VOLUME I

# OUTCOMES IN INDIVIDUALS WITH NEURODEVELOPMENTAL DISORDERS OVER THE AGE OF 15

BY

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A thesis submitted to the University of Birmingham for the degree of
DOCTOR OF CLINICAL PSYCHOLOGY

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# OVERVIEW

This thesis is submitted as a requirement of the Doctor of Clinical Psychology degree at the School of Psychology at Birmingham University and is comprised of two volumes; a research and, a clinical volume.

## Volume I: Research

The research volume contains a literature review and an empirical paper. The literature review is a review of the literature into mental health problems in individuals over the age of 16 with a neurodevelopmental syndrome (Angelmans, Cri-du-chat, Cornelia de Lange, Fragile X, Prader-willi, Smith-Magenis and Williams syndromes). Each of these syndromes is associated with specific cognitive and behavioural characteristics that are risk factors for mental health. Despite this, the psychological features of these syndromes are largely unknown. This literature review seeks to assess the prevalence and descriptions of symptoms of mental health disorders within these syndromes to assist with early identification and treatment.

The empirical paper is a 10 year longitudinal study into fourteen individuals with Smith-Magenis Syndrome (SMS); a neurodevelopmental disorder first described in 1982. This syndrome is associated with high sociability, moderate/severe intellectual disabilities and high levels of challenging behaviour and sleep disturbances. The behavioural characteristics and communicative abilities of participants were compared between 2003/2004 and 2014/2015 to determine how the support needs of these individuals have changed over time. This study attempts to answer the question; what happens to individuals with SMS as they become adults, and, what the resulting impact is upon their quality of life.

## Volume II: Clinical Component

The Clinical Component consists of five clinical practice reports. The first clinical practice report is of a young girl with trichotillomania, formulated from the behavioural and systemic models. The second clinical practice report is a service evaluation of a Child and Adolescent Mental Health Service (CAMHS), using the CORE quantitative tool and a semi-structured interview to make recommendations on how client satisfaction could be improved. The third clinical practice report is a case study of a young woman who had a diagnosis of borderline personality disorder and anxiety, and who engaged in self-injurious behaviour. Her presenting issues are formulated using a psychodynamic formulation and the intervention used is described and evaluated. The fourth clinical practice report is a forensic single case experimental design study of a man with an intellectual disability who was engaging in risky behaviours. The assessment process, formulation and intervention are described and

evaluated. The final clinical practice report is a neuropsychological report of an elderly lady who was presenting with symptoms of dementia. The dementia assessment process and formulation is described with recommendations given around intervention.

DEDICATION

I dedicate this thesis to my family who have always supported me in everything I do, and in loving memory of my Grandma and Granddad Jones who have always made me believe anything is possible.

"*All our dreams can come true, if we have the courage to pursue them*"
- Walt Disney

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I would like to thank my friends, family, course cohort and the Clinical Psychology team at Birmingham University (especially Liz Kent and Ruth Butterworth) who have all supported me throughout the doctorate course.

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# CHAPTER 1: LITERATURE REVIEW

# SYSTEMATIC REVIEW OF THE PREVALENCE AND PRESENTATION OF MENTAL HEALTH DISORDERS EXPERIENCED BY ADULTS WITH NEURODEVELOPMENTAL SYNDROMES


## ABSTRACT

### Purpose of Review

This is a systematic review of the research about the prevalence and presentation of mental health disorders experienced by individuals over 16-years-old in Angelman, Cornelia de Lange, Cri-du-chat, Fragile X, Prader-Willi, Smith-Magenis and Williams Syndromes to assist clinicians with identification and treatment of mental health disorders.

### Method

The search terms were applied to Psychinfo and Web of Science search engines and the abstracts and references for each article were reviewed. Twenty-seven articles were located; fourteen for Prader-Willi, five for Fragile X, seven for Williams Syndrome and 1 for Cri-du-chat Syndrome. No articles met the inclusion criteria for Angelman, Cornelia de Lange and Smith-Magenis syndromes

### Findings

The overall prevalence of mental health disorders appeared higher than idiographic intellectual disabilities. The prevalence of psychosis and bipolar depression appeared higher in Prader-Willi syndrome although, the variance in symptoms of these disorders (e.g. angry explosive moods in bipolar), made definitive diagnosis difficult. The research indicated that

physical health issues may be an early warning sign for psychotic symptoms**,** and, obsessive rituals appeared to increase during the psychotic episode. Individuals with Williams syndrome appeared to have a high prevalence of anxiety and those with Fragile X had a high prevalence of anxiety and depression, as well as presenting with singular psychotic symptoms (e.g. delusions).

**Summary**

The findings suggest that mental health disorders are not only prevalent in neurodevelopmental syndromes; but also differ in presentation from typically developing and idiographic intellectual disability populations, thereby making identification and diagnosis difficult. The low quantity and quality of the papers available does raise questions over the validity of these results meaning further longitudinal research and cross-sectional studies using suitable measures and diagnostic criteria, are required in order to confirm findings.

# SYSTEMATIC REVIEW OF THE PREVALENCE AND PRESENTATION OF MENTAL HEALTH DISORDERS EXPERIENCED BY ADULTS WITH NEURODEVELOPMENTAL SYNDROMES

## INTRODUCTION

Neurodevelopmental syndromes as described throughout this article relate to neurodevelopmental disorders considered to be caused by a genetic anomaly (mutation, addition or deletion of genetic material). Whilst the psychological elements of many genetic neurodevelopmental syndromes generally remain under-researched, there has been a recent increase in research focusing on the behavioural, social, emotional and cognitive phenotypes of some genetic neurodevelopmental syndromes associated with intellectual disability (ID), such as Angelman, Fragile X and Cornelia de Lange syndromes (e.g., Dykens, 1995; Oliver et al., 2011;Summers et al., 1995; Wolff et al., 2012). It has become apparent that many of these syndromes have risk markers that may make individuals more vulnerable to mental health disorders such as anxiety, affective disorders and psychosis (e.g., Vogels et al., 2004). This link is better defined in certain neurodevelopmental syndromes, with mental health difficulties being described within some syndromes' phenotypes (e.g., Harris, 2002). Researching the prevalence and course of common mental health disorders (see Cooper et al., 2007; Deb et al., 2001), such as anxiety, depression, affective disorders and psychosis, in individuals with genetic syndrome groups is important for developing services that adequately cover individuals' needs over their life span to improve their quality of life. The quality of life of individuals with Intellectual Disabilities (ID) currently remains lower than for individuals from typically developing populations on objective measures (e.g. Health as indicator of quality of life; Hensel, Rose, Stenfert Kroese, & Banks-Smith, 2002). More broadly, further

research into mental health disorders in syndrome groups could also provide further insight into particular genetic variations that may be risk markers for mental health disorders.

The majority of research into mental health disorders thus far has focused on typically developing populations, and has proven the complexity involved with defining and diagnosing mental health disorders (Stein et al., 2010). This level of complexity increases with individuals with ID due to physical health co-morbidities and communication difficulties (Emerson, Baines, Allerton, & Welch, 2012). This is further exacerbated, as behaviours that may be used for emotional regulation in typically developing populations (e.g. self injury) may perform an alternative function in individuals with ID (Klonsky, 2007). Therefore, both self-report measures and observations of behaviour may not be reliable indicators of mental health disorders. To reflect the differences in the presentation of mental health issues in individuals with ID, attempts have been made to develop suitable measures (e.g. the clinical interview of the Psychiatric Assessment Schedule for Adults with Developmental Disabilities (PAS-ADD; Moss, Prosser & Goldberg, 1996) and the Glasgow Depression Scale for Intellectual Disability (Cooper, Cuthill & Espie, 2003) or to adapt self-report measures to use with individuals with mild/moderate ID (e.g., adapted HADS; Dagnan et al., 2008). Measures used with individuals with severe ID or communication problems tend to rely heavily on observed behaviour and carer reports (e.g., Mood, Interest and Pleasure Questionnaire, Ross & Oliver, 2003; Anxiety, Mood and Depression Scale, Esbensen, Rojahn, Aman & Ruedrich, 2003).

The majority of research into neurodevelopmental syndromes to date has focused on children. There are various reasons for this. First, unidentified health problems mean that some

individuals do not reach adulthood. Second, the increasing use of genetic testing, and the advent of more sophisticated techniques, means that the proportion of younger people with a neurodevelopmental disorder receiving an accurate genetic diagnosis is greater than the proportion of older people (Dykens, 2013). Furthermore, families of younger children may be more likely to be in contact with specific services and support groups, which are often the recruitment base for studies. Data collection may also be simpler for younger individuals as it can be easier to match age/ability to contrast groups and there may be more suitable standardised tests available (e.g. Conner's Rating Scale; Conner, 2008). However, it is important to study the course of neurodevelopmental syndromes across the lifespan, following individuals into adulthood, especially within the area of mental health disorders, as studies of typically developing populations have highlighted that the majority of long-term mental health disorders first occur in the mid-teens to early twenties (Kessler et al., 2007). For individuals with genetic neurodevelopmental syndromes, the prevalence, symptomology and typical course of mental health disorders (as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM; APA, 1994)/ International Classification of Diseases (ICD; WHO, 1993) diagnostic criterion is largely unknown. Considering the research into ID populations, the presentation of mental health disorders within individuals with neurodevelopmental syndromes is likely to be complex given the high levels of physical health and communication difficulties present. Greater clarity on the prevalence and presentation of mental health disorders is therefore necessary to assist Services with identification of mental health disorders whilst enabling Services to support the individuals' needs. This therefore, is the topic of the current literature review, which assesses the prevalence and descriptions of mental health disorders and explores what information, if any, is available on potential genetic variations that may be risk markers for mental health

disorders in adults (defined as aged 16 years and above) with neurodevelopmental syndromes. This will be assessed in seven neurodevelopmental syndromes that have the strongest research base as indicated by Powis (2013): Angelman, Prader-Willi, Cri du Chat, Cornelia de Lange, Fragile X, Williams and Smith-Magenis syndromes. In all of the syndrome groups assessed in the current article, behaviours potentially related to mental health disorders have been reported repeatedly (e.g., anxiety in Williams syndrome, Moldavsky, Lev & Lerman-Sagie, 2001; psychosis in Prader-Willi syndrome, Clarke et al., 1998; self-injury in Smith-Magenis syndrome and aggression in Angelman syndrome, Arron et al., 2011; specific fears in Angelman syndrome, Artigas-Pallarés et al., 2005; depression in Cri-du-Chat, Ferreiros-Martinez, Lopez-Manzanares, and Alonso-Cerezo, 2014, and social anxiety in Cornelia de Lange and Fragile X syndromes, Richards et al., 2009; Moldavsky, Lev & Lerman-Sagie, 2001).

*Angelman syndrome (AS)*: AS, was first described by Angelman (1965) and has a prevalence of approximately 1 in 10,000-40,000 (Buckley, Dinno & Weber, 1998; Clayton-smith, 1993), is caused by a deletion, translocation, mutation or uniparental disomy at chromosome 15q11-13. AS is associated with severe ID, sleep disturbances, hyperactivity and aggression and, stereotyped behaviours (Clayton-Smith, 2001; Summers & Feldman, 1999; Summers et al., 1995). In comparison to individuals with ID of unknown aetiology, people with AS may have lower levels of irritability and mood disorders (Summers & Feldman, 1999), although Artigas-Pallarés et al. (2005) reported fear of noise in a third of their participants and a fear of crowds in half of them.

*Cri-du-chat syndrome (CdCS)*: Cri-du-chat (deletion 5p syndrome) described by Lejeune (1963) with a prevalence of 1 in 50,000 (Dykens, Hodapp, & Finucane, 2000)**.** Alongside moderate to severe ID, it is characterised by sleep disturbances (Cornish et al., 2004), self-injury (70.3% of children), and physical aggression (33.3% of children) (Cornish et al., 2004; Cornish, Oliver, Standen, Bramble, and Collins, 2003; Cornish & Pigram, 1996;). There have also been anecdotal links with mental health disorders, such as, Ferreiros-Martinez, Lopez-Manzanares, and Alonso-Cerezo's (2014) report of a woman with CdCS who had depression.

*Cornelia de Lange syndrome (CdLS):* This was first described in 1916 with an estimated prevalence of 1 in 50,000 (Opitz, 1985) caused by a genetic mutation in NIPBL (60%), SMC1A (<1%), and SMC3 (5%) genes (Borck et al., 2004; Deardorff et al., 2007) HDAC8 (5%; Deardorff et al., 2012a) RAD21 (<1%; Deardorff et al., 2012b). CdLS is diagnosed clinically in a proportion of cases as, the genetic origin may not be known. It is associated with gastrointestinal issues, moderate to severe ID, self-injurious behaviour (over 50% of children), social anxiety (Richards et al., 2009) and socially avoidant behaviours. Reports also identify physical aggression (49% of children), hyperactivity (40% of children) and autistic traits in 55-60% (Basile, Villa, Selicorni & Molteni, 2007; Berney, Ireland & Burn, 1999; Bhyuian et al., 2006; Hyman, Oliver & Hall, 2002; Luzzani, Macchini, Valade, Milani, & Selicorni, 2003; Moss et al., 2005; Oliver et al., 2006; Oliver et al., 2008).

*Fragile X Syndrome (FXS):* FXS is caused by excessive CGG trinucleotide repeats in the FMR1 gene on the X chromosome (Sherman, 2002). Characteristics associated with full mutation are mild to severe ID, social difficulties with social anxiety and high levels of autistic features in addition to, high irritability and hyperarousal (Hagerman & Cronister,

1996; Mazzocco, 2000; Moldavsky, Lev & Lerman-Sagie, 2001; Turk & Cornish, 1998; Turk, 2011). Common mental health disorders in children with FXS include hyperactivity and inattention (80% of boys and girls, Hagerman, 2002), anxiety (70% boys and 56% girls), self-injurious behaviour (41% boys and 10% girls) and there are some reports of depression (12% boys and 22% girls) (Bailey et al., 2008).

*Prader-Willi Syndrome (PWS):* PWS is caused by a deletion (65-75%), uniparental disomy (most commonly maternal uniparental disomy (mUPD); 20-30% of individuals with PWS), imprinting deficits (10%) or balanced translocation of SNURF/SNRPN region (0.1%) on chromosome 15q11-13 (Constantine Samaan, 2014). Features of PWS include borderline (IQ 70-85) to mild ID, social withdrawal and anxiety, obsessions and compulsions with food, impulsivity and disturbed affect regulation. The prevalence of mental health disorder diagnoses in children with PWS is estimated at higher than 50% (Whitman & Accardo, 1987), including ADHD (up to 25%), anxiety (3.4%) (Wigren & Hansen, 2005) and auditory hallucinations (34%) (Whitman & Accardo, 1987).

*Smith-Magenis syndrome* (SMS): SMS was identified in 1982 with a prevalence of 1 in 25,000 caused by a deletion of chromosome 17p 11.2 (Greenberg et al., 1991) and is characterised by moderate ID, sleep disturbances, high levels of challenging behaviour and hyperarousal (Greenberg et al., 1996). Hyperactivity, restlessness and impulsivity has been reported in 50-100% of children with SMS in addition to high levels of aggression (70%-100%) and self- injurious behaviour (67-100%) (Dykens & Smith, 1998; Greenberg et al., 1991; Rijk-van Andel et al., 1991; Webber; 1999).

*Williams Syndrome (WS):* WS is caused by a genetic deletion of a region containing 26 genes on the long arm of chromosome 7 (Martens, Wilson, & Reutens, 2008). It has been characterised by mild to moderate ID, hypersociability and high levels of anxiety and fears (Einfeld, Tonge, & Florio, 1997; Mervis & Morris, 2007; Moldavsky, Lev & Lerman-Sagie, 2001).

All empirical articles with an identifiable adult sample assessing common mental health disorders in the above neurodevelopmental syndromes were reviewed. However, Autistic Spectrum Disorders (ASD), Attention Deficit Hyperactivity Disorder (ADHD) and behavioural problems were excluded (in line with studies such as Cooper at al., 2007 and Smiley, 2005).

## METHOD

### *Search Strategy*

As few of the syndromes had been described prior to 1967, the search engines Psych Info and Web of Science were checked between 1967 and 03 October 2014 (Figure 1 depicts the search process, an extensive version of this can be seen in Appendix A). Anxiety disorders, affective disorders (depression and bipolar disorder) and psychosis were used as search terms based on the most common adult mental health disorders in ID (Cooper et al., 2007; Smiley, 2005). In addition, the search term 'mental health' was exploded in the search engines to create additional search terms. For the purposes of this literature review, FXS refers to individuals with the full mutation; studies assessing solely pre-mutation carriers or studies where it was not possible to discriminate participants with pre and full mutations were excluded.

### *Inclusion and exclusion criteria*

Most studies within this field were found to use the term "adult" to refer to individuals over the age of 16, therefore this review includes studies with participants exclusively over the age of 16, as well as any mixed-age studies that enabled the data for over 16s to be extracted for review. Consequently, any studies failing to publish the age of participants were excluded.

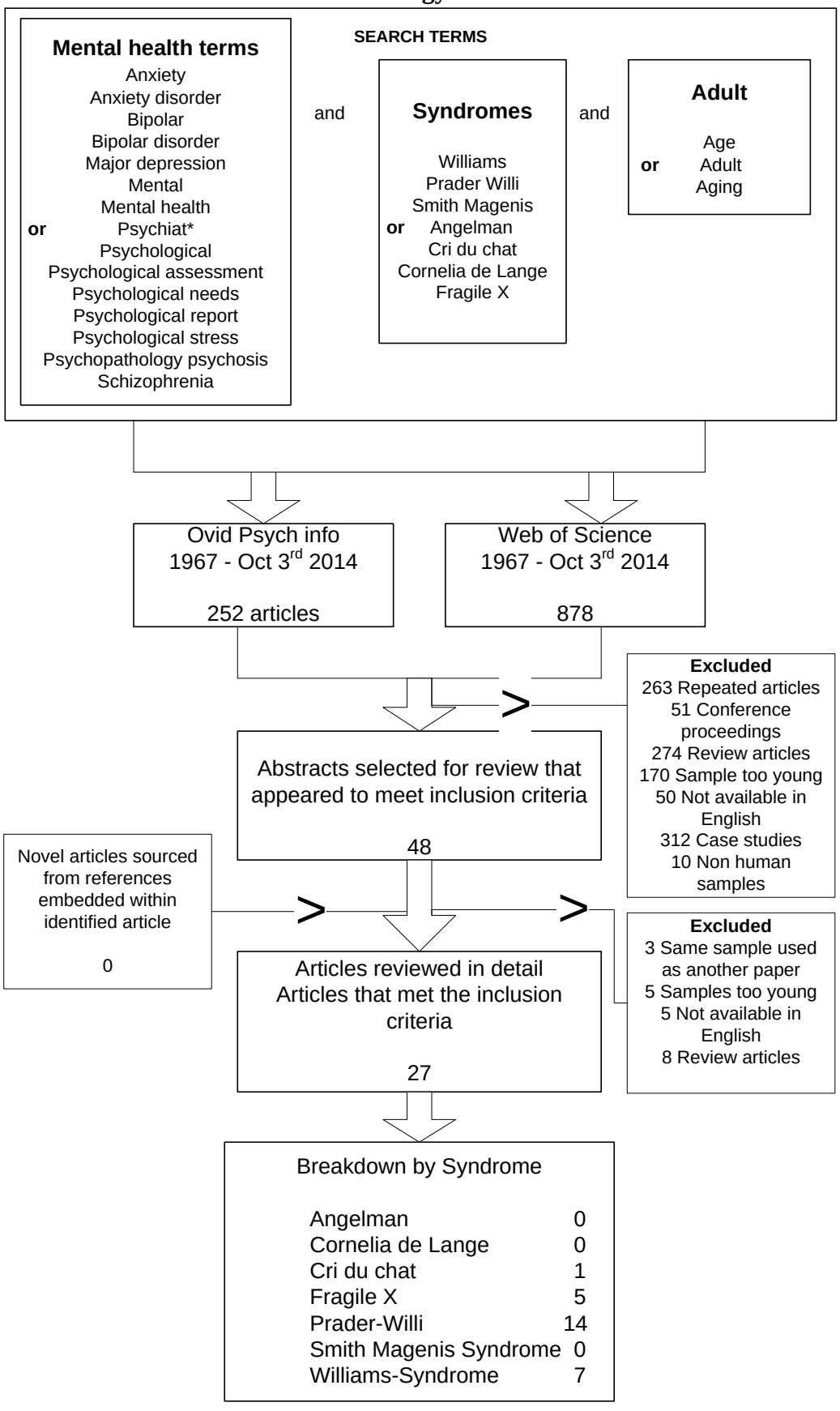
Unless information was provided on the prevalence or nature of the mental health disorders involved, articles focusing purely on treatment were excluded. Articles unavailable in English, conference proceedings and pure abstracts were excluded as it was not possible to determine whether these studies met the inclusion/exclusion criteria. Autism spectrum

disorders (ASD), Attention Deficit Hyperactive Disorder (ADHD) and behavioural problems, whilst common in ID (Cooper et al. 2007), were not included as mental health disorder search terms for review in line with ID research (Deb et al., 2001). Case series with less than five participants were excluded to increase the chance the samples would be representative of the syndromes. The reference sections of all papers were also examined to identify any additional relevant articles; however articles reproducing data were excluded to reduce re-sampling.

### *Quality Criteria*

As the number of papers was small, a quality criterion was not used to exclude papers based on poor methodology. However, aspects of the Effective Public Health Practice Project "Quality Assessment Tool for Quantitative Studies" (EPHPP; Thomas et al., 2004) were used to appraise the studies, as this tool was designed for use in all areas of Public Health Services, enabling comparison of different methodologies using the same quality assessment tool. These aspects included selection bias, study design, confounding variables, participant/analyser blinding, and data collection methods (see Table 2).

**Figure 1: The literature review search strategy**



## Results

The results of the literature review can be seen in Table 1. There were no papers found assessing the prevalence of mental health disorders in adults with AS, CdLS and SMS.

**Table 1: Table of papers researching the relationship between mental health disorders and adulthood in neurodevelopmental syndromes**

| Study | Age Range (years) | Sample | Method | Genetic confirmation | Assessments Used | Findings | Diagnostic Criteria Used |
|---|---|---|---|---|---|---|---|
| **Prader Willi Syndrome (PWS)** | | | | | | | |
| Bartolucci and Younger (1994) | 21-34 | N=9<br>5 Males<br>3 Females<br>1 Unknown | Case Studies from a dual diagnosis clinic (Hamilton Psychiatric Hospital) in Canada | Not noted | No assessments described | All participants were admitted to hospital with poor self-image and feelings of sadness.<br>Depression was dysphoric, angry and explosive.<br>Most participants had threatened to commit suicide to escape an adverse situation however one participant committed suicide under extreme stress.<br>There were three patterns in participants mental health disorders:<br>• Mental health trait fluctuation (cyclic food/drink refusal, weight loss/food binge and increase | Unknown |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | in antisocial behaviour)<br>• Lethargic refusal states (refusing food/drink and company), soiling and incontinence (no physical issues). Florid psychotic episodes (hallucinations, mood disturbance, delusional thoughts, agitation and insomnia). | |
| Boer et al. (2002) | 29-47 | N=25<br>15 Studied in detail<br>8 Males<br>7 Females. | Case studies of individuals in the UK with PWS. Viagnettes were made of participants' information that 2 blinded psychiatrists diagnosed to determine prevalence of mental health disorders in | 9 Deletion<br>1 Imprinting mutation<br>5 mUPD[1] | Initial screening, interview and full psychiatric assessment. | Based on the 15 participants studied in detail the mean age of onset for mental health disorders was 26. The prevalence of mental health disorders were:-<br>13% Depressive psychosis<br>- 20% Bipolar affective disorder<br>- 7% Depressive episode<br>- 13% Psychotic | ICD-10[2] |

[1] Maternal uniparental disomy (mUPD)
[2] International Classification of Diseases – 10th Edition (ICD-10)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | individuals with PWS. | | | disorder - 33% Paranoid delusions and hallucinations<br>- 7% Behavioural problems<br>- 60% Psychiatric illness<br>- 28% Major affective or psychotic illness.<br>Characteristic features of mental health disorders were a combination of bipolar/depression and psychotic symptoms. | |
| Beardsmore, Dorman, Cooper, and Webb (1998) | 21-38 | N=23<br>9 Males<br>14 Females | Prevalence study based on individuals with PWS in Northamptonshire, UK. Participants were compared against an ID control group in a neighbouring county. | 100% Clinical diagnosis and 87% genetically tested.<br>10 Deletion<br>1 mUPD[1]<br>PWS pattern in 13 | PPS-LD[3], Adaptive Behavior Scale, and the mini PAS-ADD[4]. | The prevalence of mental health disorders were:<br>- 17.4% Self-harm<br>- 34.8% Skin picking<br>- 17.4% Affective disorder and psychotic symptoms<br>- 4.3% Recurrent depression<br>- 4.3% Schizophrenia<br>- 4.3% OCD[5]<br>- 17.4% Affect | The ICD-10[2],DSM-IV[6], Kettering/ Leicester diagnostic criteria for depression in adults with learning disabilities and the |

[3] Present Psychiatric State for People with Learning Disabilities (PSS-LD)
[4] Psychiatric Assessment Schedules for Adults with Developmental Disabilities (PAS-ADD)
[5] Obsessive Compulsive Disorder (OCD)

| | | | | | | | |
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| | | | | | | disorder<br>- 21.7% None<br>- 17.4% Met the ICD-10[2] criteria for a depressive episode<br>- 4.3% Met the ICD-10[2] persistent delusional disorder and DSM-IV[6] criteria for schizophrenia. | Perris Criteria for cycloid psychosis were used. |
| Clarke et al. (1998) | 28-46 | N=6<br>2 Males<br>4 Females | This was a UK based study assessing the prevalence of mental health disorders and compared blood samples against individuals with AS. | 83.3% Had genetically confirmed PWS<br>2 Chromosome 15 deletion<br>2 mUPD[1]<br>1 Mutation | Case note review and interview with participant and their carer. Assessments used were the ABC[7] and VABS[8] | - 66.7% Participants were diagnosed with cycloid psychosis (age of onset 12-21)<br>- 16.7% Participants had paranoid psychosis (age of onset 20)<br>- 16.7% Participants had bipolar affective disorder.<br>- Participants scored highest on the irritability/agitation, lethargy/withdrawal and hyperactivity/non-compliance subscales | Unknown |

[6] Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)
[7] Aberrant Behavior Checklist (ABC)
[8] Vineland Adaptive Behavior Schedule (VABS)

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| | | | | | | on the ABC[7].<br>- The authors determined that reported psychotic symptoms were unlikely to be caused by a single gene abnormality. | |
| Clarke (1998) | 16-51 | N=95 | Prevalence study of individuals with PWS in the UK. | 34 Deletion<br>4 mUPD[1]<br>2 Other<br>55 Unknown | PAS-ADD[4] Checklist – scores modified to take account of repetitive speech.<br>ABC[7] | - 14.7% Participants had a PAS-ADD[4] score indicative of a psychotic disorder.<br>- 6.3% Past the threshold for a possible psychotic disorder.<br>- Participants scored highest on the Irritability/agitation subscale of the ABC[7]. | PAS-ADD[4] Checklist scoring criteria |
| Dykens and Roof (2008) | Over 16 | N=63 | This study compared the behavioural issues in individuals with PWS in the United States of America across age and genetic subtype. | 20 Type 1 Deletion<br>23 Type 2 Deletion<br>20 UPD[9] | The assessments used were the CBCL[10], Y-BOCS[11], Hyperphagia Questionnaire and VABS[8]. | 50% of UPD[9], 20% Type 1 deletion and 26% Type 2 deletion subgroups were hospitalised due to their mental health disorder.<br>30% UPD[9] participants | Unknown |

[9] Uniparental disomy (UPD)
[10] Child Behavior Checklist (CBCL)
[11] Yale-Brown Obsessive Compulsive Scale (Y-BOCS)

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| | | | | | | were on anti-psychotic medication but not hospitalised. | |
| Hiraiwa, Maegaki, Oka, and Ohno (2007) | 18-31 | N=29<br>14 Male<br>14 Female<br>1 Unknown | Prevalence study of mental health diagnoses across the population of WS in Japan and compared against ID controls | Unknown | Semi-structured questionnaire on behavioural problems and psychiatric symptoms | The authors described:<br>- 20.7% Inactivity, "lack of spirit"<br>- 10.3% Depressive state<br>- 6.9% Manic state<br>- 10.3% Hallucination<br>- 20.7% Delusion<br>- 37.9% Any psychiatric symptoms<br>- 65.5% Emotional Liability<br>- 24.6% More adults had psychiatric symptoms than children.<br>- Adults with WS scored significantly higher for inactivity, delusion and overall prevalence of psychiatric symptoms than ID controls. | Unknown |
| Larson, Whittington, Webb, and Holland (2014) | Over 18 | N=28 | This is a longitudinal study of individuals with PWS in the UK and their psychotic | 8 mUPD[1], never psychotic<br>11 mUPD[1], psychotic<br>9 deletion, psychotic | Interview about their mental health disorders. | In the original sample 10% had previously had psychosis. At follow up there were no new diagnoses of psychosis. | Unknown |

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| | | | symptoms. | | | Out of those diagnosed with psychosis 10% now receive medication for psychosis and 10% had relapsed. Mood instability was still reported at follow up. Those without psychosis had better outcome. | |
| Sinnema et al. (2011b) | 18-66 | N=102 49 Males 53 Females | This is a prevalence study comparing the prevalence of mental health disorders in individuals in the Netherlands with PWS across genetic sub group. | 55 Paternal deletion 44 mUPD[1] 3 Imprinting centre deficit | Semi-structured interviews, PAS-ADD[4]. | 55% Participants with mUPD[1] had psychotic symptoms compared to 13% with a deletion. 64% Participants with mUPD[1] had a history of psychopathology compared to 17% with deletion. Mean age of onset for 1st psychiatric episode was 21.9yrs. | PAS-ADD[4] scoring criteria. |
| Sinnema et al. (2011a) | 18-66 Grouping <25 25-34 34-44 | N=98 | This is a prevalence study comparing individuals in the Netherlands with | Genetic confirmation used to separate participants into Type 1 deletion, | The DBC-A[12] was used. | Participants aged 25-34 scored highest on "rapid mood changes", "stubbornness" and "hiding things". | DBC-A[12] scoring criteria |

[12] Developmental Behaviour Checklist for Adults (DBC-A)

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| | 45< | | PWS across age and genetic sub group. | Type 2 deletion and mUPD[1]. | | Participants with mUPD[1] scored highest on the items "unhappy", "abusive", "poor attention", "strips" and "screams a lot".<br>Participants with mUPD[1] scored significantly higher on the depressive, disrupted and self-absorbed subscales. | |
| Sinnema, Schrander-Stumpel, Maaskant, Boer, and Curfs (2012) | 50-66 | N=12 | This is a study focusing on aging in PWS individuals in the Netherlands with PWS comparing physical characteristics and mental health disorders in older adults with PWS against working age adults with PWS (age 18-49) and drawing comparisons against participants' genetic sub | 4 Paternal deletion<br>8 mUPD[1] | Semi-structured interview, Observational Questionnaire for Elderly Residents with ID, DBC-A[12], PAS-ADD[4], and Food related Problem Questionnaire. | Participants with paternal deletion had no psychiatric illness.<br>In the mUPD[1] group:<br>- 25% Participants had bipolar illness with psychotic symptoms,<br>- 16.7% Participants had psychotic illness where affective symptoms are not prominent,<br>- 8.3% Participants had non-psychotic depressive illness,<br>- 8.3% Participants had bipolar illness with psychotic symptoms | ICD-10[2] |

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| | | | groups. | | | - 8.3% Participants had no psychiatric history<br>- 8.3% Participants had dementia. | |
| Verhoeven, Tuinier, and Curfs (2003) | 17-43 | N=19<br>10 Male<br>6 Females | This is a report of symptoms of individuals with PWS in the Netherlands with relapsing mental health disorders. | 10 UPD[9]<br>1 Del 15<br>5 Clinical Diagnosis | Comprehensive Psychopathological Rating Scale and the ABC[7] | Participants either had a diagnosis of Bipolar affective disorder (15.8%) or Cycloid psychosis (84.2%).<br>The most common symptoms were anxiety, confusion, mood swings, emotional turmoil and increased obsessive rituals in their psychotic state.<br>Previous diagnoses were depression (26.3%), bipolar (10.5%), paranoid psychosis (10.5%), pervasive developmental disorder (10.5%), psychotic depression (5.3%), psychotic disorder (2), delirious state (5.3%) cycloid psychosis (5.3%) and | ICD-10[2] |

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| | | | | | | paranoid psychosis (5.3%). | |
| Vogels et al. (2004) | 16-33 | 4 Males<br>2 Females | This was a study of Psychosis in individuals from Belgium with PWS. | Unknown | OPCRIT[13], clinical interviews and observations. | Most participants (83%) experienced a loss or potential loss prior to their first psychotic episode.<br>All 4 adults required hospitalisation (mean length 7 months).<br>All experienced prodromal phase and physical complaints in the days leading up to an episode.<br>On the DSM-IV[6] 83% of participants met psychotic disorder not specified diagnosis.<br>On the ICD-10[2] 66.7% of participants met diagnosis for bipolar with psychosis and 16.7% schizophrenia. | DSM-IV[6] and ICD-10[2] |
| Webb et al. (2008) | 17-56 | N=53<br>26 Males<br>27 Females | A study comparing the presence of psychosis across genetic sub groups of individuals | 25 with 15q11-q13 deletion no psychosis.<br>12 with15q11-q13 deletion with psychosis | Screening Questionnaire, PAS-ADD[4] and OPCRIT[13] | The authors found that all the participants with psychosis (PWS and 15q11q13) had mUPD[1] in the IVS5-6 section of the | Unknown |

[13] Operational Criteria for Psychotic and Affective Illness (OPCRIT)

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| | | | with PWS in the UK to determine the genetic origin of psychosis. | 4 UPD$^{9}$ no psychosis<br>12 UPD$^{9}$ with psychosis | | GABRG3 gene, indicating this genetic mutation may be linked to psychosis. | |
| **Fragile X Syndrome (FXS)** | | | | | | | |
| Hartley et al. (2011) | 22.1-63.5 | N=328<br>239 Males<br>89 Females | National survey of adults with FXS in the United States of America. | Unknown | Participants were asked in survey if their son/daughter has been diagnosed/ treated for affect problems (depression and anxiety), attention problems, hyperactivity, aggressiveness self-injury and/or autism. | Men had significantly more co-occurring mental health problems (Mean 1.61, SD 1.21) than women (Mean 2.80, SD 1.49) and higher prevalence of affect disorders (anxiety and depression; Males 72%, Females 59%) | Unknown |
| Hagerman (2009) | 18-31 | N=29<br>14 Male<br>14 Female<br>1 No response | This is a prevalence study of mental health disorders in adults with FXS in the United States of America. | Unknown | Semi-structured questionnaire | 37.9% Demonstrated some evidence of a psychiatric illness (e.g. delusion 20.7%, hallucinations 10.3%, depressive state 10.3% and manic state 6.9%). 10% Participants had been admitted to hospital for psychotic states. | Unknown |

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| Kerby and Dawson (1994) | Mean age 44 (SD 10.2) | N=9<br>9 Males | This is a prevalence study comparing against individuals with ID in the United States of America. | Genetically tested. | Adult Functional Scale, VABS[8], EASI[14]. | Participants with FXS had significantly higher emotionality, schizoid, and schizotypical personality disorder traits than learning disability controls. | DSM-III[15] |
| Sabaratnam, Venkatesha Murthy, Wijeratne, Buckingham, and Payne, (2003) | 21-76 | N=18<br>18 Males | A 10-year follow-up of mental health disorders and autistic traits in individuals with FXS in Essex, UK. | Clinical and anthropometric criteria for screening was used to select whether to perform genetic testing for FXS in the sample. Participants that did not meet this were excluded. | B-DAS[16], HBS[17] and mini PAS-ADD[18] | In 1989 11.1% had a diagnosis of schizophrenia and 5.6% had a mood disorder (not specified).<br>In 2000 16.7% had a diagnosis of schizophrenia and 16.7% met the cut-off score for anxiety. | DSM-III[15] |
| Utari et al. (2010) | 40-71 | N=62<br>44 Males<br>18 Females | Retrospective study of individuals referred for an FXS assessment in the United States of America. | 3.2% Exact genetic mutation unknown<br>6.7% Hypermenthylated full mutation<br>23.3% Mosaic | Retrospective study of files, assessments not noted. | 9.7% Participants had experienced Dementia/cognitive decline.<br>46.8% Participants were on psychotropic medication. | Unknown |

[14] The Emotionality, Activity and Sociability Impulsivity Temperament Scale (EASI)
[15] Diagnostic and Statistical Manual of Mental Disorders - Third Edition (III)
[16] Brief Disability Assessment Schedule (B-DAS)
[17] Handicaps, Behaviours and Skills Schedule (HBS)
[18] Mini Psychiatric Assessment Schedules for Adults with Developmental Disabilities (Mini PAS-ADD)

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| **Williams Syndrome (WS)** | | | | | | | |
| Cherniske et al. (2004) | 30-51 | N=20<br>10 males<br>10 females | Prevalence study of individuals with WS in the United States of America. | 17 Elastin deletion confirmed by FISH[19], 3 clinically confirmed | ADIS[20], SADS[21] and open ended interviews. | 95% Described as having depression and/or anxiety.<br>65% Diagnosed with mod-severe anxiety (most common specific phobia and GAD[22]). Other diagnoses included:<br>- Simple Phobia (50%)<br>- Depression (10%)<br>- Manic Depression (5%)<br>- Panic Disorder (5%)<br>- OCD[5] (5%) | DSM-IV[6] |
| Davies, Udwin, and Howlin (1998) | 19-39.9 | N=70<br>33 Males<br>37 Females | Prevalence study of social, emotional and behavioural difficulties in individuals with WS in the UK. | Unknown | Interview items from Social and Emotional Functioning Interview, Autistic diagnostic interview and VABS[8] were used. | 21 Participants (30%) were referred to mental health services over last 2 years for anxiety, panic attacks, phobias, depression.<br>50% Participants had pre-occupations/ obsessions that were disruptive. Disruptive levels of mood | Unknown |

[19] Fluorescence in Situ Hybridisation (FISH) genetic testing
[20] Anxiety Disorder Interview Schedule (ADIS)
[21] Schedule for Affective Disorders and Schizophrenia (SADS)
[22] General Anxiety Disorder (GAD)

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| | | | | | | disturbance (not specified) were reported by 10% of participants, disruptive phobias 41% and disruptive anxiety 16%. | |
| Dodd and Porter (2009) | 18-50 | N=20<br>8 Males<br>12 Females | Cross-sectional study of prevalence of psychopathology in individuals with WS in Australia. | Unknown | K-SADS-PL[23] and the WJ-COG-R[24]. | Adults had significantly higher rates of depressive disorders (25%) compared to children (3%).<br>Age of onset of depressive disorders was 15-20 years.<br>Anxiety disorders were reported in 40% of adults.<br>30% Met at least one diagnosis, though 50% did not meet any diagnosis. | DSM-IV[6] |
| Dykens (2003) | 19-48 | N=41 | Cross-sectional prevalence study of anxiety, fears and phobias in individuals with | Molecular testing available for 65% | FSSC-R[25] | WS participants FSSC-R[25] scores were significantly higher than ID controls.<br>The interaction | FSSC-R[25] scores |

[23] Schedule for Affective Disorders and Schizophrenia for school-age children – present and lifetime version (K-SADS-PL)
[24] Woodcock-Johnson Test of Cognitive Ability-Revised (WJ-COG-R)
[25] Fear Survey Schedule for Children Revised (FSSC-R)

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| | | | WS in the United States of America. | | | between age and scores was mediated by gender (men scored higher than boys and females higher than girls).<br>Adults scored higher than children on fears of criticism, injury/animals and danger/death. | |
| Howlin and Udwin (2006) | 19-56 | N=239<br>118 Males<br>121 Females | A study of the outcomes in adults with WS in the UK. | Genetic confirmation by FISH[19] in 108 the remaining 115 had one or more symptoms associated with WS. | 42 Item self-created Questionnaire. | Psychological issues mainly began at ages 20-30.<br>Depression and anxiety were most prevalent (51%).<br>Aggression/angry outbursts were experienced by 4%, panic attacks by 2%, and severe phobias and obsessions by1%, 1 Participant had attempted suicide and 1 participant was admitted to hospital with stress. | Unknown |
| Stinton, | 19-55 | N=92<br>42 Males | Prevalence study of mental health | Genetic Confirmation by | Parental interview, WAIS III[26], | The most prevalent issues were: | ICD-10[2] |

[26] Weschler Adults Intelligence Scale third edition (WAIS III)

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| Elison, and Howlin, (2010) | | 50 Females | disorders in adults with WS in the UK. | FISH[19]. | VABS[8], Expressive One Word Picture Vocabulary Test, British Picture Vocabulary Scale (2nd edition), and the PAS-ADD[4]. | - 43.5% Phobias<br>- 8% OCD[5]<br>- 5% Psychosis.<br>- 29% Diagnosable disorder<br>- 13% Depression<br>- 19% Anxiety | |
| Stinton, Tomlinson, and Estes (2012) | 20-42 | N=19<br>10 Males<br>9 Females | Prevalence study of individuals with WS in the UK. | Genetic confirmation by FISH[19]. | Stroop test and the PAS-ADD[4] | 10.6% Reported significant issues with mood.<br>5.3% Diagnosed with Depression.<br>Participants rated higher on anxiety scales and words than depression. | Unknown |
| **Cri-du-Chat Syndrome (CdCS)** | | | | | | | |
| Van Buggenhout et al. (2000) | 16-47 | N=7<br>4 Males<br>3 Females | Case Studies of individuals with CdCS in the Netherlands. | 1 Del(5)(p14.1)<br>5 Del (5) (p13.3) and 1 Del (5) (p15.31) | Case studies measures not described. | Participants become more nervous and aggressive. 29% Had a fear of loud noises. | Unknown |

## Prader-Willi Syndrome

There were fourteen articles identified for PWS, eleven of which reported the prevalence of mental health disorders in adults with PWS. The *N* ranged from 6 to 102 and the age range was 16-76. The mental health diagnostic measures used in these studies were versions of the PAS-ADD, the Comprehensive Psychopathological Rating Scale, the OPCRIT or clinical interviews (e.g. Boer et al., 2002; Beardsmore et al., 1999; Clarke et al., 1998; Clarke, 1998). Clarke et al. (1998) and Larson et al. (2014) reported existing mental health diagnoses from Mental Health Services, rather than assessing participants directly. The diagnostic criteria used were reported in eight studies (Boer et al., 2002; Beardsmore et al., 1998; Clarke, 1998; Sinnema et al., 2011b; Sinnema et al., 2011a; Sinnema et al., 2012; Verhoeven et al., 2003; and Vogels et al., 2004), consisting of the ICD-10, DSM-IV, the Perris criteria for cycloid psychosis, and the PAS-ADD and DBC-A scoring criteria's. Only one study used a diagnostic criteria designed for individuals with ID (the Kettering/Leicester diagnostic criteria, Beardsmore et al., 1998). There were three studies with comparison groups, one population study comparing prevalence against children with PWS (Hiraiwa et al., 2007), and two studies using adults with idiopathic ID as a comparison group (Hiraiwa et al., 2007; Beardsmore et al., 1998). Most were cross-sectional studies with only one longitudinal study (Larson et al., 2014).

### *Prevalence*

Prevalence of diagnosable mental health disorders in individuals with PWS varied across studies from 28% (Boer et al., 2002) to 58.3% (Sinnema et al., 2012). This is somewhat higher than the estimated prevalence of 20.1% - 31.7% in people with ID of unknown

aetiology (Cooper, Smiley, Morrison, Williamson, & Allan, 2007; Taylor, Hatton, Dixon, & Douglas, 2004; Morgan, Leonard, Bourke, & Jablensky, 2008).

Reported prevalence of psychosis varied between 1.4% (Beardsmore et al., 1998) and 84% (Verhoeven et al., 2003). This contrasts with an estimated prevalence of 3.7–5.2% in people with idiographic ID (Morgan et al., 2008) and 34% of adolescents with PWS experiencing hallucinations (Whitman & Accardo, 1987), reflecting a high co-morbidity between PWS and psychosis that may increase with age. This is not unexpected given that the age of onset for psychosis tends to be late adolescence to early adulthood. Diagnosed levels of cycloid psychosis were particularly high at 66.7% (Clarke et al., 1998) to 84% (Verhoeven et al., 2003). However, there appeared to be a large overlap between the symptoms of psychosis and bipolar disorder, with many studies describing participants having bipolar illness or depression with psychotic symptoms, ranging in prevalence from 5.5% (Beardsmore et al., 1998) to 25% (Sinnema et al., 2011b). The prevalence of bipolar disorder alone remains high within this group at 8.3% (Sinnema et al., 2011b) to 16.7% (Clarke et al., 1998), especially when compared to estimates of people with ID of unknown origin (1.5%; Smiley, 2005) and rates of depressive states in children with PWS (0-2.2%; Hiraiwa et al., 2007).

Individuals with mUPD appeared to have a higher prevalence of mental health disorders (50% (Dykens & Roof, 2008) to 87.5% (Sinnema et al., 2012) than individuals with a deletion gene, for whom prevalence was 0% (Sinnema et al., 2012) to 17% (Sinnema et al., 2011b). This could explain the overall high prevalence of mental health disorders in Sinnema et al.'s (2012) study and psychosis in Verhoeven et al.'s (2003) study, where the proportion of participants with mUPD was 66.7% and 52.6% respectively, both being higher than the average PWS

mUPD prevalence (20-30%; Constantine Samaan, 2014). Webb et al. (2008) suggested that all participants with psychotic experiences had two maternal copies of GABRG3 gene and suggesting this may be a genetic risk marker for psychosis. It is unclear whether this is supported by the other studies as the genetic subtype of individuals experiencing psychotic symptoms was not reported in all studies.

### *Specific manifestations*

Whilst the studies of PWS suggested a high prevalence of psychosis and depression, the symptoms failed to fit neatly into the diagnostic criteria for depression or psychosis due to complicated presentation of symptoms. Some studies reported high scores of depression on behavioural assessments (Jauregi et al., 2013; Sinnema et al., 2011a), fitting with a typical presentation, whilst Bartolucci and Younger (1994) suggest more of an angry and explosive mood than the typical lethargic state seen in depression, with threats of suicide being driven less by mood than by attempts to escape adverse situations. Most studies noted cyclical mood instability, anxiety, emotional turmoil, and confusion consistent with the prodromal phase of schizophrenia (Addington, 2003), with the diagnosis of participants in some studies being converted from depression to cycloid psychosis after further assessment (e.g. Verhoeven et al., 2003). Anecdotal reports of individuals with PWS with depression appear to corroborate this finding, describing cyclical remission and ideas of persecution (e.g. Watanabe, Ohmori, & Abe, 1997). This may lend support to the argument that the ICD-10 (WHO, 1993) and DSM-IV (APA, 1994) criteria are not sensitive enough to use with ID populations as the symptoms of mental health disorders are atypical (e.g. depression; Marston et al., 1997).

The case studies provided detailed accounts of psychosis in individuals with PWS, suggesting differences in presentation to typically developing individuals. Whilst individuals may have hallucinations and delusional and/or paranoid thoughts, an increase in the individuals' obsessive rituals was also described during psychotic episodes (Verhoeven et al., 2003). Studies noted some differences in the lead up to a psychotic episode with Vogels et al. (2004) noting that individuals with PWS had experienced physical complaints in the days leading up to and during the initial days of a psychotic episode. In contrast, Bartolucci and Younger (1994) describe cyclical patterns, with individuals with PWS refusing food/drink, withdrawing socially and becoming incontinent (with no physical health reason) in the days leading up to a psychiatric episode. However, it must be noted that this information is based on case studies with small sample sizes and no description of assessments used. Clearly, larger sample sizes are needed to assess how broadly such patterns apply.

**Fragile X Syndrome**

Five papers were identified for FXS, with *N* varying from 9 to 328 and ages ranging from 18 to 76. There was one 10-year follow-up study of mental health disorders in males (Sabaratnam et al., 2003), one national survey (Hartley et al., 2011) and one retrospective review of referrals for evaluation of FXS (Utari et al., 2010). Only one study used a comparison group of individuals with idiopathic ID (Kerby & Dawson, 1994). Assessment methods included non-standardised questionnaires, the VABS, The EASI, B-DAS, and HBS and only two studies noted the diagnostic criteria used (DSM-III; Kerby & Dawson, 1994; Sabarstnam et al., 2003).

### *Prevalence*

The reported prevalence of mental health disorders within adults with FXS were also higher than for individuals with idiopathic ID/ID of unknown origin (Cooper et al., 2007; Morgan et al., 2008; Taylor et al., 2004), ranging between 37.9% (Hagerman, 2009) and 46.8% (Utari et al., 2010).

The overall prevalence of psychosis appears lower in adults with FXS than in adults with PWS, at 10.3% (Hagerman, 2009) to 16.7% (Sabaratnam et al., 2003). However, there is a high prevalence of specific psychotic symptoms, such as delusions (20.7%; Hagerman, 2009), suggesting a possible connection between FXS and certain symptoms of psychosis rather than psychosis more generally. Studies have not reported the levels of co-morbidity between psychosis and depression that were reported in the studies on PWS. The prevalence of anxiety and depression in FXS ranged between 5.6% (Sabaratnam et al., 2003) and 72% (Hartley et al., 2011). This seems fairly consistent when compared to children with FXS (anxiety 56-70%, depression 12-22%; Bailey et al., 2008). However, this is difficult to assess given the different presentations of the results (some studies reported mood disorders as combined figures (e.g. anxiety and depression) and others presented rates for individual disorders). There was one report of an individual with dementia (Dykens & Roof, 2008).

### *Specific manifestations*

Despite reported links between anxiety and FXS, there were no detailed descriptions of the course of mental health disorders in people with FXS other than Kerby and Dawson (1994), who note that individuals displayed more emotionality, and schizoid and schizotypical personality disorder traits, than individuals with idiopathic ID.

## Williams Syndrome

There were seven papers assessing people with WS, with *N* varying from 20 to 239, and ranging in age from 18 to 56. There were no longitudinal studies for WS and only two used a control group (school children with WS; Dodd & Porter, 2009; Dykens, 2011;). The remaining five studies were prevalence studies exploring the psychological, emotional and behavioural issues within adults with WS. The assessments used within these studies tended to be individual measures assessing aspects of emotion and behaviour (e.g. ADIS, SADS, K-SADS-PL, WJ-COG-R, FSSC-R and VABS). The PAS-ADD was mainly used as a diagnostic tool (Stinton et al., 2010; Stinton et al., 2012), with two studies using a version of the DSM (Cherniske et al., 2004; Dodd & Porter, 2009) and one using the ICD-10 (Stinton et al., 2010) as a diagnostic criteria. The remaining four studies do not report using a diagnostic criterion.

### *Prevalence*

The overall prevalence of psychopathology reported within WS varied between 29% (Stinton et al., 2010) and 95% (Cherniske et al., 2004). The most common issues appeared to be depression and anxiety with prevalence of 10% (Davies et al., 1998) to 95% (Cherniske et al., 2004). The prevalence of depression in adults with WS is higher than prevalence rates for individuals with idiopathic ID (4%; Smiley, 2005) and 22% higher than for children with WS (Dodd & Porter, 2009), which is consistent with Woodruff-Borden et al.'s (2010) longitudinal study of anxiety in children and adolescents. The prevalence of anxiety (19%, Stinton et al., 2010; to 65% Cherniske et al., 2004) was higher than depression (5%, Stinton et al., 2012; to 25%, Dodd & Porter, 2009). Phobias (1.3%, Howlin & Udwin, 2006; to 50%, Cherniske et al., 2004) and general anxiety disorder (specific prevalence rates not available) were

reportedly the most common types of anxiety. It is unclear the extent to which assessment tools and diagnostic criteria may have played within the differences seen in prevalence, for example, Howlin and Udwin (2006) reported on past diagnoses, without reporting the means by which such diagnoses were made.

Obsessive-compulsive behaviours appear more prevalent within this group, although individuals may not necessarily meet diagnostic criteria since studies discussed obsessive-compulsive traits rather than diagnoses. However, anecdotally, there are reports of individuals with WS whose obsessive traits have had significant impact on their lives, such as a man whose obsessive thoughts about the sexual practices of others had led to many police warnings (Klein-Tasman & Albano, 2007). In contrast, the prevalence of psychosis was lower than in PWS and FXS, with one report of 5% (Stinton et al., 2010).

### *Specific manifestations*

Within the sample of studies on WS, there is some disparity in the age of onset of mental health disorders. Whilst Dodd and Porter (2009) describe a typical age of onset for depression between the 15 and 20 years, Howlin and Udwin (2006) suggest an age of onset of 20-30 years for psychological disorder (including depression and anxiety). Both are a little lower than the age of onset for anxiety or depression within a typically developing population (25-45 years; Kessler et al., 2007). Whilst no detailed descriptions of the mental health disorders are available, Dykens (2003) described fear increasing with age in both males and females. Dykens (2003) describes a difference in the content of fears with age. Fears of danger/death, injury/animals and criticism were more prevalent in adulthood, though it was not noted

whether this was to a clinically significant level. This variation in the severity and content of fears with age may reflect increased knowledge and experience that comes with age.

### Cri du Chat syndrome

A single study was found reporting mental health disorders in adults with CdCS. Van Buggenhout et al. (2000) describe a case series of seven adults with CdCS, finding that individuals with CdCS became more nervous with age with 29% becoming afraid of loud noises. However, it is unclear whether participants' symptoms were at clinically significant levels.

### Quality Assessment

As seen in Table 2 whilst the focus of these studies was on diagnosed mental health disorders**,** the measures used for diagnosis on most studies were either not available (Bartolucci and Younger, 1994; Boer et al., 2002; Utari et al., 2010; Van Buggenhout et al., 2000) or novel measures were used and not included in the appendix (Hagerman, 2009; Howlin & Udwin, 2009) making it difficult to determine how accurate or valid the diagnosis were. This is particularly problematic as based on the literature presented there is debate about diagnoses, especially in PWS where symptoms seem to lie between psychosis and bipolar. Arguably, amongst the studies available**,** it is the case study data that provides the most rich detail that would assist in early identification and treatment of mental health disorders amongst individuals with neurodevelopmental syndromes however, it is difficult to determine how representative the sample is.

Whilst NICE guidelines is still developing guidance on assessing mental health disorders in individuals with ID (NICE, 2014), BPS guidelines on assessing dementia recommend the use of the PAS-ADD Checklist or mini PAS-ADD or the Glasgow depression and anxiety scales when assessing for mental health disorders (BPS, 2015). Only six of the studies report using a version of the PAS-ADD (Beardsmore et al., 1998; Clarke, 1998; Sinnema et al., 2011b; Sinnema et al., 2012; Stinton et al., 2010; Stinton et al., 2012; Webb et al., 2008;) and none of the studies used any of the Glasgow Scales, despite assessing anxiety and depression. Furthermore, research into ID suggests that the DSM (e.g. APA, 1994) and ICD-10 (WHO, 1993) criteria should be supplemented by a diagnostic criterion for individuals with ID, which only one study used (Beardsmore et al., 1998). Instead, most studies relied highly on non-direct measures designed for children or behavioural measures, which impacts on the reliability of the data (Jauergi et al., 2013). Overall, this makes the results of these studies questionable and in greater need of investigation.

**Table 2: Assessment of the Quality of the Papers Reviewed**

| Study | Selection Bias | Study Design | Confounders | Genetic confirmation | Blinding | Data Collection Methods- Diagnostic criteria | Withdrawal/ drop out | Analysers? Who analysed? Method? Checked? |
|---|---|---|---|---|---|---|---|---|
| **Prader Willi Syndrome (PWS)** | | | | | | | | |
| Bartolucci and Younger (1994) | It is unclear how representative the sample is as the study has a small sample size, the genetic subtypes are not described by the study and one participant has a lower than average IQ for PWS based on the typical population. | Case Studies. | No contrast group used. | Not noted | None | The data collection methods are not reported in the case studies. | Unknown | Unknown |
| Boer et al. (2002) | The sample has a higher than average percentage of imprinting mutation (7%) and (13%) had a moderate ID. Only 15 of the participants were | Case vignettes of clinical material. | No contrast group used. | Information provided on the genetic subtypes: 60% Deletion 7% Imprinting mutation 33% Maternal Heterodisomy. | The diagnosing Psychiatrists were blinded over whether the participants had PWS. | Initial screening, interview and full psychiatric assessment were given, but no specific tools were mentioned. | Unknown. | All the assessment information was collated to be diagnosed by blinded Psychiatrists. |

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| | selected to study in detail creating a small sample. Therefore, the sample may not be representative of all individuals with PWS. | | | | | | | |
| Beardsmore, et al. (1998) | This study has a medium sized sample of 25 participants, which appears small in comparison to the ID control group. There was a high response rate (92%) and 100% of the participants had a diagnosis of PWS. Therefore, this sample is likely to be representative of individuals with PWS. | Comparison study against ID controls. | Comparison with 73 randomly selected Intellectual disability controls matched controlling for age, gender and IQ. | All participants had a clinical diagnosis and 87% were genetically tested.<br>10 Participants had the deletion<br>1 had mUPD[1] and 13 had the PWS pattern. | None. | The study used measures designed for ID populations and a diagnostic criteria designed for individuals with ID (the Kettering/ Leicester diagnostic criteria for depression in adults with learning disabilities.) | Unknown. | The authors analysed the measures. |
| Clarke et al. (1998) | Little information is provided about the background of the cases discussed in the | Case note review. | Blood samples were compared against individuals | 83.3% Participants had genetically confirmed PWS | None. | The measures used have been designed for or validated for use with | Unknown. | Information came from interviews with participants |

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| | study, other than their physical characteristics (e.g. height and weight) making it difficult to determine how representative this small sample of individuals with PWS. | | with Angelman Syndrome. However, there was no control group for the clinical features. | 2 Chromosome 15 deletion<br>2 mUPD[1]<br>1 mutation | | individuals with ID. | | and carers, being analysed by the treating professional reducing the chance of bias. |
| Clarke (1998) | Participants varied in ID from mild (27.4%), moderate (54.7%), to severe (11.6%) with 6.3% unknown and the genetic subtype of PWS for the majority of the participants is unknown. The response rate was 41.5%; therefore the representativeness of this sample is questionable despite the large sample size. | Cohort study. | No control group used. | Genetic confirmation was only available for 40 participants. | None | The measures used were either designed for or validated for use with individuals with ID. Whilst this is based on the ICD-10[2], the results were not independently checked using a diagnostic criterion designed for individuals with ID. | Unknown | The information was analysed by the author. |
| Dykens and | This study has a | Cross- | This study | Genetic | None | The study uses | Unknown | Data was |

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| Roof (2008) | relatively large sample of individuals with PWS, with a relatively proportionate representation of the genetic subtypes and a range of IQs. Therefore, this sample is likely to be highly representative of individuals with PWS. | sectional study of individuals with PWS. | controlled for age and genetic subtype, grouping results into age, and then separating results for adults by genetic subtype. | subtype was available for all participants: 32% Type 1 Deletion 36% Type 2 Deletion 32% UPD | | a combination of child measures (e.g. CBCL[10]), gold standard measure for OCD[5] symptoms (Y-BOCS[11]) measures for typically developing individuals (e.g. hyperphagia questionnaire) and those designed for individuals with ID. | | analysed by the authors. |
| Hiraiwa et al. (2007) | The response rate was 41%, little the demographic information about these participants is known. Participants had a range of ID (Borderline IQ 4.2%, Mild 33.3%, Moderate 62.5%). However, | Population study of mental health problems across the population of WS in Japan | A control group of age matched individuals with ID was used. | Unknown | None | The authors created a Semi-structured questionnaire on behavioural problems and psychiatric symptoms, which was not included in the paper. Individuals | Unknown | The data was analysed by the authors. |

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| | the genetic subtype of these participants is unknown; therefore, the representativeness of this sample is unclear. | | | | | were asked about past mental health disorders. The interview is not included; therefore, it is unclear whether it was valid for the sample. | | |
| Larson et al. (2014) | The response rate for this study was 41.7%. It is not clear whether the participants that did not respond were untraceable/ declined/ died. There was a high percentage of participants with mUPD (67.9%) compared to the PWS population, therefore, the sample may not be entirely representative of the population. | Longitudinal study taken over 10 years. | None | Genetic subtype available for all participants: 29% mUPD[1], never psychotic 39% mUPD[1], psychotic 31% delPWS, psychotic | None | Participants were interviewed by the author about any mental health problems or diagnoses. The interview is not included; therefore, it is unclear whether it was valid for the sample. | Unknown | The authors analysed the results. |
| Sinnema et al. (2011b) | 5 Participants were excluded as | Cross-sectional | The study separated | Genetic confirmation | None. | This study used a semi- | The study excluded 5 | Interviews with carers |

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| | the researcher was unable to assess the individuals due to their psychiatric state at the time. Therefore, this study may not fully represent all participants with PWS and a mental health issue. Little demographic information was given on participants other than their age and genetic subtype. | study of genetic subtypes. | groups by genetic subtype rather than matching based on age or IQ, therefore, the study may not have controlled for these variables. | was provided for all participants: 54% Paternal deletion 43% mUPD[1] 3% Imprinting centre deficit | | structured interview, though no details are provided about this and the PAS-ADD which has been validated for use with individuals with ID. The study does not report if a separate diagnostic criteria was used. | participants as their psychiatric problems meant they were unable to be interviewed. | and participants were assessed by the author. |
| Sinnema et al. (2011a) | From the identified sample 72.5% consented to the study with a response rate of 96% of those with a genetic confirmation of PWS. It was not possible to determine the genetic subtypes of the adults | Cross-sectional study. | This study controlled for age and genetic subtype, though not for IQ. | Genetic confirmation was used to separate participants into Type 1 deletion, Type 2 deletion and mUPD[1]. | The DBC-A[12] was used. | The assessment used has been validated for use with individuals with ID, though, no independent diagnostic criteria appears to have been used. | Unknown | The results were analysed by the author. |

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| | involved in this study, or any other demographic variables to determine the representativeness of this sample. | | | | | | | |
| Sinnema et al. (2012) | This a small sample with a higher than average percentage of mUPD participants. The IQ of participants ranged between mild (33% participants), mod (50% participants), and severe (17% participants). No information is given on how the participants were selected, but there was no significant difference in the age or gender of non- responders. The | Cross-sectional study. | The comparison group in this study was made up of younger adults with PWS (aged 18-49), not controlled for age, IQ or genetic subtype. Results were further separated within the older adult group to control for genetic subtype. | Genetic confirmation was provided purely for the older adult group: 33%Paternal deletion 67% mUPD[1] | None | This study used measures designed for individuals with ID and one assessment designed for older adults with ID (The Observational Questionnaire for Elderly Residents with Intellectual Disability). The authors report comparing the results of these against the ICD-10[2], rather than a diagnostic criterion designed for | Unknown | The results were analysed by the author. |

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| | representativeness of this sample therefore, is unknown. | | | | | individuals with ID. | | |
| Verhoeven et al. (2003) | This is a medium sized sample with a higher percentage of mUPD[1] than the average for PWS. Little other demographic details available, therefore it is unclear how representative this sample is. | Case Studies. | No control group reported. | Genetic confirmation provided for all participants with psychosis:<br>63% UPD[9]<br>7% Del 15<br>30% Clinical Diagnosis | None. | This study used measures that have been validated against ID population, assessing the behaviour and psychopathy of individuals. Results were compared against the ICD-10[2] rather than diagnostic criteria designed for individuals with ID. | Unknown. | Results were analysed by the authors. |
| Vogels et al. (2004) | This study has a small sample size, with no information on the genetic subtype of individuals or their level of ID. | Cohort study based on case studies. | No control group used. | No genetic confirmation provided. | None. | This study used a range of assessment methods including standardised assessments for typically developing | Unknown. | Results were analysed by the authors creating the potential for bias. |

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| | | | | | | individuals, interviews and observations. The results of which were assessed against the DSM-IV[6] and ICD-10[2]. | | |
| Webb et al., (2008) | This study had a relatively large sample size for studies on PWS; however, there was a greater proportion of individuals with UPD than the reported average for PWS. | Cohort study. | The study controlled for genetic subtype, without allowing for differences in age, gender or IQ. | Genetic confirmation was provided for all participants: 47% Had 15q11-q13 deletion no psychosis 23% Had 15q11-q13 deletion with psychosis 7% HadUPD no psychosis 23% Had UPD with psychosis | None. | The authors note using a screening questionnaire, though, the exact content of this is unknown. Similar to other studies the measures of mental health disorders are designed for or have been used in other studies with individuals with ID. | Unknown | The results were analysed by the authors. |
| **Fragile X Syndrome (FXS)** | | | | | | | | |
| Hartley et | As a population | Population | No control | No genetic | None | This study used | Unknown | The surveys |

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| al. (2011) | study with a large sample size the results are likely to be fairly representative of individuals with the full mutation of FXS, though, there is no evidence of genetic confirmation. | study. | group used. | confirmation is provided. | | a specifically designed, but not standardised survey asking whether the individual had ever been diagnosed with a mental health disorder. | | were answered by parents/carers and analysed by authors. |
| Hagerman (2009) | This study has a medium sized sample for this group and it seems fairly representative of individuals with FXS. | Cohort study. | No control group used. | No genetic confirmation is provided. | None. | The authors report using a semi-structured questionnaire, however, as it was not included it was not possible to determine the validity of this tool. | Unknown. | Questionnaires were completed by parents/carers and analysed by authors. |
| Kerby and Dawson, (1994) | This study has a small sample size from two ID residential facilities in USA all of whom were male. Therefore, the sample may not be | Cohort study with a control group. | The control group used were individuals with ID from the same dorms as the individuals with WS. | Genetically tested. | None. | The VABS was validated against individuals with ID. Whilst the EASI[14] was designed for typically developing | Unknown. | Assessments were administered by and analysed by the authors. |

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| | representative of all individuals with FXS. | | However, the IQ level appears higher in the control group than the WS group. | | | individuals. The results were compared against the DSM-III[15]. | | |
| Sabaratnam et al. (2003) | This is a medium sized sample and it is unclear how representative it is of individuals with FXS. | Longitudinal study. | No control group used | A clinical and anthropometric criterion was used for screening to select for cytogenetic confirmation. Participants were excluded if they failed to meet this. | None. | The authors used tools designed for or validated against use with individuals with ID; however the HBS[17] was designed for use with children. The assessment results were compared against the DSM-III[15]. | Unknown. | Assessments were administered and analysed by the authors. |
| Utari et al. (2010) | This is a fairly large sample; however, there was a higher proportion of male participants. | Retrospective case studies. | No control group used. | The distribution of genetic subtype was: 3.2% Exact CGG unknown 76.7% | None. | Retrospective study of files. | Unknown. | The results were analysed by the authors. |

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| | | | | Hypermenthylated full mutation 23.3% Mosaic | | | | |
| **Williams Syndrome (WS)** | | | | | | | | |
| Cherniske et al., (2004) | Recruited through the Genetic clinic (clinicians, colleagues and website) and the Williams Syndrome Association. There is a medium sized sample for this study with a varying level of ID (15% borderline ID, 70% mild ID and 15% moderate ID). The sample appears fairly representative of individuals with WS. | Cohort Study | No control group used. | 85% Participants had an elastin deletion confirmed by FISH[19] and 15% were clinically confirmed by one of the authors | Not noted | This study used standardised mental health assessment not designed for typically developed adults and compared the results against the DSM-IV[6]. | Unknown | Parent/carer measures checked by a Child Psychiatrist compared against the DSM-IV[6]. There was no reasoning given why a child psychiatrist was used instead of a Psychiatrist in adult mental health disorders. |
| Davies et al. (1998) | The authors selected 62 participants from 128 as being representative of | Cohort study. | No control groups used. | Unknown. | None. | The assessments were standardised assessments | Unknown. | Two authors independently rated the results of all of the |

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| | the total group, rather than testing all participants, no reasoning was given as to why all participants weren't assessed. Therefore, the representativeness of this sample is questionable. | | | | | validated for use with individuals with ID, although, it is unclear whether a diagnostic criteria was used. | | assessments. The inter-rater agreement level is not reported. |
| Dodd and Porter (2009) | No IQ levels were reported, however, the authors report that the mental age of the adult participants was (4.5-10.58 years). | Cross-sectional study. | Control group of children (age 6-19). | All participants had a genetic FISH[19] analysis confirming Williams Syndrome. | None. | The mental health measure (K-SADS-PL[23]) was designed for use with children aged 7-17. | Unknown. | Analysed by author. |
| Dykens (2003) | It is unclear how representative of the population these participants are with little demographic information available. | Cross-sectional prevalence study of anxiety, fears and phobias in WS. | Contrasted against children aged 6-12, 13 to 18 and 31 adults aged over 18 with mixed aetiologies of ID. | All participants had a clinical diagnosis of Williams Syndrome and molecular testing available for 65%. There is no description of the aetiologies of | None. | The FSSC-R[25] is designed for children aged 7-16, and not standardised for use with ID adults. | Unknown. | Results collected and analysed by author. |

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| | | | | the ID control group. | | | | |
| Howlin and Udwin (2006) | This study used a fairly large sample with a high response rate (82%), therefore, is fairly likely to be representative of individuals with WS. | Cohort study. | No control group. | Genetic confirmation by FISH[19] in 48% the remaining 52% had one or more symptoms associated with Williams Syndrome. | None | 42 Item Questionnaire created by the authors. A copy of this was not included in the paper. Therefore it is not possible to see what questions were asked and how. Understanding of the participants activities of daily living was tested by rating their daily living skills on a Likert scale. Whilst they appear to ask about diagnosed mental health disorders, no information is known about | Unknown. | The results were analysed by author. |

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| | | | | | | the assessment process. | | |
| Stinton et al. 2010) | The large number of participants and high response rate (92/108) indicates that the sample is representative of Williams Syndrome, however, all but two had the verbal ability to complete the PAS-ADD[4]; therefore, the sample may not reflect participants who may be less able to discuss their mental health disorder. | Prevalence study of mental health in adults with WS. | No control group was used. | All the participants had genetic confirmation of WS by FISH[19]. | None. | The measures used were a parental interview, the WAIS III[26], the VABS[8], the Expressive One Word Picture Vocabulary Test, the British Picture Vocabulary Scale (2nd edition), PAS-ADD[4]. Two participants lacked the verbal skill to complete the PAS-ADD[4]. Only mental health problems over the last 3 years were explored. This demonstrated limitations in purely using the PAS-ADD[4] | Unknown. | Direct and informant measures were used that demonstrated significant differences in the results, creating the question as to which measurement was most accurate. ICD-10[2] used to compare results against. |

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| | | | | | | that it was not sensitive enough to detect participants taking medication for mental health problems. | | |
| Stinton et al. (2012) | This sample is based on the average abilities of individuals with WS, though excludes less cognitively able participants who are unable to read or self-report their mood. Most individuals with WS were considered able to read words at this level. | Cohort study. | No control group used. | Genetic confirmation by FISH[19] | None | The assessments used have been validated for assessment of mental health problems in individuals with ID. | 38.7% Participants were excluded due to withdrawal and incomplete information as participants were unable to either complete the Stroop task or answer questions on their mental health. There was a response | The results were analysed by the author with responses being trimmed to exclude incorrect responses. |

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| | | | | | | | rate of 28.2%. | |
| **Cri du chat Syndrome (CdCS)** | | | | | | | | |
| Van Buggenhout et al. (2000) | This is a small sample; therefore, the representativeness is unclear. | Case Studies. | No control group used. | Genetic confirmation was obtained for all participants: 17% Del(5)(p14.1) 66% Del (5) (p13.3) and 17% Del (5) (p15.31) | None. | The assessments used for data collection are unknown to assess suitability. | Unknown. | Results analysed by authors. |

## DISCUSSION

The review found no papers assessing mental health disorders in individuals over the age of 16 with AS, CdLS and SMS. This is a curious finding as these syndromes have a relatively good research base and no papers were excluded based on quality alone. More research was available for PWS, FXS and WS using a variety of designs (including case studies, cross-sectional, and longitudinal), assessments, diagnostic criterion, sample sizes, age ranges, and control groups. The level of description of the diagnostic process also varied with some describing "blind" analysers and others not noting the assessments or diagnostic criteria used, making comparison difficult.

### Angelman Syndrome

Adults with AS appear to have been overlooked within research into mental health disorders, as no papers were found in the review suggesting more attention is required in future research.

### Cornelia de Lange Syndome

The lack of articles for CdLS seems surprising given studies reporting mental health disorders, such as social anxiety and low mood (e.g. Richards et al., 2009) in children with CdLS. There has also been anecdotal evidence and some cross-sectional studies suggesting that lower mood may be more of an issue in older individuals than younger individuals with CdLS (Berney, Ireland & Burn, 1999; Nelson, Moss & Oliver, 2014). This indicates a need for more research or research to be presented in a format that adult results can be extracted.

### Smith Magenis Syndrome

Whilst SMS is a more recently discovered syndrome, it has several defined features that are risk markers for mental health disorders including self-injury, temper tantrums, aggressive behaviours and sleep disturbances. Therefore, there is a clear need for further research in this syndrome both for mental health and adult outcomes in general.

### Cri-du-Chat Syndrome

Only one study was found for CdCS, indicating issues with "hyperaffectivity". Given the lack of detail about the assessments used within these case studies, and the small participant number, the generalisability of these findings is limited. This reflects the mainly anecdotal evidence of mental health disorders in adults (e.g. Ferreiros-Martinez, Lopez-Manzanares, & Alonso-Cerezo, 2014) demonstrating the need for further research with larger sample sizes to explore these findings.

### Prader-Willi Syndrome

The research into mental health disorders in adults with PWS suggests high prevalence of psychopathology, with evidence to suggest this may be particularly high within individuals with the mUPD subtype. The presentation of depression and psychosis in PWS appears to vary from that seen in typically developed individuals; therefore, typical diagnostic criteria (e.g. DSM (APA, 1994) and ICD (WHO, 1993)) may not be specific enough to reliably diagnose these individuals. The use of multiple case studies has enabled more detailed description of mental health disorders than for the other syndromes, though more longitudinal studies could provide greater clarity about mental health disorders throughout the lifespan and the factors appearing to impact on this.

## Fragile X Syndrome

The studies identified for FXS reported anxiety, depression and psychosis (especially delusions), however, little detail was provided around the presentation or course. Whilst there is a good evidence base for FXS, the majority of studies combine the results of individuals with the full mutation and individuals that have a pre-mutation therefore; the interaction between the genetic mutation and mental health disorders is not greatly understood and requires further research.

## Williams Syndrome

For WS there was also a high prevalence of both anxiety and depression. Whilst high levels of anxiety have previously been reported within children (e.g. Moldavsky, Lev & Lerman-Sagie, 2001), these studies suggest that the prevalence may increase further into adulthood. There are indicators from longitudinal and cross-sectional studies that the nature of anxiety experienced by children may change in adulthood (Dodd & Porter, 2009; Dykens, 2003). Further research into the nature of these changes may elucidate further aspects of the impact on individuals' lives and the possible relationship between the anxiety and depression.

## Clinical Implications

The results suggested some interesting findings that could assist with identification of mental health disorders in individuals with neurodevelopmental disorders, especially in PW**S,** where it is difficult to differentiate between a psychotic state and a bipolar manic state due to the angry explosive mood described. The evidence suggests there are increases in physical health symptoms prior to psychotic episodes and that obsessive rituals may increase as the psychotic episode progresses. This may assist in early detection and identification of psychosis.

Furthermore, the research also indicates that mUPD mutations may be a vulnerability factor for mental health disorders, therefore, individuals with this type of genetic mutation may be more at risk. For individuals with FXS, the finding that there is a higher prevalence for specific psychotic symptoms (e.g. delusions) than psychosis is interesting. This may indicate that either individual psychotic symptoms are common in this population or that the overall presentation of psychosis may be different within this population. The suggestion that the content and severity of anxiety increases with age in individuals with WS suggests the need for ongoing monitoring to ensure that treatment plans reflect the dynamic shifts in the anxiety. However, due to the methodological limitations of the evidence, further research would be needed to confirm these results prior to clinical use to clarify how typical these variations in presentation of mental health disorders really are. What the research fails to demonstrate is how mental health disorders progress in individuals with neurodevelopmental syndromes to assist not only in identifying what mental health disorder they are presenting with, also at what stage, to determine what intervention is necessary.

### Limitations of the studies

Overall, the studies available highlighted several issues in research into mental health disorders in neurodevelopmental syndromes that need addressing to develop research in this field further. Within the adult literature, there appears to be a bias towards neurodevelopmental syndromes associated with milder ID (PWS, FXS and WS). For syndromes known to be associated with a high prevalence of severe ID (AS, CdLS and CdCS), understanding of mental health disorders in adulthood remains very limited. One potential barrier to research within syndromes with higher prevalence of ID may be issue of the lack of appropriate assessment tools.

Research into neurodevelopmental syndromes currently depends heavily on measures and psychiatric taxonomy developed for children (e.g. FSSC-R; Ollendick, 1983) or typically developing adults (ICD-10 (WHO, 1993) or the DSM (APA, 1994) criteria's). As demonstrated by these articles, this may not accurately reflect, or fit the atypical presentation of mental health disorders, as found in studies of individuals with ID (e.g. depression; Marston et al., 1997) and studies are not utilising diagnostic criteria's developed for ID (e.g. Diagnostic Criteria for Psychiatric Disorder for Use with Adults with Learning Disabilities; Smiley & Cooper, 2003). This means that mental health disorders may be missed or misdiagnosed and individuals may fail to get appropriate support. There is a clear need for the development of suitable measures and diagnostic criteria for mental health disorders in ID. There is also potential for measures specific to certain syndromes, as have been developed for eating behaviours in PWS (Dykens et al., 2007; Russell & Oliver, 2003).

More research into the different presentation of mental health disorders across the neurodevelopmental syndromes would be needed to develop further valid tools. This may require more case studies, with a greater depth of description of the measures and criteria used in addition to the mental health disorders noted. Further research into mental health disorders in people with specific genetic subtypes of syndromes may also provide clearer links to potential genetic risk markers for mental health disorders.

In addition, as many of the measures used (e.g. PAS-ADD) in the studies focus on current mental health disorders, rather than psychiatric history there is clearly a need for a greater number of longitudinal studies to track the development of mental health disorders over time.

Additionally, larger samples sizes will aid generalisation and allow a further analysis of on risk factors and risk markers for mental health disorders within the groups.

## Research Implications

Overall research into mental health disorders in individuals with neurodevelopmental disorders needs:

- A general consensus of the best measures to use to assess mental health disorders taking into account communication difficulties and physical health co-morbidity, which may mean creation of new measures. These then need to be used consistently across studies.
- The use of ID based mental health diagnostic criterion in addition to diagnostic criterions for typically developing populations.
- Greater level of descriptions of the presentation and progression of mental health disorders.

In summation, there is a clear need to research mental health disorders across neurodevelopmental syndromes further, and more consideration needs to be given to measures used for this. This research needs to be more precise in the description of the procedure (especially in case studies) and consideration given to how data is displayed in cross-sectional studies (e.g. presenting adult data separately to child data).

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# CHAPTER 2: EMPIRICAL PAPER

## COGNITIVE, BEHAVIOURAL, EMOTIONAL AND QUALITY OF LIFE OUTCOMES IN A TEN YEAR LONGITUDINAL STUDY OF INDIVIDUALS OVER THE AGE OF 15 WITH SMITH MAGENIS SYNDROME


## ABSTRACT

**Introduction:** Smith Magenis Syndome (SMS) is a neurodevelopmental disorder associated with high levels of challenging behaviour, particularly aggressive behaviours and sleep disturbances. However, research into SMS lacks longitudinal studies assessing how features change over time and how they affect outcomes in this group making anticipation of needs and identification of early warning signs difficult in considering future needs from Services

**Method:** A 10-year longitudinal study of fourteen individuals with SMS currently aged between 15 and 42 years old assessing how their cognitive, emotional and behavioural characteristics have changed over time and consequently what impact this may have had on their quality of life. Comparisons were made of scores on measures of challenging and repetitive behaviours, sleep, adaptive functioning, mental health disorders and quality of life at Time 1 and Time 2. Linear regression analyses were also used to assess factors affecting quality of life.

**Results:** Whilst some challenging behaviours reduced (including aggression) over time, these levels remain higher than for individuals with idiopathic ID and for typically developing populations. There was an increase in possible environmental functions for behaviours. Individuals remained highly reliant upon parents/carers for activities of daily living, and appeared to have poor quality of life in some areas.

**Conclusion:** Individuals with SMS continue to have high levels of challenging behaviour, sleep disturbances and be highly reliant upon parents/carers. In some areas (e.g., health and productivity) participants had low levels of quality of life and parents/carers reported difficulties functioning.

# COGNITIVE, BEHAVIOURAL, EMOTIONAL AND QUALITY OF LIFE OUTCOMES IN A TEN YEAR LONGITUDINAL STUDY OF INDIVIDUALS OVER THE AGE OF 15 WITH SMITH MAGENIS SYNDROME

## INTRODUCTION

Smith-Magenis Syndrome (SMS) is a neurodevelopmental disorder first described in two case studies in 1982 (Smith, McGavran, & Waldstein, 1982). Known genetic causes of SMS include a deletion in the chromosomal region of 17p11.2 or mutation of the RAI1 gene (Elsea & Girirajan, 2008; Slager et al., 2003), resulting in a malfunction of the RAI1 protein which is involved in communication between DNA and RNA. SMS is relatively rare, with a prevalence of approximately 1 in 25,000 live births (Greenberg et al., 1991), although the prevalence level is being debated as the move away from clinical diagnosis and introduction of more sophisticated cytogenetic testing (e.g. fluorescent insitu hybridisation (FISH)), means many individuals previously misdiagnosed with other developmental disorders (e.g. Prader-Willi; Dykens & Smith, 1998) are now receiving a diagnosis of SMS. Whilst the morphological characteristics of SMS (e.g. brachycephaly and midface hypoplasia; Gropman et al., 1998) are relatively well established, the associated behavioural, social and emotional characteristics are increasingly being assessed (e.g. Dykens & Smith, 1998; Udwin, Webber, & Horn, 2001), leading to characterisation of a specific behavioural phenotype (Dykens & Smith, 1998).

### *Behavioural characteristics*

Up to 100% of individuals with SMS are documented to have difficulties with sleeping (e.g. continually waking in the night and drowsiness in the day), related to an inverted circadian rhythm/melatonin release pattern (Potocki et al., 2000). These sleep problems are a particular

area of concern for parents/carers as, in addition to posing enormous difficulties with general family exhaustion and stress, individuals with SMS have been reported to complete risky behaviours during the night, such as attempting to cook, abscond, and rearrange furniture (Horn, 1999). Parents report particular difficulties in managing their child's safety during night awakenings (Horn, 1999; Webber, 1999). Studies have also shown that not only quantity, but good quality sleep is related to good quality of life and satisfaction for health (Pilcher, Ginter & Sadowsky, 1996), suggesting quality of life may be poor in individuals with SMS.

Challenging behaviours are extremely prevalent in people with SMS. For instance, over 90% of individuals in mixed-age samples of people with SMS demonstrate some form of self-injurious behaviour (SIB) (Arron, Oliver, Moss, Berg, & Burbidge, 2011; Dykens & Smith, 1998; Finucane, Dirrigl, & Simon, 2001). Based on a group of adults with SMS, Horn (2001) reported that 100% exhibited SIB, raising the hypothesis that prevalence may increase with age.

The topographies of SIB within this population are varied (e.g. hand biting, skin picking, polyembolokoilamania, self pinching, scratching, onychotillomania; Finucane et al., 2001; Smith et al., 1986) and, intriguingly, research suggests differences between child and adult samples, with the prevalence of skin picking, self slapping and onyctillomania potentially greater in adults than children (Finucane et al., 2001). There is also a very high prevalence of aggression, with up to 100% of individuals displaying behaviours such as temper tantrums, destroying property, punching and kicking (Dykens, Finucane, & Gayley, 1997; Dykens & Smith, 1998; Greenberg et al., 1996; Webber, 1999). Anecdotal accounts of adults with SMS

include attempts to strangle carers or pets, individuals sectioned under the Mental Health Act, and carers having to call out the Police during violent outbursts (Horn, 1999), demonstrating the severity of challenging behaviours within this group. Whilst studies into neurodevelopmental disorders have indicated gender and age related differences in behaviours displayed (e.g. the high prevalence of ADHD mostly seen in males with Fragile X; Tranfaglia, 2011) and varying levels of aggression across the lifespan of individuals with developmental disorders (Dykens, 2004), this remains unclear in SMS.

The exhibited SIB may partly relate to the purported high tolerance for pain exhibited by individuals with SMS (Webber, 1999). Individuals with SMS are also clinically known to meet many of the risk markers for challenging behaviour (McClintock, 2003; Sloneem, Oliver, Udwin, & Woodcock, 2011) (including autistic spectrum disorder, impulsivity, communication difficulties and cognitive impairment (Dykens et al., 1997; Dykens & Smith, 1998; Sloneem et al., 2011; Webber, 1999). Research indicates high levels of challenging behaviour adversely affect individuals' quality of life, especially within ID. For example, high levels of challenging behaviours create higher risks of residential placement breakdowns and less routine (Broadhurst & Mansell, 2007).

### *Cognition*

Most studies suggest that individuals with SMS tend to have a moderate/severe intellectual disability (ID) (Greenberg et al., 1991), although there have been reported cases of individuals with mild ID (Udwin et al., 2001). Cognitive strengths in SMS tend to be long term memory, perceptual abilities and computer skills (Dykens et al., 1997). Particular cognitive difficulties appear to be visual motor skills, speed of response, sequencing and expressive language skills

(Greenberg et al., 1996; Udwin & Horn, 2001). Amongst children, speech delays, hearing loss and ocular impairments appear common (Greenberg et al., 1991; Greenberg et al., 1996), which could explain some of these cognitive difficulties and contribute to challenging behaviours as individuals attempt to communicate their needs. Most reports suggest that individuals are highly dependent upon carers to complete activities of daily living, with carers reporting they cannot be left alone for more than an hour, and in some cases no longer than a few minutes (Udwin & Horn, 2001), putting immense pressure on carers to meet their needs. In the literature on adults with SMS, there are no known cases of individuals who are able to live entirely independently (Udwin & Horn, 2001).

### *Social and Emotional characteristics*

Research indicates high levels of Autistic Spectrum Disorder (ASD) characteristics in people with SMS, with a high proportion (over 90%) of people meeting criteria for ASD on screening tools (Laje et al., 2010a; Webber, 1999). However, the specific nature of possible ASD in SMS has yet to be fully explored, including the relative degree to which it is driven by high levels of repetitive behaviours as opposed to social impairments. Individuals with SMS typically display high levels of specific forms of sociability, with a preference for adults (especially attachment figures; Wilde, Silva & Oliver, 2013) over peers. Research also indicates a trigger for challenging behaviour in some individuals with SMS is the removal of attention (Taylor and Oliver, 2008).

In comparison to individuals with idiopathic ID or Prader-Willi syndrome, individuals with SMS are reported to be more emotionally labile (Dykens & Smith, 1998), with sudden changes in mood and withdrawal. In the context of the previously reported high levels of

aggression and temper tantrums, this may indicate compromised emotional regulation. Despite anecdotal reports of difficulties in areas, such as, mood and emotional regulation, and frequent prescription of psychoactive medication (Laje et al., 2010b), mental health problems are not well researched in SMS. Further understanding in this area is arguably of particular importance in adolescents and adults, since the onset of most long term mental health problems in the typically developing population during adolescence and early adulthood (Kessler et al., 2007).

It is clear that care giving for individuals with SMS can be extremely challenging and demanding; therefore, it is perhaps unsurprising that stress levels amongst families of children with SMS are higher than for families of people with idiographic ID (Hodapp, Fidler, & Smith, 1998). This may relate in part to the high level of social demand on carers as well as the (related) extreme levels of challenging behaviours. There have been links between high levels of maladaptive behaviours and high levels of pessimism in parents (Hodapp et al., 1998). This is exacerbated by long term sleep deprivation, which is known to negatively impact mood, as well as cognitive and motor performance (Pilcher & Huffcutt, 1996). Whilst research into SMS is increasing, there are some notable gaps in knowledge. First, little is understood of the ways that behaviour might develop into later childhood and adulthood, as there are few large sample studies assessing adults with SMS (Udwin et al., 2001; Udwin, 2003). This may be due to a variety of factors, including the rarity of SMS, the lack of genetic identification until recently and the potential of reduced life expectancy (Dykens, 2013). Cross-sectional studies assessing varying age groups of people with SMS suggest that challenging behaviours may be different in topography in older people (Finucane et al., 2001), and that the prevalence and severity of behaviours may increase (Horn, 1999; Webber, 1999).

There have also been suggestions that sleep problems may be less extreme in older individuals (Horn, 1999) and that cognitive abilities may be approximately equivalent at different ages (Udwin & Horn, 2001). However, less is known about the areas of mental health problems, quality of life, adult relationships, achievement of adult milestones (e.g. learning how to drive, or living independently) and factors that influence adult outcomes. Research in this area has been based on cross-sectional studies, which have well-known limitations to drawing conclusions about the effects of aging (Levin, 2006). For studies of people with SMS, the potential for cohort effects is substantial, with a likelihood of greater rates of diagnosis in younger individuals and failure to thrive in youth (Greenberg et al., 1996, Webber, 1999). It is possible, for example, that older people diagnosed with SMS are more likely to have displayed more severe phenotypes than younger people with the diagnosis, since the clinical threshold for genetic testing may have been higher at the point of likely diagnosis.

The increasing number of individuals diagnosed with SMS, and the evidence of extreme behavioural, emotional and cognitive difficulties associated with the syndrome, mean that it is imperative that we develop a greater understanding of the phenotypes of SMS, including, crucially, development beyond childhood. This may help to reduce families' uncertainty and aid development of intervention strategies to reduce negative outcomes.

The current study comprises, to our knowledge, the first longitudinal assessment of psychological characteristics of people with SMS. It represents a ten year follow-up of individuals with SMS first seen by Sloneem et al. (2011) in 2003-2005. Sloneem et al. (2011)

assessed 32 individuals with SMS recruited through the SMS Foundation UK aged 6-39 to determine the impact of cognitive and behavioural characteristics on levels of challenging behaviour (e.g. aggressive behaviour, destruction of property and self-injurious behaviour). At that time aggressive behaviour was the most prevalent behaviour (87% prevalence) in the sample and was associated with high levels of impulsivity. This study seeks to address some unanswered questions about development of individuals with SMS into adolescence and adulthood.

Building upon Sloneem et al. (2011) study the aims of this study were:

1) To determine how challenging behaviours (including SIB) develop over time. This will aid assessment of whether the suggested increase in prevalence and severity of challenging behaviours (Horn, 1999) is supported by longitudinal analysis.
2) To assess change over time in repetitive behaviours given the high prevalence of autistic like behaviours in youth, including stereotyped behaviours (Laje et al., 2010a).
3) To track adaptive ability over time (including communication, activities of daily living and social skills) assessing whether these remain stable as suggested by Udwin et al. (2001) or if there are age related changes.
4) To determine whether there is any variation in impulsivity and hyperactivity over time, or if these issues persist from childhood to adulthood.
5) To explore whether there is a link between SMS and any specific categories of mental health problems in older people with SMS and whether there is evidence of sectioning under the mental health act, as indicated by Horn (1999).
6) To explore quality of life for individuals with SMS in adolescence and adulthood.

7) To explore what factors may impact upon quality of life amongst individuals with SMS.
8) To begin to assess outcomes within adults with SMS, in particular, their level of independence, employment status and interpersonal relationship skills.

## METHOD

This is a longitudinal study of individuals with SMS over the age of 15. Participants were initially recruited to the study in 2003-2005 (Sloneem et al., 2011) (Time 1) and followed up in 2014-2015 (Time 2).

### Participants

#### *Time 1*

Sloneem et al. (2011) recruited participants through the Smith-Magenis Syndrome Foundation UK support group (SMS Foundation UK) advertising the study on their website and at their biannual conference. All families caring for an individual with Smith-Magenis Syndrome over the age of six and who had consented to be contacted about research were invited to take part in the study. Thirty-two individuals aged 6 to 39 (MDN 10.5, IQR 10.25) participated in the study, over half of whom were females (56%). Participants currently resided at home with parents (84%) or in residential care (16%) and had a range of ID (12% mild, 16% mild-moderate, 28% moderate and 44% severe-profound) based on their scores on the Wechsler Adult Intelligence Scale – third edition WAIS-III) or Wechsler Intelligence Scale for Children – third edition (WISC III) administered at Time 1.

#### *Time 2*

The 32 participants were contacted 9-11 years after the initial study either by phone call or by letter (see Appendix B and C) if researchers were unable to contact participants by telephone.

#### *Consent*

Consent forms were sent out to potential participants with an information sheet (see Appendices D and E) about the study for participants to go through with their carers.

Parents/carers were asked to go through the consent forms with participants (see Appendices F, H and I), with parents/carers taking on the role of consultee if participants were over the age of 16. Information was provided for carers on the role of a consultee (see Appendix G) to assist with this. The consent process was repeated for any participants that turned 16 during the course of the study.

## Measures

Participants parents/carers completed a series of questionnaires and interviews, assessing behavioural, cognitive, emotional and quality-of-life factors, most of which were utilised in Sloneem et al. (2011) allowing comparison between time points. Additional measures were included to assess outcomes and quality of life for individuals with SMS.

### Time 1 and Time 2 measures

#### *Demographic Information*

A demographic questionnaire (see Appendix 10) was utilised to determine the demographic characteristics of the participants, including age of participant, gender, relationship to informant, and confirmation of diagnosis (including genetic variant).

#### *Challenging Behaviour*

The Checklist for Challenging Behaviour (CCB) (Harris, Humphreys, and Thomson, 1994) was used to determine the frequency, severity and management difficulty of fourteen topographies of aggressive challenging behaviour (including hitting, biting, and kicking) and

seventeen topographies of other challenging behaviours (e.g. refusing to do things and causing a night time disturbance) each rated on a five-point Likert scale. The data were collated into scores for frequency, management difficulty, severity, number of behaviours displayed and total for each subdomain (aggressive and other challenging behaviour). Higher scores are indicative of higher levels of challenging behaviours. The CCB has an inter-rater reliability Spearman's correlation co-efficient of 0.67-0.70 and test-re-test Spearman's correlation co-efficient of 0.53-0.69.

The Challenging Behaviour Interview (CBI) (Oliver et al., 2003) is a 14-item interview validated for use with adults and children with ID with high test-re-test (Pearson's correlation co-efficient 0.90) and inter-rater reliability (0.69 overall severity score). The CBI assesses the frequency, duration and severity of 13 topographies of challenging behaviours over the last month, including four types of aggressive behaviour (self-injurious behaviour (SIB), physical aggression (PAG), verbal aggression (VAG) and disruption and destruction of property or the environment (DBT) rated against a four- or five-point Likert scale. High scores on this assessment indicate high levels of challenging behaviour.

The Questions about Behavioral Function Scale (QABF) (Matson & Volmer, 1995) assesses the function of behaviour displayed by individuals by exploring the setting events of the behaviour in a 25-item questionnaire designed for individuals with ID. This can help to determine, for instance, if the behavioural function of self-injury for participants may be for attention, demand escape, self-stimulation, pain or discomfort or to gain tangible goods. The higher a score for the function on the QABF, the more likely it is to be a function of the behaviour. The QABF has good internal consistency (Cronbach's alpha score 0.79-0.99)

across the five functions and test-re-test reliability (Pearson's correlation co-efficient 0.64-1.0).

### *Hyperactivity and impulsivity*

Characteristics of Attention Deficit Hyperactivity Disorder were assessed using the Conners' Parent Rating Scale Revised, Long version (Conners', 1997) and the Dysexecutive Questionnaire (DEX) (Wilson, Alderman, Burgess, Emslie, & Evans, 1996)/Dysexecutive Questionnaire for Children (DEX-C) (Emslie, Wilson, Burden, Nimmo-Smith, & Wilson, 2003) were used to assess impulsivity based on age and cognitive ability of the participant (i.e. above or below 16). The Conners' is an 80-item questionnaire rated upon a five-item Likert scale based upon the clinical criteria for the DSM-IV (APA, 1994) for inattention, hyperactivity, and ADHD and is used clinically to assess ADHD. The test-re-test reliability co-efficient on the scales varied between 0.47 and 0.85 and the internal reliability co-efficient of 0.77-0.94. The DEX is a 20-item questionnaire based on a four-item Likert scale based on typically developing individuals, designed to assess for executive functioning difficulties, such as, impulsivity based on questions about their cognitive, behaviour and emotional functioning and can be used to track changes in executive functioning over time (Gerstof et al., 2008). The scores for each item on the DEX are summed with a maximum score of 80; the higher a participant scores on this scale, the higher the level of difficulty with executive functioning. The Cronbach's alpha scores for inter-rater reliability and internal consistency for the DEX is above 0.90.

### *Cognitive and Social Characteristics*

The Vineland Adaptive Behavior Scales – Interview edition, Survey Form (VABS-SF) (Sparrow, Balla, and Chiccetti, 1984) is a semi-structured interview administered to care givers as a measure of adaptive ability (communication skills, activities of daily living, socialisation skills, and motor skills); this scale assists in putting participants' cognitive functioning into a context of daily living. These scores can then be compared against typically developing individuals to describe the age of their abilities (e.g. writing ability expected by a 7 year old typically developing child). The VABS has an internal consistency Cronbach's alpha score of 0.70-0.94 and inter-rater reliability correlational score of 0.96-0.99 across the domains. The communication domain was completed for the original study (Sloneem et al., 2011) and assesses the expressive, receptive and written abilities of individuals, comparing these against age and context related peers with ID (e.g. inpatient or in the community). The entire VABS was completed with participants including the activities of daily living, socialisation and motor skills domains, which will be described using descriptive statistics. The activities of daily living skills domain assesses an individuals' personal care, engagement with domestic chores and independence within the community, whilst the socialisation domain assesses an individuals' abilities to develop interpersonal relationships, coping skills and their use of play/leisure activities. The motor skills component assesses fine and gross motor abilities. Whilst these domains were only completed by a few participants at Time 1 the measures were completed by all participants at Time 2 to get a greater understanding of the independent living and social abilities of individuals with SMS.

*Stereotyped Behaviours*

The Repetitive Behaviour Questionnaire (RBQ) (Moss and Oliver, 2007) was used to assess repetitive behaviours, with carers reporting the occurrence of 19 specific behaviours using a 4-point Likert scale to describe the current behavioural characteristics of participants in addition to determining any autistic traits. The RBQ has a test-re-test reliability of 0.61-0.93 and inter-rater reliability of 0.46-0.80. There is maximum total score of 80 on this scale, with higher scores indicating higher levels of stereotyped behaviour. The RBQ has five sub domains: stereotyped behaviours; compulsive behaviour; insistence on sameness; restrictive preferences, and, repetitive use of language. As the restrictive preferences and repetitive use of language domains rely upon responses for language, these domains were not completed for any non-verbal participants (as defined by a score of <30 on the communication domain of the VABS-SF). Total scores for non-verbal participants are pro-rated with the removal of verbal items on the scale.

**Measures not used at Time 1**

*Sleep*

The Modified Sigmond and Parraga Sleep Questionnaire (MSPSQ) (Wiggs and Stores, 1996) and Infant Sleep Questionnaire (ISQ) (Morrell, 1999) were used to assess sleep. The MSPSQ was modified for use with individuals with ID. It consists of a 55-item questionnaire assessing the prevalence of a series of sleep problems, sleep behaviours and interventions used. It has good test-retest reliability (Pearson's correlation ranging from 0.83 to 1.0).

This will be supported by the ISQ, a 7-item assessment assessing the environment an individual sleeps in, the length of sleep/wakefulness during the night and the frequency of

wakening per night. Whilst this assessment was designed to assess sleep within infants, it has been used with older individuals (Sadeh, 2004). The ISQ has a test-retest Pearson's correlation score of 0.92.

### *Mental Health*

The Psychiatric Assessment for Adults with a Developmental Disability Checklist (PAS-ADD Checklist) (Moss et al., 1984) was used to assess current mental health problems in individuals with SMS. The PAS-ADD Checklist is a 25-item checklist developed to screen for symptoms within the DSM-IV (APA, 1994) in individuals with ID for an affective disorder (maximum score 8, cut off score 5), possible organic condition (e.g. dementia) (maximum score 25, cut off score 6) and a psychotic disorder (maximum score 4, cut off score 2) based on symptoms seen over the last 4 weeks. This measure is often used both clinically and in research for individuals with ID. It has a Cronbach's alpha score of 0.51-0.87 for internal consistency and 0.55-0.79 for inter-rater reliability.

Given the high levels of parental stress reported in parents of children with SMS (Hodapp et al., 1998), the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) was used as a mood screen for parents/carers. The HADS is a 14-item questionnaire used clinically as a screening tool for anxiety and depression. Each scale is scored out of 21, with scores between 0 and 7 considered to be 'normal' and above this clinically relevant. Scores above 15 are classed as 'severe'. The HADS has an internal consistency Cronbach's alpha score of 0.51-0.87 and inter-rater reliability correlational score of 0.55-0.79 across the scales.

*Quality of Life*

The Client Service Receipt Inventory - Intellectual disability version (CSRI-ID version) (Beecham and Knapp, 1992), and the Comprehensive Quality of Life Scale – Intellectual disability version (ComQoL – I5) (Cummins, 1997) were administered to assess outcomes and participants' quality of life. The CSRI-ID investigates the current health and social care resources accessed by participants and carers over the prior 6 months. Parents/carers are asked about the services that the participant currently receives both socially (e.g. daily activities, residential care, education) and individuals health needs through the number and reason for contacts with inpatient, outpatient, A and E and community based services for the individual. This provides an indicator of health and productivity outcomes, in addition to questioning parents/carers about areas of unmet needs. The results of this will reported through descriptive statistics.

The ComQoL-I5 informant interview is designed to assess quality of life in individuals with intellectual disabilities using a 5-point Likert scale to determine the importance of and satisfaction with seven factors of quality of life (material wellbeing, health, productivity, safety, intimacy, community and emotion) for each individual. Scores on the importance scale vary between -1 and +5 and scores for satisfaction vary between -4 and +4. The importance and satisfaction scores are multiplied for each factor to provide an indicator of quality of life. Possible scores vary between -20 and +20. Participants' scores will be recorded as descriptive statistics, though will be compared against ID and typically developing individuals to provide context. The ComQoL-I5 has a test-re-test reliability of 0.82-0.87 and inter-rater reliability Pearson's correlation co-efficient of 0.48-0.68.

## Procedure

Once consent was gained from parents/carers/participants, parents/carers were sent a questionnaire pack containing the demographic questionnaire, the CCB, the QABF, the Connors' Parent Rating Scale Revised, the RBQ, the HADS, the ISQ, the MSPSQ and the DEX/DEX-C.

Following return of the questionnaire packs, telephone interviews were conducted with parents/carers lasting between 1.5 hours and 2.5 hours. During the interviews the VABS-SF, the PAS-ADD checklist, CSRI-ID, and the informant subjective measure section of the ComQol-I5 were completed.

## Data Analysis

Data were analysed using IBM SPSS Statistics 19. Descriptive statistics were used to determine if the data would meet the assumptions for parametric statistics. This demonstrated most of the data was non-normally distributed; therefore, the data were mainly analysed using non-parametric statistical tests.

Mann Whitney U tests were used to assess whether there were any significant differences in age or ability between the participants followed up ($N$=14) and those unable or unwilling to be followed up in this study ($N$=18).

To assess any significant differences in scores from Time 1 to Time 2 on the repeated measures (the CBI, CCB, QABF, DEX/DEX-C, Connors', RBQ and VABS-SF), Wilcoxon Signed Rank Tests and McNemar analyses were used to compare total scores and sub-domain scores, and prevalence of behaviours, between the two time points on each measure.

Spearmans Rho correlations were also employed on all scale and subscale scores on the repeated measures to determine if there was a linear relationship between scores at the two time points.

To assess differences in scores between older and younger individuals, or between males and females, Mann Whitney U analyses were performed on all total scale and subscale scores for all measures. The median age (21.5 years) was used to perform a median split for comparison of age groups for all measures, except for the CBI where individuals were separated into age groups of above and below 19 to enable comparison with individuals with idiopathic ID (Joyce et al., 2001). Descriptive statistics were used to describe all data collected solely at time 2. In accordance with the non-parametric measures used for Time 1 and Time 2 data, the median scores (Mdn) and inter quartile range (IQR) are presented with the exception of the ComQol-I5, as only means and standard deviations (SD) were available to make comparisons with ComQol-I5 control groups. One sample t-tests were used to compare scores for the current sample against scores for comparison groups. These data were assessed using descriptive statistics to determine it met the assumptions needed for parametric statistics to use a t-test.

To assess the possible influence of challenging behaviours and sleep issues on quality of life, bootstrapped linear regression analyses were used to determine whether scores on the challenging behaviour scales (CCB, CBI, QABF), items from the MSPSQ (how often they wake in the night, the number of awakenings per night, frequency of sleep medication use, how often they have uncontrollable and controllable urges to sleep during the day, whether advice was sought for sleep, and whether the child has a sleep problem) and ISQ (hours of

sleep at night and during the day, and how many hours they are awake) predicted quality of life on the ComQol-I5.

An alpha of 0.05 was adopted throughout. It is acknowledged that, given the number of tests employed, this may increase the risk of making type 1 errors. However, the low *N* (a frequent issue in studies of rare disorders, compounded by the attrition rate typical of a follow-up study) reduces power. Therefore, whilst results are reported as significant at $p < 0.05$, the risk of type 1 errors is acknowledged as a point of exploration in future work.

## Ethical Considerations

Ethical approval was sought and approved by NHS Ethics (see Appendix K).

### *Confidentiality*

The results of the assessments were anonymised to protect the confidentiality of the individuals involved and stored within a locked cabinet.

### *Debrief*

Each participant received an individualised report of their abilities (both at Time 1 and Time 2) alongside the mean results for the whole sample. If any results were deemed a potential cause for concern to the individual or their family (e.g. the results of the PAS-ADD) these were discussed with the family prior to the report being sent out.

## RESULTS

### Demographics of the sample

From the original sample fourteen participants were unable to be contacted, one person was able to be contacted but refused to participate as their child was transitioning to a new Service and seventeen people were able to be contacted and consented to take part in the study. Of these, one participant died prior to the data collection and two participants did not return their stage one questionnaire packs. The results shown are for the 14 participants (follow-up rate of 44%) who returned data. Variation in *N* between measures reflects where data sets were incomplete.

The sample was made up of seven males and seven females aged 15-42 (Mdn 21.5, IQR 11.5) years. The participants had varying cognitive abilities based on their IQ results from WAIS III or WISC III administered by Sloneem et al. (2011) at Time 1. Five participants had mild ID, three participants had moderate ID, five participants had profound ID and the IQ of one participant was unknown as they did not complete the WAIS-III because they had no verbal communication. These scores are similar to those described by Udwin et al. (2001) in their sample of adults with SMS. The follow up time between the data collection from the original time point to the data collection from this study ranged between 9 and 11 years (Mdn 10, IQR 0). There were no significant differences in the age, gender or level of ID between participants who were and were not able to be followed up. The demographic details of the participants followed up can be seen in Table 1. As can be seen in Table 1, four of the participants were no longer residing at home, and the majority now attend day centres. The data presented from Time 1 and Time 2 were collected from parents/carers. The measures were completed with

the same parents/carers for twelve participants, and in combination between the original parent/carer and the key worker or manager currently working with the participant.

**Table 1: Demographic details of the participants at Time 1 and 2**

| Participant Number | Age at Time 1 (years) | Age at Time 2 (years) | Length of follow up (years) | Gender | ID | Place of residence at Time 1 | Place of residence at Time 2 | Daily activities | Reported physical health problems and medication |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 10 | 21 | 11 | Male | Severe/ Profound | Family home | Residential home | Unknown | Unknown as the participant did not complete this measure. |
| 2 | 9 | 19 | 10 | Female | Severe/ Profound | Family home | Family home | Day Centres | This participant had visual ataxia and needed to wear hearing aids. She struggled continuously with cellulitis resulting in many trips to hospital and also had some difficulties with lympodema. She was on medication for sleep (Melatonin), acne (Tetralysal) and incontinence (Desmopressin and Oxybutynin). |
| 3 | 8 | 18 | 10 | Male | Borderline | Family home | Residential school | Day Centres | This participant had become blind in his left eye and was only partially sighted in his right eye due to SIB. He used to take melatonin but was not currently on any medication |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 4 | 6 | 16 | 10 | Male | Mild | Family home | Family home | Specialist ID school | This participant had issues with acid reflux and had been diagnosed with Raynaud's disease. He was not reported to be on any medication. |
| 5 | 11 | 22 | 11 | Male | Severe/ Profound | Family home | Family home | Day Centre | No physical health problems or medication were noted for this participant. |
| 6 | 6 | 15 | 9 | Male | Borderline | Family home | Residential home | Specialist ID school | This participant had auditory problems requiring hearing aids. He was on a mood stabiliser (Sertraline) to reduce aggression. |
| 7 | 6 | 16 | 10 | Female | Severe/ Profound | Family home | Family home | Unknown | Unknown as the participant did not complete this measure. |
| 8 | 13 | 23 | 10 | Female | Mild | Family home | Family home | Day Centre | This participant had kidney dysfunction and was taking blood pressure medication (Ramipril). |
| 9 | 12 | 22 | 10 | Female | Mild | Family home | Family home | Family | No physical health problems or medications were noted. |
| 10 | 32 | 42 | 10 | Female | Borderline | Residential home | Residential home | 1:1 Activities at residence | Unknown as the participant did not complete this measure. |
| 11 | 28 | 38 | 10 | Male | Severe/ Profound | Family home | Residential home | Day Centre | No physical health problems or medication were noted. |
| 12 | 19 | 29 | 10 | Male | Unknown | Family | Family | Day Centre | This participant was taking |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | home | home | | medication for his diabetes (Insulin), epilepsy, and a fatty liver. He had also lost his sight in his right eye due to his SIB. He was taking a mood stabiliser (Fluvoxamine) and anti-psychotic (Amisulpride) to reduce aggressive behaviour in addition to anti-convulsants (Procyclidene and Carbamazepine and Topiramate), sleep medication (Propiomazine). |
| 13 | 6 | 15 | 9 | Female | Mild | Family home | Family home | Mainstream school | No physical health problems or medication were noted. |
| 14 | 18 | 27 | 9 | Female | Mild | Family home | Family home | Day Centre | This participant had medication for epilepsy, sleep difficulties (Melatonin), asthma, incontinence (Oxybutynin) and an underactive thyroid. She also had a leaky heart valve that required constant monitoring and urinary incontinence. |

## Challenging Behaviour

The types and frequencies of the challenging behaviour were assessed using the CBI and CCB. The QABF was used to determine the function of self-injurious behaviour performed by participants.

### *The CBI*

There was no significant difference between the two time points in the prevalence of challenging behaviours (see Table 2), number of aggressive behaviours ($Z=-1.706$, $n=12$, $p=0.09$) displayed or the aggressive behaviours overall score ($Z=-1.844$, $n=12$, $p=0.07$) on the CBI, indicating no significant change in the frequency or severity of the aggressive behaviours over time.

**Table 2: Presence of Challenging Behaviour on the CBI**

| Type of Challenging Behaviour | Present during Time 1 (n=12) | Present during Time 2 (n=12) | Differences in presence of challenging behaviour between Time 1 and Time 2 (Significance, p-value) |
|---|---|---|---|
| Self-Injurious Behaviour | 92% | 83% | 0.24 |
| Physical Aggression | 67% | 50% | 0.50 |
| Verbal Aggression | 25% | 50% | 0.45 |
| Destruction of Property | 83% | 42% | 0.06 |
| Stereotyped Behaviour | 67% | 33% | 0.07 |
| Inappropriate Vocalisations | 47% | 33% | 0.66 |
| Inappropriate Removal of clothing | 25% | 17% | 0.63 |
| Inappropriate Sexual Behaviour | 47% | 17% | 0.45 |
| Pica | 33% | 8% | 0.25 |
| Self-induced vomiting | 0 | 17% | 0.32 |
| Anal Poking | 0 | 0 | |
| Smearing | 0 | 0 | |
| Stealing | 0 | 0 | |
| Number of aggressive behaviours displayed by participants at time point. | Mdn 3 (IQR 2) | Mdn 3 (IQR 3.75) | Z=--1.706, n=12 p=0.09 |
| Total score for aggressive behaviours | Mdn 27 (IQR 57.25) | Mdn 53 (IQR 42.0) | Z=-1.844, n=12 p=0.07 |

*The CCB*

On the aggressive behaviours scale there was a significant decrease over time in the number of behaviours displayed by participants (Z=-2.250, n=12, p=0.024; Time 1 Mdn 8.0, IQR 7.5, Time 2 Mdn 4.0, IQR 7.0) and the frequency of aggressive behaviours (Z=-2.943, n=12, p=0.003; Time 1 Mdn 23.5, IQR 18.5; Time 2 Mdn 23.0, IQR 20.5). This resulted in an

overall reduction in the total aggression scores (Z=-1.923, n=12, p=0.055; Time 1 Mdn 69.0, IQR 57.0, Time 2 Mdn 67.0, IQR 66.0) despite no significant change in the management difficulty (Z=-0.490, n=12, p=0.624) or severity (Z=-0.525, n=13, p=0.600) of the aggressive behaviour. There was no significant correlation between the overall scores at Time 1 and Time 2 ($r_s$=-0.283, n=13, p=0.372), suggesting there is no linear relationship.

In comparison to other adults with mixed ID (Joyce et al., 2001), despite the reduction of aggressive challenging behaviours over time, the prevalence of the majority of aggressive behaviours in individuals with SMS over the age of 19 remains higher than for adults with mixed ID (see Table 3). The results indicate a potential shift in the topography of challenging behaviours in individuals with SMS over the age of 19, with grabbing (66.7%) becoming the most prevalent type of aggressive behaviour and the number of participants hitting out at people almost halving.

**Table 3: Frequency of aggressive behaviours on the CCB**

| Aggressive Behaviour | Total percentage of SMS participants at time 1 displaying the behaviour (n=13) | Total percentage of participants at time 2 displaying the behaviour (n=13) | Difference between time 1 and time 2 (McNemar significance, p-values) | Percentage of SMS participants at time 1 over the age of 19 displaying the behaviour (n=8) | Percentage of participants at time 2 over the age of 19 displaying the behaviour (n=9) | Percentage of mixed ID group over the age of 19 (Joyce et al. 2001) (n=448) |
|---|---|---|---|---|---|---|
| Pinching people | 77 | 31 | 0.03* | 50 | 22 | 21 |
| Biting people | 61 | 31 | 0.22 | 50 | 11 | 9 |
| Scratching people | 46 | 38 | 0.93 | 25 | 22 | 26 |
| Hitting out at people | 11 | 69 | 0.50 | 100 | 56 | 49 |
| Grabbing | 100 | 69 | 0.13 | 88 | 67 | 56 |
| Kicking | 85 | 61 | 0.25 | 75 | 44 | 26 |
| Head butting people | 23 | 15 | 0.51 | 12 | 0 | 4 |
| Pulling hair | 54 | 31 | 0.45 | 25 | 22 | 17 |
| Choking or throttling | 46 | 8 | 0.06* | 25 | 11 | 5 |
| Using objects as weapons | 39 | 15 | 0.25 | 37 | 0 | 13 |
| Throwing things at people | 54 | 54 | 0.99 | 62 | 44 | 27 |

*Statistical significance at an alpha of p=0.05.

In contrast, there was no significant difference in the number (Z=-0.118, n=13, p=0.906)), frequency (Z=-1.155, n=13, p=0.248), management difficulty (Z=-1.218, n=13, p=0.223) severity (Z=-0.350, n=13, p=0.726) or overall scores for other challenging behaviours (Z=-0.785, n=13, p=0.432) between the time points suggesting there was little systematic change in these behaviours over time (see Table 4). Significant positive correlations are seen between the two time points for the frequency ($r_s(13)=0.699$, p=0.008), management difficulty ($r_s(13)=0.816$, p=0.001) and severity ($r_s(13)=0.839$, p<0.001).

**Table 4: Frequency of Other Challenging behaviours on the CCB**

| Other Challenging Behaviours | Percentage of SMS sample displaying the behaviour at Time 1 (n=13) | Percentage of sample currently displaying the behaviour (n=13) | Difference (p value) |
|---|---|---|---|
| Damaging clothes, furniture or other objects | 61 | 69 | 0.57 |
| Smashing windows | 8 | 8 | 0.99 |
| Slamming doors | 61 | 46 | 0.57 |
| Making loud noises | 69 | 69 | 0.99 |
| Threatening to hurt others | 54 | 61 | 0.53 |
| Taking food and drink from others | 31 | 31 | 0.99 |
| Eating inappropriate things | 31 | 8 | 0.25 |
| Displaying ritualistic or repetitive behaviour | 46 | 38 | 0.63 |
| Engaging in stereotyped behaviour | 77 | 69 | 0.13 |
| Showing withdrawn behaviour | 38 | 46 | 0.43 |
| Spitting at people | 23 | 38 | 0.63 |
| Deliberately soiling, wetting or vomiting | 31 | 23 | 0.13 |
| Smearing or flicking faeces | 31 | 8 | 0.25 |
| Exposing his or her body inappropriately | 31 | 46 | 0.69 |
| Refusing to do things | 92 | 69 | 0.25 |
| Absconding or trying to abscond from facility | 8 | 23 | 0.50 |
| Causing night time disturbance | 69 | 77 | 0.13 |

*Statistical significance at an alpha of p=0.05.

*The QABF*

The results of the QABF can be seen in Table 5. Overall there was a significant increase in the functional scores for attention (Z=-3.064, n=13, p=0.002), escape (Z=-3.066, n=13, p=0.002), self-stimulation (Z=-2.984, n=13, p=0.003), pain and discomfort (Z=-3.068, n=13, p=0.002) and tangible (Z=-2.952, n=13, p=0.003) for SIB at Time 2.

**Table 5: Functions of SIB on the QABF**

| Function of SIB | Time 1 Mdn (IQR) (n=13) | Time 2 Mdn (IQR) (n=13) | Significance |
|---|---|---|---|
| Attention | 4.0 (5.0) | 8.5 (5.5) | p=0.002* |
| Demand Escape | 3.0 (4.5) | 9.0 (5.25) | p=0.002* |
| Self-stimulation | 3.0 (4.5) | 11.0 (5.75) | p=0.003* |
| Pain and discomfort | 1.0 (4.0) | 6.5 (3.0) | p=0.002* |
| Tangible goods | 3.0 (5.0) | 9.5 (5.75) | p=0.003* |

*Statistical significance at an alpha of p=0.05.

**Repetitive Behaviour**

Participants' total scores on this assessment were significantly higher (Z=-2.594, n=12, p=0.009) at time 2, indicating higher levels of repetitive behaviours as participants have got older (see Table 6). At a subdomain level, participants' scores on insistence on sameness (Z=-2.536, n=12, p=0.011) and repetitive use of language (Z=-2.094, n=12, p=0.036) were significantly higher at Time 2 than Time 1.

**Table 6: Comparison of scores on the RBQ at Time 1 and Time 2.**

| Scale | Time 1 Mdn (IQR) (n=12) | Time 2 Mdn (IQR) (n=12) | Significance |
|---|---|---|---|
| Stereotyped behaviour | 9.0 (8.5) | 8.0 (5.75) | Z=-0.715, n=12, p=0.475 |
| Compulsive Behaviour | 2.5 (8.25) | 3.5 (7.25) | Z=-1.474, n=12, p=0.141 |
| Insistence on sameness | 1.5 (4.5) | 3.0 (4.5) | Z=-2.536, n=12, p=0.011* |
| Restricted preferences | 4.0 (3.5) | 4.0 (3.75) | Z=-1.798, n=12, p=0.072 |
| Repetitive use of language | 4.0 (2.0) | 5.5 (3.75) | Z=-2.094, n=12, p=0.036* |
| RBQ Total (including non verbal pro-rated) | 18.5 (12.25) | 27.0 (18) | Z=-2.594, n=12, P=0.009* |

*Statistical significance at an alpha of p=0.05.

**Hyperactivity and Impulsivity**

*DEX/DEX-C*

There was no significant change in scores on this measure (Z=-1.059, n=14, p=0.289), indicating that levels of impulsivity are fairly consistent within the group over time. There was a significant correlation within these scores ($r_s(13)=0.839$, $p<0.001$) suggesting a strong positive, linear relationship. At Time 1 the item with the highest score was "sometimes getting over excited about things", whilst this continued to have a high score at Time 2 the greatest endorsed item was "difficulty planning or thinking about the future". This may be due to the changing demands placed upon the participants as they have grown, making problems with planning for the future become more apparent with time. This may have been an issue as at both time points participants scored highly on having a lack of insight into their ability, acting without thinking and being easily distracted. Other item scores that appeared to

increase with age were items suggesting that participants seemed less concerned about their behaviour in social situations.

*The Conners'*

There was no significant difference in the DSM total score (Z=-1.837, n=12, p=0.066) on the Conners' between Time 1 and Time 2. However, scores were significantly lower at time 2 on the oppositional scale (Z=-2.433, n=12 p=0.015), global index emotional liability (Z=-2.401, n=12,pP=0.016), global index total (Z=-2.048, n=12, p=0.041), DSM inattentive (Z=-2.096, n=12, p=0.036), and DSM hyperactive impulsive (Z=-2.373, n=12, p=0.018). This indicates that individuals were reported to be less defiant, hyperactive, inattentive, and had greater control of their emotions at Time 2. However, there was little variation in the number of participants that met clinical level on the scales between the time periods. As seen in Table 7, all sub domain scores on the Conners' had a significant positive correlation between Time 1 and Time 2. This indicates there is a linear relationship between these scores.

**Table 7: Scores on the Conners' at time 1 and time 2**

| Conners' Scale | Time 1 MDN (IQR) (N=12) | Time 2 MDN (IQR) (N=12) | Results of Wilcoxon Signs Test | Results of Spearman's Rho | Number of participants meeting clinical level^ at Time 1 | Number of participants meeting clinical level^ at Time 2 |
|---|---|---|---|---|---|---|
| Oppositional Scale | 14.7 (15.8) | 8.0 (13.25) | Z=-2.433, n=12, p=0.015* | $r_s$ (13)=0.666 p=0.013* | 5 | 6 |
| Cognitive Problems | 25.8 (9.4) | 25.0 (14.0) | Z=-0.445, n=12, p=0.657 | $r_s$ (13)=0.807, p=0.001* | 7 | 8 |
| Hyperactivity | 15.0 (15.4) | 12.0 (14.25) | Z=-1.959, n=12, p=0.05 | $r_s$ (13)=0.845, p=0.000* | 9 | 10 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Anxious/shy | 4.0 (8.5) | 4.5 (4.75) | Z=-0.613, N=12, p=0.540 | $r_s$ (13)$R^2$=0.788, p=0.001* | 5 | 2 |
| Perfectionism | 8.0 (9.8) | 5.5 (6.25) | Z=-1.602, n=12, p=0.109 | $r_s$ (13)=0.856, p=0.000* | 5 | 2 |
| Social Problems | 4.0 (6.3) | 4.5 (4.75) | Z=-0.409, n=12, p=0.682 | $r_s$ (13)=0.504, p=0.079* | 4 | 6 |
| Psychosomatic | 4 (5.5) | 3.5 (5.5) | Z=-0.567, n=12, p=0.571 | $r_s$ (13)=0.699, p=0.008* | 5 | 5 |
| ADHD index | 28 (10.0) | 26.0 (16.7) | Z=-0.904, n=12, p=0.366 | $r_s$ (13)=0.816, p=0.001* | 10 | 9 |
| Global index restless impulsive | 15.5 (6.5) | 13.0 (11.5) | Z=-1.586, n=12, p=0.113 | $r_s$ (13)=0.839, n=13, p=0.000* | 10 | 10 |
| Global index emotional lability | 5.5 (5.3) | 2.0 (4.7) | Z=-2.401, n=12, p=0.016* | $r_s$ (13)=0.946, p=0.000* | 7 | 5 |
| Global index total | 20.0 (10.3) | 15.5 (16.5) | Z=-2.048, n=12, p=0.041* | $r_s$ (13)=0.666, p=0.013* | 10 | 9 |
| DSM Inattentive | 19.5 (19.0) | 15.0 (10.8) | Z=-2.096, n=12, p=0.036* | $r_s$ (13)=0.807, N=13 p=0.001* | 8 | 7 |
| DSM Hyperactive impulsive | 18.0 (13.8) | 13.0 (17.0) | Z=-2.373, n=12, p=0.018 | $r_s$ (13)=0.845, p=0.000* | 9 | 8 |
| DSM Total | 33.3 (17.8) | 33.0 (21.0) | Z=-1.837, n=12, p=0.066 | $r_s$ (13)=0.788, p=0.001* | 10 | 9 |

*Statistical significance at an alpha of p=0.05

^ Clinical level was defined as meeting the criteria for Moderately Atypical or Markedly Atypical on the Conners' rating scale indicating a Significant Problem.

**Cognitive and Social Functioning**

'Communication' domain on the VABS-SF was completed at Time 1 and Time 2 (see Table 8). Scores for the Communication domain had not significantly ($Z=-1.363$, $n=10$, $p=0.173$) changed over time (remaining at an age equivalent of 1 year 2 months to 8 years 9 months at Time 2), with only a significant difference found in the written subdomain, which had increased by Time 2 ($Z=-2.803$, $n=10$, $p=0.005$) to age equivalent scores of 1 year 6 months to 8 years 9 months. This indicates that the participants' written abilities increase over time. The participants scored the highest on the 'Daily Living Skills' domain (raw score Mdn 110.0, IQR 44.25) of the VABS-SF. However, there was great variation in the scores with age equivalent scores of 1 year 10 months to 9 years 10 months. Whilst parents/carers reported that individuals were able to engage in domestic chores, it was universally agreed that none of the individuals with SMS were completely independent and lack of road safety skills was a particular issue. Only 16.7% were able to safely cross the road independently and only 41.7% were able to do so with assistance. When describing social relationships parents/carers tended to note that their child did not have any specific friends despite high levels of sociability, and that their child displayed little awareness of stranger danger instead being described as "over friendly" with strangers.

**Table 8: Scores on the VAB-SF with age equivalent scores for typically developing population.**

| Domain | Time 1 Mdn Raw score (IQR) (n=10) | Time 2 Mdn Raw score (IQR) (n=10) | Time 1 Mdn age equivalent in years/months (IQR) | Time 2 Mdn age equivalent in years/months (IQR) | Significance of difference between raw score at time 1 and time 2 |
|---|---|---|---|---|---|
| Communication | 63.0 (42.7) | 89.0 (56.0) | 3.2 (4.7) | 6.2 (4.1) | Z=-1.363, n=10, p=0.173 |
| Expressive | 31.0 (25.5) | 46.0(34.5) | 2.5 (2.6) | 5.7 (3.2) | Z=-0.665, n=10, p=0.506 |
| Receptive | 22.5 (3.0) | 25.0 (3.0) | 2.10 (2.2) | 5.9 (4.8) | Z=-1.725, n=10, p=0.084 |
| Written | 9.0 (12.0) | 21.0 (21.5) | 5.10 (11.2) | 6.9 (5.6) | Z=-2.803, n=10, p=0.005* |
| Daily Living Skills | | 110.0 (44.3) | | 6.8 (3.8) | |
| Personal | | 64.5 (12.7) | | 6.6 (2.10) | |
| Domestic | | 24.0 (17.3) | | 8.10 (6.3) | |
| Community | | 27.5 (23.3) | | 6.9 (4.5) | |
| Socialisation | | 79.5 (13.5) | | 5.5 (2.9) | |
| Interpersonal relationships | | 37.0 (10.5) | | 4.5 (3.7) | |
| Play and Leisure | | 26.0 (11.7) | | 5.6 (7.5) | |
| Coping Skills | | 15.5 (9.8) | | 5.5 (1.10) | |
| Motor Skills | | 63.5 (14.5) | | 4.5 (2.3) | |
| Gross | | 33.0 (9.0) | | 3.5 (3.0) | |
| Fine | | 30.5 (4.3) | | 5.10 (1.4) | |

*Statistical significance at an alpha of p=0.05.

## Sleep

### *Sleep Questionnaire and Infant Sleep*

The participants had high levels of sleep problems with all of the participants exceeding the clinical cut-off score of 6, details of which can be seen in Table 9. Specific issues that parents/carers noted were; being overexcited when waking up, frequent awakenings, and sleeping during the day. One parent/carer noted this was subsequently impacting upon their child's functioning. The majority of participants (42%) had approximately 6-7 hours sleep a night, 8% had 8 hours sleep and 8% had 4-5 hours asleep. Sleep length was unknown for the remaining participants. The frequency of sleep waking during the night varied between 1 and 4 (Mdn 2, IQR 1.5).

Strategies used to keep their child safe during night waking included using a Safespace bed (8%), staff support/waking night staff (17%), locking rooms at night (8%), sleeping on the floor of their child's room (8%) and taking them back to bed (8%). Three parents/carers described their management strategy for when their child resisted going to bed. Two parents/carers described letting their child read in their bed, whilst one noted letting them (their child) stay up, but starting a countdown. Out of the eight participants that had received interventions for sleep, all the participants had been given medication (Melatonin) and one participant had also had their bedroom re-designed by an Occupational Therapist. Only three parents/carers found this useful, including the participant who had had a room re-design. There is evidence of the sleep problems impacting upon participants parents/carers with a vast majority (80%) reporting they did not have enough sleep. Parents/carers reported they often felt exhausted, lacked in energy, napped during the day, had difficulties with concentration and generally found it hard to function.

**Table 9: Presence of sleep problems on the Sleep Questionnaire**

| Sleep Behaviours | Percentage of participants (n=12) |
|---|---|
| Talk in sleep | 25 |
| Walk in sleep | 8 |
| Head bang at night | 0 |
| Sleep Apnoea | 17 |
| Bites tongue in sleep | 8 |
| Moves a lot in sleep | 33 |
| Snores loudly | 58 |
| Incontinence at night | 75 |
| Sleeps during the day | 67 |
| Drowsy during the day but can stay awake | 50 |
| Rolls rhythmically in sleep | 33 |
| Needs a security object to sleep | 50 |
| Has a bedtime ritual | 75 |
| Reluctant to go to bed | 67 |
| Afraid of the dark | 42 |
| Complains of headaches upon wakening | 25 |
| Wakes up before 5 am and stays up | 83 |
| Parents/carers report child has a sleep problem | 83 |
| Received intervention for sleep | 67 |
| Currently on sleep medication (e.g. melatonin) | 58 |
| Parents/carers do not get enough sleep | 67 |

## Mental Health Problems

### *Individuals with SMS*

None of the participants met the cut off scores for a 'Possible organic condition', 'Affective Neurotic disorder', or 'Psychotic disorder' on the PAS-ADD Checklist (see Table 10). Three participants were reported to be seeing a psychologist or psychiatrist on the CSRI and ComQol-I5. Of these, two individuals were taking SSRIs for the stated aim of mood stabilisation (Fluvoxamine and Sertraline; Selective Serotonin Reuptake Inhibitors) and one

person was taking an anti-psychotic (Propiomazine). Reasons given for these appointments/medications were for behavioural problems (sleep problems or reducing aggression) rather than mental health problems per se.

**Table 10: Participants' scores on the PAS-ADD Checklist**

| Domain on PAS-ADD Checklist | Cut off scores for domains | Participants scores at Time 2 Mean (SD) (n=12) |
|---|---|---|
| Possible Organic Condition | 5 | 0.6 (1.0) |
| Affective Neurotic Disorder | 6 | 0.7 (1.5) |
| Psychotic Disorder | 2 | 0.2 (0.4) |

*Parents/carers*

The HADS was completed with parents/carers. On the HADS, 14.2% met criteria for anxiety (scored above 7) with scores ranging between 0 and 11 for anxiety (Mdn 3.5, IQR 6.25) and none met the criteria for depression with scores ranging between 0 and 5 (Mdn 1.5, IQR 2.5). On the CSRI, none of the participants' parents/carers reported seeing any Mental Health Services in the last 6 months for themselves.

**Quality of Life**

Scores on the COMQol-I5 informant measure are created by multiplying the importance of this factor to the individual by their satisfaction with this aspect of their life (scores ranging from -4 to 20). Higher scores indicate a greater importance and satisfaction with this area of quality of life. The results of this scale are shown in Table 11 compared against 256 individuals with mixed ID recruited from group homes and sheltered workshops, and 794 randomly sampled typically developing adults (Cummins, 1997). Individuals with SMS scored lower than typically developing adults and adults with ID across all the domains of

quality of life with the exception of 'Intimacy' (relationships with family and friends). Participants with SMS scored the lowest on the 'Productivity' subscale (Mean 0.8, SD 7.87); although**,** there was great variation within these scores. There were strong positive correlations between the importance and satisfaction elements on the 'Safety' ($r_s(10)=0.834$, $p=0.03$) and 'Community' ($r_s(10)=0.705$, $p=0.023$) subscales, meaning participants who placed higher importance on these factors also had a high level of satisfaction in these areas. However, the satisfaction score for 'Safety' (Mean 0.1, SD 1.03) and 'Community' (Mean 0.4, SD 2.5) remained low. There was no significant correlation between the importance and satisfaction scores for 'Material Wellbeing' ($r_s=0.091$, $p=0.803$), 'Health' ($r_s=-0.142$, $p=0.696$), 'Productivity' ($r_s=0.519$, $p=0.124$), 'Intimacy' ($r_s=0.000$, $p=1$), or 'Emotion' ($r_s=-0.285$, $p=0.423$).

**Table 11: Comparison of participants scores on the ComQol-I5 against typically developing adults and adults with ID.**

| Quality of Life Indicator | Participants with SMS (n=8). Mean (SD) | Individuals with mixed ID (Cummins, 1997) (n=256) Mean (SD) | Difference between SMS sample and ID (Cummins, 1997) | Typically developing individuals (Cummins, 1997) (n=794) | Difference between SMS and typically developing individuals (Cummins, 1997) |
|---|---|---|---|---|---|
| Material Wellbeing | 5.7 (7.8) | 7.41 (1.7) | t(1)=7.667, p=0.083 | 8.44 (4.65) | t(1)=5.161, p=0.122 |
| Health | 3.2 (6.3) | 11.98 (2.6) | t(1)=1.729, p=0.334 | 8.78 (6.92) | t(1)=2.147, p=0.277 |
| Productivity | 0.8 (7.9) | 10.56 (2.9) | t(1)=1.164, P=0.452 | 7.45 (5.50) | t(1)=1.241, p=0.432 |
| Intimacy | 14.4 (3.4) | 11.69 (2.6) | t(1)=9.627, p=0.066 | 11.51 (6.34) | t(1)=8.965, p=0.071 |
| Safety | 3.3 (5.6) | 12.54 (2.2) | t(1)=1.714, p=0.336 | 10.00 (5.04) | t(1)=1.985, p=0.297 |
| Community | 3.2 (7.6) | 6.31 (1.9) | t(1)=3.058, p=0.201 | 7.14 (5.09) | t(1)=2.624, p=0.232 |
| Emotion | 2.3 (5.5) | 10.34 (2.8) | t(1)=1.572, p=0.361 | 8.98 (6.09) | t(1)=1.689, p=0.340 |

**Factors predicting Quality of Life**

Regression analyses with bootstrapping were used to determine whether challenging behaviour scores and or sleep scores were related to the factors of quality of life on the ComQol-I5 at each time point. All items that had a significant relationship to factors on the ComQol-I5 can be seen in Table 8.

Material wellbeing appeared to be related to other challenging behaviours at time 2 with significant relationships to the overall severity in addition to individual behaviour scores (damage to property, making threats, loud noises, withdrawn, night time disturbances and refusal to do things). Material wellbeing was the only factor that appeared to have a relationship with sleep, with a significant relationship to uncontrollable urges to sleep during the day.

There were no items that were significantly related to health on the ComQol-I5 at both points, however, at a behavioural level there was a link with other challenging behaviours (smashing windows, stereotyped behaviours, absconding, and pica. Productivity appeared related to be using SIB for self-stimulation at Time 1. Community also appeared linked to functions of SIB (self-stimulation and pain) some individual behaviours (making unwanted sexual contact and stereotyped behaviours). There were no items that were significantly related to intimacy or emotion and no other significant relationships were found.

**Table 12: Significant Predictors of Quality of Life**

| Quality of life domain | Significant predictor | Time point | Regression analysis |
|---|---|---|---|
| Material Wellbeing | CCB: Total for pinch | Time 1 | β=1.309, p=0.036 $R^2$=0.47, F(1,8)=7.05, p=0.017 |
| | CCB: Total for refusing to do things | Time 1 | Time 1: β=3.208, p=0.001 $R^2$= 0.86, F(1,9)=47.72, p<0.001 |
| | CCB: Total SIB | Time 2 | β=1.76, p=0.007 $R^2$= 0.729, F(1,7)=18.83, p<0.01 |
| | CCB: Damage to clothing, furniture and property | Time 2 | β=2.043, p=0.022 $R^2$= 0.582, F(1,7)=9.74, p=0.02 |
| | CCB: Making loud noises | Time 2 | β=2.79, p=0.044 $R^2$= 0.577, F(1,7)=9.57, p=0.02 |
| | CCB: Threatening to hurt others | Time 2 | β=1.83, p=0.032 $R^2$= 0.487, F(1,7)=6.654, p=0.04 |
| | CCB: Withdrawn Behaviour | Time 2 | β=2.36, p=0.034 $R^2$= 0.530, F(1,7)=7.88, p=0.015 |
| | CCB: Night time disturbance | Time 2 | β=1.94, p=0.034 $R^2$= 0.587, F(1,7)=9.95, p=0.02 |
| | CCB: Total severity of other challenging behaviours | Time 2 | β=0.168, p=0.33, $R^2$= 0.602, F(1,7)=10.602, p=0.01 |
| | MSPSQ: Urges to sleep during the day and can't stop themselves | Time 2 | β=3.216, p=0.029 $R^2$= 0.665, F(1,7)=13.90, p=0.016 |
| Health | CCB: Total score for Smashing windows | Time 1 | β =-2.296, p=0.002 $R^2$= 0.477, F(1,8)=7.29, p=0.027 |
| | CCB: Absconding | Time 1 | β=-2.296, p=0.027 $R^2$=0.477, F(1,8)=7.29, p=0.006 |
| | CCB: Eating inappropriate things | Time 2 | β=-1.529, p=0.021 $R^2$= 0.455, F(1,7)=5.84, p=0.046 |
| | CCB: Stereotyped | Time 2 | β=-1.505, p=0.031 |

| | | | |
|---|---|---|---|
| | behaviours | | $R^2$= 0.466, F(1,7)=6.11, p=0.026 |
| Productivity | QABF: Self-stimulation | Time 1 | β = 2.842, p=0.018 $R^2$=0.552, F(1,7)=8.627, p=0.022 |
| Community | CCB: Making unwanted sexual contact total | Time 2 | β=2.850, p=0.08, p=0.036 $R^2$=0.61, F(1,8)=12.585, p=0.01 |
| | CC: Stereotyped behaviour total | Time 2 | β=1.309, p=0.040 $R^2$=0.605, F(1,8)=12.239, p=0.008 |
| | QABF: Self stimulation | Time 1 | β=-2.605, p=0.044 $R^2$=0.530, F(1,7)=7.908, p=0.026 |
| | QABF: Pain | Time 1 and time 2 | Time 1: β=3.109, p=0.008 $R^2$=0.588, F(1,7)=9.972, p=0.016 Time 2: β=2.546, p=0.028 $R^2$=0.446, F(1,8)=5,631, p=0.049 |

*Statistical significance at an alpha of p=0.05.

**Impact of demographic variables on assessment scores**

The impact of gender and age (whether participants were above or below the age of 21) were assessed on all the assessments at time 2 using Mann Whitney U analyses. There was also an impact of gender on the 'Social Problems' (U=4.0, Z=-2.240, p=0.025; male Mdn 8, IQR 4, female Mdn 3, IQR 3.75), and 'ADHD index' (U=5.0, Z=-2.037, p=0.042; male Mdn 30, IQR 7.5, female Mdn 7.5, IQR 15) on the Conners' with males scoring higher than females across this domain. This finding appears to be common across both ID and typically developing populations, with males with Fragile X scoring higher than female counterparts for ADHD symptoms (Tranfaglia; 2011).

When comparing older and younger people at Time 2, there was a significant effect of age on choking/throttling others (U=8.5, Z=-1.987, p=0.004; 15-21 years Mdn, IQR, 22-42 years Mdn, IQR), taking food and drink from others (U=4.5, Z=-2.193, p=0.028 and withdrawn behaviour (U=4.0, Z=-2.480, p=0.013; 15-21 years Mdn, IQR, 22-42 years Mdn, IQR) on the CCB. There was, however, an effect of age on changes in scores on the VAB-SF for the 'Communication' domain (U=4.0, n=13 p=0.015; 15-21 years Mdn 30.5, 22-42 years Mdn 7.0) and 'Written' sub-domain (U=6.0, n=13, p=0.002; 15-21 years Mdn 15.5, 22-42 years Mdn= 3.0).

There were no other effects that reached significance for age or gender across the measures.

## DISCUSSION

This study represents the first longitudinal study, to our knowledge, to assess how behavioural and psychological traits of SMS change over time. Of particular clinical importance, this is the first study to assess mental health difficulties, adult outcomes and quality of life in adolescents and adults with SMS. Whilst the sample size is small, this is common in studies of rare genetic disorders and the follow up rate of just under 50% is relatively high given the ten year follow up period. In addition, the individuals who were followed up were representative of the original sample, with equivalent demographic characteristics including gender, level of ID and variation in age.

Data from this study provide a relatively broad and in-depth characterisation of life for people over 15 with SMS. None of the individuals live independently, with participants either living in the family home or in highly structured residential care homes/schools with other individuals with ID. Whilst one individual was able to complete a mainstream education, all the other adolescents with SMS eventually attended a special school or college and despite the introduction of direct payments providing choice around activities, the majority of adults with SMS attended some form of day centre. Unmet needs raised by parents/carers were the lack of suitable respite and community activities for individuals with SMS. Indeed, one individual was dependent upon family for daytime activities after being excluded from all community services due to high levels of challenging behaviour. Whilst respite was available the lack of suitable consistent placements rendered the support “not worth the hassle”.

Individuals' communication abilities overall appeared stable, with receptive abilities continuing to be lower than expressive abilities. This appears to contrast with other studies indicating that individuals with SMS have better receptive skills than expressive (Gropman, Duncan & Smith, 2006; Smith, Dykens & Greenberg, 1998).

The results of this study also found some increase in the writing abilities of individuals with SMS, particularly amongst the younger participants (aged 15-21). Whilst participants' scores on most scales fitted with previous findings by Udwin et al. (2001) of being lower than an eight year old, some participants' writing abilities surpassed this, with the highest score having an age equivalent of approximately 8 years 6 months.

Overall, the data suggest a possible decrease in a number of aspects of challenging behaviour, in particular the overall frequency and number of aggressive behaviours displayed by the individuals. The prevalence of pinching and choking others significantly reduced from Time 1 to Time 2, and when looking at participants over the age of 19 on the CCB, some aggressive behaviours reduced by over a half (pinching, biting, scratching, head butting, pulling hair, using objects as weapons and, contrary to Webber (1999), choking/throttling). The most prevalent aggressive behaviour displayed changed from hitting (previously, 100%, currently 55.6%) to grabbing (previously 87.5%, currently 66.7%). However, when compared to individuals with ID related to other causes, the levels of challenging behaviour remain high and prevalence of many challenging behaviours (e.g. destruction of property, making loud noises and threatening others) remained largely unchanged.

This potential decrease in aggressive behaviour with time contrasts with data reported by Horn (1999) and Webber (1999), which indicates that levels and severity of challenging behaviour are higher in adults than children. As only the frequency of aggressive behaviours changed, rather than the management difficulty or severity, one hypothesis may be that proactive behavioural strategies may have reduced the frequency of the behaviours, but when they do occur the behaviours are severe and difficult to manage. In typically developing populations lower levels of aggression are often seen in adults compared to children, perhaps related to learned emotional regulation skills (García-Sancho, Salguero, & Fernández-Berrocal, 2014). However, in people with ID and neurodevelopmental disorders, many studies have noted either an increase or maintenance of aggression levels as individuals reach adulthood; Boer & Clark, 1999; Sinnema et al., 2011) followed by a decrease into older adulthood (Dykens, 2004). Whilst the data does not fully support this pattern, the decrease in scores may indicate that individuals with SMS are able to develop some emotional regulation over time, as suggested by the reduction in their emotional lability scores on the Connors'. Alternatively, this reduction in aggression could indicate a reduction in the risk factors for aggression, for example, the reduced level of impulsivity and hyperactivity seen on the Conners' also seen in Horn (1999).

Possible decreases notwithstanding, the severe long-term impacts of challenging behaviours are striking, with two participants becoming blind in one eye as a result of severe SIB, demonstrating a clear need for intervention. The data indicates an apparent increase in all functional scores on the QABF for SIB. Oliver and Richards (in press) suggest that function of SIB may be pain related in youth, and develops further functions as the individual develops. This variation in scores on the QABF could be due to a variety of factors, such as

parents'/carers' increased understanding or sensitivity to the environmental contingencies related to SIB, or SIB being increasingly used to display a variety of functions. As research suggests the topography of SIB seen in adults may differ from that observed in children (Finucane et al., 2001), it may be interesting to explore whether specific types of SIB perform specific functions for adolescents/adults with SMS. This may aid formulation of potential intervention pathways for SIB.

This study found a significant increase in the need for sameness in the cohort on the RBQ, which is a known trigger for challenging behaviour within individuals with SMS (Webber, 1999). This increase in scores on the RBQ for insistence on sameness from childhood to adulthood is commensurate with that found in some other developmental disorders (e.g. Cornelia de Lange; Penhallow et al., 2015).

The exploration of, mental health problems using the PAS-ADD checklist indicated no specific mental health problems in the current group of individuals with SMS. This contrasts with some other neurodevelopmental disorders (e.g. Prader-Willi syndrome, Clarke et al., 1998) and possibly with peers with mixed-cause ID (Cooper, Smiley, Morrison, Williamson, & Allan, 2007). Most participants who had been referred to mental health teams were referred for challenging behaviour and were receiving medication as a mood stabiliser to reduce levels of aggression. This confirms that reports of adults with SMS being sectioned (Horn, 1999) reflects risk ostensibly due to behaviour problems. However, it should be noted that many vulnerability factors for mental health problems (such as ID; Cooper et al., 2007), and poor emotional coping strategies) are prominent in people with SMS and there is evidence to suggest the presentation of mental health problems may differ for different populations. For instance, presentation of depression in individuals with ID may differ from presentation in

typically developing individuals (Marston et al., 1997). Therefore, it remains possible that emotional difficulties are obscured by the severe behavioural issues seen in this group, and/or that the presentation of potential mental health problems is somewhat atypical. Parents/carers have argued that because of the challenging nature of behaviour associated with SMS, individuals require more support from mental health services rather than less, not least because, to date, no universal medication has been successful in managing these challenging behaviours (Laje et al., 2010b). Fourteen percent of parents/caregivers met the criteria on a screening tool for anxiety, and none met the criteria for depression. None of the parents/carers had accessed mental health services. Sleep continued to be an issue for participants, with most continuing to wake in the night and sleep during the day. A majority of participants had been given sleep medication for this, but had not found this effective. However, perceptions of sleep problems may differ between individuals with SMS and their parents/carers as one person noted "it's not an issue for (my child) but it's an issue for everyone else". Indeed, 80% of carers reported they did not get enough sleep, felt exhausted and found it hard to function despite low scores on the HADS.

The overall quality of life appears low in individuals with SMS when compared to both individuals with ID and typically developing populations. The issue of quality of life demonstrates a particular deficit within the area of productivity, despite many of the sample attending school or day centres. Parents/carers noted particular issues in finding appropriate services, with some individuals being reliant upon family members following exclusion from day centres and respite centres due to challenging behaviour. Despite this, individuals scored the highest on the 'intimacy' domain, reflecting that their relationship with their family was the most important factor of quality of life for them and they gained the greatest level of

satisfaction from this area. This, perhaps, is not unexpected given the strong attachment that individuals with SMS make to care givers and their social nature (Wilde, 2012).

Even within this sample; where over half the participants had borderline/mild ID, the average scores on both the daily living skills and socialisation domains of the VABS-SF were the equivalent of those expected by a 5-6 year old, demonstrating that the daily functioning of individuals with SMS is lower than would be expected based on their IQ. Within the daily living skills domain, parents/carers reported little care and attention was given to tasks, and individuals demonstrated little road safety awareness. When discussing social skills, parents/carers noted adolescents and adults with SMS had no particular friends or relationships, although there was often some evidence of awareness of the opposite sex (e.g. females preferring the attention of male staff). However, a lack of knowledge of social boundaries continued to be an issue. Adolescents and adults with SMS continue to need constant supervision, placing high demands on carers, who report getting little sleep or respite and having to manage high levels of challenging behaviour daily.

The results suggest some potential areas that, with further investigation, could be used to increase quality of life; in particular environmental functions of SIB appeared to be related to 'productivity' and 'community' (pain and self-stimulation), which is interesting given the increase in these scores at Time 2. Clearly, this may be an area for further research to clarify the relationship between the variables.

**Limitations**

The small sample size is a limitation of this study. However, this has been an issue in most research into individuals with SMS for the previously mentioned reasons of issues of rarity,

lack of accurate diagnosis in adults, and, failure to thrive in youth. This is compounded in some areas by missing data. There were two main contributors to this latter factor. First, some named child measures were used, which parents/carers saw as not applicable. The issue of appropriate measures for use with adults with developmental disorders is ongoing. Due to a lack of suitable measures for adults with ID or developmental disorders, the Time 1 sample was reliant upon child measures, some of which do not have a directly comparable adult equivalent (e.g. the Conners'). This may impact on the validity of the measure as, for example, adults may have different daily activities and demands placed on them from those experienced by children attending school. However, in the absence of suitable, directly comparable measures for people of all ages with ID, there is no simple solution to this issue. One reason that measures developed for children may, in some cases, be more suitable for adults with ID than measures developed for typically developing adults is that many adult participants are engaged in structured activities (e.g. day centres and supported living placements) seen more often in typically developing children than in typically developing adults. The measures chosen for this study were selected based on a combination of factors including psychometric properties (e.g. test-re-test and inter-rater reliability), possibly ecological validity for the sample, the known phenotypes of the group and the methods at Time point 1. As further measures are developed, findings from the current study may be confirmed and/or refined.

A further limitation is due to the fact that a number of adults with SMS in the current study are in residential care. Whilst parents tended to report perceiving the research as important, and were therefore likely to make time for the measures, many whose adult child lived in residential care relied upon professional carers for up-to-date information, and these

professionals were less likely to return measures. This could perhaps have been reduced by completing all measures through a series of telephone interviews or using direct measures with participants, although this would have decreased the convenience of the study for participants. However, again given the length of follow up, the number of parents/carers able to complete the data at both time points is a great strength of this study as it reduces the likelihood of error due to low inter-rater reliability.

The use of informant report measures rather than direct assessment of individuals with SMS has substantial advantages. It allows a greater number of participants to be assessed, at greater distances, and does not involve the risk of distress to participants reported by Sloneem et al. (2011) in relation to IQ assessments. However, there are also some considerable limitations since many potential caregiver/parent related factors also impact the results. This will be partially addressed in extensions to the current study (see below).

A further limitation of this study is the $p<0.05$ criterion adopted to indicate statistical significance, which increases the chance of type 1 errors given the large number of analyses completed. However, given the small sample size used within the study, had a $p<0.01$ criterion been used, there may have been a substantial chance of making type 2 errors, accepting the null hypothesis when it should be rejected, which given the small literature base for SMS and the exploratory nature of this study, would be a great potential disservice to individuals with SMS, their parents/carers and services supporting them. However, it is acknowledged that this is an issue for future consideration and that the findings should be interpreted tentatively.

## Future Research

The data presented are a small aspect of a wider research project studying aging in individuals with SMS, during which direct data will be collected from individuals with SMS to further explore the issues of cognition and quality of life in adults with SMS, rectifying the limitation that the study relies solely upon informant measures. Furthermore, the sample will be increased to include a greater number of adults with SMS, enabling greater exploration and generalisation of findings presented. Further questions raised by this study, which may form a basis for future work, include whether the potentially increasing functions of self-injurious behaviour are more pronounced with age and with respect to specific topographies of SIB, whether there are indeed no associations between SMS and specific categories of mental health problems or whether presentations of mental ill-health may be atypical, and whether social abilities and daily living skills change over time.

## CONCLUSION

This study has provided an overview of how fourteen individuals with SMS have changed over the last 10 years, suggesting areas of change (including increased functions of SIB, increased repetitive behaviours, reductions in aggressive behaviours and possibly impulsivity and emotional lability, and improvements in writing ability) and areas of stability (e.g. expressive and receptive communication and scores on the DEX/DEX-C). Furthermore, from the data, it has been possible to suggest links between aggressive behaviour and functions of SIB with factors of quality of life for individuals with SMS, which could be explored further to develop interventions aimed at improving quality of life.

It is becoming increasingly apparent that SMS poses extreme challenges for families. The psychological impact of SMS in adolescence and adulthood remains poorly understood, and an understanding of change over time is of great clinical importance and relevance for families in ensuring services are able to support the complex and extensive needs of these individuals. The lack of available respite services, reports from parents/carers of exhaustion and difficulties functioning, and lack of change in management difficulties of challenging behaviours, suggest that, in at least some of these areas, families' needs are not currently being met. Addressing these issues should be of high priority for professionals in years to come.

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## CHAPTER 3: PUBLIC BRIEFING DOCUMENT

This is a public briefing document about two pieces of research, a literature review on mental health issues in individuals over the age of 16 with a neurodevelopmental syndrome and an empirical piece of research on the progression of cognitive, behavioural and emotional traits of adolescents and adults with Smith-Magenis Syndrome.

### LITERATURE REVIEW: *Systematic Review of the Prevalence and Presentation of Mental Health Disorders Experienced by Adults with Neurodevelopmental Syndromes*

Neurodevelopmental syndromes are developmental disorders caused by a genetic abnormality. This literature review focuses on seven relatively well known syndromes; Angelman, Cornelia de Lange, Cri-du-chat, Fragile X, Prader-Willi, Smith-Magenis and Williams. Each is characterised by its own cognitive, behavioural and emotional features. Less is known overall about the psychological features of each syndrome and how these change with time, as most research focuses upon children. The aim of this literature review was to assess the prevalence, and descriptions of mental health disorders to gain a better understanding of how these can be identified enabling mental health services to meet the potential needs of individuals with neurodevelopmental syndromes.

In the literature review, no studies were found assessing mental health issues in Angelman, Cornelia de Lange or Smith-Magenis syndromes. There was research available on mental health issues in adults in four syndromes; one study was found for Cri-du-Chat syndrome; five studies for Fragile X syndrome; seven studies for Williams syndrome, and fourteen for Prader-Willi syndrome.

Overall, the number and type of mental health problems were different across syndromes. There were high levels of depression and psychosis amongst individuals with Prader-Willi syndrome; anxiety appeared to be an issue for people with Williams Syndrome; and for individuals with Fragile X syndrome, problems with anxiety and depression appeared more common. However, descriptions of symptoms suggest that symptoms experienced by individuals with neurodevelopmental syndromes seemed different than those typically described by individuals with these mental health issues. However, as only a small number of studies were found for each syndrome, and in some cases none, more research is needed to better understand what the mental health needs are of individuals with neurodevelopmental syndromes and how these can be identified.

**EMPIRICAL PAPER:** ***Cognitive, Behavioural, Emotional and Quality of Life Outcomes in a Ten Year Longitudinal Study of Individuals over the Age of 15 with Smith Magenis Syndrome***

Smith-Magenis Syndrome (SMS) is a neurodevelopmental disorder first described in 1982. Individuals with SMS have been reported to be very sociable individuals with moderate to severe intellectual disabilities and depend highly upon carers for activities of daily living (e.g. personal care). The most well known characteristics are sleeping problems (particularly sleeping in the day and waking at night) and challenging behaviours (including aggressive behaviour and self-injurious behaviour). Both of these factors are linked to poor quality of life, however, most studies of people with SMS have focused on children and little is known about what happens to individuals with SMS as they get older. This is important to ensure that services are not only able to meet the needs of the individual, but their carers'; as parents are reported to suffer high levels of exhaustion and stress.

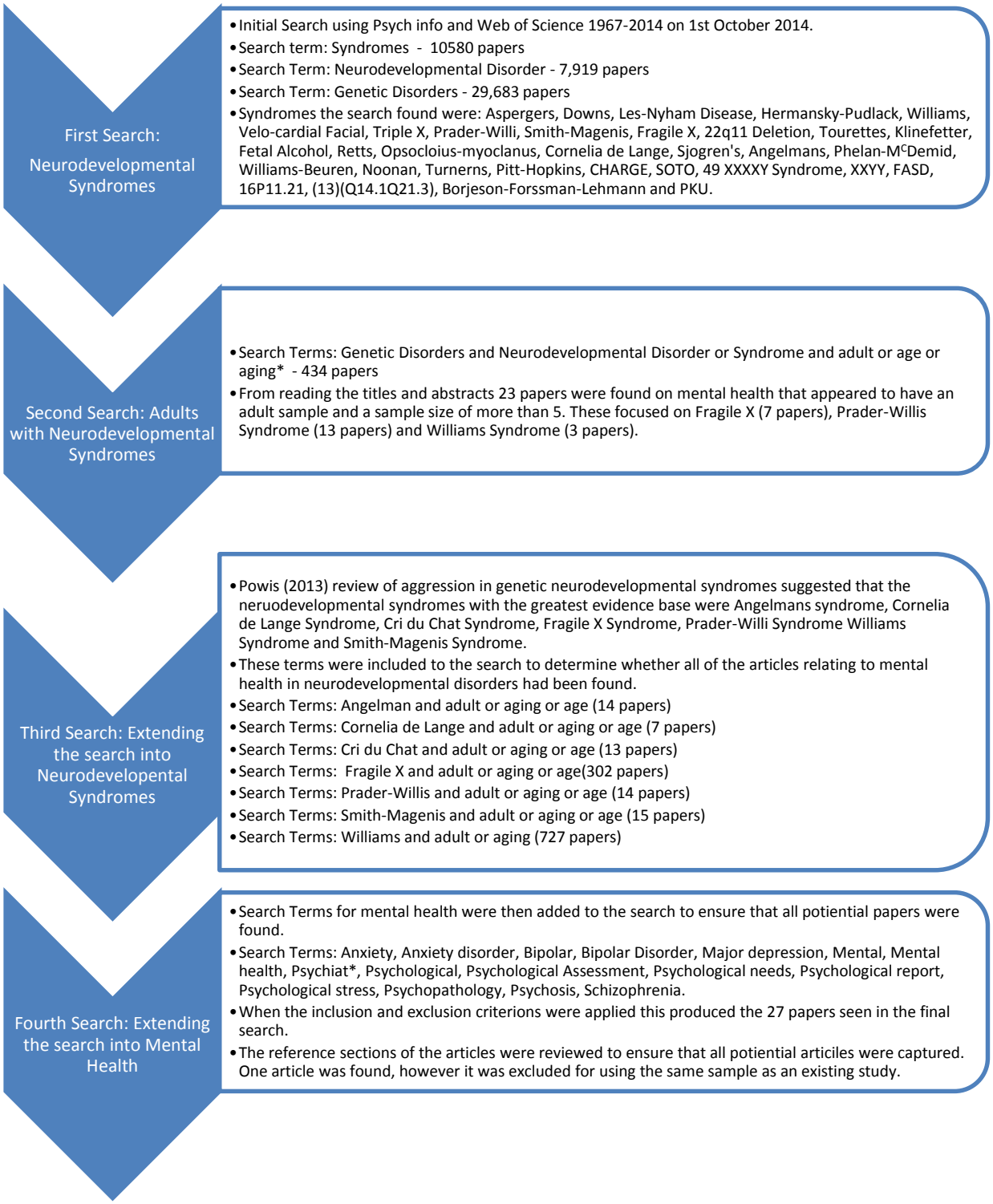
This study followed fourteen individuals with SMS over 10 years to see how their characteristics change over time, in particular, their challenging and repetitive behaviours, and communication abilities, comparing their scores on measures in 2003/2004 to present day (2014/2015). The study also sought to find out what has happened to the individuals and what their quality of life is like now they are all aged 15 and above.

Overall, some challenging behaviours had reduced over time, such as aggressive behaviours; however, these levels are still higher than seen in individuals with idiopathic ID. At the same time, the potential functions for self-injurious behaviours had increased. Participants' communication abilities had largely remained the same, although, there had been an increase in their ability to read and write. They continued to be highly reliant upon parents/carers for activities of daily living and most individuals had problems with sleep. Carers also reported having issues sleeping, which was leaving them exhausted and struggling to function. Despite this, carers reported they did not use respite as the lack of suitable, consistent placements caused distress to the individual with SMS. Participants' quality of life appeared low, particularly in the areas of productivity and health, where two individuals had lost sight in one eye due to self-injurious behaviour.

The findings of this study demonstrate that individuals with SMS continue to have very complex needs as they grow older, requiring high levels of support that services need to be aware of and help support improving the quality of life for individuals with SMS and their carers'.

# APPENDICES

## APPENDIX A: THE EXTENDED LITERATURE REVIEW SEARCH STRATEGY



**Appendix B: Speculative letter sent to parents/carers of children under the age of 16**

## Understanding Smith-Magenis syndrome in people over 14 years of age

Dear **<<Title>> <<First Name>> <<Surname>>** and <<name of participant>>,

We would like to invite you and <<name of participant>> to take part in a research study to be conducted by the Cerebra Centre for Neurodevelopmental Disorders at the University of Birmingham, headed by Professor Chris Oliver.
The aim of the research study is to increase the understanding of behaviour and quality of life in Smith-Magenis syndrome after the age of 14 years. We are really interested to find out about <<name of participant>>'s behaviour and quality of life is now that (s)he is <<x>> year old.

We have enclosed an information sheet providing further details about the project. This should provide you with all the information you need about the study and help you to decide whether or not you and <<name of participant>> wish to take part.

If you feel it is appropriate, you may wish to discuss the research with <<name of participant>>; we've enclosed a simplified information sheet which you might find useful.

If, after reading the information sheet, you would like to take part in the study, please complete and sign the consent form enclosed and complete the questionnaire pack in your own time. Should <<name of participant>> turn 16 during the process of completing this study, we would also seek consent from you and <<name of participant>> using the procedures relevant to people over the age of 16 years. Please contact the research team if you have any questions about this.

You can fill out the questionnaires all in one go or, if this is easier for you, in short sittings over the course of one week.

Once you have completed the questionnaires, we would be grateful if you could please return them, along with the form, in the prepaid return envelope provided, **within four weeks** of the date on this letter.

We will then arrange a time to call you on the telephone to conduct a telephone interview, and arrange a time to visit you and <<name of participant>> in person.

If you have previously indicated that you are happy to be contacted about research, we will in any case call you in the next week to discuss any questions you may have about the research project.

During this call, if you are happy to participate in the research, we will arrange a convenient time to conduct a phone interview with you.

In the meantime, if you have any queries then please contact **** by telephone: ******, email: ***** or at the above address.

***Thank you for your time and continued support for our research at the University of Birmingham. We look forward to speaking with you.***

Yours Sincerely,

**Appendix C: Speculative letter for individuals with SMS over the age of 16**

## Understanding behaviour in Smith-Magenis syndrome into adolescence and adulthood

Dear **<<Title>> <<First Name>> <<Surname>>** and <<name of participant>>,

We would like to invite you and <<name of participant>> to take part in a research study to be conducted by the Cerebra Centre for Neurodevelopmental Disorders at the University of Birmingham, headed by Professor Chris Oliver.

The aim of the research study is to increase the understanding of behaviour and quality of life in Smith-Magenis syndrome after the age of 14 years. We are really interested to find out about <<name of participant>>'s behaviour and quality of life now that (s)he is <<x>> year old.
We have enclosed an information sheet providing further details about the project. This should provide you with all the information you need about the study and help you to decide whether or not you and <<name of participant>> wish to take part.

As <<participant>> is over 16 it is important for you to consider whether they are able to understand the research and to make and communicate an informed decision. If you feel they are able, please discuss the research with them, we've enclosed a simplified information sheet which you might find useful and then complete **Form B**.

Alternatively if you do not feel that <<participant>> is able to make an informed decision, we are required to ask a "consultee" to advise on <<participant>>'s involvement. Please read the attached guidance on what it means to be a consultee.

If you are willing to be <<participants>> consultee, we ask you to read the information sheet and consider what you know of <<participants>> wishes and feelings about research. If you decide <<participant>> would have no objection to taking part we will ask you to complete **Form A.**

If you decide that <<participant>> would not wish to take part it will not affect the standard of care they receive in any way.

If you feel unable to give advice about this, please let us know. We will understand if you do not want to take on this responsibility.

If, however, after reading the information sheet, you would like to take part in the study, please sign the relevant form enclosed and complete the questionnaire pack in your own time.

You can fill out the questionnaires all together or in short sittings over one week if this is easier for you.

Once you have completed the questionnaires, we would be grateful if you could please return them, along with the form, in the prepaid return envelope provided, **within four weeks** of the date on this letter.

We will then arrange a time to call you on the telephone to conduct a telephone interview and arrange a time to meet you and <<name of participant>>.

We will in any case call you in the next week to discuss any questions you may have about the research project. During this call if you are happy to participate in the research we will arrange a convenient time to conduct a phone interview with you.
In the meantime, if have any queries then please contact Professor Chris Oliver by telephone: *****, email: ***** or at the above address.

***Thank you for your time and continued support for our research at the University of Birmingham. We look forward to speaking to you in the next 7 days.***

Yours Sincerely,

**Appendix D: Information form for Carers**

# Understanding Smith-Magenis syndrome in people over 14 years of age

We would like to invite you and your child to take part in a research study. To help you decide if you wish to take part, we would like you to understand why the research is being done and what it would involve for you and your child. Please take the time to look through the information below.

**If you would like a spoken explanation of the study or have any questions please contact the researchers using the contact details at the end.**

## What is the purpose of the study?

Researchers from the Cerebra Centre at the University of Birmingham are carrying out some new research which aims to better understand behaviour and quality of life in older children and adults with Smith-Magenis Syndrome (SMS). We are also interested in the services received and the mental wellbeing of parents and carers.

As well as assessing quality of life, behaviour and parent/carer mental wellbeing in people with SMS over 14 years old, we aim to see how these things have developed over time for some of our participants. This will be possible because in 2003-4, thirty-two people with Smith-Magenis syndrome were assessed by Jenny Sloneem, Chris Oliver and colleagues at the Cerebra Centre, University of Birmingham. We are now re-contacting all of these people in order to re-assess them and establish how things have changed over the intervening years. We are also contacting people with SMS over 14 years who were not in the original study, as it is important to assess as many people with SMS as possible to make sure our results are representative.

## Why have I been invited?

You have been invited to take part in this study because <<name of participant>> is over 14 years of age and has Smith-Magenis Syndrome.

## Do I have to take part?

No, we ask that you take some time to read this information sheet, which should help you to make an informed decision. You do not have to take part if you do not want to. Even once you've agreed to take part you can change your mind at any point, without having to give a reason.

## What will happen if I take part?

If you agree to take part then we ask if you could complete the questionnaires enclosed, returning them in the stamped addressed envelope. We ask if you could do this within four weeks of receiving them. Feel free to look over the questionnaires before agreeing to take part. If you would rather complete the questionnaire pack over the phone with one of our researchers please contact us on the details below. Additionally we would like to ask you some further questions over the phone. Prior to this we will ring to discuss the most convenient time to arrange this telephone interview. This first call will also be an ideal opportunity to ask any further questions you might have about the study. Finally, we would like to arrange to meet with you and <<name of participant>>, in order to directly assess some aspects of <<name of participant>>'s behaviour and abilities.

## What will I have to do?

There are three parts to this study.

Firstly there is the questionnaire pack to fill out (Stage 1); this should take 2 to 3 hours, and is to be completed by a parent/caregiver. You can complete this all in one go, or if it's easier spread it out across one week.

The second part (Stage 2) is a telephone interview with a parent/caregiver, which should take approximately 1 to 2 hours. Together we will arrange a convenient time for us to ring you and do the interview. This part can be split into shorter interviews if preferred.

Finally, for the third part (Stage 3) we would like to visit and carry out some assessments with <<name of participant>>, which will take a total of around 3 hours. This third stage will include in-person interviews with you and <<name of participant>>, a period of time during which we will observe <<name of participant>>'s behaviour and rate it for certain features of social behaviour, and a computerised cognitive demand task.

## What are the potential risks and benefits of the study?

***Risks***

There are unlikely to be any risks associated with participation in this study. However the questionnaires used within this study will ask, amongst other things, about challenging behaviour that your child may have displayed, alongside their quality of life and receipt of services. We would also like to ask you about your own mental wellbeing as a parent/carer. In the unlikely event that these questions cause you any distress please contact your GP, Consultant or national syndrome group for further support. We would also be happy to discuss any difficulties with you and to signpost you to people who could help.

Whilst the direct assessments of <<name of participant>> are not expected to expose him/her to unusual levels of distress, it is possible that he/she will experience a degree of frustration or boredom associated with a task. You and <<name of participant>> will be

able to terminate this at any stage, should you feel it is causing unusual distress. In the highly unlikely event that any aspect of the study leads to difficulties of any sort for your child, please contact your GP, Consultant or national syndrome group for further support. We would also be happy to discuss any difficulties with you and to signpost you to people who could help.

Please see also the section below, "What if there is a problem?".

***Benefits***

<<name of participant>> will benefit from receiving a report about their current behaviour and quality of life that can be shown to professionals to support their work with <<name of participant>>. It may also be that <<name of participant>> will enjoy or find stimulating the direct assessment stage (third stage) of the study. It may be that you, as parent/carer/guardian will find the interview aspects of the assessments (in stages 2 and 3) interesting.

## What happens at the end of the study?

This study does not affect any current support or treatment you and your child might be receiving. Once the information from your questionnaire pack and the telephone interview has been complied you will receive personalised feedback about our findings as well as information about the finding of the study as a whole.

## Where will data be stored?

The data collected will be kept in locked or password protected storage at the University of Birmingham. All information gathered about you and your child will be stored separately from any information that would allow someone to identify who you or your child are (this is known as personal identifying information, e.g. your full names, your address, your contact details). Your personal identifying information will be stored in a locked space at the University of Birmingham and only members of our research team will have access to it. We will only be able to trace the information we have collected about you and your child back to you using a special reference number which we will store in a password protected database held at the University of Birmingham. Only members of our research team will have access to that database. Personal identifying information will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998.

Any video and/or audio recordings are considered to necessarily contain personal identifying information. We will therefore store the recordings of you and your child separately to the other information we have collected about you. These recordings will not be labelled with your names or any other personal identifying information but will be labelled with your special reference number. Recordings will be stored in a locked cabinet at the University of Birmingham and only members of our research team will have access to it.

**If participant is not known to us already:**

At the end of the study, personal details will be ***destroyed unless you tell us otherwise.*** This means that we would no longer be able to trace the results of your assessments back to you. ***The section below on 'The Regular Participant Database Information'*** gives information about a database that we use to store the personal details of some participants. Please read this section in order to decide if you would like to join that database.

**If participant is known to us already and has previously agreed for us to keep their details and contact them for future research:**

Since you have previously been involved in our research projects at the University of Birmingham and have agreed to be contacted by the research team with information about future research work, we have a copy of your personal details on the 'Regular Participant Database'. This database is password protected and only approved members of out research team have access to your details. We do not share your details with anyone outside the research team.

*What happens if I decide that I no longer want my details on the Regular Participant Database?*

All you would need to do is contact ****** on ****** or at ******* or at the School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT. Your details would be removed from the database immediately.

**For participants who are not known to us already: Regular Participant Database Information**

*What is the regular participant database?*

We have a database that we keep in the Cerebra Centre where we store the names and contact details of some previous participants. If you would like us to, we can add your details to this database. We would use this information for two things:

1) We will contact you with information about future research work to find out whether or not you would like to participate.

2) It is often important to find out how things change over time. By keeping your details we would be able to trace the results of the previous assessments that you have done with us back to you. This means that if you take part in other studies with us we would be able to look at how things have changed over time.

*Who would have access to my details?*

Only approved members of our research team would have access to your details. We would not share your details with anyone outside the research team.

*When would I be contacted?*
You would only be contacted by an approved member of the research team when we are starting another study or phase of a study that we think you might like to participate in or when we need to clarify some information that you have provided us with from participation in a research study.

*What happens if I decide that I want my details to be added to the database but then I change my mind?*
All you would need to do is contact **** on ******** or at ********** or at the School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT. Your details would be removed from the database immediately.

## Withdrawal

Even after consent has been granted, you or your child/person you care for can request to be withdrawn from the study and for your research data to be destroyed. You will have up to 4 months after participation to indicate you or your child/person you care for's withdrawal from the study, without giving a reason. This will not restrict access to other services and will not affect the right to treatment. After 24 months of participating in the study, your personal details will no longer be linked to the information collected as part of this study. This means that we would no longer be able to trace the results of your assessments back to you and withdraw you from the study.

## What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. Please contact ***** on ********** or at ********** in the first instance. If you remain unhappy and wish to complain formally, you can contact:

## Will my taking part remain confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. Your personal information will be kept confidential within the team, and identifying information will be stored separately from data from the study.
In the unlikely event that any illegal activities were to become apparent during the study, we would share this information with the relevant authorities. Similarly, should information be disclosed which caused concerns about your or another person's safety, we would share this information with the relevant professionals.

**Appendix E: Information sheets for Participants over 16.**

# Information Sheet for Participants
# Understanding behaviour in Smith-Magenis syndrome over 14 years of age

We would like to invite you and your parent/carer to take part in a research study. To help you decide if you wish to take part we would like you to understand why the research is being done and what it would involve for you and your child. Please take the time to look through the information below.

**If you would like a verbal explanation of the study or have any questions please contact the researchers using the contact details at the end.**

## What is the purpose of the study?

Researchers from the Cerebra Centre at the University of Birmingham are carrying out some new research which aims to better understand behaviour and quality of life in people 14 years old with Smith-Magenis Syndrome. We are also interested in the services received and the mental wellbeing of parents and carers.

## Why have I been invited?

You have been invited to take part in this study because you are over 14 years of age and have Smith-Magenis Syndrome.

## Do I have to take part?

No, we ask that you take some time to read this information sheet with a parent/guardian/carer, which should help you to make an informed decision. You do not have to take part if you do not want to. Even once you've agreed to take part you can change your mind at any point, without having to give a reason.

## What will happen if I take part?

If you agree to take part then we ask if your parent/carer could complete the questionnaires enclosed, returning them in the stamped addressed envelope. Feel free to look over the questionnaires before agreeing to take part. Additionally we would like to ask your parent/carer some further questions over the phone. Prior to this we will ring to discuss the most convenient time to arrange this telephone interview. This first call will also be an ideal opportunity to ask any further questions you might have about the study. Finally, we would like to arrange to meet with you and your parent/carer, in order to directly assess some aspects of your behaviour and abilities.

## What will I have to do?

There are three parts to this study. Firstly there is the questionnaire pack for your parent/carer to fill out; this should take approximately 1 hour 20 minutes. The second part is a telephone interview with your parent/carer this should take around 2 hours 40 minutes. Together we will arrange a convenient time for us to ring you and do the interview. Finally, for the third part we would like to visit you and carry out some assessments , which will take around 1 hour 20 minutes.

## What are the potential risks and benefits of the study?

***Risks***

There are unlikely to be any risks associated with participation in this study. However the questionnaires used within this study will ask, amongst other things, about challenging behaviour that you may have displayed, alongside your quality of life and receipt of services. We would also like to ask your parent/carer about their mental wellbeing as a parent/carer. In the unlikely event that these questions cause you any distress please contact your GP, Consultant or national syndrome group for further support.

It is possible that you might find some of the tasks we ask you to do frustrating (although we hope you may find them enjoyable). If you want to stop at any point, that is fine.

***Benefits***

You will benefit from receiving a report about their current behaviour and quality of life that can be shown to professionals to support their work with you. You may also enjoy some of the tasks and interviews involved during the third stage of the study.

## What happens at the end of the study?

This study does not affect any current support or treatment you and your parent/carer might be receiving. Once the information from your questionnaire pack and the telephone interview has been complied you will receive personalised feedback about our findings as well as information about the finding of the study as a whole.

## What if there's a problem?

If during the study you have any problems or wish to make a complaint. You can contact the research team or speak to someone independent of this study.

## Will my taking part remain confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence.

**Appendix F: Consent form for participants under the age of 16**

## Understanding Smith-Magenis syndrome over 14 years of age

### Consent Form

**Please read through the statements below. If you agree with the statement please put your initials in the box next to it. Remember, your decision will NOT affect the care you receive now or in the future.**

I confirm that I have read and understood the information sheet provided and have been given the opportunity to ask questions ☐

I have had all my questions answered to a satisfactory standard by the researcher ☐

I understand that my child's and my participation in the study is voluntary and that we have the right to withdraw from the study at any time, without having to give a reason ☐

I agree to participation in the above study ☐

I feel that my child was <u>able</u> to understand the information provided

They have agreed (assented) to participate ☐

They do not wish to participate ☐

I feel that my child was <u>not able</u> to understand the information provided ☐

I agree to the participation of my child in the above study ☐

I agree for the data obtained here to be transported to and analysed at the University of Birmingham. ☐

**P.T.O**

**Please complete the information below**

Child's name: ……..... Date of birth: …….

Parent/guardian's signature:……..…….Mr/Mrs/Miss/Ms (please circle)

Date: ……

Please state relationship to child:…….

Contact address:

……..……..……

…….……Contact telephone number: ……

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**FOR OFFICE USE ONLY**

Researcher Name…….…..

Signature of Researcher:…….…..Date:……..

When completed: 1 for Parent/guardian's signature; 1 (original) for researcher site file

**Appendix G: Consultee Information sheet for parents/carers over the age of 16**

## Personal and Nominated Consultee Information Sheet

Please read this information sheet if you care for a person who you have judged *is not* able to make an 'informed' decision about whether or not they would like to take part in the study or *is not* able to communicate that decision to you.

If you are an unpaid carer (e.g. parent, legal guardian etc) we would like to invite you to act as a ***personal consultee*** for the person that you care for. If you are a paid carer (e.g. paid carer, key worker, support worker etc) and there are no unpaid carers (e.g. parent, legal guardian etc) to act as a personal consultee for the person you care for then we would like to invite you to act as a ***nominated consultee*** **(go to page 3)**.

### Information for Personal Consultees

**What is a Personal Consultee?**

In order to understand illness and disability, and to improve treatment and care, research is essential. That research may focus on the people with the illness or disability or on children under the age of 16, and may invite those people to participate. Some people will have capacity to make their own decision whether to take part in the research.

Others, possibly the youngest children or those most affected by the illness or disability, may not have that capacity. They may not be able to understand enough of the research to be able to give 'informed consent'. They may not be able to communicate a decision. The research provisions of the Mental Capacity Act are designed to allow such people to take part in research even though they cannot give valid consent of their own.

First, the research has to be approved by a Research Ethics Committee. Then, instead of asking the research participant for consent, the researcher must ask a consultee for an opinion whether the research participant would have wished to take part in the research.

**Who can be a personal consultee?**

Any person interested in the welfare of the proposed participant, for example:

- A family member, unpaid carer or friend
- A person acting under a Lasting Power of Attorney
- A court appointed deputy

**Who cannot be a personal consultee?**

- Paid carers and professionals (if you are a paid carer or professional please refer to **page 3**)
- People connected with the research (e.g. members of the research team)

**Why have I been asked?**

You have been asked to act as a personal consultee by a researcher because the researcher thinks you might be willing and able to do this because of your close relation with the proposed research participant.

**If I agree to be a personal consultee, what will I have to do?**

You will need to think about what the proposed participant's wishes and feelings about the research would be if they had capacity to make an informed decision and decide whether in your view the person should be involved in the research or not. This means you need to

- Look at the study information sheet.
- Think about whether or not the person would want to be involved in the research project if he or she had the capacity to make that decision.

You should not put forward your personal views on participation in the specific project or research in general, you must consider only what the person's views and interests are or would likely be. You should think about:

- What the broad aims of the research and the practicalities of taking part will mean for the proposed participant.
- How the specific activities in the research might impact the participant. For example, if the study involves activities in the afternoon when the person is most tired they might find it a strain or the research might involve an activity that the person particularly enjoys and thus would give them more pleasure.
- Any view previously expressed by the person on the overall nature of the research.

If you advise that the proposed participant would not have wanted to be involved in the research, they cannot be included in the research.

If you advise that the proposed participant would want to be involved, they may be included in the research. If the research commences but the person shows any sign at any stage that they are not happy to be involved in the research you can change your advice at any time without giving a reason, whereby the researcher must withdraw the person from the research. If the person seems unhappy at any point or shows any signs of objection, then they will be withdrawn from the research.

The research project has been approved by the Coventry NHS Research Ethics Committee. If you wish to see proof of approval from this body, or you wish to discuss any concerns about acting as a personal consultee for the person that you care for, please contact Chris Oliver on 0121 414 7206 or by email at c.oliver@bham.ac.uk.

**I don't want to be a personal consultee/ I am a paid carer and so cannot be a personal consultee- what do I do?**

Please try to suggest an alternative person who might like to act as a personal consultee for the potential participant, please pass the project information pack on to that person.

**Where can I get more information and guidance?**

More information is available from:
Department for Constitutional Affairs (2007) *Mental Capacity Act 2005 Code of Practice*
http://www.dca.gov.uk/legal-policy/mental-capacity/mca-cp.pdf

Mental Capacity Implementation Programme (2007) *Making Decisions: a guide for family, friends and unpaid carers. Second edition*
http://www.dca.gov.uk/legal-policy/mental-capacity/mibooklets/booklet02.pdf
A printed copy of this booklet is available by telephoning 023 80878038.

**I have decided that I want to be a personal consultee- what do I do?**
Please go back to the 'Functions of Challenging Behaviour' Information Sheet and continue reading.

## Information for Nominated Consultees

**What is a Nominated Consultee?**
In order to understand illness and disability, and to improve treatment and care, research is essential. That research may focus on the people with the illness or disability or on children under the age of 16, and may invite those people to participate. Some people will have capacity to make their own decision whether to take part in the research.
Others, possibly the youngest children or those most affected by the illness or disability, may not have that capacity. They may not be able to understand enough of the research to be able to give 'informed consent'. They may not be able to communicate a decision. The research provisions of the Mental Capacity Act are designed to allow such people to take part in research even though they cannot give valid consent of their own.
First, the research has to be approved by a Research Ethics Committee. Then, instead of asking the research participant for consent, the researcher must ask a consultee for an opinion whether the research participant would have wished to take part in the research.

**Who can be a nominated consultee?**

- Any person interested in the welfare of the proposed participant who works with the participant in a professional capacity.

**Who cannot be a nominated consultee?**

- People connected with the research (e.g. members of the research team)

**Why have I been asked?**
You have been asked to act as a nominated consultee by a researcher because the researcher thinks you might be willing and able to do this because of your professional relationship with the proposed research participant.

**If I agree to be a nominated consultee, what will I have to do?**

You will need to think about what the proposed participant's wishes and feelings about the research would be if they had capacity to make an informed decision and decide whether in your view the person should be involved in the research or not. This means you need to

- Look at the study information sheet.
- Think about whether or not the person would want to be involved in the research project if he or she had the capacity to make that decision.
- You may need to seek the advice of friends/ family/ other paid carers of the person you care for in order for you to best advise us on what the person's wishes and feelings would be.

You should not put forward your personal views on participation in the specific project or research in general, you must consider only what the person's views and interests are or would likely be. You should think about:

- What the broad aims of the research and the practicalities of taking part will mean for the proposed participant.
- How the specific activities in the research might impact the participant. For example, if the study involves activities in the afternoon when the person is most tired they might find it a strain or the research might involve an activity that the person particularly enjoys and thus would give them more pleasure.
- Any view previously expressed by the person on the overall nature of the research.

If you advise that the proposed participant would not have wanted to be involved in the research, they cannot be included in the research.
If you advise that the proposed participant would want to be involved, they may be included in the research. If the research commences but the person shows any sign at any stage that they are not happy to be involved in the research you can change your advice at any time without giving a reason, whereby the researcher must withdraw the person from the research. If the person seems unhappy at any point or shows any signs of objection, then they will be withdrawn from the research.
The research project has been approved by the Coventry NHS Research Ethics Committee. If you wish to see proof of approval from this body, or you wish to discuss any concerns about acting as a personal consultee for the person that you care for, please contact

**I don't want to be a nominated consultee - what do I do?**

Please try to suggest an alternative person who might like to act as a nominated consultee for the potential participant, please pass the project information pack on to that person.
If no-one can be found who is willing and able to act as a consultee for the person you care for then the person will not be able to participate in the research study.

**Where can I get more information and guidance?**

More information is available from:

Department for Constitutional Affairs (2007) *Mental Capacity Act 2005 Code of Practice*
http://www.dca.gov.uk/legal-policy/mental-capacity/mca-cp.pdf
Mental Capacity Implementation Programme (2007) *Making Decisions: a guide for family, friends and unpaid carers. Second edition*
http://www.dca.gov.uk/legal-policy/mental-capacity/mibooklets/booklet02.pdf
A printed copy of this booklet is available by telephoning 023 80878038.

**I have decided that I want to be a nominated consultee- what do I do?**

Please go back to the 'Describing and Understanding Challenging Behaviour and Parent/Carer Well-being' Information Sheet and continue reading.

**Appendix H: Consent form for participants over 16 who are unable to consent**

## Form A

**Complete this only if you feel that the person you care for <u>is not</u> able to make an informed decision**

**Please read through the statements below. If you agree with the statement please put your initials in the box next to it. Remember, your decision will NOT affect the care you receive now or in the future.**

I have been consulted about <<participant>>'s participation in this research project. I have had the opportunity to ask questions about the study and understand what is involved. ☐

In my opinion they would have no objection to taking part in the above study. ☐

I also consent to participate in the above study ☐

I understand that my participation and that of the person I care for is voluntary and that we are free to withdraw at any time without giving any reason, without my or that of person I care for's medical care or legal rights being affected. ☐

**Please complete the information below**

Participant's Name……Participant's Date of Birth……..

Consultee's name:……..…….Mr/Mrs/Miss/Ms (please circle)

Please state relationship to participant:…….

Contact address:

……..……..……

……..……..

…….……

Contact telephone number: ……

Consultee's signature:

……..…….Date:

……

---

**FOR OFFICE USE ONLY** Researcher Name……..

Signature of researcher:……..Date:……..

When completed: 1 for consultee; 1 (original) for researcher site file

**Appendix I: Consent form for Participants over the age of 16 who are able to consent**

## Form B

**Complete this only if you feel that the person you care for <u>is able</u> to make an informed decision**

**<u>SECTION 1:</u>**
**To be completed by <<Participant>> or by a parent/carer on their behalf.**

1. Has somebody explained the project to you or have you read the information? YES/NO
2. Do you understand what the project is about? YES/NO
3. Have you asked all of the questions you want? YES/NO
4. Have you had your questions answered in a way you understand? YES/NO
5. Do you understand it is OK to stop taking part at any time? YES/NO
6. Are you happy to take part? YES/NO

If <u>any</u> answers are 'no' or you don't want to take part, don't sign your name!

If you <u>do</u> want to take part, you can write your name below

Your name:
_____

Date:_____

The person who explained this project to you needs to sign too.
Print name:……..
Sign:……
Date:…….

PTO…continued overleaf

**SECTION 2:**

**To be completed by the parent/carer/guardian of <<Participant>>.**

**Please read through the statements below. If you agree with the statement please put your initials in the box next to it. Remember, your decision will NOT affect the care you receive now or in the future.**

**Please initial box…**

1. I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation and that of the person I care for is voluntary and that we are free to withdraw at any time without giving any reason, without my or that of person I care for's medical care or legal rights being affected. ☐

3. I consent to take part in the above study. ☐

**Please complete the information below**

Print Name: _____ Telephone number: _____

Relationship to participant:_____

Address:

_____

_____Email: _____

Signature: _____Date: _____

---

**FOR OFFICE USE ONLY** Researcher

Name……..

Signature of researcher:……Date:……..

**When completed: 1 for Signatory and 1 (original) for researcher site**

**Appendix J: Demographic Information Questionnaire**

## BACKGROUND INFORMATION

**Please tick or write your response to these questions concerning background details:**

**Please answer the following about the person you care for:**

1. **Today's date:** _____

2. **Gender:** Male ☐ Female ☐

3. **Date of Birth**: ___/___/____ **Age:_____**

4. **Is the person you care for verbal?** (i.e. more than 30 signs/words in their vocabulary)

   Yes/No (delete as appropriate)

5. **Is the person you care for able to walk unaided?**

   Yes/No (delete as appropriate)

6. **Has the person you care for been diagnosed with a syndrome?** Yes/No (delete as appropriate)

*If yes, please indicate which syndrome in 5a. and answer questions 6 to 8. If no, please move on to question 9*

6.a

| | | | |
|---|---|---|---|
| Cornelia de Lange syndrome | ☐ | Cri du Chat syndrome | ☐ |
| Prader-Willi syndrome | ☐ | Rubinstein Taybi syndrome | ☐ |
| Fragile X syndrome | ☐ | Down syndrome | ☐ |
| Lowe syndrome | ☐ | Soto Syndrome | |
| Rubinstein-Taybi syndrome | ☐ | 9q34 deletion | |
| 8p23deletion | ☐ | Tuberous Sclerosis | ☐ |
| Other _____ | | | |

7. **What is the genetic mechanism causing the syndrome in the person you care for?**

| | | | |
|---|---|---|---|
| Uni-parental disomy | ☐ | Sequence repetition | ☐ |
| Deletion | ☐ | Translocation | ☐ |
| Unknown | ☐ | Other | |

_____

8. **When was the person you care for diagnosed?** _____

**9. Who diagnosed the person you care for?**

| | | | |
|---|---|---|---|
| Paediatrician | ☐ | Clinical Geneticist | ☐ |
| GP | ☐ | Other | |

_____

**10. Has the person you care for had any medical/health difficulties in the last six months? If yes, please give details:**

**_____**

**_____**

**_____**

*In the information sheet and consent form we informed you that we may need to contact your child's/person you care for's GP in order to clarify any information regarding your child's health and diagnostic status (see consent form and information sheet for more information). If you are happy for us to do this, please complete the relevant details below:*

**11. Name of your child's/person you care for's**

**GP_____**

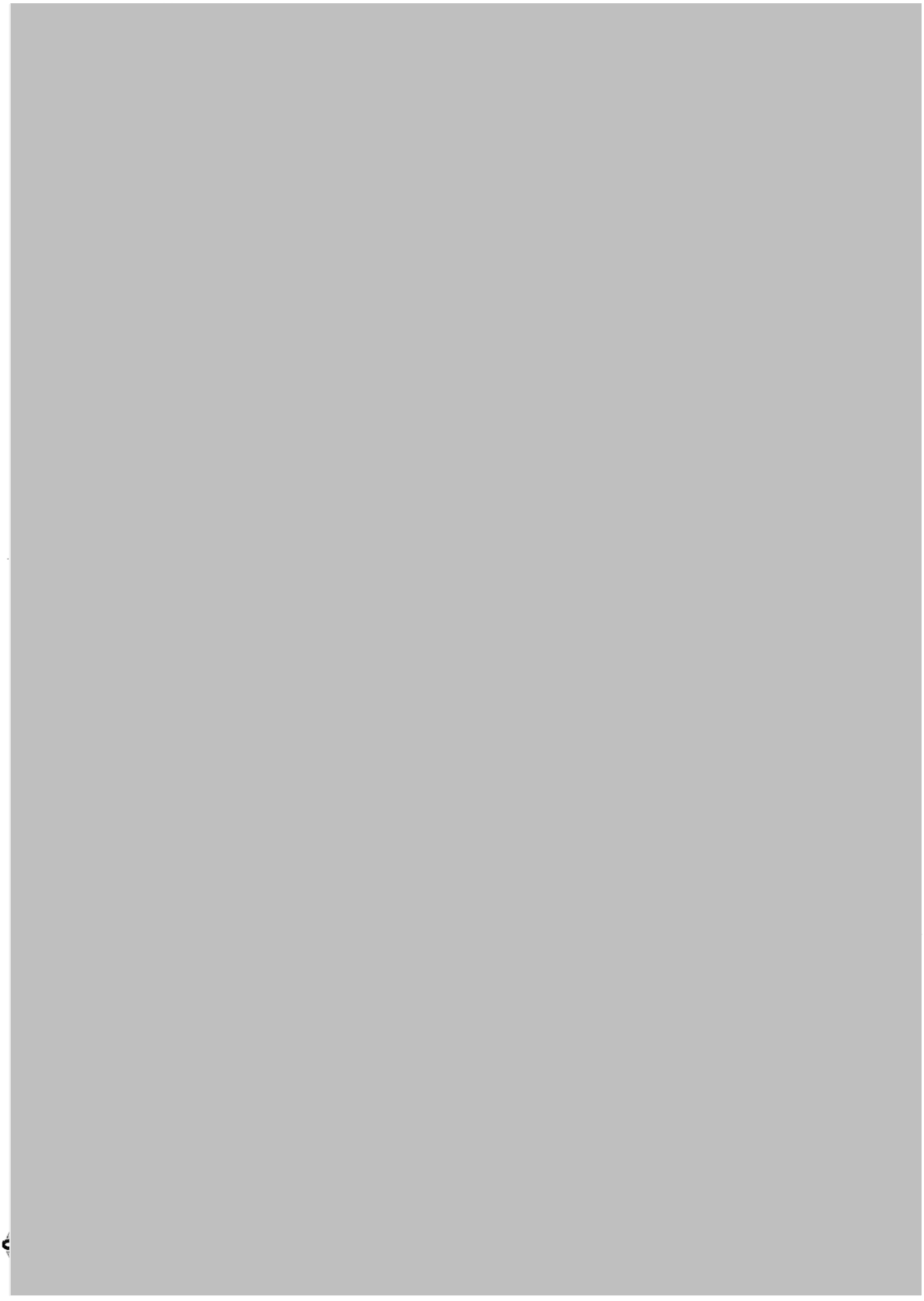
**GP**

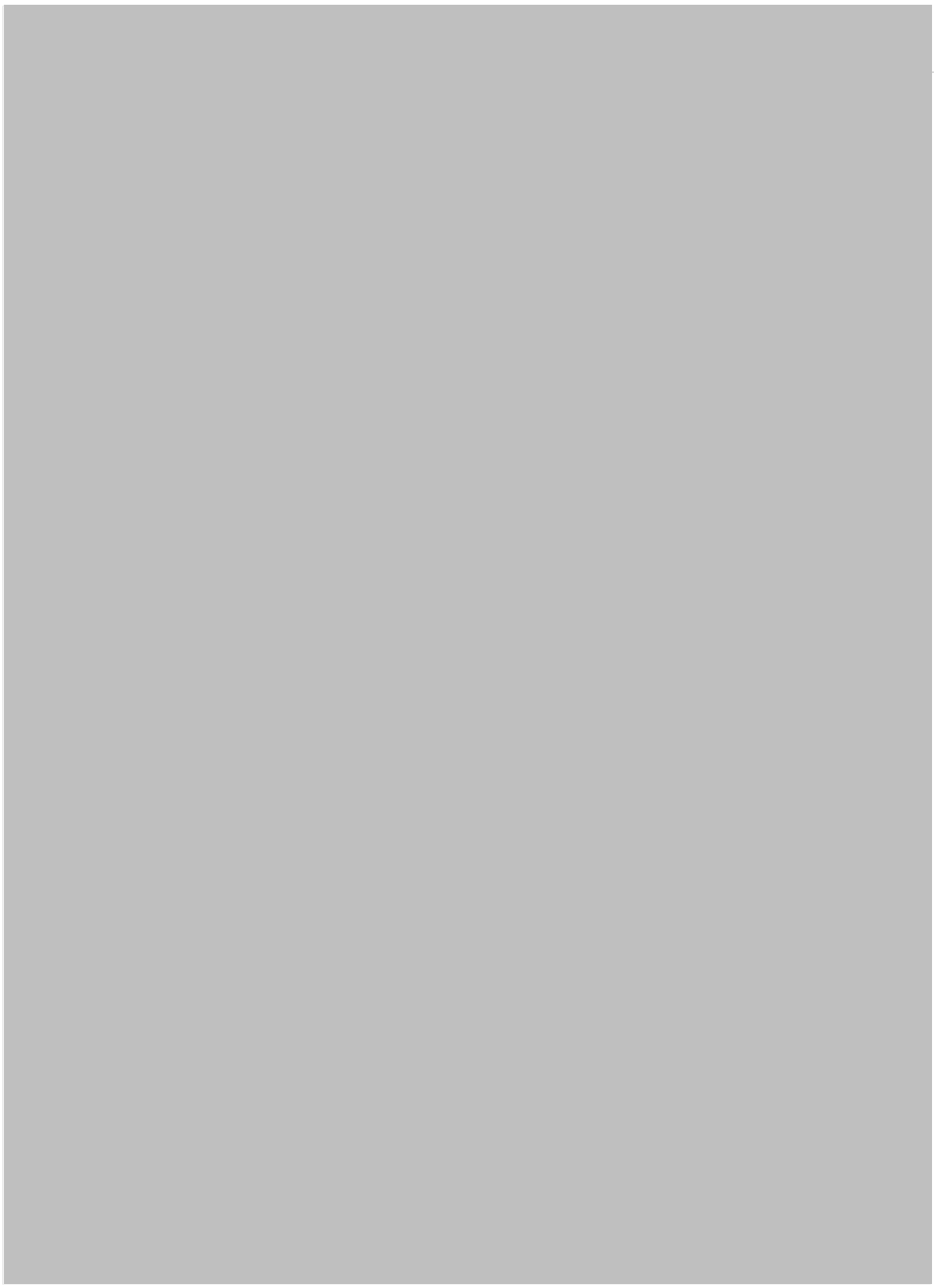
**Address_____**

**_____**

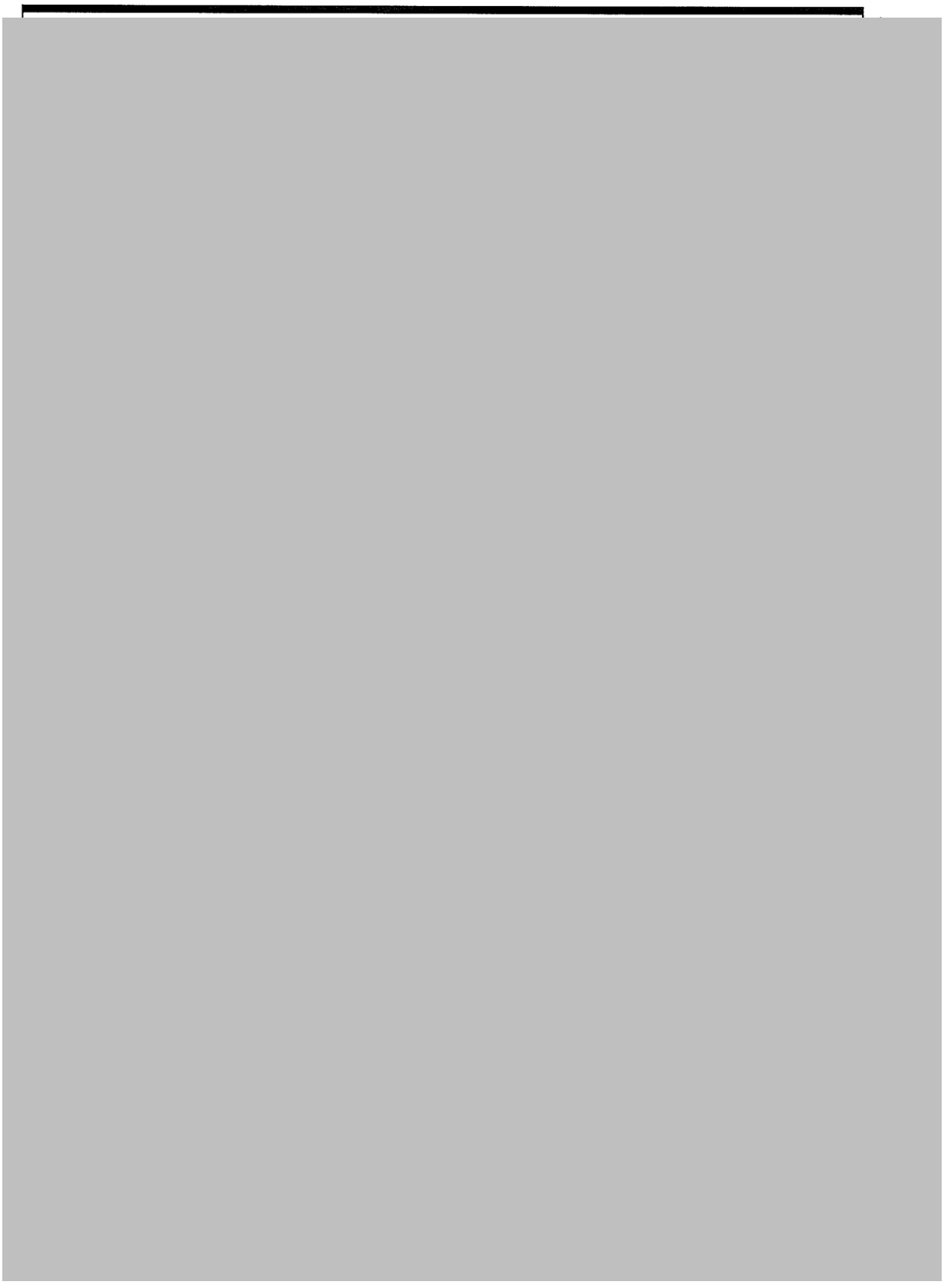
**GP Telephone number_____**

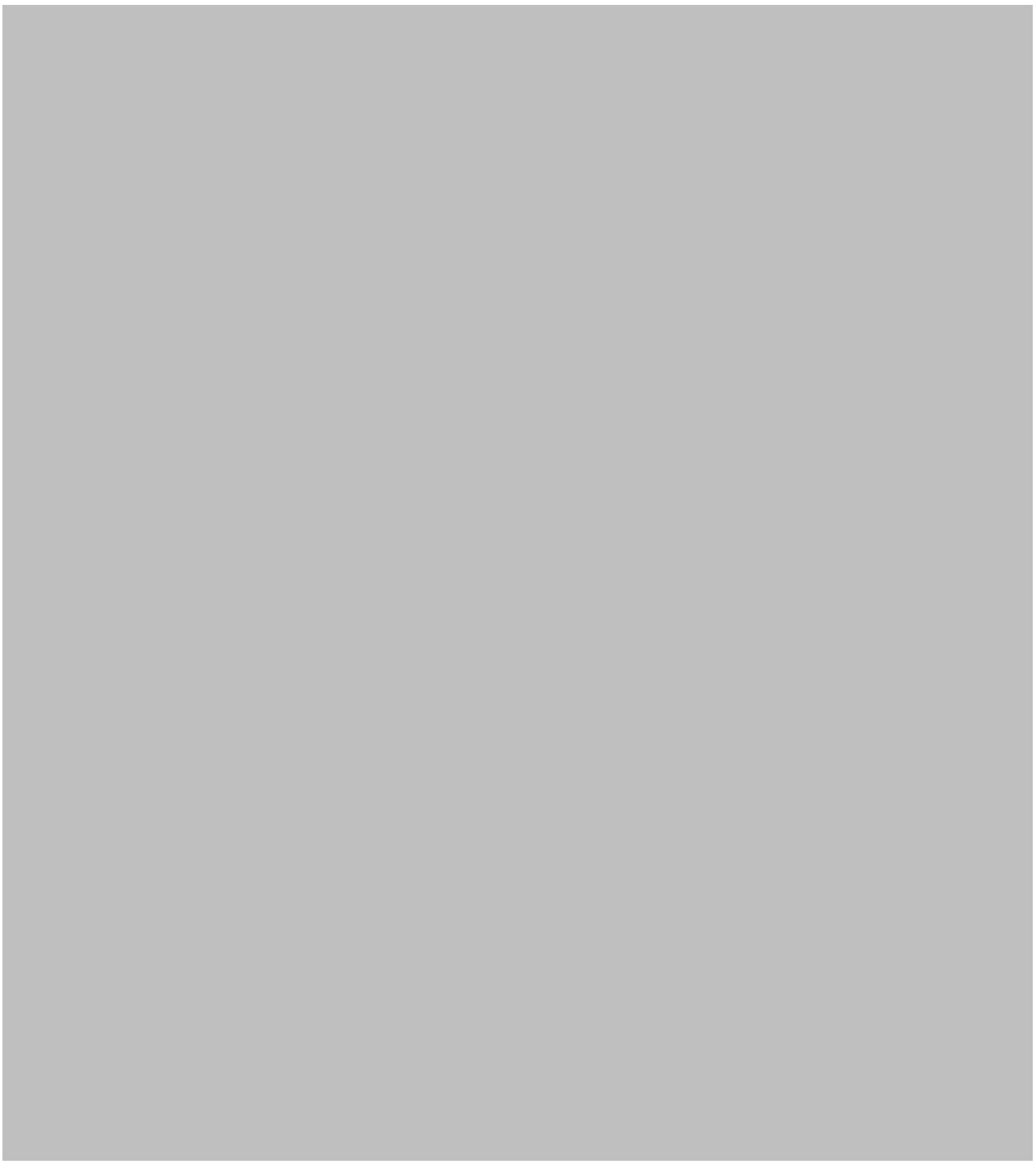
## Appendix K: NHS Ethical Approval

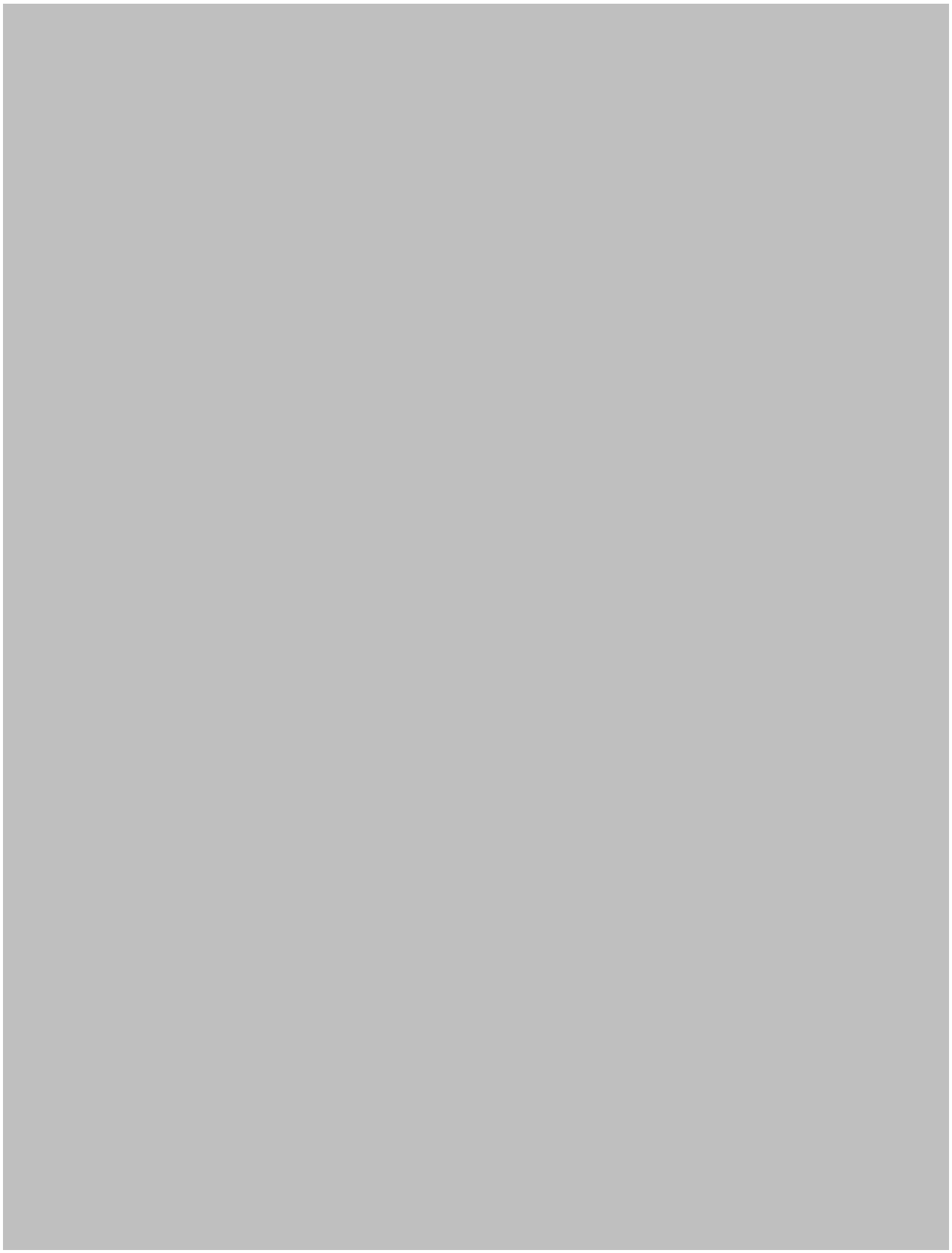


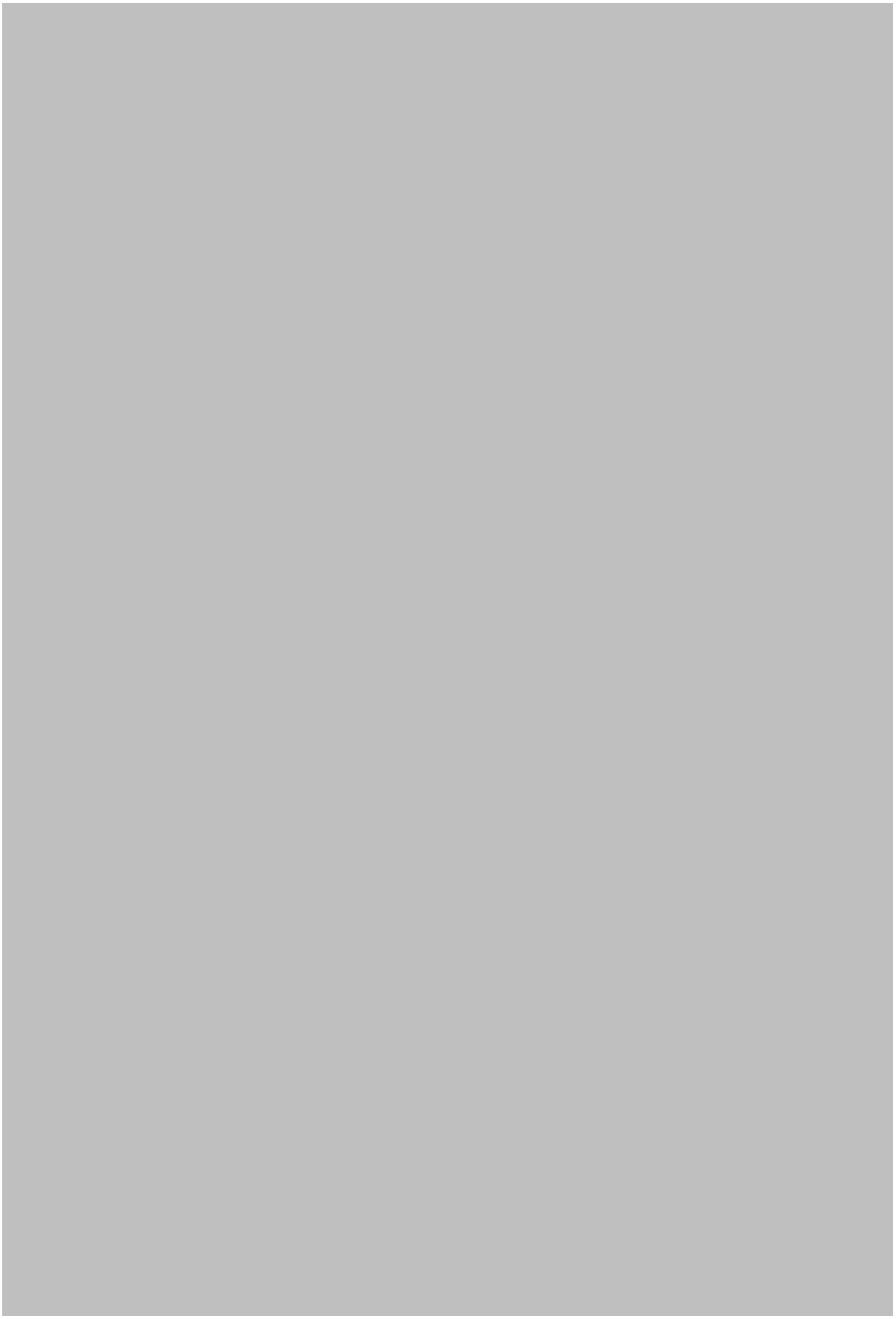


## Appendix L: Author instructions for literature review











## Appendix M: Author instructions for Empirical Paper

