DOCTOR OF CLINICAL PSYCHOLOGY (DCLINPSY)

Doctorate in Clinical Psychology: Main Research Portfolio

1) Pubertal development and mental health in autism: a scoping review; 2) The demographic representativeness of Pain Management Service patients at Great Western Hospital, Swindon; 3) Characterising homotypic and heterotypic continuity of mental health symptoms in autism: a longitudinal study across childhood

Roberts, Elystan

Award date:
2024

Awarding institution:
University of Bath

Research Portfolio Submitted in Part Fulfilment of the requirements for the Degree of Doctorate in Clinical Psychology

Pubertal development and mental health in autism: a scoping review

The demographic representativeness of Pain Management Service patients at Great Western Hospital, Swindon

Characterising homotypic and heterotypic continuity of mental health symptoms in autism: a longitudinal study across childhood

Elystan Roberts

Doctorate in Clinical Psychology

University of Bath

Department of Psychology

May 2024

Declaration of any previous submission of the work

The material presented here for examination for the award of a higher degree by research **has not** been incorporated into a submission for another degree. (If applicable, provide the relevant details i.e. those parts of the work which have previously been submitted for a degree, the University to which they were submitted and the degree, if any, awarded).

Candidate's signature……  …….

Declaration of authorship

I am the author of this portfolio, and the work described therein was carried out by myself personally, with the exception of ……. article/chapter where …… (detail the amount in percentage terms) of the work was carried out by other researchers (e.g. detail any collaborative works included in the portfolio in terms of formulation of ideas, design of methodology, experimental work, and presentation of data in journal format).

Candidate's signature……  …….

Word Counts

Critical Review of the Literature	6,669
Service-Related Project	4,287
Main Research Project	3,325
Executive Summary	988
Total Word Count	15,269

Table of Contents

Abstracts

Critical Review of the Literature

Pubertal development and mental health in autism: a scoping review

The transition through puberty is a complex biopsychosocial experience that has been associated with a wide range of negative mental health outcomes in typically developing young people. There is some evidence that the experience of puberty might be different for autistic young people, a group who are also at high risk of experiencing mental health problems. However, it is not clear whether pubertal development is associated with mental health outcomes in autism. This review aims to systematically assess the existing evidence for an association between puberty and mental health in autism. A systematic search was conducted using the APA PsycNET, PubMed, and Web of Science electronic databases in June 2023, and eight studies meeting inclusion and exclusion criteria were reviewed. Overall, the review identified a small, heterogenous, and low-quality evidence base. The results do not provide strong evidence for an association between pubertal development and mental health outcomes in autism, a finding which does not align with the results in typically developing populations. Possible explanations, implications, and directions for future research are discussed.

Service-Related Project

The demographic representativeness of Pain Management Service patients at Great Western Hospital, Swindon

Purpose:

A core philosophy of the National Health Service (NHS) in the United Kingdom is equal, universal access to healthcare. However, there is evidence of substantial health inequalities for some groups of society, for both physical and mental health care. The demographic make-up of many areas of the UK have changed drastically over the past decade, which may put a greater number of individuals at risk of exclusion from services. The first step in ensuring equal access to a service is to establish how representative the present patient population is. The current study therefore aimed to establish the representativeness of the patient population of a local Pain Management and pain psychology service.

Methods:

Demographic information (comprising age, sex, and ethnicity) was drawn from hospital and national census data for four levels of population: the service catchment area, the hospital as a whole, the Pain Management Service, and pain psychology. The levels were compared descriptively and cross-referenced with published prevalence estimates to establish whether the observed demographic distributions reflect the expected distributions.

Results:

The observed patient demographics were largely reflective of the wider hospital and local area demographics in the context of expected prevalence estimates of chronic pain. Three groups appeared to be underrepresented in the Pain Management Service and pain psychology: men, individuals aged over 70 years, and individuals of Asian heritage.

Conclusion:

This is the first study to investigate the demographic profile of patients seen by the Pain Management Service and pain psychology at Great Western Hospital. The results indicated that some groups may be underrepresented in the service. Possible explanations for this result are discussed and recommendations for future research and improving access to care and are made.

Keywords:

Pain management, psychology, equality, accessibility, ethnicity, service evaluation

Main Research Project

Characterising homotypic and heterotypic continuity of mental health symptoms in autism: a longitudinal study across childhood

Objective:

Among typically developing (TD) preschool-age children, mental health symptoms show instability over time: symptoms at earlier ages predict different symptoms later on. Mental health problems are highly prevalent among autistic children, even during the preschool years. However, it is unclear whether mental health symptoms show the same instability over the preschool years in autistic as in TD children. The current study aimed to answer this question by examining the homotypic and heterotypic continuity of mental health symptoms across early childhood in an autistic sample.

Method:

The sample (*n* = 360, 84% male) were drawn from a longitudinal cohort study of autistic children. Mental health symptoms were assessed using the Anxious/Depressed, Aggressive Behaviour and Attention Problems subscales of the Child Behavior Checklist at three timepoints (T1 mean age = 3.4 years, SD = 0.78; T2 = 7.73 years, SD = 0.22; T3 = 10.76 years, SD = 0.24). The homotypic and heterotypic continuity of the three subscales across the three timepoints were examined using cross-lagged panel models.

Results:

There was strong evidence for all homotypic pathways across timepoints. There was evidence for one heterotypic pathway, from Aggressive Behaviour at T1 to Anxious/Depressed symptoms at T2 (β = 0.08, *p* = .013).

Conclusion:

The results align with TD literature in finding evidence for homotypic and heterotypic continuity during the preschool years. The findings indicate the possibility of an early developmental window during which mental health symptoms are more labile in autistic children. Autistic children may benefit from early screening and intervention for mental health symptoms.

University of Bath
Doctorate in Clinical Psychology

Critical Review of the Literature

Pubertal timing and mental health in autism: a scoping review

Elystan Roberts

Department of Psychology, University of Bath

egr22@bath.ac.uk

Word count: 6,309

Supervised by: Prof Rachael Bedford, Queen Mary University of London

Proposed journal for publication: Clinical Psychology Review

Author guidelines for this journal can be found here: https://www.sciencedirect.com/journal/clinical-psychology-review/publish/guide-for-authors

Introduction

Puberty and its measurement

Puberty represents an important developmental milestone: the transition from childhood towards nascent adulthood and the reaching of sexual maturity. This transition is associated with a range of endocrinological, physical, emotional, and neurocognitive changes. Two of the key measures of the pubertal transition are pubertal stage and pubertal timing. Pubertal stage represents the level of pubertal development an individual has reached by a particular point in time, and is typically measured using methods such as the Tanner scale (Marshall & Tanner, 1969, 1970), which defines five possible stages of development from pre-pubertal to fully developed. The gold-standard approach is for these stages to be assessed by a qualified clinician, but they can also be self-reported or parent-reported (Coleman & Coleman, 2002). Pubertal stage can also be assessed using questionnaires like the Pubertal Development Scale (PDS; Petersen et al., 1988), which is self-reported, or single measures of pubertal milestones, such as whether or not an individual has experienced menarche, the first menstrual period. Pubertal timing, in contrast, represents the age at which an individual has reached a particular point of pubertal development. Pubertal timing is generally measured using age at a reliable developmental milestone, most commonly age at menarche. However, in many studies pubertal timing is estimated by regressing pubertal stage on chronological age and using the residuals as proxies for relative pubertal timing (Barendse et al., 2022).

Pubertal development and mental health

In typically developing (TD) populations, it has been well established that both pubertal stage and pubertal timing are associated with mental health difficulties. Research has consistently shown that young people who experience the onset of puberty earlier than their peers are at higher risk of experiencing mental health difficulties, including eating disorders (Berger et al., 2009), alcohol and substance misuse (Costello, 2007) depressive symptoms (Joinson et al., 2012), and self-harm (Roberts et al., 2020). More advanced pubertal stage has similarly been identified as a risk factor for a number of negative outcomes, including transdiagnostic processes such as rumination (Mendle et al., 2020), and mental health conditions such as depression (Stumper & Alloy, 2023).

A number of possible mechanisms have been proposed to explain the observed effect of pubertal development on mental health. The *social deviance hypothesis* proposes that individuals who start pubertal development either earlier or later than the majority of their peers – i.e. those whose pubertal development differs most from the population norm – are at greatest risk for developing mental health difficulties, because they differ socially and physically from their peers (Petersen & Taylor, 1980). Underlying this hypothesis, there is evidence that going through transition events at unexpected times reduces the opportunity for appropriately planning for and anticipating the transition, which increases the risk of adjustment difficulties (Caspi & Moffitt, 1991). Further, adolescence is a period where peer group influence is particularly strong (Brown & Larson, 2009) and there is evidence that social comparison can lead to negative affective consequences (Buunk et al., 1990).

The *early timing hypothesis* proposes that early developers are most likely to experience mental health difficulties because they experience the greatest mismatch between their pubertal development and their cognitive and emotional development (Ge & Natsuaki, 2009). Neurocognitively, evidence suggests that earlier developers experience a disparity in the temporal development of sensation- and reward-seeking limbic pathways, which develop with puberty, and the inhibition- and planning-related prefrontal cortex, which develops with age (Shulman et al., 2016). This disparity puts individuals at risk for behaviours which are associated with increased likelihood of mental health difficulties, such as substance use (Al-Sahab et al., 2012). Psychosocially, it has been proposed that earlier-developing girls are perceived and treated as older than they are (Sontag et al., 2011), and are therefore more likely to experience situations with more psychosocial complexity, such as sexual relationships (Baams et al., 2015). However, they may lack the cognitive and emotional skills to effectively manage these experiences, which may lead to psychological distress (Ge & Natsuaki, 2009; Graber, 2013).

Autism

Autism is a neurodevelopmental condition characterised by deficits in social communication and interaction in addition to restricted or repetitive behaviours (American Psychiatric Association, 2013). A recent meta-analysis estimated the global prevalence of autism at around 100 cases per 10,000 people and found some evidence that prevalence estimates are increasing over time (Zeidan et al., 2022). There is some evidence that there may be differences in pubertal development between autistic and TD populations. For example, a recent cohort study of 163 American adolescents examined the association between pubertal timing and ASD diagnosis. The authors found a significant association between

pubertal timing and diagnosis (t = 2.71, p = .007), reporting that participants in the ASD diagnosis group began puberty nearly five months earlier than those without a diagnosis (Corbett et al., 2022). However, the findings of other studies have varied: whilst some have also reported earlier pubertal timing in autism (Corbett et al., 2020; Pohl et al., 2014), some report an association between autism and later pubertal timing (Hergüner & Hergüner, 2016; Whitehouse et al., 2011), and others report no difference between autism and TD groups (May et al., 2017).

Autism is also associated with a range of co-occurring mental health difficulties, including many of those associated with pubertal timing. For example, studies have found a higher prevalence of anxiety and depressive disorders (Lai et al., 2019), eating disorders (Huke et al., 2013), and self-harm (Blanchard et al., 2021) in autistic populations. Around 70% of autistic children have a co-occurring mental health problem (Chandler et al., 2016) and a similar prevalence has been observed in autistic adolescents (Abdallah et al., 2011; Simonoff et al., 2008). This is approximately double the prevalence of psychiatric disorders in non-autistic adolescents (Costello et al., 2003; Simonoff et al., 2008).

The current study

Given the well-established association between pubertal timing and mental health difficulties in the TD population, the mixed evidence regarding differences in pubertal development in autism, and the increased prevalence of mental health difficulties in autism, it is important to establish whether pubertal development represents the same risk for mental health difficulties in this vulnerable population. The aim of the current paper is to

review the evidence examining the association between pubertal development and mental health in autism to establish the current state of the evidence base.

Methods

The protocol for this review was registered online with PROSPERO, the international prospective register of systematic reviews (registration number: CRD42023393259). Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Page et al., 2021) guidelines were followed throughout the review process. A systematic search was conducted using the APA PsycNET, PubMed, and Web of Science electronic databases for peer-reviewed published literature and the PsyArXiv database for preprints, capturing studies published at any time prior to June 2023. The search strategy, database choices, and search terms used were based on existing systematic reviews (e.g. Cook et al., 2021; Ullsperger & Nikolas, 2017) and are presented in Table 1 below. The reference lists of relevant articles identified from the initial search were scanned to identify any articles the search had missed, and forward citation searching was used to identify any relevant articles which had cited the initially identified articles. The review diverged from the registered protocol by not using searches of WorldCAT and ETHoS. This decision was made because research dissertations are already included in APA PsycNET searches (EBSCO, 2023).

Studies were included in the review if they included participants either identified as autistic or with autistic traits, assessed using formal measures such as clinician diagnosis, semi-structured diagnostic interviews such as the Autism Diagnostic Observation Schedule (Lord et al., 2000), or questionnaire measures such as the Autism Quotient (Baron-Cohen et al., 2001). Studies must have formally measured pubertal development using an appropriate

method, such as clinician assessment of Tanner stage, PDS, or age at menarche. Studies must also have collected data on mental health, measured either at the symptom level using a questionnaire such as the Child Behavior Checklist (CBCL; Achenbach, 2001; Achenbach & Rescorla, 2000) or at the disorder level using clinical diagnosis

Table 1 Search terms used for systematic database searching

Autism	**Pubertal development**	**Mental health**
Autis*	Pubert*	Mental health
ASD	Pubescen*	Depress*
Asperger*	Menarch*	Anxi*
PDD-NOS	Spermarch*	Mood
Kanner	Early maturation	Internali*
	Late maturation	Externali*
		Problem behavior
		Antisocial behavior
		Attention problems
		Conduct problems
		Risky sexual behavior
		Substance use
		Eating pathology
		Anorexia
		Bulemia
		Binge eating

based on internationally recognised criteria (e.g. the DSM-V; American Psychiatric Association, 2013). All study designs were considered for the review, excluding intervention, qualitative studies, and reviews. Only studies written in English were included.

Identified studies were stored in a single database using Covidence (Covidence, 2023), a web-based software platform for the production of systematic reviews. The initial search identified 381 articles. After the removal of duplicates, the titles and abstracts of 141 studies were screened by the first author and a second reviewer (DW). Inter-rater reliability for this stage of screening was 89% (Cohen's $\kappa = 0.50$). Disagreements were discussed until resolutions were agreed. Full-text review included 14 studies, of which eight were included in the current review. Inter-rater agreement at the stage of full-text review was 100%. The review process is depicted in the PRISMA diagram in Figure 1. A standardised extraction form was developed and completed for the current review, which included study information such as design, location, and sample size; participant characteristics such as age, sex, and autism diagnosis; exposure and outcome variables measuring pubertal development and mental health; and relevant study results.

The quality of the included studies was assessed using the *Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies*, which categorises observational studies as poor, fair, or good quality based on 14 key criteria (Ma et al., 2020; National institutes of Health, 2021). The criteria capture factors such as sample size and power, clear definition of exposure and outcome variables, and adjustment for potential confounding variables. Each criterion is marked as *Yes/No/Other,* where *Other* includes *Cannot Determine, Not Applicable,* and *Not Reported*. An overall critical appraisal of each study's quality was then

made based on the individual criteria results. Quality assessment was completed by the lead author.

Results

Study characteristics

The systematic search identified eight studies which investigated the association between puberty and mental health symptoms in autism, which are presented in Appendix A. In total, the studies examined 1,021 participants, of whom 56% (n = 572) were autistic and 44% (n = 449) were TD. Males were overrepresented in both autistic and TD samples, with a slightly higher proportion of males in the autistic (n = 364, 63%) than TD group (n = 268, 60%). The mean age of participants across all samples was 12.15 years (SD 2.79)[1]. Study sizes ranged from N = 53 to N = 395. The vast majority of studies employed cross-sectional study designs, with only one longitudinal study identified (Corbett et al., 2022). All studies recruited participants from the community and all but three (Bitsika & Sharpley, 2020; Bronsard et al., 2010; Sharpley et al., 2021) examined both autistic and TD samples. The quality of seven of the identified studies were rated as 'fair', with only one rated as 'good' (Corbett et al., 2022). In general, the studies were marked down for quality because variables were not clearly defined or reliable, sample sizes were not justified or power not calculated, and confounders were not considered.

[1] This estimate excludes data from Corbett et al. (2022), who reported sample age as median and inter-quartile range (*Md* (TD sample) = 11.6 years, IQR = 10.6-12.6; *Md* (Autistic sample) = 11.2 years, IQR = 10.5-12.2).

Autistic participants were generally identified using the ADOS (Lord et al., 2000). Only two studies did not use the ADOS, instead employing the Autism Quotient (Groenman et al., 2024) and the ADI-R (Bronsard et al., 2010). The methods used to measure pubertal timing

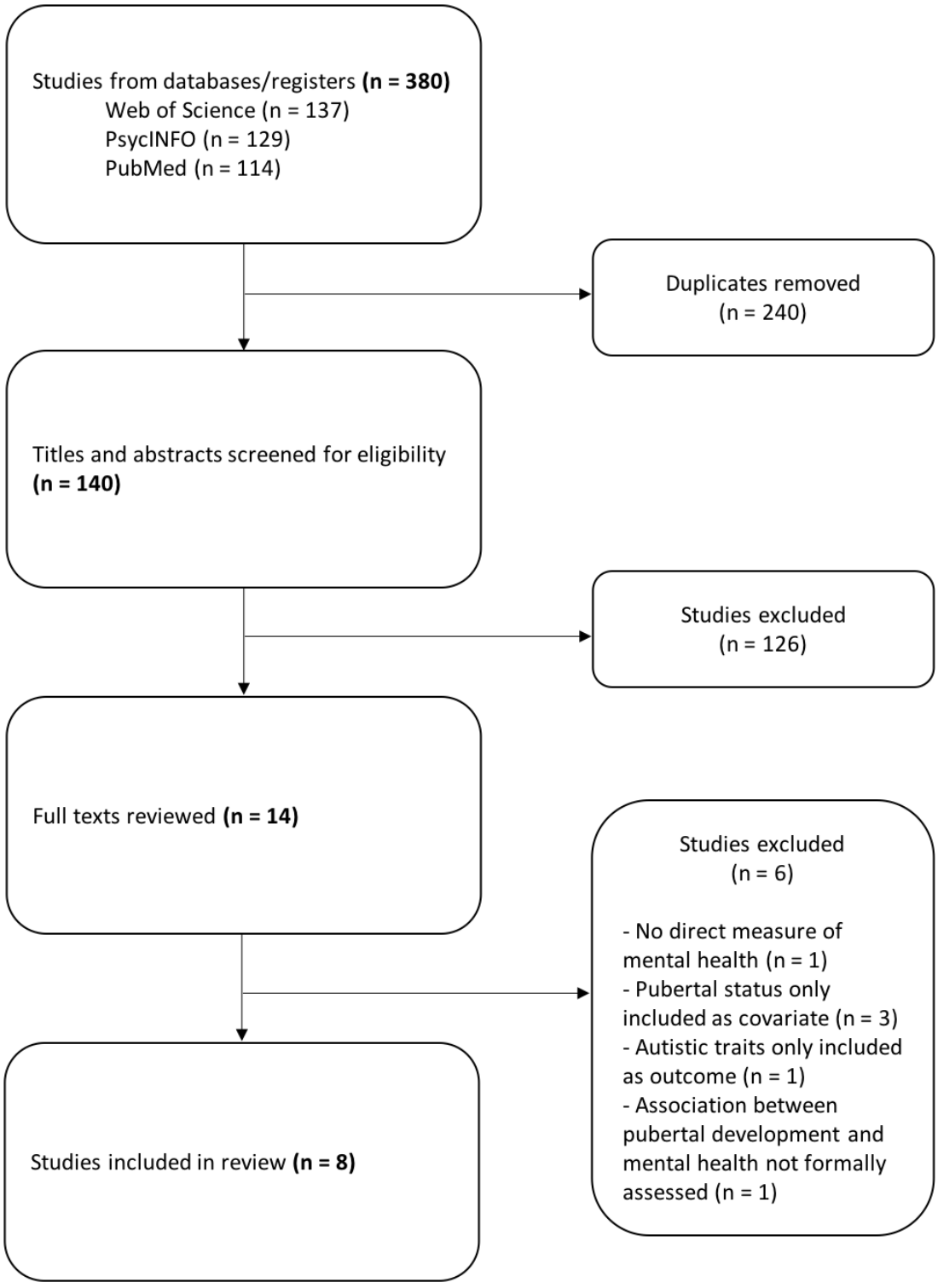

Figure 1 PRISMA diagram showing study identification and exclusion process.

differed between studies. The most common method was the parent-reported Pubertal Development Scale, which was used in four studies (Groenman et al., 2024; Muscatello & Corbett, 2018; Phan, 2020a, 2020b), followed by menarche status (Bitsika & Sharpley, 2020; Sharpley et al., 2021) and clinician assessment using the Tanner scale (Bronsard et al., 2010; Corbett et al., 2022), each of which were used in two studies. There was substantial heterogeneity in the measures of mental health outcomes used across studies. The most common measure used was the CASI (Gadow & Sprafkin, 2010), although different subscales were measured by different authors (Bitsika & Sharpley, 2020; Phan, 2020a; Sharpley et al., 2021). The only other measure used in more than one study was the Child Behavior Checklist (Achenbach, 2001; Achenbach & Rescorla, 2000), which was used in two studies (Corbett et al., 2022; Phan, 2020a). The other mental health measures used were the Other-Injurious Behavior scale (Tordjman et al., 2008), used by Bronsard et al. (2010); cortisol level (as a proxy for stress; Young et al., 2004), used by Muscatello and Corbett (2018); the Center for Epidemiologic Studies Depression Scale (Eaton et al., 2004), used by Phan (2020b); and the Children's Depression Inventory (Saylor et al., 1984), SCARED-71 (Bodden et al., 2009), and Strengths and Difficulties Questionnaire (Goodman, 1997), which were all used by Groenman et al. (2024). Given the substantial heterogeneity between measures and analysis techniques, as well as the small number of identified studies, meta-analysis was not feasible for the current review and a narrative synthesis approach was used.

Study findings

As noted above, the factor shared most commonly between studies is method of assessment of pubertal development – there is substantial heterogeneity in mental health measure, methodology used, and overall findings. The results are therefore presented below grouped according to pubertal development measure.

Pubertal Development Scale

Four studies used the PDS as a measure of pubertal development. In one (Phan, 2020a), the total PDS score was converted into equivalent Tanner stages. These stage scores were then regressed on chronological age and the residuals used as a measure of pubertal timing. For this study, Phan (2020a) reports using data from the National Database for Autism Research (NDAR), a database created and managed by the National Institute for Health in the USA. The author does not specify from which dataset within the NDAR the data used for the study are drawn. This study has the largest sample of the studies identified in the current review (N = 395). Autistic participants were identified using the ADOS-2 and represented 45% of the sample (n = 176). The mean age of autistic participants was 12.14 (SD 2.78), compared with 13.02 (SD 3.01) in the TD sample. The author examined two main outcome measures: repetitive behaviours and mental health symptoms. The latter were measured using both the Child Behavior Checklist (CBCL) and the Child and Adolescent Symptom Inventory (CASI). The author used parent reported CBCL data, and analysed responses at the level of the internalising and externalising domains, which were comprised of the anxious/depressed, withdrawn/depressed, and somatic complaints subscales (internalising) and the rule-breaking and aggressive behaviour subscales (externalising). The CASI data were also parent reported, and the author analysed symptom counts for oppositional

defiant disorder (ODD), conduct disorder (CD), generalised anxiety disorder (GAD), and major depressive disorder (MDD).

The author conducted linear regression analyses to examine the association between pubertal development and mental health symptoms. In the overall sample, the results showed no evidence for an association between pubertal development and internalising (p = .762) or externalising symptoms (p = .370) using the CBCL. There was also no evidence for an association between pubertal development and internalising (p = .599) or externalising symptoms (p = .537). The study similarly found no evidence for an association between pubertal development and any of the disorders addressed by the CASI (Gadow & Sprafkin, 2010; p(ODD) > .301; p(CD) > .441; p(GAD) = .248; p(MDD) > .121). The study does not report beta values or standard errors for these analyses. Following the main analysis, the author split the CBCL analysis according to sex and diagnosis group. These analyses included a third diagnosis group who did not meet the criteria for an autism diagnosis but scored either ≥3 and ≤6 on the ADOS or t ≥ 55 on the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005). This group is referred to as the *below ASD dx cutoff* group (N = 55; 40% male; mean age 13.86, SD = 2.88). The results showed no association between pubertal timing and CBCL score in any diagnosis group (p > .369), but some evidence for an association between pubertal status and externalising symptoms for male participants in the autistic group (b = -3.54, p = .01) and female participants in the *below ASD dx cutoff* group (b = -5.50, p = .03), such that more advanced pubertal status was associated with fewer externalising symptoms.

A second study identified for the current review, and also using the PDS, was also conducted by Phan as part of the same thesis but using a different analysis sample (Phan, 2020b). The second study examined a sample of N = 74 adolescent males, of whom 42% (n = 31) were autistic, as measured using clinical cut-offs on the Autism Diagnostic Observation Schedule, Social Responsiveness Scale, Autism Spectrum Rating Scale, and DSM-5. Among other measures, the author examined data on pubertal status and depressive symptoms. Pubertal status was assessed using the self-reported PDS, which was again converted into equivalent Tanner stages. In this study, the converted Tanner stages were then split into two measures proposed to broadly map onto gonadal vs adrenal development – two different endocrinological processes which underlie puberty – based on Shirtcliff et al. (2009). Depressive symptoms were examined using the Center for Epidemiologic Studies Depression Scale (Radloff, 1977). The study results showed some evidence for an association between adrenal development and depressive symptoms in autistic (*b* = 0.244, p = .007) but not TD participants (*b* = 0.006, p = .865). However, this association attenuated to the null after adjustment for restrictive and repetitive behaviours (*p* = .492 [no beta reported]). Given autistic traits and diagnosis have been associated with both pubertal timing (Corbett et al., 2022; Hergüner & Hergüner, 2016) and mental health symptoms (Chandler et al., 2016), these findings may indicate a confounding effect of autism symptom severity. There was no evidence of an association between gonadal development and depressive symptoms (*p* = .139 [no beta reported]).

The third study to use the PDS as its measure of puberty is also the most recent identified in the current review. Groenman et al. (2024) examined the association between pubertal status and mental health symptoms in a community sample of Dutch adolescents (N = 68),

50% of whom were autistic (n = 34) and 53% of whom were male (n = 36). Autistic participants were categorised according to the clinical cut-offs on the Developmental, Dimensional and Diagnostic interview (Slappendel et al., 2016) and Dutch Social Responsiveness Scale (Roeyers et al., 2011). The authors followed the same procedure as Phan (2020b) in splitting PDS scores into separate adrenal and gonadal scales. They then created a new variable proposed to capture relative pubertal development. First, they created predicted pubertal status values by regressing the adrenal and gonadal scale scores on age and sex in the TD group. They then subtracted the observed pubertal status scores for all participants from the predicted reference scores. This created a relative pubertal development variable, where negative values reflected less developed status compared to predictions based on the TD data and positive values reflected more developed status compared to the predicted values. The authors also collected data on three mental health symptom clusters: depression, using the Children's Depression Inventory; anxiety, using the SCARED-71; and externalising symptoms, using the hyperactivity/attention problems and behavioural problems subscales of the parent-reported Strengths and Difficulties questionnaire. The authors reported associations between more advanced pubertal development and increased depressive (adrenal $r = 0.26$, $p = .002$; gonadal $r = 0.14$, $p = .03$) and externalising symptoms (adrenal $r = 0.13$, $p = .04$; gonadal $r = 0.18$, $p = .01$) in the autistic group, but no association between pubertal development and anxiety symptoms (adrenal $r = 0.03$, $p = .30$; gonadal $r = 0.06$, $p = .16$).

The fourth study to use the PDS as its measure of pubertal development was conducted by Muscatello and Corbett (2018). In this study, the authors investigated the association between pubertal development and daily cortisol rhythm, a proxy for HPA axis function and

emotional stress response, in a US cohort of autistic and TD adolescents. Just over half the sample were identified as autistic (n = 64, 57%), using previous diagnosis, current clinical judgment, and meeting the clinical cut-off on the ADOS as diagnostic criteria. The majority of the sample (n = 99, 88%) were male. The authors found that PDS score was positively associated with evening cortisol levels in the overall sample, even after adjustment for age and IQ (b = 0.45, p = .04). However, when results were stratified by diagnosis group, partial correlations showed an association between more advanced pubertal development and higher evening cortisol level in the TD group (r = 0.30, p = .05) but not in the autistic group (r = 0.17, p = .25).

Overall, these studies provide contradictory results and do not provide strong evidence for an association between pubertal development and mental health symptoms in autism. One study showed a protective effect of more advanced pubertal development on externalising symptoms, but only in autistic males (Phan, 2020a), while another study showed a negative effect of more advanced pubertal development on externalising and depressive symptoms in autistic adolescents (Groenman et al., 2024). Groenman and colleagues also reported no association between pubertal development and anxiety symptoms, a finding that aligns with the results of Muscatello and Corbett (2018), who found no correlation between pubertal stage and evening cortisol levels in autistic adolescents, and with Phan (2020b), who reported no association between pubertal development and depressive symptoms after analyses were adjusted for the potential confounder of restrictive and repetitive behaviours.

Menarche status

Two studies identified for the current review used menarche status as the measure of pubertal development. Both studies drew on the same sample but differed in their choice of outcome measure. The sample consisted of a cohort of Australian participants (N = 53), all of whom were autistic and female. Participants were around mean age 10 years (SD = 2.7). Participants were recruited from the community, and autism diagnoses were established using a clinical interview with parents and confirmed using the ADOS-2 at the time of recruitment to the study. Parents were asked whether or not their daughters had commenced menarche and 26% (n = 14) reported that they had. In the study by Bitsika and Sharpley (2020), the authors investigated the association between menarche status and anxiety using both self- and parent-reports on the GAD subscale of the Child and Adolescent Symptom Inventory (CASI-4). In a two-way MANOVA, the authors reported no main effect of menarche status on CASI-GAD score (F = 1.84, p = .169). They also found no association between menarche status and self-reported CASI-GAD score after restricting the sample to only participants who reported not taking any medication (F = 0.171, p = .682). However, there was evidence of an association between menarche status and mother-reported CASI-GAD score in this group (F = 6.507, p = .017). The second study to use this sample used the depression (MDD) and social phobia (SP) subscales of the CASI as its primary outcome measures (Sharpley et al., 2021). The CASI-MDD was both self- and mother-reported, whereas the CASI-SP was self-reported only. In regression analyses, there was no association between menarche status and self-reported CASI-MDD (b = .050, p > .05) or mother-reported CASI-MDD (b = .098, p > .05). In a separate MANOVA analysis, the authors found a significant effect of menarche status on parent-reported CASI-MDD (F = 11.36, p = .001) but not CASI-SP (F = 0.04, p = .835).

Both studies using menarche status as the measure of puberty used the same sample of participants. Both studies reported no association between menarche status and self-reported measures of mental health symptoms. However, both did find evidence for an association between menarche status and parent-reported mental health measures, such that individuals who had commenced menarche were rated as having higher levels of depression and anxiety symptoms than those who had not commenced menarche.

Clinician assessment

Two studies used clinician assessment of pubertal stage, using Tanner scales, as their measure of pubertal development. This method is considered the gold standard (Coleman & Coleman, 2002). Bronsard and colleagues (2010) investigated the association between pubertal stage and externalising symptoms, indexed by aggression towards others, in a sample of French autistic adolescents (n = 74). The sample was 66% male (n = 49). Autistic status was determined by direct clinical observation and confirmation using the ADI-R. The authors used the Other-Injurious Behavior (OIB) scale as the outcome measure. Using ANOVA and *t*-tests, the authors found no association between pubertal status and OIB score. Test statistics were not reported.

Corbett and colleagues (2022) used a longitudinal community cohort study to compare pubertal timing and tempo in autistic and TD adolescents. The sample consisted of 244 adolescents, of whom 66% (n = 162) were male and 57% (n = 140) were autistic. Participants underwent physical examination by a medical clinician to establish their Tanner stage. This assessment was completed annually, at Time 1 (where participants were aged 10 years to

13 years 11 months), Time 2 (age 11 to 14 years), and Time 3 (age 12 to 15 years). In addition to physical examination, mental health data were collected annually using the anxiety and affective domains of the CBCL, although only mental health data from Time 3 were used for analysis. To examine the association between pubertal timing and mental health, the authors used a non-linear mixed effects model to estimate pubertal timing from the collected Tanner stage data. The extracted random effects from this model were used as the exposure variable in a linear regression analysis, with Time 3 CBCL scores as the outcome and age and BMI as covariates. The analysis sample included both autistic and TD participants. The results showed no association between pubertal timing and CBCL scores in females (anxiety p = .25, affective p = .054) or males (anxiety p = .16, affective p = .70).This result is in line with Bronsard et al. (2010): both studies using clinician assessment report no association between pubertal development and mental health outcomes in autistic samples.

Overall, the results of the reviewed studies do not provide strong evidence for an association between pubertal development and mental health outcomes in autism. Half of the studies found no evidence for an association (Bronsard et al., 2010; Corbett et al., 2022; Muscatello & Corbett, 2018; Phan, 2020b) and all of the studies which do report associations find pubertal development effects for some mental health outcomes but not others (Bitsika & Sharpley, 2020; Groenman et al., 2024; Phan, 2020a; Sharpley et al., 2021). Three of these four studies reported associations between earlier pubertal timing, or more advanced pubertal status, and poorer mental health outcomes (Bitsika & Sharpley, 2020; Groenman et al., 2024; Sharpley et al., 2021). One study (Phan, 2020a) reported a protective effect of more advanced pubertal status. Moderator variables were not routinely analysed in the reviewed studies, though all did report data on participant sex. The results of the

studies variously show associations between pubertal development and mental health in males but not females (Phan, 2020a), no association in males (Phan, 2020b), an association in females (Bitsika & Sharpley, 2020; Sharpley et al., 2021), no association in either sex (Bronsard et al., 2010; Corbett et al., 2022; Muscatello & Corbett, 2018), and associations in both sexes (Groenman et al., 2024). The mixed overall results mean that no conclusions can be confidently drawn about any differential effect of pubertal development on mental health in males or females with autism.

Discussion of identified studies

The heterogeneous nature of the above results may point to methodological explanations. For example, while the study benefits from a large sample size and well validated measures, it does not appear that any of the regression analyses in Phan (2020a) were adjusted for any potential confounders, for example socioeconomic status (Hiatt et al., 2021; Reiss, 2013) or adverse childhood experiences like sexual abuse (Hailes et al., 2019; Noll et al., 2017). This leaves open the possibility that the observed effects are due to the confounding effect of one or more unmeasured variables. Indeed, in the study where potential confounders are included in the regression analyses, Phan reports no effect of pubertal development (Phan, 2020b). Both studies by Phan were conducted as part of a doctoral research project, and hence have not been peer reviewed. They must be interpreted in that context.

In addition to the unadjusted analyses, in both studies by Phan the author does not report important information like beta values, meaning null results cannot be further interrogated. Robust reporting of results is also a consideration for other studies. For example, Bronsard et al. (2010) do not make clear what their analysis methods for investigating the association

between pubertal status and OIB were; they report conducting ANOVA, *t*-tests, correlation analyses, and χ^2 tests, but do not specify which of these were used to assess the effect of pubertal status, and do not report any test statistics for their null finding. Corbett et al. (2022) explicitly describe their analysis method – linear regression – and report *p* values for the analyses, but do not report beta values or any other test statistics. The way these results are reported mean that evaluating the findings, for example by studying standard errors to gauge confidence in the estimates, is not possible.

In other studies, the construct validity of some of the measures used is questionable. In Groenman et al. (2024), the process by which the relative pubertal development variable is created is unclear and the variable itself is unvalidated. Further, it appears that the relative pubertal development of the autistic sample is calculated relative to the TD sample, even though the authors report "suggestions for earlier … pubertal development in autistic boys and girls compared to non-autistic participants" (Groenman et al., 2024, pp.7). If pubertal development differed between the groups, a variable based only on the TD group will not, by its nature, accurately represent the relative pubertal development of the autistic group in the context of the whole sample – it will overestimate divergence from the mean. A comparison variable based on the whole sample may have produced less pronounced effects for the autistic group. In Muscatello and Corbett (2018), the primary outcome measure is cortisol rhythm. The authors justify this measure as a proxy for HPA function, which itself is a proxy for the body's response to stress. However, the authors also collected mental health data using the CBCL and found no evidence for an association between the measured cortisol levels and any CBCL outcomes (Muscatello & Corbett, 2018). The study

may have been unintentionally measuring a construct unrelated to mental health symptoms.

Sample size is also an important factor in many of the identified studies. Both studies using menarche status as the measure of puberty utilise the same sample of participants, and both find evidence for an association between menarche status and parent-reported mental health measures. Whilst it is possible that mothers are more sensitive to their children's affective symptoms than the children themselves – previous research has identified that parent reports of children's anxiety are consistently more severe than child reports (van Steensel & Heeman, 2017) – the results should be interpreted in light of the size of the studies' analysis samples. Although Sharpley et al. (2021) used the full sample for their analysis, only a small number of participants (n = 14) reported having commenced menarche. In the study by Bitsika and Sharpley (2020), the significant effect of menarche status is only observed after restricting the sample to participants who reported not taking any medication – a total analysis sample of n = 14. Of this already small sample, only n = 5 reported having commenced menarche. The associations reported by Groenman et al. (2024) are found only after splitting the sample by autism diagnosis group, which leaves an analysis sample of n = 34. Any conclusions taken from these analyses must therefore be drawn with caution as the small samples increase the risk of error and bias (Pickles & Bedford, 2015).

In summary, the studies identified for the current review are generally of 'fair' quality and their results should be interpreted in the context of the important methodological

considerations identified. Overall, the studies do not provide strong evidence for an association between pubertal development and mental health in autism.

Discussion

The aim of this review was to review the current evidence examining the association between pubertal development and mental health in autistic populations to answer two questions: what is the current state of the evidence base, and what do the findings of the research so far tell us? The results of the review indicate that the evidence base is limited – the existing literature base is small and of only 'fair' quality. The research so far provides mixed results, but overall does not provide strong evidence for an association between pubertal development and mental health in autism.

Interpretations of review findings

The findings of the current review contrast with the TD literature, in which the finding of an association between pubertal development is consistent and robust (Ullsperger & Nikolas, 2017). As noted above, an important consideration is the quality of the evidence in autistic populations. The overall quality of the studies was rated as 'fair'. Higher quality research may yield more consistent results from which more confident conclusions about the relationship between pubertal development and mental health in autism can be drawn.

Assuming the observed difference between autistic and TD populations is a true difference, there are a number of possible explanations. The assumed mechanisms underlying the association between pubertal development and mental health in TD populations, such as the social deviance and early timing hypotheses, may operate differently in autism. The

social deviance hypothesis, for example, proposes that experiencing pubertal timing differently to one's peers – either earlier or later – increases feelings of anxiety and insecurity following social comparison (Buunk et al., 1990) at a time when peer group influence is particularly important (Brown & Larson, 2009). For autistic adolescents, it may be that social comparison to peers does not take place in the same way; for example, the self in relation to others may be conceptualised differently due to deficits in theory of mind (Frith & Happé, 1999). Alternatively, social comparison, stigma, feelings of 'difference', and negative emotional consequences may have already taken place prior to puberty (Mesa & Hamilton, 2022; Turnock et al., 2022) so the effect of the pubertal transition is not as pronounced as in TD populations.

The early timing hypothesis proposes that it is individuals who experience puberty earlier than their peers who show increased risks for mental health difficulties. This phenomenon is proposed to occur because of a mismatch between physical development and cognitive and emotional development (Ge & Natsuaki, 2009). This mismatch contains neurocognitive and psychosocial components, each of which may operate differently in autism. For example, autistic individuals show increased sensation-seeking compared to TD individuals throughout childhood and adolescence (Ben-Sasson et al., 2009), as well as more difficulties in inhibition and control (Geurts et al., 2014). It may be that the neurocognitive disparity seen at puberty in TD populations exists in autistic populations independently of puberty, so the pubertal transition does not confer any increased risk. In terms of social expectations, the burden of increased social expectations on early developers may not apply to autistic young people in the same way as to their TD peers. Qualitative interviews with parents and educators have identified lower expectations for autistic children to participate at school

than for their TD peers (Hodges et al., 2020), and parents of autistic children often express concern about their children's ability to live as independent adults (Kirby et al., 2020). Conversely, it may be the case that the pre-pubertal social expectations perceived as manageable by TD populations are experienced as unmanageable by autistic populations. Social communication difficulties are a defining characteristic of autism (American Psychiatric Association, 2013), and autistic individuals are more likely to be victims of social rejection as children (Locke et al., 2013) and bullying as adolescents (Humphrey & Symes, 2010). Whether social expectations are not raised as a result of the pubertal transition, or whether they have been subjectively unmanageable since pre-puberty, pubertal development may not increase the risk of distress in autism as in TD populations.

Implications of the overall findings

The results of the current review have a number of important implications. Most importantly, the number and quality of the studies identified by this review demonstrate the need for further research into the association between pubertal development and mental health outcomes in autism. Future research should use multiple objective, high-quality measures of pubertal timing and development, such as age at menarche and clinician-assessed Tanner stage. In addition, mental health measures validated for use in autistic young people, such as the CBCL, should be employed. The research should be longitudinal and follow participants from late childhood across adolescence in order to capture pubertal timing contemporaneously. Finally, future research should use large, representative samples so that findings are more likely to be accurate, reliable, and generalisable.

Clinically, the results of this review indicate that mental health interventions aimed at autistic young people starting puberty may not have any more benefit than an intervention delivered earlier in childhood. The results of the review indicate that differences in pubertal timing do not confer any additional risk of mental health problems in autistic populations. This may be because the mechanisms that increase risk at puberty in TD populations are already operating in autistic populations during earlier childhood. This finding highlights the importance of early identification and intervention for mental health difficulties in autism. It is well documented that mental health difficulties are more prevalent in autism than in TD populations (Simonoff et al., 2008), even from early in childhood (Hayashida et al., 2010). Interventions aimed at young autistic children, perhaps through parent-focused or behavioural interventions, may be the most effective approach to improving mental health symptoms (Kulasinghe et al., 2023; Wong et al., 2015).

Limitations

The results of the current review must be considered in light of its limitations. Although the search strategy was based on existing reviews and constructed to identify as much available literature as possible, it is possible that some findings, for example from unpublished research or studies examining less common mental health outcomes, were not captured. The studies identified by the current review suggest a weaker association between pubertal development and mental health outcomes in autism compared to in TD. Given the well-established publication bias towards positive results (Thornton & Lee, 2000), other research supporting this null finding may not have been published and therefore not captured in the current review. Future reviews may benefit from searching collections of unpublished research, for example conference proceedings (Korevaar et al., 2020). Further, the small

number of identified studies and the heterogeneity of their methods meant a meta-analysis was not possible for the current review, so pooled estimates of effect sizes were not produced.

Conclusion

The current review highlights a lack of high-quality studies investigating the association between pubertal development and mental health outcomes in autism. The results of the studies that were identified for the review do not provide strong evidence for an effect of pubertal development on mental health in autism, a result which contrasts with the TD literature. Further research is needed to increase confidence in this finding.

References

Abdallah, M. W., Greaves-Lord, K., Grove, J., Nørgaard-Pedersen, B., Hougaard, D. M., & Mortensen, E. L. (2011). Psychiatric comorbidities in autism spectrum disorders: findings from a Danish Historic Birth Cohort. *European child & adolescent psychiatry*, *20*(11), 599-601.

Achenbach, T. M. (2001). Manual for ASEBA school-age forms & profiles. *University of Vermont, Research Center for Children, Youth & Families*.

Achenbach, T. M., & Rescorla, L. A. (2000). *Manual for the ASEBA preschool forms and profiles* (Vol. 30). Burlington, VT: University of Vermont.

Al-Sahab, B., Ardern, C. I., Hamadeh, M. J., & Tamim, H. (2012). Age at menarche and current substance use among Canadian adolescent girls: results of a cross-sectional study [journal article]. *BMC Public Health*, *12*(1), 195. https://doi.org/10.1186/1471-2458-12-195

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. American Psychiatric Publishing.

Baams, L., Dubas, J. S., Overbeek, G., & Van Aken, M. A. (2015). Transitions in body and behavior: A meta-analytic study on the relationship between pubertal development and adolescent sexual behavior. *Journal of Adolescent Health*, *56*(6), 586-598.

Barendse, M. E., Byrne, M. L., Flournoy, J. C., McNeilly, E. A., Guazzelli Williamson, V., Barrett, A.-M. Y., Chavez, S. J., Shirtcliff, E. A., Allen, N. B., & Pfeifer, J. H. (2022). Multimethod assessment of pubertal timing and associations with internalizing psychopathology in early adolescent girls. *Journal of psychopathology and clinical science*, *131*(1), 14.

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): Evidence from asperger syndrome/high-functioning autism, malesand females, scientists and mathematicians. *Journal of autism and developmental disorders*, *31*, 5-17.

Ben-Sasson, A., Hen, L., Fluss, R., Cermak, S. A., Engel-Yeger, B., & Gal, E. (2009). A Meta-Analysis of Sensory Modulation Symptoms in Individuals with Autism Spectrum Disorders. *Journal of autism and developmental disorders*, *39*(1), 1-11. https://doi.org/10.1007/s10803-008-0593-3

Berger, U., Weitkamp, K., & Strauss, B. (2009). Weight limits, estimations of future BMI, subjective pubertal timing and physical appearance comparisons among adolescent girls as precursors of disturbed eating behaviour in a community sample. *European Eating Disorders Review: The Professional Journal of the Eating Disorders Association*, *17*(2), 128-136.

Bitsika, V., & Sharpley, C. F. (2020). Self-vs parent reports of generalised anxiety disorder symptomatology in mildly impaired girls with an autism spectrum disorder. *Journal of autism and developmental disorders*, *50*(3), 1045-1055.

Blanchard, A., Chihuri, S., DiGuiseppi, C. G., & Li, G. (2021). Risk of Self-harm in Children and Adults With Autism Spectrum Disorder: A Systematic Review and Meta-analysis. *JAMA Network Open*, *4*(10), e2130272-e2130272. https://doi.org/10.1001/jamanetworkopen.2021.30272

Bodden, D. H., Bögels, S. M., & Muris, P. (2009). The diagnostic utility of the screen for child anxiety related emotional disorders-71 (SCARED-71). *Behaviour Research and Therapy*, *47*(5), 418-425.

Bronsard, G., Botbol, M., & Tordjman, S. (2010). Aggression in low functioning children and adolescents with autistic disorder. *PLoS One*, *5*(12), e14358.

Brown, B. B., & Larson, J. (2009). Peer relationships in adolescence. *Handbook of adolescent psychology*, *2*(Pt I), 74-104.

Buunk, B. P., Collins, R. L., Taylor, S. E., VanYperen, N. W., & Dakof, G. A. (1990). The affective consequences of social comparison: either direction has its ups and downs. *Journal of personality and social psychology*, *59*(6), 1238.

Caspi, A., & Moffitt, T. E. (1991). Individual differences are accentuated during periods of social change: the sample case of girls at puberty. *Journal of personality and social psychology*, *61*(1), 157.

Chandler, S., Howlin, P., Simonoff, E., O'sullivan, T., Tseng, E., Kennedy, J., Charman, T., & Baird, G. (2016). Emotional and behavioural problems in young children with autism spectrum disorder. *Developmental Medicine & Child Neurology*, *58*(2), 202-208.

Coleman, L., & Coleman, J. (2002). The measurement of puberty: a review. *Journal of adolescence*, *25*(5), 535-550.

Constantino, J., & Gruber, C. (2005). Social responsive scale (SRS) manual. *Los Angeles, CA: Western Psychological Services*.

Cook, J., Hull, L., Crane, L., & Mandy, W. (2021). Camouflaging in autism: A systematic review. *Clinical Psychology Review*, *89*, 102080. https://doi.org/https://doi.org/10.1016/j.cpr.2021.102080

Corbett, B. A., Muscatello, R. A., Kim, A., Vandekar, S., Duffus, S., Sparks, S., & Tanguturi, Y. (2022). Examination of pubertal timing and tempo in females and males with autism spectrum disorder compared to typically developing youth. *Autism Research*.

Corbett, B. A., Vandekar, S., Muscatello, R. A., & Tanguturi, Y. (2020). Pubertal Timing During Early Adolescence: Advanced Pubertal Onset in Females with Autism Spectrum Disorder. *Autism Research*, *13*(12), 2202-2215. https://doi.org/https://doi.org/10.1002/aur.2406

Costello, E. J. (2007). Psychiatric predictors of adolescent and young adult drug use and abuse: What have we learned? *Drug and Alcohol Dependence*, *88*, S97-S99.

Costello, E. J., Mustillo, S., Erkanli, A., Keeler, G., & Angold, A. (2003). Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of general psychiatry*, *60*(8), 837-844.

Covidence. (2023). *Covidence systematic review software*. Veritas Health Innovation. Melbourne, Australia. Available at www.covidence.org.

Eaton, W. W., Muntaner, C., Smith, C., Tien, A., Ybarra, M., & Maruish, M. (2004). Center for epidemiologic studies depression scale: Review and revision. *The use of psychological testing for treatment planning and outcomes assessment*, p363-p377.

EBSCO. (2023). *APA PsychInfo*. https://www.ebsco.com/products/research-databases/apa-psycinfo

Frith, U., & Happé, F. (1999). Theory of mind and self-consciousness: What is it like to be autistic? *Mind & language*, *14*(1), 82-89.

Gadow, K. D., & Sprafkin, J. (2010). *Child and adolescent symptom inventory 4R: Screening and norms manual.* Checkmate Plus.

Ge, X., & Natsuaki, M. N. (2009). In search of explanations for early pubertal timing effects on developmental psychopathology. *Current directions in psychological science*, *18*(6), 327-331.

Geurts, H. M., van den Bergh, S. F., & Ruzzano, L. (2014). Prepotent response inhibition and interference control in autism spectrum disorders: Two meta-analyses. *Autism Research*, *7*(4), 407-420.

Goodman, R. (1997). The Strengths and Difficulties Questionnaire: a research note. *Journal of child psychology and psychiatry*, *38*(5), 581-586.

Graber, J. A. (2013). Pubertal timing and the development of psychopathology in adolescence and beyond. *Hormones and Behavior*, *64*(2), 262-269.

Groenman, A. P., van der Oord, S., & Geurts, H. M. (2024). Navigating adolescence: pubertal development in autism spectrum conditions and its relation to mental health. *Archives of Women's Mental Health*. https://doi.org/10.1007/s00737-023-01414-0

Hailes, H. P., Yu, R., Danese, A., & Fazel, S. (2019). Long-term outcomes of childhood sexual abuse: an umbrella review. *The Lancet Psychiatry*, *6*(10), 830-839.

Hayashida, K., Anderson, B., Paparella, T., Freeman, S. F., & Forness, S. R. (2010). Comorbid psychiatric diagnoses in preschoolers with autism spectrum disorders. *Behavioral Disorders*, *35*(3), 243-254.

Hergüner, A., & Hergüner, S. (2016). Association between age at menarche and autistic traits in Turkish university students. *American Journal of Human Biology*, *28*(1), 44-47. https://doi.org/https://doi.org/10.1002/ajhb.22739

Hiatt, R. A., Stewart, S. L., Deardorff, J., Danial, E., Abdiwahab, E., Pinney, S. M., Teitelbaum, S. L., Windham, G. C., Wolff, M. S., Kushi, L. H., & Biro, F. M. (2021). Childhood Socioeconomic Status and Menarche: A Prospective Study. *Journal of Adolescent Health*, *69*(1), 33-40. https://doi.org/https://doi.org/10.1016/j.jadohealth.2021.02.003

Hodges, A., Joosten, A., Bourke-Taylor, H., & Cordier, R. (2020). School participation: The shared perspectives of parents and educators of primary school students on the autism spectrum. *Research in Developmental Disabilities*, *97*, 103550. https://doi.org/https://doi.org/10.1016/j.ridd.2019.103550

Huke, V., Turk, J., Saeidi, S., Kent, A., & Morgan, J. F. (2013). Autism spectrum disorders in eating disorder populations: a systematic review. *European Eating Disorders Review*, *21*(5), 345-351.

Humphrey, N., & Symes, W. (2010). Perceptions of social support and experience of bullying among pupils with autistic spectrum disorders in mainstream secondary schools. *European Journal of Special Needs Education*, *25*(1), 77-91.

Joinson, C., Heron, J., Araya, R., Paus, T., Croudace, T., Rubin, C., Marcus, M., & Lewis, G. (2012). Association between pubertal development and depressive symptoms in girls from a UK cohort. *Psychological Medicine*, *42*(12), 2579-2589.

Kirby, A. V., Feldman, K. J. C., Hoffman, J. M., Diener, M. L., & Himle, M. B. (2020). Transition preparation activities and expectations for the transition to adulthood among parents of autistic youth. *Research in Autism Spectrum Disorders*, *78*, 101640. https://doi.org/https://doi.org/10.1016/j.rasd.2020.101640

Korevaar, D. A., Salameh, J. P., Vali, Y., Cohen, J. F., McInnes, M. D. F., Spijker, R., & Bossuyt, P. M. (2020). Searching practices and inclusion of unpublished studies in systematic reviews of diagnostic accuracy. *Res Synth Methods*, *11*(3), 343-353. https://doi.org/10.1002/jrsm.1389

Kulasinghe, K., Whittingham, K., Mitchell, A. E., & Boyd, R. N. (2023). Psychological interventions targeting mental health and the mother–child relationship in autism:

Systematic review and meta-analysis. *Developmental Medicine & Child Neurology*, *65*(3), 329-345. https://doi.org/https://doi.org/10.1111/dmcn.15432

Lai, M.-C., Kassee, C., Besney, R., Bonato, S., Hull, L., Mandy, W., Szatmari, P., & Ameis, S. H. (2019). Prevalence of co-occurring mental health diagnoses in the autism population: a systematic review and meta-analysis. *The Lancet Psychiatry*, *6*(10), 819-829. https://doi.org/https://doi.org/10.1016/S2215-0366(19)30289-5

Locke, J., Kasari, C., Rotheram-Fuller, E., Kretzmann, M., & Jacobs, J. (2013). Social network changes over the school year among elementary school-aged children with and without an autism spectrum disorder. *School Mental Health*, *5*, 38-47.

Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Leventhal, B. L., DiLavore, P. C., Pickles, A., & Rutter, M. (2000). The Autism Diagnostic Observation Schedule—Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of autism and developmental disorders*, *30*, 205-223.

Ma, L. L., Wang, Y. Y., Yang, Z. H., Huang, D., Weng, H., & Zeng, X. T. (2020). Methodological quality (risk of bias) assessment tools for primary and secondary medical studies: what are they and which is better? *Mil Med Res*, *7*(1), 7. https://doi.org/10.1186/s40779-020-00238-8

Marshall, W. A., & Tanner, J. M. (1969). Variations in pattern of pubertal changes in girls. *Archives of disease in childhood*, *44*(235), 291.

Marshall, W. A., & Tanner, J. M. (1970). Variations in the pattern of pubertal changes in boys. *Archives of disease in childhood*, *45*(239), 13-23.

May, T., Pang, K. C., O'Connell, M. A., & Williams, K. (2017). Typical Pubertal Timing in an Australian Population of Girls and Boys with Autism Spectrum Disorder. *Journal of*

autism and developmental disorders, *47*(12), 3983-3993. https://doi.org/10.1007/s10803-017-3281-3

Mendle, J., Beam, C. R., McKone, K. M., & Koch, M. K. (2020). Puberty and transdiagnostic risks for mental health. *Journal of Research on Adolescence*, *30*(3), 687-705.

Mesa, S., & Hamilton, L. G. (2022). "We are different, that's a fact, but they treat us like we're different-er": understandings of autism and adolescent identity development. *Advances in Autism*, *8*(3), 217-231.

Muscatello, R. A., & Corbett, B. A. (2018). Comparing the effects of age, pubertal development, and symptom profile on cortisol rhythm in children and adolescents with autism spectrum disorder. *Autism Research*, *11*(1), 110-120.

National institutes of Health. (2021). *Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies*. Retrieved 15/04/24 from https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

Noll, J. G., Trickett, P. K., Long, J. D., Negriff, S., Susman, E. J., Shalev, I., Li, J. C., & Putnam, F. W. (2017). Childhood sexual abuse and early timing of puberty. *Journal of Adolescent Health*, *60*(1), 65-71.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., & Moher, D. (2021). Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. *Journal of clinical epidemiology*, *134*, 103-112.

Petersen, A. C., Crockett, L., Richards, M., & Boxer, A. (1988). A self-report measure of pubertal status: Reliability, validity, and initial norms. *Journal of Youth and Adolescence*, *17*(2), 117-133.

Petersen, A. C., & Taylor, B. (1980). The biological approach to adolescence: Biological change and psychological adaptation. *Handbook of adolescent psychology*, *117155*.

Phan, J. M. (2020a). Chapter 4: Repetitive behaviors and pubertal status predicts psychopathology symptoms in adolescents with and without autism. In *Puberty as a moderator on risk for psychopathology symptoms and autistic stereotypy exacerbation in adolescents with and without ASD* [PhD thesis, Iowa State University] Retrieved from https://dr.lib.iastate.edu/server/api/core/bitstreams/d490215d-cf7c-4038-ad6e-89691595a5ff/content.

Phan, J. M. (2020b). Chapter 5: Pubertal development and repetitive behavior predited depressive symptoms in autistic adolescent males. In *Puberty as a moderator on risk for psychopathology symptoms and autistic stereotypy exacerbation in adolescents with and without ASD*. [PhD thesis, Iowa State University]

Retrieved from https://dr.lib.iastate.edu/server/api/core/bitstreams/d490215d-cf7c-4038-ad6e-89691595a5ff/content.

Pickles, A., & Bedford, R. (2015). What clinicians need to know about statistical issues and methods. In *Rutter's Child and Adolescent Psychiatry* (pp. 188-200). https://doi.org/https://doi.org/10.1002/9781118381953.ch15

Pohl, A., Cassidy, S., Auyeung, B., & Baron-Cohen, S. (2014). Uncovering steroidopathy in women with autism: a latent class analysis. *Molecular Autism*, *5*(1), 27. https://doi.org/10.1186/2040-2392-5-27

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied psychological measurement*, *1*(3), 385-401.

Reiss, F. (2013). Socioeconomic inequalities and mental health problems in children and adolescents: a systematic review. *Social Science & Medicine*, *90*, 24-31.

Roberts, E., Joinson, C., Gunnell, D., Fraser, A., & Mars, B. (2020). Pubertal timing and self-harm: a prospective cohort analysis of males and females. *Epidemiology and psychiatric sciences*, *29*.

Roeyers, H., Thys, M., Druart, C., De Schryver, M., & Schittekatte, M. (2011). SRS, Screeningslijst voor autismespectrumstoornissen.

Saylor, C. F., Finch, A., Spirito, A., & Bennett, B. (1984). The children's depression inventory: a systematic evaluation of psychometric properties. *Journal of consulting and clinical psychology*, *52*(6), 955.

Sharpley, C. F., Bitsika, V., McMillan, M. E., & Agnew, L. L. (2021). Physiological, psychosocial, and environmental factors in depression among autistic girls. *International Journal of Developmental Neuroscience*, *81*(6), 502-509.

Shirtcliff, E. A., Dahl, R. E., & Pollak, S. D. (2009). Pubertal Development: Correspondence Between Hormonal and Physical Development. *Child Development*, *80*(2), 327-337. https://doi.org/https://doi.org/10.1111/j.1467-8624.2009.01263.x

Shulman, E. P., Smith, A. R., Silva, K., Icenogle, G., Duell, N., Chein, J., & Steinberg, L. (2016). The dual systems model: Review, reappraisal, and reaffirmation. *Developmental cognitive neuroscience*, *17*, 103-117.

Simonoff, E., Pickles, A., Charman, T., Chandler, S., Loucas, T., & Baird, G. (2008). Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child & Adolescent Psychiatry*, *47*(8), 921-929.

Slappendel, G., Mandy, W., van der Ende, J., Verhulst, F. C., van der Sijde, A., Duvekot, J., Skuse, D., & Greaves-Lord, K. (2016). Utility of the 3Di short version for the

diagnostic assessment of autism spectrum disorder and compatibility with DSM-5. *Journal of autism and developmental disorders*, *46*, 1834-1846.

Sontag, L. M., Graber, J. A., & Clemans, K. H. (2011). The Role of Peer Stress and Pubertal Timing on Symptoms of Psychopathology During Early Adolescence. *Journal of Youth and Adolescence*, *40*(10), 1371-1382. https://doi.org/10.1007/s10964-010-9620-8

Stumper, A., & Alloy, L. B. (2023). Associations Between Pubertal Stage and Depression: A Systematic Review of the Literature. *Child Psychiatry & Human Development*, *54*(2), 312-339. https://doi.org/10.1007/s10578-021-01244-0

Thornton, A., & Lee, P. (2000). Publication bias in meta-analysis: its causes and consequences. *Journal of clinical epidemiology*, *53*(2), 207-216. https://doi.org/https://doi.org/10.1016/S0895-4356(99)00161-4

Tordjman, S., Cohen, D., & Haag, G. (2008). Manual OIBS-SIBS for the Other-Injurious Behavior Scale (OIBS), Echelle des Conduites HétéroAgressives (ECHA) and the Self-Injurious Behavior Scale (SIBS), Echelle des Conduites AutoAgressives (ECAA). *Paris: Les Editions du Centre de Psychologie Appliquée (ECPA)*.

Turnock, A., Langley, K., & Jones, C. R. (2022). Understanding stigma in autism: A narrative review and theoretical model. *Autism in Adulthood*, *4*(1), 76-91.

Ullsperger, J. M., & Nikolas, M. A. (2017). A meta-analytic review of the association between pubertal timing and psychopathology in adolescence: Are there sex differences in risk? *Psychological bulletin*, *143*(9), 903.

van Steensel, F. J., & Heeman, E. J. (2017). Anxiety levels in children with autism spectrum disorder: A meta-analysis. *Journal of Child and Family Studies*, *26*(7), 1753-1767.

Whitehouse, A. J. O., Maybery, M. T., Hickey, M., & Sloboda, D. M. (2011). Brief Report: Autistic-Like Traits in Childhood Predict Later Age at Menarche in Girls. *Journal of*

autism and developmental disorders, *41*(8), 1125-1130. https://doi.org/10.1007/s10803-010-1129-1

Wong, C., Odom, S. L., Hume, K. A., Cox, A. W., Fettig, A., Kucharczyk, S., Brock, M. E., Plavnick, J. B., Fleury, V. P., & Schultz, T. R. (2015). Evidence-Based Practices for Children, Youth, and Young Adults with Autism Spectrum Disorder: A Comprehensive Review. *Journal of autism and developmental disorders*, *45*(7), 1951-1966. https://doi.org/10.1007/s10803-014-2351-z

Young, E. A., Abelson, J., & Lightman, S. L. (2004). Cortisol pulsatility and its role in stress regulation and health. *Frontiers in neuroendocrinology*, *25*(2), 69-76.

Zeidan, J., Fombonne, E., Scorah, J., Ibrahim, A., Durkin, M. S., Saxena, S., Yusuf, A., Shih, A., & Elsabbagh, M. (2022). Global prevalence of autism: A systematic review update. *Autism Research*, *15*(5), 778-790.

University of Bath
Doctorate in Clinical Psychology

Service-Related Project

The demographic representativeness of Pain Management Service patients at Great Western Hospital, Swindon

Elystan Roberts

Department of Psychology, University of Bath

egr22@bath.ac.uk

Word count: 3,959

Supervised by: Dr Flora Wilson, Great Western Hospital

Proposed journal for publication: Journal of Pain Research

Author guidelines for this journal can be found here:

https://www.tandfonline.com/action/authorSubmission?show=instructions&journalCode=djpr20

Introduction

Background

Equal access to medical care is fundamental to the philosophy of the National Health Service (NHS): according to the NHS Constitution, services should be available to all, irrespective of age, gender, race, or ability to pay (Department of Health, 2021). Specific medical disciplines have also identified the importance of inclusive services: the Royal College of Anaesthetists' Faculty of Pain Medicine, for example, has spoken of the need to "*actively search for and address barriers that may impede access and prevent a person with pain achieving maximum benefit*" from services (Faculty of Pain Medicine, 2021, page 3). However, evidence suggests that for many patients, equal access is not the reality. A recent NHS Race and Health Observatory report identified evidence of inequalities in healthcare across a variety of services, including mental health services (Kapadia et al., 2022). There is also evidence that people from ethnic minority backgrounds are less likely than White people to receive treatment for mental health difficulties, more likely to be detained under the Mental Health Act, and more likely to have poorer outcomes following interventions (Cabinet Office, 2018; NHS Digital 2023).

Service context

Many areas across the UK are witnessing increases in population size and diversity. One example of this is in Swindon, a large town in Wiltshire, England. Its population was estimated to be 220,363 in 2017 and had increased by around 6% to 233,400 by 2021 (Jones, 2019; Office for National Statistics, 2023). The demography of Swindon has shifted over the last two decades and is expected to continue to change. For example, in 2001, 8.5% of Swindon's population was made up of minoritised ethnicity individuals; this number had

increased to 15.4% by 2011 (Jones, 2019) and by the 2021 census had further increased to 18.54% (Office for National Statistics, 2022a). The age distribution of Swindon's population is also expected to undergo dramatic changes in the near future – of the projected population growth up to 2038, over 50% is expected to be in individuals aged ≥65 (Jones, 2019). As the population of Swindon shifts and changes, it is imperative that local health services remain sensitive to the population they are serving to ensure the population's health needs are adequately met.

Swindon's local hospital is Great Western Hospital (GWH), a large hospital containing a range of specialist health departments. One of these is the Pain Management Service, a multidisciplinary team consisting of specialist pain doctors and nurses, clinical psychologists, and physiotherapists. The team accepts both outpatient and inpatient referrals. Outpatients are referred if they are experiencing chronic pain (defined as pain that lasts for longer than three months; Merskey, 1986) and inpatients are referred when, for example, experiencing pain following surgery. Medical staff initially receive referrals into the team and refer on to physiotherapy or pain psychology if appropriate. Patients who have been referred to pain psychology are sent an opt-in letter, and then those who opt in are offered an initial assessment and short-term psychological support if appropriate. The UK prevalence of chronic pain is estimated to be between 35 and 51% (Fayaz et al., 2016). The prevalence of chronic pain increases with age (NHS Digital, 2019), but the prevalence among 18-25 year-olds has been estimated at around one in four (Fayaz et al., 2016). Chronic pain is associated with a range of negative mental health outcomes, such as anxiety, depression, self-harm, and suicide (Bair et al., 2003; van Tilburg et al., 2011) and evidence-based psychological

interventions such as cognitive behavioural therapy are recommended for chronic pain by the National Institute for Health and Care Excellence (NICE, 2021).

Given the well-established negative consequences of chronic pain, the shifting demographic picture of Swindon, and the robust evidence of health inequalities across the health service, it is important to monitor whether the demographic distribution of patients currently being supported by the Pain Management Service reflects the population it serves. However, to date, the Pain Management Service has not evaluated the representativeness of its patient population. Understanding how closely the observed patient population resembles the expected patient population, based on both wider population demographics and established pain prevalence estimates, may help to identify unconscious biases or barriers to care which can be resolved to improve access and reduce health inequality.

The current study

The current study aims to describe the demographics of the Pain Management Service and pain psychology patient populations in the year 2021-2022, comparing these with the populations from which they are drawn, at the hospital and local area levels (see Figure 1, below). The study aims to address the research question: “are there groups of patients who are underrepresented in the Pain Management Service at Great Western Hospital?”. In order to accurately answer this question, the study also takes into account the expected patient group demographics based on epidemiological studies of chronic pain and associated distress. The key demographic factors considered are age, sex, and ethnicity.

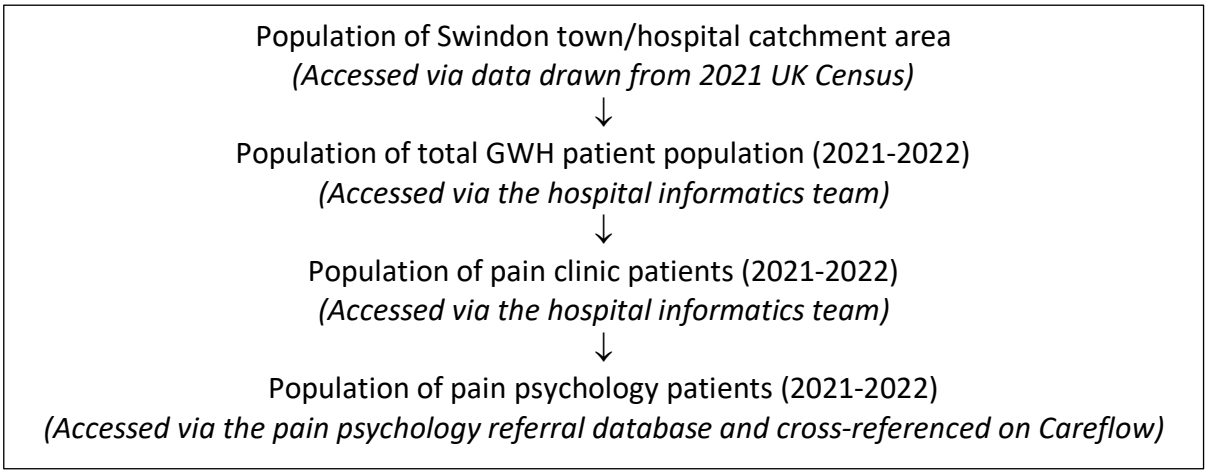

Figure 2 Population levels and their data sources.

Methods

The study was classed as a service evaluation and did not require registration with the trust's Clinical Audit Programme or formal ethical approval. Demographic data for individuals at each level of population were drawn from different sources and summarised separately. All data correspond to the year 2021-2022, though the census data represents a population snapshot on one particular date (21st March 2021). For each dataset, data were categorised according to sex as a binary variable, age in ten-year bands, and simplified ethnicity categories in order to standardise across datasets. The categories used follow guidance from the UK Government on reporting ethnicity (UK Government 2021).

Data describing patients seen by pain psychology were drawn from the referral database managed by the team. When individuals are referred to the pain psychology service, their details are added to a database which contains, amongst other information, name, hospital number, referral date, and date of assessment. Patients' hospital numbers were cross-referenced on Careflow, the hospital data system, to obtain the relevant demographic data. The data were then anonymised and saved into a new database containing only unique

patient IDs and demographic data relevant to the current project. Summary data describing patients seen by the Pain Management Service and in GWH as a whole were provided by the hospital informatics team in an already anonymised format. Data describing the general population of the area were taken from the 2021 UK Census, released online to the public in June 2022 (Office for National Statistics, 2022b).

It was noted that around 2/3^{rds} of the patients in the Pain Management Service dataset were registered as living in Swindon and around 1/3rd registered as living in Wiltshire, the surrounding county. It was hypothesised that there may be differences in demographic distribution between these two settings. For example, given Swindon's more urban setting, it was predicted that the population of Swindon would be proportionally younger and more ethnically diverse than Wiltshire. These hypotheses were confirmed by comparing the demographic distribution of the regions in the 2021 UK Census data (see Table 1). A *weighted catchment* dataset was therefore produced, which combined the 2021 UK Census data for Swindon and Wiltshire and weighted each according to the proportions observed in the Pain Management Service dataset. This enabled more accurate comparison between the patient populations of the Pain Management Service and pain psychology and the populations from which they were drawn.

Formal statistical comparison was not considered appropriate due to substantial variation in sample sizes between the population levels (see Table 2). Although equal sample size is not an assumption of a statistical test like the ANOVA, the vast differences in sample sizes meant that the variances between groups were unequal, which does violate the

assumptions of the ANOVA. In addition, the primary purpose of the study was to provide results which were understandable and actionable to a wide range of stakeholders,

Table 1 Demographic distributions of Swindon and Wiltshire samples, taken from the 2021 UK Census

Variable	Swindon n	Swindon %	Wiltshire n	Wiltshire %
Age				
00-09	28,800	12.33	55,100	10.80
10-19	27,100	11.60	57,600	11.29
20-29	27,300	11.69	52,800	10.34
30-39	34,700	14.85	61,600	12.07
40-49	32,700	14.00	63,000	12.34
50-59	32,800	14.04	75,600	14.81
60-69	23,700	10.15	61,900	12.13
70-79	16,800	7.19	52,300	10.25
80-89	8,000	3.42	24,900	4.88
90+	1,700	0.73	5,600	1.10
Sex				
Male	116,100	49.74	251,700	49.32
Female	117,300	50.26	258,600	50.68
Ethnicity				
Asian	27,173	11.64	10,876	2.13
Black	6,123	2.62	5,786	1.13
Mixed	4,717	2.02	6,343	1.24
White British	173,231	74.22	459,594	90.06
White other	16,911	7.25	21,829	4.28
Any other ethnic group	5,256	2.25	5,915	1.16

including nurses, physiotherapists, doctors, and service managers, some of whom may not have received formal training in interpreting test statistics. Results were therefore presented as descriptive statistics and visualised graphically to maximise their accessibility.

Table 2 Datasets and their sample sizes

Dataset	N
Pain psychology	107
Pain Management Service	1,621
Great Western Hospital	162,696
Weighted catchment	284,268

Results

Age

The distribution of individuals in each age band are presented in Table 1. The distribution of ages in the general population of the weighted catchment area is the most even, with roughly 10-15% of the population falling in each age category from 0-89 years. The age distribution of the GWH patient population broadly follows the same distribution as the weighted catchment, though with slightly fewer individuals aged 10-29 and slightly more aged >60. The relative risk of hospital admissions is low in <30 age group, while the risk is higher in the >60 age group (NHS Digital 2022), so this distribution is in line with expectations.

This equal distribution shifts to a more normal distribution for patients of the pain clinic, where we see relatively fewer patients aged <30 and >80 years and a peak in population aged 50-59 years. This distribution is maintained in the population of pain psychology patients, but is even more truncated, with more than half of the population aged 40-59 years and fewer than 10% of the population falling outside the 30-69 age bracket. No individuals aged <18 years are present in either pain group as the service only treats adult

patients. This distribution, differs somewhat to the expected prevalence of chronic pain: the risk of chronic pain generally increases linearly with age (Fayaz et al., 2016), with a peak in prevalence in the >75 age group (Croft et al., 1993; Elliott et al., 1999).

Table 1. Proportions of age (in 10-year bands) across population levels

Age bands	Weighted catchment	GWH patients	Pain clinic patients	Pain psychology patients
00-09	12.33	11.26	0.00	0.00
10-19	11.60	8.66	1.42	0.00
20-29	11.69	9.50	7.53	5.61
30-39	14.85	12.43	15.36	16.82
40-49	14.00	10.80	19.31	29.91
50-59	14.04	13.02	23.32	23.36
60-69	10.15	12.27	16.22	20.56
70-79	7.19	11.78	11.35	2.80
80-89	3.42	7.88	4.94	0.93
90+	0.73	2.41	0.56	0.00

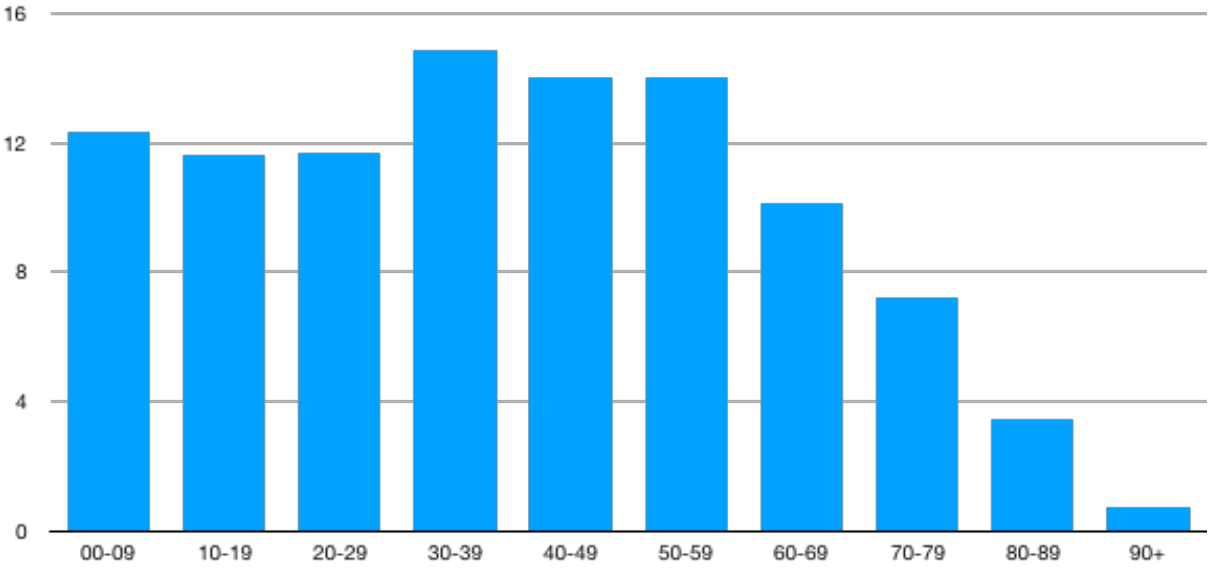

Figure 3 Bar chart showing age distribution (in 10-year bands) in the weighted catchment sample

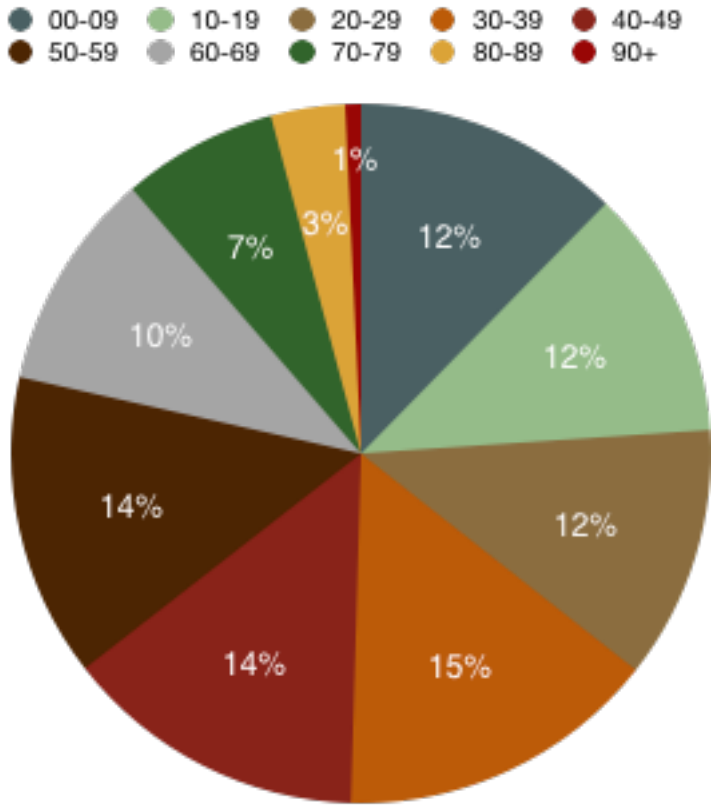

Figure 4 Pie chart showing age distribution (in 10-year bands) in the weighted catchment sample

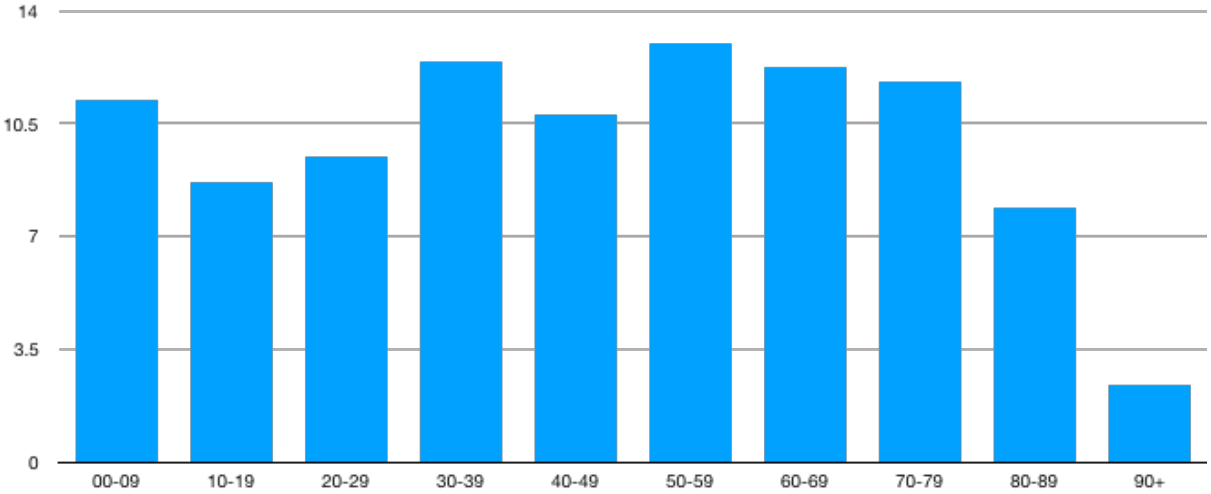

Figure 5 Bar chart showing age distribution (in 10-year bands) in Great Western Hospital sample

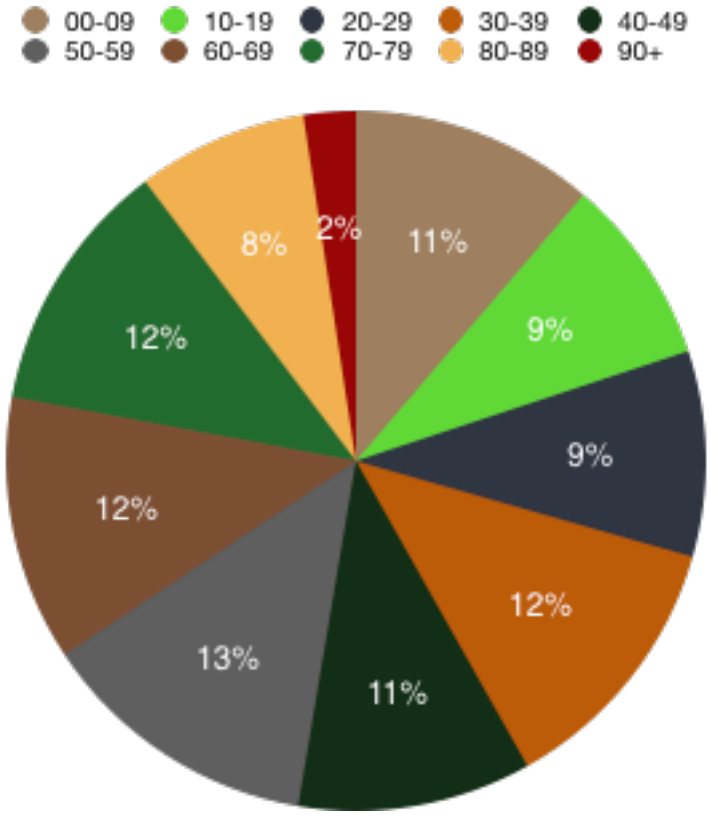

Figure 6 Pie chart showing age distribution (in 10-year bands) in Great Western Hospital sample

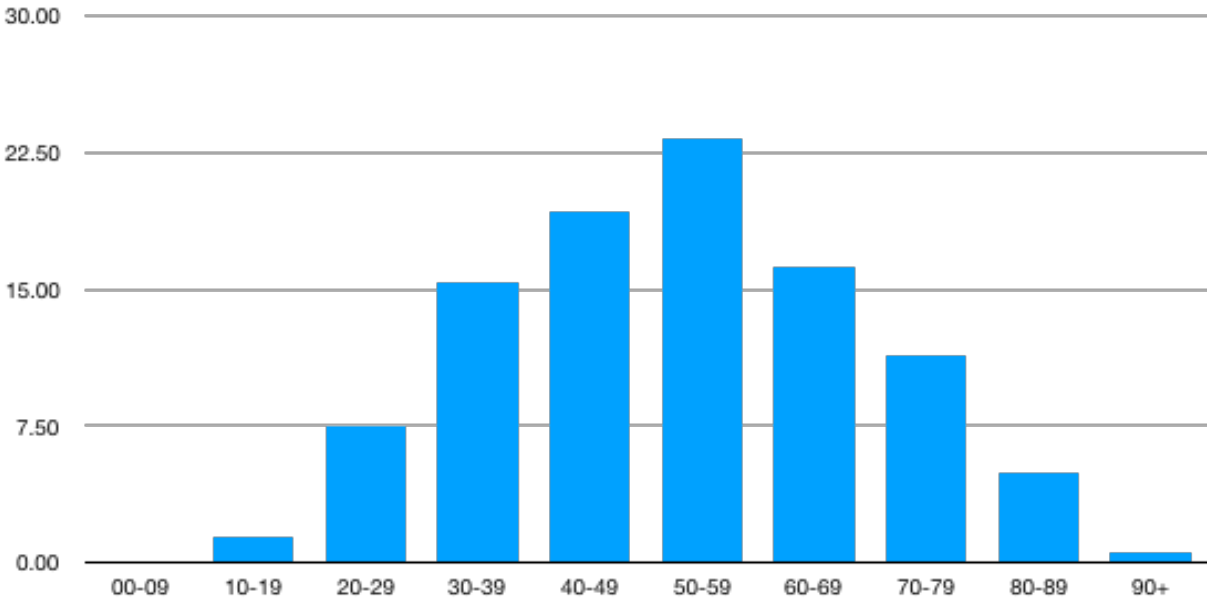

Figure 7 Bar chart showing age distribution (in 10-year bands) in the pain clinic sample

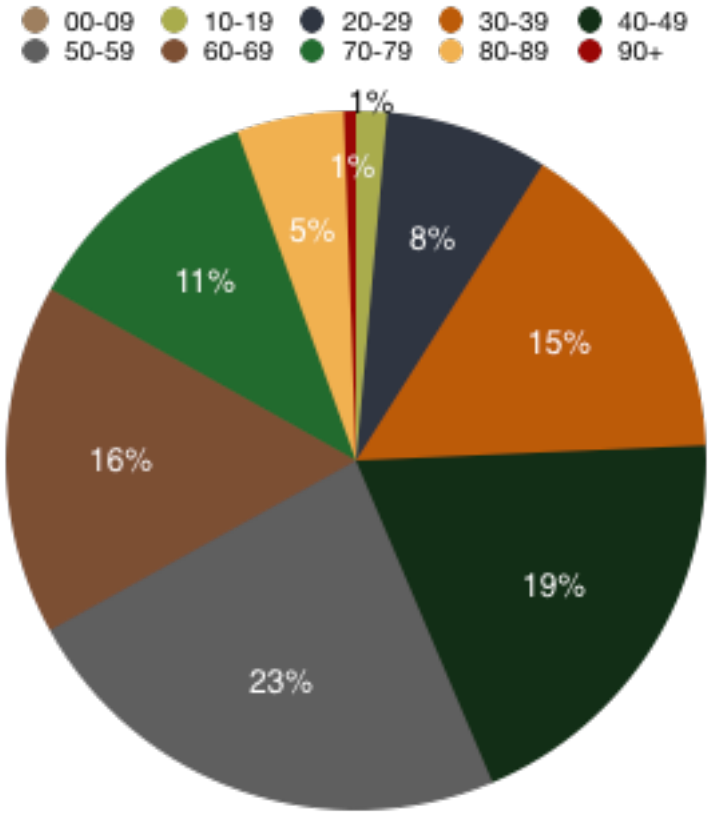

Figure 8 Pie chart showing age distribution (in 10-year bands) in the pain clinic sample

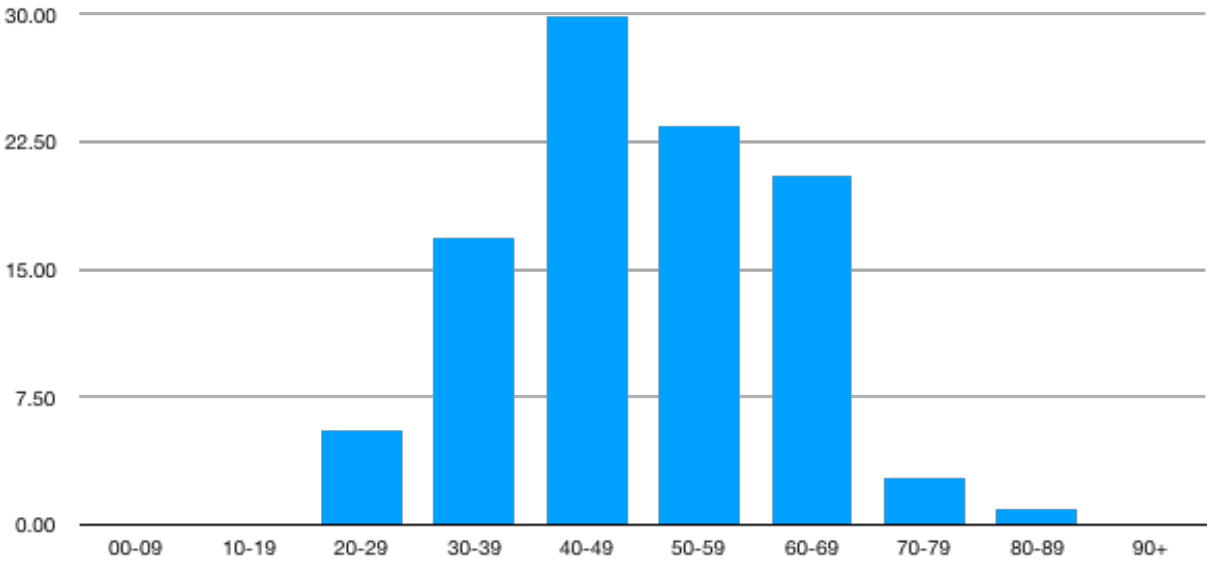

Figure 9 Bar chart showing age distribution (in 10-year bands) in the pain psychology sample

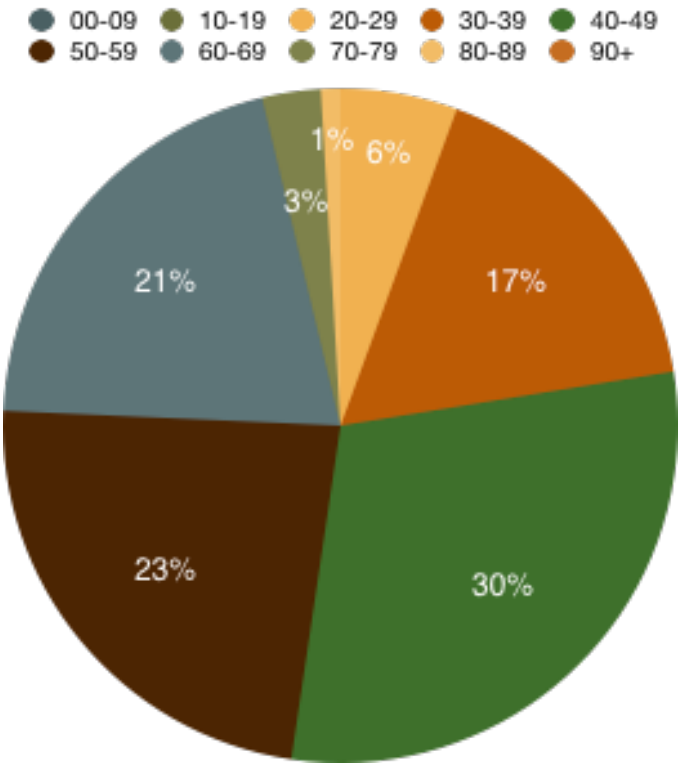

Figure 10 Pie chart showing age distribution (in 10-year bands) in the pain psychology sample.

Sex

The distribution of males and females at each level of population is displayed in Table 2. Whilst the data from the census shows the expected 50% split in the sexes, the hospital populations show a higher proportion of female patients. In the GWH population there is marginally more female patients (54%), while in both the pain clinic and pain psychology more than 70% of the patients are female.

Table 2. Proportions of sex across population levels

Sex	Weighted catchment	GWH patients	Pain clinic patients	Pain psychology patients
Male	49.74	45.75	27.45	28.97
Female	50.26	54.25	72.55	71.03

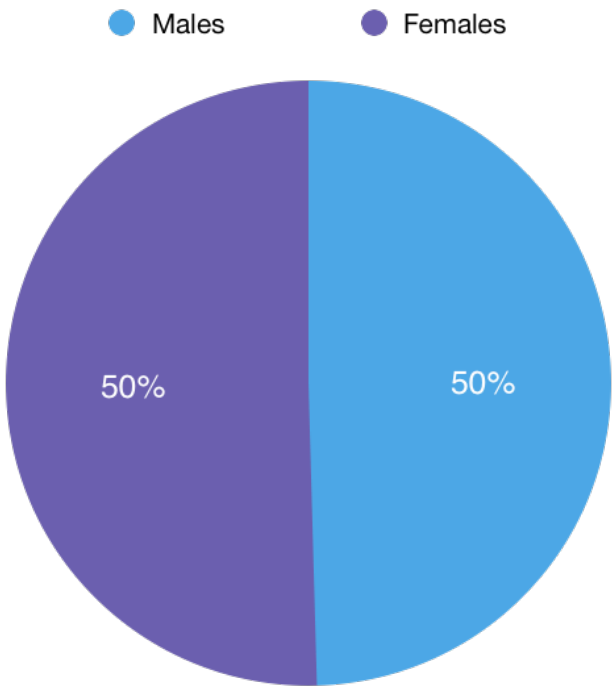

Figure 11 Pie chart showing sex split in the weighted catchment sample

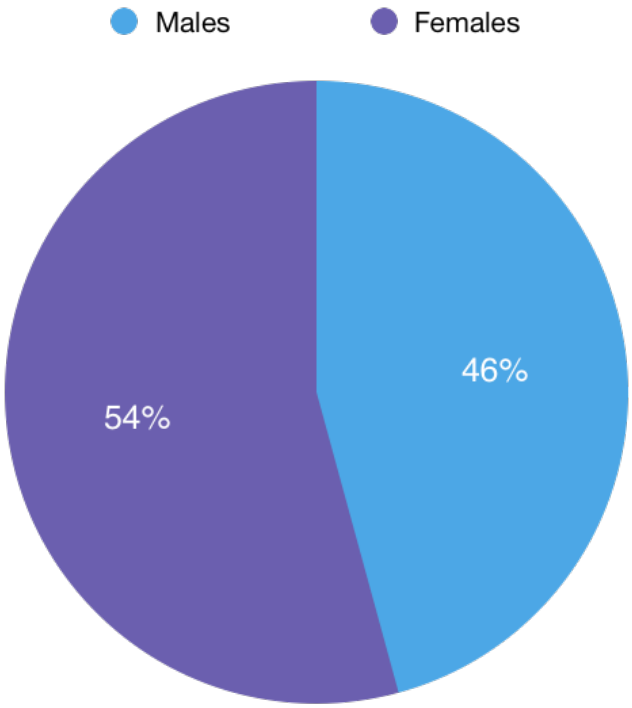

Figure 12 Pie chart showing sex split in the Great Western Hospital sample

Pain clinic

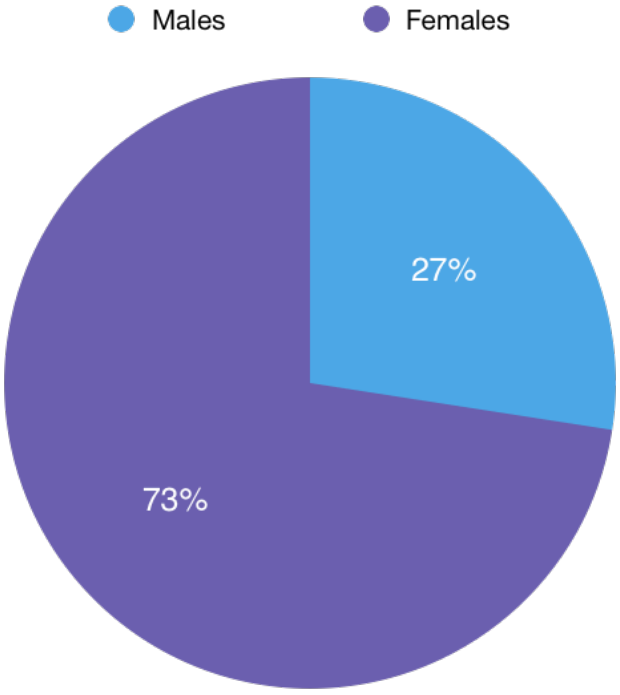

Figure 13 Pie chart showing sex split in the pain clinic sample

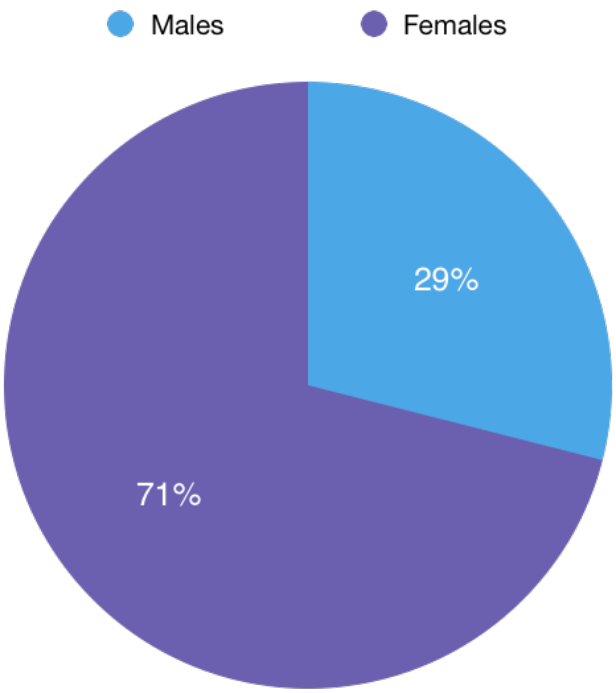

Figure 14 Pie chart showing sex split in the pain psychology sample

Ethnicity

The vast majority of individuals across all levels of population were White. The proportion of White individuals ranged from 79% in the GWH population to 88% in the pain clinic population. The largest minoritised ethnicity group in the weighted catchment area was the Asian group, which made up 7.38% of the total population. Examining the weighted catchment data, the vast majority (72.44%) of the individuals in the Asian group identified as being of south Asian heritage (Indian, Bangladeshi, or Pakistani), with 5.48% identifying as Chinese and 22.08% identifying as "Asian other". The Asian group was followed by the White other group, which made up 5.92% of the population. All other groups constituted no more than 2% of the population each. The ethnicity of all participants in the national census was captured, whereas for a small proportion of the patients in the hospital groups (<5%) ethnicity data were missing.

Table 3. Proportions of ethnicity across population levels

Ethnicity	Weighted catchment	GWH patients	Pain clinic patients	Pain psychology patients
Asian	7.38	5.50	2.28	4.67
Black	1.96	1.73	1.79	2.80
Mixed	1.67	0.88	0.68	1.87
White British	81.31	78.97	88.28	82.24
White other	5.92	5.07	3.58	1.87
Any other ethnic group	1.76	2.89	1.60	1.87
Not known	0.00	4.96	1.79	4.67

The distribution of ethnicity seen in the weighted catchment area was broadly repeated at the GWH patient population and the pain psychology levels, with most patients falling in the

White British group and the next highest proportion group being the Asian group (GWH = 5.50%, pain psychology = 4.67%). While the White other group at the GWH level was in line with the weighted catchment level (5.07%), it was lower at the pain psychology level (1.87%). The distribution of ethnicity categories differed most at the level of the pain clinic, with a higher proportion (88.28%) of individuals falling in the White British group and a lower proportion identifying as Asian (2.28%) and White other (3.58%).

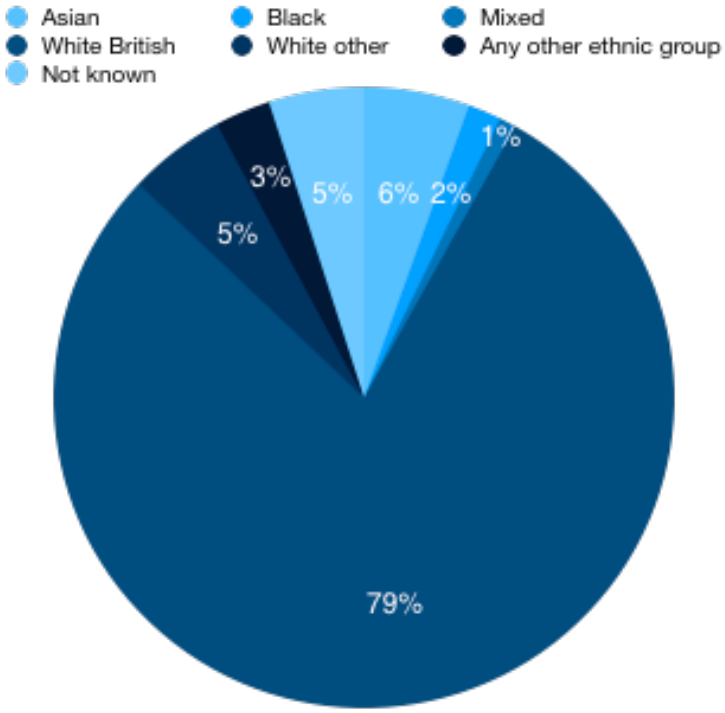

Figure 15 Pie chart showing ethnicity groups in the weighted catchment sample

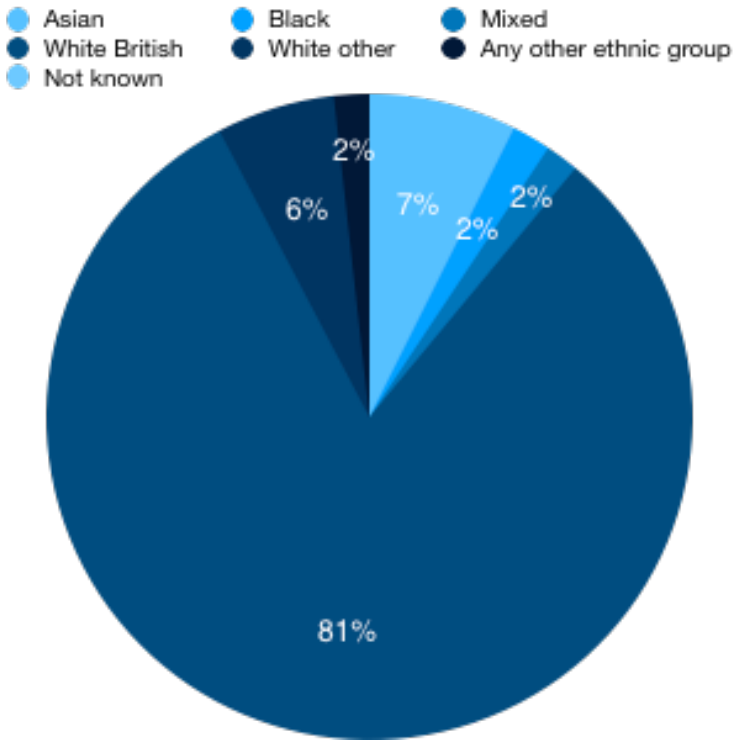

Figure 16 Pie chart showing ethnicity groups in the Great Western Hospital sample

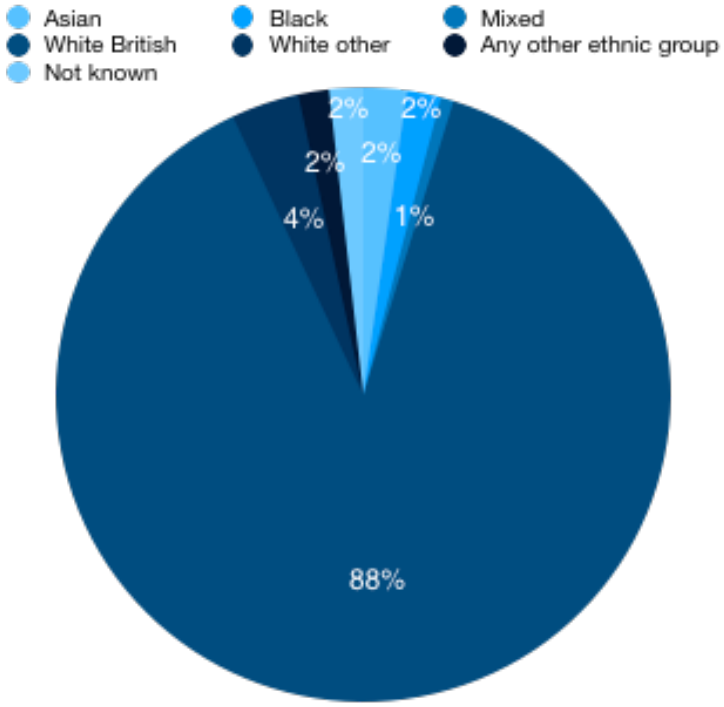

Figure 17 Pie chart showing ethnicity groups in the pain clinic sample

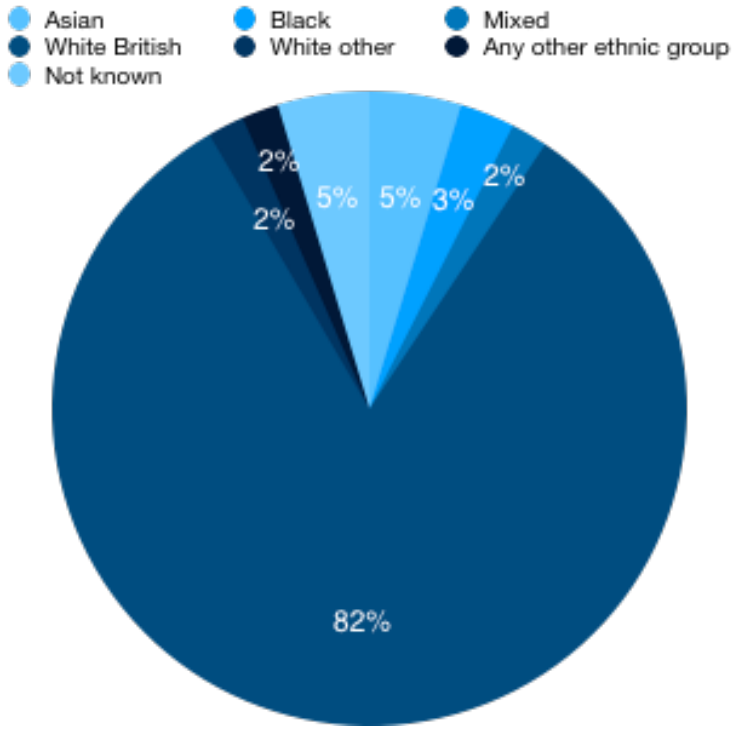

Figure 18 Pie chart showing ethnicity groups in the pain psychology sample

Discussion

The aim of the current study was to establish whether the patient groups treated by the pain clinic and pain psychology at Great Western Hospital were demographically representative of the local population, with a view to identifying whether any groups were being underserved by the service. The findings showed that, in general, GWH and the pain service treat a patient sample broadly representative of the wider population in the context of the epidemiological expectations of chronic pain. However, some groups appeared to be underrepresented: individuals aged >70 years old, men, and individuals of Asian heritage.

The proportion of individuals aged >70 years seen by pain psychology was markedly lower than in other groups – less than 4% versus 10-20% – and lower than the proportion that would be expected from prevalence estimates (Fayaz et al., 2016). This difference may be due to differences in this group's need for or seeking of psychological support. For example, individuals are generally referred to pain psychology for support managing distress related to pain. It is possible that adults aged >70 years are more accepting of pain as an expected feature of life and therefore experience less pain-related distress (Rustøen et al., 2005); studies have shown, for example, an association between older age and higher pain acceptance and a lower negative impact of fibromyalgia (Tangen et al., 2020). It may also be that chronic pain causes less role interference in older adults than in adults of working age, which could also lead to lower levels of distress and therefore less need for psychological support (Gignac et al., 2013). Alternatively, the lower proportion of >70s seen by pain psychology may be due to systemic factors. For example, the attitude described above – that increased pain is an expected part of growing older – may be the attitude of clinicians,

rather than patients, which may mean older adults are less likely to be referred for psychological support.

The results also showed a higher number of female than male patients in the pain clinic, a result that is in line with prevalence estimates of chronic pain, which is more prevalent in women (Andrews et al., 2018; Fayaz et al., 2016). Many conditions which lead to chronic pain, and which are seen often in clinic, affect either only (eg endometriosis) or predominantly (eg fibromyalgia) birth-registered females (Fillingim, 2023; Wolfe et al., 1995). However, some prevalence estimates suggest that the difference in chronic pain prevalence between the sexes is small – for example, the 2017 NHS Health Survey for England found that 38% of women and 30% of men reported chronic pain. The differences between the sexes observed in the pain clinic and pain psychology here are more substantial and may be due to additional factors, such as help-seeking behaviour. It has been robustly shown that women are more likely to seek help for health concerns than men (Kessler et al., 1981; Wang et al., 2013). There may be a cohort of men in Swindon and Wiltshire who experience chronic pain and associated distress but do not seek professional support, so the proportion of patients seen in clinic is more heavily skewed towards women. Alternatively, men may be less likely to be referred to the pain clinic despite presenting to services. It has been proposed that men are socialised to minimise their expression of pain (Bernardes et al., 2008) – referring clinicians may perceive male patients as less in need of specific pain interventions based on less overtly distressed presentations.

One of the most notable features of the ethnicity categories across population levels is the drop in proportion of Asian individuals from the weighted catchment area to the hospital

level and Pain Management Service (7.38% to 5.50% and 2.28%, respectively). This finding is unexpected, as research broadly shows a higher prevalence of chronic pain in Asian populations compared with White populations (Choudhury et al., 2013; Palmer et al., 2007). For example, Williams et al. (1993), reported that south Asian women were more likely to report musculoskeletal pain than European women of the same age, and Njobvu et al. reported an association between south Asian heritage and a higher risk of chronic pain disorders such as arthritis (Njobvu et al., 1999). There is also evidence that south Asian men display lower levels of pain tolerance than British men in experimental studies of pain (Watson et al., 2005), and that the association between chronic pain and depressive symptoms is similar in British Asian and White populations (Nicholl et al., 2015).

It may be the case that individuals from Asian backgrounds are less likely to seek support for chronic pain. However, there is evidence that south Asian individuals are at least as or more likely than White individuals to visit their GP for medical concerns (Brewin, 1980). The explanation for the current findings, then, may lie in the intersection between how pain is experienced by patients from Asian backgrounds and how that experience is understood by medical professionals. The way that pain is defined, described, and perceived is heavily culturally dependent – as noted in the review by Brady et al. (2016), emotional responses to pain, such as stoicism and coping strategies, are mediated by beliefs and values which are culturally influenced. These differences may impact, for example, an individual's likelihood of receiving support for their pain (Jacobs & Pentaris, 2021). There is evidence that Asian individuals are more likely to believe that pain should be handled bravely (Im et al., 2008), and to show stoic pain behaviour (Im et al., 2007). If healthcare workers such as GPs and

hospital doctors are unaware of these cultural attitudes, they may be less likely to recognise chronic pain and refer Asian individuals to the pain clinic.

A further barrier which may prevent healthcare professionals from referring patients onto the pain clinic and pain psychology is language. A shared understanding of subjective pain is essential for appropriate care planning, and studies have shown that patient- and nurse-reported pain ratings align best when both individuals share the same language (Harrison et al., 1996). Linguistic differences may lead to misunderstandings about the need for specialist pain intervention. Further, qualitative feedback from pain doctors as part of the current project revealed that medical staff regularly make informal assessments about whether individuals have the English language capability to engage with psychological therapy, and that this will influence whether they are referred to pain psychology. These informal assessments may also be being conducted by other medical staff, such as GPs or other medical doctors at the hospital, preventing referral to the pain clinic in the first place. Thus, language may influence referrals in two ways: first, linguistic differences may lead to misunderstandings about subjective pain, which could lead to patients' pain or distress being underestimated, and second, perceived English competence may influence whether individuals are considered appropriate for onward referral, regardless of pain.

The below-expected proportion of Asian patients in the pain clinic may also be due to structural features of the way in which the service is designed and run. The Pain Management Service exists in the context of a health service designed by, and primarily for, White people, and is currently led by White members of staff. This may limit the ability of

the team to identify internalised racism, unconscious prejudices, or other barriers to access in the design of the service.

Recommendations

Two broad strategies could be employed to improve the inclusion of the underrepresented groups identified in the current study. The first assumes that these individuals are not being seen by the pain team because they are not presenting to medical services in the first place. Following this assumption, the service could improve the representativeness of its patient population by engaging in active outreach. This would involve increasing education about chronic pain, pain medicine, and pain psychology in the general population, with a view to increasing awareness, reducing stigma, and improving signposting to appropriate services (Rickwood et al., 2005). This outreach would be aimed at individuals aged >70 years, men, and individuals of Asian heritage. The outreach could involve information campaigns like leaflets being distributed at universal medical settings such as GP surgeries. Alternatively, outreach could utilise community centres and leaders to raise awareness in non-medical settings. For example, in the 2021 Census, over 60% of south Asian respondents identified as being either Muslim or Hindu (Office for National Statistics, 2022b). Recruiting faith leaders like Imams and Pūjari and distributing information in religious settings like mosques and temples may help to spread awareness to a wide collection of individuals in the community, rather than just individuals attending their GP service. Settings which attract predominantly men, for example football matches, barbershops, or organisations like the Men Shed, could be targeted in similar ways to encourage help-seeking behaviour. Outreach towards >70s could be achieved by distributing information about the pain service via charities such as Age UK, organisations like the Lions or University of the Third Age, or using

social media. There is robust evidence that community outreach programmes are effective in improving mental health stigma, literacy, and help-seeking behaviours (Thornicroft et al., 2014; Xu et al., 2018).

The second strategy for improving representation in the pain service assumes that individuals are presenting to medical services, but not being appropriately referred on. This strategy involves improving education and awareness among medical staff with a view to changing referral behaviour (Marcelin et al., 2019). Staff who typically refer patients to the pain service, for example GPs and hospital doctors, could receive training on factors like cultural sensitivity to improve their understanding of how pain is perceived and communicated by different ethnic and cultural groups. In addition, training on unconscious bias may help referring staff become more aware of their own attitudes towards pain and different ethnicities, and how these attitudes might shape referral behaviour (Marcelin et al., 2019). Staff may also benefit from specific education on pain and distress across the lifespan, to better understand how the experience of pain might change as individuals age. Further, staff could receive training on trust policies about the use of interpreters and reasonable adjustments for language barriers. This training could be mandated, or encouraged by counting as continuous professional development, to maximise participation.

Related to this second strategy, the White-centric structure of the Pain Management Service may mean that the service practices systematic racism and exclusion without conscious awareness. A key recommendation based on the current findings is the active inclusion of minoritised ethnicity voices in service design and implementation. This may take the form of

steering groups led by experts by experience or the recruitment of minoritised ethnicity clinicians into senior roles within the team.

The results of the current study were formally fed back to the Pain Management Service via presentation and discussion. Some of the interpretations of the data, for example regarding referrals based on English language proficiency, were suggested by members of the team. In response to the findings of the study, the team agreed to begin the process of creating a group of experts by experience with whom possible interventions to improve the representation of the service could be co-designed.

Strengths and limitations

The current study has many strengths. For example, the study benefited from large sample sizes and very little missing data, with no missing data in the age and sex variables and an average of 2.86% falling in the 'Not known' category for ethnicity. This lowers the risk of bias and increases confidence in the validity and representativeness of the data (Sterne et al., 2009).

However, the study must also be interpreted in light of its limitations. The comparisons between population levels were descriptive and not tested using formal statistical analysis, which means conclusions cannot be drawn about the statistical significance of any differences between the population levels. However, as noted in the methods section above, the substantial differences in sample size between the datasets meant that statistical comparison would have been inappropriate. Further, the results of the study were intended to be understood by a broad spectrum of stakeholders, with the goal being to identify

clinically meaningful, rather than statistically significant, differences on which decisions about service design could be based.

A further limitation of the study is that it was not possible to conduct multivariate analyses as three of the four datasets (weighted catchment, GWH, and the pain clinic) were available only as summary statistics, rather than raw data with unique patient IDs. It may be the case that groups with combinations of characteristics, for example Asian individuals aged >70, are particularly underrepresented in the pain clinic and pain psychology. However, this intersectionality could not be examined.

The current study consisted of analysis of secondary data, and hence none of the study participants were directly involved in its production. The study would have benefited from the involvement of patient experts by experience, particularly in interpreting its results and making recommendations for the service, for example around potential help-seeking behaviour and attitudes towards pain (Sacristán et al., 2016). Future studies, particularly projects exploring the recommendations made above, should involve experts by experience at each stage of development, from conception to dissemination.

Directions for future research

Future studies should aim to conduct formal multivariate tests of demographic representativeness to establish a greater depth of understanding of underrepresented groups. These findings were presented to the pain team and their interpretations and perspectives were considered in the writing of this manuscript. However, future research could be conducted to qualitatively examine the perspective of both pain clinicians and

referring clinicians to better understand barriers to treatment. For example, to the author's knowledge, no research has been published examining how the perception of patients' English language skills influence decisions to refer to psychology. It would be valuable to explore these factors in order to guide recommendations and service improvements. Future research should also include the perspectives of patients to help guide decision-making in both research project and service design.

Conclusion

The current study aimed to establish the demographic representativeness of the patient groups treated by the pain clinic and pain psychology at Great Western Hospital, Swindon, in order to identify whether any groups were being underserved. The results showed that men, individuals aged >70 years, and individuals of Asian heritage may be underrepresented in the service. Interventions such as community outreach and clinician education may help to improve representation in these groups.

References

Andrews, P., Steultjens, M., & Riskowski, J. (2018). Chronic widespread pain prevalence in the general population: A systematic review. *European Journal of Pain*, *22*(1), 5-18. https://doi.org/https://doi.org/10.1002/ejp.1090

Bair, M. J., Robinson, R. L., Katon, W., & Kroenke, K. (2003). Depression and Pain Comorbidity: A Literature Review. *Archives of Internal Medicine*, *163*(20), 2433-2445. https://doi.org/10.1001/archinte.163.20.2433

Bernardes, S. F., Keogh, E., & Lima, M. L. (2008). Bridging the gap between pain and gender research: a selective literature review. *European Journal of Pain*, *12*(4), 427-440.

Brady, B., Veljanova, I., & Chipchase, L. (2016). Are multidisciplinary interventions multicultural? A topical review of the pain literature as it relates to culturally diverse patient groups. *Pain*, *157*(2). https://journals.lww.com/pain/fulltext/2016/02000/are_multidisciplinary_interventions_multicultural_.7.aspx

Brewin, C. (1980). Explaining the lower rates of psychiatric treatment among Asian immigrants to the United Kingdom: a preliminary study. *Social Psychiatry*, *15*, 17-19.

Cabinet Office. (2018). *Race Disparity Audit: Summary Findings from the Ethnicity Facts and Figures website*. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/686071/Revised_RDA_report_March_2018.pdf

Choudhury, Y., Bremner, S. A., Ali, A., Eldridge, S., Griffiths, C. J., Hussain, I., Parsons, S., Rahman, A., & Underwood, M. (2013). Prevalence and impact of chronic widespread pain in the Bangladeshi and White populations of Tower Hamlets, East London. *Clinical rheumatology*, *32*, 1375-1382.

Croft, P., Rigby, A., Boswell, R., Schollum, J., & Silman, A. (1993). The prevalence of chronic widespread pain in the general population. *The Journal of rheumatology*, *20*(4), 710-713.

Department of Health. (2021). *NHS Constitution for England*

Elliott, A. M., Smith, B. H., Penny, K. I., Smith, W. C., & Chambers, W. A. (1999). The epidemiology of chronic pain in the community. *The Lancet*, *354*(9186), 1248-1252.

Faculty of Pain Medicine. (2021). *Core Standards for Pain Management Services in the UK*

Fayaz, A., Croft, P., Langford, R. M., Donaldson, L. J., & Jones, G. T. (2016). Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open*, *6*(6), e010364. https://doi.org/10.1136/bmjopen-2015-010364

Fillingim, R. B. (2023). Chapter 49 - Sex, gender, and pain. In M. J. Legato (Ed.), *Principles of Gender-Specific Medicine (Fourth Edition)* (pp. 769-792). Academic Press. https://doi.org/https://doi.org/10.1016/B978-0-323-88534-8.00011-0

Gignac, M. A. M., Backman, C. L., Davis, A. M., Lacaille, D., Cao, X., & Badley, E. M. (2013). Social role participation and the life course in healthy adults and individuals with osteoarthritis: Are we overlooking the impact on the middle-aged? *Social Science & Medicine*, *81*, 87-93. https://doi.org/https://doi.org/10.1016/j.socscimed.2012.12.013

Harrison, A., Ahmed Busabir, A., ObeidAl-Kaabi, A., & Khahd Al-Awadi, H. (1996). Does sharing a mother-tongue affect how closely patients and nurses agree when rating the patient's pain, worry and knowledge? *Journal of Advanced Nursing*, *24*(2), 229-235.

Im, E.-O., Chee, W., Guevara, E., Liu, Y., Lim, H.-J., Tsai, H.-M., Clark, M., Bender, M., Kim, K. S., & Kim, Y. H. (2007). Gender and ethnic differences in cancer pain experience: a multiethnic survey in the United States. *Nursing Research*, *56*(5), 296-306.

Im, E.-O., Liu, Y., Kim, Y. H., & Chee, W. (2008). Asian American cancer patients' pain experience. *Cancer Nursing*, *31*(3), E17-E23.

Jacobs, L., & Pentaris, P. (2021). Factors affecting the help-seeking behaviour of Black Asian Minority Ethnic (BAME) groups for mental health services in the UK: a literature review. *Greenwich Social Work Review*, *2*(1), 156-170.

Jones, C. (2019). *Joint Strategic Needs Assessment: An Overview of Health and Wellbeing in Swindon*

Kapadia, D., Zhang, J., Salway, S., Nazroo, J., Booth, A., Villarroel-Williams, N., Bécares, L., & Esmail, A. (2022). *Ethnic Inequalities in Healthcare: A Rapid Evidence Review*

Kessler, R. C., Brown, R. L., & Broman, C. L. (1981). Sex differences in psychiatric help-seeking: Evidence from four large-scale surveys. *Journal of health and social behavior*, 49-64.

Marcelin, J. R., Siraj, D. S., Victor, R., Kotadia, S., & Maldonado, Y. A. (2019). The impact of unconscious bias in healthcare: how to recognize and mitigate it. *The Journal of infectious diseases*, *220*(Supplement_2), S62-S73.

Merskey, H. E. (1986). Classification of chronic pain: Descriptions of chronic pain syndromes and definitions of pain terms. *Pain*(Suppl 3), 226.

National Institute for Health and Care Excellence. (2021). *Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain*. https://www.nice.org.uk/guidance/NG193

NHS Digital. (2019). *Health survey for England 2017*. https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2017

NHS Digital (2022). *Hospital Admitted Patient Care Activity, 2021-22*. https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2021-22

NHS Digital (2023). *Detentions under the Mental Health Act* https://www.ethnicity-facts-figures.service.gov.uk/health/mental-health/detentions-under-the-mental-health-act/latest/

Nicholl, B. I., Smith, D. J., Cullen, B., Mackay, D., Evans, J., Anderson, J., Lyall, D. M., Fawns-Ritchie, C., McIntosh, A. M., Deary, I. J., Pell, J. P., & Mair, F. S. (2015). Ethnic differences in the association between depression and chronic pain: cross sectional results from UK Biobank. *BMC Family Practice*, *16*(1), 128. https://doi.org/10.1186/s12875-015-0343-5

Njobvu, P., Hunt, I., Pope, D., & MacFarlane, G. (1999). Pain amongst ethnic minority groups of South Asian origin in the United Kingdom: a review. *Rheumatology*, *38*(12), 1184-1187.

Office for National Statistics. (2022a). *Ethnic group*. https://www.ons.gov.uk/datasets/TS021/editions/2021/versions/3

Office for National Statistics. (2022b). *UK 2021 Census* https://www.ons.gov.uk/census

Office for National Statistics. (2023). *How life has changed in Swindon: Census 2021*. https://www.ons.gov.uk/visualisations/censusareachanges/E06000030

Palmer, B., Macfarlane, G., Afzal, C., Esmail, A., Silman, A., & Lunt, M. (2007). Acculturation and the prevalence of pain amongst South Asian minority ethnic groups in the UK.

Rickwood, D., Deane, F. P., Wilson, C. J., & Ciarrochi, J. (2005). Young people's help-seeking for mental health problems. *Australian e-journal for the Advancement of Mental health*, *4*(3), 218-251.

Rustøen, T., Wahl, A. K., Hanestad, B. R., Lerdal, A., Paul, S., & Miaskowski, C. (2005). Age and the Experience of Chronic Pain: Differences in Health and Quality of Life Among Younger, Middle-Aged, and Older Adults. *The Clinical Journal of Pain*, *21*(6). https://journals.lww.com/clinicalpain/fulltext/2005/11000/age_and_the_experience_of_chronic_pain_.8.aspx

Sacristán, J. A., Aguarón, A., Avendaño-Solá, C., Garrido, P., Carrión, J., Gutiérrez, A., Kroes, R., & Flores, A. (2016). Patient involvement in clinical research: why, when, and how. *Patient preference and adherence*, 631-640.

Sterne, J. A., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G., Wood, A. M., & Carpenter, J. R. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *Bmj*, *338*.

Tangen, S. F., Helvik, A.-S., Eide, H., & Fors, E. A. (2020). Pain acceptance and its impact on function and symptoms in fibromyalgia. *Scandinavian Journal of Pain*, *20*(4), 727-736. https://doi.org/doi:10.1515/sjpain-2020-0049

Thornicroft, C., Wyllie, A., Thornicroft, G., & Mehta, N. (2014). Impact of the "Like Minds, Like Mine" anti-stigma and discrimination campaign in New Zealand on anticipated and experienced discrimination. *Australian & New Zealand Journal of Psychiatry*, *48*(4), 360-370. https://doi.org/10.1177/0004867413512687

UK Government (2021). *Writing about ethnicity*. Retrieved 25th April 2024 from https://www.ethnicity-facts-figures.service.gov.uk/style-guide/writing-about-ethnicity

van Tilburg, M. A., Spence, N. J., Whitehead, W. E., Bangdiwala, S., & Goldston, D. B. (2011). Chronic pain in adolescents is associated with suicidal thoughts and behaviors. *The Journal of Pain*, *12*(10), 1032-1039.

Wang, Y., Hunt, K., Nazareth, I., Freemantle, N., & Petersen, I. (2013). Do men consult less than women? An analysis of routinely collected UK general practice data. *BMJ open*, *3*(8), e003320.

Watson, P. J., Latif, R. K., & Rowbotham, D. J. (2005). Ethnic differences in thermal pain responses: A comparison of South Asian and White British healthy males. *Pain*, *118*(1), 194-200. https://doi.org/https://doi.org/10.1016/j.pain.2005.08.010

Williams, R., Bhopal, R., & Hunt, K. (1993). Health of a Punjabi ethnic minority in Glasgow: a comparison with the general population. *Journal of Epidemiology & Community Health*, *47*(2), 96-102.

Wolfe, F., Ross, K., Anderson, J., Russell, I. J., & Hebert, L. (1995). The prevalence and characteristics of fibromyalgia in the general population. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *38*(1), 19-28.

Xu, Z., Huang, F., Koesters, M., Staiger, T., Becker, T., Thornicroft, G., & Ruesch, N. (2018). Effectiveness of interventions to promote help-seeking for mental health problems: systematic review and meta-analysis. *Psychological medicine*, *48*(16), 2658-2667.

University of Bath
Doctorate in Clinical Psychology

Main Research Project

Characterising homotypic and heterotypic continuity of mental health symptoms in autism: a longitudinal study across childhood

Elystan Roberts

Department of Psychology, University of Bath

egr22@bath.ac.uk

Word count: 3,075

Supervised by: Prof Rachael Bedford, Queen Mary University of London

Proposed journal for publication:

Journal of the American Academy of Child & Adolescent Psychiatry

Author guidelines for this journal can be found here: https://www.jaacap.org/content/authorinfo

Introduction

Autism is a neurodevelopmental condition frequently accompanied by co-occurring difficulties, including mental health problems. The prevalence of mental health problems in autism is significantly higher than in the general population (Simonoff et al., 2020). Co-occurring difficulties appear to emerge early in life, with high rates of depression, social and specific phobias, and anxiety observed in autistic children as young as preschool age (Gadow et al., 2004; Hayashida et al., 2010). However, the stability of these mental health problems as autistic individuals transition through childhood is not well understood. Understanding how co-occurring mental health problems change over time can inform how best to support autistic young people.

Among typically developing (TD) children, mental health symptoms show substantial stability through childhood and adolescence: symptoms at earlier timepoints predict the same symptoms later on (Snyder et al., 2017). Indeed, a recent review concluded that, across the lifespan, homotypic continuity is substantially more common than *heterotypic* continuity (mental health symptoms predicting different symptoms later on; Oldehinkel & Ormel, 2023). However, earlier in development, during toddler and preschool-age years, there is evidence for both homotypic and heterotypic continuity. For example, Luby et al. (2014) examined the associations between internalising (depression and anxiety), externalising (conduct disorder and oppositional defiant disorder), and attentional (attention deficit/hyperactivity disorder, ADHD) disorders at age 4 and 10 years in a community sample. Later depression was predicted not only by an earlier diagnosis of depression, but also by an earlier diagnosis of conduct disorder, even after adjustment for potential confounders (Luby et al., 2014). Other studies have identified the reverse

heterotypic pathways, for example internalising (anxiety) symptoms predicting later externalising (oppositional defiant disorder) symptoms in 3- to 6-year-olds (Bufferd et al., 2012). These studies suggest an instability in mental health symptoms between preschool and school age in TD populations.

The research base examining the developmental stability of mental health symptoms in autistic populations is limited, particularly for the early preschool years. In later childhood and adolescence, there appears to be stronger evidence for homotypic than heterotypic continuity of mental health symptoms, in line with the TD literature. For example, in a study of parent-rated behavioural, emotional, and hyperactivity symptoms in 12- to 16-year-old autistic adolescents, Simonoff et al. (2013) reported stronger correlations between within-domain compared to between-domain factors, consistent with homotypic continuity. A recent community-based study by Carter Leno et al. (2022) assessed emotional, behavioural, and ADHD symptoms at two timepoints (at ages 4-8 years and 13-17 years) in an autistic sample. After adjusting for a range of potential confounders, strong evidence remained for all homotypic continuity pathways but only one heterotypic pathway: earlier emotional symptoms to later ADHD symptoms (Carter Leno et al., 2022).

In earlier childhood, cross-sectional studies comparing preschool and school-age samples of autistic children have shown elevated levels of anxiety compared to TD populations across childhood (Davis III et al., 2011; Vasa et al., 2013). While the cross-sectional nature of these studies means that associations over time cannot be estimated, a consistent elevation of anxiety symptoms across childhood in autism may imply homotypic continuity. Indeed, longitudinal studies have identified associations between earlier and later measures of the

same mental health symptoms in autistic children. For example, Flouri et al. (2015) found that emotional problems followed a linear, increasing trajectory from age 3 to 7 years in an autistic sample. Baribeau et al. (2021) examined change in anxiety scores on the Child Behaviour Checklist (CBCL; Achenbach, 2001; Achenbach & Rescorla, 2000) between the ages of 3 and 11 in the *Pathways in Autism Spectrum Disorder* cohort, a Canadian cohort of autistic young people on which the current research is also based. The authors identified four different developmental trajectories of anxiety: low-increasing, moderate-decreasing, moderate-increasing, and high-stable. This association between earlier anxiety scores and later anxiety scores can be taken as evidence of homotypic continuity (Baribeau et al., 2021). However, it is notable that none of the above studies have longitudinally measured multiple domains of mental health problems to examine how they relate to one another over time. Some studies have examined different domains of mental health problems – for example, Wright et al. (2023) calculated the trajectory of aggression, attention problems, and anxiety/depression symptoms across childhood in autism – but no studies have investigated how these different symptom domains might interrelate. Whilst the results of existing studies imply homotypic continuity, the possibility of heterotypic continuity from preschool age has not been examined in autistic populations.

This knowledge gap is important because if mental health symptoms first emerge during toddlerhood and become more stable after preschool age in TD populations, the first few years of life may represent a critical window during which mental health symptoms can significantly shift and develop (National Scientific Council on the Developing Child, 2008). It may be the case that the homotypic continuity of mental health symptoms seen in later childhood and adolescence in autism follows a similar pattern, with a more labile earlier

phase during which symptom adaptation is more possible. Given the high prevalence of mental health symptoms observed in autistic children from preschool age, the presence of a critical window early in development may present an opportunity for intervention that could prevent not only the development of existing symptoms, but also the shift from one symptom pattern to another. The current study aims to address this knowledge gap by longitudinally examining both heterotypic and homotypic continuity of mental health symptoms from preschool age to late childhood in an autistic sample.

Methods

Design & Participants

The study received ethical approval from the University of Bath Psychology Research Ethics Committee (reference number 22-034). The study uses data collected as part of the *Pathways in Autism Spectrum Disorder* ("Pathways") study. Pathways is an ongoing, longitudinal, multisite cohort study of children in Canada, recruited at the point of autism diagnosis (n = 421). Participants were aged between two and five years at recruitment. Children were eligible for the study if they had received an autism diagnosis from a clinician based on the DSM-IV-TR (American Psychiatric Association, 2000) criteria and confirmed using the Autism Diagnostic Interview-Revised (ADI-R; Rutter et al., 2003) and the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000). The Pathways sample is majority male (n = 355, 84.3%) and White (n = 286, 67.9%). Children were recruited from five different centres across Canada, all of which were urban centres but drew participants from the surrounding rural areas. There were no substantive differences across the sites in terms of clinical characteristics of the children recruited. Participants were initially assessed at diagnosis, six months post-diagnosis, and one-year post-diagnosis. They were subsequently

assessed annually. Participants who provided mental health data at the first timepoint (n = 360; mean T1 age 3.41 years, SD = 0.78, range = 1.98-5.28) formed the sample for the current analysis.

Measures

Mental health symptoms

The Child Behaviour Checklist (CBCL; Achenbach, 2001; Achenbach & Rescorla, 2000), which was parent-reported, was used as the primary measure of mental health symptoms. Items were rated on a 3-point Likert scale (0=Never, 1=Sometimes, 2=Often) with rating periods of the last 2 (preschool form) or 6 (school age form) months. The preschool and school-age forms are designed to be developmentally appropriate, and so differ from one another in some of their items. The raw CBCL scores were combined to create syndrome scales. In line with the domains of psychopathology proposed to co-occur highly with autism in the DSM-5 (American Psychiatric Association, 2013), we used the Anxious/Depressed, Aggressive Behaviour and Attention Problems subscales to assess emotional, behavioural and attention difficulties (Wright et al., 2023). The CBCL has shown good reliability and validity in young autistic populations (Pandolfi et al., 2009, 2012; Pandolfi et al., 2014). In the current study we used data collected at three timepoints across childhood: Time 1 (mean age 3.4 years, SD = 0.78, range = 1.98-5.28), Time 2 (mean age 7.73, SD = 0.22, range = 7.27-8.59 years), and Time 3 (mean age 10.76, SD = 0.24, range 10.14-11.90 years). The measures showed adequate reliability between timepoints (Cronbach's α Anxious/Depressed = 0.74; Aggressive Behaviour = 0.67; Attention Problems = 0.77).

Confounders

Autism symptom severity was assessed using the ADOS total score (Lord et al., 2000). Socioeconomic status was indexed using household income level and maternal education level, both of which were reported by participants' mothers. Household income was reported on an 11-point scale ranging from less than CA$5,000 to more than CA$80,000. Due to small cell counts, income was collapsed into five bands for analysis. Maternal education level was reported on a five-point scale ranging from "Did not complete high school" to "Postgraduate degree". Child IQ was assessed using Wechsler Intelligence Scale for Children (WISC; Wechsler & Kodama, 1949) data collected at visit six (mean age 8.72, range 8.13-9.60 years). Where WISC data were not available at visit six, data were taken from visit seven (n = 63; mean age 9.71, range = 9.16-10.38 years). Finally, sex and recruitment site were also included in analyses.

Missing data

As is the case for many cohort studies, attrition and missing data is an issue for the Pathways study. Primary analyses for the current study were conducted on imputed datasets based on participants with complete CBCL data at Time 1 (n = 360). Of those individuals with complete CBCL data at Time 1, 186 (51.66%) had complete CBCL data at Time 2, and 136 (37.78%) had complete CBCL data at Time 3. With the addition of confounders, the number of individuals with complete data for all variables was 89 (24.65%). This data loss is displayed in Figure 1. Missing data were imputed using Multivariable Imputation by Chained Equations (Royston & White, 2011). The use of the MICE method is based on the Missing at Random (MAR) assumption that, conditional on the variables included in the imputation model, there are no systematic differences between

missing and observed values for any given variable (Sterne et al., 2009). The imputation models included all variables used in the analysis as well as relevant auxiliary variables (see Appendix B for imputation model). Fifty imputed datasets were produced (StataCorp., 2023).

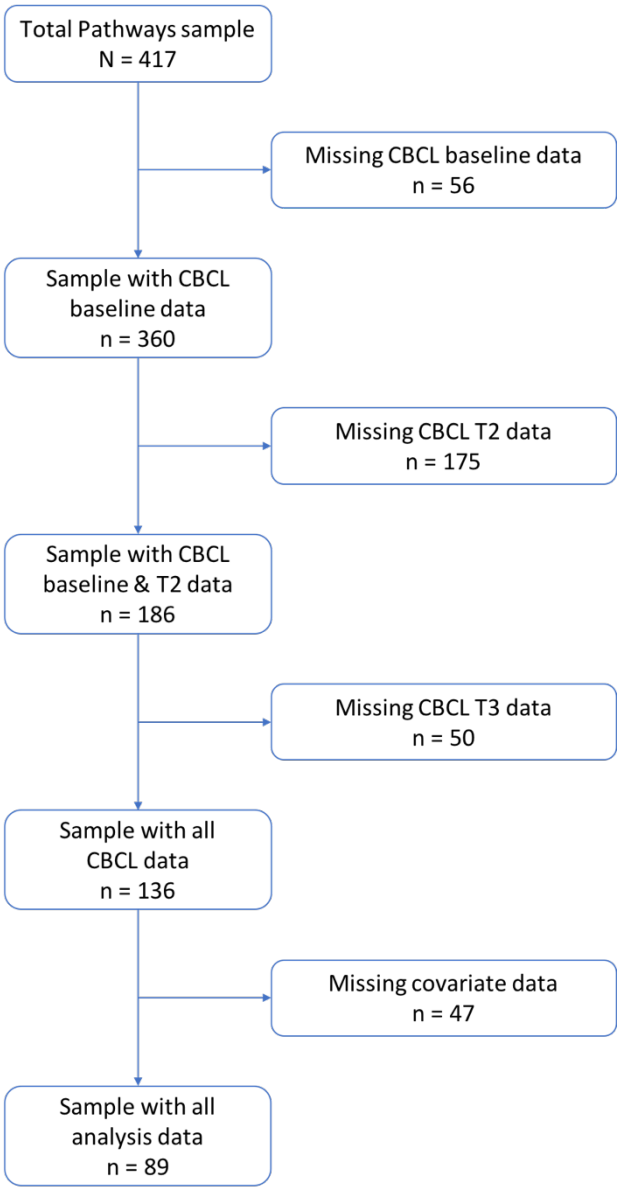

Figure 19 Diagram showing data loss in Pathways.

Statistical analysis

The main analysis of homotypic and heterotypic continuity was conducted by constructing cross-lagged panel models (CLPMs) using structural equation modelling in Stata version 17.0 (StataCorp., 2021). Cross-lagged panel models can be used to simultaneously and separately examine both concurrent and longitudinal associations between variables of interest. Robust standard errors were calculated to account for non-normality in the analysis variables and standardised estimates are presented in the results. Each of the Anxious/Depressed, Aggressive Behaviour and Attention Problems scores at Time 2 and 3 were regressed on all three of the variables at the preceding timepoint. This produced 6 autoregressive (homotypic) and 12 cross-lagged (heterotypic) pathways (see Figure 2). Model fit was assessed using the Comparative Fit Index (CFI) and Root Mean Square Error of Approximation (RMSEA). Values of CFI ≥ 0.90 and RMSEA ≤ 0.08 were considered to indicate good model fit (Hu & Bentler, 1999; Kline, 2023) .

In addition to the main analysis, a number of sensitivity analyses were conducted to test the robustness of the results. We ran the CLPM under 3 sensitivity conditions: 1) with confounder variables excluded, 2) using the complete case sample without imputation, and 3) using maximum likelihood missing value estimation as opposed to multiply imputed data. The results of these sensitivity analyses are presented in the Supplementary Material (Appendix B).

Results

Descriptive data for the analysis sample is presented in Table 1. Reflecting the overall Pathways population, the sample is majority male (84.17%; n = 303). The sample is also skewed towards higher socioeconomic status, with over 80% of participants' mothers having completed education beyond high school and over 70% reporting a household income higher than CA$40,000. Descriptive statistics for the imputed data show they follow a similar distribution to the complete case data. Table 2 shows a correlation matrix between descriptive and analytic variables in the complete case dataset.

The final, adjusted, CLPM showed acceptable model fit (CFI = 0.89, RMSEA = 0.09). The adjusted CLPM provided evidence for all homotypic pathways across all timepoints (Time 1 to Time 2 Anxious/Depressed β = 0.33, $p < .001$; Aggressive Behaviour β = 0.32, $p < .001$; Attention Difficulties β = 0.49, $p = .001$; Time 2 to Time 3 Anxious/Depressed β = 0.57, $p < .001$; Aggressive Behaviour β = 0.56, $p < .001$; Attention Difficulties β = 0.66, $p < .001$). There was evidence for one heterotypic effect, from Aggressive Behaviour at Time 1 to Anxious/Depressed at Time 2 (β = 0.08, $p = .013$), but no other heterotypic pathways were significant. These results are displayed in Figure 2 and Table 3. The results of sensitivity analyses were consistent with the main analyses (see Appendix B).

Table 1

Distributions of values of analysis and confounder variables observed in participants with complete data for all included variables, and distributions in imputed datasets

Variable	**Complete case data**	**Imputed data (n = 360)**
	Mean (SD) for continuous variables *n* (%) for categorical variables	Mean (SE) for continuous variables Proportion (SE) for categorical variables
CBCL total score Time 1 (n = 360)		
Anxiety/Depression	3.18 (2.66)	3.18 (0.14)
Attention Difficulties	4.56 (2.34)	4.56 (0.12)
Aggressive Behaviour	13.31 (7.41)	13.31 (0.39)
CBCL total score Time 2 (n = 186)		
Anxiety/Depression	3.58 (3.19)	4.26 (0.21)
Attention Difficulties	8.75 (4.54)	9.08 (0.27)
Aggressive Behaviour	7.04 (6.13)	8.10 (0.38)
CBCL total score Time 3 (n = 168)		
Anxiety/Depression	3.70 (3.64)	4.58 (0.24)
Attention Difficulties	7.21 (4.45)	8.07 (0.31)
Aggressive Behaviour	5.58 (5.63)	7.23 (0.37)
BRIEF Shift *t*-score (n = 232)	67.00 (12.95)	67.00 (0.85)
ADOS total score (n = 356)	7.63 (1.69)	7.63 (0.09)
WISC FSIQ total score (n = 174)	84.86 (18.73)	80.42 (1.37)
Sex (n = 360)		
Male	303 (84.17)	84.17 (0.02)
Female	57 (15.83)	15.83 (0.02)
Mother's education level (n = 353)		
Did not complete high school	17 (4.82)	4.88 (0.01)
Completed high school	31 (8.78)	8.88 (0.02)
Further education	154 (43.63)	43.70 (0.03)
Undergraduate degree	107 (30.31)	30.19 (0.02)
Postgraduate degree	44 (12.46)	12.35 (0.02)
Household income level (n = 347)		
Less than $20,000	38 (10.95)	11.38 (0.02)
$20,000 - $40,000	48 (13.83)	13.71 (0.02)
$40,000 - $60,000	71 (20.46)	20.26 (0.02)
$60,000 - $80,000	58 (16.71)	16.71 (0.02)
More than $80,000	132 (38.04)	37.94 (0.03)
Research Site (n = 360)		
Halifax	47 (13.06)	13.06 (0.02)
Montreal	122 (33.89)	33.89 (0.02)
Hamilton	53 (14.72)	14.72 (0.02)
Vancouver	89 (24.72)	24.72 (0.02)
Edmonton	49 (13.61)	13.61 (0.02)

Table 2

Correlation matrix of analysis and confounder variables

		Time 1			Time 2			Time 3									
		Anxiety/ Depression	Aggressive Behaviour	Attention Problems	Anxiety/ Depression	Aggressive Behaviour	Attention Problems	Anxiety/ Depression	Aggressive Behaviour	Attention Problems	BRIEF t-score	ADOS Total Score	WISC FSIQ	Sex	Maternal Education Level	Income	Site
Time 1	Anxiety/Depression	1.00	0.47***	0.26***	0.43***	0.22**	0.11	0.41***	0.20**	0.12	0.09	-0.08	0.14	-0.10	-0.08	-0.16**	0.08
	Aggressive Behaviour	0.47***	1.00	0.50***	0.38***	0.45***	0.27***	0.13	0.32***	0.23**	0.08	-0.16**	-0.01	-0.01	-0.12*	-0.16**	0.11*
	Attention Problems	0.26***	0.50***	1.00	0.15*	0.23**	0.39***	0.03	0.08	0.24**	0.13*	0.05	-0.14	0.01	-0.11*	-0.12*	0.20***
Time 2	Anxiety/Depression	0.43***	0.38***	0.15*	1.00	0.52***	0.33***	0.63***	0.39***	0.16	0.15*	-0.15*	0.10	-0.18*	-0.08	-0.10	0.08
	Aggressive Behaviour	0.22**	0.45***	0.23**	0.52***	1.00	0.55***	0.40***	0.65***	0.40***	0.23**	0.03	-0.04	-0.16*	-0.14	-0.18*	0.03
	Attention Problems	0.11	0.27***	0.39***	0.33***	0.55***	1.00	0.20*	0.37***	0.74***	0.22**	0.09	-0.29**	-0.02	-0.04	-0.11	0.05
Time 3	Anxiety/Depression	0.41***	0.13	0.03	0.63***	0.40***	0.20*	1.00	0.51***	0.35***	0.17*	-0.07	0.23*	-0.12	0.00	0.03	0.16*
	Aggressive Behaviour	0.20**	0.32***	0.08	0.39***	0.65***	0.37***	0.51***	1.00	0.57***	0.15	0.05	0.08	-0.08	-0.15	-0.12	0.14
	Attention Problems	0.12	0.23**	0.24**	0.16	0.40***	0.74***	0.35***	0.57***	1.00	0.11	0.08	-0.22*	0.03	-0.03	0.01	0.10
	BRIEF t-score	0.09	0.08	0.13*	0.15*	0.23**	0.22**	0.17*	0.15	0.11	1.00	0.15*	-0.21*	-0.30***	-0.11	-0.11	0.14*
	ADOS Total Score	-0.08	-0.16**	0.05	-0.15*	0.03	0.09	-0.07	0.05	0.08	0.15*	1.00	0.08	0.02	-0.04	0.05	0.07
	WISC FSIQ	0.14	-0.01	-0.14	0.10	-0.04	-0.29**	0.23*	0.08	-0.22*	-0.21*	0.08	1.00	-0.01	0.12	0.09	0.10

Table 2 cont.

	Time 1		Time 2			Time 3										
	Anxiety/ Depression	Aggressive Behaviour	Attention Problems	Anxiety/ Depression	Aggressive Behaviour	Attention Problems	Anxiety/ Depression	Aggressive Behaviour	Attention Problems	BRIEF t-score	ADOS Total Score	WISC FSIQ	Sex	Maternal Education Level	Income	Site
Sex	-0.10	-0.01	0.01	-0.18*	-0.16*	-0.02	-0.12	-0.08	0.03	-0.30***	0.02	-0.01	1.00	0.02	0.08	-0.05
Maternal Education Level	-0.08	-0.12*	-0.11*	-0.08	-0.14	-0.04	0.00	-0.15	-0.03	-0.11	-0.04	0.12	0.02	1.00	0.34***	-0.00
Income	-0.16**	-0.16**	-0.12*	-0.10	-0.18*	-0.11	0.03	-0.12	0.01	-0.11	0.05	0.09	0.08	0.34***	1.00	0.13*
Site	0.08	0.11*	0.20***	0.08	0.03	0.05	0.16*	0.14	0.10	0.14*	0.07	0.10	-0.05	-0.00	0.13*	1.00
N	360															

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

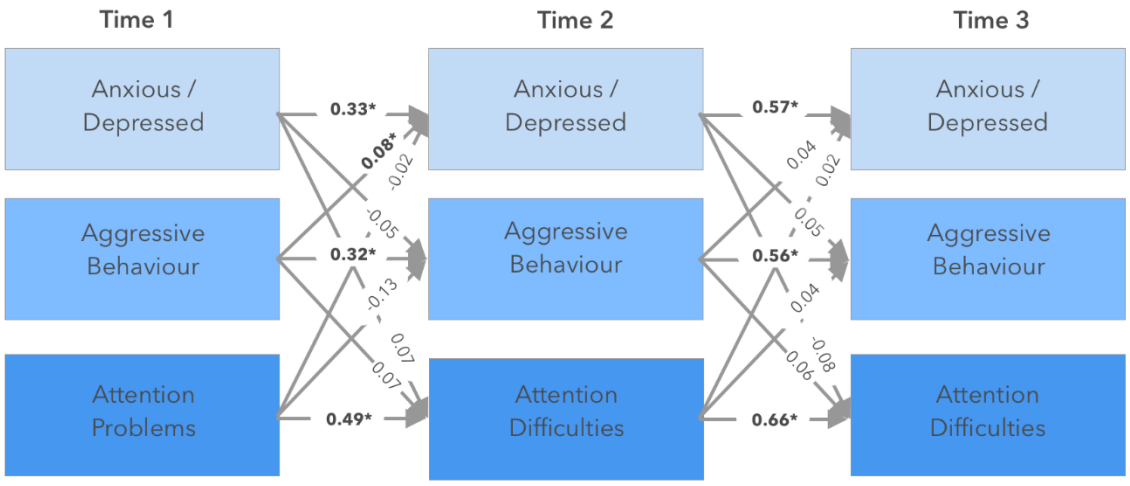

Figure 2 Cross-lagged panel model of homotypic and heterotypic pathways across Times 1, 2, and 3. Standardised beta values are displayed. Estimates of $p < .05$ are bolded and asterisked.

Table 3

Coefficients, 95% confidence intervals, and p values for adjusted homo- and heterotypic pathways

Variable	*Beta* (95% CI)	*P*
Anxious/Depressed Time 2		
Anxious/Depressed Time 1	0.33 (0.18, 0.49)	<.001
Aggressive Behaviour Time 1	0.08 (0.02, 0.14)	.013
Attention Problems Time 1	-0.02 (-0.19, 0.16)	.866
Aggressive Behaviour Time 2		
Anxious/Depressed Time 1	0.05 (-0.25, 0.35)	.751
Aggressive Behaviour Time 1	0.32 (0.20, 0.43)	<.001
Attention Problems Time 1	-0.13 (-0.46, 0.20)	.438
Attention Problems Time 2		
Anxious/Depressed Time 1	0.07 (-0.14, 0.28)	.509
Aggressive Behaviour Time 1	0.07 (-0.02, 0.16)	.121
Attention Problems Time 1	0.49 (0.23, 0.75)	<.001
Anxious/Depressed Time 3		
Anxious/Depressed Time 2	0.57 (0.36, 0.77)	<.001
Aggressive Behaviour Time 2	0.04 (-0.05, 0.14)	.376
Attention Problems Time 2	0.02 (-0.08, 0.13)	.644
Aggressive Behaviour Time 3		
Anxious/Depressed Time 2	0.05 (-0.21, 0.31)	.690
Aggressive Behaviour Time 2	0.56 (0.42, 0.69)	<.001
Attention Problems Time 2	0.04 (-0.12, 0.20)	.632
Attention Problems Time 3		
Anxious/Depressed Time 2	-0.08 (-0.27, 0.10)	.382
Aggressive Behaviour Time 2	0.06 (-0.05, 0.17)	.281
Attention Problems Time 2	0.66 (0.53, 0.80)	<.001

Discussion

The current study investigated homotypic and heterotypic pathways of mental health symptoms across childhood in a community sample of autistic children. It extended previous research by longitudinally examining multiple mental health symptom clusters and their continuity across three time points from preschool age through to late childhood. The results suggest evidence for homotypic continuity across childhood in autistic children. This aligns with previous research in both autistic and typically developing populations, which has broadly found stronger evidence for homotypic than heterotypic continuity, particularly in later childhood and adolescence (Carter Leno et al., 2022; Oldehinkel & Ormel, 2023). This stability in mental health symptomatology may reflect underlying genetic risk factors, which are thought to explain around 30% of the variance in internalising and externalising behaviour (Nikstat & Riemann, 2020; van der Valk et al., 2003). Specific mental health symptoms may also be maintained by learned patterns of thinking, relating, and behaving, which sustain symptoms by looping individuals in *vicious cycles* (Beck, 2002; Kuyken et al., 2005). The results of the current study show stronger homotypic associations between Time 2 and Time 3 than between Time 1 and Time 2, implying a strengthening of symptom stability over time. This result aligns with existing literature (Oldehinkel & Ormel, 2023) and may be explained at the intrapersonal level – the entrenchment of the *vicious cycles* mentioned above – or at the interpersonal level, where a bidirectional, negatively reinforcing relationship forms between an individual's mental health and their environment (Esch et al., 2014; Oldehinkel & Ormel, 2023). Understanding that later mental health symptoms are predicted by their earlier counterparts provides an important

foundation for the development of effective tools for screening and supporting mental health problems in autistic populations. It also speaks to the importance of early identification of mental health symptoms in young people with autism, as it shows that mental health symptoms observed at age 10 are predicted by symptoms observed as early as age 3.

Evidence for heterotypic continuity was less clear, with only one significant cross-lagged pathway, namely from Aggressive Behaviour at Time 1 to Anxious/Depressed at Time 2. This aligns with the TD literature, which has previously identified an association between preschool-age conduct disorder and school-age depression (Luby et al., 2014). This finding is consistent with a developmental cascade, or failure, model (Burke & Loeber, 2010; Masten & Cicchetti, 2010), which hypothesises that behavioural problems have a negative impact on factors such as interpersonal relationships, which in turn leads to later symptoms of anxiety and depression (Burke & Loeber, 2010; Carter Leno et al., 2024). The result indicates that autistic children may follow a similar pattern to TD children in the development of mental health symptoms across early childhood. The identified heterotypic pathway provides further evidence for the importance of early screening for mental health symptoms in autistic children, as it suggests that symptoms observed during the preschool years predict the development of different symptoms in later childhood.

We did not replicate the finding of an association between earlier emotional symptoms and later ADHD symptoms that was found in Carter Leno et al. (2022).

The authors acknowledge that the finding was not hypothesised and does not align with existing results (Carter Leno et al., 2022, pp. 1451). Nonetheless, it may be possible that this pathway only becomes apparent in adolescence, given that the mean age of participants in Carter Leno et al. (2022) was 15 compared to 9 in the current study. It may be that factors like the transition to secondary school, with its increased demands on personal organisation and academic challenge, exacerbate or activate ADHD symptoms to a greater extent in young autistic people who have experienced earlier emotional difficulties (Palmu et al., 2024; Zendarski et al., 2021).

The results of the current study provide evidence for an early developmental window during which mental health symptoms may be more labile in autistic children. This finding has important clinical implications. For example, it may be particularly beneficial to screen autistic children for aggressive behaviour during the preschool years. This may provide early indications of increased risk not only for aggressive behaviour, but also internalising symptoms during their later school years. Following early identification, autistic children demonstrating high levels of aggressive behaviour may benefit from being offered specific psychological or behavioural interventions targeting that aggressive behaviour (Wong et al., 2015). It is possible that these interventions may have the added benefit of reducing the risk of later internalising symptoms – future research should examine the longitudinal, heterotypic impact of early psychological interventions.

The current study considers mental health outcomes at the symptom level (i.e., continuous scores on the CBCL), as opposed to the disorder level (i.e., categorised according to meeting diagnostic cut-offs). A key strength of this approach is that it provides a nuanced picture of the range and intensity of symptom severity that may be lost if individuals were collapsed into diagnostic groups. This means analyses are sensitive to changes in symptom levels which may not meet the threshold of causing an individual to move between diagnostic categories. A potential risk of this approach is privileging statistically significant rather than clinically meaningful symptom change. However, given the increase in the strength of symptom stability over time seen in the results, it is crucial to detect the subtle but important changes in symptom severity during the early years. Disorder-level analysis may have been insensitive to these changes.

An important strength of the current study is the use of a large, well characterised community sample of autistic young people. The use of longitudinal data, as well as repeated measurement of mental health symptoms across three timepoints spanning toddlerhood to late childhood, are also important strengths. Further, the age range of participants within the timepoints was narrower than in other studies of autistic children (e.g., Carter Leno et al., 2022), enabling the identification of specific developmental windows. However, the study should also be considered in light of its limitations. As for many cohort studies, a proportion of participants were lost to follow-up in Pathways, which may have biased the complete case analysis. However, missing data were imputed in line with the MAR assumption and sensitivity analyses showed consistent results between different analysis samples.

Another limitation of the study is the disproportionate number of male participants. Although this is common in studies of autistic populations, it means that analysis stratified by sex was not possible. Given the emergence of sex differences in mental health symptoms during childhood (Oswald et al., 2016), it is possible that patterns of symptom stability may differ by sex. Further, the current study relied solely on parent-reported outcome measures, which means a proportion of the observed effect may be due to shared methods variance. Future research should examine whether the effects observed in the current study are consistent across sex and examine whether the effects are replicated with multi-informant outcome measures.

Summary

The current study provides clear evidence for homotypic continuity in mental health symptoms across childhood in autistic youth. We found evidence for a single heterotypic pathway between preschool aggressive behaviour and school-age internalising symptoms, possibly indicating a critical window of symptom lability for autistic children during the preschool years. These results support the need for early identification and intervention for this at-risk population.

References

Achenbach, T. M. (2001). Manual for ASEBA school-age forms & profiles. *University of Vermont, Research Center for Children, Youth & Families*.

Achenbach, T. M., & Rescorla, L. A. (2000). *Manual for the ASEBA preschool forms and profiles* (Vol. 30). Burlington, VT: University of Vermont.

American Psychiatric Association. (2000). *Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.).*

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. American Psychiatric Publishing.

Baribeau, D. A., Vigod, S., Pullenayegum, E., Kerns, C. M., Mirenda, P., Smith, I. M., Vaillancourt, T., Volden, J., Waddell, C., & Zwaigenbaum, L. (2021). Co-occurring trajectories of anxiety and insistence on sameness behaviour in autism spectrum disorder. *The British Journal of Psychiatry*, *218*(1), 20-27.

Beck, A. T. (2002). Cognitive models of depression. *Clinical advances in cognitive psychotherapy: Theory and application*, *14*(1), 29-61.

Bufferd, S. J., Dougherty, L. R., Carlson, G. A., Rose, S., & Klein, D. N. (2012). Psychiatric disorders in preschoolers: continuity from ages 3 to 6. *American Journal of Psychiatry*, *169*(11), 1157-1164.

Burke, J., & Loeber, R. (2010). Oppositional defiant disorder and the explanation of the comorbidity between behavioral disorders and depression. *Clinical Psychology: Science and Practice*, *17*(4), 319-326.

Carter Leno, V., Hollocks, M. J., Chandler, S., White, P., Yorke, I., Charman, T., Pickles, A., Baird, G., & Simonoff, E. (2022). Homotypic and heterotypic continuity in psychiatric symptoms from childhood to adolescence in autistic

youth. *Journal of the American Academy of Child & Adolescent Psychiatry*, *61*(12), 1445-1454.

Carter Leno, V., Wright, N., Pickles, A., Bedford, R., Zaidman-Zait, A., Kerns, C., Zwaigenbaum, L., Duku, E., Bennett, T., Georgiades, S., Smith, I. M., Richards, A., Vaillancourt, T., Szatmari, P., & Elsabbagh, M. (2024). Longitudinal associations between early childhood irritability and adolescent depression symptoms in autistic children are mediated by peer relationships but not educational engagement. *Development and Psychopathology*, *36*(1), 443-453. https://doi.org/10.1017/S0954579422001316

Davis III, T. E., Hess, J. A., Moree, B. N., Fodstad, J. C., Dempsey, T., Jenkins, W. S., & Matson, J. L. (2011). Anxiety symptoms across the lifespan in people diagnosed with autistic disorder. *Research in Autism Spectrum Disorders*, *5*(1), 112-118.

Esch, P., Bocquet, V., Pull, C., Couffignal, S., Lehnert, T., Graas, M., Fond-Harmant, L., & Ansseau, M. (2014). The downward spiral of mental disorders and educational attainment: a systematic review on early school leaving. *BMC PSYCHIATRY*, *14*, 1-13.

Flouri, E., Midouhas, E., Charman, T., & Sarmadi, Z. (2015). Poverty and the growth of emotional and conduct problems in children with autism with and without comorbid ADHD. *Journal of autism and developmental disorders*, *45*, 2928-2938.

Gadow, K. D., DeVincent, C. J., Pomeroy, J., & Azizian, A. (2004). Psychiatric symptoms in preschool children with PDD and clinic and comparison samples. *Journal of autism and developmental disorders*, *34*, 379-393.

Hayashida, K., Anderson, B., Paparella, T., Freeman, S. F., & Forness, S. R. (2010). Comorbid psychiatric diagnoses in preschoolers with autism spectrum disorders. *Behavioral Disorders*, *35*(3), 243-254.

Hu, L. t., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural equation modeling: a multidisciplinary journal*, *6*(1), 1-55.

Kline, R. B. (2023). *Principles and practice of structural equation modeling*. Guilford publications.

Kuyken, W., Watkins, E., & Beck, A. T. (2005). Cognitive-behavior therapy for mood disorders.

Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Leventhal, B. L., DiLavore, P. C., Pickles, A., & Rutter, M. (2000). The Autism Diagnostic Observation Schedule—Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of autism and developmental disorders*, *30*, 205-223.

Luby, J. L., Gaffrey, M. S., Tillman, R., April, L. M., & Belden, A. C. (2014). Trajectories of preschool disorders to full DSM depression at school age and early adolescence: continuity of preschool depression. *American Journal of Psychiatry*, *171*(7), 768-776.

Masten, A. S., & Cicchetti, D. (2010). Developmental cascades. *Development and Psychopathology*, *22*(3), 491-495.

National Scientific Council on the Developing Child. (2008). *Mental Health Problems in Early Childhood Can Impair Learning AndBehavior for Life. Working Paper# 6*.

Nikstat, A., & Riemann, R. (2020). On the etiology of internalizing and externalizing problem behavior: A twin-family study. *PLoS One*, *15*(3), e0230626.

Oldehinkel, A. J., & Ormel, J. (2023). Annual Research Review: Stability of psychopathology: lessons learned from longitudinal population surveys. *Journal of child psychology and psychiatry*, *64*(4), 489-502.

Oswald, T. M., Winter-Messiers, M. A., Gibson, B., Schmidt, A. M., Herr, C. M., & Solomon, M. (2016). Sex differences in internalizing problems during adolescence in autism spectrum disorder. *Journal of autism and developmental disorders*, *46*, 624-636.

Palmu, I. R., Määttä, S. J., Närhi, V. M., & Savolainen, H. K. (2024). ADHD-symptoms and transition to middle school: the effects of academic and social adjustment. *European Journal of Special Needs Education*, *39*(1), 48-63.

Pandolfi, V., Magyar, C. I., & Dill, C. A. (2009). Confirmatory factor analysis of the Child Behavior Checklist 1.5–5 in a sample of children with autism spectrum disorders. *Journal of autism and developmental disorders*, *39*(7), 986-995.

Pandolfi, V., Magyar, C. I., & Dill, C. A. (2012). An initial psychometric evaluation of the CBCL 6–18 in a sample of youth with autism spectrum disorders. *Research in Autism Spectrum Disorders*, *6*(1), 96-108.

Pandolfi, V., Magyar, C. I., & Norris, M. (2014). Validity study of the CBCL 6–18 for the assessment of emotional problems in youth with ASD. *Journal of Mental Health Research in Intellectual Disabilities*, *7*(4), 306-322.

Royston, P., & White, I. R. (2011). Multiple imputation by chained equations (MICE): implementation in Stata. *Journal of statistical software*, *45*, 1-20.

Rutter, M., Le Couteur, A., & Lord, C. (2003). ADI-R. *Autism diagnostic interview revised. Manual. Los Angeles: Western Psychological Services*.

Simonoff, E., Kent, R., Stringer, D., Lord, C., Briskman, J., Lukito, S., Pickles, A., Charman, T., & Baird, G. (2020). Trajectories in symptoms of autism and cognitive ability in autism from childhood to adult life: findings from a longitudinal epidemiological cohort. *Journal of the American Academy of Child & Adolescent Psychiatry*, *59*(12), 1342-1352.

Snyder, H. R., Young, J. F., & Hankin, B. L. (2017). Strong homotypic continuity in common psychopathology-, internalizing-, and externalizing-specific factors over time in adolescents. *Clinical Psychological Science*, *5*(1), 98-110.

StataCorp. (2021). *Stata Statistical Software: Release 17*. StataCorp LLC.

StataCorp. (2023). *Stata Multiple-Imputation Reference Manual Release 18*. Stata Press. https://www.stata.com/manuals/mi.pdf

Sterne, J. A., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G., Wood, A. M., & Carpenter, J. R. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *Bmj*, *338*.

van der Valk, J. C., van den Oord, E. J. C. G., Verhulst, F. C., & Boomsma, D. I. (2003). Genetic and Environmental Contributions to Stability and Change in Children's Internalizing and Externalizing Problems. *Journal of the American Academy of Child & Adolescent Psychiatry*, *42*(10), 1212-1220. https://doi.org/https://doi.org/10.1097/00004583-200310000-00012

Vasa, R. A., Kalb, L., Mazurek, M., Kanne, S., Freedman, B., Keefer, A., Clemons, T., & Murray, D. (2013). Age-related differences in the prevalence and correlates

of anxiety in youth with autism spectrum disorders. *Research in Autism Spectrum Disorders*, *7*(11), 1358-1369.

Wechsler, D., & Kodama, H. (1949). *Wechsler intelligence scale for children* (Vol. 1). Psychological corporation New York.

Wong, C., Odom, S. L., Hume, K. A., Cox, A. W., Fettig, A., Kucharczyk, S., Brock, M. E., Plavnick, J. B., Fleury, V. P., & Schultz, T. R. (2015). Evidence-Based Practices for Children, Youth, and Young Adults with Autism Spectrum Disorder: A Comprehensive Review. *Journal of autism and developmental disorders*, *45*(7), 1951-1966. https://doi.org/10.1007/s10803-014-2351-z

Wright, N., Courchesne, V., Pickles, A., Bedford, R., Duku, E., Kerns, C., Bennett, T., Georgiades, S., Hill, J., & Richard, A. (2023). A longitudinal comparison of emotional, behavioral and attention problems in autistic and typically developing children. *Psychological medicine*, *53*(16), 7707-7719.

Zendarski, N., Mensah, F., Hiscock, H., & Sciberras, E. (2021). Trajectories of emotional and conduct problems and their association with early high school achievement and engagement for adolescents with ADHD. *Journal of Attention Disorders*, *25*(5), 623-635.

Executive Summaries

Critical Review of the Literature

Pubertal development and mental health in autism: a scoping review

There is robust evidence that pubertal development is associated with mental health outcomes in typically developing (TD) populations. There is evidence that the timing of puberty may differ in autistic samples compared to TD samples, and also consistent evidence that mental health problems are more prevalent in autistic samples than in TD samples. However, little is known about the association between pubertal development and mental health in autism. This review therefore aimed to establish the state of the current evidence base and to summarise the results of this literature to improve our understanding of this association.

A systematic search was conducted across four electronic databases to identify any studies which had investigated the association between pubertal development and mental health outcomes in autistic samples. The reference lists of identified studies were also scanned and forward citation searching was employed to identify any further relevant articles. Eight studies were ultimately identified as meeting inclusion criteria for the review. Due to the heterogenous nature of the studies identified, a narrative synthesis method was employed to draw overall conclusions.

The overall quality of the evidence was rated as 'fair', so overarching conclusions from the literature should be drawn with caution. The review did not provide strong evidence for an association between pubertal development and mental health outcomes in autism. Most of the studies reviewed did not find evidence for an association, and of the studies reporting positive results, most also reported null findings. This does not align with results in TD samples, which report an association between pubertal development and mental health problems.

Whilst the lack of association in autistic samples may be related to the low quality of the evidence, it is possible that pubertal development does not confer the same risk of poorer mental health outcomes for autistic young people as it does for TD populations. This may be due to differences in neurocognitive development or psychosocial experiences during puberty in autistic individuals. Some of the mechanisms that increase the risk of poor mental health during puberty in TD populations may be operating earlier in childhood in autistic children. The results highlight the importance of early identification of autistic individuals experiencing mental health problems.

Service-Related Project

The demographic representativeness of Pain Management Service patients at Great Western Hospital, Swindon

Equal access to healthcare, regardless of age, sex, or race, is a core tenet of the National Health Service (NHS) and forms part of the NHS Constitution. However, evidence suggests that many groups in society experience significant health inequalities. Many areas of the UK have seen substantial demographic changes over the past decade, which may put an even greater number of people at risk of exclusion from services. The first step in ensuring health services are representative of the populations they serve is to establish what current patient populations look like. The aim of the current project, therefore, was to examine the demographic representativeness of patients seen by the Pain Management Service and pain psychology team at Great Western Hospital, Swindon.

Data on age, sex, and ethnicity were examined. Demographic data for four levels of population were collected: the service catchment area, drawn from the national census; the total hospital patient population and the Pain Management Service population, both accessed via the hospital informatics team; and the pain psychology patient population, accessed via the local referral database. Data were presented visually and compared descriptively, contextualised using expected prevalence estimates of chronic pain and distress taken from published evidence.

The results showed that the Pain Management Service and pain psychology patient groups were broadly reflective of the wider population in the context of expected prevalence estimates. Three groups appeared to be underrepresented in the service: individuals aged >70 years, individuals of Asian heritage, and men. A number of factors may explain these results, for example biases on the part of referring clinicians, cultural differences in the management and communication of pain, and help-seeking behaviour. Recommendations for improving the representativeness of the service include outreach to different communities and education of healthcare professionals on topics like unconscious bias and cultural attitudes towards pain.

Characterising homotypic and heterotypic continuity of mental health symptoms in autism: a longitudinal study across childhood

The homotypic continuity of mental health symptoms – that is, that symptoms at earlier timepoints predict the same symptoms later on – is a consistent finding across the lifespan. However, among typically developing (TD) populations, this stability is less pronounced during the preschool years: some mental health symptoms (for example, conduct problems) can predict different symptoms (for example, depressive symptoms) later on. This is known as heterotypic continuity. The prevalence of mental health problems among autistic populations is significantly higher than among TD populations, even at preschool age. However, it is not clear whether the heterotypic continuity of mental health symptoms seen in TD preschoolers is also experienced by autistic children. This study aimed to examine the stability of mental health symptoms across childhood in an autistic sample.

The study used data from a longitudinal cohort study of Canadian autistic children – the *Pathways in Autism Spectrum Disorder* study. Mental health symptoms were measured using the Child Behavior Checklist, and three subscales in particular were examined: Anxious/Depressed, Aggressive Behaviour and Attention Problems. Data were collected at three timepoints across childhood (T1 mean age = 3.4 years, T2 mean age = 7.7 years, T3 mean age 10.7 years). Cross-

lagged panel models were constructed to assess the association between each subscale and its later equivalents, as well as with each of the other subscales, to test homotypic and heterotypic continuity.

The results showed strong evidence for all homotypic pathways across timepoints, as well as evidence for one heterotypic pathway: Aggressive Behaviour at Time 1 to Anxious/Depressed symptoms at Time 2. These results are in line with findings in TD populations in showing evidence for homotypic and heterotypic continuity during the preschool years. The results are consistent with a developmental cascade model, and also evidence of an early developmental window during which mental health symptoms may be more changeable in autistic children. The findings demonstrate the importance of early identification of and intervention for autistic children experiencing mental health problems.

Research Appendices

Appendix A – table showing studies included in the systematic review, including key information extracted and relevant results.

Study	Sample	Design	Autism measure	Pubertal timing measure	Mental health measure	Confounders	Main results
Bronsard et al, 2010	France N = 74 Community Males and females (66% male) Autistic only Mean age 11.6 years (SD = 4.5)	Cross-sectional	DSM-IV, confirmed with ADI-R	Clinician assessment – Tanner scale	Externalising symptoms: Other-Injurious Behavior Scale	N/A	No association between pubertal stage and OIB score
Muscatello & Corbett, 2018	USA N = 113 Community Males and females (88% male) Autistic and TD (57% autistic) Age 7-17 years, mean age 12.02	Cross-sectional	ADOS	Pubertal Development Scale (parent report)	Cortisol level (proxy)	N/A	Pubertal stage significant predictor of evening cortisol level across autistic + TD samples (β = 0.45, *p* = .04). Partial correlations

	(ASD) / 11.17 (TD) [no SD reported]						between evening cortisol and pubertal stage (adjusted for age) significant for TD (r = 0.40, p = .05) but not for ASD (r = 0.17, p = .25).
Bitsika & Sharpley, 2020	Australia N = 53 Community Females only Autistic only Mean age = 10.10 years (SD = 2.7)	Cross-sectional	ADOS	Menarche status (maternal report)	Child and Adolescent Symptom Inventory (CASI-4) GAD subscale	N/A	Main effect of menarche status on mother-rated CASI-GAD score for girls not taking medication ($F(1,26)$ = 6.507, p = .017). No other significant effects.
Phan, 2020a	USA N = 395 Community	Cross-sectional	Autism Diagnostic Interview, Revised (ADI-R),	Pubertal Development Scale (PDS) –	Child Behavior Checklist (CBCL)	N/A	No effect of pubertal timing on internalising (p = .60) or

	Males and females (54% male) Autistic and TD (45% autistic) Mean age (Autistic) = 12.13 (SD = 2.78; mean age (TD) = 13.86 (SD = 2.88)		ADOS-2, or clinician diagnosis	self-report and parent-report. Pubertal timing calculated by regressing stage on age and saving residuals	Internalising and externalising domains (parent-report) Child and Adolescent Symptom Inventory (CASI) - ODD, CD, MDD, GAD (parent-report)		externalising (*p* = .54) symptoms in overall sample. Pubertal status negatively associated with externalising domain in autistic males (b = -3.537, p = 0.012, N = 52). No association between pubertal status and any CASI symptoms.
Phan, 2020b	USA N = 74 Males only Autistic and TD (42% autistic) Mean age (Autistic) = 14.66 years; mean age (TD) =	Cross-sectional	ADOS, SRS, Autism Spectrum Rating Scale DSM-V	Pubertal Development Scale (self-report) PDSA (adrenal) + PDSG (gonadal)	Center for Epidemiologic Studies Depression Scale	Repetitive behaviours	Association between PDSA and depressive symptoms in autistic sample (b = 0.244, p = 0.007) but not TD (b = 0.006, p = 0.865). No

	14.83 years [no SD reported]						association after adjustment for repetitive behaviours. No association between PDSG and depression.
Sharpley et al, 2021	Australia N = 53 Cross-sectional Community Females only Autistic sample Mean age = 10.00 years (SD = 2.74)	Cross-sectional	ADOS	Menarche status (parent-report)	Child and Adolescent Symptom Inventory (CASI-4) MDD (self- and parent-report) & Social Phobia (self-report) subscales	N/A	Menarche status associated with mother-reported MDD score (F = 11.36, p = .001). No other significant effects.
Corbett et al, 2022	USA N = 244 Longitudinal Community Males and females (66% male) Autistic and TD (57% autistic)	Longitudinal	Diagnosis according to DSM-V, confirmed by clinician and corroborated with ADOS-2	Clinician assessment – Tanner scale. Random effects from non-linear mixed effects model	Child Behavior Checklist (CBCL) anxiety and affective domains	WASI-II	Pubertal timing not associated with CBCL domains in either females (anxiety p = .25, affective p = .054) or males (anxiety p = .16,

	T1 median age (Autistic) = 11.2 years (IQR = 10.5, 12.2); T1 median age (TD) = 11.6 years (IQR = 10.6, 12.6)						affective *p* = .70).
Groenman et al, 2024	Netherlands N = 68 Community Males and females (53% male) Autistic and TD (50% autistic) Mean age (Autistic) = 14.14 (SD = 1.42); mean age (TD) = 14.20 (SD = 1.44)	Cross-sectional	Autism Quotient (self-report & parent report)	Pubertal Development Scale (self-report) PDSA (adrenal) + PDSG (gonadal) Relative pubertal development calculated from regression predictions	Children's Depression Inventory (self-report) SCARED-71 Strengths and difficulties questionnaire	SES	More advanced puberty associated with depressive and externalising symptoms in autistic but not TD group. Depression: adrenal p = 0.00, r = 0.28; gonadal p = 0.05, r = 0.14 Externalising: adrenal p = 0.04, r = 0.13; gonadal p = 0.02, r = 0.18. No association

							between pubertal development and anxiety symptoms (adrenal r = 0.03, p = .30; gonadal r = 0.06, p = .16).

Appendix B – MRP supplementary material

Supplementary Table 1. Imputation model

Variable name	Details	Type of variable
Anxiety/Depression Time 1	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
Aggressive Behaviour Time 1	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
Attention Problems Time 1	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
Anxiety/Depression Time 2	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
Aggressive Behaviour Time 2	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
Attention Problems Time 2	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
Anxiety/Depression Time 3	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
Aggressive Behaviour Time 3	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
Attention Problems Time 3	Syndrome scale calculated from relevant raw scores on CBCL	Continuous
ADOS (Baseline)	Total score on the Autism Diagnostic Observation Schedule	Continuous
Household income (Baseline)	Reported on 11-point scale from <CA$5,000 to >CA$80,000	Ordered categorical
Maternal education (Baseline)	Reported on a five-point scale from "Did not complete high school" to "Postgraduate degree"	Ordered categorical
Recruitment site (Baseline)	Five possible recruitment sites across Canada	Categorical
Sex (Baseline)	Collected at baseline	Binary categorical
Age (Time 1)	Age at time of completion of CBCL	Continuous
Age (Time 2)	Age at time of completion of CBCL	Continuous
Age (Time 3)	Age at time of completion of CBCL	Continuous
Maternal depression (Baseline)	Maternal depressive symptoms self-reported using the SCL-90	Continuous
WISC (Visit 6)	Wechsler Intelligence Scale for Children total FSIQ score	Continuous
WISC (Visit 7)	Wechsler Intelligence Scale for Children total FSIQ score	Continuous
Vineland (Visit 6)	Standard scores on the parent-reported Vineland Adaptive Behaviour Scale Communication domain	Continuous
Merrill-Palmer (Visit 6)	Ratio of cognitive age to chronological age on Merrill-Palmer Scale	Continuous

Supplementary Table 2. Coefficients, 95% confidence intervals, and *p* values for homo- and heterotypic pathways unadjusted for confounders using imputed data (N = 360)

	***Beta* (95% CI)**	***p***
Anxious/Depressed Time 2		
Anxious/Depressed Time 1	0.37 (0.20, 0.53)	<.001
Aggressive Behaviour Time 1	0.09 (0.03, 0.15)	.006
Attention Problems Time 1	-0.05 (-0.22, 0.12)	.535
Aggressive Behaviour Time 2		
Anxious/Depressed Time 1	0.04 (-0.24, 0.33)	.773
Aggressive Behaviour Time 1	0.30 (0.18, 0.43)	<.001
Attention Problems Time 1	-0.05 (-0.38, 0.29)	.773
Attention Problems Time 2		
Anxious/Depressed Time 1	0.01 (-0.21, 0.22)	.946
Aggressive Behaviour Time 1	0.04 (-0.05, 0.13)	.397
Attention Problems Time 1	0.57 (0.30, 0.84)	<.001
Anxious/Depressed Time 3		
Anxious/Depressed Time 2	0.62 (0.45, 0.80)	<.001
Aggressive Behaviour Time 2	0.03 (-0.06, 0.12)	.482
Attention Problems Time 2	0.01 (-0.11, 0.12)	.898
Aggressive Behaviour Time 3		
Anxious/Depressed Time 2	0.13 (-0.10, 0.36)	.266
Aggressive Behaviour Time 2	0.54 (0.39, 0.70)	<.001
Attention Problems Time 2	-0.03 (-0.15, 0.20)	.764
Attention Problems Time 3		
Anxious/Depressed Time 2	-0.07 (-0.23, 0.09)	.386
Aggressive Behaviour Time 2	0.07 (-0.04, 0.17)	.195
Attention Problems Time 2	0.66 (0.54, 0.78)	<.001

Supplementary Table 3. Coefficients, 95% confidence intervals, and *p* values for adjusted homo- and heterotypic pathways in the complete case sample (N = 93)

	***Beta* (95% CI)**	***p***
Anxious/Depressed Time 2		
Anxious/Depressed Time 1	0.48 (0.31, 0.65)	<.001
Aggressive Behaviour Time 1	0.22 (0.04, 0.40)	.017
Attention Problems Time 1	-0.08 (-0.26, 0.11)	.403
Aggressive Behaviour Time 2		
Anxious/Depressed Time 1	0.24 (0.06, 0.42)	.008
Aggressive Behaviour Time 1	0.34 (0.17, 0.52)	<.001
Attention Problems Time 1	-0.09 (-0.29, 0.11)	.368
Attention Problems Time 2		
Anxious/Depressed Time 1	0.15 (-0.04, 0.34)	.124
Aggressive Behaviour Time 1	0.04 (-0.14, 0.22)	.667
Attention Problems Time 1	0.19 (0.01, 0.40)	.066
Anxious/Depressed Time 3		
Anxious/Depressed Time 2	0.47 (0.21, 0.74)	<.001
Aggressive Behaviour Time 2	0.10 (-0.09, 0.29)	.293
Attention Problems Time 2	0.08 (-0.11, 0.27)	.417
Aggressive Behaviour Time 3		
Anxious/Depressed Time 2	0.17 (-0.11, 0.45)	.227
Aggressive Behaviour Time 2	0.61 (0.39, 0.83)	<.001
Attention Problems Time 2	-0.05 (-0.21, 0.11)	.543
Attention Problems Time 3		
Anxious/Depressed Time 2	-0.01 (-0.21, 0.19)	.916
Aggressive Behaviour Time 2	0.12 (-0.06, 0.29)	.183
Attention Problems Time 2	0.65 (0.46, 0.84)	<.001

Supplementary Table 4. Coefficients, 95% confidence intervals, and *p* values for adjusted homo- and heterotypic pathways using maximum likelihood missing value estimation (N = 360)

	***Beta* (95% CI)**	***p***
Anxious/Depressed Time 2		
Anxious/Depressed Time 1	0.33 (0.19, 0.47)	<.001
Aggressive Behaviour Time 1	0.23 (0.07, 0.38)	.005
Attention Problems Time 1	-0.03 (-0.17, 0.11)	.691
Aggressive Behaviour Time 2		
Anxious/Depressed Time 1	0.23 (-0.12, 0.16)	.745
Aggressive Behaviour Time 1	0.48 (0.34, 0.61)	<.001
Attention Problems Time 1	-0.04 (-0.19, 0.11)	.615
Attention Problems Time 2		
Anxious/Depressed Time 1	0.06 (-0.06, 0.18)	.337
Aggressive Behaviour Time 1	0.15 (0.08, 0.29)	.038
Attention Problems Time 1	0.28 (0.13, 0.43)	<.001
Anxious/Depressed Time 3		
Anxious/Depressed Time 2	0.56 (0.36, 0.77)	<.001
Aggressive Behaviour Time 2	0.05 (-0.15, 0.24)	.653
Attention Problems Time 2	0.05 (-0.11, 0.21)	.540
Aggressive Behaviour Time 3		
Anxious/Depressed Time 2	0.38 (-0.16, 0.23)	.699
Aggressive Behaviour Time 2	0.60 (0.47, 0.73)	<.001
Attention Problems Time 2	-0.07 (-0.05, 0.20)	.251
Attention Problems Time 3		
Anxious/Depressed Time 2	-0.04 (-0.18, 0.10)	.553
Aggressive Behaviour Time 2	0.09 (-0.04, 0.22)	.189
Attention Problems Time 2	0.71 (0.59, 0.84)	<.001