a true biopsychosocial approach.

1.2. A true biopsychosocial approach.

Whilst a biopsychosocial approach was first promoted by Engel in the 1970s (Adler, 2009), critics such as Read, Mosher and Bentall (2004) have pointed out that for three decades only lip service was paid to this approach, when a biomedical model remained the dominant discourse in the study and treatment of psychosis. However, by combining the role of cognitive appraisals and incorporating the role of social factors into a true biopsychosocial model of psychosis, a fuller understanding of psychosis may be reached. Cognitive models view psychosis as lying on a continuum of experiences, rather than being a discreet biomedical illness with clear evidence that many people in the general population have anomalous experiences (Bentall, Claridge & Slade, 1989; Johns & van Os, 2001). There is also support for the proposition that a need for care occurs as a result of maladaptive appraisals and coping styles in response to the unusual experiences (Ward et al., 2014). Maladaptive coping styles associated with developing psychosis include escape / avoidance, denial, self-blame and behavioural disengagement (Cooke et al., 2007; Meyer, 2001). In their
cognitive model of persecutory delusions, Freeman, Garety, Kuipers, Fowler and Bebbington (2002) point out how some coping strategies may be used as safety-seeking behaviours, which prevent change in the delusional belief. In 2001, Garety, Kuipers, Fowler, Freeman and Bebbington proposed a cognitive model of positive symptoms of psychosis. Their model places a central role for biased conscious appraisals, beliefs about the self as vulnerable to threat, and deficits in understanding social situations and the intentions of others, in the development of psychosis. The model proposes that cognitive architecture involving attributional and reasoning biases drive threat-based appraisals.

Experimental support for such cognitive architecture comes from a study by Ward et al., (2014), which found significant differences in appraisals and coping styles between a non-clinical group and a clinical group when presented with analogues of psychotic symptoms. A computer-based card trick was presented to both groups, where participants chose a card from a choice of five cards on a screen, and were told that the computer would be able to identify their card and remove it from the pile. The computer then displayed five different cards for three seconds. The trick works because participants only scan for their own card and do not notice that all the cards are different. This analogue of thought interference (which can include thought insertion, thought broadcasting, thought control and mind reading) was appraised differently by the two groups. The clinical group rated the experience as more threatening and personally significant, and were more likely to incorporate the experience with their own anomalous experiences than the non-clinical group. They were also more likely to endorse maladaptive coping responses and appraisals, as well as rating the experience as distressing. Further support for distress being linked to maladaptive appraisals was found by Taylor, Parker, Mansell and Morrison (2013), using the same card trick, with participants who reported a psychotic explanation (e.g. “It works because the computer can read my mind.”) showing higher levels of distress.

One factor that appears to predispose someone to developing a cognitive architecture where threatening appraisals are more readily reported, is trauma. Lovatt, Mason, Brett and Peters (2010) compared two groups (one clinical / one non-clinical) who were experiencing psychotic-like experiences. The groups were compared on types of psychotic experiences, appraisals of these experiences, distress and trauma. The clinical group showed more distress and had more externalising and personalising appraisals and fewer normalising appraisals, despite not having a higher incidence of trauma, suggesting that negative trauma appraisals may lead to distress rather than experiencing trauma per se. In this study, interpersonal
trauma was found to be associated with more personalising appraisals, with the authors concluding that interpersonal trauma in the clinical group may have predisposed individuals to a paranoid worldview. Underwood, Kumari and Peters (2016) defines such personalising appraisals in clinical groups as seeing anomalous experiences as being produced by an outside source, which has the intention of causing harm, so that threat stimuli are more salient than safety cues, with such attentional biases towards threatening stimuli leading to the formation of maladaptive externalising attributional biases. Trauma severity and negative appraisals were also linked to psychotic symptoms (hallucinations) in a study by Kilcommons and Morrison (2005) who concluded that psychosis may be trauma-induced. Several other studies add to the weight of evidence demonstrating that trauma is consistently found to be a contributing factor in psychosis (e.g. Bebbington 2004; Janssen et al., 2004; Read, Bentall & Fosse, 2009; Read, van Os, Morrison, & Ross, 2005; Shevlin, Houston, Dorahy, & Adamson, 2008; Spence, Mulholland, Lynch, McHugh, Dempster, & Shannon, 2006; Varese et al., 2012).

However, this is not to say that trauma is necessary or sufficient for psychosis to develop, and it does not mean that biology does not have a role. In fact, trauma has been found to be related to biological differences, such as dysregulation of the hypothalamic-pituitary adrenal (HPA) axis with blunted cortisol response (Carpenter et al., 2007; Chaunette et al., 2016), abnormalities in neurotransmitter function, e.g. dopaminergic systems (De Bellis & Zisk, 2014), hippocampus damage (Hoy et al., 2012; Woon, Sood & Hedges, 2015), and cerebral atrophy (De Bellis, Spratt, & Hooper, 2011). Whilst all of these studies focus on the structure and/or functioning of the central nervous system and endocrine systems, research in recent years has begun to consider a role for the immune system in the development and maintenance of psychosis.

It is widely understood that the inflammatory response of the immune system is a defense mechanism that removes harmful agents (e.g. viruses) and damaged tissue so that the body can heal. Pro-inflammatory cytokines are part of this immune response which, in the acute phase, promotes recovery from injury, but chronically elevated levels of inflammatory cytokines have been associated with heart disease (Kaptoge et al., 2014), liver disease (Tilg, 2010) and autoimmune disorders (Kroemer & Martinez, 1991; Timoteo et al., 2017). As well as physical injury or infection, research has also shown an association between childhood abuse and activation of the inflammatory response (Altemus, Cloitre, & Dhabhar, 2003), which may be associated with diseases of inflammation. For example, Dong et al. (2004)
found that adverse childhood experiences such as emotional abuse, neglect or witnessing marital discord, were associated with a higher risk prevalence of ischemic heart disease. This proxy measure of inflammation was followed up by studies directly measuring inflammation. For example, Danese, Pariante, Caspi, Taylor & Poulton (2007) found that hsCRP levels were significantly higher in participants who had experienced childhood maltreatment. As well as biomarkers being associated with childhood trauma, psychoneuroimmunology studies have found elevated levels of cytokines in people with schizophrenia (Monji, Kato, & Kanba, 2009) which are known to regulate the action of neurotransmitters such as dopamine (Felger & Lotrich, 2013; Millar, Haroon, Raison, & Felger, 2013), which is known to play a role in psychosis, as mentioned above.

1.3 Theoretical clinical and importance of the study.
These recent findings of trauma, such as childhood abuse, being associated with an inflammatory response, and inflammatory responses (elevated cytokines) being present in psychosis, raises the question of how these findings might be related? From a theoretical perspective, this study aimed to investigate possible answers to this question by firstly examining if there is a relationship between these findings and, secondly, by investigating if any such relationship is mediated by cognitive architecture (i.e. maladaptive appraisals, and coping style). From a clinical perspective, the study is novel in that there is little research considering inflammation and cognitive architecture together with individuals from the ultra-high risk and first-episode psychosis populations. As Underwood, Kumari and Peters (2016) put it, given the evidence of different cognitive architecture between those with a need for care and those without a need for care being an important role in moving from at-risk to psychotic disorder, cognitive architecture should be investigated as aetiologically relevant in the transition to a need for care. Therefore, by comparing a clinical group with healthy controls, it may be possible to detect differences in cognitive architecture and possible related biomarkers that lead to a need for care. Further, from a clinical viewpoint, a relationship between cytokines and cognitive architecture / coping style, may help in the development of treatments from both psychological and pharmaceutical approaches. To address the above issues, the study aimed to examine the role of trauma, pro-inflammatory cytokines, cognitive architecture and coping style in psychosis by answering the questions below.
1.4 Research questions.

1) Does trauma predict the level of pro-inflammatory cytokines?
2) If so, is there a direct link, or is it mediated by cognitive architecture / coping style?
3) Does group membership (control vs clinical group) predict levels of pro-inflammatory cytokines?
4) If so, is there a direct link, or is it mediated by trauma or cognitive architecture (trauma appraisals, coping)?

2.0 Research Methodology.

2.1 Participants.
The sample consisted of two groups of participants. The healthy control group \((n = 29)\) were students aged 18 to 45 years from Queen’s University Belfast (QUB). The clinical group \((n = 19)\) consisted of individuals (aged 16 to 42) recruited from specialist mental health services treating patients with psychosis or a risk of developing psychosis. To be included in the study, participants had to be either a student of Queen’s University Belfast or must have been referred to (and met the criteria for) the specialist mental health service outlined above. The following exclusion criteria were applied: inability to speak English fluently, poor literacy skills, history of neurological problems, presence of a physical disorder known to have high levels of inflammation (e.g. rheumatoid arthritis), an estimated IQ lower than 70.

2.2 Method of recruitment.
Students of Queen’s University Belfast were invited to participate in the study via an online research system (SONA). The SONA system allows for inclusion and exclusion criteria to be set for students who wish to register for studies, and therefore students self-selected via this system. Students received course credit for their participation. Patients of the specialist mental health services who met the inclusion criteria were identified by their direct care team and were invited to participate in the research. Individuals interested in participating in the study were given a copy of the participant information sheet and were offered the opportunity to have any queries they might have answered by members of the research team. Those who decided to participate completed a form showing informed consent.

2.3 Materials.
Materials required for obtaining blood samples included: tourniquets, Vacuette® tubes, and hypodermic needles. Enzyme-linked immunosorbent assay (ELISA) equipment has been
procured to measure levels of soluble cytokines in the blood samples. Self-report measures have been found to be reliable in trauma-related research (Klewchuck, McCusker, Mulholland & Shannon, 2007) and the following questionnaires were used to detect the presence of trauma, quantify the impact of trauma and measure trauma appraisals. The Trauma Experiences Checklist (TEC: Nijenhuis, Van der Hart, and Kruger, 2002) is a self-report measure used in both clinical and research settings, which assess trauma such as emotional and physical abuse, sexual harassment, bodily threat from another person, as well as neglect and other traumas, e.g. losing someone close or parental separation. For each item, the respondent answers whether the event happened and, if so, at what age the event started and ended. Answers to this question were used to assess for the presence of trauma. As well as asking the age that the trauma occurred, the TEC also measures the impact of the trauma, by asking, “What impact did this have on you?” with answers being on a scale from 1 (not at all) to 5 (very much). The TEC has good reliability (internal consistency showing a Cronbach’s α score of .90, and a retest reliability of r = 0.91) and strong convergent and criterion related validity (Nijenhuis, Van der Hart, and Kruger, 2002).

The Trauma Appraisal Questionnaire (TAQ) is a 54-item questionnaire of post-trauma appraisals. It has six subscale scores for the following appraisal categories: anger, alienation, fear, betrayal, shame, and self-blame. The TAQ has excellent internal consistency and test-retest reliability, as well as excellent convergent, discriminant, and concurrent validity (DePrince, Zurbriggen, Chu, & Smart, 2010). The Brief COPE (Carver, 1997) is a 28-item instrument, which asks questions on a four-point Likert scale, with answers ranging from 1 “I haven’t been doing this at all” to 4 “I’ve been doing this a lot”. The questionnaire measures fourteen coping scales. Carver (1997) found high Cronbach’s alpha for some scales (Religion: α =0.82, Substance Use: α = 0.90) with other scales having acceptable internal consistency values (Active Coping: α = 0.68, Planning: α = 0.73, Positive Reframing: α = 0.64, Acceptance: α = 0.57, Humour α = 0.73, Using Emotional Support: α = 0.71, Using Instrumental Support: α = 0.64, Self-distraction: α = 0.71, Denial: α = 0.54, Venting: α = 0.50, Behavioural disengagement: α = 0.65 and Self-blame: α 0.69). The Brief COPE has been assessed as having use in evaluating coping strengths and impairments in psychiatric patients (Meyer, 2001), thus meriting use with the sample in the present study.

2.4 Procedure.
Members of the research team met with participants individually by appointment. The researchers answered any questions before gaining informed consent to complete the
following procedure: i) Blood sample - A fully trained member of the research team took blood samples from superficial veins in participants’ arms. Samples were labelled and were stored in the regional Immunology Laboratory at Queen’s University Belfast. ii) Participants were asked to complete the Trauma Experiences Checklist, the Trauma Appraisal Questionnaire, and the Brief COPE. Participant codes were used to match each questionnaire with the blood samples for analysis.

2.5 Data analysis.
At the time of submission of this thesis, the blood samples were currently in storage awaiting to be analysed for inflammatory markers, using a multiplex assay system to measure the levels of cytokines. The results of this analysis will be used as the dependent variable in answering the research questions.
References.


