FULL TITLE: People with **A**u**T**ism detained within hospitals: defining the population, understanding aetiology and improving **C**are pat**H**ways (The mATCH study).

SPONSOR: Hertfordshire Partnership University NHS Foundation Trust.

CHIEF INVESTIGATOR: Dr Peter Langdon, University of Kent

COLLABORATORS: Dr Regi Alexander, Partnerships in Care Ltd.; Sabyasachi Bhaumik, Leicestershire Partnership NHS Trust; Dr John Devapriam, Leicestershire Partnership NHS Trust; Professor Conor Duggan, Partnerships in Care Ltd.; Professor Lee Shepstone, University of East Anglia; Dr Ekkehart Staufenburg, Hertfordshire Partnership University NHS Foundation Trust; Mr David Turner, University of East Anglia; Professor. Professor Essi Viding, University College, London

NORWICH CLINICAL TRIALS UNIT STAFF: Mr Anthony Dyer; Mr Antony Colles.

PLAN ENGLISH ABSTRACT: Some people with autistic spectrum disorders (ASD) are detained in hospitals under the Mental Health Act (2007) because of mental health problems, behavioural problems and risk. While all these patients have a diagnosis of ASD, their clinical presentations, risk behaviours, treatment needs and responses to treatment are very different. An inability to capture these differences adequately means that some patients stay in restrictive hospital settings for longer than needed. To minimise this risk and improve care, we need to tailor the care pathway to the needs of each individual patient. The current study aims to do this in two ways (1) systematically investigate a subtypology of people with ASD within psychiatric hospitals to examine whether this may help allocate people to receive the appropriate care, and (2) collect information over 1 year which can be used to improve their care pathway. This study will help to design better inpatient services and directly benefit patients by minimising the risk of them being in restrictive hospital settings for longer than necessary. From published work and consultation with experts, we have developed some proposed subtypes of people with ASD who are detained in hospital. We will initially ask clinicians, patients and family members to take part in a focus group to refine these further. We will collect data from at least 150 patients about behaviour, engagement in treatment and risk, and invite 100 of these patients to take part in some psychological testing. This will help determine if the subtypes are valid. We will follow-up patients for 12-months to see whether outcomes are different for different subtypes of patients and how this relates to the care pathway. We have asked people with ASD, and carers and family members to take part in this and share in the oversight of our research.

ABSTRACT: Background: Some people with autistic spectrum disorders (ASD) are detained within hospitals because of the risk of violence, but we know little about the relationship between autism and this risk, nor do we fully understand the differences within this group and the implications for clinical care. There is little information about the most appropriate care-pathway for this population. There is a lack of evidence linking risk of future violence and ASD, and there is evidence that diagnosis alone is not an appropriate predictor of outcome from secure hospitals. It is more likely that comorbid factors, related to neurocognitive functioning and personality explain the relationship between violence and autism. Considering that secure beds are expensive, it is important to clarify the relationships between these variables to help manage risk carefully, target resources correctly, and ensure care pathways are appropriate. We have developed a sub-typology of people with ASD who have been detained in hospital. While these subtypes have face validity, they have not been examined thoroughly for people with ASD detained in hospital either in respect to treatment

needs or outcome within the hospital care pathway. Aims: This study has three aims, 1) to further develop a proposed sub-typology for people with autistic spectrum disorders (ASD) detained within hospital, 2) to test the validity of these subtypes, by examining the relationship between these subtypes, clinical data, and neurocognitive variables, and 3) to examine the relationship between these subtypes and patient outcome in order to understand the most appropriate care pathway. Methods: The aims will be investigated within three related Workstreams: 1) Workstream I will involve using focus group work and consensus methods with clinicians and services users to refine our sub-typology. Clinicians will then be asked to rate all their current inpatients with ASD according to the subtypes, 2) Workstream II will involve examining the validity of our subtypes within two sub-streams: i) Workstream IIa will involve collecting data about behaviour, resource use and risk from clinical records and staff members, describing factors related to care-pathways, and then making comparisons between subtypes on a minimum of 150 patients, and ii) Workstream IIb will involve asking 100 of these patients to complete a battery of neurocognitive tests to allow us to test the validity of our subtypes further. It is anticipated that differences between the subtypes can be characterised by key indicators (e.g. aggression and psychopathy) and 3) Workstream III involves those patients from Workstream IIa being followed up in 12 months, allowing us to collect behavioural data over time. This will allow us to examine how outcome differs between our subtypes, and whether the care pathway differs between subtypes. Potential Benefits to Patients: This study has direct implications for hospital care pathways. Importantly, the study will also allow us to examine the differences between patients, describe their care needs more effectively, and design better hospital care pathways. The Autism Act (2009) directed the government to publish a strategy document which was subsequently titled, "Fulfilling and rewarding lives: the strategy for adults with autism in England." This document states that people with autism should be able to access services and derive benefit from them, while the Equality Act (2010) states that all services need to make reasonable adjustments to enable access to services for people with disabilities. This project will help the NHS to understand patients with ASD who are detained within hospital effectively, consider risk more appropriately and design better in-patient services and care pathways to the community. This will directly benefit patients by minimising the risk of them being in restrictive hospital settings for longer than necessary.

BACKGROUND AND RATIONALE: There is often a misconception that people with ASD are at risk of committing crimes, which is inherently stigmatising for a group who already have marked disability and co-morbidity. While a large volume of case study work investigating the offending behaviours of people with ASD has been published [1-10], Howlin [11] suggested that some people with autism may be at risk of engaging in criminal offending behaviours because they have specific neurocognitive difficulties. On the surface, and considering that autism is associated with difficulties with social interaction, communication and perspective-taking, it is seems sensible to hypothesise that this group may be at risk of engaging in behaviours that are likely to attract the attention of criminal justice agencies. However, there is some limited evidence that constructs such as psychopathy, which increase the probability of criminal behaviour, are aetiologically distinct from ASD [12], while there is further evidence that the neurocognitive profiles of people with ASD and people with ASD and psychopathic traits are different [13, 14]. This has considerable implications for the care-pathway of patients with ASD detained in hospital, as patients with co-morbid psychopathy, will require intensive longer term support, while those without psychopathy, may require shorter stays, and different clinical interventions. This has implications for inpatient care-pathways, but has not been thoroughly examined.

The known prevalence data about offending behaviours amongst people with ASD suggest that this population is no more at risk, or actually have less risk of committing crimes, than the general population [15, 16]. Recently, Mouridsen [17] reviewed the literature in this area, concluding that forensic risk differs between people with different types of autism, and went on to argue that our understanding of forensic mental health problems amongst people with ASD needs to be improved, as does risk assessment and interventions. Mouridsen [17] also suggested that neurocognitive problems and associated psychiatric illness are important risk factors to consider when working with this population. Others have drawn similar conclusions [18, 19], and pointed out that there may be a higher prevalence of antisocial personality disorder amongst people with ASD who have forensic mental health problems [18, 20]. Långström et al. [19] reported that people with ASD who had committed violent crimes more likely to have comorbid psychosis, substance misuse and personality disorder. Meta-analytic work has indicated that personality disorder is associated with violence [21].

There are studies indicating that people with ASD are overrepresented in secure hospitals in the United Kingdom and elsewhere [22-29]. Studies involving single hospitals have suggested that between 15 to 30% of patients detained within specialist hospitals have ASD [27, 28]. There are an estimated 2500 beds within hospitals for people with intellectual and developmental disabilities within the United Kingdom, costing an estimated £320 million [27, 30], but we know little about the clinical profile and care-pathways of these patients. Defining the population, and understanding the comorbidity will help define the care-pathway for patients, and allow resources to be effectively targeted.

There is evidence that a diagnosis of ASD per se does not predict treatment outcomes (defined either by length of hospital stay or rates of aggression) within secure hospitals [28], suggesting that other variables need to be considered. The suggestion that specific neurocognitive problems and comorbid psychopathology explain forensic risk amongst people with ASD, rather than autism itself, is important, but has received little attention. Woodbury-Smith and colleagues [20] reported that offenders with ASD, compared with non-offenders with ASD, had an impaired ability to recognise fear, suggesting that offenders with ASD may have co-morbid psychopathy. A study of adolescents with ASD and behavioural problems has also documented that some (but not all) of these individuals have a neurocognitive profile that is indicative of co-morbid ASD and psychopathic features [31]. Some behaviours, (e.g. unemotionality and behavioural dyscontrol) seen in both individuals with psychopathy and those with ASD may appear superficially similar, however the neurocognitive underpinnings of these behaviours may be quite different. Indeed, a recent general population study suggests that different aspects of empathy are impaired in those individuals with high levels of ASD traits and those with high levels of psychopathic traits (33). Whilst individuals with high levels of ASD have difficulty in understanding what others think ('cognitive empathy'), individuals with high levels of psychopathic traits have difficulty in resonating with other people's feelings ('affective empathy'). Resonating with other people's feelings is thought to be particularly important for feeling true empathy for their suffering and this suggests that psychopathy would be a particularly important feature to consider when assessing and treating forensic mental health problems, while autistic symptomatology, although related, may be of less clinical importance. However, it remains that we know very little about the relationship between these constructs forensic risk, and importantly, the care-pathway within secure hospitals.

The current care-pathways for people with ASD detained within hospital are poorly defined. NICE define generic care-pathways for autism, incorporating psychosocial and biomedical

interventions, while there are no specific care-pathways described by NICE for people with ASD who are detained within hospital because of forensic mental health problems. Hence, there may be a group of people with specific neurocognitive difficulties, and/or associated problems with psychopathology, separate from ASD, which has implications for our understanding of risk and pathways. There have been case reports outlining how people with ASD who have forensic mental health problems present with marked complexity and as a consequence may be excluded from services [32]. Little is known about the clinical profile of patients with ASD within inpatient services, and related to this, forensic risk assessment and management often does not consider factors associated with autism [33]. Some initial work is needed in order to understand the clinical profile of people with ASD who have forensic mental health problems to inform the development of the most appropriate care-pathway, and our understanding of co-morbidities. This will clarify factors associated with risk and treatment outcome and generate knowledge that can be used to help clarify diagnostic issues, define care pathways, target resources appropriately and increase our knowledge and understanding of forensic risk.

AIMS AND OBJECTIVES: There are three aims to this study:

1. To further develop a proposed sub-typology for people with autistic spectrum disorders (ASD) detained within hospital.
2. To test the validity of these subtypes, by examining the relationship between these subtypes, clinical data, and neurocognitive variables.
3. To examine the relationship between these subtypes and patient outcome in order to understand the most appropriate care pathway for each subtype.

The objectives of the study are:

1) To use focus groups and consensus methods with clinicians to further refine subtyping of ASD within a hospital setting.
2) Clinicians from fifteen hospitals will rate all inpatients with ASD under their care using the subtypes in a systematic manner.
3) Collect behavioural and risk data on these patients which can be used to describe the current care-pathway for patients.
4) Use the behavioural and risk data to examine differences between patients of different subtypes and make use of finite mixture modelling to explore the group-structure within our data and revise our subtypes as appropriate.
5) Invite 100 of these patients with ASD to take part in neurocognitive assessments and examine the differences between patients in order to examine the validity of the subtypes further.
6) Follow up these patients for 12 months, collecting behavioural data, and examine the relationship between the follow-up data and our revised subtypes in order to examine the relationship between the different subtypes and care-pathways.

RESEARCH PLAN: This project has been developed collaboratively with members of the NIHR Forensic Intellectual and Developmental Disabilities Clinical Research Group (CRG), including service users and clinicians, who have prioritised increasing our understanding of the different clinical presentations of ASD, clinical needs, and care pathways for this group within hospital. Our CRG have developed a subtyping method for characterising the clinical presentation of ASD within forensic settings, based around several key variables, which include the spectrum of psychopathy, psychosis, and frequency and intensity of aggression.

The subtypes (**Figure 1**) are characterised as follows: 1) *Low Psychopathy*, which is further characterised into those with and without psychosis, and within these two groups, there are those with higher and lower behaviour difficulties, and 2) *High Psychopathy*, which again includes those with and without psychosis, which are again further characterised into those with higher and lower behaviour difficulties. In total, there are eight subtypes. There are hypothesised differences between these subtypes in terms of their clinical presentation and neurocognitive functioning, which has associated implications for treatment and care pathways. For example, for those with low psychopathy + psychosis, but with lower behavioural difficulties, the priority would be the successful treatment of their mental health problems, suggesting a relatively shorter length of hospital stay, while for those with low psychopathy, who do not have psychosis, but have higher behavioural difficulties, there is likely to be a need for careful interventions and staff training, based upon strategies such as the Structure, Positive, Empathy, Low arousal, Links (SPELL) approach for autism, but again, hospital stay may be shorter because their difficulties are associated with autism, rather than comorbid psychopathy. Those with comorbid psychopathy are likely to require careful supervision, but this may not have to be within medium or high security, and will vary according to whether they have psychosis and the frequency and intensity of their behavioural difficulties. For example, the group with psychopathy and no psychosis, plus lower behaviour difficulties, are likely to engage in offending behaviours linked to their circumscribed interests, which may be unpredictable at times, but they may be relatively easy to manage. They are likely to have some features of psychopathy, but as this is a spectrum, their difficulties may not be as marked. For those who have higher levels of psychopathy, and behaviour problems, they are likely to require a high degree of careful management within conditions of security because of behavioural problems; they are likely to need the longest length of stay within hospital. However, the clinical challenges posed by those with comorbid psychopathy are likely to be associated with neurocognitive processing and psychopathy, which will be investigated thoroughly within Workstreams IIb.

Identifying valid subtypes is beneficial because they inherently provide a wealth of information about appropriate care pathways which will improve the commissioning of better services. We have asked three different psychiatrists to independently assign 23 patients with ASD detained within hospital to one of our subtypes, revealing excellent agreement, multirater k_{free} = .90. However, we need to test these proposed subtypes further, and examine their validity, and as such, this study aims to investigate this and examine how these relate to patient outcome. There are three separate workstreams to this study:

<u>Workstream I</u> - Aim: To further develop a proposed sub-typology for people with autistic spectrum disorders (ASD) detained within hospital.

<u>Workstream Ia</u>: Initially, we will hold a focus group with clinicians from inpatient services, and people with ASD, along with family members and carers to refine our subtypes. Clinicians will be recruited from our NIHR CRG network, while people with ASD and family members will be recruited from the community and/or inpatient services, including existing service user organisations. We aim to recruit three clinicians, and three people with ASD or their family members/carers.

We will use consensus development methods during our focus groups in order to arrive at consensus. Initially, we will present a brief review of the project and the background

literature, followed by a presentation about our subtypes and their descriptions. The group will then be asked to consider the subtypes, and discuss them until consensus is reached. The group will be asked to provide comments on the validity of the subtypes and whether any further characteristics need to be considered.

Our inclusion and exclusion criteria for this part of the project are:

a. *Inclusion Criteria*: 1) A registered health care professional working in services for people with ASD, or 2) a person with ASD, or 3) a family member or carer of someone with ASD.
b. *Exclusion Criteria*: 1) Inability to give or withhold consent to take part as defined within the Mental Capacity Act, 2007.

Workstream Ib: Following on from this, and incorporating any changes, we will further refine our descriptions of each of our subtypes. We will then work with five clinicians working within inpatient services for people with developmental disabilities to prepare ten anonymous clinical vignettes. These five clinicians are from our NIHR CRG and will be invited to take part in a later consensus rating exercise using a similar methodology to that employed by Cooray et al. [34] where they will be asked to assign vignettes to our proposed subtypes independently and ratings compared. Again, using consensus development methods, clinicians will be asked discuss and give their expert opinion regarding the subtypes and provide any feedback once consensus has been reached. This will be used to further refine our subtypes. A final summary of each subtype will be produced which will be used to categorise patients.

Our inclusion and exclusion criteria for this part of the project are:

a. *Inclusion Criteria*: 1) A clinician who is a member of our NIHR CRG group.
b. *Exclusion Criteria*: 1) Inability to give or withhold consent to take part as defined within the Mental Capacity Act, 2007.

Workstream II – Aim: To test the validity of the subtypes within two concurrent workstreams.

Workstream IIa: This workstream aims to test the validity of the subtypology by comparing data on patient and hospital variables between people characterised according to our subtypes. This workstream will use a cross-sectional design. We will work with at least fifteen clinicians from our NIHR CRG from fifteen different inpatient hospitals, but have additional sites identified.

1. Target Population: One hundred and fifty to 200 people aged 18 or older who have a confirmed diagnosis of ASD detained within hospital.
    a. *Inclusion Criteria*: 1) aged 18 or older, 2) diagnosis of ASD made by a Clinical Psychologist, Psychiatrist or other appropriately qualified professional, 3) detained within hospital using the Mental Health Act (2007) or detained within hospital using the Mental Capacity Act (2007).
    b. *Exclusion Criteria*: None.
    c. *Sampling and Sample Size*: Participants will be recruited from inpatient hospitals in the United Kingdom. As this is not a typical hypothesis testing

study, the sample size cannot be translated into terms of statistical power for a given effect size or association strength. However, using a binomial distribution, the probability of observing at least 10 individuals of a particular subtype, within a sample of 150, for a given prevalence of that subtype can be calculated. If the prevalence is at least 10%, then there is a 94% chance of observing 10 or more individuals; for a prevalence of at least 5%, the chance is 22%. Thus, we are confident that all but the rarest subtypes would be well represented in a sample of 150 individuals. However, it is important to recognise, while some of the subtypes may prove to be less frequent, this is actually a useful finding which will not have a negative impact upon the success of the project.

2. Data Collection and Analysis: We will collect information from patient records and staff members. This data will be passed to the research team in an anonymous format. The majority of these data can be collected from clinical records, as they are already routinely collected by hospitals using standardised measures. Some of the measures will be completed directly by clinical staff who know the patient well (e.g. GEEQ). Data collection will involve collecting information on a variety of demographic and clinical variables as follows:
    a. *Primary Measures*: i) Demographics and associated clinical information: 1) age on admission, 2) sex, 3) level of security: low, medium or high, 4) Mental Health Act Section: civil, criminal, restricted, 5) diagnosis, 6) length of stay, 7) leave status, 8) levels of observation, 9) body mass index, 10) medication, 11) psychological interventions, 12) ASD Subtype Allocation. ii) Risk, Psychopathy, and Violence: 1) Psychopathy Checklist: Short Version (PCL: SV), 2) Historical, Clinical, Risk Management – 20 (HCR-20), 3) Short Term Assessment of Risk and Treatability (START), 4) HONOS-Secure, 5) coded forensic history, including index offence, 6) coded offending-like behaviours, 7) index of institutional aggression by calculating the number of seclusions and restraints over the last 12 months, and 8) the Modified Overt Aggression Scale (MOAS), which has good psychometric properties when used with people with intellectual disabilities [35]. iii) Engagement in Treatment: Group Emotional Engagement Questionnaire (GEEQ) [36]. iv) Resource Use and Quality of Life: Resource use will be extracted from patient notes. A proxy EQ5D-5L will be completed by clinical staff. v) General Intellectual Functioning: Most recent scores from the Wechsler Scales.
    b. *Analysis*: Following the collection of the data, we will make comparisons between subtypes. It is hypothesised, for example, that some groups will score higher than others on the PCL-SV and this will be related to behavioural difficulties. We are hypothesising that the likely key variables are, a) aggression, including frequency and severity, b) co-morbid diagnosis, especially psychosis, and c) psychopathy. We anticipate that our keys variables are likely to distinguish between our proposed subtypes, although we recognise and expect that some revision is probable. Formally, we will use multivariate hypothesis tests (e.g. MANOVA) to test for differences between sub-types on key variables. Following on from this, we will also carry out dimension reducing techniques (such as Principal Components Analysis) on

all variables and again used this to make comparison between groups. Finally, we will use cluster analyses and multidimensional scaling to examine the relationships between variables, and determine possible alternative subtypes, with revisions to the original subtyping, as indicated.

c. *Clinical Trials Unit*: Norwich CTU will provide statistical and health economics analysis for this trial, as well as data management services. A secure web-based service will be used by clinicians and research staff to remotely enter and securely store data on CTU servers which are backed-up regularly. Clinicians and researchers will be given individual login details which will allow them to access the Clinical Record Form (CRF) and enter data. Paper based records will also be kept and securely stored.
d. *Blinding*: While this is not a clinical trial, clinicians and staff who are collecting data about patients will not be told about the ASD Subtype to which a patient has been allocated. Patients will be allocated to a particular ASD Subtype by their Responsible Clinician who will then be asked not to share this information with the clinical team. Responsible Clinicians who inadvertently share this information will be asked to report such incidents to the research team.

Workstream IIb – This Workstream aims to further test the validity of our subtypes by examining their relationship with neurocognitive variables. Specifically, we are hypothesising that patients scoring higher on measures of psychopathy will have greater difficulties with both affective empathy, emotion recognition, and moral tasks, than those scoring lower on psychopathy, but this may vary according to frequency and severity of behavioural difficulties, and may be related to psychosis. Symptoms of autism will be related with difficulties with cognitive perspective-taking. This means that our subtypology should be supported by neurocognitive data, demonstrating validity further, and adding further weight to the proposition that patients with ASD detained within hospital have different treatment needs which have to be considered when designing appropriate care-pathways. Describing how information processing difficulties vary according to subtype will directly inform treatment as it will highlight different biases in information processing across our subtypology, which can be addressed through tailored psychological interventions [37], which would be defined within the care-pathway. This portion of the study uses a cross-sectional design.

1. Target Population: One hundred people aged 18 or older who have a confirmed diagnosis of ASD detained within hospital.
    a. *Inclusion Criteria*: 1) aged 18 or older, 2) diagnosis of ASD made by a Clinical Psychologist, Psychiatrist or other appropriately qualified professional, 3) detained within hospital using the Mental Health Act (2007) or detained within hospital using the Mental Capacity Act (2007).
    b. *Exclusion Criteria*: 1) Inability to give or withhold consent to take part as defined within the Mental Capacity Act, 2007, and 2) Full Scale IQ of <50.
    c. *Sampling and Sample Size*: Participants will be recruited from inpatient hospitals in the United Kingdom. We will ask clinicians taking part in Workstream IIa to distribute information about Workstream IIb to inpatients with ASD, as these patients will have already been assigned to a subtype by their clinician. Patients will be invited to take part in this study by their own

clinical team, and will be told that taking part in this study has no bearing on their clinical treatment or care pathway. Patients who agree will be asked to provide signed consent to indicate that they agree to take part, and all patients will be afforded the opportunity to have someone they trust present throughout the study procedures. Effect sizes vary according to our comparisons, d = .53 to d = 1.05, comparing young people or adults, with and without psychopathy, who either have autism, or "autistic traits". The largest sample size calculation indicated that we need to recruit 90 patients with ASD living within secure hospitals. This number has been rounded to 100 in order to account for potential missing data. However, this is a preliminary study and it is difficult to estimate parameters with a degree of certainty at this stage.

2. Data Collection and Analysis: Patients will be invited to take part in standardised assessments and tasks, which have good reliability and validity. Patients will completed these instruments once, but not necessarily on the same day. Data collection will involve collecting information on a variety of clinical variables as follows:
    a. *Primary Measures*: i) Autism: We will use the Autism Quotient [38] to measure autism traits. ii) Empathy: We will use the SAM-stories described by Seara-Cardoso et al. [39] which involves reading 12 short stories depicting emotion and participants are asked to rate their emotional response. We will include a second measure of empathy, namely the Empathy Quotient [40, 41], which has been developed for use with people with ASD, and successfully used with people with mild intellectual disabilities [42]. iii) Cognitive-Perspective Taking: In order to measure how well participants understand the mental states of others, we will use the same method described by Lockwood et al. [14]. In this theory of mind animations task participants watch shapes interact with each other or moving randomly on a computer screen. Participants are asked to describe what is happening on the screen and the verbal descriptions are coded by independent raters for comments describing intentionality and appropriateness. iv) General Intellectual Functioning: Where a patient has not had an estimate of their general intellectual functioning completed within the last two years, we will administered the Wechsler Adult Intelligence Scale – IV. v) Executive Functioning: The Go/No-Go task from the Maudsley Attention and Response Suppression Task Battery (MARS) will be used to measure response suppression, while flexibility and set-shifting will be measured using the Intra/Extra Dimensional (ID/ED) Shift Task from the Cambridge Neuropsychological Test Automated Battery (CAN-TAB). vi) Emotional Recognition: We will use the Emotion Multimorph Task used by others [39] which involves presenting a neutral face on a computer screen which slowly changes or morphs into one of several facial expressions. vii) Moral Reasoning: We will use both the Moral Dilemmas Task [39] and the Sociomoral Reasoning Measure- Short Form [43] which has been used with people who have developmental disabilities detained within hospital [44, 45]. viii) EQ5D-5L: Participants will be asked to complete the EQ5D-5L and clinicians will be asked to complete a proxy EQ5D-5L independently. Comparisons will allow us to assess the usefulness

of the proxy EQ5D scores collected during Workstreams IIa and III. iv) Positive and Negative Syndrome Scale (PANSS): This is a measure of psychosis symptom severity [46].

b. *Analysis*: Formally, we will use multivariate hypothesis tests (e.g. MANOVA) to test for differences between sub-types on key variables. Following on from this, we will also carry out dimension reducing techniques (such as Principal Components Analysis) on all variables and again used this to make comparison between groups. Finally, we will use cluster analyses and multidimensional scaling to examine the relationships between variables, and determine possible alternative subtypes, with revisions to the original subtyping, as indicated.
c. *Clinical Trials Unit*: Norwich CTU will provide statistical and health economics analysis for this trial, as well as data management services. A secure web-based service will be used by clinicians and research staff to remotely enter and securely store data on CTU servers which are backed-up regularly. Clinicians and researchers will be given individual login details which will allow them to access the Clinical Record Form (CRF) and enter data. Paper based records will also be kept and securely stored.

Workstream III – Aim: To examine the relationship between these subtypes and patient outcome in order to understand the most appropriate care pathway for each subtype.

This part of the study is longitudinal. We will collect more data about the sample recruited as part of Workstream IIa, 12 months later, in order to test the relationship between our subtypes and outcome. For example, we have hypothesised that people who have ASD and co-morbid psychopathy are likely to have higher rates of aggression, and this may be associated with poorer outcome, while outcomes for patients with lower psychopathy should be relatively more positive. The data we aim to collect during Workstream III is exactly the same as the data collected during Workstream IIa. Again, this will be taken from patient records and staff, and will be collected anonymously. Collecting information after 12-months will allow us to look at discharges out of inpatient services, and to other inpatient services, providing valuable information about the care pathway. We will collect data on resource use such as costs incurred during inpatient stays and other health economic and social care events. These will be costed to illustrate the resources required by subtype. Similarly, the EQ5D will be used to examine differences in health related quality of life (HRQoL) across subtypes.

1. Target Population: One hundred and fifty to 200 people aged 18 or older who have a confirmed diagnosis of ASD detained within hospital.
    a. *Inclusion Criteria*: 1) aged 18 or older, 2) diagnosis of ASD made by a Clinical Psychologist, Psychiatrist or other appropriately qualified professional, 3) detained within hospital using the Mental Health Act (2007) or detained within hospital using the Mental Capacity Act (2007).
    b. *Exclusion Criteria*: None.
    c. *Sampling and Sample Size*: Participants will be recruited from inpatient hospitals in the United Kingdom. As this is not a typical hypothesis testing study, the sample size cannot be translated into terms of statistical power for a given effect size or association strength. A formal sample size estimate has not been completed for this portion of the study as our aim is to follow up as

many patients as possible. The maximum number of patients that may be included, assuming no attrition or loss, is 200.

2. Data Collection and Analysis: We will collect information from patient records and staff members using the same methods within Workstream IIa. This data will be passed to the research team in an anonymous format. The majority of these data can be collected from clinical records, as they are already routinely collected by hospitals using standardised measures. Some of the measures will be completed directly by clinical staff who know the patient well (e.g. GEEQ). Data collection will involve collecting information on a variety of demographic and clinical variables as follows:
    a. *Primary Measures*: i) Demographics and associated clinical information: 1) age on admission, 2) sex, 3) level of security: low, medium or high, 4) Mental Health Act Section: civil, criminal, restricted, 5) diagnosis, 6) length of stay, 7) leave status, 8) levels of observation, 9) body mass index, 10) medication, 11) psychological interventions, 12) ASD Subtype Allocation. ii) Risk, Psychopathy, and Violence: 1) Psychopathy Checklist: Short Version (PCL: SV), 2) Historical, Clinical, Risk Management – 20 (HCR-20), 3) Short Term Assessment of Risk and Treatability (START), 4) HONOS-Secure, 5) coded forensic history, including index offence, 6) coded offending-like behaviours, 7) index of institutional aggression by calculating the number of seclusions and restraints over the last 12 months, and 8) the Modified Overt Aggression Scale (MOAS), which has good psychometric properties when used with people with intellectual disabilities [35]. iii) Engagement in Treatment: Group Emotional Engagement Questionnaire (GEEQ) [36]. iv) Resource Use and Quality of Life: Resource use will be extracted from patient notes. A proxy EQ5D-5L will be completed by clinical staff. v) General Intellectual Functioning: Most recent scores from the Wechsler Scales.
    b. *Analysis*: We will use multivariate hypothesis tests (e.g. MANOVA) to test for differences between sub-types on key variables. Using regression models, we will examine which variables can be used to predict behaviour.
    c. *Clinical Trials Unit*: Norwich CTU will provide statistical and health economics analysis for this trial, as well as data management services. A secure web-based service will be used by clinicians and research staff to remotely enter and securely store data on CTU servers which are backed-up regularly. Clinicians and researchers will be given individual login details which will allow them to access the Clinical Record Form (CRF) and enter data. Paper based records will also be kept and securely stored.
    d. *Blinding*: While this is not a clinical trial, clinicians and staff who are collecting data about patients will not be told about the ASD Subtype to which a patient has been allocated. Patients will be allocated to a particular ASD Subtype by their Responsible Clinician who will then be asked not to share this information with the clinical team. Responsible Clinicians who inadvertently share this information will be asked to report such incidents to the research team.

BARRIERS TO SUCCESS: *Key Risks*: 1) Difficulties recruiting successful numbers, 2) analysis reveals "subtypes" are not valid, 3) clinicians do not participate in consensus ratings, 4) loss of patients at follow-up, and 5) errors or missing data. *Success Criteria*: 1) Complete

our focus groups and consensus work, 2) recruit clinicians from inpatient services and collect patient data, and 3) retain at least 80% of our patient sample for follow-up, 4) recruit 100 patients with ASD. *Contingency Plans*: 1) Use NIHR CRG with network of 30 inpatient hospitals. Recruit 15 patients from 15 hospitals, with alternative sites as needed. Recruiting 15 to 20 participants from 15 hospitals is feasible within the context of our network, considering the estimated the prevalence of autism within secure hospitals and the number of specialist beds [27, 28, 30]. This means that there are approximately 375 to 750 patients with ASD in psychiatric hospitals in the United Kingdom, 2) the finding that there are no "subtypes" based on our analysis is actually a useful result, but unlikely, considering findings that there are differences between children with ASD on measures of psychopathy and behaviour (30), 3) use clinicians involved in NIHR CRG, but include others if needed, 4) track patients monthly, monitoring discharges and location, and 5) design and test well developed Clinical Record Form (CRF) and use Clinical Trials Unit systems to securely collect and store data.

DISSEMINATION AND OUTPUTS: We will disseminate our findings through the publication of open access peer review journal articles, and presentations at national and international conferences. We will also host stakeholder events, delivered jointly with our service-user members and carers, following the completion of the study which will include service providers, service users, commissioners, and clinicians amongst other representatives from charities, the NHS and the private sector. We will also provide a high-level summary of our findings to the NHS which will be publically available, and we will work directly with service users to produce materials that are easier for service users to read and understand. We will develop and host a website, providing information about the study, which will be updated and provide information about all of our findings, including our reports, summaries and publications. This will be maintained after the study has finished. This project will contribute to our understanding of people with ASD living within inpatient hospitals in the United Kingdom. This information will be of marked importance to commissioners, service providers and service users. Specifically, this project will: 1) improve our understanding of the relationship between ASD and forensic mental health problems, including forensic risk, 2) help identify which constructs relate to our understanding of forensic risk which can be used to help inform care pathways, 3) improve our understanding of the aetiology and prognosis of forensic mental health problems amongst people with ASD, 4) the further development of our subtypes will allow for clarification about which interventions are likely to be most appropriate and provide vital prognostic information about length of stay, 5) lead to improvements in the hospital care-pathway for patients with ASD, which may lead to shorter hospital stays and, subsequently, cost savings which will help commission more efficient services, and 6) in addition to outputs in the form of peer review papers, we wish to engage with stakeholders in order to share our findings, and further consider the implications for service development. Our subtypes also provide valuable information about appropriate interventions, and following the completion of this study, we would wish to apply for further funding to formally test out changes to the secure hospital care-pathway for patients with ASD, based upon our subtypology, working jointly with commissioners and hospitals.

PROJECT MANAGEMENT: The sponsor of this study will be Hertfordshire Partnership University NHS Foundation Trust, and will provide indemnity and compensation in the event of a claim for negligent harm.

1. Steering Committee: The project will be governed by a Steering Group who will have responsibility for monitoring progress. This group will be chaired by a commissioner and will meet every six months. The research team will report to the Steering Committee, providing information about recruitment, and the committee will monitor data collection. The following PPI members will be on our steering group, 1) at least two people with developmental disabilities who have been or are detained in hospital, 2) at least two carer/family members of someone with developmental disabilities who has been detained in hospital, 3) Ms Robyn Stewart has been invited and agreed to join our steering group. She has an autistic spectrum disorder (ASD) and has worked with us before on studies involving people with ASD, 4) a representative from a charity for people with ASD, namely Asperger East Anglia and 5) Mr Alan Rosenbach, Senior Policy Advisor, Care Quality Commission.
2. Project Reviews: Alongside this, the study team and staff will meet once every three months to again monitor performance against our targets. We aim to recruit and appoint a research assistant at the postdoctoral level. They will have responsibility for managing the day to day conduct of the research project, and will report into the study team and Steering Group. The Chief Investigator will meet monthly with the study manager to also monitor progress.

TIMETABLE: A breakdown of our timetable is found in Table 1.

Table 2

Time	Work Programme
-6 to 0 months	Apply for an ethical opinion and R&D approvals; recruit research staff. Initial Steering Group meeting.
0 to 5 months	Study set up at sites (training); Workstream Ia and IIb completed.
5 to 16 months	Workstream IIa (minimum accrual rate: 13 per month) and IIb (minimum accrual rate: 9 per month) complete; initiate patient tracking for Workstream III. Two Steering Group meetings.
17 to 28 months	Workstream III complete (Minimum accrual rate: 10 per month); Steering Group meeting.
29 to 33 months	Final analysis and writing up; Steering Group meeting.
34 to 36 months	Dissemination events; final Steering Group meeting; final report to NIHR.

ETHICAL ISSUES: An ethical opinion for this study is required from an NHS Research Ethics Committee in England, along with associated Research Governance permissions. There are several issues which we wish to draw to the attention of the Research Ethics Committee: 1) Workstream Ia/b involves the use of consensus methods which are not normally considered to be research. However, as they form an important part of this project they should be treated as research and an ethical opinion is being sought, 2) Workstream IIa/III will involve the collection of anonymous patient data. Data will be uploaded to the Clinical Trials Unit using online secure systems accessible from research sites. Researchers will only have access to anonymous patient data for this portion of the study. All participants will be assigned a unique identifier. It is not entirely clear whether this portion of the study would be classified as research because: a) the purpose is to capture data that allows us to describe the current patient population within hospital without making any changes to care; in

other words, the purpose is to describe how standard care is delivered, and b) we are not randomising patients to different groups. However, we are attempting to generate new knowledge that may be generalisable to the broader patient population, and therefore, an ethical opinion is appropriate, 2) patient consent will be required for Workstream IIb, and although this portion of the overall project is observational, it would be considered research as the purpose is to generate new knowledge by addressing defined research questions. The patient population is vulnerable and issues around coercion and power are important. Informed consent will be sought from all participants. We have adapted our trial documentation to try to improve accessibility for participants, including the provision of study documents in an audio format. Patients who do not have capacity to consent as defined within the Mental Capacity Act (2007) will be excluded from this study. The Chief Investigator has completed Good Clinical Practice training, along with additional training in the Mental Capacity Act, 2007. It is the responsibility of the person seeking to enrol someone within a study to determine whether they have mental capacity to give or withhold consent, and in this study, this responsibility will fall to the clinicians and researchers seeking informed consent from participants. These individuals know the patients very well and as a consequence, will be well placed to make a decision with respect to capacity, Taking part in this study is likely to take patients away from their rehabilitative programmes, and as a consequence, we feel that it is appropriate to offer a small payment to express our appreciation for taking part. All data collected will be stored in an anonymous secure format making use of appropriate encryption in order to protect confidentiality, 3) patients taking part in this trial will be detained in hospital, and as a consequence, clinicians seeking consent will be part of the clinical team working with the participants during their detention. In order to reduce the probability of coercion, all patients will be afforded time to make a decision as to whether they wish to take part in this study, which can be up to 14 days. Alongside this, participants will be given the contact details for the researcher team, and will be encouraged to contact them as they need. They will be available to visit participants at their request and answer any questions or provide any further information. We will also encourage participants to ask another person to attend the meeting where the study is explained to them, and participants will be advised that this could be anyone they choose. This could be a family member, and advocate, or a different member of staff.

PATIENT AND PUBLIC INVOLVEMENT: This project was developed by the Forensic Intellectual and Developmental Disabilities Clinical Research Group (CRG) that was funded by NIHR in 2012, and PPI consultation started in 2013. The CRG includes applicants and members from over 30 hospitals and 10 universities across the UK, as well as people with developmental disabilities who are currently detained for treatment in psychiatric hospitals. Aspects of this project have been developed jointly with members of the CRG, including patients detained within hospital who have been consulted during the development of this work. Our PPI members have directly commented on this proposal, and their comments incorporated. They have said (1) “this project will allow you to work out how to place people in hospital better, and help get the support right”, (2) “the subtypes are not stereotyping, as they are categories which outline needs”, (3) “the subtypes will help clinicians to identify needs better”, (4) “it is important to have people with ASD, and their carers in the focus groups to get their views, especially parents because they are the first to notice these problems”, and (5) “some people might do better in a care home, rather than hospital, or need to stay in hospital shorter so this project could help them move on better”. The CRG website

www.forensiclearningdisability.com has a plain English summary of this project. The project has also been discussed with the Care Quality Commission and they support it; their national clinical advisor on learning disability is a named applicant and their senior policy advisor will be part of the study's steering group, and will help with dissemination. Service users, carers and staff will be full members of our steering group, who will have responsibility for monitoring the progress of the study. We will also invite a commissioner to chair our steering group. The following PPI members will be on our steering group, 1) at least two people with developmental disabilities who have been or are detained in hospital, 2) at least two carer/family members of someone with developmental disabilities who has been detained in hospital, 3) Ms Robyn Stewart has been invited and agreed to join our steering group. She has an autistic spectrum disorder (ASD) and has worked with us before on studies involving people with ASD, 4) a representative from a charity for people with ASD, namely Asperger East Anglia and 5) Mr Alan Rosenbach, Senior Policy Advisor, Care Quality Commission. Mr Rosenbach will act as a consultant throughout the project and we work collaboratively with the CQC to help disseminate our findings. All of the applicants and research workers will be members of the steering group. We will also actively involve service users and family carers to take part in our focus group work, working as researchers. We also plan to hold a series of dissemination events for stakeholders, clinicians, commissioners, service providers, including the third sector, which will be delivered jointly with service users and carers and has been costed.

1. Baron-Cohen, S., *An assessment of violence in a young man with Asperger's Syndrome.* Journal of Child Psychology and Psychiatry and Allied Disciplines, 1988. **29**: p. 351-360.
2. Chen, P., et al., *Asperger's disorder: a case report of repeated stealing and the collecting behaviours of an adolescent patient.* Acta Psychiatrica Scandinavica, 2003. **107**(1): p. 73-76.
3. Chesterman, P. and S.C. Rutter, *Case report: Asperger's syndrome and sexual offending.* The Journal of Forensic Psychiatry, 1993. **4**(3): p. 555-562.
4. Schwartz-Watts, D.M., *Asperger's disorder and murder.* Journal of the American Academy of Psychiatry and the Law Online, 2005. **33**(3): p. 390-393.
5. Cooper, S., W. Mohamed, and R.A. Collacott, *Possible Asperger's syndrome in a mentally handicapped transvestite offender.* Journal of Intellectual Disability Research, 1993. **37**(2): p. 189-194.
6. Everall, I.P. and A. Lecouteur, *Firesetting in an adolescent boy with Asperger's syndrome.* The British Journal of Psychiatry, 1990. **157**(2): p. 284-287.
7. Mawson, D.C., A. Grounds, and D. Tantam, *Violence and Asperger's syndrome: a case study.* The British Journal of Psychiatry, 1985.
8. Milton, J., et al., *Case history of co-morbid Asperger's syndrome and paraphilic behaviour.* Medicine, science and the law, 2002. **42**(3): p. 237-244.
9. Murrie, D.C., et al., *Asperger's syndrome in forensic settings.* International Journal of Forensic Mental Health, 2002. **1**(1): p. 59-70.
10. Silva, J.A., M.M. Ferrari, and G.B. Leong, *The case of Jeffrey Dahmer: Sexual serial homicide from a neuropsychiatric developmental perspective.* Journal of forensic sciences, 2002. **47**(6): p. 1347-1359.
11. Howlin, P., *Legal issues*, in *Autism and Asperger Syndrome: Preparing for Adulthood*, P. Howlin, Editor. 2004, Routledge: London. p. 300-312.
12. Jones, A.P., et al., *Phenotypic and aetiological associations between psychopathic tendencies, autistic traits, and emotion attribution.* Criminal Justice and Behavior, 2009. **36**(11): p. 1198-1212.
13. Viding, E., P.J. Frick, and R. Plomin, *Aetiology of the relationship between callous–unemotional traits and conduct problems in childhood.* The British Journal of Psychiatry, 2007. **190**(49): p. s33-s38.
14. Lockwood, P.L., et al., *Dissecting empathy: high levels of psychopathic and autistic traits are characterized by difficulties in different social information processing domains.* Frontiers in human neuroscience, 2013. **7**.
15. Mouridsen, S.E., et al., *Pervasive developmental disorders and criminal behaviour: A case control study.* International Journal of Offender Therapy and Comparative Criminology, 2008. **52**: p. 196-205.
16. Allen, D., et al., *Offending behaviour in adults with Asperger syndrome.* Journal of Autism and Developmental Disorders, 2008. **38**: p. 748-758.
17. Mouridsen, S.E., *Current status of research on autism spectrum disorders and offending.* Research in Autism Spectrum Disorders, 2012. **6**: p. 79-86.
18. Dein, K. and M. Woodbury-Smith, *Asperger syndrome and criminal behaviour.* Advances in Psychiatric Treatment, 2010. **16**(1): p. 37-43.
19. Långström, N., et al., *Risk Factors for Violent Offending in Autism Spectrum Disorder A National Study of Hospitalized Individuals.* Journal of Interpersonal Violence, 2009. **24**(8): p. 1358-1370.

20. Woodbury-Smith, M.R., et al., *A case-control study of offenders with high functioning autistic spectrum disorders.* Journal of Forensic Psychiatry and Psychology, 2005. **16**: p. 747-763.
21. Yu, R., J.R. Geddes, and S. Fazel, *Personality disorders, violence, and antisocial behavior: a systematic review and meta-regression analysis.* Journal of personality disorders, 2012. **26**(5): p. 775-792.
22. Scragg, P. and A. Shah, *Prevalence of Asperger syndrome in a secure hospital.* British Journal of Psychiatry, 1994. **165**: p. 679-682.
23. Hare, D., et al., *A preliminary study of individuals with autistic spectrum disorders in three special hospitals in England*. 1999, London: National Autistic Society.
24. Haskins, B.G. and J.A. Silva, *Asperger's disorder and criminal behavior: forensic-psychiatric considerations.* Journal of the American Academy of Psychiatry and the Law Online, 2006. **34**(3): p. 374-384.
25. Alexander, R.T., et al., *Personality disorders in offenders with intellectual disabilities: a comparison of clinical, forensic and outcome variables and implications for service provision.* Journal of Intellectual Disability Research, 2010. **54**: p. 650-658.
26. Crocombe, J., R. Mills, and L. Wing, *Austism Spectrum Disorders in the High Security Hospitals of the United Kingdom*. 2006: The National Autistic Society.
27. Alexander, R., et al., *Evaluation of treatment outcomes from a medium secure unit for people with intellectual disability.* Advances in Mental Health and Intellectual Disabilities, 2011. **5**(1): p. 22-32.
28. Alexander, R.T., et al., *The clinical, forensic and treatment outcome factors of patients with autistic spectrum disorder treated in forensic intellectual disability services.* Under Review.
29. Woodbury-Smith, M.R. and F.R. Volkmar, *Asperger syndrome.* European Child & Adolescent Psychiatry, 2009. **18**(1): p. 2-11.
30. Royal College of Psychiatrists, *People with learning disability and mental health, behavioural or forensic problems: the role of in-patient services*. 2013, London: Royal College of Psychiatrists, Faculty of Psychiatry of Intellectual Disability.
31. Rogers, J., et al., *Autism spectrum disorder and psychopathy: shared cognitive underpinnings or double hit?* Psychological Medicine, 2006. **36**(12): p. 1789-1798.
32. Baliousis, M., et al., *Autistic spectrum disorder, personality disorder and reading disability: a complex case that falls between the cracks?* The Journal of Forensic Psychiatry & Psychology, 2013. **24**(2): p. 286-292.
33. Gunasekaran, S., *Assessment and management of risk in autism.* Advances in Mental Health and Intellectual Disabilities, 2012. **6**(6): p. 314-320.
34. Cooray, S.E., P. Tyrer, and Parkside Learning Disability Research Initiative (PLDRI), *Utility of an ICD-10/DSM IV based multiaxial classificatory system for people with developmental disabilities.* NADD Journal - International Congress Proceedings, 2000. **Philadelphia, USA**.
35. Oliver, P.C., et al., *Modfied Overt Aggression Scale (MOAS) for people with intellectual disability and aggressive challenging behaviour: a reliability study.* Journal of Applied Research in Intellectual Disabilities, 2007. **20**: p. 368-372.
36. Casey, H., *Psychometric Evaluation of the Group Emotional Engagement Questionnaire.* PhD Thesis: University of Oxford, 2014.
37. Langdon, P.E., et al., *An Evaluation of the EQUIP Treatment Programme with Men who have Intellectual or Other Developmental Disabilities.* Journal of Applied Research in Intellectual Disabilities, 2013. **26**: p. 167-180.

38. Baron-Cohen, S., et al., *The autism-spectrum quotient (AQ): evidence from Asperger syndrome/high functioning autism, males and females, scientists and mathematicians.* Journal of Autism and Developmental Disorders, 2001. **31**: p. 5-17.
39. Seara-Cardoso, A., et al., *Investigating associations between empathy, morality and psychopathic personality traits in the general population.* Personality and Individual Differences, 2012. **52**(1): p. 67-71.
40. Baron-Cohen, S. and S. Wheelright, *The Empathy Quotient: An investigation of adults with Asperger Syndrome or high functioning autism, and normal sex differences.* Journal of Autism and Developmental Disorders, 2004. **34**: p. 163-175.
41. Lawrence, E.J., et al., *Measuring empathy: reliabilty and validity of the Empathy Quotient.* Psychological Medicine, 2004. **34**: p. 911-924.
42. Hockley, O.J. and P.E. Langdon, *Men with intellectual disabilities with a history of sexual offending: empathy for victims of sexual and non-sexual crimes.* Journal of Intellectual Disability Research, In Press.
43. Gibbs, J.C., K.S. Basinger, and D. Fuller, *Moral maturity: Measuring the development of sociomoral reflection*. 1992, Hillsdale, NJ: Erlbaum.
44. Langdon, P.E., et al., *Relationships among moral reasoning, empathy and distorted cognitions amongst men with intellectual disabilities and a history of criminal offending.* American Journal on Intellectual and Developmental Disabilities, 2011. **116**: p. 438-456.
45. Langdon, P.E., et al., *The psychometric properties of the Socio-Moral Reflection Measure – Short Form and the Moral Theme Inventory for men with and without intellectual disabilities.* Research in Developmental Disabilities, 2010. **31**: p. 1204-1215.
46. Kay, S.R., A. Flszbein, and L.A. Opfer, *The positive and negative syndrome scale (PANSS) for schizophrenia.* Schizophrenia bulletin, 1987. **13**(2): p. 261.

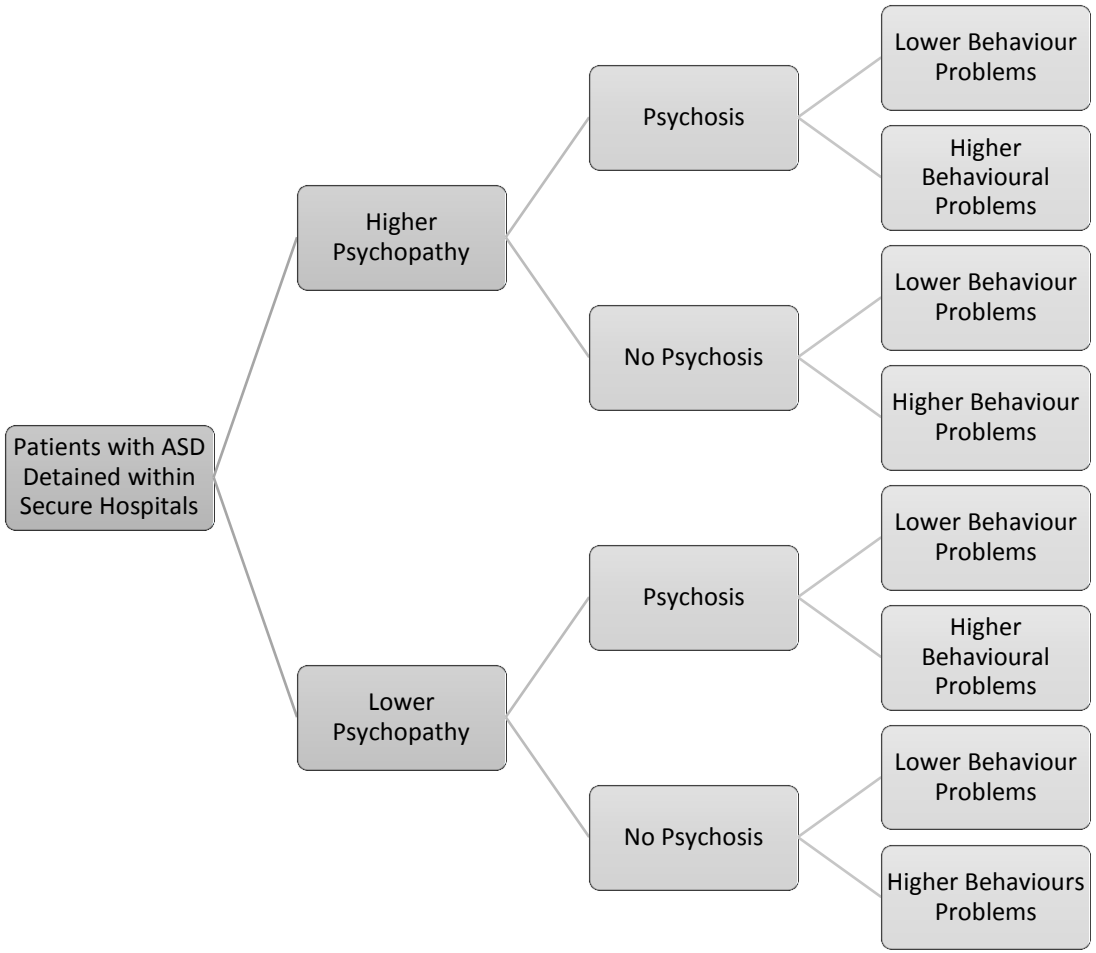

Figure 1: The proposed descriptive subtypes of patients with ASD detained within secure hospitals. It is important to stress that all patients would have a history of behavioural problems, but differences between the subtypes are characterised by the severity and frequency of behavioural problems. For example, a patient with ASD may have committed murder on one occasion while in the community, but within a ward environment, they may exhibit infrequent behavioural problems, and as a consequence would be categorised as having low behavioural problems, relative to others who exhibit behaviour difficulties frequently. Additionally, within this context, psychopathy is seen as a spectrum, where one group will score lower or higher, relative to the other.